

#01#

Artículos originales (todos) *** Original articles (all)

RESPIRATORY TRACT TUMORS

(Conceptos / Keywords: NSCLC; SCLC, Mesotheliomas; Tracheal tumors; Bronchial tumors; etc).

October / November 2013

El sistema de alerta de literatura biomédica© es un servicio GRATUITO. La literatura ha sido compuesta en base a una patente que permite la indexación y ordenación de los artículos por orden de importancia. Consecuentemente existe un copyright de carácter compilativo (todos los derechos reservados). Este documento sólo contiene artículos escritos en Castellano y/o Inglés. Para mayor información visite el portal de la compañía haciendo un clic en la palabra [Enlace/Link](#)

The biomedical literature© alert system is a FREE service. The literature has been arranged according to a patent, which entitles the right to cataloguing and sorting articles by true relevance. Consequently, a compilation copyright exists (all rights reserved). Only articles written in Spanish and/or English are included. For more information please visit the website of the company by clicking on the following [Enlace/Link](#)

[1]

TÍTULO / TITLE: - Randomized Phase II Trial of Onartuzumab in Combination With Erlotinib in Patients With Advanced Non-Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 10;31(32):4105-14. doi: 10.1200/JCO.2012.47.4189. Epub 2013 Oct 7.

●● [Enlace al texto completo \(gratis o de pago\) 1200/JCO.2012.47.4189](#)

AUTORES / AUTHORS: - Spigel DR; Ervin TJ; Ramlau RA; Daniel DB; Goldschmidt JH Jr; Blumenschein GR Jr; Krzakowski MJ; Robinet G; Godbert B; Barlesi F; Govindan R; Patel T; Orlov SV; Wertheim MS; Yu W; Zha J; Yauch RL; Patel PH; Phan SC; Peterson AC

INSTITUCIÓN / INSTITUTION: - David R. Spigel, Thomas J. Ervin, and Davey B. Daniel, Sarah Cannon Research Institute; David R. Spigel, Tennessee Oncology, Nashville; Davey B. Daniel, Chattanooga Oncology Hematology Associates, Chattanooga, TN; Thomas J. Ervin, Florida Cancer Specialists, Fort Myers; Michael S. Wertheim, Hematology/Oncology Associates, Port St Lucie, FL; Rodryg A. Ramlau, Poznan University of Medical Sciences, Poznan; Maciej J. Krzakowski, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; Jerome H. Goldschmidt Jr, Blue Ridge Cancer Care, Christianburg, VA; George R. Blumenschein Jr, The University of Texas MD Anderson Cancer Center, Houston, TX; Gilles Robinet, University Hospital Morvan, Brest; Benoit Godbert, Centre Hospitalier Universitaire Nancy, Vandoeuvre-les-Nancy; Fabrice Barlesi, Assistance Publique-Hopitaux de

Marseille, Aix Marseille University, Marseille, France; Ramaswamy Govindan, Washington University School of Medicine, St Louis, MO; Taral Patel, Mid Ohio Oncology/Hematology, Columbus, OH; Sergey V. Orlov, St Petersburg Pavlov State Medical University, St Petersburg, Russia; Wei Yu, Robert L. Yauch, Premal H. Patel, and See-Chun Phan, Genentech; Amy C. Peterson, Medivation, San Francisco, CA; and Jiping Zha, Crown Bioscience, Taicang City, China.

RESUMEN / SUMMARY: - PURPOSE: Increased hepatocyte growth factor/MET signaling is associated with poor prognosis and acquired resistance to epidermal growth factor receptor (EGFR) -targeted drugs in patients with non-small-cell lung cancer (NSCLC). We investigated whether dual inhibition of MET/EGFR results in clinical benefit in patients with NSCLC. PATIENTS AND METHODS: Patients with recurrent NSCLC were randomly assigned at a ratio of one to one to receive onartuzumab plus erlotinib or placebo plus erlotinib; crossover was allowed at progression. Tumor tissue was required to assess MET status by immunohistochemistry (IHC). Coprimary end points were progression-free survival (PFS) in the intent-to-treat (ITT) and MET-positive (MET IHC diagnostic positive) populations; additional end points included overall survival (OS), objective response rate, and safety. RESULTS: There was no improvement in PFS or OS in the ITT population (n = 137; PFS hazard ratio [HR], 1.09; P = .69; OS HR, 0.80; P = .34). MET-positive patients (n = 66) treated with erlotinib plus onartuzumab showed improvement in both PFS (HR, .53; P = .04) and OS (HR, .37; P = .002). Conversely, clinical outcomes were worse in MET-negative patients treated with onartuzumab plus erlotinib (n = 62; PFS HR, 1.82; P = .05; OS HR, 1.78; P = .16). MET-positive control patients had worse outcomes versus MET-negative control patients (n = 62; PFS HR, 1.71; P = .06; OS HR, 2.61; P = .004). Incidence of peripheral edema was increased in onartuzumab-treated patients. CONCLUSION: Onartuzumab plus erlotinib was associated with improved PFS and OS in the MET-positive population. These results combined with the worse outcomes observed in MET-negative patients treated with onartuzumab highlight the importance of diagnostic testing in drug development.

[2]

TÍTULO / TITLE: - ATLAS: Randomized, Double-Blind, Placebo-Controlled, Phase IIIB Trial Comparing Bevacizumab Therapy With or Without Erlotinib, After Completion of Chemotherapy, With Bevacizumab for First-Line Treatment of Advanced Non-Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 1;31(31):3926-34. doi: 10.1200/JCO.2012.47.3983. Epub 2013 Oct 7.

●● [Enlace al texto completo \(gratis o de pago\) 1200/JCO.2012.47.3983](#)

AUTORES / AUTHORS: - Johnson BE; Kabbinavar F; Fehrenbacher L; Hainsworth J; Kasubhai S; Kressel B; Lin CY; Marsland T; Patel T; Polikoff J; Rubin M; White L; Yang JC; Bowden C; Miller V

INSTITUCIÓN / INSTITUTION: - Bruce E. Johnson, Dana-Farber Cancer Institute, Boston, MA; Fairouz Kabbinavar, University of California Los Angeles, Translational Oncology Research International, Los Angeles; Louis Fehrenbacher, Kaiser Permanente Northern California, Vallejo; Chin-Yu Lin and Chris Bowden, Genentech, South San Francisco; Jonathan Polikoff, Southern California Permanente Medical

Group, San Diego, CA; John Hainsworth, Sarah Cannon Research Institute, Nashville, TN; Saifuddin Kasubhai, Northwest Medical Specialties, Tacoma, WA; Bruce Kressel, Sibley Memorial Hospital, Washington, DC; Thomas Marsland, Integrated Community Oncology Network, Orange Park; Mark Rubin, Florida Cancer Specialists, Fort Myers, FL; Taral Patel, The Mark H. Zangmeister Center, Columbus, OH; Leonard White, Arch Medical Services, The Center for Cancer Care and Research, Saint Louis, MO; Vincent Miller, Weill Cornell Medical College and Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, NY; and James Chih-Hsin Yang, National Taiwan University, Taipei, Taiwan.

RESUMEN / SUMMARY: - PURPOSE: This phase III trial was performed to assess the potential benefit of adding maintenance erlotinib to bevacizumab after a first-line chemotherapy regimen with bevacizumab for advanced non-small-cell lung cancer (NSCLC). PATIENTS AND METHODS: One thousand one hundred forty-five patients with histologically or cytologically confirmed NSCLC (stage IIIB with malignant pleural effusion, stage IV, or recurrent) received four cycles of chemotherapy plus bevacizumab. Seven hundred forty-three patients without disease progression or significant toxicity were then randomly assigned (1:1) to bevacizumab (15 mg/kg, day 1, 21-day cycle) plus either placebo or erlotinib (150 mg per day). The primary end point was progression-free survival (PFS). RESULTS: Median PFS from time of random assignment was 3.7 months with bevacizumab/placebo and 4.8 months with bevacizumab/erlotinib (hazard ratio [HR], 0.71; 95% CI, 0.58 to 0.86; P < .001). Median overall survival (OS) times from random assignment were 13.3 and 14.4 months with bevacizumab/placebo and bevacizumab/erlotinib, respectively (HR, 0.92; 95% CI, 0.70 to 1.21; P = .5341). During the postchemotherapy phase, there were more adverse events (AEs) overall, more grade 3 and 4 AEs (mainly rash and diarrhea), more serious AEs, and more AEs leading to erlotinib/placebo discontinuation in the bevacizumab/erlotinib arm versus the bevacizumab/placebo arm. The incidence of AEs leading to bevacizumab discontinuation was similar in both treatment arms. CONCLUSION: The addition of erlotinib to bevacizumab significantly improved PFS but not OS. Although generally well tolerated, the modest impact on survival and increased toxicity associated with the addition of erlotinib to bevacizumab maintenance mean that this two-drug maintenance regimen will not lead to a new postchemotherapy standard of care.

[3]

TÍTULO / TITLE: - Second-line therapy in elderly patients with advanced non-small cell lung carcinoma: analysis of the IFCT-0501 Phase III study comparing single-agent therapy to carboplatin-based doublet therapy with fixed second-line erlotinib therapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur Respir J. 2013 Oct 10.

●● [Enlace al texto completo \(gratis o de pago\) 1183/09031936.00048213](#)

AUTORES / AUTHORS: - Quiox E; Westeel V; Moreau L; Pichon E; Lavole A; Dauba J; Debieuvre D; Souquet PJ; Bigay-Game L; Dansin E; Poudenx M; Molinier O; Vaylet F; Moro-Sibilot D; Herman D; Sennelart H; Tredaniel J; Mennequier B; Morin F; Baudrin L; Milleron B; Zalcman G

INSTITUCIÓN / INSTITUTION: - CHU Strasbourg, France.

RESUMEN / SUMMARY: - There is no dedicated study on second-line treatment for elderly patients with advanced non-small cell lung cancer (NSCLC). We report the results on second-line erlotinib therapy from our previously published Phase III study comparing single-agent therapy with platinum-based doublet (carboplatin + paclitaxel) therapy in 451 elderly patients. Erlotinib was given to patients exhibiting disease progression (PD) or experiencing excessive toxicity during first-line therapy, until further PD or non-acceptable toxicity. In total, 292 (64.7%) patients received erlotinib in second-line. Initial performance status (PS) 0-1, Stage IV NSCLC, and ADL6 were independent factors for receiving erlotinib. Median overall survival was 4 months (95% CI: 3.2-6.7) vs. 6.8 months (95% CI: 5.0-8.3) in single-agent arm and doublet arm, respectively (p=0.089). PS 0-1, never-smoking, adenocarcinoma, and weight loss $\leq 5\%$ were favorable independent prognostic factors of survival, whereas the randomization arm had no significant impact. Among the 292 patients who received erlotinib, 60 (20.5%) experienced Grade 3-4 toxic effects, the most frequent being rash. Erlotinib as second-line therapy is feasible, leading to efficacy results similar to those obtained in a previous randomized study that was not dedicated to elderly patients, with acceptable toxicity.

[4]

TÍTULO / TITLE: - Prediction of overall survival or progression free survival by disease control rate at week 8 is independent of ethnicity: Western versus Chinese patients with first-line non-small cell lung cancer treated with chemotherapy with or without bevacizumab.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Pharmacol. 2013 Oct 3. doi: 10.1002/jcph.191.

●● Enlace al texto completo (gratis o de pago) [1002/jcph.191](#)

AUTORES / AUTHORS: - Claret L; Gupta M; Han K; Joshi A; Sarapa N; He J; Powell B; Bruno R

INSTITUCIÓN / INSTITUTION: - Pharsight Consulting Services, Pharsight, A Certara Company, Marseille, France.

RESUMEN / SUMMARY: - Categorizations of best response observed at week 8 (between week 3 and 14) of first-line treatment in two studies of bevacizumab plus chemotherapy in Western (878 patients) and Chinese (198 patients) patients with non-small cell lung cancer were assessed together with baseline prognostic factors in multivariate parametric models to predict overall survival (OS) and progression free survival (PFS). Predictive performances of the models were assessed by simulating multiple replicates of the studies. Disease control rate (DCR) was the best response categorization to predict OS and PFS. In the OS model, DCR fully captured bevacizumab effect. For PFS, DCR did not fully capture bevacizumab treatment effect. The models adequately predicted OS and PFS distributions in each arm as well as bevacizumab hazard ratio (HR) for OS and PFS, for example, in Western patients (model prediction [95% prediction interval]: 0.84 [0.71-0.98] vs. observed: 0.77 for OS and 0.59 [0.49-0.72] vs. observed: 0.58 for PFS). Covariates in the models captured endpoint differences seen in Chinese patients. There was no impact of Chinese ethnicity on the DCR relationship to OS or PFS. DCR predicted OS benefit with bevacizumab in first-line NSCLC patients. Western data can be used to inform design of studies in Chinese patients.

[5]

TÍTULO / TITLE: - Phase II trial of dose-dense chemotherapy followed by dose-intense erlotinib for patients with newly diagnosed metastatic non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Dec;43(6):2057-63. doi: 10.3892/ijo.2013.2122. Epub 2013 Oct 3.

●● Enlace al texto completo (gratis o de pago) [3892/ijo.2013.2122](#)

AUTORES / AUTHORS: - Petty WJ; Laudadio J; Brautnick L; Lovato J; Dotson T; Streer NP; Weaver KE; Miller AA

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Section on Hematology and Oncology, Wake Forest School of Medicine, Winston-Salem, NC 27157, USA.

RESUMEN / SUMMARY: - This phase II study investigated dose-intense erlotinib maintenance after dose-dense chemotherapy for patients with metastatic non-small cell lung cancer and examined two cell cycle biomarkers. Patients with newly diagnosed metastatic non-small cell lung cancer received docetaxel 75 mg/m² and cisplatin 75 mg/m² on day 1 and pegfilgrastim on day 2 every 14 days for four cycles. Patients then received erlotinib with initial doses based on smoking status. Doses were increased in 75 mg increments every two weeks depending on toxicities until each patient's maximal tolerable dose (MTD) was achieved. Cyclin D1 and D3 biomarkers were measured by immunohistochemistry. The objectives of the study were to evaluate time to progression (TTP) and overall survival (OS) for the entire population and biomarker subgroups. Forty-five patients were enrolled. Intra-patient erlotinib MTD ranged from 0 to 525 mg. Median MTD achieved in smokers was higher than in non-smokers (300 vs. 150 mg; P=0.019). TTP for the entire cohort was not significantly improved compared to historical controls. Patients with high cyclin D1 expressing tumors demonstrated improved TTP on erlotinib (8.2 vs. 4.7 months; hazard ratio, 4.1; 95% CI, 1.6-0.6; P=0.003) and improved OS (20.5 vs. 8.0 months; hazard ratio 2.8; 95% CI, 1.2-6.3; P=0.016). Intratumoral cyclin D3 expression did not impact clinical outcomes. Current smokers but not former smokers exhibit a higher erlotinib MTD. High cyclin D1 expression was associated with favorable TTP and OS.

[6]

TÍTULO / TITLE: - Phase II trial of erlotinib in patients with advanced non-small-cell lung cancer harboring epidermal growth factor receptor mutations: additive analysis of pharmacokinetics.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct 12.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2307-6](#)

AUTORES / AUTHORS: - Motoshima K; Nakamura Y; Sano K; Ikegami Y; Ikeda T; Mizoguchi K; Takemoto S; Fukuda M; Nagashima S; Iida T; Tsukamoto K; Kohno S

INSTITUCIÓN / INSTITUTION: - Second Department of Internal Medicine, Nagasaki University School of Medicine, 1-7-1 Sakamoto, Nagasaki, 852-8501, Japan.

RESUMEN / SUMMARY: - BACKGROUND: We conducted a phase II trial of erlotinib in patients with advanced non-small-cell lung cancer (NSCLC) harboring epidermal growth factor receptor (EGFR) mutations and evaluated the relationship between

plasma concentration and efficacy of erlotinib. METHODS: Patients who were previously treated but naive to epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKIs), with advanced NSCLC harboring EGFR mutations, were enrolled. Erlotinib was given at 150 mg once daily until disease progression. The primary end point was objective response rate (ORR). Plasma trough levels of erlotinib were measured on Days 2 (D2) and 8 (D8) by high-performance liquid chromatography. RESULTS: In total, 29 patients were enrolled from September 2008 to January 2011. ORR was 61.5 % (95 % confidence interval [CI] 40.57-79.8) of 26 assessable patients. The median progression-free survival (PFS) and overall survival (OS) were 6.3 months and 16.9 months, respectively. Skin rash was observed in 24 patients, mostly at grade 1 or 2. Grade 2 pneumonitis was observed in one patient. We collected blood samples from 16 patients. The median PFS of the high and low D8/D2 ratio group was 11.2 months and 5.7 months, respectively (p = 0.044, hazard ratio = 0.301, 95 % CI 0.094-0.968). CONCLUSION: Erlotinib showed an ORR comparable to that seen in previous studies for patients with NSCLC harboring EGFR mutations, although response, the primary end point, did not reach the predetermined threshold level. The D8/D2 ratio of erlotinib plasma trough levels might be a predictive factor for PFS.

[7]

TÍTULO / TITLE: - Oncogenic and drug-sensitive NTRK1 rearrangements in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Med. 2013 Nov;19(11):1469-72. doi: 10.1038/nm.3352. Epub 2013 Oct 27.

●● Enlace al texto completo (gratis o de pago) [1038/nm.3352](#)

AUTORES / AUTHORS: - Vaishnavi A; Capelletti M; Le AT; Kako S; Butaney M; Ercan D; Mahale S; Davies KD; Aisner DL; Pilling AB; Berge EM; Kim J; Sasaki H; Park SI; Kryukov G; Garraway LA; Hammerman PS; Haas J; Andrews SW; Lipson D; Stephens PJ; Miller VA; Varella-Garcia M; Janne PA; Doebele RC

INSTITUCIÓN / INSTITUTION: - 1] Department of Medicine, Division of Medical Oncology, University of Colorado School of Medicine, Aurora, Colorado, USA. [2].

RESUMEN / SUMMARY: - We identified new gene fusions in patients with lung cancer harboring the kinase domain of the NTRK1 gene that encodes the high-affinity nerve growth factor receptor (TRKA protein). Both the MPRIP-NTRK1 and CD74-NTRK1 fusions lead to constitutive TRKA kinase activity and are oncogenic. Treatment of cells expressing NTRK1 fusions with inhibitors of TRKA kinase activity inhibited autophosphorylation of TRKA and cell growth. Tumor samples from 3 of 91 patients with lung cancer (3.3%) without known oncogenic alterations assayed by next-generation sequencing or fluorescence in situ hybridization demonstrated evidence of NTRK1 gene fusions.

[8]

TÍTULO / TITLE: - PointBreak: A Randomized Phase III Study of Pemetrexed Plus Carboplatin and Bevacizumab Followed by Maintenance Pemetrexed and Bevacizumab Versus Paclitaxel Plus Carboplatin and Bevacizumab Followed by

Maintenance Bevacizumab in Patients With Stage IIIB or IV Nonsquamous Non-Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Dec 1;31(34):4349-57. doi: 10.1200/JCO.2012.47.9626. Epub 2013 Oct 21.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2012.47.9626](#)

AUTORES / AUTHORS: - Patel JD; Socinski MA; Garon EB; Reynolds CH; Spigel DR; Olsen MR; Hermann RC; Jotte RM; Beck T; Richards DA; Guba SC; Liu J; Frimodt-Moller B; John WJ; Obasaju CK; Pennella EJ; Bonomi P; Govindan R

INSTITUCIÓN / INSTITUTION: - Jyoti D. Patel, Northwestern University; Philip Bonomi, Rush University Medical Center, Chicago, IL; Mark A. Socinski, University of Pittsburgh, Pittsburgh, PA; Edward B. Garon, University of California at Los Angeles, Los Angeles, CA; Craig H. Reynolds, US Oncology Research, Ocala, FL; David R. Spigel, Sarah Cannon Research Institute-Tennessee Oncology, Nashville, TN; Mark R. Olsen, Tulsa Cancer Institute, Tulsa, OK; Robert C. Hermann, Northwest Georgia Oncology Centers, Marietta, GA; Robert M. Jotte, Rocky Mountain Cancer Centers, Denver, CO; Thaddeus Beck, Highlands Oncology Group, Fayetteville, AR; Donald A. Richards, US Oncology Research, Tyler, TX; Susan C. Guba, Jingyi Liu, Bente Frimodt-Moller, and William J. John, Eli Lilly, Indianapolis, IN; Coleman K. Obasaju and Eduardo J. Pennella, Lilly USA, Indianapolis, IN; and Ramaswamy Govindan, Washington University School of Medicine, St. Louis, MO.

RESUMEN / SUMMARY: - PURPOSE: PointBreak (A Study of Pemetrexed, Carboplatin and Bevacizumab in Patients With Nonsquamous Non-Small Cell Lung Cancer) compared the efficacy and safety of pemetrexed (Pem) plus carboplatin © plus bevacizumab (Bev) followed by pemetrexed plus bevacizumab (PemCBev) with paclitaxel (Pac) plus carboplatin © plus bevacizumab (Bev) followed by bevacizumab (PacCBev) in patients with advanced nonsquamous non-small-cell lung cancer (NSCLC). PATIENTS AND METHODS: Patients with previously untreated stage IIIB or IV nonsquamous NSCLC and Eastern Cooperative Oncology Group performance status of 0 to 1 were randomly assigned to receive pemetrexed 500 mg/m² or paclitaxel 200 mg/m² combined with carboplatin area under the curve 6 and bevacizumab 15 mg/kg every 3 weeks for up to four cycles. Eligible patients received maintenance until disease progression: pemetrexed plus bevacizumab (for the PemCBev group) or bevacizumab (for the PacCBev group). The primary end point of this superiority study was overall survival (OS). RESULTS: Patients were randomly assigned to PemCBev (n = 472) or PacCBev (n = 467). For PemCBev versus PacCBev, OS hazard ratio (HR) was 1.00 (median OS, 12.6 v 13.4 months; P = .949); progression-free survival (PFS) HR was 0.83 (median PFS, 6.0 v 5.6 months; P = .012); overall response rate was 34.1% versus 33.0%; and disease control rate was 65.9% versus 69.8%. Significantly more study drug-related grade 3 or 4 anemia (14.5% v 2.7%), thrombocytopenia (23.3% v 5.6%), and fatigue (10.9% v 5.0%) occurred with PemCBev; significantly more grade 3 or 4 neutropenia (40.6% v 25.8%), febrile neutropenia (4.1% v 1.4%), sensory neuropathy (4.1% v 0%), and alopecia (grade 1 or 2; 36.8% v 6.6%) occurred with PacCBev. CONCLUSION: OS did not improve with the PemCBev regimen compared with the PacCBev regimen, although PFS was significantly improved with PemCBev. Toxicity profiles differed; both regimens demonstrated tolerability.

[9]

TÍTULO / TITLE: - Does Routine Clinical Practice Reproduce the Outcome of Large Prospective Trials? The Analysis of Institutional Database on Patients with Limited-Disease Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Invest. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [3109/07357907.2013.861470](#)

AUTORES / AUTHORS: - Wzietek I; Suwinski R; Nowara E; Bialas M; Bentzen S; Tukiendorf A

INSTITUCIÓN / INSTITUTION: - Departments of Radiation Oncology, 1.

RESUMEN / SUMMARY: - We performed the analysis of database on 409 patients with LD-SCLC to evaluate as to what extent the clinical outcome of large prospective trials was reproduced in routine practice. The analysis has shown that the hazard rate of death in the absence of prophylactic cranial irradiation (PCI) adjusted for the effects of confounding factors, appeared larger than that reported in the trials on PCI in LD-SCLC, and was comparable to that estimated for extensive disease. Less intense routine staging procedures, compared to the trial settings, contributed for such outcome. Hyperfractionated thoracic radiotherapy provided survival advantage similar to that reported in the literature.

[10]

TÍTULO / TITLE: - Comparison of efficacy for postoperative chemotherapy and concurrent radiochemotherapy in patients with IIIA-pN2 non-small cell lung cancer: An early closed randomized controlled trial.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Oct 31. pii: S0167-8140(13)00512-4. doi: 10.1016/j.radonc.2013.10.008.

●● Enlace al texto completo (gratis o de pago) [1016/j.radonc.2013.10.008](#)

AUTORES / AUTHORS: - Shen WY; Ji J; Zuo YS; Pu J; Xu YM; Zong CD; Tao GZ; Chen XF; Ji FZ; Zhou XL; Han JH; Wang CS; Yi JG; Su XL; Zhu WG

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, People's Hospital of Lianshui County, Huai'an, PR China.

RESUMEN / SUMMARY: - **OBJECTIVE:** The efficacy of postoperative concurrent radiochemotherapy (POCRT) on IIIA-pN2 non-small cell lung cancer (NSCLC) is still unclear. The aim of this randomized controlled trial was to compare POCRT with postoperative chemotherapy (POCT) alone in terms of survival and relapse patterns. **METHODS:** Patients with completely resected IIIA-pN2 NSCLC were randomized into POCRT or POCT groups. Chemotherapy consisted of paclitaxel (175mg/m²) and cisplatin (60mg/m²) administered intravenously for four cycles on day 1, 22, 43, and 64. Patients in the POCRT group received radiotherapy (50.4Gy/28 fractions) concurrently with the first 2 cycles of chemotherapy. **RESULTS:** This study recruited 140 participants and was closed early because of slow accrual. Data were analyzed for 135 of them including 66 cases in the POCRT group and 69 cases in the POCT group. Patients were followed-up for a median period of 45months. The POCRT group had a median survival (MS) of 40months and a 5-year overall survival (OS) rate of 37.9%. The POCT group had a MS of 28months and a 5-year OS rate of 27.5%. The hazard

ratio for death in the POCRT group was 0.69 (95% CI: 0.457-1.044, P=0.073). We observed a disease-free survival (DFS) of 28months and a 5-year DFS rate of 30.3% in the POCRT group. Likewise, we observed a DFS of 18months and a 5-year DFS rate of 18.8% in the POCT group. The recurrence hazard ratio in the POCT group was 1.49 (95% CI: 1.008-2.204, P=0.041). Subgroup analysis revealed that POCRT significantly increased the OS rate of the patients with 2 pN2 lymph nodes (P=0.021). The POCRT group had a significantly lower local relapse (P=0.009) and distant metastasis (P=0.05) rates as compared to that of the POCT group. One case died of pyemia and 9 cases suffered from grade 3 and 4 acute radiation esophagitis. The two groups had similar and tolerable hematologic toxicities. CONCLUSIONS: Compared with POCT, POCRT increased both local/regional and distant DFS rate of the patients with IIIA-pN2 NSCLC, but not the OS rate. Considering the relatively small sample size of the current study, caution should be taken when adopting the conclusions.

[11]

TÍTULO / TITLE: - Dosing to rash: A phase II trial of the first-line erlotinib for patients with advanced non-small-cell lung cancer an Eastern Cooperative Oncology Group Study (E3503).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Cancer. 2013 Nov 15. pii: S0959-8049(13)00932-5. doi: 10.1016/j.ejca.2013.10.006.

●● Enlace al texto completo (gratis o de pago) [1016/j.ejca.2013.10.006](#)

AUTORES / AUTHORS: - Brahmer JR; Lee JW; Traynor AM; Hidalgo MM; Kolesar JM; Siegfried JM; Guaglianone PP; Patel JD; Keppen MD; Schiller JH

INSTITUCIÓN / INSTITUTION: - Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, MD, United States. Electronic address: brahmju@jhmi.edu.

RESUMEN / SUMMARY: - BACKGROUND: The development of a rash has been retrospectively associated with increased response and improved survival when treated with erlotinib at the standard dose of 150mg per day. The objective of this trial was to evaluate the association of the activity of erlotinib in the first-line setting in patients with advanced non-small-cell lung cancer (NSCLC) with the development of a tolerable rash via dose escalation of erlotinib or tumour characteristics. METHODS: Patients, with advanced NSCLC without prior systemic therapy, were treated with erlotinib 150mg orally per day. The dose was increased by 25mg every two weeks until the development of grade 2/tolerable rash or other dose limiting toxicity. Tumour biopsy specimens were required for inclusion. RESULTS: The study enrolled 137 patients, 135 were evaluable for safety and 124 were eligible and evaluable for response. Only 73 tumour samples were available for analysis. Erlotinib dose escalation occurred in 69/124 patients. Erlotinib was well tolerated with 70% of patients developing a grade ½ rash and 10% developing grade 3 rash. Response rate and disease control rate were 6.5% and 41.1% respectively. Median overall survival was 7.7months. Toxicity and tumour markers were not associated with response. Grade 2 or greater skin rash and low phosphorylated mitogen-activated protein kinase (pMAPK) were associated with improved survival. CONCLUSIONS: Overall survival was similar in this trial compared to first-line chemotherapy in this unselected patient population. Dose escalation to the development of grade 2 skin rash was associated with improved survival in this patient population.

[12]

TÍTULO / TITLE: - Phase II Trial of Biweekly Chemotherapy with Docetaxel and Cisplatin in High-Risk Patients with Unresectable Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chemotherapy. 2013 Oct 9;59(3):159-166.

●● Enlace al texto completo (gratis o de pago) [1159/000354983](#)

AUTORES / AUTHORS: - Kim MJ; Kim SH; Kang JH; Kim HG; Cho YJ; Jeong YY; Kim HC; Lee JD; Hwang YS; Kim MG; Choi JY; Lee GW

INSTITUCIÓN / INSTITUTION: - Division of Hematology-Oncology, Department of Internal Medicine, Gyeongsang National University School of Medicine, Jinju, Republic of Korea.

RESUMEN / SUMMARY: - Purpose: We investigated the efficacy and toxicity of a biweekly schedule of docetaxel and cisplatin in high-risk patients with unresectable (stages IIIB-IV) non-small cell lung cancer (NSCLC). Methods: In this study, 48 high-risk patients with previously untreated locally advanced or metastatic NSCLC were treated with combination chemotherapy consisting of docetaxel 40 mg/m² and cisplatin 40 mg/m²; both drugs were given biweekly, on days 1 and 15, every 4 weeks in an outpatient setting. Results: Complete response, partial response, and stable disease were observed in 1 (2.1%), 30 [62.5%, 95% confidence interval (CI) 47.9-77.1], and 4 (8.3%) patients. The median overall survival was 15.1 months (95% CI 11.7-18.5) and the median time to progression was 7.5 months (95% CI 6.4-8.6). The major toxicity was grade 3 anemia in 7 (14.6%) patients. Grade 3 neutropenia was observed in 5 (10.4%) patients. Among the nonhematologic toxicities, grade 3 infection and grade 3 diarrhea were observed in 5 (10.4%) and 4 (8.3%) patients, respectively. No treatment-related mortality was found. Conclusions: As a front-line chemotherapy for high-risk patients with unresectable NSCLC in an outpatient setting, the biweekly schedule of docetaxel and cisplatin showed feasible efficacy with acceptable hematologic toxicities, comparable to the results of previous studies of triweekly or weekly schedules. Additional large randomized studies are needed to optimize the schedule and dosage of combination therapy with docetaxel and cisplatin in high-risk patients with unresectable NSCLC. © 2013 S. Karger AG, Basel.

[13]

TÍTULO / TITLE: - Clinicopathologic Characteristics of Malignant Mesotheliomas Arising in Patients With a History of Radiation for Hodgkin and Non-Hodgkin Lymphoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2013.49.9616](#)

AUTORES / AUTHORS: - Chirieac LR; Barletta JA; Yeap BY; Richards WG; Tilleman T; Bueno R; Baldini EH; Godleski J; Sugarbaker DJ

INSTITUCIÓN / INSTITUTION: - Lucian R. Chirieac, Justine A. Barletta, William G. Richards, Tamara Tilleman, Raphael Bueno, Elizabeth H. Baldini, John Godleski, and David J. Sugarbaker, Brigham and Women's Hospital; Beow Y. Yeap, Massachusetts General Hospital; and William G. Richards, Tamara Tilleman, Raphael Bueno, Elizabeth H. Baldini, and David J. Sugarbaker, Harvard Medical School, Boston, MA.

RESUMEN / SUMMARY: - PURPOSE: Studies have reported an association between pleural diffuse malignant mesothelioma (PDMM) and chest radiation for lymphoma. The clinicopathologic characteristics of malignant mesotheliomas arising in these patients have not been established. PATIENTS AND METHODS: We studied 1,618 consecutive patients diagnosed with pleural PDMM from July 1993 to February 2008 and identified patients with a history of radiation for Hodgkin and non-Hodgkin lymphoma. We evaluated the histology in the surgical resection specimens and compared clinicopathologic features with overall survival. RESULTS: We identified 22 patients who developed PDMM after chest radiation as part of their treatment for lymphoma (mean latency time, 21.4 years; 95% CI, 17.0 to 25.8 years). Asbestos bodies in lymphoma-associated PDMM were lower than in asbestos-associated PDMM (median count, 15 v 325 bodies, respectively; $P < .001$) and similar to an unexposed control group (median count, 15 v 10 bodies, respectively; $P = .6$). Seventeen lymphoma-associated PDMMs (77%) were epithelioid and five (23%) were biphasic. Seven PDMMs (32%) had unusual histologies (pleomorphic, myxoid, clear cell, and signet ring cell). Patients with lymphoma-associated PDMM were younger than patients with asbestos-associated PDMM (median age, 45 v 64 years, respectively; $P < .001$) and had a significantly longer overall survival time (median, 32.5 v 12.7 months, respectively; $P = .018$). In multivariate analysis, independent favorable predictors for overall survival were history of prior radiation ($P = .022$), female sex ($P < .001$), age ≤ 65 years ($P = .005$), cytoreductive surgery ($P < .001$), and epithelioid histology ($P < .001$). CONCLUSION: Patients with lymphoma-associated PDMM are likely to have unusual histologic features, are significantly younger, and seem to have a longer overall survival compared with patients with asbestos-associated PDMM.

[14]

TÍTULO / TITLE: - Systematic identification of molecular subtype-selective vulnerabilities in non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cell. 2013 Oct 24;155(3):552-66. doi: 10.1016/j.cell.2013.09.041. Epub 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) [1016/j.cell.2013.09.041](#)

AUTORES / AUTHORS: - Kim HS; Mendiratta S; Kim J; Pecot CV; Larsen JE; Zubovych I; Seo BY; Kim J; Eskiocak B; Chung H; McMillan E; Wu S; De Brabander J; Komurov K; Toombs JE; Wei S; Peyton M; Williams N; Gazdar AF; Posner BA; Brekken RA; Sood AK; Deberardinis RJ; Roth MG; Minna JD; White MA

INSTITUCIÓN / INSTITUTION: - Department of Cell Biology, University of Texas Southwestern Medical Center, Dallas, TX 75390, USA.

RESUMEN / SUMMARY: - Context-specific molecular vulnerabilities that arise during tumor evolution represent an attractive intervention target class. However, the frequency and diversity of somatic lesions detected among lung tumors can confound efforts to identify these targets. To confront this challenge, we have applied parallel screening of chemical and genetic perturbations within a panel of molecularly annotated NSCLC lines to identify intervention opportunities tightly linked to molecular response indicators predictive of target sensitivity. Anchoring this analysis on a matched tumor/normal cell model from a lung adenocarcinoma patient identified three distinct target/response-indicator pairings that are represented with significant

frequencies (6%-16%) in the patient population. These include NLRP3 mutation/inflammasome activation-dependent FLIP addiction, co-occurring KRAS and LKB1 mutation-driven COPI addiction, and selective sensitivity to a synthetic indolotriazine that is specified by a seven-gene expression signature. Target efficacies were validated in vivo, and mechanism-of-action studies informed generalizable principles underpinning cancer cell biology.

[15]

TÍTULO / TITLE: - A comparison of individualized treatment guided by VeriStrat with standard of care treatment strategies in patients receiving second-line treatment for advanced non-small cell lung cancer: A cost-utility analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):461-8. doi: 10.1016/j.lungcan.2013.08.021. Epub 2013 Sep 3.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.08.021](#)

AUTORES / AUTHORS: - Nelson RE; Stenehjem D; Akerley W

INSTITUCIÓN / INSTITUTION: - VA Salt Lake City Health Care System, Salt Lake City, UT, United States; University of Utah School of Medicine, Salt Lake City, UT, United States. Electronic address: Richard.Nelson@utah.edu.

RESUMEN / SUMMARY: - OBJECTIVES: Two therapies are appropriate as 2nd-line treatment of non-small cell lung cancer (NSCLC) patients: chemotherapy and epidermal growth factor receptor (EGFR) inhibitor therapy. VeriStrat, a serum proteomic test, can be used to guide treatment decisions for NSCLC patients. The test classifies patients as likely to benefit from either of these two treatment options. The objective of this research was to model the anticipated survival and cost-effectiveness of four different treatment strategies: chemotherapy for all patients (C-all), EGFR inhibitor for all (E-all), a performance status guided selection strategy (PS-guided), and a strategy guided by VeriStrat test results (V-guided). MATERIALS AND METHODS: We developed a Markov model with the perspective of the U.S. health care system. Model inputs were taken from published literature for the base-case analysis. One-way and probabilistic sensitivity analyses were performed. RESULTS AND CONCLUSION: The C-all treatment strategy showed the best overall survival outcome (10.1 months), followed by V-guided (9.6 months), PS-guided (9.2 months), and E-all (8.2 months) strategies. The incremental cost-effectiveness ratio (ICER) of a V-guided treatment strategy was \$91,111 (vs. E-all) and \$8462 (vs. PS-guided) per quality-adjusted life year (QALY). The ICER for C-all compared to V-guided was \$105,616. This cost-utility analysis indicates that a treatment strategy guided by the VeriStrat test in patients receiving second-line therapy for NSCLC may experience an overall survival benefit at an incremental cost-effectiveness ratio that is reasonable when compared with other practices, including cancer treatments, generally covered in the U.S. health care system. However, treating all patients with chemotherapy yielded the greatest expected survival.

[16]

TÍTULO / TITLE: - Phase I trial of carboplatin and etoposide in combination with panobinostat in patients with lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Oct;33(10):4475-81.

AUTORES / AUTHORS: - Tarhini AA; Zahoor H; McLaughlin B; Gooding WE; Schmitz JC; Siegfried JM; Socinski MA; Argiris A

INSTITUCIÓN / INSTITUTION: - University of Pittsburgh Cancer Institute, UPMC Cancer Pavilion, 5150 Centre Avenue (555), Pittsburgh, PA 15232, U.S.A.

tarhiniaa@upmc.edu.

RESUMEN / SUMMARY: - A phase I trial consisting of panobinostat (a HDAC inhibitor), carboplatin and etoposide was conducted in patients with lung cancer. **PATIENTS AND METHODS:** Patients received carboplatin AUC5 on day 1 and etoposide 100 mg/m² on days 1, 2 and 3, every 21 days. Concurrent oral panobinostat was given 3 times weekly on a 2-weeks-on and 1-week-off schedule during the 4-6 cycles of chemotherapy and then continued as maintenance therapy. **RESULTS:** Six evaluable patients were treated at the first dose level of panobinostat (10 mg). Dose-limiting toxicity occurred in two patients (33%) during the first cycle. One patient developed grade 4 thrombocytopenia and another grade 4 febrile neutropenia. Therefore, the study was suspended based on the pre-specified study design. No recommended phase II starting dose was established. **CONCLUSION:** The addition of panobinostat to carboplatin and etoposide was not tolerable at the lowest dose level tested in this trial. Further research and development into this combination is not recommended.

[17]

TÍTULO / TITLE: - A population-based review of the feasibility of platinum-based combination chemotherapy after tyrosine kinase inhibition in EGFR mutation positive non-small cell lung cancer patients with advanced disease.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 19. pii: S0169-5002(13)00451-0. doi: 10.1016/j.lungcan.2013.10.007.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.lungcan.2013.10.007](#)

AUTORES / AUTHORS: - Mariano C; Bosdet I; Karsan A; Ionescu D; Murray N; Laskin JJ; Zhai Y; Melosky B; Sun S; Ho C

INSTITUCIÓN / INSTITUTION: - British Columbia Cancer Agency, Department of Medical Oncology, 600 West 10th Avenue, Vancouver, BC, Canada V5Z 4E6.

Electronic address: cmariano@bccancer.bc.ca.

RESUMEN / SUMMARY: - **INTRODUCTION:** The IPASS trial demonstrated superior progression free survival for Asian, light/never smoking, advanced, pulmonary adenocarcinoma patients treated with first-line gefitinib compared to carboplatin/paclitaxel, of which 59% of those tested were epidermal growth factor receptor (EGFR) mutation positive. In IPASS 39% of gefitinib treated patients went on to receive platin based polychemotherapy. We hypothesized that in a population-based setting fewer patients receive second-line platin based chemotherapy than those enrolled in a clinical trial. **METHODS:** The Iressa Alliance program provided standardized EGFR mutation testing and appropriate access to gefitinib to all patients in British Columbia with advanced, non squamous non small cell lung cancer (NSCLC). We retrospectively analyzed clinical, pathologic data and outcomes for all patients tested in this program between March 2010 and June 2011. **RESULTS:** A total of 548 patients were referred for testing and 22% of patients were mutation positive. Baseline

characteristics of mutation negative and mutation positive; median age 67/65, male 41%/31%, Asian 15%/51%, never smoker 21%/58%, stage IV 80%/91%. Median overall survival was 12 months in mutation negative patients and not yet reached in mutation positive ($p < 0.0001$). In mutation positive patients 5% of patients had a complete response, 46% partial response, 34% stable disease, 6% progressive disease. Twenty percent of patients continued on gefitinib after radiographic progression and clinical stability. Sixty-one gefitinib treated patients progressed at the time of analysis; 10% of patients received further gefitinib only, 38% platinum based doublet, 8% other chemotherapy and 44% no further treatment. Performance status most strongly predicted for delivery of second line chemotherapy. CONCLUSIONS: This North American population based study shows similar efficacy of gefitinib in mutation positive patients compared to the IPASS trial. Contrary to our hypothesis, delivery of second line chemotherapy was feasible in a significant proportion of gefitinib treated patients.

[18]

TÍTULO / TITLE: - Long-lasting disease stabilization in the absence of toxicity in metastatic lung cancer patients vaccinated with an epitope derived from indoleamine 2,3 dioxygenase.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 11.

- [Enlace al texto completo \(gratis o de pago\) 1158/1078-0432.CCR-13-1560](#)

AUTORES / AUTHORS: - Zeeberg Iversen T; Engell-Noerregaard L; Ellebaek E; Andersen R; Kiaer Larsen S; Bjoern J; Zeyher C; Gouttefangeas C; Moerck Thomsen B; Holm B; Thor Straten P; Mellemgard A; Andersen MH; Svane IM

INSTITUCIÓN / INSTITUTION: - Department of Haematology and Oncology, Center for Cancer ImmuneTherapy.

RESUMEN / SUMMARY: - PURPOSE: To investigate targeting of indoleamine 2.3 dioxygenase (IDO) enzyme using a synthetic peptide vaccine administered to patients with metastatic NSCLC. EXPERIMENTAL DESIGN: In a clinical phase I study we treated 15 HLA-A2 positive patients with stage III-IV NSCLC in disease stabilization (SD) after standard chemotherapy. Patients were treated with Imiquimod ointment and subcutaneous vaccinations (100 microg IDO5 peptide, sequence ALLEIASCL, formulated in 900 microL Montanide). Primary end point was toxicity. Clinical benefit and immunity were assessed as secondary endpoints. RESULTS: No severe toxicity was observed. One patient developed a partial response (PR) after 1 year of vaccine treatment while long-lasting disease stabilization ($SD \geq 8.5$ months) was demonstrated in another 6 patients. The median overall survival (OS) was 25.9 months. Patients demonstrated significant improved OS ($P=0.03$) when compared to the group of patients excluded due to HLA-A2 negativity. IDO specific CD8+ T cell immunity was demonstrated by IFN- γ Elispot and Tetramer staining. FACS analyses demonstrated a significant reduction of the Treg population ($P=0.03$) after the 6th vaccine (2.5 months) compared to pre-treatment levels. Furthermore, expression of IDO was detected in 9/10 tumour biopsies by immunohistochemistry. HPLC analyses of Kynurenine/Tryptophan (Kyn/Trp) ratio in sera were performed. In long term analyses of two clinical responding patients the ratio of Kyn/Trp remained stable.

CONCLUSIONS: The vaccine was well-tolerated with no severe toxicity occurring. A median OS of 25.9 months was demonstrated and long-lasting PR+SD were seen in 47% of the patients.

[19]

TÍTULO / TITLE: - Do Angiotensin-converting enzyme inhibitors reduce the risk of symptomatic radiation pneumonitis in patients with non-small cell lung cancer after definitive radiation therapy? Analysis of a single-institution database.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Dec 1;87(5):1071-7. doi: 10.1016/j.ijrobp.2013.08.033. Epub 2013 Oct 22.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijrobp.2013.08.033](#)

AUTORES / AUTHORS: - Wang H; Liao Z; Zhuang Y; Xu T; Nguyen QN; Levy LB; O'Reilly M; Gold KA; Gomez DR

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Nanfang Hospital, Southern Medical University, Guangzhou, Guangdong Province, P.R. of China.

RESUMEN / SUMMARY: - PURPOSE: Preclinical studies have suggested that angiotensin-converting enzyme inhibitors (ACEIs) can mitigate radiation-induced lung injury. We sought here to investigate possible associations between ACEI use and the risk of symptomatic radiation pneumonitis (RP) among patients undergoing radiation therapy (RT) for non-small cell lung cancer (NSCLC). METHODS AND MATERIALS: We retrospectively identified patients who received definitive radiation therapy for stages I to III NSCLC between 2004 and 2010 at a single tertiary cancer center. Patients must have received a radiation dose of at least 60 Gy for a single primary lung tumor and have had imaging and dosimetric data available for analysis. RP was quantified according to Common Terminology Criteria for Adverse Events, version 3.0. A Cox proportional hazard model was used to assess potential associations between ACEI use and risk of symptomatic RP. RESULTS: Of 413 patients analyzed, 65 were using ACEIs during RT. In univariate analysis, the rate of RP grade ≥ 2 seemed lower in ACEI users than in nonusers (34% vs 46%), but this apparent difference was not statistically significant ($P=.06$). In multivariate analysis of all patients, ACEI use was not associated with the risk of symptomatic RP (hazard ratio [HR] = 0.66; $P=.07$) after adjustment for sex, smoking status, mean lung dose (MLD), and concurrent carboplatin and paclitaxel chemotherapy. Subgroup analysis showed that ACEI use did have a protective effect from RP grade ≥ 2 among patients who received a low (≤ 20 -Gy) MLD ($P<.01$) or were male ($P=.04$). CONCLUSIONS: A trend toward reduction in symptomatic RP among patients taking ACEIs during RT for NSCLC was not statistically significant on univariate or multivariate analyses, although certain subgroups may benefit from use (ie, male patients and those receiving low MLD). The evidence at this point is insufficient to establish whether the use of ACEIs does or does not reduce the risk of RP.

[20]

TÍTULO / TITLE: - Mutated Ephrin Receptor Genes in Non-Small Cell Lung Carcinoma and Their Occurrence with Driver Mutations-Targeted Resequencing Study on Formalin-Fixed, Paraffin-Embedded Tumor Material of 81 Patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Genes Chromosomes Cancer. 2013 Oct 7. doi: 10.1002/gcc.22109.

●● Enlace al texto completo (gratis o de pago) [1002/gcc.22109](#)

AUTORES / AUTHORS: - Maki-Nevala S; Kaur Sarhadi V; Tuononen K; Lagstrom S; Ellonen P; Ronty M; Wirtanen A; Knuutila A; Knuutila S

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Haartman Institute, University of Helsinki, Finland.

RESUMEN / SUMMARY: - Non-small cell lung carcinoma (NSCLC) is the most common subtype of lung cancer. The oncogenic potential of receptor tyrosine kinases (RTKs) is widely known and they are potential targets for tailored therapy. Ephrin receptors (Ephs) form the largest group of RTKs. Nevertheless, Ephs are not widely studied in NSCLC so far. The aim of our study was to investigate novel mutations of Eph genes (EPHA1-8, EPHB1-4, EPHB6) and their association with clinically relevant mutations in BRAF, EML4-ALK, EGFR, INSR, KDR, KRAS, MET, PDGFRA, PDGFRB, PIK3, PTEN, RET, and TP53 in NSCLC patients. Targeted resequencing was conducted on 81 formalin-fixed, paraffin-embedded NSCLC tumor specimens. We analyzed missense and nonsense mutations harbored in the coding regions of the selected genes. We found 18 novel mutations of Ephs in 20% (16 of 81) of the patients. Nearly half of these mutations occurred in the protein kinase domain. The mutations were not mutually exclusive with other clinically relevant mutations. Our study shows that Ephs are frequently mutated in NSCLC patients, and occur together with other known mutations relevant to the pathogenicity of NSCLC. © 2013 Wiley Periodicals, Inc.

[21]

TÍTULO / TITLE: - Circulating Inflammation Markers and Prospective Risk of Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Natl Cancer Inst. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1093/jnci/djt309](#)

AUTORES / AUTHORS: - Shiels MS; Pfeiffer RM; Hildesheim A; Engels EA; Kemp TJ; Park JH; Katki HA; Koshiol J; Shelton G; Caporaso NE; Pinto LA; Chaturvedi AK

INSTITUCIÓN / INSTITUTION: - Affiliations of authors: Infections and Immunoepidemiology Branch (MSS, AH, EAE, JK, AKC), Biostatistics Branch (RMP, HAK), and Genetic Epidemiology Branch (NEC), Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD; HPV Immunology Laboratory, SAIC-Frederick Inc., Frederick, MD (TJK, GS, LAP); Department of Statistics, Dongguk University, Seoul, Korea (J-HP).

RESUMEN / SUMMARY: - **BACKGROUND:** Despite growing recognition of an etiologic role for inflammation in lung carcinogenesis, few prospective epidemiologic studies have comprehensively investigated the association of circulating inflammation markers with lung cancer. **METHODS:** We conducted a nested case-control study (n = 526 lung cancer patients and n = 592 control subjects) within the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. Control subjects were matched to lung cancer case patients on age, sex, follow-up time (median = 2.9 years), randomization year, and smoking (pack-years and time since quitting). Serum levels of 77 inflammation markers were measured using a Luminex bead-based assay. Conditional logistic regression

and weighted Cox models were used to estimate odds ratios (ORs) and cumulative risks, respectively. RESULTS: Of 68 evaluable markers, 11 were statistically significantly associated with lung cancer risk (P trend across marker categories < .05), including acute-phase proteins (C-reactive protein [CRP], serum amyloid A [SAA]), proinflammatory cytokines (soluble tumor necrosis factor receptor 2 [sTNFRII]), anti-inflammatory cytokines (interleukin 1 receptor antagonist [IL-1RA]), lymphoid differentiation cytokines (interleukin 7 [IL-7]), growth factors (transforming growth factor alpha [TGF-A]), and chemokines (epithelial neutrophil-activating peptide 78 [ENA 78/CXCL5], monokine induced by gamma interferon [MIG/CXCL9], B cell-attracting chemokine 1 [BCA-1/CXCL13], thymus activation regulated chemokine [TARC/CCL17], macrophage-derived chemokine [MDC/CCL22]). Elevated marker levels were associated with increased lung cancer risk, with odds ratios comparing the highest vs the lowest group ranging from 1.47 (IL-7) to 2.27 (CRP). For IL-1RA, elevated levels were associated with decreased lung cancer risk (OR = 0.71; 95% confidence interval = 0.51 to 1.00). Associations did not differ by smoking, lung cancer histology, or latency. A cross-validated inflammation score using four independent markers (CRP, BCA-1/CXCL13, MDC/CCL22, and IL-1RA) provided good separation in 10-year lung cancer cumulative risks among former smokers (quartile [Q] 1 = 1.1% vs Q4 = 3.1%) and current smokers (Q1 = 2.3% vs Q4 = 7.9%) even after adjustment for smoking. CONCLUSIONS: Some circulating inflammation marker levels are associated with prospective lung cancer risk.

[22]

TÍTULO / TITLE: - Short and long-term effects of supervised versus unsupervised exercise training on health-related quality of life and functional outcomes following lung cancer surgery - A randomized controlled trial.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 30. pii: S0169-5002(13)00459-5. doi: 10.1016/j.lungcan.2013.10.015.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.lungcan.2013.10.015](#)

AUTORES / AUTHORS: - Brocki BC; Andreassen J; Nielsen LR; Nekrasas V; Gorst-Rasmussen A; Westerdahl E

INSTITUCIÓN / INSTITUTION: - Department of Occupational Therapy and Physiotherapy, Aalborg University Hospital, Denmark; School of Health and Medical Sciences, Orebro University, Sweden. Electronic address: bcb@rn.dk.

RESUMEN / SUMMARY: - OBJECTIVE: Surgical resection enhances long-term survival after lung cancer, but survivors face functional deficits and report on poor quality of life long time after surgery. This study evaluated short and long-term effects of supervised group exercise training on health-related quality of life and physical performance in patients, who were radically operated for lung cancer. METHODS: A randomized, assessor-blinded, controlled trial was performed on 78 patients undergoing lung cancer surgery. The intervention group (IG, n=41) participated in supervised out-patient exercise training sessions, one hour once a week for ten weeks. The sessions were based on aerobic exercises with target intensity of 60-80% of work capacity, resistance training and dyspnoea management. The control group (CG, n=37) received one individual instruction in exercise training. Measurements consisted of: health-related quality of life (SF36), six minute walk test (6MWT) and lung function (spirometry),

assessed three weeks after surgery and after four and twelve months. RESULTS: Both groups were comparable at baseline on demographic characteristic and outcome values. We found a statistically significant effect after four months in the bodily pain domain of SF36, with an estimated mean difference (EMD) of 15.3 (95% CI:4 to 26.6, p=0.01) and a trend in favour of the intervention for role physical functioning (EMD 12.04, 95% CI: -1 to 25.1, p=0.07) and physical component summary (EMD 3.76, 95% CI:-0.1 to 7.6, p=0.06). At 12 months, the tendency was reversed, with the CG presenting overall slightly better measures. We found no effect of the intervention on 6MWT or lung volumes at any time-point. CONCLUSION: Supervised compared to unsupervised exercise training resulted in no improvement in health-related quality of life, except for the bodily pain domain, four months after lung cancer surgery. No effects of the intervention were found for any outcome after one year.

[23]

TÍTULO / TITLE: - CK-19 mRNA-positive cells in peripheral blood predict treatment efficacy and survival in small-cell lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):755. doi: 10.1007/s12032-013-0755-9. Epub 2013 Nov 1.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0755-9](#)

AUTORES / AUTHORS: - Shi WL; Li J; Du YJ; Zhu WF; Wu Y; Hu YM; Chen YC

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, Affiliated Hospital of Jiangsu University, 438 North Jiefang Street, Zhenjiang, 212001, China.

RESUMEN / SUMMARY: - Small-cell lung cancer (SCLC) is the most aggressive form of lung cancer. The aim of this study was to investigate whether the presence of cytokeratin-19 (CK-19) mRNA-positive circulating tumor cells (CTCs) predicts treatment response, progression-free survival (PFS), and overall survival (OS) in SCLC patients who received standard therapy. Fifty-five SCLC patients were enrolled in this single-center prospective study. CK-19 mRNA-positive CTCs in blood samples were detected using real-time quantitative-PCR assay before the initiation of chemotherapy (B0) and after one chemotherapy cycle (B1) and three chemotherapy cycles (B3). The association with known prognostic factors and the effect of CK-19 mRNA-positive CTCs on patients' prognosis were analyzed. Patients with positivity for CK-19 mRNA-positive CTCs at B0, B1, and B3 time points had shorter PFS and OS compared with patients without (P = 0.014 and P = 0.01, respectively, at B0; P = 0.008 and P = 0.002, respectively, at B1; P = 0.003 and P = 0.001, respectively, at B3). Conversion of initial positivity for CK-19 mRNA-positive CTCs to negativity at B1 and B3 time points was associated with longer PFS and OS compared with patients with persistent positivity at three time points (P = 0.008 and P = 0.010, respectively). Multivariate analysis demonstrated that the presence of CK-19 mRNA-positive CTCs at B0, B1, and B3 time points remained strong predictors of PFS and OS after adjustment for clinically significant factors. In conclusion, detection of CK-19 mRNA-positive CTCs before and during chemotherapy is an accurate indication of subsequent disease progression and mortality for SCLC patients.

[24]

TÍTULO / TITLE: - Rebiopsy of non-small cell lung cancer patients with acquired resistance to epidermal growth factor receptor-tyrosine kinase inhibitor: Comparison between T790M mutation-positive and mutation-negative populations.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer. 2013 Sep 16. doi: 10.1002/cncr.28364.

●● Enlace al texto completo (gratis o de pago) [1002/cncr.28364](#)

AUTORES / AUTHORS: - Hata A; Katakami N; Yoshioka H; Takeshita J; Tanaka K; Nanjo S; Fujita S; Kaji R; Imai Y; Monden K; Matsumoto T; Nagata K; Otsuka K; Tachikawa R; Tomii K; Kunimasa K; Iwasaku M; Nishiyama A; Ishida T; Nishimura Y

INSTITUCIÓN / INSTITUTION: - Division of Integrated Oncology, Institute of Biomedical Research and Innovation, Kobe, Japan.

RESUMEN / SUMMARY: - BACKGROUND: The secondary epidermal growth factor receptor (EGFR) mutation Thr790Met (T790M) accounts for approximately half of acquired resistances to EGFR-tyrosine kinase inhibitor (TKI). Recent reports have demonstrated that the emergence of T790M predicts a favorable prognosis and indolent progression. However, rebiopsy to confirm T790M status can be challenging due to limited tissue availability and procedural feasibility, and little is known regarding the differences among patients with or without T790M mutation. METHODS: The study investigated 78 EGFR-mutant patients who had undergone rebiopsy after TKI failure. The peptide nucleic acid-locked nucleic acid polymerase chain reaction clamp method was used in EGFR mutational analyses. Various patient characteristics and postprogression survivals (PPSs) after initial TKI failure were retrospectively compared in patients with and without T790M. RESULTS: The T790M mutation was identified in 4 (17%) of 24 central nervous system lesions, and in 22 (41%) of 54 other lesions ($P = .0417$). No other characteristics had a statistical association with T790M prevalence. Median PPS was 31.4 months in 26 patients with T790M, and 11.4 months in 52 patients without T790M ($P = .0017$). In the multivariate analysis, statistically significant factors for longer PPS included T790M-positive, good performance status, and no carcinomatous meningitis. CONCLUSIONS: The emergence of T790M in central nervous system lesions was rare, compared with other lesions. Patients with T790M after TKI failure appear to have better prognoses than those without T790M. TKI rechallenge or continuous administration beyond progression may be effective after initial TKI failure. Cancer 2013. © 2013 American Cancer Society.

[25]

TÍTULO / TITLE: - Clinical Outcomes After First-line EGFR Inhibitor Treatment for Patients with NSCLC, EGFR Mutation, and Poor Performance Status.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):5057-64.

AUTORES / AUTHORS: - Okuma Y; Hosomi Y; Nagamata M; Yamada Y; Sekihara K; Kato K; Hishima T; Okamura T

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious diseases Center Komagome Hospital, 3-18-22 Honkomagome, Bunkyo, Tokyo 113-8677, Japan. y-okuma@cick.jp.

RESUMEN / SUMMARY: - BACKGROUND: The phase II NEJ001 trial suggested that gefitinib was active against advanced non-small cell lung cancer (NSCLC) even in patients with poor performance status (PS). Clinical response among the patients

harboring epidermal growth factor receptor (EGFR) mutation with poor PS is fair; however, gefitinib does not have as much continued efficacy as in patients with good PS. This study has retrospectively investigated the clinical outcomes of gefitinib treated patients with advanced NSCLC, EGFR mutations, and poor PS. PATIENTS AND METHODS: A total of 208 patients with advanced NSCLC and poor PS treated with gefitinib from 2004 to 2013 were retrospectively evaluated. Outcomes were studied after stratification for gender, smoking status, histological subtype, and EGFR mutation status. RESULTS: Fifty-two patients (25.0%) with advanced NSCLC, EGFR mutation, and poor PS were treated with gefitinib. The overall response rate was 65.4%. The median progression-free survival, median survival time, and one-year survival rate was 6.6 months, 19.6 months, and 62.9%, respectively. Death due to interstitial lung disease occurred in 11.5% of the patient population. In multivariate analysis, a PS of 4 was independently associated with poor outcomes (hazard ratio=10.5; 95% Confidence interval=1.92-50.19; p=0.0091). CONCLUSION: Patients with advanced NSCLC, EGFR mutation, and poor PS have poor outcomes in response to gefitinib. However, the indication of gefitinib for such patients will not be changed in clinical practice and oncologists should treat these patients with more careful follow-up since for those with poor PS, therapy may be more toxic than for patients with good PS.

[26]

TÍTULO / TITLE: - Nicotine Induces the Up-regulation of the alpha7-Nicotinic Receptor (alpha7-nAChR) in Human Squamous Cell Lung Cancer Cells via the Sp1/GATA Protein Pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Biol Chem. 2013 Nov 15;288(46):33049-59. doi: 10.1074/jbc.M113.501601. Epub 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago) [1074/jbc.M113.501601](#)

AUTORES / AUTHORS: - Brown KC; Perry HE; Lau JK; Jones DV; Pulliam JF; Thornhill BA; Crabtree CM; Luo H; Chen YC; Dasgupta P

INSTITUCIÓN / INSTITUTION: - From the Department of Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall University, Huntington, West Virginia 25755.

RESUMEN / SUMMARY: - Nicotine, the addictive component of cigarettes, promotes lung cancer proliferation via the alpha7-nicotinic acetylcholine receptor (alpha7-nAChR) subtype. The present manuscript explores the effect of nicotine exposure on alpha7-nAChR levels in squamous cell carcinoma of the lung (SCC-L) in vitro and in vivo. Nicotine (at concentrations present in the plasma of average smokers) increased alpha7-nAChR levels in human SCC-L cell lines. Nicotine-induced up-regulation of alpha7-nAChR was confirmed in vivo by chicken chorioallantoic membrane models. We also observed that the levels of alpha7-nAChR in human SCC-L tumors (isolated from patients who are active smokers) correlated with their smoking history. Nicotine increased the levels of alpha7-nAChR mRNA and alpha7-nAChR transcription in human SCC-L cell lines and SCC-L tumors. Nicotine-induced up-regulation of alpha7-nAChR required GATA4 and GATA6. ChIP assays showed that nicotine induced the binding of GATA4 or GATA6 to Sp1 on the alpha7-nAChR promoter, thereby inducing its transcription and increasing its levels in human SCC-L. Our data are clinically

relevant because SCC-L patients smoked for decades before being diagnosed with cancer. It may be envisaged that continuous exposure to nicotine (in such SCC-L patients) causes up-regulation of $\alpha 7$ -nAChRs, which facilitates tumor growth and progression. Our results will also be relevant to many SCC-L patients exposed to nicotine via second-hand smoke, electronic cigarettes, and patches or gums to quit smoking.

[27]

TÍTULO / TITLE: - EBUS-centred versus EUS-centred mediastinal staging in lung cancer: a randomised controlled trial.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Thorax. 2013 Oct 30. doi: 10.1136/thoraxjnl-2013-203881.

●● [Enlace al texto completo \(gratis o de pago\) 1136/thoraxjnl-2013-203881](#)

AUTORES / AUTHORS: - Kang HJ; Hwangbo B; Lee GK; Nam BH; Lee HS; Kim MS; Lee JM; Zo JI; Lee HS; Han JY

INSTITUCIÓN / INSTITUTION: - Center for Lung Cancer, Research Institute and Hospital, National Cancer Center, , Goyang, Korea.

RESUMEN / SUMMARY: - BACKGROUND: The impact of procedure sequence and primary procedure has not been studied in the combined application of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) and endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) in lung cancer staging. METHODS: In a randomised controlled trial, 160 patients with histologically confirmed or strongly suspected potentially operable non-small cell lung cancer were enrolled (Group A, n=80, EBUS-centred; Group B, n=80, EUS-centred). EBUS-TBNA and EUS-FNA with an ultrasound bronchoscope were used as the first procedures in Groups A and B, respectively, and secondary procedures (EUS-FNA in Group A, EBUS-TBNA in Group B) were added. RESULTS: Diagnostic values were evaluated in 148 patients (74 in each group). In Groups A and B the diagnostic accuracy (93.2% (95% CI 87.5% to 99.0%) vs 97.3% (95% CI 93.6% to 101.0%), p=0.245) and sensitivity (85.3% (95% CI 68.9% to 95.0%) vs 92.0% (95% CI 74.0% to 99.0%), p=0.431) in detecting mediastinal metastasis were not statistically different. In Group A, adding EUS-FNA to EBUS-TBNA did not significantly increase the accuracy (from 91.9% to 93.2%, p=0.754) or sensitivity (from 82.4% to 85.3%, p=0.742). In group B, adding EBUS-TBNA to EUS-FNA increased the accuracy (from 86.5% to 97.3%, p=0.016) and sensitivity (from 60.0% to 92.0%, p=0.008). There were no intergroup differences in procedure time, cardiorespiratory parameters during procedures, complications or patient satisfaction. CONCLUSIONS: Using a combination of EBUS-TBNA and EUS-FNA in mediastinal staging, we found that diagnostic values and patient satisfaction were not different between the EBUS-centred and EUS-centred groups. However, the necessity for EBUS-TBNA following EUS suggests that EBUS-TBNA is a better primary procedure in endoscopic mediastinal staging of potentially operable lung cancer. TRIAL REGISTRATION NUMBER: ClinicalTrials.gov number NCT01385111.

[28]

TÍTULO / TITLE: - Associations between Single-Nucleotide Polymorphisms in the PI3K-PTEN-AKT-mTOR Pathway and Increased Risk of Brain Metastasis in Patients with Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 15;19(22):6252-60. doi: 10.1158/1078-0432.CCR-13-1093. Epub 2013 Sep 27.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-1093](#)

AUTORES / AUTHORS: - Li Q; Yang J; Yu Q; Wu H; Liu B; Xiong H; Hu G; Zhao J; Yuan X; Liao Z

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Department of Oncology, Tongji Hospital, Huazhong University of Science and Technology, Wuhan, Hubei Province, China; and Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas.

RESUMEN / SUMMARY: - PURPOSE: Non-small cell lung cancer (NSCLC) metastasizes fairly often to the brain, but identifying which patients will develop brain metastases is problematic. The phosphoinositide 3-kinase (PI3K)-AKT-mTOR signaling pathway is important in the control of cell growth, tumorigenesis, and cell invasion. We hypothesized that genotype variants in this pathway could predict brain metastasis in patients with NSCLC. Methods: We genotyped 16 single-nucleotide polymorphisms (SNP) in five core genes (PIK3CA, PTEN, AKT1, AKT2, and FRAP1) by using DNA from blood samples of 317 patients with NSCLC, and evaluated potential associations with the subsequent development of brain metastasis, the cumulative incidence of which was estimated with Kaplan-Meier analysis. Multivariate Cox regression analysis was used to analyze correlations between genotype variants and the occurrence of brain metastasis. RESULTS: In analysis of individual SNPs, the GT/GG genotype of AKT1: rs2498804, CT/TT genotype of AKT1: rs2494732, and AG/AA genotype of PIK3CA: rs2699887 were associated with higher risk of brain metastasis at 24-month follow-up [respective HRs, 1.860, 95% confidence interval (CI) 1.199-2.885, P = 0.006; HR 1.902, 95% CI 1.259-2.875, P = 0.002; and HR 1.933, 95% CI 1.168-3.200, P = 0.010]. We further found that these SNPs had a cumulative effect on brain metastasis risk, with that risk being highest for patients carrying both of these unfavorable genotypes (P = 0.003). CONCLUSIONS: Confirmation of our findings, the first to indicate that genetic variations in PI3K-AKT-mTOR can predict brain metastasis, in prospective studies would facilitate stratification of patients for brain metastasis prevention trials. Clin Cancer Res; 19(22); 6252-60. ©2013 AACR.

[29]

TÍTULO / TITLE: - Clinical management patterns and treatment outcomes in patients with non-small cell lung cancer (NSCLC) across Europe: EPICLIN-Lung study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Med Res Opin. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1185/03007995.2013.860372](#)

AUTORES / AUTHORS: - Carrato A; Vergnenegre A; Thomas M; McBride K; Medina J; Cruciani G

INSTITUCIÓN / INSTITUTION: - Ramon y Cajal University Hospital , Madrid , España.

RESUMEN / SUMMARY: - Abstract Background: Throughout Europe, physicians face similar challenges in non-small cell lung cancer (NSCLC) management, but comprehensive international information on usual clinical practice is lacking so the burden of NSCLC is not fully understood. Methods: This multinational, multicentre, non-interventional study (NCT00831909) was conducted in eight European countries. Patients with confirmed NSCLC were consecutively enrolled from January to March 2009 and followed for 12 months or until death. Information was collected on patient and disease characteristics, diagnosis and treatment patterns, and clinical outcomes. Spontaneously reported adverse events (AEs) were also recorded. Results: Data were available for 3508 patients. Most patients (77.5%) were male, median (range) age was 65.0 years (21.6-90.7), the majority of patients had a World Health Organization performance status of ≤ 1 (74.7%), and 10.8% were never smokers. The most prevalent histologies were adenocarcinoma (43.8%) and squamous-cell carcinoma (29.4%). Most patients presented with advanced disease (11.6% with stage IIIA, 18.7% with stage IIIB, 48.6% with stage IV). In stage IV disease, median progression-free survival and overall survival (months) by first-line treatment cluster were platinum regimens: 6.5, 10.8; non-platinum regimens: 4.3, 8.5; regimens with bevacizumab 8.7, 12.9; investigational regimens: 5.6, 10.8; best supportive care: 5.4, 6.6. The most frequently reported severe (Common Terminology Criteria for Adverse Events v3.0 >2) AEs were blood/bone marrow (16.0%) and pulmonary/upper respiratory (7.8%). Key limitations of this study related to its non-interventional nature and wide regional focus; for example, achieving a representative sample of the overall NSCLC population, variation in recruitment between countries, and data based on information from medical records derived from routine visits. Conclusions: The Epidemiological Study to Describe NSCLC Clinical Management Pattern in Europe-Lung (EPICLIN-Lung) study provides new insights into the descriptive patterns and clinical management strategies for NSCLC across Europe, and how they affect patient outcomes.

[30]

TÍTULO / TITLE: - A phase III concurrent chemoradiotherapy trial with cisplatin and paclitaxel or docetaxel or gemcitabine in unresectable non-small cell lung cancer: KASLC 0401.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Dec;72(6):1247-54. doi: 10.1007/s00280-013-2308-5. Epub 2013 Oct 5.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2308-5](#)

AUTORES / AUTHORS: - Oh IJ; Kim KS; Kim YC; Ban HJ; Kwon YS; Kim YI; Lim SC; Chung WK; Nam TK; Song JY; Yoon MS; Ahn SJ

INSTITUCIÓN / INSTITUTION: - Lung and Esophageal Cancer Clinic, Chonnam National University Hwasun Hospital, 322 Seoyang-ro, Hwasun-eup, Jeonnam, 519-809, Republic of Korea.

RESUMEN / SUMMARY: - PURPOSE: Concurrent chemoradiotherapy (CCRT) is recommended for the management of patients with unresectable non-small cell lung cancer (NSCLC). This prospective study aimed to compare the efficacy of concurrently delivered cisplatin doublets with paclitaxel, or docetaxel, or gemcitabine. METHODS: The main eligibility criteria consisted of previously untreated stage IIIB NSCLC. The subjects were randomized into three arms: paclitaxel 45 mg/m²/week (TP), docetaxel

20 mg/m²/week (DP), and gemcitabine 350 mg/m²/week (GP) in addition to cisplatin 20 mg/m²/week. Three-dimensional conformal radiotherapy was given once daily, weekly 5 fractions and the total prescription dose was 60-66 Gy. The primary endpoint was response rate, and the secondary endpoints were survival and toxicity. RESULTS: A total of 101 patients were recruited into this trial of whom 93 (TP: 33, DP: 29, GP: 31) patients were treated with CCRT from March 2005 to July 2007. Similar response rates were observed across arms: TP: 63.6 %, DP: 72.4 %, GP: 61.3 % (p = 0.679). There was no statistically significant difference of median survival (TP: 27.3, DP: 27.6, GP: 16.5 months, p = 0.771). In subgroup analysis, a survival benefit of consolidation chemotherapy was not seen, but leucopenia (63.2 %) and neutropenia (68.4 %) more than grade 3 were significantly high in DP arm. The grade \geq 3 radiation esophagitis was more frequent in the GP arm (22.6 %, p = 0.163). CONCLUSIONS: Among the three arms, no statistically significant difference in response rate, survival, and toxicity was observed. However, clinically significant radiation toxicity was more frequent in the GP arm.

[31]

TÍTULO / TITLE: - Correction for Red Brewer et al., Mechanism for activation of mutated epidermal growth factor receptors in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Nov 15.

- Enlace al texto completo (gratis o de pago) [1073/pnas.1320849110](https://doi.org/10.1073/pnas.1320849110)

[32]

TÍTULO / TITLE: - Quality of life during chemotherapy in lung cancer patients: results across different treatment lines.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Cancer. 2013 Oct 29;109(9):2301-8. doi: 10.1038/bjc.2013.585. Epub 2013 Oct 3.

- Enlace al texto completo (gratis o de pago) [1038/bjc.2013.585](https://doi.org/10.1038/bjc.2013.585)

AUTORES / AUTHORS: - Wintner LM; Giesinger JM; Zabernigg A; Sztankay M; Meraner V; Pall G; Hilbe W; Holzner B

INSTITUCIÓN / INSTITUTION: - Department of Psychiatry and Psychotherapy, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria.

RESUMEN / SUMMARY: - Background: Most lung cancer patients are diagnosed at an advanced disease stage and predominantly receive palliative treatment, which increasingly consists of several chemotherapy lines. We report on patients' quality of life (QOL) to gain knowledge on QOL during and across multiple lines of chemotherapy. This includes patients with (neo)adjuvant therapy up to 3rd or above line palliative chemotherapy. Methods: Lung cancer patients receiving outpatient chemotherapy at the Kufstein County Hospital completed an electronic version of the EORTC QLQ-C30. Linear mixed models were used for statistical analysis. Results: One hundred and eighty seven patients were included in the study. Surprisingly, irrespective of the chemotherapy line patients reported stable QOL scores during treatment. None of the calculated monthly change rates attained clinical significance, referring to established guidelines that classify a small clinical meaningful change as 5 to 10

points. According to treatment line, 3rd or above line palliative chemotherapy was associated with the worst QOL scores, whereas patients undergoing (neo)adjuvant or 1st line palliative chemotherapy reported fairly comparable QOL. Conclusion: The essential finding of our study is that all QOL aspects of the EORTC QLQ-C30 questionnaire remained unchanged during each chemotherapy line in an unselected population of lung cancer patients. Between treatment lines pronounced differences were found, indicating that later palliative chemotherapy lines are associated with higher QOL impairments. These changes in QOL may not primarily be related to the treatment, but rather refer to impairments due to disease progression and may be partly due to a consequence of the prior therapies.

[33]

TÍTULO / TITLE: - The validation of estrogen receptor 1 mRNA expression as a predictor of outcome in patients with metastatic non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Cancer. 2013 Oct 31. doi: 10.1002/ijc.28571.

●● [Enlace al texto completo \(gratis o de pago\) 1002/ijc.28571](#)

AUTORES / AUTHORS: - Atmaca A; Al-Batran SE; Wirtz RM; Werner D; Zirlik S; Wiest G; Eschbach C; Claas S; Hartmann A; Ficker JH; Jager E; Brueckl WM

INSTITUCIÓN / INSTITUTION: - Department of Hematology and Oncology, Krankenhaus Nordwest, Frankfurt am Main, Germany.

RESUMEN / SUMMARY: - The prognostic role of estrogen receptors in lung cancer is not validated. Results from patients with early stage non-small lung cancer patients indicate a prognostic role of estrogen receptor 1 (ESR1) mRNA expression in these patients. Automated RNA extraction from paraffin and RT-quantitative PCR was used for evaluation of tumoral ESR1 and progesterone receptor (PGR) mRNA expression. The test cohort consisted of 31 patients with advanced or metastatic non-small cell lung cancer (NSCLC) patients, treated in a first-line registry trial. For validation, 53 patients from a randomized multicentre first-line study with eligible tumor samples were evaluated. There was no significant correlation of ESR1 expression with clinical characteristics. ESR1 high expression was of significant positive prognostic value in the training set with a median overall survival (OS) of 15.9 versus 6.2 months for high versus low ESR1 expression patients ($p = 0.0498$, HR 0.39). This could be confirmed in the validation cohort with a median OS of 10.9 versus 5.0 months in ESR1 high versus low patients, respectively ($p = 0.0321$, HR 0.51). In the multivariate analysis adjusted for histological subtype, gender, age and performance status, ESR1 expression remained an independent prognostic parameter for survival in both cohorts. In contrast to ESR1, PGR expression was not able to separate prognostic groups or to predict outcome significantly (for OS; $p = 0.94$). Our study shows that ESR1 mRNA as assessed by qPCR represents a reliable method for detecting ESR1 expression in NSCLC and that ESR1 expression is an independent prognostic factor in metastatic NSCLC.

[34]

TÍTULO / TITLE: - Drug-induced reduction in estimated glomerular filtration rate in patients with ALK-positive non-small cell lung cancer treated with the ALK inhibitor crizotinib.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer. 2013 Nov 20. doi: 10.1002/cncr.28478.

●● Enlace al texto completo (gratis o de pago) [1002/cncr.28478](#)

AUTORES / AUTHORS: - Brosnan EM; Weickhardt AJ; Lu X; Maxon DA; Baron AE; Chonchol M; Camidge DR

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology, University of Colorado Anschutz Medical Campus, Aurora, Colorado.

RESUMEN / SUMMARY: - **BACKGROUND:** To the best of the authors' knowledge, the renal side effects of crizotinib have not been investigated previously. **METHODS:** The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration creatinine-based prediction equation during the first 12 weeks of crizotinib therapy and after crizotinib but before the introduction of any further systemic therapy. **RESULTS:** A total of 38 patients with stage IV anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer who were treated with crizotinib were identified. The mean eGFR decreased by 23.9% compared with baseline ($P < .0001$; 95% confidence interval, 21.3%-26.6%), with the majority of the decrease occurring within the first 2 weeks of therapy. Clinical history and blood urea nitrogen/creatinine ratios did not suggest prerenal causes. The objective response rate among evaluable patients ($n = 27$) was 41%. Tumor shrinkage was not correlated with changes in eGFR (correlation coefficient, -0.052 ; $P = .798$). Among the 16 patients for whom data after treatment with crizotinib were available, recovery to within 84% of the baseline eGFR occurred in all patients. After adjusting for the number of scans with intravenous contrast and the use of known nephrotoxic drugs, the issue of whether a patient was on or off crizotinib treatment was found to be significantly associated with changes in eGFR ($P < .0001$). **CONCLUSIONS:** As assessed by the Chronic Kidney Disease Epidemiology Collaboration prediction equation, eGFR is reduced by treatment with crizotinib, but the majority of patients will recover their eGFR after the cessation of therapy. The early onset, size of the change, minimal cumulative effect, and rapid reversibility raise the possibility that this may be a pharmacological and/or tubular creatinine secretion effect rather than a direct nephrotoxic effect. Increased vigilance with regard to the concomitant use of renally cleared medications or nephrotoxic agents should be considered for patients receiving crizotinib and, when eGFR is reduced, additional renal investigations should be undertaken. Cancer 2013. Esta es una cita bibliográfica que va por delante de la publicación en papel. La fecha indicada en la cita provista, NO corresponde con la fecha o la cita bibliográfica de la publicación en papel. La cita bibliográfica definitiva (con el volumen y su paginación) saldrá en 1 ó 2 meses a partir de la fecha de la emisión electrónica-online. *** This is a bibliographic record ahead of the paper publication. The given date in the bibliographic record does not correspond to the date or the bibliographic citation on the paper publication. The publisher will provide the final bibliographic citation (with the volume, and pagination) within 1 or 2 months from the date the record was published online. © 2013 American Cancer Society.

TÍTULO / TITLE: - Docetaxel or pemetrexed with or without cetuximab in recurrent or progressive non-small-cell lung cancer after platinum-based therapy: a phase 3, open-label, randomised trial.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lancet Oncol. 2013 Dec;14(13):1326-36. doi: 10.1016/S1470-2045(13)70473-X. Epub 2013 Nov 12.

●● Enlace al texto completo (gratis o de pago) [1016/S1470-2045\(13\)70473-](#)

[X](#)

AUTORES / AUTHORS: - Kim ES; Neubauer M; Cohn A; Schwartzberg L; Garbo L; Caton J; Robert F; Reynolds C; Katz T; Chittoor S; Simms L; Saxman S

INSTITUCIÓN / INSTITUTION: - Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC, USA. Electronic address: Edward.Kim@carolinashealthcare.org.

RESUMEN / SUMMARY: - BACKGROUND: Available preclinical and phase 2 clinical data suggest that the addition of cetuximab, a monoclonal antibody directed against the epidermal growth factor receptor (EGFR), to chemotherapy might improve outcome in patients with advanced non-small-cell lung cancer (NSCLC). We aimed to assess whether the addition of cetuximab to chemotherapy improved progression-free survival in patients with recurrent or progressive NSCLC after platinum-based therapy.

METHODS: In this unmasked, open-label randomised phase 3 trial we enrolled patients with metastatic, unresectable, or locally advanced NSCLC from 121 sites in Canada and the USA. Eligible patients were those aged 18 years or older who had experienced progressive disease during or after one previous platinum-based regimen. Initially, patients were randomly assigned to receive either pemetrexed (500 mg/m²) or docetaxel (75 mg/m²) and then randomly assigned within each group to receive their chemotherapy with or without cetuximab (400 mg/m² at first dose and 250 mg/m² weekly thereafter) until disease progression or unacceptable toxicity.

However, after a change in the standard of care, investigators chose whether to treat with pemetrexed or docetaxel on a patient-by-patient basis. The primary analysis was changed to compare progression-free survival with cetuximab plus pemetrexed versus pemetrexed, on an intention-to-treat basis. This study is registered with ClinicalTrials.gov, number NCT00095199. FINDINGS: Between Jan 10, 2005, and Feb 10, 2010, we enrolled 939 patients; data for one patient was accidentally discarded. Of the remaining 938 patients, 605 received pemetrexed (301 patients with cetuximab and 304 alone) and 333 received docetaxel (167 in combination with cetuximab and 166 alone). Median progression-free survival with cetuximab plus pemetrexed was 2.9 months (95% CI 2.7-3.2) versus 2.8 months (2.5-3.3) with pemetrexed (HR 1.03, 95% CI 0.87-1.21; p=0.76). The most common grade 3-4 adverse events with cetuximab plus pemetrexed were fatigue (33 [11%] of 292 patients), acneiform rash (31 [11%]), dyspnoea (29 [10%]), and decreased neutrophil count (28 [10%]), and with pemetrexed alone were dyspnoea (35 [12%] of 289 patients), decreased neutrophil count (26 [9%]), and fatigue (23 [8%]). A significantly higher proportion of patients in the cetuximab plus pemetrexed group (119 [41%] of 292 patients) experienced at least one serious adverse event than those patients in the pemetrexed group (85 [29%] of 289 patients; p=0.0054). Nine (3%) of 292 treated patients in the cetuximab and pemetrexed group died of adverse events compared with five (2%) of 289 treated patients in the pemetrexed alone group. INTERPRETATION: The use of cetuximab is not recommended in combination with chemotherapy in patients previously treated with

platinum-based therapy. FUNDING: Eli Lilly and Company and ImClone Systems LLC, a wholly owned subsidiary of Eli Lilly and Company.

[36]

TÍTULO / TITLE: - A phase II study of pemetrexed in patients with previously heavily treated non-squamous non-small cell lung cancer (HANSHIN Oncology Group 001).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Oct 20.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2290-y](#)

AUTORES / AUTHORS: - Hattori Y; Satouchi M; Katakami N; Fujita S; Kaji R; Hata A; Urata Y; Shimada T; Uchida J; Tomii K; Morita S; Negoro S

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology, Hyogo Cancer Center, 13-70 Kitaoji-cho, Akashi-shi, Hyogo, 673-8558, Japan.

RESUMEN / SUMMARY: - PURPOSE: Pemetrexed has shown substantial activity in non-squamous non-small cell lung cancer (NSCLC) and is one of the current standard agents in second-line settings due to its efficacy and favorable tolerability profile. We conducted phase II study to evaluate the safety and efficacy of pemetrexed in Japanese patients with previously heavily treated, advanced non-squamous NSCLC. METHODS: Patients with stage IIIB or IV non-squamous NSCLC, performance status (PS) 0-2, previous two to five regimens of chemotherapy were enrolled and received pemetrexed (500 mg/m²) on day 1 every 21 days until disease progression. The primary endpoint was progression-free survival (PFS). The secondary endpoints included overall survival (OS), objective response rate (ORR), disease control rate (DCR), and safety. RESULTS: From August 2009 to May 2010, 46 patients were enrolled: median age 65 years; 52 % women; PS 0/1/2 26/67/7 %; previous treatment regimen 2/3/4/5 48/28/20/4 %; epidermal growth factor receptor activating mutation positive/wild/unknown 30/48/22 %. The median follow-up period was 13.5 months. The median number of treatment cycles was 4 (range 1-18 cycles). The median PFS was 5.2 months (95 % CI 3.0-5.8 months). The median OS was 14.4 months (95 % CI 9.4-21.3 months). The ORR was 8.7 % and DCR was 63.0 %. The grade $\frac{3}{4}$ hematological adverse events include 8 patients with leukopenia, 11 with neutropenia, 5 with anemia, and 2 with thrombocytopenia. There were no reports of febrile neutropenia and no treatment-related death was observed. CONCLUSION: Treatment with pemetrexed in previously heavily treated Japanese non-squamous NSCLC patients is feasible and shows encouraging activity.

[37]

TÍTULO / TITLE: - Concomitant chemoradiotherapy and antiretroviral therapy for HIV-infected patients with locoregionally advanced non-small cell lung cancer: benefit and tolerability of treatment in 2 cases.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onkologie. 2013;36(10):586-90. doi: 10.1159/000355162. Epub 2013 Sep 17.

●● Enlace al texto completo (gratis o de pago) [1159/000355162](#)

AUTORES / AUTHORS: - Okuma Y; Yanagisawa N; Hosomi Y; Imamura A; Okamura T; Kato K; Negishi K

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology and Respiratory Medicine, Tokyo Metropolitan Cancer and Infectious diseases Center, Komagome Hospital, Tokyo, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Human immunodeficiency virus (HIV)-infected patients are surviving longer since the advent of antiretroviral therapy. Therefore, more patients are developing non-AIDS-defining cancers which increasingly determine mortality. CASE REPORTS: Here we present 2 cases of locally advanced non-small cell lung cancer treated initially with concomitant chemoradiotherapy and antiretroviral therapy. Both patients were male, ages 69 and 66, with known HIV infection and immunologically stable on antiretroviral therapy. Presenting symptoms included superior sulcus tumor with left arm immobility and sensory disturbance in case 1 and right lower bronchus constriction in case 2. Symptoms were controlled by chemoradiotherapy. CONCLUSION: These cases illustrate that intensive anticancer therapy administered to the HIV-infected population can be tolerated even though these patients seem to be too fragile for both chemotherapy and radiotherapy, especially since the potential benefit remains uncertain. Recent improvements in chemoradiotherapy and supportive care have enhanced tolerance for such therapy.

[38]

TÍTULO / TITLE: - KDM2A promotes lung tumorigenesis by epigenetically enhancing ERK1/2 signaling.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Invest. 2013 Dec 2;123(12):5231-46. doi: 10.1172/JCI68642. Epub 2013 Nov 8.

●● [Enlace al texto completo \(gratis o de pago\) 1172/JCI68642](#)

AUTORES / AUTHORS: - Wagner KW; Alam H; Dhar SS; Giri U; Li N; Wei Y; Giri D; Cascone T; Kim JH; Ye Y; Multani AS; Chan CH; Erez B; Saigal B; Chung J; Lin HK; Wu X; Hung MC; Heymach JV; Lee MG

RESUMEN / SUMMARY: - Epigenetic dysregulation has emerged as a major contributor to tumorigenesis. Histone methylation is a well-established mechanism of epigenetic regulation that is dynamically modulated by histone methyltransferases and demethylases. The pathogenic role of histone methylation modifiers in non-small cell lung cancer (NSCLC), which is the leading cause of cancer deaths worldwide, remains largely unknown. Here, we found that the histone H3 lysine 36 (H3K36) demethylase KDM2A (also called FBXL11 and JHDM1A) is frequently overexpressed in NSCLC tumors and cell lines. KDM2A and its catalytic activity were required for in vitro proliferation and invasion of KDM2A-overexpressing NSCLC cells. KDM2A overexpression in NSCLC cells with low KDM2A levels increased cell proliferation and invasiveness. KDM2A knockdown abrogated tumor growth and invasive abilities of NSCLC cells in mouse xenograft models. We identified dual-specificity phosphatase 3 (DUSP3) as a key KDM2A target gene and found that DUSP3 dephosphorylates ERK1/2 in NSCLC cells. KDM2A activated ERK1/2 through epigenetic repression of DUSP3 expression via demethylation of dimethylated H3K36 at the DUSP3 locus. High KDM2A levels correlated with poor prognosis in NSCLC patients. These findings uncover an unexpected role for a histone methylation modifier in activating ERK1/2 in lung tumorigenesis and metastasis, suggesting that KDM2A may be a promising therapeutic target in NSCLC.

[39]

TÍTULO / TITLE: - CRL4A-FBXW5-mediated degradation of DLC1 Rho GTPase-activating protein tumor suppressor promotes non-small cell lung cancer cell growth.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Oct 15;110(42):16868-73. doi: 10.1073/pnas.1306358110. Epub 2013 Sep 30.

●● Enlace al texto completo (gratis o de pago) [1073/pnas.1306358110](#)

AUTORES / AUTHORS: - Kim TY; Jackson S; Xiong Y; Whitsett TG; Lobello JR; Weiss GJ; Tran NL; Bang YJ; Der CJ

INSTITUCIÓN / INSTITUTION: - Lineberger Comprehensive Cancer Center, Department of Pharmacology, and Department of Biochemistry and Biophysics, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599.

RESUMEN / SUMMARY: - DLC1 encodes a RhoA GTPase-activating protein and tumor suppressor lost in cancer by genomic deletion or epigenetic silencing and loss of DLC1 gene transcription. We unexpectedly identified non-small cell lung cancer (NSCLC) cell lines and tumor tissue that expressed DLC1 mRNA yet lacked DLC1 protein expression. We determined that DLC1 was ubiquitinated and degraded by cullin 4A-RING ubiquitin ligase (CRL4A) complex interaction with DDB1 and the FBXW5 substrate receptor. siRNA-mediated suppression of cullin 4A, DDB1, or FBXW5 expression restored DLC1 protein expression in NSCLC cell lines. FBXW5 suppression-induced DLC1 reexpression was associated with a reduction in the levels of activated RhoA-GTP and in RhoA effector signaling. Finally, FBXW5 suppression caused a DLC1-dependent decrease in NSCLC anchorage-dependent and -independent proliferation. In summary, we identify a posttranslational mechanism for loss of DLC1 and a linkage between CRL4A-FBXW5-associated oncogenesis and regulation of RhoA signaling.

[40]

TÍTULO / TITLE: - Concordance of National Cancer Registration with self-reported breast, bowel and lung cancer in England and Wales: a prospective cohort study within the UK Collaborative Trial of Ovarian Cancer Screening.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 26;109(11):2875-9. doi: 10.1038/bjc.2013.626. Epub 2013 Oct 15.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.626](#)

AUTORES / AUTHORS: - Gentry-Maharaj A; Fourkala EO; Burnell M; Ryan A; Apostolidou S; Habib M; Sharma A; Parmar M; Jacobs I; Menon U

INSTITUCIÓN / INSTITUTION: - Gynaecological Cancer Research Centre, Women's Cancer, Institute for Women's Health, University College London, London, UK.

RESUMEN / SUMMARY: - Background:It has been suggested that lower UK cancer survival may be due to incomplete case ascertainment by cancer registries.Methods:We assessed concordance between self-reported breast, bowel and lung cancer and cancer registration (CR) for 1995-2007 in England and Wales in the UK Collaborative Trial of Ovarian Cancer Screening.Results:Concordance of breast cancer CR was higher (94.7%:95% CI: 94.1-95.3%) than for bowel (85.1%:95% CI:

82.1-87.8%) and lung (85.4%:95% CI: 76.3-92.0%). CR concordance was lower in breast cancer (94.5% vs 98.8%) survivors compared with deceased but the difference was small. No difference was found for bowel (85.3% vs 94.6%) or lung (87.1% vs 90.5%) cancer. Conclusion: Concordance of CR and self-reported cancer is high. Incomplete registration is unlikely to be a major cause of lower UK survival rates.

[41]

TÍTULO / TITLE: - Minimal-dose computed tomography is superior to chest x-ray for the follow-up and treatment of patients with resected lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Oct 18. pii: S0022-5223(13)01042-8. doi: 10.1016/j.jtcvs.2013.08.060.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.08.060](#)

AUTORES / AUTHORS: - Hanna WC; Paul NS; Darling GE; Moshonov H; Allison F; Waddell TK; Cypel M; de Perrot ME; Yasufuku K; Keshavjee S; Pierre AF

INSTITUCIÓN / INSTITUTION: - Division of Thoracic Surgery, University of Toronto, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - OBJECTIVES: A minimal-dose computed tomography scan of the thorax (MnDCT) delivers a radiation dose comparable with a chest x-ray (CXR). We hypothesized that in patients with completely resected lung cancer, surveillance with MnDCT, when compared with CXR, leads to earlier detection and a higher rate of treatment of new or recurrent lung cancer. METHODS: After lung cancer resection, patients prospectively were enrolled for surveillance with MnDCT and CXR at 3, 6, 12, 18, 24, 36, 48, and 60 months. Images were interpreted by different blinded radiologists. When new or recurrent cancer was suspected, standard-dose CT and/or a tissue biopsy were performed for confirmation. RESULTS: Between 2007 and 2012, 271 patients were included and 1137 pairs of CXR and MnDCT were analyzed. MnDCT was more sensitive (94% vs 21%; $P < .0001$) and had a higher negative predictive value (99% vs 96%; $P = .007$) than CXR for the diagnosis of new or recurrent lung cancer. The prevalence of new or recurrent lung cancer was 23.2% (63 of 271), of whom 78% (49 of 63) had asymptomatic disease. The majority of asymptomatic patients (75%; 37 of 49) were treated with curative intent and had a median survival of 69 months. The remainder of patients received palliative treatment (24%; 12 of 49) and had a median survival of 25 months ($P < .0001$). CONCLUSIONS: After curative resection of lung cancer, MnDCT is superior to CXR for the detection of new or recurrent lung cancer. The majority of new or recurrent cancer was detected by MnDCT at an asymptomatic phase, allowing for curative treatment, leading to a long survival.

[42]

TÍTULO / TITLE: - Epigenetic inactivation of microRNA-34b/c predicts poor disease-free survival in early stage lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Oct 15.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-](#)

[0736](#)

AUTORES / AUTHORS: - Nadal E; Chen G; Gallegos M; Lin L; Ferrer-Torres D; Truini A; Wang Z; Lin J; Reddy RM; Llatjos R; Escobar I; Moya J; Chang AC; Cardenal F; Capella G; Beer DG

INSTITUCIÓN / INSTITUTION: - Surgery, University of Michigan.

RESUMEN / SUMMARY: - PURPOSE: The microRNA-34b/c (miR-34b/c) has been considered a tumor suppressor in different tumor types and it is a known transcriptional target of the tumor suppressor gene TP53. The main objectives of this study were to investigate the clinical implications of miR-34b/c methylation in early stage lung adenocarcinoma (AC) patients and to determine the functional role of miR-34b/c re-expression in lung AC cell lines. EXPERIMENTAL DESIGN: Aberrant methylation and expression of miR-34b/c were assessed in 15 lung AC cell lines and a cohort of 140 early stage lung AC. Lung AC cell lines were transfected with miR-34b/c and the effects upon cell proliferation, migration, invasion and apoptosis were investigated. RESULTS: Aberrant methylation of miR-34b/c was detected in 6 (40%) of 15 lung AC cell lines and 64 out of 140 (46%) primary lung adenocarcinomas. Expression of miR-34b/c was significantly reduced in all methylated cell lines and primary tumors, especially in those harboring a TP53 mutation. Patients with high levels of miR-34b/c methylation had significantly shorter disease-free survival and overall survival as compared to patients with unmethylated miR-34b/c or low level of miR-34b/c methylation. Ectopic expression of miR-34b/c in lung AC cell lines decreased cell proliferation, migration and invasion. CONCLUSIONS: Epigenetic inactivation of miR-34b/c by DNA methylation has independent prognostic value in early stage lung AC patients with surgically resected tumors. Re-expression of miR-34b/c leads to a less aggressive phenotype in lung AC cell lines.

[43]

TÍTULO / TITLE: - Rare EGFR exon 18 and exon 20 mutations in non-small-cell lung cancer on 10 117 patients: a multicentre observational study by the French ERMETIC-IFCT network.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Oncol. 2013 Nov 26.

●● [Enlace al texto completo \(gratis o de pago\) 1093/annonc/mdt418](#)

AUTORES / AUTHORS: - Beau-Faller M; Prim N; Ruppert AM; Nanni-Metellus I; Lacave R; Lacroix L; Escande F; Lizard S; Pretet JL; Rouquette I; de Cremoux P; Solassol J; de Fraipont F; Bieche I; Cayre A; Favre-Guillevin E; Tomasini P; Wislez M; Besse B; Legrain M; Voegeli AC; Baudrin L; Morin F; Zalcman G; Quoix E; Blons H; Cadranel J

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Strasbourg University Hospital, Strasbourg.

RESUMEN / SUMMARY: - BACKGROUND: There is scarce data available about epidermal growth factor receptor (EGFR) mutations other than common exon 19 deletions and exon 21 (L858R) mutations. PATIENTS AND METHODS: EGFR exon 18 and/or exon 20 mutations were collected from 10 117 non-small-cell lung cancer (NSCLC) samples analysed at 15 French National Cancer Institute (INCa)-platforms of the ERMETIC-IFCT network. RESULTS: Between 2008 and 2011, 1047 (10%) samples were EGFR-mutated, 102 (10%) with rare mutations: 41 (4%) in exon 18, 49 (5%) in exon 20, and 12 (1%) with other EGFR mutations. Exon 20 mutations were related to never-smoker status, when compared with exon 18 mutations (P < 0.001).

Median overall survival (OS) of metastatic disease was 21 months [95% confidence interval (CI) 12-24], worse in smokers than in non-smoker patients with exon 20 mutations (12 versus 21 months; hazard ratio [HR] for death 0.27, 95% CI 0.08-0.87, P = 0.03). Under EGFR-tyrosine kinase inhibitors (TKIs), median OS was 14 months (95% CI 6-21); disease control rate was better for complex mutations (6 of 7, 86%) than for single mutations (16 of 40, 40%) (P = 0.03). CONCLUSIONS: Rare EGFR-mutated NSCLCs are heterogeneous, with resistance of distal exon 20 insertions and better sensitivity of exon 18 or complex mutations to EGFR-TKIs, probably requiring individual assessment.

[44]

TÍTULO / TITLE: - ASAP3 expression in non-small cell lung cancer: association with cancer development and patients' clinical outcome.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Sep 27.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1205-1](#)

AUTORES / AUTHORS: - Fan C; Tian Y; Miao Y; Lin X; Zhang X; Jiang G; Luan L; Wang E

INSTITUCIÓN / INSTITUTION: - Department of Pathology, First Affiliated Hospital and College of Basic Medical Sciences of China Medical University, 110001, Shenyang, China.

RESUMEN / SUMMARY: - ASAP3 belongs to Arf-specific GTPase-activating proteins which regulate Arfs by stimulating their intrinsic GTP hydrolysis. ASAP3 expression and the clinical significance in malignant tumors are largely unknown. In this study, we examined ASAP3 expression in non-small cell lung cancer (NSCLC) to find out its clinicopathological significance. Immunohistochemistry shows elevated expression of ASAP3 in cancer tissues (54.8 % (57/104)) compared to normal lung tissues (18.0 % (9/50)) (p < 0.05). Increased ASAP3 expression was associated with poor differentiation, lymph node metastasis, and advanced TNM stages in NSCLC (p < 0.05). Survival analysis reveals that ASAP3 expression contributes to patients' poor clinical outcome (p < 0.05). We also examined ASAP3 expression in several lung cancer cell lines using Western blotting. We downregulated ASAP3 expression in LTE cell which has a relative high level of ASAP3 expression using siRNA and found that reduced ASAP3 leads to significant inhibition of cancer cell invasion (p < 0.05). These data indicate that ASAP3 is elevated in NSCLC and may contribute to cancer development and patients' poor clinical outcome, which is possibly due to its critical roles in regulating cancer invasion.

[45]

TÍTULO / TITLE: - Comparative physicochemical and biological characterization of NIST Interim Reference Material PM2.5 and SRM 1648 in human A549 and mouse RAW264.7 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Toxicol In Vitro. 2013 Dec;27(8):2289-98. doi: 10.1016/j.tiv.2013.09.024. Epub 2013 Oct 4.

●● Enlace al texto completo (gratis o de pago) [1016/j.tiv.2013.09.024](#)

AUTORES / AUTHORS: - Mitkus RJ; Powell JL; Zeisler R; Squibb KS

INSTITUCIÓN / INSTITUTION: - University of Maryland School of Medicine, 11 South Paca Street, Baltimore, MD 21201, United States. Electronic address: maryland2@comcast.net.

RESUMEN / SUMMARY: - The epidemiological association between exposure to fine particulate matter (PM_{2.5}) and adverse health effects is well-known. Here we report the size distribution, metals content, endotoxin content, and biological activity of National Institute of Standards and Technology (NIST) Interim Reference Material (RM) PM_{2.5}. Biological activity was measured in vitro by effects on cell viability and the release of four inflammatory immune mediators, from human A549 alveolar epithelial cells or murine RAW264.7 monocytes. A dose range covering three orders of magnitude (1-1000µg/mL) was tested, and biological activity was compared to an existing Standard Reference Material (SRM) for urban PM (NIST SRM 1648). Robust release of IL-8 and MCP-1 from A549 cells was observed in response to IRM PM_{2.5} exposures. Significant TNF-α, but not IL-6, secretion from RAW264.7 cells was observed in response to both IRM PM_{2.5} and SRM 1648 particle types. Cytokine or chemokine release at high doses often occurred in the presence of cytotoxicity, likely as a result of externalization of preformed mediator. Our results are consistent with a local cytotoxic and pro-inflammatory mechanism of response to exposure to inhaled ambient PM_{2.5} and reinforce the continued relevance of in vitro assays for mechanistic research in PM toxicology. Our study furthers the goal of developing reference samples of environmentally relevant particulate matter of various sizes that can be used for hypothesis testing by multiple investigators.

[46]

TÍTULO / TITLE: - Effects of respiratory motion on passively scattered proton therapy versus intensity modulated photon therapy for stage III lung cancer: are proton plans more sensitive to breathing motion?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Nov 1;87(3):576-82. doi: 10.1016/j.ijrobp.2013.07.007.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.ijrobp.2013.07.007](#)

AUTORES / AUTHORS: - Matney J; Park PC; Bluett J; Chen YP; Liu W; Court LE; Liao Z; Li H; Mohan R

INSTITUCIÓN / INSTITUTION: - Department of Radiation Physics, University of Texas MD Anderson Cancer Center, Houston, Texas; The University of Texas Graduate School of Biomedical Sciences, Houston, Texas.

RESUMEN / SUMMARY: - **PURPOSE:** To quantify and compare the effects of respiratory motion on paired passively scattered proton therapy (PSPT) and intensity modulated photon therapy (IMRT) plans; and to establish the relationship between the magnitude of tumor motion and the respiratory-induced dose difference for both modalities. **METHODS AND MATERIALS:** In a randomized clinical trial comparing PSPT and IMRT, radiation therapy plans have been designed according to common planning protocols. Four-dimensional (4D) dose was computed for PSPT and IMRT plans for a patient cohort with respiratory motion ranging from 3 to 17 mm. Image registration and dose accumulation were performed using grayscale-based deformable image registration algorithms. The dose-volume histogram (DVH) differences (4D-3D

[3D = 3-dimensional]) were compared for PSPT and IMRT. Changes in 4D-3D dose were correlated to the magnitude of tumor respiratory motion. RESULTS: The average 4D-3D dose to 95% of the internal target volume was close to zero, with 19 of 20 patients within 1% of prescribed dose for both modalities. The mean 4D-3D between the 2 modalities was not statistically significant ($P < .05$) for all dose-volume histogram indices (mean +/- SD) except the lung V5 (PSPT: +1.1% +/- 0.9%; IMRT: +0.4% +/- 1.2%) and maximum cord dose (PSPT: +1.5 +/- 2.9 Gy; IMRT: 0.0 +/- 0.2 Gy). Changes in 4D-3D dose were correlated to tumor motion for only 2 indices: dose to 95% planning target volume, and heterogeneity index. CONCLUSIONS: With our current margin formalisms, target coverage was maintained in the presence of respiratory motion up to 17 mm for both PSPT and IMRT. Only 2 of 11 4D-3D indices (lung V5 and spinal cord maximum) were statistically distinguishable between PSPT and IMRT, contrary to the notion that proton therapy will be more susceptible to respiratory motion. Because of the lack of strong correlations with 4D-3D dose differences in PSPT and IMRT, the extent of tumor motion was not an adequate predictor of potential dosimetric error caused by breathing motion.

[47]

TÍTULO / TITLE: - A Randomized Trial of Weekly Symptom Telemonitoring in Advanced Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Pain Symptom Manage. 2013 Nov 7. pii: S0885-3924(13)00481-8. doi: 10.1016/j.jpainsymman.2013.07.013.

●● Enlace al texto completo (gratis o de pago)

[1016/j.jpainsymman.2013.07.013](#)

AUTORES / AUTHORS: - Yount SE; Rothrock N; Bass M; Beaumont JL; Pach D; Lad T; Patel J; Corona M; Weiland R; Del Ciello K; Cella D

INSTITUCIÓN / INSTITUTION: - Northwestern University, Chicago, Illinois, USA.

Electronic address: s-yount@northwestern.edu.

RESUMEN / SUMMARY: - CONTEXT: Lung cancer patients experience multiple, simultaneous symptoms related to their disease and treatment that impair functioning and health-related quality of life (HRQL). Computer technology can reduce barriers to nonsystematic, infrequent symptom assessment and potentially contribute to improved patient care. OBJECTIVES: To evaluate the efficacy of technology-based symptom monitoring and reporting in reducing symptom burden in patients with advanced lung cancer. METHODS: This was a prospective, multisite, randomized controlled trial. Two hundred fifty-three patients were enrolled at three sites and randomized to monitoring and reporting (MR) or monitoring alone (MA). Patients completed questionnaires at baseline, 3, 6, 9, and 12 weeks and symptom surveys via interactive voice response weekly for 12 weeks. MR patients' clinically significant symptom scores generated an e-mail alert to the site nurse for management. The primary endpoint was overall symptom burden; secondary endpoints included HRQL, treatment satisfaction, symptom management barriers, and self-efficacy. RESULTS: This randomized controlled trial failed to demonstrate efficacy of symptom monitoring and reporting in reducing symptom burden compared with monitoring alone in lung cancer. HRQL declined over 12 weeks in both groups ($P < 0.006$ to $P < 0.025$); at week 12, treatment satisfaction was higher in MA than MR patients ($P < 0.012$, $P < 0.027$). Adherence to

weekly calls was good (82%) and patient satisfaction was high. CONCLUSION: Feasibility of using a technology-based system for systematic symptom monitoring in advanced lung cancer patients was demonstrated. Future research should focus on identifying patients most likely to benefit and other patient, provider, and health system factors likely to contribute to the system's success.

[48]

TÍTULO / TITLE: - Severe late esophagus toxicity in NSCLC patients treated with IMRT and concurrent chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Aug;108(2):337-41. doi: 10.1016/j.radonc.2013.08.017. Epub 2013 Sep 24.

●● Enlace al texto completo (gratis o de pago) [1016/j.radonc.2013.08.017](#)

AUTORES / AUTHORS: - Chen C; Uytendinck W; Sonke JJ; de Bois J; van den Heuvel M; Belderbos J

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: We reported the incidence of severe late esophagus toxicity (LET) in locally advanced NSCLC patients treated with intensity-modulated radiation therapy (IMRT) and concurrent chemotherapy. Acute esophagus toxicity (AET) and the dose to the esophagus were analyzed for their associations with severe LET. MATERIAL AND METHODS: Two hundred and thirty-one patients treated from 2008 to 2011 with hypofractionated IMRT (66Gy/24fx) and concurrent daily low dose cisplatin were included. The association between AET and severe LET (grade ≥ 3 RTOG/EORTC) was tested through Cox-proportional-hazards model. Equivalent uniform dose (EUD) to the esophagus and the volume percentage receiving more than x Gy (Vx) were applied by Lyman-Kutcher-Burman (LKB) model. RESULTS: A total of 171 patients were eligible for this study. Severe LET was observed in 6% patients. Both the maximum grade and the recovery rate of AET were significantly associated with severe LET. In the EUDn-LKB model, the fitted values and 95% confidence intervals (CIs) were $TD_{50}=76.1$ Gy (73.2-78.6), $m=0.03$ (0.02-0.06) and $n=0.03$ (0-0.08). In the Vx-LKB model, the fitted values and 95% CIs were $Tx_{50}=23.5\%$ (16.4-46.6), $m=0.44$ (0.32-0.60) and $x=76.7$ Gy (74.7-77.5). CONCLUSIONS: Severe AET, EUD ($n=0.03$) and $V_{76.7}$ to the esophagus were significantly associated with severe LET. An independent validation study is required.

[49]

TÍTULO / TITLE: - Predictive and prognostic value of early response assessment using 18FDG-PET in advanced non-small cell lung cancer patients treated with erlotinib.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Nov 21.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2356-x](#)

AUTORES / AUTHORS: - Tiseo M; Ippolito M; Scarlattei M; Spadaro P; Cosentino S; Latteri F; Ruffini L; Bartolotti M; Bortesi B; Fumarola C; Caffarra C; Cavazzoni A; Alfieri RR; Petronini PG; Bordonaro R; Bruzzi P; Ardizzoni A; Soto Parra HJ

INSTITUCIÓN / INSTITUTION: - Oncologia Medica, Azienda Ospedaliero-Universitaria di Parma, Via Gramsci 14, 43100, Parma, Italy, mtiseo@ao.pr.it.

RESUMEN / SUMMARY: - BACKGROUND: [18F]fluorodeoxyglucose (FDG)-PET is being evaluated as a tool for the early detection of response to various targeted agents in solid tumors. The aim of this study was to evaluate the predictive value of PET response after 2 days of erlotinib in unselected pretreated patients with stage IV NSCLC. PATIENTS AND METHODS: FDG-PET/CT scans were conducted at baseline and after 2 days of erlotinib, with a CT evaluation performed at baseline and after 45-60 days of therapy. PET responses were evaluated by quantitative changes on SUVmax tumor/non-tumor ratio and classified according to EORTC criteria. PET responses were compared with RECIST responses and related to progression-free (PFS) and overall (OS) survival. Erlotinib effects on glucose uptake were also studied in a panel of NSCLC cell lines. RESULTS: Fifty-three patients were enrolled. At 2 days of erlotinib, 20 (38 %) patients showed partial metabolic response (PMR), 25 (47 %) had stable metabolic disease (SMD) and 8 (15 %) had progressive metabolic disease (PMD). All patients with PMD had confirmed RECIST progression at 45-60 days. Patients with early PMR and SMD had significantly longer PFS ($p < 0.001$ and $p = 0.001$, respectively) and OS ($p = 0.001$ for both) than PMD patients. CONCLUSIONS: FDG-PET assessment after 2 days of erlotinib could be useful to identify early resistant patients and to predict survival in unselected NSCLC pretreated population.

[50]

TÍTULO / TITLE: - MET and AXL inhibitor NPS-1034 exerts efficacy against lung cancer cells resistant to EGFR kinase inhibitors due to MET or AXL activation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Oct 28.

- [Enlace al texto completo \(gratis o de pago\) 1158/0008-5472.CAN-13-](#)

[1103](#)

AUTORES / AUTHORS: - Rho JK; Choi YJ; Kim SY; Kim TW; Choi EK; Yoon SJ; Park BM; Park E; Bae JH; Choi CM; Lee JC

INSTITUCIÓN / INSTITUTION: - Oncology, Asan Medical Center.

RESUMEN / SUMMARY: - In non-small cell lung cancer (NSCLC) with EGFR mutations, acquired resistance to EGFR kinase inhibitors (EGFR-TKIs) can occur through generation of bypass signals such as MET or AXL activation. In this study, we investigated the antitumor activity of NPS-1034, a newly developed drug that targets both MET and AXL, in NSCLC cells with acquired resistance to gefitinib or erlotinib (HCC827/GR and HCC827/ER, respectively). Characterization of H820 cells and evaluation of NPS-1034 efficacy in these cells were also performed. The resistance of HCC827/GR was mediated by MET activation, whereas AXL activation led to resistance in HCC827/ER. The combination of gefitinib or erlotinib with NPS-1034 synergistically inhibited cell proliferation and induced cell death in both resistant cell lines. Accordingly, suppression of Akt was noted only in the presence of treatment with both drugs. NPS-1034 was also effective in xenograft mouse models of HCC827/GR. Although the H820 cell line was reported previously to have T790M and MET amplification, we discovered that AXL was also activated in this cell line. There were no antitumor effects of siRNA or inhibitors specific for EGFR or MET, whereas combined treatment with AXL siRNA or NPS-1034 and EGFR-TKIs controlled H820 cells,

suggesting that AXL is the main signal responsible for resistance. In addition, NPS-1034 inhibited cell proliferation as well as ROS1 activity in HCC78 cells with ROS1-rearrangement. Our results establish the efficacy of NPS-1034 in NSCLC cells rendered resistant to EGFR-TKIs due to MET or AXL activation or ROS1 rearrangement.

[51]

TÍTULO / TITLE: - Identification of a Subset of Human Non-Small Cell Lung Cancer Patients with High PI3Kbeta and Low PTEN Expression, more prevalent in SCC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 27.

- Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-1638](https://doi.org/10.1158/1078-0432.CCR-13-1638)

AUTORES / AUTHORS: - Cumberbatch M; Tang X; Beran G; Eckersley S; Wang X; Ellston RP; Dearden SP; Cosulich S; Smith PD; Behrens C; Kim ES; Su X; Fan S; Gray N; Blowers D; Wistuba II; Womack C

INSTITUCIÓN / INSTITUTION: - Molecular Pathology, AstraZeneca.

RESUMEN / SUMMARY: - PURPOSE: The phosphoinositide 3-kinase (PI3K) pathway is a major oncogenic signalling pathway and an attractive target for therapeutic intervention. Signalling through the PI3K pathway is moderated by the tumor suppressor phosphatase and tensin homolog (PTEN) which is deficient or mutated in many human cancers. Molecular characterization of the PI3K signalling network has not been well defined in lung cancer; in particular, the role of PI3Kbeta and its relation to PTEN in NSCLC remains unclear. EXPERIMENTAL DESIGN: Antibodies directed against PI3Kbeta and PTEN were validated and used to examine, by immunohistochemistry, expression in 240 NSCLC resection tissues (TMA Set 1). Preliminary observations were extended to an independent set of tissues (TMA Set 2) comprising 820 NSCLC patient samples analyzed in a separate laboratory applying the same validated antibodies and staining protocols. The staining intensities for PI3Kbeta and PTEN were explored and co-localization of these markers in individual tumour cores correlated. RESULTS: PI3Kbeta expression was elevated significantly in squamous cell carcinomas (SCC) compared with adenocarcinomas (AC). In contrast, PTEN loss was greater in SCC than AC. Detailed correlative analyses of individual patient samples revealed a significantly greater proportion of SCC in TMA Set 1 with higher PI3Kbeta and lower PTEN expression when compared with AC. These findings were reinforced following independent analyses of TMA Set 2. CONCLUSIONS: We identify for the first time a subset of NSCLC more prevalent in SCC, with elevated expression of PI3Kbeta accompanied by a reduction/loss of PTEN, for whom selective PI3Kbeta inhibitors may be predicted to achieve greater clinical benefit.

[52]

TÍTULO / TITLE: - DNA crosslinks, DNA damage and repair in peripheral blood lymphocytes of non-small cell lung cancer patients treated with platinum derivatives.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):391-6. doi: 10.3892/or.2013.2805. Epub 2013 Oct 23.

- Enlace al texto completo (gratis o de pago) [3892/or.2013.2805](#)

AUTORES / AUTHORS: - Fikrova P; Stetina R; Hrniciarik M; Hrniciarikova D; Hronek M; Zadak Z

INSTITUCIÓN / INSTITUTION: - Department of Biological and Medical sciences, Faculty of Pharmacy, Charles University in Prague, Hradec Kralove, Czech Republic.

RESUMEN / SUMMARY: - Lung cancer is the leading cause of cancer-related mortality in the world. Chemotherapy has been the mainstay of treatment for advanced non-small cell lung cancer (NSCLC) and platinum-based derivatives have been shown to improve overall survival. The aim of the present study was to investigate the DNA damage [single strand breaks (SSBs) and DNA crosslinks] and DNA repair in peripheral blood lymphocytes in patients with NSCLC treated with platinum derivatives using modified comet assay. Twenty patients in the final (4th) stage of NSCLC and 10 age-corresponding healthy controls participated in the study. Alkaline comet assay was performed according to the appropriate protocol. The DNA base excision repair (BER) activity of the controls was significantly higher compared to that of cancer patients, and the activity of DNA nucleotide excision repair (NER) was almost at the same level both in controls and patients. We observed changes in the amount of SSBs and DNA crosslinks during the course of chemotherapy. We found a significantly higher level of SSBs immediately after administration of chemotherapy. Similarly, we found the highest incidence of DNA crosslinks immediately or 1 day after chemotherapy (compared to measurement before chemotherapy). Moreover, we compared the levels of DNA repair in patients who survived chemotherapy with those in patients who died in the course of chemotherapy: the activity of BER was higher in the case of surviving patients, while the levels of NER were essentially the same. The data arising from the present study confirm the findings of other studies dealing with DNA damage and repair in cancer patients treated with chemotherapy. Moreover, our results indicated that despite the fact that cisplatin-DNA adducts are removed by the NER pathway, BER may also play a role in the clinical status of patients and their survival.

[53]

TÍTULO / TITLE: - Survival of patients with small cell lung cancer undergoing lung resection in England, 1998-2009.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Thorax. 2013 Oct 30. doi: 10.1136/thoraxjnl-2013-203884.

- Enlace al texto completo (gratis o de pago) [1136/thoraxjnl-2013-203884](#)

AUTORES / AUTHORS: - Luchtenborg M; Riaz SP; Lim E; Page R; Baldwin DR; Jakobsen E; Vedsted P; Lind M; Peake MD; Mellempgaard A; Spicer J; Lang-Lazdunski L; Moller H

INSTITUCIÓN / INSTITUTION: - Cancer Epidemiology and Population Health, King's Health Partners Cancer Centre, , London, UK.

RESUMEN / SUMMARY: - INTRODUCTION: Chemotherapy or chemoradiotherapy is the recommended treatment for small cell lung cancer (SCLC), except in stage I disease where clinical guidelines state there may be a role for surgery based on favourable outcomes in case series. Evidence supporting adjuvant chemotherapy in resected SCLC is limited but this is widely offered. METHODS: Data on 359 873 patients who were diagnosed with a first primary lung cancer in England between 1998 and 2009 were grouped according to histology (SCLC or non-SCLC (NSCLC)) and

whether they underwent a surgical resection. We explored their survival using Kaplan-Meier analysis and Cox regression, adjusting for age, sex, comorbidity and socioeconomic status. RESULTS: The survival of 465 patients with resected SCLC was lower than patients with resected NSCLC (5-year survival 31% and 45%, respectively), but much higher than patients of either group who were not resected (3%). The difference between resected SCLC and NSCLC diminished with time after surgery. Survival was superior for the subgroup of 198 'elective' SCLC cases where the diagnosis was most likely known before resection than for the subgroup of 267 'incidental' cases where the SCLC diagnosis was likely to have been made after resection. CONCLUSIONS: These data serve as a natural experiment testing the survival after surgical management of SCLC according to NSCLC principles. Patients with SCLC treated surgically for early stage disease may have survival outcomes that approach those of NSCLC, supporting the emerging clinical practice of offering surgical resection to selected patients with SCLC.

[54]

TÍTULO / TITLE: - Afatinib for the treatment of patients with EGFR-positive non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Drugs Today (Barc). 2013 Sep;49(9):523-35. doi: 10.1358/dot.2013.49.9.2016610.

●● Enlace al texto completo (gratis o de pago) [1358/dot.2013.49.9.2016610](#)

AUTORES / AUTHORS: - Bowles DW; Weickhardt A; Jimeno A

INSTITUCIÓN / INSTITUTION: - University of Colorado School of Medicine, Division of Medical Oncology, and Denver Veterans Affairs Medical Center, Denver, Colorado, USA. antonio.jimeno@ucdenver.edu.

RESUMEN / SUMMARY: - Epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) are valuable treatments for EGFR-mutated non-small cell lung cancer (NSCLC). Anti-EGFR antibodies are widely used in the treatment of head and neck squamous cell carcinomas (HNSCC) and in KRAS wild-type colorectal cancer. The first-generation, reversible EGFR inhibitors erlotinib and gefitinib in the first-line setting provide superior progression-free survival and quality of life compared to conventional chemotherapy in NSCLC harboring activating EGFR mutations. However, these therapies eventually fail and new options are needed. Afatinib is a novel irreversible inhibitor of the ErbB family members EGFR, tyrosine kinase-type cell surface receptors HER2 and HER4. It shows preclinical efficacy in NSCLC with common EGFR-activating mutations and the T790M mutation typically associated with EGFR TKI resistance. Preclinical activity is seen in other tumor types as well, including HNSCC. Clinically, afatinib has been evaluated in the broad-reaching LUX Lung trial program, with significant activity seen in the first and later-line settings. It is also under investigation in multiple other tumor types. This review will stress on afatinib's preclinical pharmacology, pharmacokinetics and clinical activity with a focus on NSCLC.

[55]

TÍTULO / TITLE: - MicroRNA 4423 is a primate-specific regulator of airway epithelial cell differentiation and lung carcinogenesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Nov 19;110(47):18946-51. doi: 10.1073/pnas.1220319110. Epub 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) [1073/pnas.1220319110](https://doi.org/10.1073/pnas.1220319110)

AUTORES / AUTHORS: - Perdomo C; Campbell JD; Gerrein J; Tellez CS; Garrison CB; Walser TC; Drizik E; Si H; Gower AC; Vick J; Anderlind C; Jackson GR; Mankus C; Schembri F; O'Hara C; Gomperts BN; Dubinett SM; Hayden P; Belinsky SA; Lenburg ME; Spira A

INSTITUCIÓN / INSTITUTION: - Division of Computational Biomedicine, Genetics and Genomics Program, and Pulmonary Center, Department of Medicine, Boston University, Boston, MA 02118.

RESUMEN / SUMMARY: - Smoking is a significant risk factor for lung cancer, the leading cause of cancer-related deaths worldwide. Although microRNAs are regulators of many airway gene-expression changes induced by smoking, their role in modulating changes associated with lung cancer in these cells remains unknown. Here, we use next-generation sequencing of small RNAs in the airway to identify microRNA 4423 (miR-4423) as a primate-specific microRNA associated with lung cancer and expressed primarily in mucociliary epithelium. The endogenous expression of miR-4423 increases as bronchial epithelial cells undergo differentiation into mucociliary epithelium in vitro, and its overexpression during this process causes an increase in the number of ciliated cells. Furthermore, expression of miR-4423 is reduced in most lung tumors and in cytologically normal epithelium of the mainstem bronchus of smokers with lung cancer. In addition, ectopic expression of miR-4423 in a subset of lung cancer cell lines reduces their anchorage-independent growth and significantly decreases the size of the tumors formed in a mouse xenograft model. Consistent with these phenotypes, overexpression of miR-4423 induces a differentiated-like pattern of airway epithelium gene expression and reverses the expression of many genes that are altered in lung cancer. Together, our results indicate that miR-4423 is a regulator of airway epithelium differentiation and that the abrogation of its function contributes to lung carcinogenesis.

[56]

TÍTULO / TITLE: - Clinician Perceptions of Care Difficulty, Quality of Life, and Symptom Reports for Lung Cancer Patients: An Analysis from the Symptom Outcomes and Practice Patterns (SOAPP) Study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov 1.

●● Enlace al texto completo (gratis o de pago)

[1097/01.JTO.0000437501.83763.5d](https://doi.org/10.1097/01.JTO.0000437501.83763.5d)

AUTORES / AUTHORS: - Hamann HA; Lee JW; Schiller JH; Horn L; Wagner LI; Chang VT; Fisch MJ

INSTITUCIÓN / INSTITUTION: - *Harold C. Simmons Cancer Center, Departments of Psychiatry and Clinical Sciences, University of Texas Southwestern Medical Center, Dallas, Texas; daggerDana Farber Cancer Institute, Boston, Massachusetts; double daggerHarold C. Simmons Cancer Center, Department of Internal Medicine, University

of Texas Southwestern Medical Center, Dallas, Texas; section signDepartment of Medical Oncology, Vanderbilt University, Nashville, Tennessee; ||Department of Medical Social Sciences, Northwestern University, Feinberg School of Medicine, Chicago, Illinois; paragraph signDepartment of Veterans Affairs, Rutgers - New Jersey Medical School, Newark, New Jersey; and #Department of General Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas.

RESUMEN / SUMMARY: - INTRODUCTION:: Despite recent therapeutic advances, lung cancer is a difficult disease to manage. This study assessed clinicians' perceptions of care difficulty, quality of life (QOL), and symptom reports for their lung cancer patients compared with their patients with breast, prostate, and colon cancer. METHODS:: This report focused on secondary analyses from the Eastern Cooperative Oncology Group Symptom Outcomes and Practice Patterns study (E2Z02); outcome measures included clinician ratings of 3106 solid tumor patients. Univariate analyses focused on patterns of disease-specific perceptions; multivariable analyses examined whether disease-specific differences persisted after covariate inclusion. RESULTS:: In univariate comparisons, clinicians rated lung cancer patients as more difficult to treat than other solid tumor patients, with poorer QOL and higher symptom reports. After covariates were adjusted, the odds of clinicians perceiving lower QOL for their lung cancer patients were 3.6 times larger than for patients with other solid tumors (odds ratio = 3.6 [95% confidence interval, 2.0-6.6]; $p < 0.0001$). In addition, the odds of clinicians perceiving weight difficulties for their lung cancer patients were 3.2 times larger (odds ratio = 3.2 [95% confidence interval, 1.7-6.0]; $p = 0.0004$). No other outcome showed significant differences between lung versus other cancers in multivariable models. CONCLUSION:: Clinicians were more pessimistic about the well-being of their lung cancer patients compared with patients with other solid tumors. Differences remained for clinician perceptions of patient QOL and weight difficulty, even after controlling for such variables as stage, performance status, and patient-reported outcomes. These continuing disparities suggest possible perception bias. More research is needed to confirm this disparity and explore the underpinnings.

[57]

TÍTULO / TITLE: - Neuropilin-2 Is Upregulated in Lung Cancer Cells during TGF-beta1-Induced Epithelial-Mesenchymal Transition.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Dec 1;73(23):7111-21. doi: 10.1158/0008-5472.CAN-13-1755. Epub 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [1158/0008-5472.CAN-13-](#)

[1755](#)

AUTORES / AUTHORS: - Nasarre P; Gemmill RM; Potiron VA; Roche J; Lu X; Baron AE; Korch C; Garrett-Mayer E; Lagana A; Howe PH; Drabkin HA

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Division of Hematology-Oncology, Department of Public Health Sciences, Department of Biochemistry, The Hollings Cancer Center and Medical University of South Carolina, Charleston, South Carolina; Department of Biostatistics and informatics; Division of Medical Oncology, University of Colorado Denver, Anschutz Medical Campus, Aurora, Colorado; and Department of Molecular Virology, Immunology, and Medical Genetics, School of Medicine, The Ohio State University, Columbus, Ohio.

RESUMEN / SUMMARY: - The epithelial-mesenchymal transition (EMT) and its reversal, mesenchymal-epithelial transition (MET), are fundamental processes involved in tumor cell invasion and metastasis. SEMA3F is a secreted semaphorin and tumor suppressor downregulated by TGF-beta1 and ZEB1-induced EMT. Here, we report that neuropilin (NRP)-2, the high-affinity receptor for SEMA3F and a coreceptor for certain growth factors, is upregulated during TGF-beta1-driven EMT in lung cancer cells. Mechanistically, NRP2 upregulation was TbetaRI dependent and SMAD independent, occurring mainly at a posttranscriptional level involving increased association of mRNA with polyribosomes. Extracellular signal-regulated kinase (ERK) and AKT inhibition blocked NRP2 upregulation, whereas RNA interference-mediated attenuation of ZEB1 reduced steady-state NRP2 levels. In addition, NRP2 attenuation inhibited TGF-beta1-driven morphologic transformation, migration/invasion, ERK activation, growth suppression, and changes in gene expression. In a mouse xenograft model of lung cancer, NRP2 attenuation also inhibited locally invasive features of the tumor and reversed TGF-beta1-mediated growth inhibition. In support of these results, human lung cancer specimens with the highest NRP2 expression were predominantly E-cadherin negative. Furthermore, the presence of NRP2 staining strengthened the association of E-cadherin loss with high-grade tumors. Together, our results demonstrate that NRP2 contributes significantly to TGF-beta1-induced EMT in lung cancer. Cancer Res; 73(23); 7111-21. ©2013 AACR.

[58]

TÍTULO / TITLE: - Improved survival associated with neoadjuvant chemoradiation in patients with clinical stage IIIA (N2) non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):e100. doi: 10.1097/JTO.0b013e3182a47552.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a47552](#)

AUTORES / AUTHORS: - Poullis M

INSTITUCIÓN / INSTITUTION: - Consultant Cardiothoracic Surgeon Liverpool Heart and Chest Hospital Liverpool, England.

[59]

TÍTULO / TITLE: - A primate-specific microRNA enters the lung cancer landscape.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Proc Natl Acad Sci U S A. 2013 Nov 19;110(47):18748-9. doi: 10.1073/pnas.1318740110. Epub 2013 Nov 4.

●● Enlace al texto completo (gratis o de pago) [1073/pnas.1318740110](#)

AUTORES / AUTHORS: - Robles AI; Harris CC

INSTITUCIÓN / INSTITUTION: - Laboratory of Human Carcinogenesis, National Cancer Institute, Center for Cancer Research, National Institutes of Health, Bethesda, MD 20892.

[60]

TÍTULO / TITLE: - Signaling Control by Epidermal Growth Factor Receptor and MET: Rationale for Cotargeting Strategies in Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 10;31(32):4148-50. doi: 10.1200/JCO.2013.50.8234. Epub 2013 Oct 7.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2013.50.8234](#)

AUTORES / AUTHORS: - Haura EB; Smith MA

INSTITUCIÓN / INSTITUTION: - H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.

[61]

TÍTULO / TITLE: - Pro-Surfactant Protein B as a Biomarker for Lung Cancer Prediction.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2013.50.6105](#)

AUTORES / AUTHORS: - Sin DD; Tammemagi CM; Lam S; Barnett MJ; Duan X; Tam A; Auman H; Feng Z; Goodman GE; Hanash S; Taguchi A

INSTITUCIÓN / INSTITUTION: - Don D. Sin, Stephen Lam, and Anthony Tam, University of British Columbia; Don D. Sin and Anthony Tam, Institute of Heart and Lung Health, James Hogg Research Center, St. Paul's Hospital; Stephen Lam and Xiaobo Duan, British Columbia Cancer Agency, Vancouver, British Columbia; C. Martin Tammemagi, Brock University, St. Catharines, Ontario, Canada; Matt J. Barnett, Ziding Feng, and Gary E. Goodman, Fred Hutchinson Cancer Research Center, Seattle, WA; Heidi Auman, Canary Foundation, Palo Alto, CA; and Ziding Feng, Samir Hanash, and Ayumu Taguchi, University of Texas MD Anderson Cancer Center, Houston, TX.

RESUMEN / SUMMARY: - PURPOSE: Preliminary studies have identified pro-surfactant protein B (pro-SFTPb) to be a promising blood biomarker for non-small-cell lung cancer. We conducted a study to determine the independent predictive potential of pro-SFTPb in identifying individuals who are subsequently diagnosed with lung cancer. PATIENTS AND METHODS: Pro-SFTPb levels were measured in 2,485 individuals, who enrolled onto the Pan-Canadian Early Detection of Lung Cancer Study by using plasma sample collected at the baseline visit. Multivariable logistic regression models were used to evaluate the predictive ability of pro-SFTPb in addition to known lung cancer risk factors. Calibration and discrimination were evaluated, the latter by an area under the receiver operating characteristic curve (AUC). External validation was performed with samples collected in the Carotene and Retinol Efficacy Trial (CARET) participants using a case-control study design. RESULTS: Adjusted for age, sex, body mass index, personal history of cancer, family history of lung cancer, forced expiratory volume in one second percent predicted, average number of cigarettes smoked per day, and smoking duration, pro-SFTPb (log transformed) had an odds ratio of 2.220 (95% CI, 1.727 to 2.853; P < .001). The AUCs of the full model with and without pro-SFTPb were 0.741 (95% CI, 0.696 to 0.783) and 0.669 (95% CI, 0.620 to 0.717; difference in AUC P < .001). In the CARET Study, the use of pro-SFTPb yielded an AUC of 0.683 (95% CI, 0.604 to 0.761). CONCLUSION: Pro-SFTPb in plasma is an independent predictor of lung cancer and may be a valuable addition to existing lung cancer risk prediction models.

[62]

TÍTULO / TITLE: - Dose-limiting toxicity after hypofractionated dose-escalated radiotherapy in non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Dec 1;31(34):4343-8. doi: 10.1200/JCO.2013.51.5353. Epub 2013 Oct 21.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2013.51.5353](#)

AUTORES / AUTHORS: - Cannon DM; Mehta MP; Adkison JB; Khuntia D; Traynor AM; Tome WA; Chappell RJ; Tolakanahalli R; Mohindra P; Bentzen SM; Cannon GM

INSTITUCIÓN / INSTITUTION: - Donald M. Cannon, Pranshu Mohindra, Soren M. Bentzen, Anne M. Traynor, Richard J. Chappell, University of Wisconsin School of Medicine and Public Health, Madison, WI; Minesh P. Mehta, University of Maryland, Baltimore, MD; Jarrod B. Adkison, Southeast Alabama Medical Center, Dothan, AL; Deepak Khuntia, Varian Medical Systems, Palo Alto, CA; Wolfgang A. Tome, Albert Einstein College of Medicine, Bronx, NY; George M. Cannon, Intermountain Medical Center, Salt Lake City, UT; Ranjini Tolakanahalli, Juravinski Cancer Center, Hamilton, Canada.

RESUMEN / SUMMARY: - PURPOSE: Local failure rates after radiation therapy (RT) for locally advanced non-small-cell lung cancer (NSCLC) remain high. Consequently, RT dose intensification strategies continue to be explored, including hypofractionation, which allows for RT acceleration that could potentially improve outcomes. The maximum-tolerated dose (MTD) with dose-escalated hypofractionation has not been adequately defined. PATIENTS AND METHODS: Seventy-nine patients with NSCLC were enrolled on a prospective single-institution phase I trial of dose-escalated hypofractionated RT without concurrent chemotherapy. Escalation of dose per fraction was performed according to patients' stratified risk for radiation pneumonitis with total RT doses ranging from 57 to 85.5 Gy in 25 daily fractions over 5 weeks using intensity-modulated radiotherapy. The MTD was defined as the maximum dose with $\leq 20\%$ risk of severe toxicity. RESULTS: No grade 3 pneumonitis was observed and an MTD for acute toxicity was not identified during patient accrual. However, with a longer follow-up period, grade 4 to 5 toxicity occurred in six patients and was correlated with total dose ($P = .004$). An MTD was identified at 63.25 Gy in 25 fractions. Late grade 4 to 5 toxicities were attributable to damage to central and perihilar structures and correlated with dose to the proximal bronchial tree. CONCLUSION: Although this dose-escalation model limited the rates of clinically significant pneumonitis, dose-limiting toxicity occurred and was dominated by late radiation toxicity involving central and perihilar structures. The identified dose-response for damage to the proximal bronchial tree warrants caution in future dose-intensification protocols, especially when using hypofractionation.

[63]

TÍTULO / TITLE: - Activation of proteinase-activated receptor 2 prevents apoptosis of lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Invest. 2013 Nov;31(9):578-81. doi: 10.3109/07357907.2013.845674. Epub 2013 Oct 18.

- Enlace al texto completo (gratis o de pago) [3109/07357907.2013.845674](https://doi.org/10.1186/1745-7256-3-10)

AUTORES / AUTHORS: - Huang SH; Li Y; Chen HG; Rong J; Ye S

INSTITUCIÓN / INSTITUTION: - Departments of 1 Cardiothoracic Surgery, 2 Anesthesiology, and 3 Medical Oncology, The Third Affiliated Hospital, Sun Yat-Sen University, Guangzhou, China.

RESUMEN / SUMMARY: - The therapeutics of lung cancer (LC) is unsatisfactory. The pathogenesis of LC remains unclear. Protease-activated receptors (PAR) are involved in the immunoregulation. The present study aims to investigate the activation of PAR2 in regulation of the expression of EGFR and apoptosis of LC cells. The results showed that exposure to tryptase increased EGFR expression in A549 cells and suppressed the cell apoptosis. Tryptase also decreased the expression of Bax and increased Bcl-xL levels in A549 cells. We conclude that activation of PAR2 by tryptase can decrease the ratio of Bax/Bcl-xL and reduce the LC cell line, A549 cells, and apoptosis.

[64]

TÍTULO / TITLE: - A randomized, double-blind, placebo-controlled phase 2 study of tigatuzumab (CS-1008) in combination with carboplatin/paclitaxel in patients with chemotherapy-naïve metastatic/unresectable non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):441-8. doi: 10.1016/j.lungcan.2013.09.014. Epub 2013 Oct 1.

- Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.014](https://doi.org/10.1016/j.lungcan.2013.09.014)

AUTORES / AUTHORS: - Reck M; Krzakowski M; Chmielowska E; Sebastian M; Hadler D; Fox T; Wang Q; Greenberg J; Beckman RA; von Pawel J

INSTITUCIÓN / INSTITUTION: - LungClinic Grosshansdorf, Member of the German Centre for Lung Research (DZL), Grosshansdorf, Germany. Electronic address: dr.martin.reck@web.de.

RESUMEN / SUMMARY: - INTRODUCTION: Tigatuzumab, a humanized monoclonal DR5 agonist antibody induces apoptosis in human cancer cell lines. The objective of this study was to investigate the antitumor effects of tigatuzumab combined with carboplatin/paclitaxel in chemotherapy-naïve patients with metastatic/unresectable non-small cell lung cancer (NSCLC). METHODS: Patients with histologically or cytologically confirmed NSCLC stage IIIB/IV disease by RECIST (version 1.0) and ECOG-PS 0-1 were enrolled at 15 European sites. Patients received tigatuzumab or placebo intravenously with carboplatin/paclitaxel every 3 weeks (1 cycle) for up to 6 cycles. The primary end point was progression-free survival (PFS). Secondary end points were overall survival (OS), objective response rate and safety. RESULTS: 97 patients were analyzed for efficacy (49 tigatuzumab; 48 placebo). Median PFS (95% CI) was 5.4 months (3.3, 6.6) for tigatuzumab compared with 4.3 months (4.1, 5.8) for placebo. Median OS (95% CI) was 8.4 months (6.9, 16.3) for tigatuzumab versus 9.0 months (7.6, 14.5) for placebo. 12 patients (24.5%) in the tigatuzumab arm and 11 patients (22.9%) in the placebo arm had partial response. No patient had complete response. In a prospectively-defined Fc gamma receptor genotype subset (n=25), there was a non-significant trend toward increased PFS with tigatuzumab versus placebo (HR=0.47; 95% CI: 0.16, 1.35) but no difference in OS. Tigatuzumab was well tolerated. However, grade 3/4 neutropenia was reported in 10 patients (20.4%) receiving tigatuzumab compared with 4 patients (8.3%) receiving placebo. CONCLUSIONS:

Tigatuzumab was well tolerated but did not improve efficacy of carboplatin/paclitaxel in systemic therapy-naive, unselected advanced NSCLC patients. Clinical trials identifier: NCT00991796.

[65]

TÍTULO / TITLE: - Increased Lung Cancer Risk Among Patients with Pneumococcal Pneumonia: A Nationwide Population-Based Cohort Study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Oct 23.

●● Enlace al texto completo (gratis o de pago) [1007/s00408-013-9523-z](#)

AUTORES / AUTHORS: - Lin TY; Huang WY; Lin JC; Lin CL; Sung FC; Kao CH; Yeh JJ

INSTITUCIÓN / INSTITUTION: - Division of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan.

RESUMEN / SUMMARY: - BACKGROUND: The possible effects of pneumonia on subsequent lung cancer have been reported, but no relevant publications have focused on the association between pneumococcal pneumonia and lung cancer. The purpose of this study was to perform a nationwide population-based cohort study to investigate the risk of lung cancer after pneumococcus infection. METHODS: This nationwide population-based cohort study was based on data obtained from the Taiwan National Health Insurance Database. In total, 22,034 pneumococcal pneumonia patients and 88,136 controls, matched for age and sex, were recruited for the study from 1997 to 2010. RESULTS: The incidence rate of lung cancer (28.2 per 1,000 person-years) was significantly higher in pneumococcal pneumonia patients than in controls (8.7 per 1,000 person-years; incidence rate ratio, 3.25; 95 % confidence interval, 3.09-3.42; $p < 0.001$). Cox proportional hazards regression analysis showed a hazard ratio of 4.24 (95 % confidence interval, 3.96-4.55) for the pneumococcal pneumonia cohort after adjustment for age, gender, and comorbidities. CONCLUSIONS: Pneumococcal pneumonia is associated with an increased risk of lung cancer. Thus, physicians should remain aware of this association when assessing patients with pneumococcal pneumonia.

[66]

TÍTULO / TITLE: - A prognostic DNA methylation signature for stage I non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 10;31(32):4140-7. doi: 10.1200/JCO.2012.48.5516. Epub 2013 Sep 30.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2012.48.5516](#)

AUTORES / AUTHORS: - Sandoval J; Mendez-Gonzalez J; Nadal E; Chen G; Carmona FJ; Sayols S; Moran S; Heyn H; Vizoso M; Gomez A; Sanchez-Cespedes M; Assenov Y; Muller F; Bock C; Taron M; Mora J; Muscarella LA; Liloglou T; Davies M; Pollan M; Pajares MJ; Torre W; Montuenga LM; Brambilla E; Field JK; Roz L; Lo Iacono M; Scagliotti GV; Rosell R; Beer DG; Esteller M

INSTITUCIÓN / INSTITUTION: - Juan Sandoval, Jesus Mendez-Gonzalez, F. Javier Carmona, Sergi Sayols, Sebastian Moran, Holger Heyn, Miguel Vizoso, Antonio

Gomez, Montse Sanchez-Cespedes, and Manel Esteller, Bellvitge Biomedical Research Institute; Josefina Mora, Hospital de la Santa Creu i Sant Pau; Manel Esteller, University of Barcelona and Institutio Catalana de Recerca i Estudis Avancats, Barcelona; Miquel Taron and Rafael Rosell, Catalan Institute of Oncology, Badalona, Catalonia; Marina Pollan, Instituto de Salud Carlos III, Madrid; Maria J. Pajares and Luis M. Montuenga, University of Navarra; Wenceslao Torre, Clinica University de Navarra, Pamplona, España; Ernest Nadal, Guoan Chen, and David G. Beer, University of Michigan Medical School, Ann Arbor, MI; Yassen Assenov and Fabian Muller, Max Planck Institute, Saarbrucken, Germany; Christoph Bock, Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria; Lucia A. Muscarella, Istituto Di Ricovero e Cura a Carattere Scientifico (IRCCS) Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy; Triantafillos Liloglou, Michael Davies, and John K. Field, The University of Liverpool Cancer Research Centre, Liverpool, United Kingdom; Elisabeth Brambilla, Centre Hospitalier Universitaire A Michallon, Grenoble, France; Luca Roz, IRCCS Foundation National Cancer Institute, Milan; Marco Lo Iacono and Giorgio V. Scagliotti, University of Torino, Orbassano (Torino), Italy.

RESUMEN / SUMMARY: - PURPOSE: Non-small-cell lung cancer (NSCLC) is a tumor in which only small improvements in clinical outcome have been achieved. The issue is critical for stage I patients for whom there are no available biomarkers that indicate which high-risk patients should receive adjuvant chemotherapy. We aimed to find DNA methylation markers that could be helpful in this regard. PATIENTS AND METHODS: A DNA methylation microarray that analyzes 450,000 CpG sites was used to study tumoral DNA obtained from 444 patients with NSCLC that included 237 stage I tumors. The prognostic DNA methylation markers were validated by a single-methylation pyrosequencing assay in an independent cohort of 143 patients with stage I NSCLC. RESULTS: Unsupervised clustering of the 10,000 most variable DNA methylation sites in the discovery cohort identified patients with high-risk stage I NSCLC who had shorter relapse-free survival (RFS; hazard ratio [HR], 2.35; 95% CI, 1.29 to 4.28; P = .004). The study in the validation cohort of the significant methylated sites from the discovery cohort found that hypermethylation of five genes was significantly associated with shorter RFS in stage I NSCLC: HIST1H4F, PCDHGB6, NPBWR1, ALX1, and HOXA9. A signature based on the number of hypermethylated events distinguished patients with high- and low-risk stage I NSCLC (HR, 3.24; 95% CI, 1.61 to 6.54; P = .001). CONCLUSION: The DNA methylation signature of NSCLC affects the outcome of stage I patients, and it can be practically determined by user-friendly polymerase chain reaction assays. The analysis of the best DNA methylation biomarkers improved prognostic accuracy beyond standard staging.

[67]

TÍTULO / TITLE: - The cribriform pattern identifies a subset of acinar predominant tumors with poor prognosis in patients with stage I lung adenocarcinoma: a conceptual proposal to classify cribriform predominant tumors as a distinct histologic subtype.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mod Pathol. 2013 Nov 1. doi: 10.1038/modpathol.2013.188.

●● [Enlace al texto completo \(gratis o de pago\) 1038/modpathol.2013.188](#)

AUTORES / AUTHORS: - Kadota K; Yeh YC; Sima CS; Rusch VW; Moreira AL; Adusumilli PS; Travis WD

INSTITUCIÓN / INSTITUTION: - 1] Division of Thoracic Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA [2] Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA [3] Department of Diagnostic Pathology, Faculty of Medicine, Kagawa University, Kagawa, Japan.

RESUMEN / SUMMARY: - The 2011 International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS)/European Respiratory Society (ERS) lung adenocarcinoma classification emphasizes the prognostic significance of histologic subtypes. However, one limitation of this classification is that the highest percentage of patients (approximately 40%) is classified as acinar predominant tumors, and these patients display a spectrum of favorable and unfavorable clinical behaviors. We investigated whether the cribriform pattern can further stratify prognosis by histologic subtype. Tumor slides from 1038 patients with stage I lung adenocarcinoma (1995-2009) were reviewed. Tumors were classified according to the IASLC/ATS/ERS classification. The percentage of cribriform pattern was recorded, and the cribriform predominant subtype was considered as a subtype for analysis. The log-rank test was used to analyze the association between histologic variables and recurrence-free probability. The 5-year recurrence-free probability for patients with cribriform predominant tumors (n=46) was 70%. The recurrence-free probability for patients with cribriform predominant tumors was significantly lower than that for patients with acinar (5-year recurrence-free probability, 87%; P=0.002) or papillary predominant tumors (83%; P=0.020) but was comparable to that for patients with micropapillary (P=0.34) or solid predominant tumors (P=0.56). The recurrence-free probability for patients with $\geq 10\%$ cribriform pattern tumors (n=214) was significantly lower (5-year recurrence-free probability, 73%) than that for patients with $< 10\%$ cribriform pattern tumors (n=824; 84%; P<0.001). In multivariate analysis, patients with acinar predominant tumors with $\geq 10\%$ cribriform pattern remained at significantly increased risk of recurrence compared with those with $< 10\%$ cribriform pattern (P=0.042). Cribriform predominant tumors should be considered a distinct subtype with a high risk of recurrence, and presence ($\geq 10\%$) of the cribriform pattern is an independent predictor of recurrence, identifying a poor prognostic subset of acinar predominant tumors. Our findings highlight the important prognostic value of comprehensive histologic subtyping and recording the percentage of each histologic pattern, according to the IASLC/ATS/ERS classification with the addition of the cribriform subtype. Modern Pathology advance online publication, 1 November 2013; doi:10.1038/modpathol.2013.188.

[68]

TÍTULO / TITLE: - Abnormal expression of FLOT1 correlates with tumor progression and poor survival in patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1434-3](#)

AUTORES / AUTHORS: - Li H; Wang RM; Liu SG; Zhang JP; Luo JY; Zhang BJ; Zhang XG

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Shandong Cancer Hospital and Institute, No. 440, Jiyan Rd., Jinan, 250117, China, lihuidoc112@126.com.

RESUMEN / SUMMARY: - Recent studies have revealed that flotillin-1 (FLOT1) plays important roles in cancer progression. However, the role of FLOT1 in development and progression of non-small cell lung cancer (NSCLC) remains largely unknown. The objective of the current study was to investigate the expression pattern and clinicopathological significance of FLOT1 in patients with NSCLC. Real-time quantitative polymerase chain reaction was applied to examine FLOT1 mRNA expression in 52 pairs of NSCLC tissues and adjacent noncancerous tissues. Immunohistochemistry was performed to examine FLOT1 protein expression in paraffin-embedded tissues from 106 NSCLC patients. Statistical analyses were applied to evaluate the diagnostic value and associations of FLOT1 expression with clinicopathological characteristics. FLOT1 mRNA expression was evidently upregulated in NSCLC tissues compared with that in the adjacent noncancerous tissues. In the 106 cases of tested NSCLC samples, FLOT1 protein level was positively correlated with tumor size, tumor stage, and lymph node metastasis. Patients with higher FLOT1 expression had shorter overall survival time, whereas those with lower FLOT1 expression had longer survival time. Taken together, our findings indicate that FLOT1 may play an important role in NSCLC tumorigenesis. Further elucidation of the molecular mechanisms underlying the role of FLOT1 is warranted.

[69]

TÍTULO / TITLE: - Local treatment of oligometastatic recurrence in patients with resected non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):431-5. doi: 10.1016/j.lungcan.2013.08.006. Epub 2013 Sep 19.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.lungcan.2013.08.006](#)

AUTORES / AUTHORS: - Yano T; Okamoto T; Haro A; Fukuyama S; Yoshida T; Kohno M; Maehara Y

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, National Hospital Organization Beppu Medical Center, Japan. Electronic address: tokujiro@beppu.hosp.go.jp.

RESUMEN / SUMMARY: - **OBJECTIVES:** We previously reported a retrospective study indicating the prognostic impact of the local treatment of oligometastatic recurrence after a complete resection for non-small cell lung cancer (NSCLC). In the present study, we prospectively observed postoperative oligometastatic patients and investigated the effects of local treatment on progression-free survival (PFS). **METHODS:** Using a prospectively maintained database of patients with completely resected NSCLC treated between October 2007 and December 2011, we identified 52 consecutive patients with postoperative recurrence, excluding second primary lung cancer. Of these patients, 31 suffering from distant metastases alone without primary site recurrence were included in this study. According to the definition of 'oligometastases' as a limited number of distant metastases ranging from one to three, 17 patients had oligometastatic disease. Of those 17 patients, four patients with only brain metastasis were excluded from the analysis. **RESULTS:** The oligometastatic sites

included the lungs in five patients, bone in four patients, the lungs and brain in two patients, the adrenal glands in one patient and soft tissue in one patient. Eleven of the 13 patients first received local treatment. Three patients (lung, adrenal gland, soft tissue) underwent surgical resection, and the remaining eight patients received radiotherapy. The median PFS was 20 months in the oligometastatic patients who received local treatment. There were five patients with a PFS of longer than two years. The metastatic sites in these patients varied, and one patient had three lesions. On the other hand, the two remaining patients first received a systemic chemotherapy of their own selection. The PFS of these two patients was five and 15 months, respectively. CONCLUSION: Local therapy is a choice for first-line treatment in patients with postoperative oligometastatic recurrence.

[70]

TÍTULO / TITLE: - Improving care for patients with lung cancer in the UK.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Thorax. 2013 Dec;68(12):1181-5. doi: 10.1136/thoraxjnl-2013-204588.

●● Enlace al texto completo (gratis o de pago) [1136/thoraxjnl-2013-204588](#)

AUTORES / AUTHORS: - Sethi T; Lim E; Peake M; Field J; White J; Nicolson M; Faivre-Finn C; Cane P; Reynolds J; Moller H; Pinnock H

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine and Allergy, King's Health Partners, , London, UK.

[71]

TÍTULO / TITLE: - Phase I dose-escalation study of oral vinflunine in combination with erlotinib in pre-treated and unselected EGFR patients with locally advanced or metastatic non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Nov 13.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2342-3](#)

AUTORES / AUTHORS: - Krzakowski M; Bennouna J; Dansin E; Kowalski D; Hiret S; Penel N; Favrel S; Tourani JM

INSTITUCIÓN / INSTITUTION: - Institute of Oncology, Warsaw, Poland, maciekk@coi.waw.pl.

RESUMEN / SUMMARY: - BACKGROUND: Erlotinib, the epidermal growth factor receptor tyrosine kinase inhibitor, and the intra-venous vinflunine vinca alkaloid microtubule inhibitor have been shown to be effective in the setting of non-small-cell lung cancer (NSCLC) palliative patients with acceptable toxicities. This phase I study was conducted to determine the maximal tolerated dose (MTD) and the safety of an all-oral combination. A potential pharmacokinetic drug-drug interaction was also investigated. PATIENTS AND METHODS: Patients with unresectable stage IIIB or stage IV NSCLC who failed one or two previous chemotherapy regimens were treated with flat doses of oral vinflunine from day 1 to day 5 and from day 8 to day 12 every 3 weeks and erlotinib daily on a continuous basis. The dose levels of vinflunine/erlotinib were 95/100, 115/100, 115/150 and 135/100 mg. RESULTS: Thirty patients were enrolled. The recommended dose was 115/150 mg and the MTD 135/100 mg. Dose-

limiting toxicities included grade 3 febrile neutropenia (1 patient) and related death (1 patient). Non-haematologic grade $\frac{3}{4}$ toxicities included fatigue, condition aggravated, hypokalaemia, tumour pain, acneiform dermatitis, diarrhoea, hyperbilirubinaemia and pulmonary haemorrhage, in one patient each. Of 25 patients evaluable for tumour response, 2 patients had partial response and 20 patients had stable disease. CONCLUSION: The recommended doses for oral vinflunine and erlotinib combination were, respectively, 115 mg/day from day 1 to day 5 and from day 8 to day 12 every 3 weeks and 150 mg/day. There was no mutual impact on pharmacokinetics. The combination was safe but evaluation in phase II is needed to further refine the activity and toxicity that can be expected with prolonged administration of this dose schedule.

[72]

TÍTULO / TITLE: - Clinical implementation of intrafraction cone beam computed tomography imaging during lung tumor stereotactic ablative radiation therapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Dec 1;87(5):917-23. doi: 10.1016/j.ijrobp.2013.08.015. Epub 2013 Oct 8.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijrobp.2013.08.015](#)

AUTORES / AUTHORS: - Li R; Han B; Meng B; Maxim PG; Xing L; Koong AC; Diehn M; Loo BW Jr

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Stanford University School of Medicine, Stanford, California.

RESUMEN / SUMMARY: - PURPOSE: To develop and clinically evaluate a volumetric imaging technique for assessing intrafraction geometric and dosimetric accuracy of stereotactic ablative radiation therapy (SABR). METHODS AND MATERIALS: Twenty patients received SABR for lung tumors using volumetric modulated arc therapy (VMAT). At the beginning of each fraction, pretreatment cone beam computed tomography (CBCT) was used to align the soft-tissue tumor position with that in the planning CT. Concurrent with dose delivery, we acquired fluoroscopic radiograph projections during VMAT using the Varian on-board imaging system. Those kilovolt projections acquired during millivolt beam-on were automatically extracted, and intrafraction CBCT images were reconstructed using the filtered backprojection technique. We determined the time-averaged target shift during VMAT by calculating the center of mass of the tumor target in the intrafraction CBCT relative to the planning CT. To estimate the dosimetric impact of the target shift during treatment, we recalculated the dose to the GTV after shifting the entire patient anatomy according to the time-averaged target shift determined earlier. RESULTS: The mean target shift from intrafraction CBCT to planning CT was 1.6, 1.0, and 1.5 mm; the 95th percentile shift was 5.2, 3.1, 3.6 mm; and the maximum shift was 5.7, 3.6, and 4.9 mm along the anterior-posterior, left-right, and superior-inferior directions. Thus, the time-averaged intrafraction gross tumor volume (GTV) position was always within the planning target volume. We observed some degree of target blurring in the intrafraction CBCT, indicating imperfect breath-hold reproducibility or residual motion of the GTV during treatment. By our estimated dose recalculation, the GTV was consistently covered by the prescription dose (PD), that is, V100% above 0.97 for all patients, and minimum dose to GTV >100% PD for 18 patients and >95% PD for all patients. CONCLUSIONS:

Intrafraction CBCT during VMAT can provide geometric and dosimetric verification of SABR valuable for quality assurance and potentially for treatment adaptation.

[73]

TÍTULO / TITLE: - Retrospective cohort study of bronchial doses and radiation-induced atelectasis after stereotactic body radiation therapy of lung tumors located close to the bronchial tree.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Nov 1;87(3):590-5. doi: 10.1016/j.ijrobp.2013.06.2055.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijrobp.2013.06.2055](#)

AUTORES / AUTHORS: - Karlsson K; Nyman J; Baumann P; Wersall P; Drugge N; Gagliardi G; Johansson KA; Persson JO; Rutkowska E; Tullgren O; Lax I

INSTITUCIÓN / INSTITUTION: - Department of Medical Physics, Karolinska University Hospital, Stockholm, Sweden; Department of Oncology-Pathology, Karolinska Institute, Stockholm, Sweden. Electronic address: kristin.karlsson@karolinska.se.

RESUMEN / SUMMARY: - PURPOSE: To evaluate the dose-response relationship between radiation-induced atelectasis after stereotactic body radiation therapy (SBRT) and bronchial dose. METHODS AND MATERIALS: Seventy-four patients treated with SBRT for tumors close to main, lobar, or segmental bronchi were selected. The association between incidence of atelectasis and bronchial dose parameters (maximum point-dose and minimum dose to the high-dose bronchial volume [ranging from 0.1 cm³ up to 2.0 cm³]) was statistically evaluated with survival analysis models. RESULTS: Prescribed doses varied between 4 and 20 Gy per fraction in 2-5 fractions. Eighteen patients (24.3%) developed atelectasis considered to be radiation-induced. Statistical analysis showed a significant correlation between the incidence of radiation-induced atelectasis and minimum dose to the high-dose bronchial volumes, of which 0.1 cm³ (D(0.1cm³)) was used for further analysis. The median value of D(0.1cm³) (alpha/beta = 3 Gy) was EQD(2,LQ) = 147 Gy³ (range, 20-293 Gy³). For patients who developed atelectasis the median value was EQD(2,LQ) = 210 Gy³, and for patients who did not develop atelectasis, EQD(2,LQ) = 105 Gy³. Median time from treatment to development of atelectasis was 8.0 months (range, 1.1-30.1 months). CONCLUSION: In this retrospective study a significant dose-response relationship between the incidence of atelectasis and the dose to the high-dose volume of the bronchi is shown.

[74]

TÍTULO / TITLE: - First-line gefitinib in Caucasian EGFR mutation-positive NSCLC patients: a phase-IV, open-label, single-arm study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 21. doi: 10.1038/bjc.2013.721.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.721](#)

AUTORES / AUTHORS: - Douillard JY; Ostoros G; Cobo M; Ciuleanu T; McCormack R; Webster A; Milenkova T

INSTITUCIÓN / INSTITUTION: - Institut de Cancerologie de l'Ouest, Centre Rene Gauducheau, Bd J. Monod, 44805 St-Herblain, Nantes, France.

RESUMEN / SUMMARY: - Background:Phase-IV, open-label, single-arm study (NCT01203917) to assess efficacy and safety/tolerability of first-line gefitinib in Caucasian patients with stage IIIA/B/IV, epidermal growth factor receptor (EGFR) mutation-positive non-small-cell lung cancer (NSCLC).Methods:Treatment: gefitinib 250 mg day-1 until progression. Primary endpoint: objective response rate (ORR). Secondary endpoints: disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and safety/tolerability. Pre-planned exploratory objective: EGFR mutation analysis in matched tumour and plasma samples.Results:Of 1060 screened patients with NSCLC (859 known mutation status; 118 positive, mutation frequency 14%), 106 with EGFR sensitising mutations were enrolled (female 70.8%; adenocarcinoma 97.2%; never-smoker 64.2%). At data cutoff: ORR 69.8% (95% confidence interval (CI) 60.5-77.7), DCR 90.6% (95% CI 83.5-94.8), median PFS 9.7 months (95% CI 8.5-11.0), median OS 19.2 months (95% CI 17.0-NC; 27% maturity). Most common adverse events (AEs; any grade): rash (44.9%), diarrhoea (30.8%); CTC (Common Toxicity Criteria) grade \geq 3 AEs: 15%; SAEs: 19%. Baseline plasma 1 samples were available in 803 patients (784 known mutation status; 82 positive; mutation frequency 10%). Plasma 1 EGFR mutation test sensitivity: 65.7% (95% CI 55.8-74.7).Conclusion:First-line gefitinib was effective and well tolerated in Caucasian patients with EGFR mutation-positive NSCLC. Plasma samples could be considered for mutation analysis if tumour tissue is unavailable.British Journal of Cancer advance online publication, 21 November 2013; doi:10.1038/bjc.2013.721 www.bjcancer.com.

[75]

TÍTULO / TITLE: - The correlation between cell-free DNA and tumour burden was estimated by PET/CT in patients with advanced NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 14. doi: 10.1038/bjc.2013.705.

●● Enlace al texto completo (gratis o de pago) 1038/bjc.2013.705

AUTORES / AUTHORS: - Nygaard AD; Holdgaard PC; Spindler KL; Pallisgaard N; Jakobsen A

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Vejle Hospital, Kappeltoft 25, 7100 Vejle, Denmark.

RESUMEN / SUMMARY: - Background:Cell-free DNA (cfDNA) circulating in the blood holds a possible prognostic value in malignant diseases. Under malignant conditions, the level of cfDNA increases but the biological mechanism remains to be fully understood. We aimed to examine the correlation between cfDNA and total tumour burden defined by positron emission tomography (PET) parameters.Methods:Patients with advanced non-small cell lung cancer (NSCLC) were enrolled into a prospective biomarker trial. Before treatment, plasma was extracted and the level of cfDNA was determined by qPCR. An 18F-fluorodeoxyglucose (18F-FDG) PET/computed tomography (CT) scan was performed and evaluated in terms of metabolic tumour volume (MTV) and total lesion glycolysis (TLG). Tumour contours were delineated semi-automatically by a threshold standardised uptake value (SUV) of 2.5. The primary end point was correlation among cfDNA, MTV and TLG. The secondary end point was overall survival (OS) according to cfDNA, MTV and TLG.Results:Fifty-three patients were included. There were no correlations between cfDNA and MTV ($r=0.1$) or TLG ($r=0.1$). cfDNA $>75^{\text{th}}$ percentile was correlated with shorter OS ($P=0.02$), confirmed in a

multivariate analysis. MTV>the median was associated with a significantly shorter OS (P=0.02). There was no significant difference in OS according to TLG (P=0.08). Conclusion: Cell-free DNA may not be a simple measure of tumour burden, but seems to reflect more complex mechanisms of tumour biology, making it attractive as an independent prognostic marker. British Journal of Cancer advance online publication 14 November 2013; doi:10.1038/bjc.2013.705 www.bjcancer.com.

[76]

TÍTULO / TITLE: - EGFR mutation status and its impact on survival of Chinese non-small cell lung cancer patients with brain metastases.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 7.

●● Enlace al texto completo (gratis o de pago) 1007/s13277-013-1323-9

AUTORES / AUTHORS: - Luo D; Ye X; Hu Z; Peng K; Song Y; Yin X; Zhu G; Ji Q; Peng Y

INSTITUCIÓN / INSTITUTION: - Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, 510515, China.

RESUMEN / SUMMARY: - Brain metastasis (BM) is a leading cause of death in patients with non-small cell lung cancer (NSCLC). EGFR mutations in primary NSCLC lesions have been associated with sensitivity to EGFR tyrosine kinase inhibitor (TKI). Therefore, it has become important to understand EGFR mutation status in BM lesions of NSCLC, and its clinical implications. BM samples of 136 NSCLC patients from South China, in which 15 had paired primary lung tumors, were retrospectively analyzed for EGFR mutation by amplification mutation refractory system (ARMS). Effect of BM EGFR mutations on progression-free survival (PFS) and overall survival (OS) was evaluated by Kaplan-Meier curves and log-rank test. EGFR mutations were detected in 52.9 % (72 of 136) of the BM lesions, with preference in female and never-smokers. A concordance rate of 93.3 % (14 of 15) was found between the primary NSCLC and corresponding BM. Positive prediction value of testing primary NSCLCs for BM EGFR mutation is 100.0 %, and negative prediction value is 87.5 %. Median PFS of BM surgery was 12 and 10 months (P = 0.594) in the wild-type and mutant group, respectively. Median OS of BM surgery was 24.5 and 15 months (P = 0.248) in the wild-type and mutant group, respectively. In conclusion, EGFR mutation status is highly concordant between the primary NSCLC and corresponding BM. The primary NSCLC could be used as surrogate samples to predict EGFR mutation status in BM lesions or vice versa. Moreover, EGFR mutations showed no significant effect on PFS or OS of NSCLCs with BM.

[77]

TÍTULO / TITLE: - Phase II Trial of Carboplatin, Paclitaxel, Cetuximab, and Bevacizumab Followed by Cetuximab and Bevacizumab in Advanced Nonsquamous Non-Small-Cell Lung Cancer: SWOG S0536.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov 1.

●● Enlace al texto completo (gratis o de pago)

1097/JTO.0000000000000009

AUTORES / AUTHORS: - Kim ES; Moon J; Herbst RS; Redman MW; Dakhil SR; Velasco MR Jr; Hirsch FR; Mack PC; Kelly K; Heymach JV; Gandara DR

INSTITUCIÓN / INSTITUTION: - *Levine Cancer Institute, Charlotte, North Carolina; daggerSWOG Statistical Center, Seattle, Washington; double daggerYale Cancer Center, New Haven, Connecticut; section signCancer Center of Kansas and Wichita CCOP, Wichita, Kansas; ||Central Illinois CCOP and Cancer Care Specialists, Decatur, Illinois; paragraph signUniversity of Colorado Cancer Center, Aurora, Colorado; #University of California Davis Cancer Center, Sacramento, California; and **MD Anderson Cancer Center, Houston, Texas.

RESUMEN / SUMMARY: - INTRODUCTION:: Cetuximab and bevacizumab have each been demonstrated to prolong survival when added to chemotherapy in patients with advanced non-small-cell lung cancer (NSCLC). However, the potential benefit of combining cetuximab and bevacizumab together with a platinum-based doublet had not been explored. We designed this phase II trial to evaluate the safety, tolerability, and efficacy of the combination of carboplatin, paclitaxel, cetuximab, and bevacizumab in chemotherapy-naive patients with advanced, nonsquamous NSCLC. METHODS:: Patients received with up to six cycles of carboplatin (area under curve 6), paclitaxel (200 mg/m), cetuximab (400 mg/m day 1 then 250 mg/m weekly), and bevacizumab (15 mg/kg) every 21 days. Patients with an objective response or stable disease received maintenance cetuximab (250 mg/m weekly) and bevacizumab (15 mg/kg every 21 days) until disease progression. The primary endpoint was safety as defined by the frequency and severity of hemorrhagic toxicities. Secondary endpoints included response rate, progression-free survival, overall survival, and toxicity. Molecular biomarkers were assessed in an exploratory manner. RESULTS:: The primary endpoint of grade 4 or higher hemorrhage of 2% (95% confidence interval: 0%-7%) met prespecified criteria for safety. One hundred ten patients were enrolled. There were four treatment-related deaths including lung hemorrhage (2), infection (1), and unknown (1). Median progression-free survival was 7 months and median overall survival was 15 months. The response rate was 56% with an overall disease control rate of 77%. CONCLUSION:: This regimen was safe, feasible, and effective as a frontline treatment of advanced NSCLC, providing the basis for the ongoing phase III trial S0819.

[78]

TÍTULO / TITLE: - Do HIV-infected Non-Small Cell Lung Cancer Patients Receive Guidance-concordant Care?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Care. 2013 Dec;51(12):1063-8. doi: 10.1097/MLR.0000000000000003.

●● Enlace al texto completo (gratis o de pago)

[1097/MLR.0000000000000003](#)

AUTORES / AUTHORS: - Lee JY; Moore PC; Steliga MA

INSTITUCIÓN / INSTITUTION: - Departments of *Biostatistics daggerSurgery, University of Arkansas for Medical Sciences, Little Rock, AR.

RESUMEN / SUMMARY: - BACKGROUND: The incidence of lung cancer cases among HIV-infected individuals is increasing with time. It is unclear whether HIV-infected individuals receive the same care for lung cancer as immunocompetent patients

because of comorbidities, the potential for interaction between antiretroviral agents and cancer chemotherapy, and concerns regarding complications related to treatment or infection. OBJECTIVES: The objective of this study was to assess the effect of HIV infection on receipt of guidance-concordant care, and its impact on overall survival among non-small cell lung cancer Medicare beneficiaries. DESIGN: The study design was a matched case-control design where each HIV patient was matched by age group, sex, race, and lung cancer stage at diagnosis with 20 controls randomly selected among those who were not HIV infected. SUBJECTS: The patients included in this study were Medicare beneficiaries diagnosed with non-small cell lung cancer between 1998 and 2007, who qualified for Medicare on the basis of age and were 65 years of age or older at the time of lung cancer diagnosis. HIV infection status was based on Medicare claims data. A total of 174 HIV cases and 3480 controls were included in the analysis. MEASURES: Odds ratios for receiving guidance-concordant care and hazard ratios for overall survival were estimated. RESULTS: HIV infection was not independently associated with the receipt of guidance-concordant care. Among stage I/II patients, median survival times were 26 and 43 months, respectively, for those with and without HIV infection (odds ratio=1.48, P=0.021). CONCLUSIONS: HIV infection was not associated with receipt of guidance-concordant care but reduced survival in early-stage patients.

[79]

TÍTULO / TITLE: - microRNA expression profiles associated with survival, disease progression, and response to gefitinib in completely resected non-small-cell lung cancer with EGFR mutation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):750. doi: 10.1007/s12032-013-0750-1. Epub 2013 Nov 6.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0750-1](#)

AUTORES / AUTHORS: - Shen Y; Tang D; Yao R; Wang M; Wang Y; Yao Y; Li X; Zhang H

INSTITUCIÓN / INSTITUTION: - Medical College, Thoracic Surgery of the Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao, 266003, China.

RESUMEN / SUMMARY: - microRNAs have been implicated in regulating diverse cellular pathways. Although there is emerging evidence that some microRNAs can function as oncogenes or tumor suppressors, the role of microRNAs in mediating cancer progression remains unexplored. And whether expression levels of a panel of biologically relevant microRNAs can be used as prognostic or predictive biomarkers in radically resected non-small-cell lung carcinoma (NSCLC) patients still needs to be further validated. Our analyses involved two separated, retrospective cohorts. Firstly, microRNA expression profile was performed in a cohort consisted of 128 radically resected NSCLC patients [60 were positive to epidermal growth factor receptor (EGFR) mutation and 68 were negative] and 32 healthy providers to identify EGFR mutation-related microRNAs and to determine their association with survival. In addition, to validate our findings, we used quantitative reverse transcriptase polymerase chain reaction assays to measure microRNAs and assess their association with disease progression, survival, and response to gefitinib in an independent cohort of 201 patients with EGRF mutation. In radically resected NSCLC patients, the expression

levels of miR-21, 10b in patients with EGFR mutation were much higher than those without mutation. We used Cox proportional-hazards regression to evaluate the effect of treatment on survival. In both univariate and multivariate analyses, gefitinib was associated with a significant improvement in overall survival in patients with reduced miR-21 expression. Thus, miR-21 expression emerged as an independent predictor of the response to gefitinib. Additionally, miR-10b is highly expressed in progressive disease compared with complete remission or stable disease ($P < 0.001$). However, miR-21 expression has no significant prognosis for disease progression ($P = 0.720$). Meanwhile, when overall survival was considered as the end point, miR-10b did not have a significant difference between different subgroups ($P = 0.634$). The expression patterns of microRNAs differ significantly between patients with positive and negative EGFR mutation. And the expression status of miR-21 and 10b in such patients is associated with disease progression, survival, and response to adjuvant therapy with gefitinib.

[80]

TÍTULO / TITLE: - Microscopic disease extensions as a risk factor for loco-regional recurrence of NSCLC after SBRT.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Oct;109(1):26-31. doi: 10.1016/j.radonc.2013.08.028. Epub 2013 Oct 4.

●● Enlace al texto completo (gratis o de pago) [1016/j.radonc.2013.08.028](#)

AUTORES / AUTHORS: - Salguero FJ; Belderbos JS; Rossi MM; Blaauwgeers JL; Stroom J; Sonke JJ

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

RESUMEN / SUMMARY: - PURPOSE: Stereotactic body radiotherapy (SBRT) is a highly conformal technique that allows a more accurate irradiation of lung tumors. However, a highly conformal dose distribution may underdose undetected microscopic disease extensions (MDE) near the tumor leading to loco-regional failure in tumor control. The purpose of the current work is to assess the risk of loco-regional failure in SBRT by analyzing pre-treatment scans. METHODS AND MATERIALS: A model to predict the risk of occurrence of MDE from pretreatment images was developed based on pathology samples of 47 lung cancer patients. This model was used to assess the outcome of 238 SBRT treatments. RESULTS: Patients with high risk of MDE presence showed significantly lower 2-year loco-regional control (82.0% vs. 91.8%) and shorter time to loco-regional failure (8.4months vs. 20.7months) than low risk patients. The minimum dose delivered in the volume surrounding the GTV affected the model predictive power. The model remained predictive for patients who received less than 31Gy in that volume. For patients who received larger doses, the MDE risk classification was not significant. CONCLUSIONS: The results show that MDEs are, at least partially, responsible of loco-regional failure in highly conformal radiotherapy. This information could be used to optimize dose distributions.

[81]

TÍTULO / TITLE: - Expression of fibroblast growth factor 9 is associated with poor prognosis in patients with resected non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 30. pii: S0169-5002(13)00460-1. doi: 10.1016/j.lungcan.2013.10.016.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.016](#)

AUTORES / AUTHORS: - Ohgino K; Soejima K; Yasuda H; Hayashi Y; Hamamoto J; Naoki K; Arai D; Ishioka K; Sato T; Terai H; Ikemura S; Yoda S; Tani T; Kuroda A; Betsuyaku T

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: Fibroblast growth factor (FGF) 9 is a member of the FGF family, which modulates cell proliferation, differentiation, and motility. Recent studies show that the activation of FGF signals including FGF9 is associated with the pathogenesis of several cancers; however, its clinicopathological and biological significance in non-small cell lung cancer (NSCLC) is unclear. The purpose of this study was to clarify the characteristics of NSCLC with FGF9 expression. MATERIALS AND METHODS: We evaluated the expression of FGF9 in resected NSCLC specimens and corresponding non-tumorous lung tissue samples using cDNA microarray and evaluated its clinicopathological characteristics. RESULTS: Nine out of 90 NSCLC specimens (10%) had "high" FGF9 expression compared with corresponding non-cancerous lung tissues. Histologically, of the 9 NSCLC specimens with high FGF9 expression, 5 were adenocarcinoma, whereas none were squamous cell carcinoma. FGF9 expression was not associated with sex, smoking history, or clinical stage. However, in patients with high and low FGF9 expression, the postoperative recurrence rates were 78% and 24% ($p=0.033$), respectively. Overall survival was significantly shorter in patients with high FGF9 expression than in those with low FGF9 expression ($p<0.001$). CONCLUSION: Our data indicate that FGF9 may be a novel unfavorable prognostic indicator and a candidate therapeutic target of NSCLC.

[82]

TÍTULO / TITLE: - Advanced Lung Adenocarcinoma Harboring a Mutation of the Epidermal Growth Factor Receptor: CT Findings after Tyrosine Kinase Inhibitor Therapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiology. 2013 Oct 1.

●● Enlace al texto completo (gratis o de pago) [1148/radiol.13121824](#)

AUTORES / AUTHORS: - Choi CM; Kim MY; Lee JC; Kim HJ

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary and Critical Care Medicine, Department of Oncology, Department of Radiology and Research Institute of Radiology, and Department of Clinical Epidemiology and Biostatistics, University of Ulsan College of Medicine, Asan Medical Center, 86 Asanbyeongwon-Gil, Songpa-Gu, Seoul 138-736, Korea.

RESUMEN / SUMMARY: - Purpose: To study chest computed tomography (CT) in tyrosine kinase inhibitor (TKI) treatment of epidermal growth factor receptor (EGFR)-mutant adenocarcinoma. Materials and Methods: This retrospective study was approved

by the institutional review board. Informed consent was waived. One hundred thirty consecutive patients with stage IV adenocarcinoma and EGFR mutations at a single tertiary center from November 2004 to April 2010 were enrolled retrospectively. CT images were analyzed with Response Evaluation Criteria in Solid Tumor guidelines. Target lesions were classified by size, type, axial location, and metastasis. Patients were followed after TKI therapy, and treatment response was classified as partial response, stable disease, or progressive disease. A Cox proportional hazards model was used to correlate baseline CT features and EGFR mutations with progression-free survival (PFS) and overall survival. Results: All patients underwent TKI therapy after identifying exon mutations in the EGFR gene, comprising exon 19 deletion (19del) (n = 77), L858R (n = 43), and exon 18 (n = 10). Outcomes were partial response (n = 103), stable disease (n = 22), and progressive disease (n = 5). In univariate analysis, PFS was significantly longer with small lesions (hazard ratio [HR], 1.02; 95% confidence interval [CI]: 1.01, 1.03; P < .01), nodular main lesions (HR, 0.55; 95% CI: 0.34, 0.88; P = .01), or peripheral lesions (HR, 0.62; 95% CI: 0.42, 0.93; P = .02). In univariate analysis, PFS was significantly longer with smaller lesions (HR, 1.02; 95% CI: 1.01, 1.03; P < .01), nodular main lesions (HR, 0.55; 95% CI: 0.34, 0.88; P = .01), peripheral lesions (HR, 0.62; 95% CI: 0.42, 0.93; P = .02), 19del (HR, 0.33; 95% CI: 0.14, 0.77; P = .01), or L858R (HR, 0.39; 95% CI: 0.16, 0.97; P = .04). In multivariate analysis, PFS was significantly longer with 19del (HR, 0.30; 95% CI: 0.11, 0.84; P = .02) and shorter with scattered metastases (HR, 2.25; 95% CI: 1.44, 5.51; P < .01). Conclusion: Smaller nodular lesions, peripheral lesions, and 19del relate to longer PFS after EGFR TKI treatment. © RSNA, 2013.

[83]

TÍTULO / TITLE: - Survival of Patients With Unsuspected pN2 Non-Small Cell Lung Cancer After an Accurate Preoperative Mediastinal Staging.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Surg. 2013 Nov 25. pii: S0003-4975(13)02272-8. doi: 10.1016/j.athoracsur.2013.09.101.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1016/j.athoracsur.2013.09.101](#)

AUTORES / AUTHORS: - Obiols C; Call S; Rami-Porta R; Trujillo-Reyes JC; Saumench R; Iglesias M; Serra-Mitjans M; Gonzalez-Pont G; Belda-Sanchis J

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Hospital Universitari Mutua Terrassa, University of Barcelona, Barcelona, España. Electronic address: carne_obiols@hotmail.com.

RESUMEN / SUMMARY: - BACKGROUND: The aim of this study is to analyze the survival of patients with non-small cell lung cancer (NSCLC) without clinical suspicion of mediastinal lymph node involvement who underwent complete resection and whose tumors were finally proven to be pathologic N2 (pN2). METHODS: This is a retrospective study of a prospective database from January 2004 to December 2010. A total of 621 patients with NSCLC were staged and operated according to the European Society of Thoracic Surgeons guidelines. After exclusions (previous induction treatment, carcinoid tumors, small cell carcinomas), 540 patients were analyzed; 406 (75%) required surgical exploration of the mediastinum and 134 (25%) underwent surgery directly. Survival analysis was performed by the Kaplan-Meier

method and the log-rank test was used for comparisons. RESULTS: Thirty (5.5%) patients had unsuspected pN2 and complete resection was achieved in 27 (90%). Three- and 5-year survival rates were 87% and 81%, respectively, for patients with a true negative result of the protocol (pN0-1), and 79% and 40%, respectively, for those with a false negative result (unsuspected pN2) ($p < 0.0001$). CONCLUSIONS: The rate of unsuspected pN2 in patients whose tumors were staged according to the European Society of Thoracic Surgeons guidelines was low. The survival of this group of patients was better than expected. Therefore, resection of properly staged unsuspected pN2 NSCLC is reasonable and should not be avoided if complete resection can be achieved.

[84]

TÍTULO / TITLE: - Successful treatment with a combination of electrocautery using wire snares and gefitinib in patients with EGFR-mutant lung cancer and central airway obstruction.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Intern Med. 2013;52(20):2331-5.

AUTORES / AUTHORS: - Araya T; Demura Y; Kasahara K; Matsuoka H; Nishitsuji M; Nishi K

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Ishikawa Prefectural Central Hospital, Japan.

RESUMEN / SUMMARY: - One-third of lung cancer patients present with life-threatening central airway obstruction (CAO). Two elderly patients were referred to our institution with symptoms caused by CAO. In each case, thoracic computed tomography and a bronchoscopic examination revealed a tumor obstructing the central airway. The tumors were resected endoscopically, and the patients' respiratory and performance status remarkably improved. Both patients were diagnosed with an advanced stage of lung adenocarcinoma harboring epidermal growth factor receptor (EGFR) mutations. They received gefitinib monotherapy, with partial responses sustained for more than 12 months. Combination therapy with endoscopic tumor resection and gefitinib is beneficial in patients with EGFR-mutant lung cancer and CAO.

[85]

TÍTULO / TITLE: - Targeting ALK in patients with advanced Non Small Cell Lung Cancer: Biology, diagnostic and therapeutic options.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Crit Rev Oncol Hematol. 2013 Sep 26. pii: S1040-8428(13)00208-4. doi: 10.1016/j.critrevonc.2013.09.003.

●● Enlace al texto completo (gratis o de pago) 1016/j.critrevonc.2013.09.003

AUTORES / AUTHORS: - Lazzari C; Spitaleri G; Catania C; Barberis M; Noverasco C; Santarpia M; Delmonte A; Toffalorio F; Conforti F; De Pas TM

INSTITUCIÓN / INSTITUTION: - European Institute of Oncology, Division of Thoracic Oncology, Italy. Electronic address: chiaralazzari07@gmail.com.

RESUMEN / SUMMARY: - The discovery of EML4-ALK fusion gene in a subgroup of patients with lung adenocarcinoma led to the development of a new class of agents, the ALK inhibitors, and dramatically improved the clinical outcome of these patients.

The striking results from clinical trials with crizotinib, the first ALK inhibitor evaluated, allowed the accelerated approval of crizotinib from the USA Food and Drug Administration (FDA). Despite the high initial results, patients acquire resistance to crizotinib, and different next generation ALK kinase inhibitors have been developed. In the current review, we will analyze the biology of EML4-ALK gene, the acquired resistance mechanisms to crizotinib, the therapeutic strategies, currently under evaluation, designed to overcome crizotinib resistance, and the open issues that need to be addressed in order to improve outcome in ALK+ Non Small Cell Lung Cancer (NSCLC) patients.

[86]

TÍTULO / TITLE: - Therapy-induced enrichment of putative lung cancer stem-like cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Cancer. 2013 Sep 17. doi: 10.1002/ijc.28478.

●● Enlace al texto completo (gratis o de pago) [1002/ijc.28478](#)

AUTORES / AUTHORS: - Freitas DP; Teixeira CA; Santos-Silva F; Vasconcelos MH; Almeida GM

INSTITUCIÓN / INSTITUTION: - Cancer Drug Resistance Group, Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP), Porto, Portugal; Expression Regulation in Cancer Group, Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP), Porto, Portugal.

RESUMEN / SUMMARY: - Tumour drug resistance is a major issue in the management of lung cancer patients as almost all lung tumours are either intrinsically resistant or quickly develop acquired resistance to chemotherapeutic drugs. Cancer drug resistance has recently been linked, at least in part, to the existence of cancer stem-like cells (CSLCs), a small sub-population of cells within the tumour that possess stem-like properties. CSLCs are often isolated by fluorescence activated cell sorting (FACS) according to the expression of certain stem-like cell membrane markers. Conflicting results regarding the specificity of particular stem cell surface markers for isolating CSLCs have, however, been recently reported. Therefore, alternative strategies enabling the identification and study of CSLCs should be considered, particularly in tumour types where appropriate stem cell markers are not well established and validated, like in lung cancer. In this article, we review data indicating therapy-selection as a valid approach for putative lung CSLCs enrichment. We believe that this strategy would be determinant for correctly assessing and characterising the sub-populations of CSLCs that are able to survive chemo or radiotherapy regimens and, at the same time, also have the ability to recapitulate and sustain tumour growth. Using therapy-induced enrichment of CSLCs may, therefore, prove to be an extremely useful method for studying CSLCs and provide new clues regarding potential therapeutic targets for their efficient elimination, which will undoubtedly play a decisive role in improving lung cancer patients' survival.

[87]

TÍTULO / TITLE: - In vitro and in vivo antitumor effects of MPT0B014, a novel derivative aroylquinoline, and in combination with erlotinib in human non-small-cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Pharmacol. 2013 Sep 30. doi: 10.1111/bph.12427.

●● Enlace al texto completo (gratis o de pago) [1111/bph.12427](#)

AUTORES / AUTHORS: - Tsai AC; Pai HC; Wang CY; Liou JP; Teng CM; Wang JC; Pan SL

INSTITUCIÓN / INSTITUTION: - School of Pharmacy, College of Pharmacy, Taipei Medical University, Taipei, Taiwan.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: To develop a novel non-P-glycoprotein (P-gp) substrate anti-cancer drug, MPT0B014, alone and in combination with erlotinib against human non-small-cell lung cancer (NSCLC). EXPERIMENTAL APPROACH: SRB and MTT assays were performed to assess the cytotoxicity of human NSCLC cell lines. FACScan flow cytometer was used to estimate the cell cycle phase distributions. The protein expression was detected by Western blotting analysis. Rh-123 or calcein-AM efflux experiment was carried out to study the P-gp profile. The A549 xenograft model was used to assess in vivo anti-tumor activity. KEY RESULTS: B014 showed more potent anti-proliferative activity against A549, H1299, and H226 cells. It induced G2/M arrest with downregulation of Cdc (Tyr15) and Cdc25C and upregulation of cyclin B1, phospho-Cdc2 (Thr161), and Aurora A/B. P-glycoprotein-overexpressing NCI/ADR-RES cells were also sensitive to B014. B014-induced loss of Mcl-1 was accompanied by activation of caspase-3, -7, -8, -9, and initiation of apoptosis. B014 in combination with erlotinib caused significant tumor inhibition in vitro and in vivo. CONCLUSIONS AND IMPLICATIONS: MPT0B014 exerted cytotoxicity against human NSCLC cell lines with poor susceptibility to P-gp, and significant growth inhibition of A549 cells both in vitro and in vivo by the combined use of an EGFR inhibitor, erlotinib, suggesting B014 with anti-cancer activity as a therapeutic agent.

[88]

TÍTULO / TITLE: - Pattern in lung cancer pathology may predict disease recurrence.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer. 2013 Dec 1;119(23):4057. doi: 10.1002/cncr.28475.

●● Enlace al texto completo (gratis o de pago) [1002/cncr.28475](#)

AUTORES / AUTHORS: - Printz C

[89]

TÍTULO / TITLE: - Emerging paradigms in the development of resistance to tyrosine kinase inhibitors in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Oncol. 2013 Nov 1;31(31):3987-96. doi: 10.1200/JCO.2012.45.2029. Epub 2013 Oct 7.

●● Enlace al texto completo (gratis o de pago) [1200/JCO.2012.45.2029](#)

AUTORES / AUTHORS: - Gainor JF; Shaw AT

INSTITUCIÓN / INSTITUTION: - From the Massachusetts General Hospital Cancer Center, Boston, MA.

RESUMEN / SUMMARY: - The success of tyrosine kinase inhibitors (TKIs) in select patients with non-small-cell lung cancer (NSCLC) has transformed management of the disease, placing new emphasis on understanding the molecular characteristics of

tumor specimens. It is now recognized that genetic alterations in the epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) define two unique subtypes of NSCLC that are highly responsive to genotype-directed TKIs. Despite this initial sensitivity, however, the long-term effectiveness of such therapies is universally limited by the development of resistance. Identifying the mechanisms underlying this resistance is an area of intense, ongoing investigation. In this review, we provide an overview of recent experience in the field, focusing on results from preclinical resistance models and studies of patient-derived, TKI-resistant tumor specimens. Although diverse TKI resistance mechanisms have been identified within EGFR-mutant and ALK-positive patients, we highlight common principles of resistance shared between these groups. These include the development of secondary mutations in the kinase target, gene amplification of the primary oncogene, and upregulation of bypass signaling tracts. In EGFR-mutant and ALK-positive patients alike, acquired resistance may also be a dynamic and multifactorial process that may necessitate the use of treatment combinations. We believe that insights into the mechanisms of TKI resistance in patients with EGFR mutations or ALK rearrangements may inform the development of novel treatment strategies in NSCLC, which may also be generalizable to other kinase-driven malignancies.

[90]

TÍTULO / TITLE: - Longitudinal assessment of TUBB3 expression in non-small cell lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Nov 13.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00280-013-2315-6](#)

AUTORES / AUTHORS: - Jakobsen JN; Santoni-Rugiu E; Sorensen JB

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Rigshospitalet, 9 Blegdamsvej, 2100, Copenhagen, Denmark, jan.nyrop.jakobsen@rh.regionh.dk.

RESUMEN / SUMMARY: - INTRODUCTION: Class-III-beta-tubulin (TUBB3) expression may be a potential predictive factor for treatment with microtubule interfering cytotoxic drugs in non-small cell lung cancer (NSCLC). Potential changes in TUBB3 expression during chemotherapy may be of interest if future choice of chemotherapy is to be based on TUBB3 expression. If the biomarker expression changes during chemotherapy, biopsies before initiation of chemotherapy beyond first line may be needed if treatment decision is to be based on TUBB3 expression. Thus, the aim was to explore TUBB3 expression heterogeneity and changes during chemotherapy.

MATERIALS AND METHODS: TUBB3 expression was investigated by immunohistochemistry performed on diagnostic biopsies and on available subsequent resection specimens in 65 NSCLC patients stage T1-3N0-2 who received neoadjuvant carboplatin and paclitaxel (NAC-group). Another group of 53 NSCLC patients stage T1-4N0-1 was treated with surgery alone without preceding chemotherapy (OP-group). Paired repeated samples were compared in order to evaluate for changes in TUBB3 expression. **RESULTS:** No statistically significant change in TUBB3 expression was observed between initial diagnostic biopsies and subsequent surgical resections of primary tumors in either the OP-group ($p = 0.124$) or the NAC-group ($p = 0.414$). When dichotomized into high and low TUBB3 expression, discordance between diagnostic biopsies and resection specimens of the primary tumors occurred in 22 % and 40 % in

the OP-group and NAC-group, respectively ($p = 0.169$). Significantly more patients having low TUBB3 expression experienced down-staging during neoadjuvant chemotherapy compared to patients having high TUBB3 expression ($p = 0.022$).
CONCLUSION: A high degree of discordance of TUBB3 expression between paired repeated tumor samples was observed, which likely reflects intratumoral heterogeneity. This emphasizes a need for optimal tumor tissue samples in order to stratify patients based on TUBB3 expression. No significant changes in TUBB3 expression after neoadjuvant carboplatin and paclitaxel chemotherapy occurred, suggesting no need for rebiopsy in case second-line chemotherapy with microtubule interfering cytotoxic treatments is necessary.

[91]

TÍTULO / TITLE: - Marginal pulmonary function should not preclude lobectomy in selected patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Nov 16. pii: S0022-5223(13)01162-8. doi: 10.1016/j.jtcvs.2013.09.064.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.09.064](#)

AUTORES / AUTHORS: - Taylor MD; Lapar DJ; Isbell JM; Kozower BD; Lau CL; Jones DR

INSTITUCIÓN / INSTITUTION: - Division of Thoracic and Cardiovascular Surgery, Department of Surgery, University of Virginia, Charlottesville, Va.

RESUMEN / SUMMARY: - **OBJECTIVE:** Current clinical trials are investigating the role of stereotactic body radiation therapy (SBRT) versus sublobar resection for patients with non-small cell lung carcinoma (NSCLC) and marginal pulmonary function tests (M-PFTs). We compared the outcomes of patients undergoing lobectomy with M-PFTs characterized by 2 accepted M-PFT criteria. **METHODS:** A total of 1,259 consecutive patients underwent lobectomy for NSCLC between 1999 and 2011. Patients were stratified into 2 classifications of M-PFT: American College of Surgeons Oncology Group (ACOSOG) Z4099/Radiation Therapy Oncology Group (RTOG) 1021 trial or American College of Chest Physicians (ACCP) criteria. There were 206 patients classified as having M-PFT according to ACOSOG Z4099/RTOG 1021 criteria and 131 patients classified as having M-PFT by ACCP criteria. The primary endpoints of the study were post-operative complications and survival. **RESULTS:** Median follow-up was 3.8 years. Cox-proportional survival analysis found that pathologic stage ($P < .001$), age ($P < .001$), and higher Zubrod functional status ($P < .001$) were independent predictors of mortality. Using multivariable analysis for major morbidity, M-PFT status was not associated with the development of a major complication following lobectomy ($P = .68$). M-PFT classification was not an independent predictor of mortality when controlling for other variables (ACOSOG Z4099/RTOG 1021 [$P = .34$]; ACCP criteria [$P = .83$]). A composite major morbidity analysis for major morbidity following lobectomy showed no association between clinicopathologic variables or M-PFTs and the occurrence of a major postoperative morbidity. **CONCLUSIONS:** In carefully selected patients with M-PFTs, lobectomy for NSCLC can be performed with acceptable morbidity and mortality. These results need to be considered when deciding if a patient should undergo lobectomy or other therapies for resectable NSCLC.

[92]

TÍTULO / TITLE: - Surgical Treatment in Patient with Non-Small-Cell Lung Cancer with Fissure Involvement: Anatomical versus Nonanatomical Resection.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov 19.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0000000000000040](#)

AUTORES / AUTHORS: - Leuzzi G; Cesario A; Cafarotti S; Lococo F; Dall'armi V; Novellis P; Romano R; Siciliani A; Meacci E; Granone P; Margaritora S

INSTITUCIÓN / INSTITUTION: - *Thoracic Surgery Unit, Presidio Ospedaliero Maggiore-Bellaria, Bologna, Italy; daggerDepartment of Thoracic Surgery, Catholic University of Sacred Heart, Rome, Italy; double daggerIRCCS San Raffaele Pisana, Rome, Italy; section signEOC-Thoracic Surgery Unit, Bellinzona, Switzerland; ||Thoracic Surgery Unit, Arcispedale Santa Maria Nuova, IRCCS Reggio Emilia, Reggio Emilia, Italy; and paragraph signUnit of Clinical and Molecular Epidemiology, IRCCS San Raffaele Pisana, Rome, Italy.

RESUMEN / SUMMARY: - **OBJECTIVE::** Despite the intense debate concerning the prognostic impact of fissure involvement (FI) in patients with non-small-cell lung cancer, no specific surgical strategies have been yet recommended when this condition occurs. In this setting, we report our monocentric 10-years experience to investigate this issue. **METHODS::** From January 2000 to January 2010, the clinical data of 40 non-small-cell lung cancer patients with FI undergoing curative resection were retrospectively reviewed. The sample was stratified according to the type of resection: group A (28 patients): anatomical resection (bilobectomy [21 patients], pneumonectomy [7 patients]); group B (12 patients): nonanatomical resection (lobectomy plus wedge resection [LWR]). The end-points were (1) impact of different surgical approach on the pulmonary function (measured before surgery and 1 month after discharge); (2) disease-specific survival; and (3) tumor recurrence. The t test, chi, and log-rank tests, Kaplan-Meier method, and Cox and logistic regression analyses were used for the statistical analysis. **RESULTS::** No differences between the two groups were found when comparing the clinical characteristics, histology, pN or pT status, p-stage, residual (R1) disease, tumor grading, or tumor size. Similarly, the baseline preoperative function (tested as forced expiratory volume in 1 second-%-predicted, FEV1%) was likewise comparable (92.5% +/- 21.0% in group A versus 85.2% +/- 20.0% in group B; p = not significant). The decline of FEV1% after surgery was slightly higher in group A (-24.9% +/- 13.5%) when compared with that in group B (-19.5% +/- 13.3%), but this difference was not statistically significant (p = ns). Nevertheless, the 5-year disease-specific survival was 56% for group A and 47% for group B (p = ns). The recurrence rate did not differ between the patients undergoing a LWR (3 of 12 patients) and those undergoing a bilobectomy or pneumonectomy (9 of 28 patients) (p = ns). The presence of FI extended for more than 3 cm was found to be the most significant prognostic factor when analyzing survival (p = 0.002) and recurrence rate (p; < 0.001). **CONCLUSIONS::** Our results suggest that nonanatomical resection (LWR) could be considered as a feasible surgical option (especially in "frail" patients with an extent of FI less than 3 cm) in the light of the similar oncological and functional outcome compared with anatomical resection. Further studies based on

larger series are needed to confirm these preliminary data and also to investigate the impact on the postoperative quality of life.

[93]

TÍTULO / TITLE: - Clinical efficiency of quadrivalent HPV (types 6/11/16/18) vaccine in patients with recurrent respiratory papillomatosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur Arch Otorhinolaryngol. 2013 Oct 12.

●● Enlace al texto completo (gratis o de pago) [1007/s00405-013-2755-y](#)

AUTORES / AUTHORS: - Chirila M; Bolboaca SD

INSTITUCIÓN / INSTITUTION: - ENT Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, 13 Emil Isac, 400023, Cluj-Napoca, Romania, chirila_magda@yahoo.com.

RESUMEN / SUMMARY: - The aim of the study was to assess the clinical efficiency of quadrivalent HPV (types 6/11/16/18) vaccine in patients with recurrent respiratory papillomatosis (RRP). This was a prospective study of patients with RRP treated from January 2009 to July 2012 at the Ear, Nose and Throat Department of the Emergency County Hospital of Cluj-Napoca, Romania. Demographic characteristics, onset of RRP, HPV typing, use and number of cidofovir injections, number of surgeries for RRP per year, and use of human papillomavirus vaccine (types 6, 11, 16, 18) (recombinant, adsorbed)/Silgard® were considered from all the patients included in the study. Charts were reviewed for follow-up after diagnosis, after cidofovir, and after Silgard; all the statistical tests were applied at a significance level of 5 %. The recurrences were observed within 27.53 +/- 11.24 days after intralesional cidofovir injection. Thirteen patients with recurrence after cidofovir agreed and received Silgard® vaccine. 85 % [54.44-99.41] of patients had no recurrences during 1-year follow-up. The recurrence of papillomas was observed in two patients (15 %, 95 % CI [0.59-45.56]), one with adult-onset RRP and one with juvenile-onset RRP. Both recurrences appeared after the first Silgard dose; one month after the third vaccine dose each patient underwent a new surgery for remaining papillomas with no recurrences at 1-year follow-up visit. Silgard® vaccination had a good effect and proved to be efficient in the treatment of our patients with RRP without appearance of recurrence in 85 % of the patients during 1-year follow-up.

[94]

TÍTULO / TITLE: - Clinical characteristics of patients with malignant pleural mesothelioma harboring somatic BAP1 mutations.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1430-3. doi: 10.1097/JTO.0b013e31829e7ef9.

●● Enlace al texto completo (gratis o de pago) [1097/JTO.0b013e31829e7ef9](#)

AUTORES / AUTHORS: - Zauderer MG; Bott M; McMillan R; Sima CS; Rusch V; Krug LM; Ladanyi M

INSTITUCIÓN / INSTITUTION: - *Department of Medicine, Division of Solid Tumor Oncology, Thoracic Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, New York; daggerDepartment of Medicine, Weill Cornell Medical College, New

York, New York; double daggerDepartments of Pathology, section signSurgery, ||Epidemiology and Biostatistics, paragraph signHuman Oncology and Pathogenesis Program, Memorial Sloan-Kettering Cancer Center, New York, New York.

RESUMEN / SUMMARY: - INTRODUCTION: Genomic studies of malignant pleural mesothelioma (MPM) have recently identified frequent mutations in the BRCA-associated protein 1(BAP1) gene. In uveal melanoma and clear cell renal cell carcinoma, BAP1 mutations are associated with poor outcomes but their clinical significance in MPM is unknown. We therefore undertook this study to define the characteristics of patients whose MPM tumors harbor somatic BAP1 mutation and to examine the relationship between BAP1 mutation and survival. METHODS: We reviewed the charts of 121 patients with MPM tumors diagnosed between 1991 and 2009 tested for BAP1 mutation, and extracted the following information: age at diagnosis, sex, histology, stage, smoking status, asbestos exposure, family or personal history of malignancy, and treatment including surgery, chemotherapy, and radiation as well as survival status. RESULTS: Twenty-four of the 121 tumors (20%) harbored somatic BAP1 mutations. The percentage of current or former smokers among cases with BAP1 mutations was significantly higher than in BAP1 wild-type cases, (75% versus 42%; $p = 0.006$). However, the types of nucleotide substitutions in BAP1 did not suggest that this association was because of a causative role of smoking in BAP1 mutations. No other clinical feature was significantly different among those with and without BAP1 mutations in their MPM. There was also no difference in survival according to somatic BAP1 mutation status. CONCLUSION: There is no apparent distinct clinical phenotype for MPM with somatic BAP1 mutation. The significance of the more frequent history of smoking among patients with BAP1-mutated MPM warrants further study.

[95]

TÍTULO / TITLE: - The impact of tumor size on outcomes after stereotactic body radiation therapy for medically inoperable early-stage non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Dec 1;87(5):1064-70. doi: 10.1016/j.ijrobp.2013.08.020. Epub 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) 1016/j.ijrobp.2013.08.020

AUTORES / AUTHORS: - Allibhai Z; Taremi M; Bezjak A; Brade A; Hope AJ; Sun A; Cho BC

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Princess Margaret Cancer Centre, Toronto, Canada.

RESUMEN / SUMMARY: - PURPOSE: Stereotactic body radiation therapy for medically inoperable early-stage non-small cell lung cancer (NSCLC) offers excellent control rates. Most published series deal mainly with small (usually <4 cm), peripheral, solitary tumors. Larger tumors are associated with poorer outcomes (ie, lower control rates, higher toxicity) when treated with conventional RT. It is unclear whether SBRT is sufficiently potent to control these larger tumors. We therefore evaluated and examined the influence of tumor size on treatment outcomes after SBRT. METHODS AND MATERIALS: Between October 2004 and October 2010, 185 medically inoperable patients with early (T1-T2N0M0) NSCLC were treated on a prospective research ethics board-approved single-institution protocol. Prescription doses were risk-adapted based

on tumor size and location. Follow-up included prospective assessment of toxicity (as per Common Terminology Criteria for Adverse Events, version 3.0) and serial computed tomography scans. Patterns of failure, toxicity, and survival outcomes were calculated using Kaplan-Meier method, and the significance of tumor size (diameter, volume) with respect to patient, treatment, and tumor factors was tested. RESULTS: Median follow-up was 15.2 months. Tumor size was not associated with local failure but was associated with regional failure (P=.011) and distant failure (P=.021). Poorer overall survival (P=.001), disease-free survival (P=.001), and cause-specific survival (P=.005) were also significantly associated with tumor size (with tumor volume more significant than diameter). Gross tumor volume and planning target volume were significantly associated with grade 2 or worse radiation pneumonitis. However, overall rates of grade ≥ 3 pneumonitis were low and not significantly affected by tumor or target size. CONCLUSIONS: Currently employed stereotactic body radiation therapy dose regimens can provide safe effective local therapy even for larger solitary NSCLC tumors (up to 5.7 cm in tumor diameter or 100 cm³ in tumor volume) but are associated with more nonlocal failures as well as poorer survival. These observations suggest these patients may benefit from more extensive staging or consideration of adjuvant therapy.

[96]

TÍTULO / TITLE: - Sleeve Lobectomy for Non-Small Cell Lung Cancer With N1 Nodal Disease Does Not Compromise Survival.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Surg. 2013 Nov 6. pii: S0003-4975(13)02013-4. doi: 10.1016/j.athoracsur.2013.09.016.

- Enlace al texto completo (gratis o de pago)

1016/j.athoracsur.2013.09.016

AUTORES / AUTHORS: - Berry MF; Worni M; Wang X; Harpole DH; D'Amico TA; Onaitis MW

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Division of Thoracic Surgery, Duke University Medical Center, Durham, North Carolina. Electronic address: berry037@mc.duke.edu.

RESUMEN / SUMMARY: - BACKGROUND: We evaluated if sleeve lobectomy had worse survival compared with pneumonectomy for non-small cell lung cancer (NSCLC) with N1 disease, which may be a risk factor for locoregional recurrence. METHODS: Patients who underwent pneumonectomy or sleeve lobectomy without induction treatment for T2-3 N1 M0 NSCLC at a single institution from 1999 to 2011 were reviewed. Survival distribution was estimated with the Kaplan-Meier method, and multivariable Cox proportional hazards regression was used to evaluate the effect of resection extent on survival. RESULTS: During the study period, 87 patients underwent pneumonectomy (52 [60%]) or sleeve lobectomy (35 [40%]) for T2-3 N1 M0 NSCLC. Pneumonectomy and sleeve lobectomy patients had similar mean ages (60.9 +/- 10.7 vs 63.5 +/- 12.7 years, p = 0.30), gender distribution (69.2% [36 of 52] vs 60.0% [21 of 35] male, p = 0.37), mean forced expiratory volume in 1 second (66.3 +/- 15.9 vs 63.5 +/- 17.6, p = 0.47), stage (61.5% [32 of 52] vs 62.9% [22 of 35] stage II, p = 0.90), and tumor grade (51.9% [27 of 52] vs 31.4% [11 of 35] well/moderately differentiated, p = 0.17). Postoperative mortality (3.8% [2 of 52] vs 5.7% [2 of 35], p = 0.68) and median

(interquartile range) length of stay (5 [4 to 7] vs 5 [4 to 7] days, $p = 0.68$) were similar between the two groups. The 3-year survival after pneumonectomy (46.8% [95% CI, 31.8% to 60.4%]) and sleeve lobectomy (65.2% [95% CI, 45.5% to 79.3%]) was not significantly different ($p = 0.23$). In multivariable survival analysis that included resection extent, age, stage, and grade, only increasing age predicted worse survival (hazard ratio, 1.03/year; $p = 0.03$). CONCLUSIONS: Performing sleeve lobectomy instead of pneumonectomy for NSCLC with N1 nodal disease does not compromise long-term survival.

[97]

TÍTULO / TITLE: - CTCF mediates the TERT enhancer-promoter interactions in lung cancer cells: Identification of a novel enhancer region involved in the regulation of TERT gene.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Cancer. 2013 Oct 30. doi: 10.1002/ijc.28570.

●● Enlace al texto completo (gratis o de pago) [1002/ijc.28570](#)

AUTORES / AUTHORS: - Eldholm V; Haugen A; Zienolddiny S

INSTITUCIÓN / INSTITUTION: - Department of Chemical and Biological Work Environment, National Institute of Occupational Health, Oslo, Norway.

RESUMEN / SUMMARY: - Telomerase activation is a hallmark of cancer. Although the regulation of the telomerase reverse transcriptase catalytic subunit (TERT), the rate-limiting factor for telomerase activity, has been studied intensively it remains incompletely understood. In cells devoid of telomerase activity, TERT is embedded in a region of condensed chromatin and the chromatin remodeling protein CCCTC-binding factor (CTCF) has been implicated in the inhibition of TERT expression. The importance of TERT activation for cellular immortalization and carcinogenesis is attested by the fact that the gene is expressed in more than 90% of immortal cell lines and tumors and that gain of TERT is the most frequent amplification event in early stage lung cancer. This study was designed to study the mechanisms of regulation of the TERT gene expression by the CTCF transcription factor in three human lung cancer cell lines, A427, A549 and H838. Depletion of CTCF by siRNA resulted in reduced TERT mRNA levels in two (A427 and A549) of the three cell lines. A novel enhancer element was identified approximately 4.5 kb upstream of the TERT transcription start site. Chromatin immunoprecipitation experiments revealed recruitment of CTCF to this enhancer element. Chromosome conformation capture experiments demonstrated the presence of CTCF-dependent chromatin loops between this enhancer element and the TERT proximal promoter in A427 and A549 cell lines. In summary, the results show that CTCF plays an important role in maintaining TERT expression in a subset of human lung cancer cell lines. This role may be due to CTCF-dependent enhancer-promoter interactions.

[98]

TÍTULO / TITLE: - Health-related quality of life in patients with advanced nonsquamous non-small-cell lung cancer receiving bevacizumab or bevacizumab-plus-pemetrexed maintenance therapy in AVAPERL (MO22089).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1409-16. doi: 10.1097/JTO.0b013e3182a46bcf.

●● Enlace al texto completo (gratis o de pago) [1097/JTO.0b013e3182a46bcf](https://doi.org/10.1097/JTO.0b013e3182a46bcf)

AUTORES / AUTHORS: - Rittmeyer A; Gorbunova V; Vikstrom A; Scherpereel A; Kim JH; Ahn MJ; Chella A; Chouaid C; Campbell AK; Barlesi F

INSTITUCIÓN / INSTITUTION: - *Department of Thoracic Oncology, Lungenfachklinik Immenhausen, Immenhausen, Germany; daggerN.N. Blokhin Cancer Research Center of Russia, Moscow, Russia; double daggerDepartment of Pulmonary Medicine, Lungkliniken, Linköping, Sweden; section signPulmonary and Thoracic Oncology Department, Hopital Albert Calmette, CHRU de Lille, Lille, France; ||Department of Medical Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Seoul, Korea; paragraph signDepartment of Hematology and Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea; #Department of Cardio-Thoracic Medicine, University of Pisa, Pisa, Italy; **Service de Pneumologie, Assistance Publique - Hopitaux de Paris, Hopital Saint-Antoine, Paris, France; daggerdaggerGlobal Medical Affairs, Genentech, Inc., South San Francisco, California; and double daggerdouble daggerService d' Oncologie Multidisciplinaire & Innovations Therapeutiques, Aix Marseille University, Assistance Publique Hopitaux de Marseille, INSERM CIC, Multidisciplinary Oncology and Therapeutic Innovations, Marseille, France.

RESUMEN / SUMMARY: - INTRODUCTION: In the phase III AVAPERL trial, patients with advanced nonsquamous non-small-cell lung cancer receiving bevacizumab-plus-pemetrexed maintenance after first-line induction had a significant progression-free survival benefit relative to those treated with single-agent bevacizumab maintenance but with an increase in grade ≥ 3 adverse events. Here, we compare health-related quality of life (HRQOL) between AVAPERL maintenance arms. METHODS: Patient-reported outcomes were collected at designated intervals from preinduction to final visits. HRQOL was assessed using the self-administered European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 and the Quality of Life Lung Cancer-Specific Module 13. Differences in scores of 10 points or more between arms were above the minimum important difference threshold and considered clinically meaningful. RESULTS: During induction, patient-reported coughing symptoms improved slightly, whereas fatigue and appetite loss scores worsened relative to preinduction baseline. During maintenance, changes in mean global health status and the majority of Quality of Life Questionnaire Core 30 and Quality of Life Lung Cancer-Specific Module 13 subscale scores did not differ between trial arms by the minimum important difference defining clinically meaningful (better or worse) patient-reported outcomes. Exceptions were patient-reported role functional status, fatigue symptoms and appetite loss symptoms (favoring bevacizumab), and pain in arm or shoulder symptoms (favoring bevacizumab-plus-pemetrexed maintenance), which differed by clinically meaningful amounts at more than one maintenance assessment. CONCLUSIONS: In AVAPERL, HRQOL remained relatively stable throughout maintenance and was generally similar in both arms. Despite an increase in adverse event rates, the addition of pemetrexed to bevacizumab maintenance resulted in similar stabilization of disease symptoms with improved efficacy outcomes.

[99]

TÍTULO / TITLE: - Impact and predictors of acute exacerbation of interstitial lung diseases after pulmonary resection for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Nov 20. pii: S0022-5223(13)01147-1. doi: 10.1016/j.jtcvs.2013.09.050.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.09.050](#)

AUTORES / AUTHORS: - Sato T; Teramukai S; Kondo H; Watanabe A; Ebina M; Kishi K; Fujii Y; Mitsudomi T; Yoshimura M; Maniwa T; Suzuki K; Kataoka K; Sugiyama Y; Kondo T; Date H

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Kyoto University, Kyoto, Japan.

RESUMEN / SUMMARY: - OBJECTIVE: The study objective was to examine the incidence, risk factors, and mortality rate of acute exacerbation of interstitial lung diseases in patients with lung cancer undergoing pulmonary resection in a large-scale multi-institutional cohort. METHODS: We retrospectively analyzed 1763 patients with non-small cell lung cancer who had undergone pulmonary resection and presented with a clinical diagnosis of interstitial lung diseases between January 2000 and December 2009 at 61 hospitals in Japan. The incidence and outcomes of acute exacerbation within 30 days from the operation were investigated. Univariate and multivariate logistic regression analyses were used to identify independent risk factors of acute exacerbation. RESULTS: Acute exacerbation occurred in 164 patients (9.3%; 95% confidence interval, 8.0-10.8), with a mortality rate of 43.9%, and was the top cause of 30-day mortality (71.7%). The following 7 independent risk factors of acute exacerbation were identified: surgical procedures, male sex, history of exacerbation, preoperative steroid use, serum sialylated carbohydrate antigen KL-6 levels, usual interstitial pneumonia appearance on computed tomography scan, and reduced percent predicted vital capacity. Surgical procedures showed the strongest association with acute exacerbation (using wedge resection as the reference, lobectomy or segmentectomy: odds ratio, 3.83; 95% confidence interval, 1.94-7.57; bi-lobectomy or pneumonectomy: odds ratio, 5.70; 95% confidence interval, 2.38-13.7; P < .001). The effect of perioperative prophylactics, such as steroids and sivelestat, was not confirmed in this study. CONCLUSIONS: Pulmonary resection for patients with lung cancer with interstitial lung diseases may provoke acute exacerbation at a substantially high rate and has high associated mortality. Surgical procedures that proved to be a risk factor for acute exacerbation should be chosen cautiously for these high-risk patients.

[100]

TÍTULO / TITLE: - A gene signature of bone metastatic colonization sensitizes for tumor-induced osteolysis and predicts survival in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Oct 28. doi: 10.1038/onc.2013.440.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.440](#)

AUTORES / AUTHORS: - Luis-Ravelo D; Anton I; Zanduetta C; Valencia K; Ormazabal C; Martinez-Canarias S; Guruceaga E; Perurena N; Vicent S; De Las Rivas J; Lecanda F

INSTITUCIÓN / INSTITUTION: - Division of Oncology, Adhesion and Metastasis Laboratory, University of Navarra, Pamplona, España.

RESUMEN / SUMMARY: - Bone metastasis of lung adenocarcinoma (AC) is a frequent complication of advanced disease. The purpose of this study was to identify key mediators conferring robust prometastatic activity with clinical significance. We isolated highly metastatic subpopulations (HMS) using a previously described in vivo model of lung AC bone metastasis. We performed transcriptomic profiling of HMS and stringent bioinformatics filtering. Functional validation was assessed by overexpression and lentiviral silencing of single, double and triple combination in vivo and in vitro. We identified HDAC4, PITX1 and ROBO1 that decreased bone metastatic ability after their simultaneous abrogation. These effects were solely linked to defects in osseous colonization. The molecular mechanisms related to bone colonization were mediated by non-cell autonomous effects that include the following: (1) a marked decrease in osteoclastogenic activity in vitro and in vivo, an effect associated with reduced pro-osteoclastogenic cytokines IL-11 and PTHrP expression levels, as well as decreased in vitro expression of stromal rankl in conditions mimicking tumor-stromal interactions; (2) an abrogated response to TGF-beta signaling by decreased phosphorylation and levels of Smad2/3 in tumor cells and (3) an impaired metalloproteolytic activity in vitro. Interestingly, coexpression of HDAC4 and PITX1 conferred high prometastatic activity in vivo. Further, levels of both genes correlated with patients at higher risk of metastasis in a clinical lung AC data set and with a poorer clinical outcome. These findings provide functional and clinical evidence that this metastatic subset is an important determinant of osseous colonization. These data suggest novel therapeutic targets to effectively block lung AC bone metastasis. Oncogene advance online publication, 28 October 2013; doi:10.1038/onc.2013.440.

[101]

TÍTULO / TITLE: - Patient satisfaction with service quality in an oncology setting: implications for prognosis in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Qual Health Care. 2013 Dec;25(6):696-703. doi: 10.1093/intqhc/mzt070. Epub 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [1093/intqhc/mzt070](#)

AUTORES / AUTHORS: - Gupta D; Rodeghier M; Lis CG

INSTITUCIÓN / INSTITUTION: - Cancer Treatment Centers of America, 1336 Basswood Road, Schaumburg, IL 60173, USA. christopher.lis@ctca-hope.com.

RESUMEN / SUMMARY: - OBJECTIVE: /st> To evaluate the relationship between self-reported satisfaction with service quality and overall survival in non-small cell lung cancer (NSCLC). DESIGN: /st> A prospective cohort study. SETTING: /st> Cancer Treatment Centers of America(®) from July 2007 and December 2010. PARTICIPANTS: /st> Nine hundred and eighty-six returning NSCLC patients. INTERVENTION: /st> Overall patient experience 'considering everything, how satisfied are you with your overall experience' was measured on a 7-point Likert scale ranging from 'completely dissatisfied' to 'completely satisfied.'. MAIN OUTCOME MEASURE: /st> Patient survival was the primary end point. RESULTS: /st> The response rate for this study was 69%. Six hundred patients were newly diagnosed, while 386 were previously treated. Four hundred sixty-nine were males, while 517 were females. 101,

59, 288 and 538 patients had stage I, II, III and IV disease, respectively. Mean age was 58.9 years. Six hundred and thirty (63.9%) patients had expired at the time of this analysis. Seven hundred and sixty-two (77.3%) patients were 'completely satisfied'. Median overall survival was 12.1 months (95% confidence interval (CI): 10.9-13.2 months). On univariate analysis, 'completely satisfied' patients had a significantly lower risk of mortality compared with those not 'completely satisfied' [hazard ratio (HR) = 0.70; 95% CI: 0.59-0.84; P < 0.001]. On multivariate analysis controlling for stage at diagnosis, prior treatment history, age and gender, 'completely satisfied' patients demonstrated significantly lower mortality (HR = 0.71; 95% CI: 0.60-0.85; P < 0.001) compared with those not 'completely satisfied'. CONCLUSIONS: Self-reported experience with service quality was an independent predictor of survival in NSCLC patients undergoing oncologic treatment, a novel finding in the literature. Based on these provocative findings, further exploration of this relationship is warranted in well-designed prospective studies.

[102]

TÍTULO / TITLE: - Current Status of Targeted Therapy for Anaplastic Lymphoma Kinase-Rearranged Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Pharmacol Ther. 2013 Oct 3. doi: 10.1038/clpt.2013.200.

●● Enlace al texto completo (gratis o de pago) [1038/clpt.2013.200](#)

AUTORES / AUTHORS: - Solomon B; Wilner KD; Shaw AT

INSTITUCIÓN / INSTITUTION: - 1] Department of Medical Oncology, Peter MacCallum Cancer Centre, East Melbourne, Australia [2] Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia.

RESUMEN / SUMMARY: - The identification of chromosomal rearrangements involving the anaplastic lymphoma kinase (ALK) gene in ~3-5% of non-small cell lung cancer (NSCLC) tissues and the demonstration that the first-in-class ALK tyrosine kinase inhibitor, crizotinib, can effectively target these tumors represent a significant advance in the evolution of personalized medicine for NSCLC. Single-arm studies demonstrating rapid and durable responses in the majority of ALK-positive NSCLC patients treated with crizotinib have been followed by a randomized phase III clinical trial in which superiority of crizotinib over chemotherapy was seen in previously treated ALK-positive NSCLC patients. However, despite the initial responses, most patients develop acquired resistance to crizotinib. Several novel therapeutic approaches targeting ALK-positive NSCLC are currently under evaluation in clinical trials, including second-generation ALK inhibitors, such as LDK378, CH5424802 (RO5424802802), and AP26113, and heat shock protein 90 inhibitors. Clinical Pharmacology & Therapeutics (2013); advance online publication 13 November 2013. doi:10.1038/clpt.2013.200.

[103]

TÍTULO / TITLE: - Differences in RRM1 protein expression between diagnostic biopsies and resection specimens, and changes during carboplatin and paclitaxel treatment, in non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Histopathology. 2013 Aug 26. doi: 10.1111/his.12264.

- Enlace al texto completo (gratis o de pago) 1111/his.12264

AUTORES / AUTHORS: - Jakobsen JN; Santoni-Rugiu E; Sorensen JB

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Rigshospitalet, Copenhagen, Denmark.

RESUMEN / SUMMARY: - AIMS: It is of interest whether expression of potentially predictive biomarkers changes during chemotherapy, for accurate evaluation after first-line chemotherapy. This study aimed to evaluate changes in RRM1 expression during chemotherapy. MATERIALS AND METHODS: RRM1 immunohistochemistry was performed on tumour samples from a total of 118 NSCLC patients with stage T1-4N0-2M0 disease. Samples were included from 65 patients treated with paclitaxel and carboplatin before surgery [neoadjuvant chemotherapy (NAC) group], and 53 patients who had undergone surgery but not chemotherapy [operation (OP) group]. RESULTS: Discordant RRM1 expression (low versus high) was observed in 32% and 43% of paired diagnostic and subsequent resection specimens in the OP group and NAC group, respectively ($P = 0.913$). Ten (33%) and 12 (23%) tumours in the NAC group and the OP group, respectively, had increased RRM1 expression in the resection specimens ($P = 0.289$), and 12 (40%) and 19 (36%) tumours had decreased expression ($P = 0.707$). Eleven (50%) lymph node metastases had higher RRM1 expression following chemotherapy, and two (7%) had decreased expression. CONCLUSIONS: The substantial discordance between paired samples emphasizes the need for sufficient tumour tissue in biopsies when RRM1 expression is evaluated. No change in RRM1 expression was observed in primary tumours, but expression seemed to be higher in N2 lymph node metastases following chemotherapy. Tumour heterogeneity and potential post-chemotherapy changes should be considered when RRM1 expression is evaluated.

[104]

TÍTULO / TITLE: - Genetic variation in the TP63 gene is associated with lung cancer risk in the Han population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 4.

- Enlace al texto completo (gratis o de pago) 1007/s13277-013-1248-3

AUTORES / AUTHORS: - Hu QY; Jin TB; Wang L; Zhang L; Geng T; Liang G; Kang LL

INSTITUCIÓN / INSTITUTION: - Key Laboratory of High Altitude Environment and Genes Related to Diseases of Tibet Autonomous Region, School of Medicine, Tibet University for Nationalities, Xianyang, Shaanxi, 712082, China.

RESUMEN / SUMMARY: - Lung cancer is one of the most common malignant tumors that seriously threaten human health. Current evidence suggests that heredity contributes to the progression of lung cancer. To investigate and validate potential genetic associations with the risk of lung cancer, we conducted a case-control study including 309 cases and 310 controls from Xi'an City, which is located in northwest China, and genotyped six SNPs in five genes, which are related to metabolic process. Overall, our results show that the SNP rs10937405 was associated with a decreased occurrence of lung cancer (OR = 0.72; 95 % CI = 0.56-0.92; $p = 0.009$). In the genetic models analysis, we found that genotype "CT" of rs10937405 in TP63 was associated with a decreased lung cancer risk (OR = 0.71; 95 % CI, 0.51-0.99; $p = 0.031$); the genotype "TT" of rs10937405 showed a decreased lung cancer risk in the co-dominant

model (OR = 0.53; 95 % CI, 0.30-0.95; p = 0.031). The genotype "CT-TT" of rs10937405 also showed a decreased lung cancer risk in the dominant model (OR = 0.67; 95 % CI, 0.49-0.92; p = 0.014) and the log-additive model (OR = 0.72; 95 % CI, 0.56-0.92; p = 0.0085). The genotype "CC-CT" of rs10937405 confers a higher risk of lung cancer for males than females. Our results, combined with those from previous studies, suggest that genetic variation in TP63 may influence lung cancer susceptibility in the Han population.

[105]

TÍTULO / TITLE: - Outcome Analysis of 18F-Fluorodeoxyglucose Positron-Emission Tomography in Patients with Lung Cancer After Partial Volume Correction.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):5193-8.

AUTORES / AUTHORS: - Ohtaka K; Hida Y; Kaga K; Okamoto S; Shiga T; Tamaki N; Muto J; Nakada-Kubota R; Hirano S; Matsui Y

INSTITUCIÓN / INSTITUTION: - Department of Cardiovascular and Thoracic Surgery, Hokkaido University Graduate School of Medicine, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan. yhida@med.hokudai.ac.jp.

RESUMEN / SUMMARY: - BACKGROUND: This study aimed to evaluate the necessity for the partial volume effect (PVE) correction of the maximum standardized uptake value (SUVmax) in (18)F-fluorodeoxyglucose positron-emission tomography (FDG-PET) for predicting outcome in patients with non-small cell lung cancer (NSCLC). PATIENTS AND METHODS: A total of 191 patients, with tumor diameters ranging from 10-37 mm, underwent pre-operative FDG-PET and curative resection. The SUVmax (Pre-SUV) of the primary tumor was corrected (Cor-SUV) using a recovery coefficient curve based on phantom experiments. RESULTS: The 5-year overall survival (OS) and disease-free survival (DFS) of the patients with high Pre-SUVs were lower than those with low Pre-SUVs (p<0.001 and p=0.002, respectively). The 5-year OS and DFS of patients with high Cor-SUVs were significantly lower than those with low Cor-SUVs (p<0.001 and p=0.005, respectively). CONCLUSION: Even without PVE correction, SUVmax was able to predict for outcome in patients with NSCLC.

[106]

TÍTULO / TITLE: - Review: Low-dose CT screening reduces lung cancer and mortality in current or former smokers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Intern Med. 2013 Nov 19;159(10):JC3. doi: 10.7326/0003-4819-159-10-201311190-02003.

●● [Enlace al texto completo \(gratis o de pago\) 7326/0003-4819-159-10-201311190-02003](#)

AUTORES / AUTHORS: - Lathan C; Frank DA

[107]

TÍTULO / TITLE: - Effects of postoperative epidural analgesia on recurrence-free and overall survival in patients with nonsmall cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Anesth. 2013 Oct 3. pii: S0952-8180(13)00243-2. doi: 10.1016/j.jclinane.2013.06.007.

●● Enlace al texto completo (gratis o de pago) [1016/j.jclinane.2013.06.007](#)

AUTORES / AUTHORS: - Cata JP; Gottumukkala V; Thakar D; Keerty D; Gebhardt R; Liu DD

INSTITUCIÓN / INSTITUTION: - Department of Anesthesiology and Perioperative Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA. Electronic address: jcata@mdanderson.org.

RESUMEN / SUMMARY: - **STUDY OBJECTIVE:** To determine whether postoperative epidural analgesia is associated with better recurrence-free survival and overall survival after lung cancer surgery. **DESIGN:** Retrospective study. **SETTING:** Academic hospital. **MEASUREMENTS:** Data of patients with stage 1, stage 2, and stage 3 nonsmall cell lung cancer, who underwent tumor resection surgery, were studied. Patient data were grouped into three different postoperative pain management interventions: intravenous patient-controlled analgesia, patient-controlled epidural analgesia, and their combination. Univariate and multivariate Cox proportional hazards models were applied to assess the effects of covariates of interest on overall survival and recurrence-free survival. **MAIN RESULTS:** The type of postoperative analgesia used for patients who underwent surgery for nonsmall cell lung cancer did not affect recurrence-free survival or overall survival. However, certain variables, including age ≥ 65 years, male gender, body mass index ≥ 25 kg/m², ASA physical status 4, and the need for preoperative blood transfusions, pneumonectomy, and postoperative radiation, were associated with decreased recurrence-free survival and overall survival. **CONCLUSIONS:** The type of postoperative analgesia used after surgery for nonsmall cell lung cancer is not associated with better 2-year or 5-year recurrence-free survival or overall survival rates.

[108]

TÍTULO / TITLE: - MUC1 in macrophage contributions to cigarette smoke-induced lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [1158/0008-5472.CAN-13-1713](#)

AUTORES / AUTHORS: - Xu X; Padilla MT; Li B; Wells A; Kato K; Tellez C; Belinsky SA; Kim KC; Lin Y

INSTITUCIÓN / INSTITUTION: - Molecular Biology and lung cancer program, Lovelace Respiratory Research Institute.

RESUMEN / SUMMARY: - Expression of the pro-oncogenic mucin MUC1 is elevated by inflammation in airway epithelial cells, but the contributions of MUC1 to the development of lung cancer are uncertain. In this study, we developed our finding that cigarette smoke (CS) increases Muc1 expression in lung macrophages, where we hypothesized it might contribute to CS-induced transformation of bronchial epithelial cells. In human macrophages, CS extract (CSE) strongly induced MUC1 expression through a mechanism involving the nuclear receptor PPAR-gamma. CSE-induced ERK activation was also required for MUC1 expression, but it had little effect on MUC1

transcription. RNAi-mediated attenuation of MUC1 suppressed CSE-induced secretion of TNF-alpha from macrophages, by suppressing the activity of the TNF-alpha processing enzyme TACE, arguing that MUC1 is required for CSE-induced and TACE-mediated TNF-alpha secretion. Similarly, MUC1 blockade after CSE induction through suppression of PPAR-gamma or ERK inhibited TACE activity and TNF-alpha secretion. Conditioned media from CSE-treated macrophages induced MUC1 expression and potentiated CSE-induced transformation of human bronchial epithelial cells (HBEc) in a TNF-alpha-dependent manner. Together, our results identify a signaling pathway involving PPAR-gamma, ERK and MUC1 that is used by CSE to trigger TNF-alpha secretion from macrophages. Further, our results show how that MUC1 contributes to smoking-induced lung cancers that are driven by inflammatory signals driven by macrophages.

[109]

TÍTULO / TITLE: - TRAF4 Is a Critical Molecule for Akt Activation in Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Dec 1;73(23):6938-50. doi: 10.1158/0008-5472.CAN-13-0913. Epub 2013 Oct 23.

●● Enlace al texto completo (gratis o de pago) [1158/0008-5472.CAN-13-0913](#)

AUTORES / AUTHORS: - Li W; Peng C; Lee MH; Lim D; Zhu F; Fu Y; Yang G; Sheng Y; Xiao L; Dong X; Ma W; Bode AM; Cao Y; Dong Z

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: The Hormel Institute, University of Minnesota, Austin, Minnesota; Cancer Research Institute, Xiangya School of Medicine; Xiangya Hospital, Central South University, Changsha, Hunan; The First Affiliated Hospital; and Physiology and Pathophysiology, Basic Medical School, Zhengzhou University, Zhengzhou, Henan, China.

RESUMEN / SUMMARY: - TRAF4 is an adapter protein overexpressed in certain cancers, but its contributions to tumorigenesis are unclear. In lung cancer cells and primary lung tumors, we found that TRAF4 is overexpressed. RNA interference-mediated attenuation of TRAF4 expression blunted the malignant phenotype in this setting, exerting inhibitory effects on cell proliferation, anchorage-independent growth, and tumor development in a xenograft mouse model. Unexpectedly, we discovered that TRAF4, but not Skp2, was required for activation of the pivotal cell survival kinase Akt through ubiquitination. Furthermore, TRAF4 attenuation impaired glucose metabolism by inhibiting expression of Glut1 and HK2 mediated by the Akt pathway. Overall, our work suggests that TRAF4 offers a candidate molecular target for lung cancer prevention and therapy. Cancer Res; 73(23); 6938-50. ©2013 AACR.

[110]

TÍTULO / TITLE: - Adaptive radiotherapy of lung cancer patients with pleural effusion or atelectasis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Oct 31. pii: S0167-8140(13)00521-5. doi: 10.1016/j.radonc.2013.10.013.

●● Enlace al texto completo (gratis o de pago) [1016/j.radonc.2013.10.013](#)

AUTORES / AUTHORS: - Moller DS; Khalil AA; Knap MM; Hoffmann L

INSTITUCIÓN / INSTITUTION: - Department of Medical Physics, Aarhus University Hospital, Denmark. Electronic address: dittmoel@rm.dk.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: Changes in lung density due to atelectasis, pleural effusion and pneumonia/pneumonitis are observed in lung cancer patients. These changes may be an indication for adaptive radiotherapy in order to maintain target coverage and avoid increased risk of normal tissue complications. MATERIAL AND METHODS: CBCT scans of 163 patients were reviewed to score lung changes and find the incidence, the impact of geometric and dosimetric changes and the timing of appearance and disappearance of changes. RESULTS: 23% of the patients had changes in the lung related to pleural effusion, atelectasis or pneumonia/pneumonitis. In 9% of all patients, the appearance or disappearance of a change introduced a shift of the tumor or lymph nodes relative to the spine >5mm. Only major density changes affected the dose distribution, and 9% of all patients needed adaptive treatment planning due to density changes. In total, 12% of all patients did benefit from an adaptive treatment plan and in 85% of these patients, an atelectasis did change. CONCLUSIONS: An adaptive strategy was indicated for 12% of the patients due to atelectasis, pleural effusion or pneumonia/pneumonitis. The predominant cause for adaptation was atelectasis. No systematic pattern in the appearance and disappearance of the changes were observed and hence weekly evaluation is preferable.

[111]

TÍTULO / TITLE: - EZH2 Protein Expression Associates with the Early Pathogenesis, Tumor Progression, and Prognosis of Non-Small Cell Lung Carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Dec 1;19(23):6556-65. doi: 10.1158/1078-0432.CCR-12-3946. Epub 2013 Oct 4.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-12-3946](#)

AUTORES / AUTHORS: - Behrens C; Solis LM; Lin H; Yuan P; Tang X; Kadara H; Riquelme E; Galindo H; Moran CA; Kalhor N; Swisher SG; Simon GR; Stewart DJ; Lee JJ; Wistuba II

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Thoracic/Head and Neck Medical Oncology, Pathology, Biostatistics, Thoracic Surgery, and Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, Texas; and The University of Ottawa, Ottawa, Canada.

RESUMEN / SUMMARY: - PURPOSE: Enhancer of zeste homolog 2 (EZH2) promotes carcinogenesis by epigenetically silencing tumor suppressor genes. We studied EZH2 expression by immunohistochemistry in a large series of non-small cell lung carcinomas (NSCLC) in association with tumor characteristics and patient outcomes. EXPERIMENTAL DESIGN: EZH2 immunohistochemistry expression was analyzed in 265 normal and premalignant bronchial epithelia, 541 primary NSCLCs [221 squamous cell carcinomas (SCC) and 320 adenocarcinomas] and 36 NSCLCs with paired brain metastases. An independent set of 91 adenocarcinomas was also examined. EZH2 expression was statistically correlated with clinico-pathological information, and EGFR/KRAS mutation status. RESULTS: EZH2 expression was significantly (P <

0.0001) higher in SCCs compared with adenocarcinomas and in brain metastasis relative to matched primary tumors (P = 0.0013). EZH2 expression was significantly (P < 0.0001) elevated in bronchial preneoplastic lesions with increasing severity. In adenocarcinomas, higher EZH2 expression significantly correlated with younger age, cigarette smoking, and higher TNM stage (P = 0.02 to P < 0.0001). Higher EZH2 expression in adenocarcinoma was associated with worse recurrence-free survival (RFS; P = 0.025; HR = 1.54) and overall survival (OS; P = 0.0002; HR = 1.96). Furthermore, lung adenocarcinomas with low EZH2 levels and high expression of the lineage-specific transcription factor, TTF-1, exhibited significantly improved RFS (P = 0.009; HR = 0.51) and OS (P = 0.0011; HR = 0.45), which was confirmed in the independent set of 91 adenocarcinomas. CONCLUSION: In lung, EZH2 expression is involved in early pathogenesis of SCC and correlates with a more aggressive tumor behavior of adenocarcinoma. When EZH2 and TTF-1 expressions are considered together, they serve as a prognostic marker in patients with surgically resected lung adenocarcinomas. Clin Cancer Res; 19(23); 6556-65. ©2013 AACR.

[112]

TÍTULO / TITLE: - Integrins and their ligands are expressed in non-small cell lung cancer but not correlated with parameters of disease progression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Virchows Arch. 2013 Nov 26.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00428-013-1506-1](#)

AUTORES / AUTHORS: - Boger C; Kalthoff H; Goodman SL; Behrens HM; Rocken C
INSTITUCIÓN / INSTITUTION: - Department of Pathology, Christian-Albrechts-University, Arnold-Heller-Str. 3, Haus 14, 24105, Kiel, Germany.

RESUMEN / SUMMARY: - The aim of this study was to investigate the expression of integrins, their ligands, and integrin signaling-related molecules in a cohort of human primary non-small cell lung cancers (NSCLC). Formalin-fixed and paraffin-embedded tissue samples from 215 NSCLC were immunohistochemically stained using antibodies directed against α v β 3, α v β 5, α v β 6, α v β 8, α v, osteopontin, fibronectin, vitronectin, epidermal growth factor (EGFR), vascular endothelial growth factor receptor (VEGFR), and Ki67. Immunostaining of tumor, stroma, and endothelial cells was evaluated separately by quantity and intensity (tumor cells) or intensity (stroma and endothelial cells) expressed in an immunoreactivity score. We studied correlations between the staining patterns of the different markers and of marker expression with clinicopathological data and patient survival. In the majority of NSCLC, each marker was expressed in at least one tumor component. As expected, α v and α v integrin heterodimers were significantly co-expressed, as were integrins and EGFR. Vitronectin was expressed significantly more often in smaller (T-category) and in well-differentiated tumors; Ki67 index was higher in larger (T-category) and in poorly differentiated tumors. No significant correlation was found between any marker expression and gender, venous invasion, lymph vessel invasion, lymph node metastasis, or survival. Although integrin expression does not seem to be associated with indicators of progression of NSCLC, the expression of α v β 3 in 89 % and α v β 5 in 100 % of NSCLC is novel and merits to be further investigated.

[113]

TÍTULO / TITLE: - Co-expression of Rho guanine nucleotide exchange factor 5 and Src associates with poor prognosis of patients with resected non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2864-70. doi: 10.3892/or.2013.2797. Epub 2013 Oct 14.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2797](#)

AUTORES / AUTHORS: - He P; Wu W; Wang H; Liao K; Zhang W; Xiong G; Wu F; Meng G; Yang K

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, Southwest Hospital, Third Military Medical University, 400038 Chongqing, P.R. China.

RESUMEN / SUMMARY: - Specific and sensitive enough molecular biomarkers are lacking to accurately predict the survival of non-small cell lung cancer (NSCLC) patients. ARHGEF5 and Src have been shown to play an important role in tumorigenesis. However, the involvement of ARHGEF5 and Src in NSCLC remains unknown. Therefore, we evaluated the expression of ARHGEF5 and Src in resected NSCLC tissues and the correlation of co-expression of ARHGEF5 and Src and the prognosis of patients with resected NSCLC. Positive expression of ARHGEF5 was detected in 133 cases of 193 patients (68.91%). A total of 193 NSCLC patients (male: 145; female: 48; average age: 61.84 years; age range: 31-84) were enrolled in this study, of which 99 cases were squamous cell carcinomas (SCCs) (51.30%) and 94 cases were adenocarcinomas (ADCs) (48.70%). The expression of ARHGEF5 was mainly located in the cytoplasm of tumor cells, but not in the corresponding adjacent lung tissues. The levels of ARHGEF5 were significantly associated with age, differentiation and tumor stage. ARHGEF5 protein expression was associated with Src protein expression in NSCLC ($\chi^2 = 11.874$, $P < 0.01$) and in ADC ($\chi^2 = 12.194$, $P < 0.01$), but not in SCC. Co-immunoprecipitation revealed that there was a physical interaction between Src and ARHGEF5 in lung cancer cells. The patients with ARHGEF5(+)/Src(+) had a shorter survival time compared with the other patients (29.37 months versus 39.90 months, $P = 0.029$). In conclusion, ARHGEF5/Src can be considered as a prognostic biomarker and a therapeutic target for patients with resected NSCLC.

[114]

TÍTULO / TITLE: - Genetic polymorphisms involved in the inflammatory response and lung cancer risk: A case-control study in Japan.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cytokine. 2014 Jan;65(1):88-94. doi: 10.1016/j.cyto.2013.09.015. Epub 2013 Oct 15.

●● Enlace al texto completo (gratis o de pago) [1016/j.cyto.2013.09.015](#)

AUTORES / AUTHORS: - Kiyohara C; Horiuchi T; Takayama K; Nakanishi Y

INSTITUCIÓN / INSTITUTION: - Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University, Maidashi 3-1-1, Higashi-ku, Fukuoka 812-8582, Japan. Electronic address: chikako@phealth.med.kyushu-u.ac.jp.

RESUMEN / SUMMARY: - Evidence is accumulating that chronic inflammation may have an important mechanism for the development and progression of lung cancer.

Therefore, genetic polymorphisms in genes that involved in the inflammatory response may be associated with lung cancer risk. We evaluated the role of tumor necrosis factor alpha (TNFA) rs1799724, interleukin 1beta (IL1B) rs16944, IL6 rs1800796, myeloperoxidase (MPO) rs2333227 and C-reactive protein (CRP) rs2794520 in a case-control study comprised of 462 lung cancer cases and 379 controls in a Japanese population. Unconditional logistic regression was used to assess the adjusted odds ratios (OR) and 95% confidence intervals (95% CI). CRP rs2794520 (OR=1.64, 95% CI=1.19-2.26) and IL6 rs1800796 (OR=1.41, 95% CI=1.02-1.96) were associated with lung cancer risk. In addition, we assessed interactions between the polymorphisms and smoking. The polymorphisms did not significantly modify the association between smoking and lung cancer. As TNFA triggers a cytokine cascade, the modifying effect of the TNFA rs1799724 genotypes on the association of any of the remaining polymorphisms with lung cancer risk was also examined. There was a significant interaction between TNFA rs1799724 and MPO rs2333227 (Pinteraction=0.058). Future studies involving larger control and case populations will undoubtedly lead to a more thorough understanding of the role of the polymorphisms involved in the inflammation pathway in lung cancer.

[115]

TÍTULO / TITLE: - Targeting of the Hedgehog signal transduction pathway suppresses survival of malignant pleural mesothelioma cells in vitro.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Oct 3. pii: S0022-5223(13)00955-0. doi: 10.1016/j.jtcvs.2013.08.035.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.08.035](#)

AUTORES / AUTHORS: - You M; Varona-Santos J; Singh S; Robbins DJ; Savaraj N; Nguyen DM

INSTITUCIÓN / INSTITUTION: - Thoracic Surgery Section, Division of Cardiothoracic Surgery, Department of Surgery, Sylvester Comprehensive Cancer Center, Leonard M. Miller School of Medicine, University of Miami, Miami, Fla.

RESUMEN / SUMMARY: - OBJECTIVE: The present study sought to determine whether the Hedgehog (Hh) pathway is active and regulates the cell growth of cultured malignant pleural mesothelioma (MPM) cells and to evaluate the efficacy of pathway blockade using smoothened (SMO) antagonists (SMO inhibitor GDC-0449 or the antifungal drug itraconazole [ITRA]) or Gli inhibitors (GANT61 or the antileukemia drug arsenic trioxide [ATO]) in suppressing MPM viability. METHODS: Selective knockdown of SMO to inhibit Hh signaling was achieved by small interfering RNA in 3 representative MPM cells. The growth inhibitory effect of GDC-0449, ITRA, GANT61, and ATO was evaluated in 8 MPM lines, with cell viability quantified using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Cell death was determined by annexinV/propidium iodide staining and flow cytometry. RESULTS: SMO small interfering RNA mediated a two- to more than fivefold reduction of SMO and Gli1 gene expression as determined by real-time quantitative reverse-transcriptase polymerase chain reaction, indicating significant Hh pathway blockade. This was associated with significantly reduced cell viability (34% +/- 7% to 61% +/- 14% of nontarget small interfering RNA controls; P = .0024 to P = .043). Treating MPM cells with Hh inhibitors resulted in a 1.5- to 4-fold reduction of Gli1 expression. These 4 Hh

antagonists strongly suppressed MPM cell viability. More importantly, ITRA, ATO, GANT61 induced significant apoptosis in the representative MPM cells.
CONCLUSIONS: Hh signaling is active in MPM and regulates cell viability. ATO and ITRA were as effective as the prototypic SMO inhibitor GDC-0449 and the Gli inhibitor GANT61 in suppressing Hh signaling in MPM cells. Pharmaceutical agents Food and Drug Administration-approved for other indications but recently found to have anti-Hh activity, such as ATO or ITRA, could be repurposed to treat MPM.

[116]

TÍTULO / TITLE: - The Janus Kinases Inhibitor AZD1480 Attenuates Growth of Small Cell Lung Cancers In Vitro and In Vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-1110](#)

AUTORES / AUTHORS: - Lee JH; Park KS; Alberobello AT; Kallakury B; Weng MT; Wang Y; Giaccone G

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Medical Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland; and Lombardi Comprehensive Cancer Center, Georgetown University, Washington, District of Columbia.

RESUMEN / SUMMARY: - PURPOSE: The prognosis of small cell lung cancer (SCLC) is poor, and there has been very little progress in the medical treatment of SCLC in the past two decades. We investigated the potential of Janus-activated kinases (JAK) inhibitor, AZD1480, for treatment of SCLC in vitro and in vivo. EXPERIMENTAL DESIGN: JAK1 and JAK2 were inhibited by AZD1480 or siRNAs, and the effect of inhibition of JAK gene family on SCLC cell viability was evaluated. The effect of AZD1480 on cell-cycle distribution and apoptosis induction was studied. Antitumor effects of AZD1480 in tumor xenografts were assessed. RESULTS: AZD1480 significantly inhibited growth of six out of 13 SCLC cells with IC50s ranging from 0.73 to 3.08 $\mu\text{mol/L}$. Knocking down of JAK2 and JAK1 inhibited proliferation of Jak2-positive/Jak1-negative H82 cells and Jak1-positive/Jak2-negative GLC4 cells, respectively. Treatment of SCLC cells with AZD1480 for 24 hours resulted in an increase of 4N DNA content and histone 3 serine 10 phosphorylation, indicative of G2-M phase arrest. Moreover, SCLCs underwent apoptosis after AZD1480 treatment as exemplified by the downregulation of MCL1, the accumulation of cleaved caspase 3, cleaved PARP, and increase of annexin-V-positive cells. Finally, xenograft experiments showed that AZD1480 attenuated the growth of H82 and GLC4 tumors in mice, and we observed stronger apoptosis as well as decreased CD31-positive endothelial cells in H82 and GLC4 xenografts upon AZD1480 treatment. CONCLUSIONS: JAK inhibitor AZD1480 attenuated growth of SCLC cells in vitro and in vivo. Clinical development of anti-JAKs therapies in SCLC warrants further investigation. Clin Cancer Res; 19(24); 1-10. ©2013 AACR.

[117]

TÍTULO / TITLE: - FDG PET/CT metabolic tumor volume and total lesion glycolysis predict prognosis in patients with advanced lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Clin Oncol. 2013 Nov 6.

●● Enlace al texto completo (gratis o de pago) [1007/s00432-013-1545-7](#)

AUTORES / AUTHORS: - Chung HW; Lee KY; Kim HJ; Kim WS; So Y

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Konkuk University Medical Center, Research Institute of Biomedical Science, Konkuk University School of Medicine, 120-1 Neungdong-ro, Hwayang-dong, Gwangjin-gu, Seoul, 143-729, Korea, hwchung@kuh.ac.kr.

RESUMEN / SUMMARY: - PURPOSE: We investigated fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT)-assessed metabolic tumor volume (MTV) and total lesion glycolysis (TLG) as prognostic factors in lung adenocarcinoma patients. METHODS: This retrospective study included 106 patients (19 stage I/II and 87 stage III/IV lung adenocarcinoma) who underwent FDG PET/CT before treatment. Standardized uptake value (SUV), MTV, and TLG (MTV x mean SUV) of each malignant lesion were measured. Whole MTV and whole TLG were the summation of all the MTV and TLG values in each patient. Survival analysis and FDG PET/CT parameters regarding epidermal growth factor receptor (EGFR) gene mutation status were evaluated. RESULTS: Univariate survival analysis of stage III/IV patients identified high whole MTV (≥ 90), high whole TLG (≥ 600), and stage IV as significant predictors of poor progression-free survival. For overall survival, high whole MTV (≥ 90), high whole TLG (≥ 600), EGFR mutation-negative, and stage IV were significant poor prognostic predictors. After multivariate survival analysis, high whole MTV ($P = 0.001$), high whole TLG ($P = 0.027$), and stage IV ($P = 0.006$) were independent predictors of poor progression-free survival. High whole MTV ($P < 0.001$), high whole TLG ($P = 0.001$), and EGFR mutation-negative ($P = 0.001$) were independent prognostic predictors for poor overall survival. In a survival analysis of stage I/II patients, none was an independent prognostic predictor. No significant differences were found in FDG PET/CT parameters for EGFR mutation-negative and EGFR mutation-positive patients. CONCLUSIONS: Assessment of MTV and TLG by FDG PET/CT in advanced lung adenocarcinoma patients provides useful information regarding prognosis.

[118]

TÍTULO / TITLE: - A novel synthetic analog of militarin, MA-1 induces mitochondrial dependent apoptosis by ROS generation in human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Toxicol Appl Pharmacol. 2013 Oct 22. pii: S0041-008X(13)00463-8. doi: 10.1016/j.taap.2013.10.015.

●● Enlace al texto completo (gratis o de pago) [1016/j.taap.2013.10.015](#)

AUTORES / AUTHORS: - Yoon DH; Lim MH; Lee YR; Sung GH; Lee TH; Jeon BH; Cho JY; Song WO; Park H; Choi S; Kim TW

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Kangwon National University, Chuncheon 200-701, Republic of Korea.

RESUMEN / SUMMARY: - A synthetic Militarin analog-1[(2R,3R,4R,5R)-1,6-bis(4-(2,4,4-trimethylpentan-2-yl)phenoxy) hexane-2,3,4,5-tetraol] is a novel derivative of

constituents from *Cordyceps militaris*, which has been used to treat a variety of chronic diseases including inflammation, diabetes, hyperglycemia and cancers. Here, we report for the first time the synthesis of Militararin analog-1 (MA-1) and the apoptotic mechanism of MA-1 against human lung cancer cell lines. Treatment with MA-1 significantly inhibited the viability of 3 human lung cancer cell lines. The inhibition of viability and growth in MA-1-treated A549 cells with an IC₅₀ of 5 μM were mediated through apoptosis induction, as demonstrated by an increase in DNA fragmentation, sub-G₀/G₁-DNA fraction, nuclear condensation, and phosphatidylserine exposure. The apoptotic cell death caused mitochondrial membrane permeabilization through regulation of expression of the Bcl-2 family proteins, leading to cytochrome c release in a time-dependent manner. Subsequently, the final stage of apoptosis, activation of caspase-9/-3 and cleavage of poly (ADP ribose) polymerase, was induced. Furthermore, A549 lung cancer cells were more responsive to MA-1 than a bronchial epithelial cell line (BEAS-2B), involving the rapid generation of reactive oxygen species (ROS), c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) activation. The pharmacological inhibition of ROS generation and JNK/p38 MAPK exhibited attenuated DNA fragmentation in MA-1-induced apoptosis. Oral administration of MA-1 also retarded growth of A549 orthotopic xenografts. In conclusion, the present study indicates that the new synthetic derivative MA-1 triggers mitochondrial apoptosis through ROS generation and regulation of MAPKs and may be a potent therapeutic agent against human lung cancer.

[119]

TÍTULO / TITLE: - Potential diagnostic value of miR-155 in serum from lung adenocarcinoma patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - *Oncol Rep.* 2014 Jan;31(1):351-7. doi: 10.3892/or.2013.2830. Epub 2013 Nov 1.

●● [Enlace al texto completo \(gratis o de pago\) 3892/or.2013.2830](#)

AUTORES / AUTHORS: - Gao F; Chang J; Wang H; Zhang G

INSTITUCIÓN / INSTITUTION: - Division of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, Henan 450052, P.R. China.

RESUMEN / SUMMARY: - Recent studies have demonstrated that microRNAs (miRNAs) are stably detectable in plasma/serum. The expression profile of miR-21 and miR-155 was evaluated in the present study, since miR-21 is frequently reported as highly expressed in several types of cancers, while miR-155 was also found to be significantly expressed in lung cancer cell lines. Using in vitro studies, we found that miR-155 could be a candidate plasmatic biomarker for diagnosing lung cancer. We assessed the differences in levels of miR-21, miR-155, carcinoembryonic antigen (CEA) and carbohydrate antigen 125 (CA-125) expression in serum samples between lung cancer patients and healthy controls. We estimating the clinical diagnostic value of miR-155 independently and combined with CA-125 and/or CEA levels. The present study consisted of three parts: i) confirmation of the stable expression of miR-155 in the patient serum samples using quantitative PCR; ii) confirmation of higher miR-155, CEA and CA-125 levels in the patient serum samples when compared with levels in the normal controls by quantitative PCR; iii) evaluation of miR-155, CEA and CA-125

concentrations in serum samples for tumor diagnosis of lung adenocarcinoma via ROC (receiver-operating characteristic) analysis. The results showed that i) expression of miR-155 was significantly higher in the serum of lung adenocarcinoma patients than that in normal controls ($P < 0.05$); ii) testing results of serum miR-155 levels showed a much higher sensitivity (0.722) than that for CA-125 or CEA; iii) CEA associated with CA-125 had the highest Youden's index (0.639) in all terms of combinations; and iv) combined with CA-125 testing, miR-155 received a competitive sensitivity (0.889) and specificity (0.688) for diagnosing lung adenocarcinoma (OOP=14.88). In conclusion, endogenous miR-155 stably existed in patient serum and could be sensitively and specifically measured. Overexpression of miR-155 in serum specimens could constitute a diagnostic marker for the early detection of lung adenocarcinoma.

[120]

TÍTULO / TITLE: - Enhancement of antitumor immunity in lung cancer by targeting myeloid-derived suppressor cell pathways.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Nov 15;73(22):6609-20. doi: 10.1158/0008-5472.CAN-13-0987. Epub 2013 Oct 1.

●● Enlace al texto completo (gratis o de pago) [1158/0008-5472.CAN-13-](#)

[0987](#)

AUTORES / AUTHORS: - Sawant A; Schafer CC; Jin TH; Zmijewski J; Tse HM; Roth J; Sun Z; Siegal GP; Thannickal VJ; Grant SC; Ponnazhagan S; Deshane JS

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Departments of Pathology, Medicine, Microbiology, and Pediatrics, The University of Alabama at Birmingham, Birmingham, Alabama.

RESUMEN / SUMMARY: - Chemoresistance due to heterogeneity of the tumor microenvironment (TME) hampers the long-term efficacy of first-line therapies for lung cancer. Current combination therapies for lung cancer provide only modest improvement in survival, implicating necessity for novel approaches that suppress malignant growth and stimulate long-term antitumor immunity. Oxidative stress in the TME promotes immunosuppression by tumor-infiltrating myeloid-derived suppressor cells (MDSC), which inhibit host protective antitumor immunity. Using a murine model of lung cancer, we demonstrate that a combination treatment with gemcitabine and a superoxide dismutase mimetic targets immunosuppressive MDSC in the TME and enhances the quantity and quality of both effector and memory CD8(+) T-cell responses. At the effector cell function level, the unique combination therapy targeting MDSC and redox signaling greatly enhanced cytolytic CD8(+) T-cell response and further decreased regulatory T cell infiltration. For long-term antitumor effects, this therapy altered the metabolism of memory cells with self-renewing phenotype and provided a preferential advantage for survival of memory subsets with long-term efficacy and persistence. Adoptive transfer of memory cells from this combination therapy prolonged survival of tumor-bearing recipients. Furthermore, the adoptively transferred memory cells responded to tumor rechallenge exerting long-term persistence. This approach offers a new paradigm to inhibit immunosuppression by direct targeting of MDSC function, to generate effector and persistent memory cells for tumor eradication, and to prevent lung cancer relapse. Cancer Res; 73(22); 6609-20. ©2013 AACR.

[121]

TÍTULO / TITLE: - SIRT1 and AMPK mediate hypoxia-induced resistance of non-small cell lung cancers to cisplatin and doxorubicin.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Nov 15.

●● Enlace al texto completo (gratis o de pago) [1158/0008-5472.CAN-13-2620](#)

AUTORES / AUTHORS: - Shin DH; Choi YJ; Park JW

INSTITUCIÓN / INSTITUTION: - Pharmacology, Seoul National University College of Medicine.

RESUMEN / SUMMARY: - SIRT1 is an NAD⁺-dependent protein deacetylase induced by metabolic stresses, such as nutrition or oxygen deprivation. Although SIRT1 contributes to aging and metabolic disorders, its role in cancer progression and therapeutic responses remains controversial. Since hypoxia occurs widely in solid tumors where it provokes drug resistance, we investigated the involvement of SIRT1 in hypoxia-induced chemoresistance. SIRT1 was downregulated in a panel of non-small cell lung carcinoma (NSCLC) cells exposed to hypoxia for 48 hours. The master metabolic kinase AMPK was inactivated under the same conditions, likely due to attenuation of the SIRT1/LKB1-mediated AMPK activation process. Notably, hypoxic inactivation of this SIRT1-AMPK pathway led to cisplatin and doxorubicin resistance. Mechanistic investigations suggested that this pathway supported the cytotoxic response to cisplatin and doxorubicin by licensing an apoptotic process controlled by mitochondria. We confirmed the involvement of this pathway in a mouse xenograft model of human NSCLC. Further, we demonstrated that a SIRT1 activator SRT1720 augmented the antitumor effects of cisplatin, and these effects could be blocked by administration of an AMPK inhibitor compound C. Taken together, our results offer preclinical proof of concept to target the SIRT1-AMPK pathway as a strategy to overcome hypoxia-induced chemoresistance in NSCLC.

[122]

TÍTULO / TITLE: - YEATS4 is a novel oncogene amplified in non-small cell lung cancer that regulates the p53 pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [1158/0008-5472.CAN-13-1897](#)

AUTORES / AUTHORS: - Pikor LA; Lockwood WW; Thu KL; Vucic EA; Chari R; Gazdar AF; Lam S; Lam WL

INSTITUCIÓN / INSTITUTION: - Integrative Oncology Genetics Unit, BC Cancer Research Centre.

RESUMEN / SUMMARY: - Genetic analyses of lung cancer have helped find new treatments in this disease. We conducted an integrative analysis of gene expression and copy number in 261 non-small cell lung cancers (NSCLC) relative to matched normal tissues to define novel candidate oncogenes, identifying 12q13-15 and more specifically the YEATS4 gene as amplified and overexpressed in ~20% of the NSCLC

cases examined. Overexpression of YEATS4 abrogated senescence in human bronchial epithelial cells (HBECS). Conversely, RNAi-mediated attenuation of YEATS4 in human lung cancer cells reduced their proliferation and tumor growth, impairing colony formation and inducing cellular senescence. These effects were associated with increased levels of p21WAF1 and p53 and cleavage of PARP, implicating YEATS4 as a negative regulator of the p21-p53 pathway. We also found that YEATS4 expression affected cellular responses to cisplatin, with increased levels associated with resistance and decreased levels with sensitivity. Taken together, our findings reveal YEATS4 as a candidate oncogene amplified in NSCLC, and a novel mechanism contributing to NSCLC pathogenesis.

[123]

TÍTULO / TITLE: - ERK1/2 BLOCKADE PREVENTS EPITHELIAL-MESENCHYMAL TRANSITION IN LUNG CANCER CELLS AND PROMOTES THEIR SENSITIVITY TO EGFR INHIBITION.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. 2013 Oct 9.

●● [Enlace al texto completo \(gratis o de pago\) 1158/0008-5472.CAN-12-](#)

[4721](#)

AUTORES / AUTHORS: - Buonato JM; Lazzara MJ

INSTITUCIÓN / INSTITUTION: - Chemical and Biomolecular Engineering, University of Pennsylvania.

RESUMEN / SUMMARY: - Overcoming cellular mechanisms of de novo and acquired resistance to drug therapy remains a central challenge in the clinical management of many cancers, including non-small cell lung cancer (NSCLC). While much work has linked the epithelial-mesenchymal transition (EMT) in cancer cells to the emergence of drug resistance, it is less clear where tractable routes may exist to reverse or inhibit EMT as a strategy for drug sensitization. Here, we demonstrate that ERK1/2 (MAPK3/1) signaling plays a key role in directing the mesenchymal character of NSCLC cells, and that blocking ERK signaling is sufficient to heighten therapeutic responses to EGFR inhibitors. MEK1/2 (MAPKK1/2) inhibition promoted an epithelial phenotype in NSCLC cells, preventing induction of EMT by exogenous TGFbeta. Moreover, in cells exhibiting de novo or acquired resistance to the EGFR inhibitor gefitinib, MEK inhibition enhanced sensitivity to gefitinib and slowed cell migration. These effects only occurred, however, if MEK was inhibited for a period sufficient to trigger changes in EMT marker expression. Consistent with these findings, changes in EMT phenotypes and markers were also induced by expression of mutant KRAS in a MEK-dependent manner. Our results suggest that prolonged exposure to MEK or ERK inhibitors may not only restrain EMT but overcome naive or acquired resistance of NSCLC to EGFR-targeted therapy in the clinic.

[124]

TÍTULO / TITLE: - Scrib heterozygosity predisposes to lung cancer and cooperates with KRas hyperactivation to accelerate lung cancer progression in vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Nov 25. doi: 10.1038/onc.2013.498.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.498](https://doi.org/10.1038/onc.2013.498)

AUTORES / AUTHORS: - Elsum IA; Yates LL; Pearson HB; Phesse TJ; Long F; O'Donoghue R; Ernst M; Cullinane C; Humbert PO

INSTITUCIÓN / INSTITUTION: - Cell Cycle and Cancer Genetics, Research Division, Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia.

RESUMEN / SUMMARY: - Lung cancer is the leading cause of cancer deaths worldwide with non small-cell lung cancer (NSCLC) accounting for 80% of all lung cancers. Although activating mutations in genes of the RAS-MAPK pathway occur in up to 30% of all NSCLC, the cooperating genetic lesions that are required for lung cancer initiation and progression remain poorly understood. Here we identify a role for the cell polarity regulator Scribble (Scrib) in NSCLC. A survey of genomic databases reveals deregulation of SCRIB in human lung cancer and we show that Scrib^{+/-} mutant mice develop lung cancer by 540 days with a penetrance of 43%. To model NSCLC development in vivo, we used the extensively characterized LSL-KRasG12D murine model of NSCLC. We show that loss of Scrib and activated oncogenic KRas cooperate in vivo, resulting in more aggressive lung tumors, likely due to a synergistic elevation in RAS-MAPK signaling. Finally, we provide data consistent with immune infiltration having an important role in the acceleration of tumorigenesis in KRasG12D lung tumors following Scrib loss. Oncogene advance online publication, 25 November 2013; doi:10.1038/onc.2013.498.

[125]

TÍTULO / TITLE: - SOX2 regulates apoptosis through MAP4K4-Survivin signaling pathway in human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Carcinogenesis. 2013 Nov 14.

●● Enlace al texto completo (gratis o de pago) [1093/carcin/bgt371](https://doi.org/10.1093/carcin/bgt371)

AUTORES / AUTHORS: - Chen S; Li X; Lu D; Xu Y; Mou W; Wang L; Chen Y; Liu Y; Li X; Li LY; Liu L; Stupack D; Reisfeld RA; Xiang R; Li N

INSTITUCIÓN / INSTITUTION: - School of Medicine, Nankai University, 94 Weijin Road, Tianjin, China 300071.

RESUMEN / SUMMARY: - Previous studies have implicated cancer stem cells in tumor recurrence, and revealed that the stem cell gene-SOX2 plays an important role in the tumor cell resistance to apoptosis. Nonetheless, the mechanism by which SOX2 regulates apoptosis signals remained undefined. Here, we demonstrated the surprising finding that silencing of the SOX2 gene effectively induces apoptosis via the activation of death receptor and mitochondrial signaling pathways in human non-small cell lung cancer (NSCLC) cells. Unexpectedly, RT-PCR analysis suggested that down-regulation of SOX2 leads to activation of MAP4K4, previously implicated in cell survival. Evaluation of the apoptotic pathways revealed an increased expression of key inducers of apoptosis, including TNF-alpha and p53, with concurrent attenuation of Survivin. While p53 appeared dispensable for this pathway, the loss of Survivin in SOX2 deficient cells appeared critical for the observed MAP4K4 induced cell death. Rescue experiments revealed that SOX2 silencing mediated killing was blocked by ectopic expression of Survivin, or by reduction of MAP4K4 expression. Clinically, expression of Survivin and SOX2 were highly correlated with each other and with poor outcome. The results reveal a key target of SOX2 expression and highlight the

unexpected context-dependent role for MAP4K4, a pluripotent activator of several MAPK pathways, in regulating tumor cell survival.

[126]

TÍTULO / TITLE: - Association of a Genetic Variant of CYP19A1 with Multicentric Development of Lung Adenocarcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3362-2](#)

AUTORES / AUTHORS: - Ikeda K; Shiraishi K; Eguchi A; Osumi H; Matsuishi K; Matsubara E; Fujino K; Shibata H; Yoshimoto K; Mori T; Omori H; Suzuki M

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan, koei@cg7.so-net.ne.jp.

RESUMEN / SUMMARY: - BACKGROUND: The detection rate of multiple lung adenocarcinomas, which display multiple ground glass opacity nodules in the peripheral lung, is increasing because of advances in high resolution computed tomography. The genetic backgrounds of multiple nodules and the mechanisms that underlie their multicentric development are unknown. In this study, we examined single nucleotide polymorphisms (SNPs) of the cytochrome P450 19A1 gene to determine if they are associated with multiple adenocarcinomas risk. METHODS: Fifty-one cases of multiple adenocarcinomas with lepidic growth, 62 cases of a single adenocarcinoma with lepidic growth, and 126 control cases were analyzed. Three SNPs were analyzed by using a 5' nuclease assay with TaqMan minor-groove-binder probe. The expression level of CYP19A1 in the noncancerous lung was quantified by real-time reverse transcription polymerase chain reaction (RT-PCR). RESULTS: A minor allele of SNP rs3764221, which is located in the CYP19A1 gene, was significantly associated with multiple adenocarcinomas risk (adjusted odds ratio = 3.06; P = 0.006). Other polymorphisms of CYP19A1 were not significantly associated with the risk of multiple adenocarcinomas. A minor allele of SNP rs3764221 was also associated with a higher level of CYP19A1 messenger RNA expression (P = 0.03). CONCLUSIONS: SNP rs3764221 contributes to the development of multicentric adenocarcinomas in the peripheral lung by causing higher levels of CYP19A1 expression.

[127]

TÍTULO / TITLE: - Loss of CDH1 up-regulates epidermal growth factor receptor via phosphorylation of YBX1 in non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - FEBS Lett. 2013 Dec 11;587(24):3995-4000. doi: 10.1016/j.febslet.2013.10.036. Epub 2013 Nov 5.

●● Enlace al texto completo (gratis o de pago) [1016/j.febslet.2013.10.036](#)

AUTORES / AUTHORS: - Liu X; Su L; Liu X

INSTITUCIÓN / INSTITUTION: - Shandong Provincial Key Laboratory of Animal Cells and Developmental Biology, Shandong University School of Life Sciences, Jinan, China.

RESUMEN / SUMMARY: - Although loss of CDH1 promotes cancer metastasis by disrupting cell-cell adhesion and inducing transcriptional changes, the functional

pathways involved in the loss of CDH1 affecting EGFR expression in lung cancer cells still remain largely unknown. In this study, we report that down-regulation of CDH1 promoted EGFR transcription through activation of YBX1. Furthermore, knockdown of CDH1 activated the AKT signaling pathway, and inhibition of AKT suppressed the phosphorylation of YBX1 and the up-regulation of EGFR induced by CDH1 loss. These data demonstrate that loss of CDH1 induces EGFR expression via phospho-YBX1, which is activated through the AKT signaling pathway.

[128]

TÍTULO / TITLE: - Skeletal muscle glycoprotein 130's role in Lewis lung carcinoma-induced cachexia.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - FASEB J. 2013 Oct 21.

●● Enlace al texto completo (gratis o de pago) [1096/fj.13-240580](#)

AUTORES / AUTHORS: - Puppa MJ; Gao S; Narsale AA; Carson JA

INSTITUCIÓN / INSTITUTION: - *Integrative Muscle Biology Laboratory, Department of Exercise Science, and.

RESUMEN / SUMMARY: - Chronic inflammation is associated with cachexia-induced skeletal muscle mass loss in cancer. Levels of IL-6 cytokine family members are increased during cancer-related cachexia and induce intracellular signaling through glycoprotein130 (gp130). Although muscle STAT3 and circulating IL-6 are implicated in cancer-induced muscle wasting, there is limited understanding of muscle gp130's role in this process. Therefore, we investigated the role of skeletal muscle gp130 (skm-gp130) in cancer-induced alterations in the regulation of muscle protein turnover. Lewis lung carcinoma (LLC) cells were injected into 8-wk-old skm-gp130-knockout (KO) mice or wild-type mice. Skeletal muscle loss was attenuated by 16% in gp130-KO mice, which coincided with attenuated LLC-induced phosphorylation of muscle STAT3, p38, and FOXO3. gp130 KO did not restore mTOR inhibition or alter AMP-activated protein kinase (AMPK) expression. The induction of atrogen expression and p38 phosphorylation in C2C12 myotubes exposed to LLC-treated medium was attenuated by gp130 inhibition, but mTOR inhibition was not restored. STAT signaling inhibition in LLC-treated myotubes did not attenuate the induction of p38 or AMPK phosphorylation. We concluded that, during LLC-induced cachexia, skm-gp130 regulates muscle mass signaling through STAT3 and p38 for the activation of FOXO3 and atrogen, but does not directly regulate the suppression of mTOR.-Puppa, M. J., Gao, S., Narsale, A. A., Carson, J. A. Skeletal muscle glycoprotein 130's role in Lewis lung carcinoma-induced cachexia.

[129]

TÍTULO / TITLE: - Trends in Asbestos and Non-asbestos Fibre Concentrations in the Lung Tissues of Japanese Patients with Mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Occup Hyg. 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [1093/annhyg/met055](#)

AUTORES / AUTHORS: - Sakai K; Hisanaga N; Shibata E; Kamijima M; Ichihara G; Takeuchi Y; Nakajima T

INSTITUCIÓN / INSTITUTION: - Nagoya City Public Health Research Institute, 1-11 Hagiya-cho, Mizuho-ku, Nagoya, Aichi 467-8615, Japan;

RESUMEN / SUMMARY: - **OBJECTIVES:** We aimed to elucidate changes in asbestos and non-asbestos fibre concentrations in the lung tissues of Japanese patients with mesothelioma over time. **METHODS:** Lung tissues were obtained from 46 patients with mesothelioma who died or underwent surgery between 1971 and 2005. All of the patients had a history of occupational asbestos exposure. We classified patients into four groups according to the period during which their lung tissue was obtained. Asbestos and non-asbestos fibre concentrations were determined by transmission electron microscopy with energy-dispersive X-ray analysis using a low-temperature ashing procedure. **RESULTS:** From the 1970s to the 2000s, we observed a decrease in the geometric mean of total asbestos concentration (67.4-1.05 million fibres per gram dry lung), chrysotile concentration (25.0-0.66 million fibres per gram dry lung), amphibole asbestos concentration (21.3-0.76 million fibres per gram dry lung), and non-asbestos fibre concentration (326-19.3 million fibres per gram dry lung). The mean duration of asbestos exposure decreased from 33.7 to 17.6 years, and the mean duration since the last exposure increased from 0.3 to 21.5 years. The percentage of longer fibres to total fibres tended to increase over time, whereas the mean fibre length did not differ significantly. **CONCLUSIONS:** The present study suggested that asbestos and non-asbestos fibre concentrations in the lung tissues of Japanese patients with mesothelioma who have occupational histories of asbestos exposure may have decreased from the 1970s to the 2000s.

[130]

TÍTULO / TITLE: - High-throughput Molecular Genotyping for Small Biopsy Samples in Advanced Non-small Cell Lung Cancer Patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):5127-33.

AUTORES / AUTHORS: - Maeng CH; Lee HY; Kim YW; Choi MK; Hong JY; Jung HA; Lee KS; Kim H; Kwon OJ; Sun JM; Ahn JS; Park K; Um SW; Ahn MJ

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary and Critical Care Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, South Korea. sangwon72.um@samsung.com.

RESUMEN / SUMMARY: - **BACKGROUND:** Despite the key role of mutational analysis in targeted therapy, the difficulty in acquisition of adequate tumor tissues for molecular genotyping in advanced non-small cell lung cancer (NSCLC) has led to the need for a fast and efficient method for detecting genetic alterations for targeted therapy.

PATIENTS AND METHODS: We analyzed tissue specimens of advanced NSCLC. A mass spectrometry-based assay was used to investigate 471 oncogenic mutations. All tumor specimens were prepared from fresh-frozen tissues. **RESULTS:** In total, there were 59 hotspot mutations in 67% of the entire patient group (41 out of 61 patients). The most frequent mutation was in TP53 (n=24, 39.3%), followed by EGFR (n=19, 31.1%). Others included MLH1, KRAS, PIK3CA, ERBB2, ABL1 and HRAS.

CONCLUSION: Our results suggest that molecular genotyping using high-throughput technology such as OncoMap v4 is feasible, even with small biopsied specimens from patients with advanced NSCLC.

[131]

TÍTULO / TITLE: - Disturbance of DKK1 level is partly involved in survival of lung cancer cells via regulation of ROMO1 and gamma-radiation sensitivity.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Nov 20. pii: S0006-291X(13)01920-7. doi: 10.1016/j.bbrc.2013.11.038.

●● Enlace al texto completo (gratis o de pago) [1016/j.bbrc.2013.11.038](#)

AUTORES / AUTHORS: - Kim IG; Kim SY; Kim HA; Kim JY; Lee JH; Choi SI; Han JR; Kim KC; Cho EW

INSTITUCIÓN / INSTITUTION: - Department of Radiation Biology, Environmental Radiation Research Group, Korea Atomic Energy Research Institute, P.O. Box 105, Yuseong, Daejeon 305-600, Republic of Korea; Department of Radiation Biotechnology and Applied Radioisotope, University of Science and Technology (UST), 989-111 Daedeok-daero, Yuseong-gu, Daejeon 305-353, Republic of Korea. Electronic address: igkim@kaeri.re.kr.

RESUMEN / SUMMARY: - Dickkopf1 (DKK1), a secreted protein involved in embryonic development, is a potent inhibitor of the Wnt signaling pathway and has been postulated to be a tumor suppressor or tumor promoter depending on the tumor type. In this study, we showed that DKK1 was expressed differently among non-small-cell lung cancer cell lines. The DKK1 expression level was much higher in A549 cells than in H460 cells. We revealed that blockage of DKK1 expression by silencing RNA in A549 cells caused up-regulation of intracellular reactive oxygen species (ROS) modulator (ROMO1) protein, followed by partial cell death, cell growth inhibition, and loss of epithelial-mesenchymal transition property caused by ROS, and it also increased gamma-radiation sensitivity. DKK1 overexpression in H460 significantly inhibited cell survival with the decrease of ROMO1 level, which induced the decrease of cellular ROS. Thereafter, exogenous N-acetylcysteine, an antioxidant, or hydrogen peroxide, a pro-oxidant, partially rescued cells from death and growth inhibition. In each cell line, both overexpression and blockage of DKK1 not only elevated p-RB activation, which led to cell growth arrest, but also inactivated AKT/NF- κ B, which increased radiation sensitivity and inhibited cell growth. This study is the first to demonstrate that strict modulation of DKK1 expression in different cell types partially maintains cell survival via tight regulation of the ROS-producing ROMO1 and radiation resistance.

[132]

TÍTULO / TITLE: - Correction: screening for lung cancer with low-dose computed tomography.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Intern Med. 2013 Nov 5;159(9):648. doi: 10.7326/0003-4819-159-9-201311050-00019.

●● Enlace al texto completo (gratis o de pago) [7326/0003-4819-159-9-201311050-00019](#)

[133]

TÍTULO / TITLE: - [6]-Shogaol inhibits growth and induces apoptosis of non-small cell lung cancer cells by directly regulating Akt1/2.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Carcinogenesis. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [1093/carcin/bgt365](#)

AUTORES / AUTHORS: - Kim MO; Lee MH; Oi N; Kim SH; Bae KB; Huang Z; Kim DJ; Reddy K; Lee SY; Park SJ; Kim JY; Xie H; Kundu JK; Ryoo ZY; Bode AM; Surh YJ; Dong Z

INSTITUCIÓN / INSTITUTION: - The Hormel Institute, University of Minnesota, MN 55912, USA.

RESUMEN / SUMMARY: - Non-small cell lung cancer (NSCLC) is the leading cause of cancer mortality worldwide. Despite progress in developing chemotherapeutics for the treatment of NSCLC, primary and secondary resistance limits therapeutic success. NSCLC cells exhibit multiple mutations in the epidermal growth factor receptor (EGFR), which cause aberrant activation of diverse cell signaling pathways. Therefore, suppression of the inappropriate amplification of EGFR downstream signaling cascades is considered to be a rational therapeutic and preventive strategy for the management of NSCLC. Our initial molecular-target oriented virtual screening revealed that the ginger components, including [6]-shogaol, [6]-paradol and [6]-gingerol, appear to be potential candidates for the prevention and treatment of NSCLC. Among the compounds, [6]-shogaol showed the greatest inhibitory effects on the NSCLC cell proliferation and anchorage-independent growth. [6]-Shogaol induced cell cycle arrest (G1 or G2/M) and apoptosis. Furthermore, [6]-shogaol inhibited Akt kinase activity, a downstream mediator of EGFR signaling, by binding with an allosteric site of Akt. In NCI-H1650 lung cancer cells, [6]-shogaol reduced the constitutive phosphorylation of STAT3 and decreased the expression of cyclin D1/3, which are target proteins in the Akt signaling pathway. The induction of apoptosis in NCI-H1650 cells by [6]-shogaol corresponded with the cleavage of caspase-3 and caspase-7. Moreover, intraperitoneal administration of [6]-shogaol inhibited the growth of NCI-H1650 cells as tumor xenografts in nude mice. [6]-Shogaol suppressed the expression of Ki-67, cyclin D1 and phosphorylated Akt and STAT3, and increased TUNEL-positivity in xenograft tumors. The present study clearly indicates that [6]-shogaol can be exploited for the prevention and/or treatment of NSCLC.

[134]

TÍTULO / TITLE: - Impact of EBUS-TBNA on modalities for tissue acquisition in patients with lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - QJM. 2013 Nov 19.

●● Enlace al texto completo (gratis o de pago) [1093/qjmed/hct233](#)

AUTORES / AUTHORS: - Jose RJ; Shaw P; Taylor M; Lawrence DR; George PJ; Janes SM; Navani N

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Medicine, University College Hospital, London, United Kingdom.

RESUMEN / SUMMARY: - IntroductionThe impact of the introduction of EBUS-TBNA on the use of diagnostic modalities for tissue acquisition in patients with lung cancer is unknown.MethodsA retrospective review of 328 consecutive patients diagnosed with

lung cancer at a university teaching hospital, where they first presented, in London in 2007, 2009 and 2011. EBUS was introduced in 2008. Results 316 patients were included in the analysis. Comparing 2007 to 2011 there has been a significant reduction in standard bronchoscopy ($P < 0.0001$) and mediastinoscopy ($P = 0.02$). The proportion of cases diagnosed by EBUS-TBNA significantly increased from 0% in 2007 to 26.7% in 2009 and 25.4% in 2011 ($P < 0.0001$). In the same period there has also been an increased trend in the proportion of patients going directly to surgery without pathological confirmation with a 9.6% increase in diagnoses obtained at thoracotomy ($p = 0.0526$). Conclusions The use of diagnostic modalities that provide information on diagnosis and staging in a single intervention are increasing. At our hospital, the use of EBUS-TBNA for providing a lung cancer diagnosis is increasing and this has led to a significant reduction in standard bronchoscopies and mediastinoscopies. These changes in practice may have implications for future service provision, training and commissioning.

[135]

TÍTULO / TITLE: - Resolvin D1 inhibits TGF-beta1-induced epithelial mesenchymal transition of A549 lung cancer cells via lipoxin A4 receptor/formyl peptide receptor 2 and GPR32.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Biochem Cell Biol. 2013 Dec;45(12):2801-7. doi: 10.1016/j.biocel.2013.09.018. Epub 2013 Oct 10.

•• Enlace al texto completo (gratis o de pago) [1016/j.biocel.2013.09.018](#)

AUTORES / AUTHORS: - Lee HJ; Park MK; Lee EJ; Lee CH

INSTITUCIÓN / INSTITUTION: - College of Pharmacy, Dongguk University, Seoul 100-715, Republic of Korea.

RESUMEN / SUMMARY: - Epithelial-mesenchymal-transition (EMT) is a key event for tumor cells to initiate metastasis which lead to switching of E-cadherin to N-cadherin. Resolvins are known to promote the resolution of inflammation and phagocytosis of macrophages. However, the role of resolvins in EMT of cancer is not known. Therefore, we examined the effects of resolvins on transforming growth factor, beta 1 (TGF-beta1)-induced EMT. Expression of E-cadherin and N-cadherin in A549 lung cancer cells was evaluated by Western blot and confocal microscopy. Involvement of lipoxin A4 receptor/formyl peptide receptor 2 (ALX/FPR2) was examined by gene silencing. TGF-beta1 induced expression of N-cadherin in A549 lung cancer cells, and resolvin D1 and D2 inhibited the expression of N-cadherin at low concentrations (1-100nM). Resolvin D1 and D2 also suppressed the expression of zinc finger E-box binding homeobox 1 (ZEB1). The effects of resolvin D1 and D2 were confirmed in other lung cancer cell lines such as H838, H1299, and H1703. Resolvin D1 and D2 did not affect the proliferation of A549 lung cancer cells. Resolvin D1 and D2 also suppressed the TGF-beta1-induced morphological change. Resolvin D1 and D2 also inhibited the TGF-beta1-induced migration and invasion of A549 cells. Resolvin D1 is known to act via ALX/FPR2 and GPR32. Thus, we examined the involvement of ALX/FPR2 and GPR32 in the suppressive effects of resolvin D1 on TGF-beta1-induced EMT of A549 cells. Gene silencing of ALX/FPR2 and GPR32 blocked the action of resolvin D1. Overexpression of ALX/FPR2 or GPR32 increased the effects of resolvin D1. These

results suggest that resolvin D1 inhibited TGF-beta1-induced EMT via ALX/FPR2 and GPR32 by reducing the expression of ZEB1.

[136]

TÍTULO / TITLE: - Major partial response to crizotinib, a dual MET/ALK inhibitor, in a squamous cell lung (SCC) carcinoma patient with de novo c-MET amplification in the absence of ALK rearrangement.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 19. pii: S0169-5002(13)00450-9. doi: 10.1016/j.lungcan.2013.10.006.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.006](#)

AUTORES / AUTHORS: - Schwab R; Petak I; Kollar M; Pinter F; Varkondi E; Kohanka A; Barti-Juhász H; Schönleber J; Brauswetter D; Kopper L; Urban L

INSTITUCIÓN / INSTITUTION: - KPS Medical Biotechnology and Healthcare Services Ltd., Budapest, Hungary.

RESUMEN / SUMMARY: - The initial radiotherapy of a 73 years old Caucasian male patient with advanced squamous cell lung carcinoma was terminated due to severe pericarditis. Subsequently, the tumor sample was analyzed for possible targets with comprehensive molecular diagnostics. EGFR, KRAS and PIK3CA genes were wild type, ALK and ROS1 were negative for rearrangement, but c-MET was amplified by fluorescent in situ hybridization. The kinase inhibitor crizotinib is already in clinical use for the treatment of ALK positive non-small cell lung cancers, but it is also known to be a potent c-MET inhibitor. The patient was treated with the standard dose of twice a day 250mg crizotinib as a monotherapy. Major partial response to therapy was confirmed by chest CT and PET/CT after 8 weeks on therapy. C-MET expression is associated with poor prognosis and resistance to EGFR inhibitors. This case may indicate that c-MET tyrosine kinase inhibitors can be an effective targeted treatment option for squamous cell carcinoma patients, and future clinical trials should be expanded for this patient group as well.

[137]

TÍTULO / TITLE: - Multi-gene analyses from waste brushing specimens for patients with peripheral lung cancer receiving EBUS-assisted bronchoscopy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):420-5. doi: 10.1016/j.lungcan.2013.10.005. Epub 2013 Oct 14.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.005](#)

AUTORES / AUTHORS: - Tsai TH; Yang CY; Ho CC; Liao WY; Jan IS; Chen KY; Wang JY; Ruan SY; Yu CJ; Yang JC; Yang PC; Shih JY

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taipei, Taiwan. Electronic address: thtsai1971@ntu.edu.tw.

RESUMEN / SUMMARY: - OBJECTIVES: Although flexible bronchoscopy with the assistance of miniature radial-probe endobronchial ultrasound (EBUS) is increasingly employed to diagnose peripheral lung cancer, transbronchial biopsies typically offer an insufficient amount of tissue to conduct additional molecular analysis. We evaluated the

feasibility of multi-gene analyses from waste brushing samples obtained by EBUS-assisted bronchoscopy. MATERIALS AND METHODS: For lung cancer patients with positive brushing cytology, analysis of EGFR, K-ras and EML4-ALK fusions were carried out, utilizing reverse transcription-polymerase chain reaction and Sanger sequencing on the cell-derived RNA retrieved from waste brushing samples. RESULTS: EBUS-guided brushings were judged positive for tumor cells in 84 (68.9%) of the 122 patients with peripheral lung cancer receiving flexible bronchoscopy. Genotyping of EGFR and K-ras was successfully implemented in 80 (95.2%) of the 84 cytology-proven brushing samples, along with satisfactory yields to detect EGFR (55.0%) and K-ras (2.5%) mutations. The results of EGFR genotyping from the brushing specimens were highly concordant with those provided from other corresponding samples (concordance rate: 94%, kappa: 0.92). Of the 19 patients with adenocarcinoma or non-small cell lung cancer not otherwise specified harboring wild-type EGFR and K-ras, two cases (10.5%) were identified to harbor EML4-ALK fusions. CONCLUSION: Our results suggest that multi-gene analyses from waste brushing specimens using RNA-based Sanger sequencing is highly feasible. This approach offers an opportunity to overcome the dilemma of flexible bronchoscopy in molecular diagnostics for lung cancer, and could potentially recruit more patients for targeted therapy according to the molecular characteristics of the tumor cells.

[138]

TÍTULO / TITLE: - Dynamic volume perfusion CT in patients with lung cancer: Baseline perfusion characteristics of different histological subtypes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Radiol. 2013 Dec;82(12):e894-900. doi: 10.1016/j.ejrad.2013.08.023. Epub 2013 Sep 11.

●● Enlace al texto completo (gratis o de pago) [1016/j.ejrad.2013.08.023](#)

AUTORES / AUTHORS: - Shi J; Schmid-Bindert G; Fink C; Sudarski S; Apfaltrer P; Pilz LR; Liu B; Haberland U; Klotz E; Zhou C; Schoenberg SO; Henzler T

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Shanghai Pulmonary Hospital, Tongji University School of Medicine, China; Institute of Clinical Radiology and Nuclear Medicine, University Medical Center Mannheim, Medical Faculty Mannheim, Heidelberg University, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany. Electronic address: shijingyun89179@126.com.

RESUMEN / SUMMARY: - OBJECTIVE: To evaluate dynamic volume perfusion CT (dVPCT) tumor baseline characteristics of three different subtypes of lung cancer in untreated patients. MATERIALS AND METHODS: 173 consecutive patients (131 men, 42 women; mean age 61+/-10 years) with newly diagnosed lung cancer underwent dVPCT prior to biopsy. Tumor permeability, blood flow (BF), blood volume (BV) and mean transit time (MTT) were quantitatively assessed as well as tumor diameter and volume. Tumor subtypes were histologically determined and compared concerning their dVPCT results. dVPCT results were correlated to tumor diameter and volume. RESULTS: Histology revealed adenocarcinoma in 88, squamous cell carcinoma in 54 and small cell lung cancer (SCLC) in 31 patients. Tumor permeability was significantly differing between adenocarcinoma, squamous cell carcinoma and SCLC (all p<0.05). Tumor BF and BV were higher in adenocarcinoma than in SCLC (p=0.001 and p=0.0002 respectively). BV was also higher in squamous cell carcinoma compared to

SCLC ($p=0.01$). MTT was not differing between tumor subtypes. Regarding all tumors, tumor diameter did not correlate with any of the dVPCT parameters, whereas tumor volume was negatively associated with permeability, BF and BV ($r=-0.22$, -0.24 , -0.24 , all $p<0.05$). In squamous cell carcinoma, tumor diameter and volume correlated with BV ($r=0.53$ and $r=-0.40$, all $p<0.05$). In SCLC, tumor diameter and volume correlated with MTT ($r=0.46$ and $r=0.39$, all $p<0.05$). In adenocarcinoma, no association between morphological and functional tumor characteristics was observed. CONCLUSIONS: dVPCT parameters are only partially related to tumor diameter and volume and are significantly differing between lung cancer subtypes.

[139]

TÍTULO / TITLE: - Lobectomy and postoperative thromboprophylaxis with enoxaparin improve blood hypercoagulability in patients with localized primary lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Thromb Res. 2013 Nov;132(5):584-91. doi: 10.1016/j.thromres.2013.07.005. Epub 2013 Aug 29.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.thromres.2013.07.005](#)

AUTORES / AUTHORS: - Papageorgiou C; Vandreden P; Marret E; Bonnet F; Robert F; Spyropoulos A; Galea V; Elalamy I; Hatmi M; Gerotziafas GT

INSTITUCIÓN / INSTITUTION: - Service Anesthesie - Reanimation Hopital Tenon, Hopitaux Universitaires Est Parisien, Assistance Publique Hopitaux de Paris, France; ER2UPMC, Faculte de Medecine Pierre et Marie Curie, Universite Paris VI, France.

RESUMEN / SUMMARY: - BACKGROUND: Patients with lung adenocarcinoma undergoing surgery are in high risk for VTE and receive routine post-operative thromboprophylaxis with LWMH. AIM: We investigated markers of hypercoagulability in patients with primary localized adenocarcinoma and the modifications induced by lobectomy and postoperative administration of enoxaparin. MATERIALS AND METHODS: Patients suffering from localised primary lung adenocarcinoma ($n=15$) scheduled for lobectomy were studied. The control group consisted of 15 healthy age and sex-matched individuals. Blood was collected before anaesthesia induction and after surgery, at several intervals until the 7th post-operative day. Samples were assessed for thrombin generation, phosphatidylserin expressing platelet derived microparticles expressing (Pd-MP/PS(+)), tissue factor activity (TFa), FVIIa and TFPI levels, procoagulant phospholipid dependent clotting time and anti-Xa activity. RESULTS: At baseline, patients showed increased thrombin generation and Pd-MP/PS(+). After lobectomy thrombin generation significantly decreased. Administration of enoxaparin attenuated thrombin generation. In about 50% of samples collected post-operatively an increase of thrombin generation occurred despite the presence of the expected anti-Xa activity in plasma. At the 7th post-operative day, 3 out of 15 patients showed a significant increase of thrombin generation. CONCLUSION: In patients with localized lung adenocarcinoma, hypercoagulability is characterized by high thrombin generation and increased concentration of Pd-MP/PS(+). Tumor mass resection is related with attenuation of thrombin generation, which is inhibited by postoperative thromboprophylaxis with enoxaparin. The response to enoxaparin is not predicted by the concentration of the anti-Xa activity in plasma. The assessment of thrombin

generation during prophylaxis with enoxaparin allows to identify patients with high residual plasma hypercoagulability.

[140]

TÍTULO / TITLE: - EYA4 is inactivated biallelically at a high frequency in sporadic lung cancer and is associated with familial lung cancer risk.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Oct 7. doi: 10.1038/onc.2013.396.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.396](#)

AUTORES / AUTHORS: - Wilson IM; Vucic EA; Enfield KS; Thu KL; Zhang YA; Chari R; Lockwood WW; Radulovich N; Starczynowski DT; Banath JP; Zhang M; Pusic A; Fuller M; Lonergan KM; Rowbotham D; Yee J; English JC; Buys TP; Selamat SA; Laird-Offringa IA; Liu P; Anderson M; You M; Tsao MS; Brown CJ; Bennewith KL; Macaulay CE; Karsan A; Gazdar AF; Lam S; Lam WL

INSTITUCIÓN / INSTITUTION: - Integrative Oncology Genetics Unit, British Columbia Cancer Research Centre, Vancouver, BC, Canada.

RESUMEN / SUMMARY: - In an effort to identify novel biallelically inactivated tumor suppressor genes (TSGs) in sporadic invasive and preinvasive non-small-cell lung cancer (NSCLC) genomes, we applied a comprehensive integrated multiple 'omics' approach to investigate patient-matched, paired NSCLC tumor and non-malignant parenchymal tissues. By surveying lung tumor genomes for genes concomitantly inactivated within individual tumors by multiple mechanisms, and by the frequency of disruption in tumors across multiple cohorts, we have identified a putative lung cancer TSG, Eyes Absent 4 (EYA4). EYA4 is frequently and concomitantly deleted, hypermethylated and underexpressed in multiple independent lung tumor data sets, in both major NSCLC subtypes and in the earliest stages of lung cancer. We found that decreased EYA4 expression is not only associated with poor survival in sporadic lung cancers but also that EYA4 single-nucleotide polymorphisms are associated with increased familial cancer risk, consistent with EYA4s proximity to the previously reported lung cancer susceptibility locus on 6q. Functionally, we found that EYA4 displays TSG-like properties with a role in modulating apoptosis and DNA repair. Cross-examination of EYA4 expression across multiple tumor types suggests a cell-type-specific tumorigenic role for EYA4, consistent with a tumor suppressor function in cancers of epithelial origin. This work shows a clear role for EYA4 as a putative TSG in NSCLC. Oncogene advance online publication, 7 October 2013; doi:10.1038/onc.2013.396.

[141]

TÍTULO / TITLE: - Discovery of Tryptanthrin Derivatives as Potent Inhibitors of Indoleamine 2,3-Dioxygenase with Therapeutic Activity in Lewis Lung Cancer (LLC) Tumor-Bearing Mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Med Chem. 2013 Oct 25.

●● Enlace al texto completo (gratis o de pago) [1021/jm401195n](#)

AUTORES / AUTHORS: - Yang S; Li X; Hu F; Li Y; Yang Y; Yan J; Kuang C; Yang Q

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Genetic Engineering, Department of Biochemistry, School of Life Sciences, Fudan University, Handan Road 220, Shanghai 200433, China.

RESUMEN / SUMMARY: - Indoleamine 2,3-dioxygenase (IDO-1) is emerging as an important new therapeutic target for the treatment of cancer, neurological disorders, and other diseases that are characterized by pathological tryptophan metabolism. However, only a few structural classes are known to be IDO-1 inhibitors. In this study, a natural compound tryptanthrin was discovered to be a novel potent IDO-1 inhibitor by screening of indole-based structures. Three series of 13 tryptanthrin derivatives were synthesized, and the structure-activity analysis was undertaken. The optimization led to the identification of 5c, which exhibited the inhibitory activity at a nanomolar level. In vitro 5c dramatically augmented the proliferation of T cells. When administered to Lewis lung cancer (LLC) tumor-bearing mice, 5c significantly inhibited IDO-1 activity and suppressed tumor growth. In addition, 5c reduced the numbers of Foxp3+ regulatory T cells (Tregs), which are known to prevent the development of efficient antitumor immune responses.

[142]

TÍTULO / TITLE: - Frequent T cell responses against immunogenic targets in lung cancer patients for targeted immunotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):384-90. doi: 10.3892/or.2013.2804. Epub 2013 Oct 23.

●● [Enlace al texto completo \(gratis o de pago\) 3892/or.2013.2804](#)

AUTORES / AUTHORS: - Babiak A; Steinhauser M; Gotz M; Herbst C; Dohner H; Greiner J

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine III, University of Ulm, D-89081 Ulm, Germany.

RESUMEN / SUMMARY: - To date, lung cancer is one of the leading causes of cancer mortality with short overall survival despite adequate therapy. New immunotherapeutic strategies using peptides derived from tumor-associated antigens (TAAs) can induce a specific cytotoxic T cell (CTL) response leading to a targeted tumor cell death. In the present study, we addressed whether there are further significant immunogenic candidate targets that may induce strong immune reactions with a high frequency in lung cancer patients eligible for cellular immunotherapeutic approaches, such as in a polyvalent vaccination approach. In this study, we investigated specific CTL responses of 14 HLA-A*0201-positive patients (of 33 screened patients) with non-small cell lung cancer (NSCLC; n=12) or small cell lung cancer (SCLC; n=2) against several known and novel TAA-derived peptides from lung cancer and/or other tumor entities, by measuring granzyme B (GrB) and/or interferon gamma (IFN γ) secretion using enzyme-linked immunospot (ELISpot) analysis. Specific T cell responses could be detected for hTERT (4/13), two MAGE-A3-derived peptides (4/13 and 3/13, respectively), RHAMM (4/14), PRAME (8/14), G250 (7/12), survivin (3/13), HER2 (5/10) and WT1 (2/14), but also novel epitopes derived from Aurora kinase A (4/13) and B (5/13). Additionally, simultaneous CTL responses against the different peptides were examined and specific T cell responses against at least one of these TAAs could be detected in 13/14 (93%) patients. It could be shown that all patients with immune

reactions against RHAMM and hTERT showed also immune responses against PRAME. Furthermore, patients with CTL responses against the Aurora kinase A peptide (Aura A1) also demonstrated a response against the Aurora kinase B peptide (Aura B1). Taken together, we showed that these TAA-derived peptides induce frequent specific T cell responses in patients with metastatic lung cancer and are, therefore, novel candidates for targeted immunotherapies and polyvalent approaches.

[143]

TÍTULO / TITLE: - Validity of using lobe-specific regional lymph node stations to assist navigation during lymph node dissection in early stage non-small cell lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Surg Today. 2013 Oct 31.

●● Enlace al texto completo (gratis o de pago) [1007/s00595-013-0772-5](#)

AUTORES / AUTHORS: - Miyoshi S; Shien K; Toyooka S; Miyoshi K; Yamamoto H; Sugimoto S; Soh J; Hayama M; Yamane M; Oto T

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama, 700-8558, Japan, smiyoshi@md.okayama-u.ac.jp.

RESUMEN / SUMMARY: - PURPOSE: The validity of our proposed lobe-specific regional lymph node stations (LSRLNS) was evaluated as a method for navigation during lymphadenectomy in patients with early stage non-small cell lung cancer (NSCLC). METHODS: A total of 725 NSCLC patients with c-T2N1M0 or less extensive disease who had undergone a curative operation with complete mediastinal lymph node dissection (MLND) were studied. The LSRLNS were #2, #3, #4 and #10 for the right upper lobe, #11i, #11s, #7 and #8 for the right lower lobe, #4, #5 and #6 for the left superior division, #11, #5 and #7 for the left lingular division and #11, #7 and #8 for the left lower lobe. RESULTS: If the LSRLNS were used for pathological examinations during surgery, 599 p-N0 and 39 p-N1 patients diagnosed with no metastasis would have been subjected to a selective MLND, while 20 p-N1 and 65 p-N2 patients who had a diagnosis of metastasis would have been navigated to a complete MLND. Two p-N2 patients with a diagnosis of no metastasis would have inappropriately undergone a selective MLND, resulting in the false negative rate at 0.3 %. CONCLUSION: Intra-operative pathological examination using our LSRLNS may accurately reveal the status of metastasis, and appropriately lead to a selective or complete MLND in patients with c-T2N1M0 or less extensive disease.

[144]

TÍTULO / TITLE: - Anti-lymphangiogenesis effects of a specific anti-interleukin 7 receptor antibody in lung cancer model in vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Carcinog. 2013 Sep 24. doi: 10.1002/mc.22082.

●● Enlace al texto completo (gratis o de pago) [1002/mc.22082](#)

AUTORES / AUTHORS: - Jian M; Qingfu Z; Yanduo J; Guocheng J; Xueshan Q

INSTITUCIÓN / INSTITUTION: - No. 202 Hospital of People Liberation Army of China, Shenyang, P.R., China.

RESUMEN / SUMMARY: - Interleukin 7 (IL-7) is known to promote lymphangiogenesis. To study the relationship between IL-7 and the lymphangiogenesis in lung cancer cells xenograft tumors, we investigated how IL-7 regulates lymphangiogenesis by Quantitative real-time reverse transcriptase-polymerase chain reaction, Western blot, co-immunoprecipitation, chromatin immunoprecipitation, and immunohistochemistry methods. We found that, in lung cancer cells xenograft tumors IL-7/IL-7 receptor (IL-7R) increase the expression of VEGF-D and lymphangiogenesis, induce c-Fos and c-Jun heterodimer formation, and enhance c-Fos/c-Jun DNA binding activity to regulate VEGF-D. Taken together, our results provided evidence that IL-7/IL-7R induce VEGF-D upregulation and promote lymphangiogenesis via c-Fos/c-Jun pathway in lung cancer. © 2013 Wiley Periodicals, Inc.

[145]

TÍTULO / TITLE: - Fluoroscopically Guided Balloon Dilation for Benign Bronchial Stricture Occurring after Radiotherapy in Patients with Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cardiovasc Intervent Radiol. 2013 Oct 3.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00270-013-0735-7](#)

AUTORES / AUTHORS: - Cho YC; Kim JH; Park JH; Shin JH; Ko HK; Song HY

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, 388-1, Poongnap 2-dong, Songpa-gu, Seoul, 138-736, Republic of Korea, cjsakura@naver.com.

RESUMEN / SUMMARY: - PURPOSE: To evaluate the safety and clinical effectiveness of fluoroscopically guided balloon dilation in patients with benign bronchial stricture occurring after radiotherapy (RT). METHODS: From March 2002 to January 2013, ten patients with benign bronchial stricture occurring after RT underwent fluoroscopically guided balloon dilation as their initial treatment. Technical success, primary and secondary clinical success, improvement in respiratory status, and complications were evaluated. The symptomatic improvement period was calculated. RESULTS: A total of 15 balloon dilation sessions were performed in ten patients, with a range of 1-4 sessions per patient (mean 1.5 sessions). Technical success was achieved in 100 %. Six of the ten patients exhibited no symptom recurrence and required no further treatment until the end of follow-up (range 4-105 months). Four patients (40 %) experienced recurrent symptom, and two of four patients underwent repeat balloon dilations. The remaining two patients underwent cutting balloon dilation and temporary stent placement, respectively, and they exhibited symptom improvement after adjuvant treatment until the end of our study. Finally, primary clinical success was achieved in six of ten patients (60 %) and secondary clinical success was achieved in eight of ten patients (80 %). The mean symptom improvement period was 61.9 +/- 16 months (95 % confidence interval 30.6-93.3). CONCLUSION: Fluoroscopically guided balloon dilation seems to be safe and clinically effective for the treatment of RT-induced benign bronchial stricture. Temporary stent placement or cutting balloon dilation could be considered in patients with benign bronchial strictures resistant to fluoroscopically guided balloon dilation.

[146]

TÍTULO / TITLE: - Downregulation of G3BPs inhibits the growth, migration and invasion of human lung carcinoma H1299 cells by suppressing the Src/FAK-associated signaling pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Gene Ther. 2013 Nov;20(11):622-9. doi: 10.1038/cgt.2013.62. Epub 2013 Oct 25.

●● Enlace al texto completo (gratis o de pago) [1038/cgt.2013.62](#)

AUTORES / AUTHORS: - Zhang H; Zhang SH; He HW; Zhang CX; Yu DK; Shao RG

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Institute of Medicinal Biotechnology, Peking Union Medical College, Chinese Academy of Medical Sciences, Beijing, China.

RESUMEN / SUMMARY: - G3BP is a RasGAP binding protein that is overexpressed in many human cancers. We previously reported that downregulation of G3BP suppressed cell growth and induced apoptosis in HCT116 cells. Here we report that both transient and stable knockdown of G3BP suppressed the growth, migration and invasion capability of human lung carcinoma H1299 cells. Moreover, downregulation of G3BP significantly inhibited the phosphorylation of Src, FAK and ERK, and the levels of NF-kappaB were also markedly decreased in H1299 cells. Knockdown of G3BP also decreased the expression of matrix metalloproteinase-2 (MMP-2), MMP-9 and plasminogen activator (uPA), and in vivo data demonstrated that downregulation of G3BP markedly inhibited the growth of H1299 tumor xenografts. Together, these data revealed that knockdown of G3BP inhibited the migration and invasion of human lung carcinoma cells through the inhibition of Src, FAK, ERK and NF-kappaB and decreased levels of MMP-2, MMP-9 and uPA.

[147]

TÍTULO / TITLE: - Adipose-derived stem cells induced EMT-like changes in H358 lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Oct;33(10):4421-30.

AUTORES / AUTHORS: - Park YM; Yoo SH; Kim SH

INSTITUCIÓN / INSTITUTION: - DMC BioMedical Research Center, Bundang Jesaeng General Hospital, 255-2 Seohyun Ro 180 Gil, Bundang Gu, Seongnam Si, Kyungki-do 463-774, Korea. genpax@daum.net.

RESUMEN / SUMMARY: - Despite the potential utility of adipose-derived mesenchymal stem cells (ADSCs) in regenerative medicine, not much is known about their interaction with residual cancer cells. Here, we studied the direct co-culture effects of ADSCs on H358 lung cancer cells. The paracrine effects of ADSCs were compared to those of the cancer-associated fibroblasts. Extracellular matrix and conditioned media were used to determine the underlying molecules. Time-lapse photography, fluorescence-activated cell sorting (FACS), scratch assays, immunocytochemistry, and reverse-transcription polymerase chain reaction were used to analyze the effects. ADSCs differentiated into myofibroblasts expressing alphaSMA, and H358 cells strongly attached to them. EMT-like changes were observed in H358 cells which were inhibited by gamma-secretase inhibitor, a-NOTCH inhibitor. Surprisingly, both mesenchymal and epithelial genes were expressed, and the effects were readily reversed when cells were sorted by FACS.

These data suggest that ADSCs may differentiate into tumor stroma that plays supportive roles during cancer progression.

[148]

TÍTULO / TITLE: - Carboplatin plus either docetaxel or paclitaxel for Japanese patients with advanced non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Oct;33(10):4631-7.

AUTORES / AUTHORS: - Kawahara M; Atagi S; Komuta K; Yoshioka H; Kawasaki M; Fujita Y; Yonei T; Ogushi F; Kubota K; Nogami N; Tsuchiya M; Shibata K; Tomizawa Y; Minato K; Fukuoka K; Asami K; Yamanaka T

INSTITUCIÓN / INSTITUTION: - 1-5-34, Otemae, Chuo-ku, Osaka, 540-0008, Japan.
kawaharam@otemae.gr.jp.

RESUMEN / SUMMARY: - AIM: Assessment of the efficacy of docetaxel plus carboplatin vs. paclitaxel plus carboplatin in Japanese patients with advanced non-small cell lung cancer (NSCLC). PATIENTS AND METHODS: Chemotherapy-naive patients were randomly assigned at a ratio of 2 to 1 to receive six cycles of either docetaxel (60 mg/m²) plus carboplatin [area under the curve (AUC)=6 mg/ml min] or paclitaxel (200 mg/m²) plus carboplatin (same dose), on day 1 every 21 days. The primary end-point was progression-free survival (PFS). RESULTS: A total of 90 patients were enrolled. Overall response rate, median PFS and median survival time in the docetaxel-plus-carboplatin group and the paclitaxel-plus-carboplatin group were 23% vs. 33%, 4.8 months vs. 5.1 months, and 17.6 months vs. 15.6 months, respectively. The docetaxel-plus-carboplatin group had a higher incidence of grade 3 or 4 neutropenia (88% vs. 60%). CONCLUSION: Both regimens were similarly effective in Japanese patients with advanced NSCLC.

[149]

TÍTULO / TITLE: - Myelodysplastic Syndrome with Pulmonary Tumor Thrombotic Microangiopathy in an 11-Year-Old Male Patient.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pediatr Dev Pathol. 2013 Oct 7.

●● [Enlace al texto completo \(gratis o de pago\) 2350/13-05-1339-CR.1](#)

AUTORES / AUTHORS: - Perrino CM; Dehner LP; Hartman ME; Agarwal A

INSTITUCIÓN / INSTITUTION: - a Washington University, Pathology & Immunology.

RESUMEN / SUMMARY: - Abstract ABSTRACT: Myelodysplastic syndrome (MDS) and pulmonary tumor thrombotic microangiopathy (PTTM) are independently rare in the pediatric population. This report describes an 11-year-old male patient who initially presented with respiratory distress and cardiovascular collapse. A large left main pulmonary artery embolus and multiple, smaller pulmonary thromboemboli were widely dispersed throughout both lungs. Despite aggressive supportive care he expired within seven hours of admission. A complete postmortem examination was performed, leading to the diagnoses of primary MDS and microthrombi in the lungs including the characteristic fibroproliferative lesions seen in PTTM. Individually, both conditions are extremely uncommon, therefore the coincidence of these two conditions in a child is singularly unique in the setting of MDS. KEYWORDS: myelodysplastic syndrome,

refractory anemia with excess blasts-2, pulmonary tumor thrombotic microangiopathy, pulmonary hypertension, right heart failure, cor pulmonale.

[150]

TÍTULO / TITLE: - A Gene Signature Combining the Tissue Expression of Three Angiogenic Factors is a Prognostic Marker in Early-stage Non-small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Oct 22.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3330-x](#)

AUTORES / AUTHORS: - Sanmartin E; Sirera R; Uso M; Blasco A; Gallach S; Figueroa S; Martinez N; Hernando C; Honguero A; Martorell M; Guijarro R; Rosell R; Jantus-Lewintre E; Camps C

INSTITUCIÓN / INSTITUTION: - Molecular Oncology Laboratory, Fundacion Investigacion, Hospital General Universitario de Valencia, Valencia, España.

RESUMEN / SUMMARY: - BACKGROUND: Angiogenesis and lymphangiogenesis are key mechanisms for tumor growth and dissemination. They are mainly regulated by the vascular endothelial growth factor (VEGF) family of ligands and receptors. The aim of this study was to analyze relative expression levels of angiogenic markers in resectable non-small cell lung cancer patients in order to assess a prognostic signature that could improve characterization of patients with worse clinical outcomes. METHODS: RNA was obtained from tumor and normal lung specimens from 175 patients. Quantitative polymerase chain reaction was performed to analyze the relative expression of HIF1A, PIGF, VEGFA, VEGFA165b, VEGFB, VEGFC, VEGFD, VEGFR1, VEGFR2, VEGFR3, NRP1 and NRP2. RESULTS: Univariate analysis showed that tumor size and ECOG-PS are prognostic factors for time to progression (TTP) and overall survival (OS). This analysis in the case of angiogenic factors also revealed that PIGF, VEGFA, VEGFB and VEGFD distinguish patients with different outcomes. Taking into account the complex interplay between the different ligands of the VEGF family and to more precisely predict the outcome of the patients, we considered a new analysis combining several VEGF ligands. In order to find independent prognostic variables, we performed a multivariate Cox analysis, which showed that the subgroup of patients with higher relative expression of VEGFA plus lower VEGFB and VEGFD presented the poorest outcome for both TTP and OS. CONCLUSIONS: The relative expression of these three genes can be considered as an angiogenic gene signature whose applicability for the selection of candidates for targeted therapies needs to be further validated.

[151]

TÍTULO / TITLE: - Occupational exposure to crystalline silica and the risk of lung cancer in Canadian men.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Cancer. 2013 Nov 22. doi: 10.1002/ijc.28629.

●● Enlace al texto completo (gratis o de pago) [1002/ijc.28629](#)

AUTORES / AUTHORS: - Kachuri L; Villeneuve PJ; Parent ME; Johnson KC; Harris SA

INSTITUCIÓN / INSTITUTION: - Dalla Lana School of Public Health, University of Toronto, Toronto, ON; Occupational Cancer Research Centre, Toronto, ON; Prevention and Cancer Control, Cancer Care Ontario, Toronto, ON.

RESUMEN / SUMMARY: - Crystalline silica is a recognized carcinogen, but the association with lung cancer at lower levels of exposure has not been well characterized. This study investigated the relationship between occupational silica exposure and lung cancer, and the combined effects of cigarette smoking and silica exposure on lung cancer risk. A population-based case-control study was conducted in 8 Canadian provinces between 1994 and 1997. Self-reported questionnaires were used to obtain a lifetime occupational history and information on other risk factors. Occupational hygienists assigned silica exposures to each job based on concentration, frequency, and reliability. Data from 1681 incident lung cancer cases and 2053 controls were analyzed using logistic regression to estimate odds ratios (OR) and their 95% confidence intervals. Models included adjustments for cigarette smoking, lifetime residential second-hand smoke, and occupational exposure to diesel and gasoline engine emissions. Relative to the unexposed, increasing duration of silica exposure at any concentration was associated with a significant trend in lung cancer risk (OR ≥ 30 years: 1.67, 1.21-2.24; $p_{\text{trend}} = 0.002$). The highest tertile of cumulative silica exposure was associated with lung cancer (OR: 1.81, 1.34-2.42; $p_{\text{trend}} = 0.004$) relative to the lowest. Men exposed to silica for ≥ 30 years with ≥ 40 cigarette pack-years had the highest risk relative to those unexposed with < 10 pack-years (OR: 42.53, 23.54-76.83). The joint relationship with smoking was consistent with a multiplicative model. Our findings suggest that occupational exposure to silica is a risk factor for lung cancer, independently from active and passive smoking, as well as from exposure to other lung carcinogens. © 2013 Wiley Periodicals, Inc.

[152]

TÍTULO / TITLE: - Silencing of poly(ADP-ribose) glycohydrolase sensitizes lung cancer cells to radiation through the abrogation of DNA damage checkpoint.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Nov 29;441(4):793-8. doi: 10.1016/j.bbrc.2013.10.134. Epub 2013 Nov 6.

●● Enlace al texto completo (gratis o de pago) 1016/j.bbrc.2013.10.134

AUTORES / AUTHORS: - Nakadate Y; Kodera Y; Kitamura Y; Tachibana T; Tamura T; Koizumi F

INSTITUCIÓN / INSTITUTION: - Shien-Lab, National Cancer Center Hospital, 5-1-1 Tsukiji, Chuo-ku, Tokyo 104-0045, Japan; Department of Bioengineering, Graduate School of Engineering, Osaka City University, 3-3-138 Sugimoto, Sumiyoshi-ku, Osaka 558-8585, Japan.

RESUMEN / SUMMARY: - Poly(ADP-ribose) glycohydrolase (PARG) is a major enzyme that plays a role in the degradation of poly(ADP-ribose) (PAR). PARG deficiency reportedly sensitizes cells to the effects of radiation. In lung cancer, however, it has not been fully elucidated. Here, we investigated whether PARG siRNA contributes to an increased radiosensitivity using 8 lung cancer cell lines. Among them, the silencing of PARG induced a radiosensitizing effect in 5 cell lines. Radiation-induced G2/M arrest was largely suppressed by PARG siRNA in PC-14 and A427 cells, which exhibited significantly enhanced radiosensitivity in response to PARG knockdown. On the other hand, a similar effect was not observed in H520 cells, which did not exhibit a radiosensitizing effect. Consistent with a cell cycle analysis, radiation-induced checkpoint signals were not well activated in the PC-14 and A427 cells when treated

with PARG siRNA. These results suggest that the increased sensitivity to radiation induced by PARG knockdown occurs through the abrogation of radiation-induced G2/M arrest and checkpoint activation in lung cancer cells. Our findings indicate that PARG could be a potential target for lung cancer treatments when used in combination with radiotherapy.

[153]

TÍTULO / TITLE: - Volatile-Sensing Functions for Pulmonary Neuroendocrine Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Respir Cell Mol Biol. 2013 Oct 17.

●● Enlace al texto completo (gratis o de pago) [1165/rcmb.2013-0199OC](#)

AUTORES / AUTHORS: - Gu X; Karp PH; Brody SL; Pierce RA; Welsh MJ; Holtzman MJ; Ben-Shahar Y

INSTITUCIÓN / INSTITUTION: - Washington University, Biology, St. Louis, Missouri, United States.

RESUMEN / SUMMARY: - The mammalian airways are sensitive to inhaled stimuli, and airway diseases are characterized by hypersensitivity to volatile stimuli such as perfumes, industrial solvents, and others. However, the identity and function of volatile-sensing cells in the airway remains uncertain, particularly in humans. Here we show that solitary pulmonary neuroendocrine cells (PNECs), which are morphologically distinct and physiologically undefined, might serve as chemosensory cells in human airways. This conclusion is based on our finding that some human PNECs expressed members of the olfactory receptor (OR) family in vivo and in primary cell culture, and are anatomically positioned in the airway epithelium to respond to inhaled volatile chemicals. Furthermore, apical exposure of primary-culture human airway epithelial cells to volatile chemicals decreased levels of serotonin in PNEC and led to the release of the neuropeptide CGRP to the basal medium. These data suggested that volatile stimulation of PNECs can lead to the secretion of factors that are capable of stimulating the corresponding receptors in the lung epithelium. We also found that the distribution of serotonin and neuropeptide receptors may change in chronic obstructive pulmonary disease (COPD), suggesting that increased PNEC-dependent chemoresponsiveness might contribute to the altered sensitivity to volatile stimuli in this disease. Together, these data indicate that human airway epithelia harbor specialized cells that respond to volatile chemical stimuli and may help to explain clinical observations of odorant-induced airway reactions.

[154]

TÍTULO / TITLE: - Suppression of the invasive potential of highly malignant tumor cells by KIOM-C, a novel herbal medicine, via inhibition of NF-kappaB activation and MMP-9 expression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):287-97. doi: 10.3892/or.2013.2822. Epub 2013 Oct 25.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2822](#)

AUTORES / AUTHORS: - Kim A; Yim NH; Im M; Jung YP; Kim T; Ma JY

INSTITUCIÓN / INSTITUTION: - Korean Medicine (KM)-Based Herbal Drug Development Group, Korea Institute of Oriental Medicine (KIOM), Daejeon 305-811, Republic of Korea.

RESUMEN / SUMMARY: - KIOM-C, a novel herbal formula, was recently reported to be effective for treating pigs suffering from porcine circovirus-associated disease (PCVAD). In addition, administration of KIOM-C promoted clearance of influenza virus via production of antiviral cytokines, such as TNF-alpha and IFN-gamma. Since metastasis is the major cause of cancer-related death and the greatest challenge in cancer treatment, we investigated the effect of KIOM-C on the metastatic potential of HT1080 and B16F10 cells. We observed inhibitory properties of KIOM-C in colony-forming activity, migration and invasion. Matrix metalloproteinase-9 (MMP-9) activity in the resting and PMA-stimulated state in HT1080 cells was dose-dependently decreased by KIOM-C treatment via suppression of NF-kappaB activation. In addition, daily oral administration of KIOM-C at doses of 170 and 510 mg/kg, the corresponding human adult daily doses, efficiently blocked lung metastasis in C57BL/6J mice following injection of B16F10 cells in the tail veins. In particular, none of the mice administered KIOM-C during the experimental period exhibited systemic toxicity, such as body weight loss or liver and kidney dysfunction. Collectively, our results suggest that KIOM-C is a potential therapeutic formula useful as a safe herbal medicine for controlling metastatic cancer.

[155]

TÍTULO / TITLE: - Serum Biomarkers in Patients with Mesothelioma and Pleural Plaques and Healthy Subjects Exposed to Naturally Occurring Asbestos.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Oct 30.

●● Enlace al texto completo (gratis o de pago) [1007/s00408-013-9526-9](#)

AUTORES / AUTHORS: - Bayram M; Dongel I; Akbas A; Benli I; Akkoyunlu ME; Bakan ND

INSTITUCIÓN / INSTITUTION: - Department of Pulmonology, Bezmialem Vakif University, Istanbul, Turkey, drmehmetbayram@yahoo.com.

RESUMEN / SUMMARY: - PURPOSE: This study investigated the diagnostic accuracy of the serum biomarkers osteopontin and mesothelin in discriminating mesothelioma patients from those with other, benign conditions and whether levels of the biomarkers differed in subjects who had inhaled naturally occurring asbestos compared with a non-exposed control group. METHODS: This cross-sectional study studied 24 subjects with mesothelioma, 279 subjects with pleural plaques, 123 "healthy exposed," and 120 control subjects. The Kruskal-Wallis test was performed to compare mesothelin and osteopontin levels of the groups, and receiver operating characteristics curves were generated to determine diagnostic yields of both biomarkers. Multiple linear regression analyses were used to identify associated covariates with osteopontin and mesothelin levels. RESULTS: Serum osteopontin and mesothelin levels were higher in mesothelioma than in benign asbestos-related diseases and healthy exposed subjects. Both biomarker levels were independently associated with mesothelioma, age and smoking pack years. Mesothelin levels were also associated with body mass index. The sensitivity and specificity of osteopontin in distinguishing mesothelioma from the three other groups were 75 and 86 %, respectively; those of mesothelin were 58 and

83 %, respectively. The sensitivity and specificity to discriminate mesothelioma from pleural plaques and healthy subjects were 93 and 73 %, respectively, if osteopontin and mesothelin levels were higher than their optimal cut off levels. CONCLUSIONS: The combination of serum osteopontin and mesothelin levels can help to distinguish mesothelioma from benign asbestos-related diseases and asbestos-exposed subjects.

[156]

TÍTULO / TITLE: - A quantitative analysis of the polyamine in lung cancer patient fingernails by LC-ESI-MS/MS.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Chromatogr. 2013 Oct 9. doi: 10.1002/bmc.3059.

●● [Enlace al texto completo \(gratuito o de pago\) 1002/bmc.3059](#)

AUTORES / AUTHORS: - Min JZ; Matsumoto A; Li G; Jiang YZ; Yu HF; Todoroki K; Inoue K; Toyooka T

INSTITUCIÓN / INSTITUTION: - Laboratory of Analytical and Bio-Analytical Chemistry, School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Suruga-ku, Shizuoka, 422-8526, Japan; College of Pharmacy, Yanbian University, Yanji City, 133002, Jilin Province, People's Republic of China.

RESUMEN / SUMMARY: - A quantitative analysis of polyamines in lung cancer patient fingernails by the combination of 4-(N,N-dimethylaminosulfonyl)-7-fluoro-2,1,3-benzoxadiazole derivatives and liquid chromatography-electrospray ionization tandem mass spectrometry is described. The reaction of the reagent with eight kinds of polyamines, that is, N1 -acetylputrescine (N1 -actPUT), N8 -acetylspermidine, N1 -acetylspermine, 1,3-diaminopropane, putrescine (PUT), cadaverine, spermidine and spermine (SPM) effectively occurs at 60 degrees C for 30 min. The detection limits (signal-to-noise ratio 5) were 5-100 fmol. A good linearity was achieved from the calibration curves, which was obtained by plotting the peak area ratios of the analytes relative to the internal standard (IS), that is, 1,6-diaminohexane, vs the injected amounts of polyamines ($r^2 > 0.996$), and the intra-day and inter-day assay precisions were $< 9.84\%$. Furthermore, the recoveries (%) of the polyamines spiked in the human fingernails were 89.14-110.64. The present method was applied to human fingernail samples from 17 lung cancer patients and 39 healthy volunteers. The polyamine concentration was different based on the gender, that is, the N1 -actPUT and PUT contents were 3.10 times and 2.56 times higher in healthy men than in women, respectively. Additionally, in the lung cancer patient group, as compared with the healthy volunteers, the concentrations of SPM had a statistically significant ($p < 0.05$) correlation. Therefore, because the proposed method provides a good mass accuracy and the trace detection of the polyamines in human fingernails, this analytical technique could be a noninvasive technique to assist in the diagnosis and assessment of disease activity in lung cancer patients. Copyright © 2013 John Wiley & Sons, Ltd.

[157]

TÍTULO / TITLE: - Letter by Fu et al. regarding the article, "Polymorphisms in the vitamin D receptor gene and the lung cancer risk"

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 31.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1343-5](https://doi.org/10.1007/s13277-013-1343-5)

AUTORES / AUTHORS: - Gan L; Na FF; Wang JW; Xue JX

INSTITUCIÓN / INSTITUTION: - Laboratory of Cellular and Molecular biology, West China Hospital, Sichuan University, Chengdu, 610041, Sichuan Province, People's Republic of China.

[158]

TÍTULO / TITLE: - Silica nanoparticle uptake induces survival mechanism in A549 cells by the activation of autophagy but not apoptosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Toxicol Lett. 2013 Oct 16;224(1):84-92. doi: 10.1016/j.toxlet.2013.10.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.toxlet.2013.10.003](https://doi.org/10.1016/j.toxlet.2013.10.003)

AUTORES / AUTHORS: - Nowak JS; Mehn D; Nativo P; Garcia CP; Gioria S; Ojea-Jimenez I; Gilliland D; Rossi F

INSTITUCIÓN / INSTITUTION: - Nanobiosciences Unit, Institute of Health and Consumer Protection, Joint Research Centre, Via Fermi 2749, 21027 Ispra, Italy.

RESUMEN / SUMMARY: - We report here an in vitro evaluation of silica nanoparticle uptake by lung epithelial cells (A549), the cytotoxic effect of the particles and we propose autophagy as possible survival strategy. The effect of surface charge, serum proteins and the influence of inhibitors on the uptake of 20nm monodispersed nanoparticles with various functional groups are discussed. Uptake rate of the particles with various functional groups is demonstrated to be similar in the presence of serum proteins, while the uptake rate ranking is COOH>NH₂>OH under serum free conditions. Our results suggest an actin-dependent, macropinocytotic uptake process that was also confirmed by scanning and transmission electron microscopy. In spite of the intensive active uptake, significant cytotoxic effect is detected only at relatively high concentrations (above 250µg/mL). Blebbing of the cell surface is observed already at 5h of exposure and is shown to be related to autophagy rather than apoptotic cell death. The A549 cells display elevated levels of autophagosomes, however they do not express typical apoptosis markers such as increased amount of active caspase-3 and release of mitochondrial cytochrome C. Based on these results, we propose here an autophagic activity and cross-talk between autophagic and apoptotic pathways as a mechanism allowing the survival of A549 cells under exposure to silica nanoparticles.

[159]

TÍTULO / TITLE: - Combination of low-dose gemcitabine in 6-hour infusion and carboplatin is a favorable option for patients in poor performance status with advanced non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Chemother. 2013 Sep 26.

●● Enlace al texto completo (gratis o de pago)

[1179/1973947813Y.0000000139](https://doi.org/10.1179/1973947813Y.0000000139)

AUTORES / AUTHORS: - Wu ZY; Guan HH; Lin ZX; Yang HK; Zhou L; Cai QC

RESUMEN / SUMMARY: - This study sought to investigate the efficacy and tolerability of the regimen of low-dose gemcitabine combined with carboplatin in chemo-na? ve

patients with non-small cell lung cancer (NSCLC). The study involved 37 chemo-naive patients with unresectable stage IIIB or stage IV NSCLC. The predominant histological type was squamous carcinoma (22/37), and the performance status (PS) was 2 in 23 patients (62%). All received gemcitabine, 250 mg/m² in 6-hour infusion on days 1 and 8 plus carboplatin area under the curve (AUC) = 5 on day 1, every 28 days. The overall response rate (ORR) was 62.2% and disease stabilization was achieved in 21.6% of the patients. After a median follow-up duration of 13 months, the median overall survival (OS) time was 14.0 months (95% CI 13.3-16.6 months), and the median progression-free survival (PFS) time was 7.0 months (95% CI 6.1-8.9 months). Hematological toxicities were well-tolerated with the development of grade 3/4 neutropenia and thrombocytopenia in 10.3 and 10.3% of patients respectively, and the gastrointestinal toxicities were mild.

[160]

TÍTULO / TITLE: - Ca/calmodulin-dependent protein kinase IIgamma, a critical mediator of the NF-kappaB network, is a novel therapeutic target in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Lett. 2013 Nov 1. pii: S0304-3835(13)00751-9. doi: 10.1016/j.canlet.2013.10.022.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.10.022](#)

AUTORES / AUTHORS: - Chai S; Qian Y; Tang J; Liang Z; Zhang M; Si J; Li X; Huang W; Xu R; Wang K

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, the Second Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou 310009, China.

RESUMEN / SUMMARY: - The molecular mechanism that triggers constitutive activation of nuclear factor-kappa B (NF-kappaB) in non-small cell lung cancer (NSCLC) remains elusive. In this present study, we demonstrated that Ca²⁺/calmodulin-dependent protein kinase IIgamma (CaMKIIgamma) is a critical molecular switch of continuous activation of NF-kappaB in NSCLC. We found that CaMKIIgamma was aberrantly expressed in human NSCLC tissues and correlated well with the degree of malignancy. Functionally, CaMKIIgamma promoted the growth and survival of NSCLC cells via direct activation of NF-kappaB and multiple oncogenic signaling pathways in NSCLC. Taken together, our findings described a previously uncharacterized role of CaMKIIgamma in NSCLC, and suggest a novel potential therapeutic target for NSCLC treatment.

[161]

TÍTULO / TITLE: - Radiotherapy for postoperative thoracic lymph node recurrence of non-small-cell lung cancer provides better outcomes if the disease is asymptomatic and a single-station involvement.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1417-24. doi: 10.1097/JTO.0b013e3182a5097b.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a5097b](#)

AUTORES / AUTHORS: - Okami J; Nishiyama K; Fujiwara A; Konishi K; Kanou T; Tokunaga T; Teshima T; Higashiyama M

INSTITUCIÓN / INSTITUTION: - Departments of *General Thoracic Surgery and daggerRadiation Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan.

RESUMEN / SUMMARY: - OBJECTIVE: Thoracic lymph node recurrence after complete resection is common in non-small-cell lung cancer but it mostly occurs along with distant metastases. The recurrent disease might be localized and curative intent radiation therapy is the treatment of choice if no evidence of hematogenous metastasis is observed. We sought to describe the outcomes of thoracic radiotherapy for thoracic lymph node recurrences. METHODS: Fifty patients who had developed thoracic lymph node recurrence after complete resection received curative intent radiotherapy between 1997 and 2009. The clinical endpoints included the tumor response, overall survival, progression-free survival, locoregional recurrence within the irradiated field, and any other recurrence. RESULTS: The planned total radiotherapy was completed in 49 patients with minor toxicity. The median follow-up time after radiotherapy was 41 (19-98) months among the survivors. The response to treatment was complete response in 65%, partial response in 24%, and progressive disease in 10% of the evaluated patients. The median overall survival after radiotherapy was 37.3 months. The 5-year overall survival, progression-free survival, and local control rate were 36.1%, 22.2%, and 61.1%, respectively. A multivariate analysis revealed that the absence of symptoms and the involvement of a single lymph node station were significant factors associated with a better overall survival. CONCLUSIONS: Radiation therapy for thoracic lymph node recurrence after complete resection is safe and provides acceptable disease control. This treatment provides a better outcome if the disease is asymptomatic and has a single-station involvement. Early detection of the recurrence may thus improve the effectiveness of this treatment.

[162]

TÍTULO / TITLE: - Asbestos-induced mesothelioma: is fiber biopersistence really a critical factor?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Pathol. 2013 Nov;183(5):1378-81. doi: 10.1016/j.ajpath.2013.09.005. Epub 2013 Sep 29.

●● Enlace al texto completo (gratis o de pago) [1016/j.ajpath.2013.09.005](#)

AUTORES / AUTHORS: - Kagan E

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Uniformed Services University of the Health Sciences, Bethesda, Maryland. Electronic address: elliott.kagan@usuhs.edu.

RESUMEN / SUMMARY: - This Commentary highlights the research by Qi et al detailing the similarities and differences between crocidolite and chrysotile asbestos in terms of their transcriptional effects and transforming actions in human mesothelial cells.

[163]

TÍTULO / TITLE: - MET Gene Copy Number Gain is an Independent Poor Prognostic Marker in Korean Stage I Lung Adenocarcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Nov 9.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3355-1](#)

AUTORES / AUTHORS: - Jin Y; Sun PL; Kim H; Seo AN; Jheon S; Lee CT; Chung JH

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Republic of Korea.

RESUMEN / SUMMARY: - BACKGROUND: MET gene copy number gain (CNG) and protein overexpression have been reported in lung cancer, but the clinical implications in early stage adenocarcinoma remain unclear. METHODS: We investigated MET gene copy number and protein expression in 141 cases of surgically resected stage I pulmonary adenocarcinoma. MET gene CNG was determined by silver in situ hybridization, and MET protein expression was assessed by immunohistochemistry. The correlation between MET gene CNG/protein expression and clinicopathologic parameters and prognostic significance was analyzed. RESULTS: MET gene CNG was found in 24.1 % (34 of 141) of the cases and was associated with larger tumor size, pleural invasion, and lymphatic vessel invasion. MET gene CNG was inversely correlated with the presence of lepidic subtype ($r = -0.17$, $p = 0.045$) and was not associated with EGFR, KRAS mutation, or ALK gene rearrangement. In addition, MET gene CNG was significantly associated with shorter disease-free survival (DFS) (49 vs. 75 months; $p < 0.001$) and shorter overall survival (OS) (65 vs. 78 months; $p = 0.01$). Multivariate analysis confirmed that MET gene CNG was significantly associated with poorer DFS [$p < 0.001$; hazard ratio (HR) 5.5; 95 % confidence interval (CI) 2.2-13.9] but was not significantly associated with OS. MET overexpression was observed in 71.3 % of cases (97 of 136), but it was not correlated with gene CNG. CONCLUSIONS: MET gene CNG is an independent poor prognostic factor in patients with stage I lung adenocarcinoma. It is associated with aggressive pathologic features and is inversely correlated with the presence of lepidic subtype.

[164]

TÍTULO / TITLE: - Radical pleurectomy/decortication followed by high dose of radiation therapy for malignant pleural mesothelioma. Final results with long-term follow-up.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 27. pii: S0169-5002(13)00457-1. doi: 10.1016/j.lungcan.2013.10.013.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.013](#)

AUTORES / AUTHORS: - Minatel E; Trovo M; Polesel J; Baresic T; Bearz A; Franchin G; Gobitti C; Rumeileh IA; Drigo A; Fontana P; Pagan V; Trovo MG

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Centro di Riferimento Oncologico of Aviano, Italy.

RESUMEN / SUMMARY: - PURPOSE: We have previously shown the feasibility of delivering high doses of radiotherapy in malignant pleural mesothelioma (MPM) patients who underwent radical pleurectomy/decortication (P/D) or surgical biopsy. In this report, we present the long-term results of MPM patients treated with radical P/D followed by high doses of radiotherapy. METHODS AND MATERIALS: Twenty consecutive MPM patients were enrolled in this prospective study and underwent radical P/D followed by high dose radiotherapy. The clinical target volume was defined

as the entire hemithorax excluding the intact lung. The dose prescribed was 50Gy in 25 fractions. Any FDG-avid areas or regions of particular concern for residual disease were given a simultaneous boost to 60Gy. Nineteen patients received cisplatin/pemetrexed chemotherapy. Kaplan-Meier analysis was used to calculate rates of overall survival (OS), progression-free survival (PFS), and loco-regional control (LRC). RESULTS: The median follow-up was of 27 months. The median OS and PFS were 33 and 29 months, respectively. The median LRC was not reached. The Kaplan-Meier estimates of OS at 2 and 3 years were 70% and 49%, respectively. The estimates of PFS at 2 and 3 years were 65% and 46%, respectively. The estimates of LRC at 2 and 3 years were 68% and 59%, respectively. The predominant pattern of failure was distant: 7 patients developed distant metastases as the first site of relapse, whereas only 3 patients experienced an isolated loco-regional recurrence. No fatal toxicity was reported. Five Grades 2-3 pneumonitis were documented. CONCLUSIONS: High dose radiation therapy following radical P/D led to excellent loco-regional control and survival results in MPM patients. A median OS of 33 months and a 3-year OS rate of 49% are among the best observed in recent studies, supporting the idea that this approach represents a concrete therapeutic option for malignant pleural mesothelioma.

[165]

TÍTULO / TITLE: - Additional weekly Cetuximab to concurrent chemoradiotherapy in locally advanced non-small cell lung carcinoma: Efficacy and safety outcomes of a randomized, multi-center phase II study investigating.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Nov 11. pii: S0167-8140(13)00513-6. doi: 10.1016/j.radonc.2013.10.009.

●● Enlace al texto completo (gratis o de pago) [1016/j.radonc.2013.10.009](#)

AUTORES / AUTHORS: - van den Heuvel MM; Uytendaele W; Vincent AD; de Jong J; Aerts J; Koppe F; Knegjens J; Codrington H; Kunst PW; Dieleman E; Verheij M; Belderbos J

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology, The Netherlands Cancer Institute, Amsterdam, The Netherlands. Electronic address: m.vd.heuvel@nki.nl.

RESUMEN / SUMMARY: - BACKGROUND: Modest benefits from concurrent chemoradiotherapy in patients with locally advanced NSCLC warrant further clinical investigations to identify more effective treatment regimens. Cetuximab, a monoclonal antibody against the epidermal growth factor receptor has shown activity in NSCLC. We report on the safety and efficacy of the combination of daily dose Cisplatin and concurrent radiotherapy with or without weekly Cetuximab. PATIENTS AND METHODS: Patients received high dose accelerated radiotherapy (66Gy in 24 fractions) and concurrent daily Cisplatin (6mg/m²) without (Arm A) or with (Arm B) weekly Cetuximab (400mg/m² loading dose one week prior to radiotherapy followed by weekly 250mg/m²). The primary endpoint of the trial was objective local control rate (OLCR) determined at 6-8 weeks after treatment. Toxicity was reported as well. RESULTS: Between February 2009 and May 2011, 102 patients were randomized. Median follow up was 29 months. The OLCR was 84% in Arm A and 92% in Arm B (p=0.36). The one-year local progression free interval (LPFI) and overall survival (OS)

were 69% and 82% for Arm A and 73% and 71% for Arm B, respectively (LPFI p=0.39; OS p=0.99). Toxicity compared equally between both groups. CONCLUSION: The addition of Cetuximab to radiotherapy and concurrent Cisplatin did not improve disease control in patients with locally advanced NSCLC but increased treatment related toxicity.

[166]

TÍTULO / TITLE: - Degrees of dysplasia based on viral typing in patients with cidofovir use and recurrent respiratory papillomatosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Voice. 2013 Nov;27(6):765-8. doi: 10.1016/j.jvoice.2013.06.014. Epub 2013 Oct 12.

●● Enlace al texto completo (gratis o de pago) [1016/j.jvoice.2013.06.014](#)

AUTORES / AUTHORS: - Moore JE; Garcia A; Sanyal S; Saunders S; Portnoy JE; Hu A; Sataloff RT

INSTITUCIÓN / INSTITUTION: - Department of Otolaryngology-Head and Neck Surgery, Drexel University, College of Medicine, Philadelphia, Pennsylvania. Electronic address: jeaglinmoore@phillyent.com.

RESUMEN / SUMMARY: - OBJECTIVES/HYPOTHESIS: To evaluate the degree of dysplasia following cidofovir injections while documenting human papillomavirus (HPV) type in patients with recurrent respiratory papillomatosis (RRP). STUDY DESIGN: Retrospective chart review. METHODS: Demographic data, operative reports, and pathology results were reviewed from 25 patients with RRP who had had cidofovir injections. All patients included had adult onset RRP, no history of immunosuppression, well-controlled laryngopharyngeal reflux, and no current smoking history. Eight patients were excluded because they did not meet the inclusion criteria. RESULTS: Seventeen patients had adequate data for analysis and 40 subsites were identified with sufficient data for analysis. Patients negative for both low and high risk did not have progressive dysplasia at the conclusion of the study. Of the patients with positive viral typing, 70% had progressive disease at the conclusion of the study. No patients progressed to carcinoma or carcinoma in situ. The average pre- and post-treatment dysplasia scores were analyzed using a Student paired t test. There was no difference in mean dysplasia score, indicating that there was no increased risk of dysplasia following cidofovir treatment. CONCLUSIONS: To our knowledge, this is the first study looking at the degree of dysplasia while documenting HPV types in RRP. Our study suggests that HPV type appears to be relevant in the disease progression of RRP and that cidofovir does not increase the risk of dysplasia.

[167]

TÍTULO / TITLE: - Claudin-7 suppresses the cytotoxicity of TRAIL-expressing mesenchymal stem cells in H460 human non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Apoptosis. 2013 Nov 16.

●● Enlace al texto completo (gratis o de pago) [1007/s10495-013-0938-z](#)

AUTORES / AUTHORS: - Xia P; Wang W; Bai Y

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, School of Basic Medical Science, China Medical University, Shenyang, 110001, People's Republic of China, nn001007@163.com.

RESUMEN / SUMMARY: - Evidence suggests that the cytokine tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is a promising candidate for cancer therapeutics. Studies have also shown that claudin-7 (CLDN7) expression is variably dysregulated in various malignant neoplasms, with a role in lung cancer that has not been definitively decided. This work investigated the differential sensitivity of CLDN7-overexpressing human NSCLC H460 cells to TRAIL in vitro and in mouse xenografts, and explored the molecular mechanisms responsible for these effects. NCI-H460 cells were transfected or not with green fluorescent protein-tagged CLDN7. Each group was then exposed to mesenchymal stem cells (MSCs) or red fluorescent protein-tagged MSCs transduced with lentivirus expressing membrane-bound TRAIL. The effects and related mechanisms of these treatments were evaluated in vitro, and in vivo in murine xenografts. Our results indicate that TRAIL induced apoptosis in H460 cells in vitro, and in established xenograft tumors TRAIL was associated with a decrease in tumor size, tumor weight, and circulating tumor cells. CLDN7 was found to inhibit the MEK/ERK signaling pathway, leading to inhibition of death receptor 5 (TNFRSF10B). The cytotoxicity of TRAIL was confirmed in H460 cells and in vivo, and CLDN7 suppressed the cytotoxicity of TRAIL in H460 cells. Our results indicate that TRAIL may be a useful therapy to enhance apoptosis in CLDN7-negative lung cancer cells.

[168]

TÍTULO / TITLE: - Clinical Characteristics and Survival in Never Smokers With Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Arch Bronconeumol. 2013 Nov 23. pii: S0300-2896(13)00307-4. doi: 10.1016/j.arbres.2013.09.015.

●● Enlace al texto completo (gratis o de pago) 1016/j.arbres.2013.09.015

AUTORES / AUTHORS: - Parente Lamelas I; Abal Arca J; Blanco Cid N; Alves Perez MT; Dacal Quintas R; Gomez Marquez H; Garcia Montenegro RA; Marcos Velazquez P

INSTITUCIÓN / INSTITUTION: - Servicio de Neumología, Complejo Hospitalario Universitario de Ourense, Ourense, España. Electronic address: parentelamelas@gmail.com.

RESUMEN / SUMMARY: - INTRODUCTION AND OBJECTIVE: To analyze the frequency, clinical characteristics and survival of patients with lung cancer (LC) who have never smoked in comparison to patients who smoke. PATIENTS AND METHODS: A retrospective study in patients diagnosed with LC by cytohistology between 1999 and 2011. Survival was estimated by the Kaplan-Meier method. The chi2 test was used to estimate the relationship between the variables. RESULTS: A total of 2161 patients were diagnosed with LC, 396 (18.3%) of whom had never smoked. The mean age (+/-standard deviation) in this group was 72.85+/-10.52; 64.6% were women and 35.4% men. According to the cytohistology, 55.6% were adenocarcinoma, 20.5% squamous cell, 15% small cell, 2.7% large cell and 6.2% other subtypes. The diagnosis was made in advanced stage (iv) in 61.4%, and 14.4% of the patients received surgical treatment. Survival was 12.4%, with no differences between

the two groups. In the group of never smokers, women had better survival than men. CONCLUSIONS: Of the patients diagnosed with LC, 18.3% had never smoked. It was diagnosed mainly in women, at advanced stages and the most common histological type was adenocarcinoma. There were no survival differences compared to the group of smokers.

[169]

TÍTULO / TITLE: - Micropapillary and solid subtypes of invasive lung adenocarcinoma: Clinical predictors of histopathology and outcome.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Nov 4. pii: S0022-5223(13)01142-2. doi: 10.1016/j.jtcvs.2013.09.045.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.jtcvs.2013.09.045](#)

AUTORES / AUTHORS: - Cha MJ; Lee HY; Lee KS; Jeong JY; Han J; Shim YM; Hwang HS

INSTITUCIÓN / INSTITUTION: - Department of Radiology and Center for Imaging Science, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - OBJECTIVE: To evaluate the clinical effect of the presence of a micropapillary or solid subtype on the outcomes in lung adenocarcinoma and to determine the predictors of such a histopathologic diagnosis. METHODS: A total of 511 patients with lung adenocarcinoma ≤ 3 cm were included. According to the presence of micropapillary or solid subtypes, we classified the patients into 4 subgroups: both subtypes absent (MP-/S-, n = 87), either subtype present (MP+/S-, n = 207 and MP-/S+, n = 196), and both present (MP+/S+, n = 21) to determine the association between the micropapillary or solid subtype and survival outcome or clinical and imaging conditions. Univariate and multivariate analyses were undertaken to determine the parameters, allowing the prediction of the presence of the micropapillary or solid subtype. RESULTS: Overall survival (OS) and disease-free survival (DFS) differed significantly among the 4 subgroups (P < .001 and P = .004, respectively). The MP-/S- tumors showed better DFS than those containing either the micropapillary or solid subtype. Patients with the micropapillary subtype had significantly worse OS than patients without the micropapillary subtype. This difference remained significant, together with stage, after adjustment for gender, age, adjuvant therapy, tumor size, and solid subtype (DFS and OS, P = .016 and P = .002, respectively). On multivariate analysis, greater than stage I, tumor size ≥ 2.5 cm, solid mass, and maximal standardized uptake value of ≥ 7 were independent predictors of the presence of a micropapillary or solid subtype. CONCLUSIONS: Micropapillary and solid subtypes are common in tumors greater than stage I, with size ≥ 2.5 cm, pure solid type, and maximal standardized uptake value of ≥ 7 , which were predictors for poor DFS. The presence of the micropapillary subtype was a single prognostic factor for OS.

[170]

TÍTULO / TITLE: - Bevacizumab improves the antitumor efficacy of adoptive cytokine-induced killer cells therapy in non-small cell lung cancer models.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2014 Jan;31(1):777. doi: 10.1007/s12032-013-0777-3. Epub 2013 Nov 24.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0777-3](https://doi.org/10.1007/s12032-013-0777-3)

AUTORES / AUTHORS: - Tao L; Huang G; Shi S; Chen L

INSTITUCIÓN / INSTITUTION: - Medical Oncology Department of Jinling Hospital, Medical School of Nanjing University, 305 ZhongShan Eastern Road, Nanjing, 210002, People's Republic of China, taoleilei44@hotmail.com.

RESUMEN / SUMMARY: - Cytokine-induced killer cells (CIK cells) are a heterogeneous population of cells generated from peripheral blood mononuclear cells, which share phenotypic and functional properties with both natural killer and T cells. CIK cells therapy, as an adoptive immunotherapy with strong antitumor activity in vitro, represents a promising approach for the treatment of a broad array of malignant tumors. However, clinical trials in CIK cells therapy did not show more noticeable improvement as anticipated in cure rates or long-term survival. Possible explanations are that abnormal tumor vasculature and hypoxic microenvironment may highly limit the therapeutic benefits of CIK cells therapy. We hypothesized that antiangiogenesis therapy could enhance the antitumor efficacy of CIK cells by normalizing tumor vasculature and modulating tumor hypoxic microenvironment. In this study, we combined bevacizumab and adoptive CIK cells therapy in the treatment of lung adenocarcinoma bearing murine models. Flow cytometry, intravital microscopy and immunohistochemistry were applied to detect tumor vasculature and hypoxic microenvironment as well as the infiltration of CIK cells. The results indicated that bevacizumab-combined adoptive CIK cells had synergistic inhibition effects on the growth of lung adenocarcinoma. Hypoxia significantly inhibited the infiltration of CIK cells into tumor tissue. Bevacizumab could normalize tumor vasculature and decrease tumor hypoxic area. Furthermore, combination therapy enhanced more CIK cells infiltrated into tumor compared with other treatment. Bevacizumab improves antitumor efficacy of CIK cells transfer therapy in non-small cell lung cancer (NSCLC). The study provides a reasonable and beneficial strategy that combined antiangiogenesis therapy with CIK cells therapy for patients of advanced stage non-small cell lung cancer.

[171]

TÍTULO / TITLE: - Synergistic inhibition of lung cancer cell lines by (-)-epigallocatechin-3-gallate in combination with clinically used nitrocatechol inhibitors of catechol-O-methyltransferase.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Carcinogenesis. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [1093/carcin/bgt347](https://doi.org/10.1093/carcin/bgt347)

AUTORES / AUTHORS: - Forester SC; Lambert JD

INSTITUCIÓN / INSTITUTION: - Center of Excellence for Plant and Mushroom Foods for Human Health, Department of Food Science.

RESUMEN / SUMMARY: - (-)-Epigallocatechin-3-gallate (EGCG) has exhibited been studied for lung cancer inhibitory activity in vitro and in animal models, but it is rapidly methylated and inactivated by catechol-O-methyltransferase (COMT). Entacapone and tolcapone, COMT inhibitors, are used to mitigate the symptoms of Parkinson's disease. We investigated the synergistic effects of entacapone/tolcapone and EGCG against lung cancer cell lines in culture. EGCG, entacapone and tolcapone inhibited the growth

of H1299 human lung cancer cells (IC50 = 174.9, 76.8 and 29.3 microM, respectively) and CL-13 murine lung cancer cells (IC50 = 181.5, 50.7 and 19.7 microM, respectively) as single agents following treatment for 72h. Treatment with 1:10, 1:5, 1:2.5 and 1:1 combinations of EGCG and tolcapone or entacapone resulted in synergistically enhanced growth inhibition. The growth inhibitory effect of the combinations was mediated by induction of intracellular oxidative stress, cell cycle arrest and decreased nuclear translocation of nuclear factor-kappaBeta. Methylation of EGCG was dose dependently inhibited by entacapone and tolcapone (IC50 = 10 and 20 microM, respectively) in a cell-free system, and both compounds increased the intracellular levels of unmethylated EGCG. Treatment of mice with EGCG in combination with tolcapone increased the bioavailability of EGCG and decreased the methylation of plasma norepinephrine: no apparent liver or behavioral toxicity was observed. In conclusion, the combination of EGCG and entacapone/tolcapone synergistically inhibited the growth of lung cancer cells in culture, and the mechanistic basis for this synergy is likely due in part to inhibition of COMT with resultant increase in the levels of unmetabolized EGCG.

[172]

TÍTULO / TITLE: - Retreatment with icotinib in a patient with metastatic lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumori. 2013 May-Jun;99(3):124e-6e. doi: 10.1700/1334.14820.

●● Enlace al texto completo (gratis o de pago) [1700/1334.14820](#)

AUTORES / AUTHORS: - Sun X; Zheng Y

RESUMEN / SUMMARY: - A patient with advanced non-small cell lung cancer (NSCLC) was successfully treated with icotinib. The tumor relapsed after a partial response and the patient was retreated with icotinib after temporary cessation. Surprisingly we found that the tumor responded to icotinib again. The exact mechanism of this phenomenon is still unclear. A better understanding of the biological basis of involved events will help us to improve treatment of advanced NSCLC.

[173]

TÍTULO / TITLE: - Lymph node involvement and metastatic lymph node ratio influence the survival of malignant pleural mesothelioma: A French multicenter retrospective study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):415-21. doi: 10.3892/or.2013.2800. Epub 2013 Oct 18.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2800](#)

AUTORES / AUTHORS: - Hysi I; Le Pimpec-Barthes F; Alifano M; Venissac N; Mouroux J; Regnard JF; Riquet M; Porte H

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Albert Calmette Hospital, Lille, France.

RESUMEN / SUMMARY: - Malignant pleural mesothelioma (MPM) is a rare tumor with disastrous evolution. The prognostic value of nodal involvement is still debated. We

analyzed the impact of nodal involvement on overall survival (OS) in patients treated by multimodal therapy including extra pleural pneumonectomy (EPP). We evaluated the role, as a prognostic factor, of the metastatic lymph node ratio (LNR), corresponding to the number of involved nodes out of the total number of removed nodes. In this retrospective multicentric study, we reviewed the data of 99 MPM patients. Information regarding lymph node involvement was assessed from the final pathology reports. N1-N3 patients were pooled as N+ group. The OS, calculated by the Kaplan-Meier method, was compared using the logrank test. A multivariate Cox proportional hazards model was used to identify independent prognostic factors. For the whole cohort, median OS was 18.3 months and 5-year survival was 17.5%. N+ status reduced significantly the median survival (22.4 months for N0 patients vs 12.7 months for N+ patients, P=0.002). A lower metastatic LNR ($\leq 13\%$) was associated with a significantly improved median survival (19.9 vs. 11.7 months, P=0.01). OS was not related to the number of involved or total removed lymph nodes. In multivariate analysis, only adjuvant radiotherapy (P=0.001) was identified as an independent positive prognostic factor. Metastatic LNR is a more reliable prognostic factor than the number of involved lymph nodes or the total number of removed nodes. However, it could not be identified as an independent prognostic factor.

[174]

TÍTULO / TITLE: - Gefitinib and erlotinib for non-small cell lung cancer patients who fail to respond to radiotherapy for brain metastases.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Neurosci. 2013 Aug 11. pii: S0967-5868(13)00436-0. doi: 10.1016/j.jocn.2013.05.022.

●● Enlace al texto completo (gratis o de pago) [1016/j.jocn.2013.05.022](#)

AUTORES / AUTHORS: - Song Z; Zhang Y

INSTITUCIÓN / INSTITUTION: - Department of Chemotherapy, Zhejiang Cancer Hospital, 38 Guangji Road, Hangzhou 310022, China; Key Laboratory, Diagnosis and Treatment Technology on Thoracic Oncology, Zhejiang Province, Hangzhou, China.

RESUMEN / SUMMARY: - Survival and treatment options are limited for patients with brain metastases arising from non-small cell lung cancer (NSCLC). We evaluated erlotinib and gefitinib as salvage treatments for NSCLC patients with brain metastases that failed to respond to radiotherapy in a retrospective study. Survival was estimated using Kaplan-Meier analysis and log-rank tests. Multivariable predictors were assessed using the Cox proportional hazards model. Epidermal growth factor receptor (EGFR) mutations were assessed in part using sequencing methods. The 103 NSCLC patients who were treated with gefitinib or erlotinib for salvage treatment for brain metastases between January 2005 and December 2011 had overall objective response rates (ORR) of 11.7%, disease control rates (DCR) of 53.4%, 3.6 months of median progression-free survival (PFS), and 7.5 months of median survival. Intracranial disease had an ORR of 11.7% and a DCR of 70.9%. Extracranial disease had an ORR of 8.7% and a DCR of 66.0%. Nine patients (of 22 tested) were documented with EGFR mutations (five with deletion in exon 19 and four with L858R in exon 21). The median PFS for EGFR mutation patients was 9.0 months, versus 3.1 months for wild-type patients (p=0.001). The recursive partitioning analysis class was the only factor predictive of PFS using univariate analyses and was associated with survival in the

multivariate analysis. Our retrospective data suggest a potential role for gefitinib and erlotinib in advanced NSCLC patients with brain metastases which have failed to respond to radiotherapy. Patients with EGFR mutations benefited most from treatment.

[175]

TÍTULO / TITLE: - Iris Metastasis in a Patient With Small Cell Lung Cancer: Incidental Detection With 18F-FDG PET/CT.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Nucl Med. 2013 Oct 3.

●● Enlace al texto completo (gratis o de pago) [1097/RLU.0b013e3182a7549f](#)

AUTORES / AUTHORS: - Karunanithi S; Sharma P; Jain S; Mukherjee A; Kumar R

INSTITUCIÓN / INSTITUTION: - From the Department of Nuclear Medicine, All India Institute of Medical Sciences, New Delhi, India.

RESUMEN / SUMMARY: - Iris metastasis is one of the rare forms of ocular metastasis. Lung and breast cancers represent more than two thirds of the primary tumor sites in such patients. We here present the F-FDG PET/CT findings in a 60-year-old male patient with small cell lung cancer where metastasis to iris was incidentally discovered on PET/CT.

[176]

TÍTULO / TITLE: - Benign Cystic Mesothelioma: False-Positive Iodine Accumulation in a Patient With Oncocytic Follicular Thyroid Carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Nucl Med. 2013 Nov 7.

●● Enlace al texto completo (gratis o de pago)

[1097/RLU.0b013e3182a75664](#)

AUTORES / AUTHORS: - Meyer M; Godbert Y; Soubeyran I; Cazeau AL; Bonichon F

INSTITUCIÓN / INSTITUTION: - From the *Departments of Nuclear Medicine; and daggerPathology, Institut Bergonie, Bordeaux, France.

RESUMEN / SUMMARY: - Whole-body (I) scintigraphy (WBS) is used to detect residual or metastatic tissue during treatment of differentiated thyroid carcinoma in combination with thyroglobulin (Tg) and ultrasonography of the neck. It is a highly sensitive method, but there is a high rate of false positives. We report the case of a 52-year-old woman with false-positive iodine accumulation in a benign cystic mesothelioma discovered during treatment for a oncocytic follicular thyroid carcinoma (stage pT2 pNx Mx). This lesion was detected by WBS and confirmed by surgery and histopathologic analysis.

[177]

TÍTULO / TITLE: - Phosphorylation of paxillin confers cisplatin resistance in non-small cell lung cancer via activating ERK-mediated Bcl-2 expression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Oct 7. doi: 10.1038/onc.2013.389.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.389](#)

AUTORES / AUTHORS: - Wu DW; Wu TC; Wu JY; Cheng YW; Chen YC; Lee MC; Chen CY; Lee H

INSTITUCIÓN / INSTITUTION: - Graduate Institute of Cancer Biology and Drug Discovery, Taipei Medical University, Taipei, Taiwan, ROC.

RESUMEN / SUMMARY: - Paxillin (PXN) is required for receptor tyrosine kinase-mediated ERK activation, and the activation of the Raf/MEK/ERK cascade has been linked with Bcl-2 expression. We hypothesized that phosphorylation of PXN by the EGFR/Src pathway might contribute to cisplatin resistance via increased Bcl-2 expression. We show that cisplatin resistance was dependent on PXN expression, as evidenced by PXN overexpression in TL-13 and TL-10 cells and PXN knockdown in H23 and CL1-5 cells. Specific inhibitors of signaling pathways indicated that the phosphorylation of PXN at Y118 and Y31 via the Src pathway was responsible for cisplatin resistance. We further demonstrated that ERK activation was also dependent on this PXN phosphorylation. Bcl-2 transcription was upregulated by phosphorylated PXN-mediated ERK activation via increased binding of phosphorylated CREB to the Bcl-2 promoter. A subsequent increase in Bcl-2 levels by a PXN/ERK axis was responsible for the resistance to cisplatin. Animal models further confirmed the findings of in vitro cells indicating that xenograft tumors induced by TL-13-overexpressing cells were successfully suppressed by cisplatin combined with Src or ERK inhibitor compared with treatment of cisplatin, Src inhibitor or ERK inhibitor alone. A positive correlation of phosphorylated PXN with phosphorylated ERK and Bcl-2 was observed in lung tumors from NSCLC patients. Patients with tumors positive for PXN, phosphorylated PXN, phosphorylated ERK and Bcl-2 more commonly showed a poorer response to cisplatin-based chemotherapy than did patients with negative tumors. Collectively, PXN phosphorylation might contribute to cisplatin resistance via activating ERK-mediated Bcl-2 transcription. Therefore, we suggest that Src or ERK inhibitor might be helpful to improve the sensitivity for cisplatin-based chemotherapy in NSCLC patients with PXN-positive tumors. Oncogene advance online publication, 7 October 2013; doi:10.1038/onc.2013.389.

[178]

TÍTULO / TITLE: - Interfraction Displacement of Primary Tumor and Involved Lymph Nodes Relative to Anatomic Landmarks in Image Guided Radiation Therapy of Locally Advanced Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Nov 13. pii: S0360-3016(13)03190-8. doi: 10.1016/j.ijrobp.2013.09.050.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijrobp.2013.09.050](#)

AUTORES / AUTHORS: - Jan N; Balik S; Hugo GD; Mukhopadhyay N; Weiss E

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Virginia Commonwealth University, Richmond, Virginia.

RESUMEN / SUMMARY: - PURPOSE: To analyze primary tumor (PT) and lymph node (LN) position changes relative to each other and relative to anatomic landmarks during conventionally fractionated radiation therapy for patients with locally advanced lung cancer. METHODS AND MATERIALS: In 12 patients with locally advanced non-small cell lung cancer PT, LN, carina, and 1 thoracic vertebra were manually contoured on weekly 4-dimensional fan-beam CT scans. Systematic and random interfraction displacements of all contoured structures were identified in the 3 cardinal directions, and resulting setup margins were calculated. Time trends and the effect of volume

changes on displacements were analyzed. RESULTS: Three-dimensional displacement vectors and systematic/random interfraction displacements were smaller for carina than for vertebra both for PT and LN. For PT, mean (SD) 3-dimensional displacement vectors with carina-based alignment were 7 (4) mm versus 9 (5) mm with bony anatomy ($P < .0001$). For LN, smaller displacements were found with carina- (5 [3] mm, $P < .0001$) and vertebra-based (6 [3] mm, $P = .002$) alignment compared with using PT for setup (8 [5] mm). Primary tumor and LN displacements relative to bone and carina were independent ($P > .05$). Displacements between PT and bone ($P = .04$) and between PT and LN ($P = .01$) were significantly correlated with PT volume regression. Displacements between LN and carina were correlated with LN volume change ($P = .03$). CONCLUSIONS: Carina-based setup results in a more reproducible PT and LN alignment than bony anatomy setup. Considering the independence of PT and LN displacement and the impact of volume regression on displacements over time, repeated CT imaging even with PT-based alignment is recommended in locally advanced disease.

[179]

TÍTULO / TITLE: - Dynamics of the risk of smoking-induced lung cancer: a compartmental hidden markov model for longitudinal analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Epidemiology. 2014 Jan;25(1):28-34. doi: 10.1097/EDE.0000000000000032.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/EDE.0000000000000032](#)

AUTORES / AUTHORS: - Chadeau-Hyam M; Tubert-Bitter P; Guihenneuc-Jouyaux C; Campanella G; Richardson S; Vermeulen R; De Iorio M; Galea S; Vineis P

INSTITUCIÓN / INSTITUTION: - From the aMRC/HPA Centre for Environment and Health, School of Public Health, Imperial College, London, United Kingdom; bCentre for Research in Epidemiology and Population Health, INSERM, Villejuif, France; cUMRS 1018, University Paris Sud, Villejuif, France; dEA 4064, University Paris Descartes, Paris, France; eMRC Biostatistics Unit, Institute of Public Health, Cambridge, United Kingdom; fInstitute for Risk Assessment Sciences, Utrecht University, Utrecht, The Netherlands; gDepartment of Statistical Science, University College London, London, United Kingdom; and hDepartment of Epidemiology, Mailman School of Public Health, Columbia University, NY.

RESUMEN / SUMMARY: - BACKGROUND: To account for the dynamic aspects of carcinogenesis, we propose a compartmental hidden Markov model in which each person is healthy, asymptotically affected, diagnosed, or deceased. Our model is illustrated using the example of smoking-induced lung cancer. METHODS: The model was fitted on a case-control study nested in the European Prospective Investigation into Cancer and Nutrition study, including 757 incident cases and 1524 matched controls. Estimation was done through a Markov Chain Monte Carlo algorithm, and simulations based on the posterior estimates of the parameters were used to provide measures of model fit. We performed sensitivity analyses to assess robustness of our findings. RESULTS: After adjusting for its impact on exposure duration, age was not found to independently drive the risk of lung carcinogenesis, whereas age at starting smoking in ever-smokers and time since cessation in former smokers were found to be

influential. Our data did not support an age-dependent time to diagnosis. The estimated time between onset of malignancy and clinical diagnosis ranged from 2 to 4 years. Our approach yielded good performance in reconstructing individual trajectories in both cases (sensitivity >90%) and controls (sensitivity >80%). CONCLUSION: Our compartmental model enabled us to identify time-varying predictors of risk and provided us with insights into the dynamics of smoking-induced lung carcinogenesis. Its flexible and general formulation enables the future incorporation of disease states, as measured by intermediate markers, into the modeling of the natural history of cancer, suggesting a large range of applications in chronic disease epidemiology.

[180]

TÍTULO / TITLE: - Sublobar resection is equivalent to lobectomy for clinical stage 1A lung cancer in solid nodules.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Nov 23. pii: S0022-5223(13)01165-3. doi: 10.1016/j.jtcvs.2013.09.065.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.jtcvs.2013.09.065](#)

AUTORES / AUTHORS: - Altorki NK; Yip R; Hanaoka T; Bauer T; Aye R; Kohman L; Sheppard B; Thurer R; Andaz S; Smith M; Mayfield W; Grannis F; Korst R; Pass H; Straznicka M; Flores R; Henschke CI

INSTITUCIÓN / INSTITUTION: - NY Presbyterian Hospital/Weill Cornell Medical College, New York, NY.

RESUMEN / SUMMARY: - OBJECTIVES: A single randomized trial established lobectomy as the standard of care for the surgical treatment of early-stage non-small cell lung cancer. Recent advances in imaging/staging modalities and detection of smaller tumors have once again rekindled interest in sublobar resection for early-stage disease. The objective of this study was to compare lung cancer survival in patients with non-small cell lung cancer with a diameter of 30 mm or less with clinical stage 1 disease who underwent lobectomy or sublobar resection. METHODS: We identified 347 patients diagnosed with lung cancer who underwent lobectomy (n = 294) or sublobar resection (n = 53) for non-small cell lung cancer manifesting as a solid nodule in the International Early Lung Cancer Action Program from 1993 to 2011. Differences in the distribution of the presurgical covariates between sublobar resection and lobectomy were assessed using unadjusted P values determined by logistic regression analysis. Propensity scoring was performed using the same covariates. Differences in the distribution of the same covariates between sublobar resection and lobectomy were assessed using adjusted P values determined by logistic regression analysis with adjustment for the propensity scores. Lung cancer-specific survival was determined by the Kaplan-Meier method. Cox survival regression analysis was used to compare sublobar resection with lobectomy, adjusted for the propensity scores, surgical, and pathology findings, when adjusted and stratified by propensity quintiles. RESULTS: Among 347 patients, 10-year Kaplan-Meier for 53 patients treated by sublobar resection compared with 294 patients treated by lobectomy was 85% (95% confidence interval, 80-91) versus 86% (confidence interval, 75-96) (P = .86). Cox survival analysis showed no significant difference between sublobar resection and lobectomy when adjusted for propensity scores or when using propensity quintiles (P = .62 and P = .79, respectively). For those with cancers 20 mm or less in diameter, the 10-year rates were

88% (95% confidence interval, 82-93) versus 84% (95% confidence interval, 73-96) (P = .45), and Cox survival analysis showed no significant difference between sublobar resection and lobectomy using either approach (P = .42 and P = .52, respectively). CONCLUSIONS: Sublobar resection and lobectomy have equivalent survival for patients with clinical stage IA non-small cell lung cancer in the context of computed tomography screening for lung cancer.

[181]

TÍTULO / TITLE: - Restoring expression of miR-16: a novel approach to therapy for malignant pleural mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Oncol. 2013 Dec;24(12):3128-35. doi: 10.1093/annonc/mdt412. Epub 2013 Oct 22.

●● [Enlace al texto completo \(gratis o de pago\) 1093/annonc/mdt412](#)

AUTORES / AUTHORS: - Reid G; Pel ME; Kirschner MB; Cheng YY; Mugridge N; Weiss J; Williams M; Wright C; Edelman JJ; Valley MP; McCaughan BC; Klebe S; Brahmbhatt H; Macdiarmid JA; van Zandwijk N

INSTITUCIÓN / INSTITUTION: - Asbestos Diseases Research Institute, University of Sydney, Sydney, Australia.

RESUMEN / SUMMARY: - BACKGROUND: Malignant pleural mesothelioma (MPM) is recalcitrant to treatment and new approaches to therapy are needed. Reduced expression of miR-15/16 in a range of cancer types has suggested a tumour suppressor function for these microRNAs, and re-expression has been shown to inhibit tumour cell proliferation. The miR-15/16 status in MPM is largely unknown. MATERIALS AND METHODS: MicroRNA expression was analysed by TaqMan-based RT-qPCR in MPM tumour specimens and cell lines. MicroRNA expression was restored in vitro using microRNA mimics, and effects on proliferation, drug sensitivity and target gene expression were assessed. Xenograft-bearing mice were treated with miR-16 mimic packaged in minicells targeted with epidermal growth factor receptor (EGFR)-specific antibodies. RESULTS: Expression of the miR-15 family was consistently downregulated in MPM tumour specimens and cell lines. A decrease of 4- to 22-fold was found when tumour specimens were compared with normal pleura. When MPM cell lines were compared with the normal mesothelial cell line MeT-5A, the downregulation of miR-15/16 was 2- to 10-fold. Using synthetic mimics to restore miR-15/16 expression led to growth inhibition in MPM cell lines but not in MeT-5A cells. Growth inhibition caused by miR-16 correlated with downregulation of target genes including Bcl-2 and CCND1, and miR-16 re-expression sensitised MPM cells to pemetrexed and gemcitabine. In xenograft-bearing nude mice, intravenous administration of miR-16 mimics packaged in minicells led to consistent and dose-dependent inhibition of MPM tumour growth. CONCLUSIONS: The miR-15/16 family is downregulated and has tumour suppressor function in MPM. Restoring miR-16 expression represents a novel therapeutic approach for MPM.

[182]

TÍTULO / TITLE: - A common polymorphism in pre-microRNA-146a is associated with lung cancer risk in a Korean population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Gene. 2014 Jan 15;534(1):66-71. doi: 10.1016/j.gene.2013.10.014. Epub 2013 Oct 19.

●● Enlace al texto completo (gratis o de pago) [1016/j.gene.2013.10.014](#)

AUTORES / AUTHORS: - Jeon HS; Lee YH; Lee SY; Jang JA; Choi YY; Yoo SS; Lee WK; Choi JE; Son JW; Kang YM; Park JY

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Cell Biology, School of Medicine, Kyungpook National University, Dong In 2Ga 101, Daegu 700-422, South Korea; Lung Cancer Center, Kyungpook National University Medical Center, 807, Hoguk-ro, Buk-gu, Daegu 702-210, South Korea. Electronic address: jeonh@knu.ac.kr.

RESUMEN / SUMMARY: - INTRODUCTION: MicroRNAs (miRs) play important roles in the development and progression of human cancers. MiR-146a down-regulates epidermal growth factor receptor and the nuclear factor-kappaB regulatory kinase interleukin-1 receptor-associated kinase 1 genes that play important roles in lung carcinogenesis. This study was conducted to evaluate the association between rs2910164C>G, a functional polymorphism in the pre-miR-146a, and lung cancer risk. MATERIAL AND METHODS: The rs2910164C>G genotypes were determined in 1094 patients with lung cancer and 1100 healthy controls who were frequency matched for age and gender. RESULTS: The rs2910164 CG or GG genotype was associated with a significantly decreased risk for lung cancer compared to that of the CC genotype (adjusted odds ratio=0.80, 95% confidence interval=0.66-0.96, P=0.02). When subjects were stratified according to smoking exposure (never, light and heavy smokers), the effect of the rs2910164C>G genotype on lung cancer risk was significant only in never smokers (adjusted odds ratio=0.66, 95% confidence interval=0.45-0.96, P=0.03, under a dominant model for the C allele) and decreased as smoking exposure level increased (Ptrend<0.001). In line with this result, the level of miR-146a expression in the tumor tissues was significantly higher in the GG genotype than in the CC or CG genotype only in never-smokers (P=0.02). CONCLUSIONS: These findings suggest that the rs2910164C>G in pre-miR-146a may contribute to genetic susceptibility to lung cancer, and that miR-146a might be involved in lung cancer development.

[183]

TÍTULO / TITLE: - Radiotherapy for intubated patients with malignant airway obstruction: futile or facilitating extubation?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1365-70. doi: 10.1097/JTO.0b013e3182a47501.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a47501](#)

AUTORES / AUTHORS: - Louie AV; Lane S; Palma DA; Warner A; Cao JQ; Rodrigues GB

INSTITUCIÓN / INSTITUTION: - *Schulich School of Medicine and Dentistry, Western University, London, Ontario; daggerDepartment of Radiation Oncology, London Regional Cancer Program, London, Ontario; and double daggerDepartment of Epidemiology and Biostatistics, Western University, London, Ontario.

RESUMEN / SUMMARY: - INTRODUCTION: The optimal approach to patients with malignant airway obstruction who require intubation and mechanical ventilation but are

ineligible for bronchoscopic interventions is uncertain. Radiotherapy (RT) may be delivered but requires substantial resources in this patient population. In the absence of evidence, it is unknown whether RT facilitates extubation or delays an appropriate transition to end-of-life care. METHODS: We performed a 10-year retrospective review of intensive care unit (ICU) patients treated with RT while on mechanical ventilation for malignant airway obstruction. Primary study endpoints were overall survival (OS) and extubation success (ES), defined as 48 hours or more without reintubation or death. Secondary endpoints included rates of discharge from the ICU and to home. Logistic regression and Cox regression analyses were performed to identify factors associated with OS and ES. RESULTS: Twenty-six patients were eligible for analysis. Seven patients (27%) were extubated; extubations occurred between days 4 and 22 after RT initiation. All patients were discharged from the ICU and most (n = 6) were also discharged home. An association between higher radiation doses and ES was observed (odds ratio per 5 Gy increase: 0.63; p = 0.080). Median OS was only 0.36 months (range, 0-113 months), and 6-month OS was 11%. On Cox regression analysis, increased radiation dose was predictive of improved OS (hazard ratio per 5 Gy increase: 0.74; p = 0.016). CONCLUSIONS: A significant minority of patients receiving RT were successfully extubated. Higher radiation doses were predictive of improved OS and showed a trend for increased ES. Survival beyond 6 months was uncommon, however, the majority of patients with ES were able to be discharged home.

[184]

TÍTULO / TITLE: - Human Noxin is an anti-apoptotic protein in response to DNA damage of A549 non-small cell lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Cancer. 2013 Nov 10. doi: 10.1002/ijc.28600.

●● Enlace al texto completo (gratis o de pago) [1002/ijc.28600](#)

AUTORES / AUTHORS: - Won KJ; Im JY; Yun CO; Chung KS; Kim YJ; Lee JS; Jung YJ; Kim BK; Song KB; Kim YH; Chun HK; Jung KE; Kim MH; Won M

INSTITUCIÓN / INSTITUTION: - Medical Genomics Research Center, KRIBB, Daejeon, Korea; Functional Genomics, University of Science and Technology, Daejeon, Korea.

RESUMEN / SUMMARY: - Human Noxin (hNoxin, C11Orf82), a homolog of mouse noxin, is highly expressed in colorectal and lung cancer tissues. hNoxin contains a DNA-binding C-domain in RPA1, which mediates DNA metabolic processes, such as DNA replication and DNA repair. Expression of hNoxin is associated with S phase in cancer cells and in normal cells. Expression of hNoxin was induced by ultraviolet (UV) irradiation. Knockdown of hNoxin caused growth inhibition of colorectal and lung cancer cells. The comet assay and western blot analysis revealed that hNoxin knockdown induced apoptosis through activation of p38 mitogen-activated protein kinase (MAPK)/p53 in non-small cell lung carcinoma A549 cells. Furthermore, simultaneous hNoxin knockdown and treatment with DNA-damaging agents, such as camptothecin (CPT) and UV irradiation, enhanced apoptosis, whereas Trichostatin A (TSA) did not. However, transient overexpression of hNoxin rescued cells from DNA damage-induced apoptosis but did not block apoptosis in the absence of DNA damage. These results suggest that hNoxin may be associated with inhibition of apoptosis in response to DNA damage. An adenovirus expressing a short hairpin RNA against

hNoxin transcripts significantly suppressed the growth of A549 tumor xenografts, indicating that hNoxin knockdown has in vivo anti-tumor efficacy. Thus, hNoxin is a DNA damage-induced anti-apoptotic protein and potential therapeutic target in cancer.

[185]

TÍTULO / TITLE: - Percutaneous CT-Guided Radiofrequency Ablation as Supplemental Therapy After Systemic Chemotherapy for Selected Advanced Non-Small Cell Lung Cancers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - AJR Am J Roentgenol. 2013 Dec;201(6):1362-7. doi: 10.2214/AJR.12.10511.

●● Enlace al texto completo (gratis o de pago) [2214/AJR.12.10511](#)

AUTORES / AUTHORS: - Li X; Zhao M; Wang J; Fan W; Li W; Pan T; Wu P

INSTITUCIÓN / INSTITUTION: - 1 Minimally Invasive Interventional Division and Medical Imaging Center, State Key Laboratory of Oncology in South China, Sun Yat-sen University Cancer Center, 651 Dongfeng Rd East, Guangzhou 510060, P. R. China.

RESUMEN / SUMMARY: - OBJECTIVE. The purpose of this study is to evaluate the safety and efficacy of percutaneous CT-guided radiofrequency ablation (RFA) as a supplemental therapy after systemic chemotherapy for selected patients with advanced non-small cell lung cancer (NSCLC). MATERIALS AND METHODS. We retrospectively reviewed the medical records of 220 patients with advanced NSCLC who were treated with platinum-doublet chemotherapy between January 2000 and January 2012. Among them, 49 patients underwent RFA as a supplemental therapy for tumors in partial response or stable diseases after first-line chemotherapy. The progression-free survival (PFS) was evaluated by Kaplan-Meier method. RESULTS. There were nine women and 40 men (median age, 60 years; range, 24-82 years), including 28 patients with stage IIIb cancer and 21 with stage IV cancer. All 49 patients (partial response, 23 patients; stable disease, 26 patients) underwent 67 RFA sessions for 61 targeted tumors after systemic chemotherapy. There were no procedure-related deaths. Pneumothorax requiring chest tubes developed in eight sessions (11.9%). Thirty-one patients (63.3%) had complete response, 12 patients (24.5%) had partial response, six patients (12.2%) had stable disease, and no patients had progressive disease. The median follow-up period was 19 months (range, 6-34), and the median PFS was 16 weeks (95% CI, 14.5-17.5). CONCLUSION. Percutaneous CT-guided RFA can be performed as a feasible minimally invasive supplemental therapy with satisfactory PFS after systemic chemotherapy for patients with advanced NSCLC.

[186]

TÍTULO / TITLE: - Coregistered Whole Body Magnetic Resonance Imaging-Positron Emission Tomography (MRI-PET) Versus PET-Computed Tomography Plus Brain MRI in Staging Resectable Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Neurosurgery. 2013 Dec;73(6):N11-3. doi: 10.1227/01.neu.0000438331.72566.2e.

●● Enlace al texto completo (gratis o de pago)

[1227/01.neu.0000438331.72566.2e](#)

AUTORES / AUTHORS: - Parry PV; Engh JA

[187]

TÍTULO / TITLE: - NSCLC cells adapted to EGFR inhibition accumulate EGFR interacting proteins and down-regulate microRNA related to epithelial-mesenchymal transition.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Pharmacol Ther. 2013 Nov 13.

●● Enlace al texto completo (gratis o de pago) [5414/CPXCES13EA08](#)

AUTORES / AUTHORS: - Mader RM; Foerster S; Sarin N; Michaelis M; Cinatl Jr J; Kloft C; Frohlich H; Engel F; Kalayda GV; Jager W; Frotschl R; Jaehde U; Ritter CA

[188]

TÍTULO / TITLE: - Split-lobe resections versus lobectomy for lung carcinoma of the left upper lobe: a pair-matched case-control study of clinical and oncological outcomes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Cardiothorac Surg. 2013 Oct 30.

●● Enlace al texto completo (gratis o de pago) [1093/ejcts/ezt514](#)

AUTORES / AUTHORS: - Witte B; Wolf M; Hillebrand H; Huertgen M

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Katholisches Klinikum Koblenz-Montabaur, Koblenz, Germany.

RESUMEN / SUMMARY: - **OBJECTIVES:** To compare left upper split-lobe procedures, being upper trisegmentectomy and resection of the lingula, with left upper lobectomy for surgical treatment of lung carcinoma originating from the left upper lobe. **METHODS:** A pair-matched control study comparing the clinical and oncological outcomes of 22 consecutive patients after left upper split-lobe resections with those of 44 pair-matched controls that received left upper lobectomy for non-small-cell lung carcinomas. The control group was matched 1:2 for tumour diameter, histology, nodal status and patient age. In both groups, diagnosis and surgical treatment adhered to the principles of tissue-based preoperative mediastinal staging, intraoperative systematic nodal dissection, and gross surgical margins equal to the tumour diameter or at least 2 cm, a sufficient preoperative pulmonary function given. **RESULTS:** As intended by the study design, the split-lobe and lobectomy groups had similar median tumour diameters of 22.5 (range, 11-63) and 25 (range, 7-68) mm, respectively ($P = 0.98$), identical histologies (45.5% adenocarcinoma, 4.5% adenocarcinoma in situ, 45.5% squamous cell carcinoma and 4.5% neuroendocrine carcinoma) and identical pN stages (pN0 77.3%, pN1 9.1%, pN2 9.1% and ypN0 4.5%). In the split-lobe group, a lower preOP forced expiratory volume in one second (median 2.0 vs 2.3 l), a higher co-morbidity (median Charlton score of 3 vs 2) and a preponderance of video-assisted thoracoscopy procedures (63.6 vs 27.3%) were prevalent (all $P < 0.05$). There were no significant outcome differences detected, neither with regard to the postoperative clinical course assessed by intra- and postoperative complications, operation time, tissue margins, duration of drainage and hospital stay and 30-day mortality, nor with regard to 5-year overall (0.89 vs 0.81, $P = 0.90$). **CONCLUSIONS:** Left upper lobectomy might be an overtreatment for selected cases of lung carcinoma whose resection by a split-lobe procedure produces adequate margins and a complete

lymphadenectomy. Tumour diameters exceeding 2 cm, nodal involvement and previous neoadjuvant treatment do not necessarily exclude this option for selected patients under the condition of a meticulous nodal dissection. In this context, we would like to suggest a translational research of the split-lobe concept to other large pulmonary lobes.

[189]

TÍTULO / TITLE: - Fungal diseases mimicking primary lung cancer: radiologic-pathologic correlation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mycoses. 2013 Oct 22. doi: 10.1111/myc.12150.

●● Enlace al texto completo (gratis o de pago) [1111/myc.12150](#)

AUTORES / AUTHORS: - Gazzoni FF; Severo LC; Marchiori E; Irion KL; Guimaraes MD; Godoy MC; Sartori AP; Hochegger B

INSTITUCIÓN / INSTITUTION: - Radiology Department, Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil.

RESUMEN / SUMMARY: - A variety of fungal pulmonary infections can produce radiologic findings that mimic lung cancers. Distinguishing these infectious lesions from lung cancer remains challenging for radiologists and clinicians. In such cases, radiographic findings and clinical manifestations can be highly suggestive of lung cancer, and misdiagnosis can significantly delay the initiation of appropriate treatment. Likewise, the findings of imaging studies cannot replace the detection of a species as the aetiological agent. A biopsy is usually required to diagnose the infectious nature of the lesions. In this article, we review the clinical, histologic and radiologic features of the most common fungal infections that can mimic primary lung cancers, including paracoccidioidomycosis, histoplasmosis, cryptococcosis, coccidioidomycosis, aspergillosis, mucormycosis and blastomycosis.

[190]

TÍTULO / TITLE: - Monosaccharide digitoxin derivative sensitize human non-small cell lung cancer cells to anoikis through Mcl-1 proteasomal degradation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Pharmacol. 2013 Nov 11. pii: S0006-2952(13)00711-9. doi: 10.1016/j.bcp.2013.10.027.

●● Enlace al texto completo (gratis o de pago) [1016/j.bcp.2013.10.027](#)

AUTORES / AUTHORS: - Pongrakhananon V; Stueckle TA; Wang HY; O'Doherty GA; Dinu CZ; Chanvorachote P; Rojanasakul Y

INSTITUCIÓN / INSTITUTION: - Cell-Based Drug and Health Product Development Research Unit, Department of Pharmacology and Physiology, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand 10330; Department of Basic Pharmaceutical Sciences, West Virginia University, Morgantown WV 26506.

RESUMEN / SUMMARY: - Advanced stage cancers acquire anoikis resistance which provides metastatic potential to invade and form tumors at distant sites. Suppression of anoikis resistance by novel molecular therapies would greatly benefit treatment strategies for metastatic cancers. Recently, digitoxin and several of its novel synthetic

derivatives, such as alpha-L-rhamnose monosaccharide derivative (D6-MA), have been synthesized and studied for their profound anticancer activity in various cancer cell lines. In this study, we investigated the anoikis sensitizing effect of D6-MA compared with digitoxin to identify their anti-metastatic mechanism of action. D6-MA sensitized NSCLC H460 cells to detachment-induced apoptosis with significantly greater cytotoxicity (IC50=11.9nM) than digitoxin (IC50=90.7nM) by activating caspase-9. Screening of the Bcl-2 protein family revealed that degradation of anti-apoptotic Mcl-1 protein is a favorable target. Mcl-1 over-expression and knockdown studies in D6-MA and digitoxin exposed cells resulted in rescue and enhancement, respectively, indicating a facilitative role for decreased Mcl-1 expression in NSCLC anoikis. Transfection with mutant Mcl-1S159 attenuated detachment-induced cell death and correlated with a remaining of Mcl-1 level. Furthermore, D6-MA suppressed Mcl-1 expression via ubiquitin proteasomal degradation that is dependent on activation of glycogen synthase kinase (GSK)-3beta signaling. In addition, D6-MA also targeted Mcl-1 degradation causing an increased anoikis in A549 lung cancer cells. Anoikis sensitizing effect on normal small airway epithelial cells was not observed indicating the specificity of D6-MA and digitoxin for NSCLC. These results identify a novel cardiac glycoside (CG) sensitizing anoikis mechanism and provide a promising anti-metastatic target for lung cancer therapy.

[191]

TÍTULO / TITLE: - Proto-oncogene Wip1, a member of a new family of proliferative genes in NSCLC and its clinical significance.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 23.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1382-y](#)

AUTORES / AUTHORS: - Fu Z; Sun G; Gu T

INSTITUCIÓN / INSTITUTION: - Department of Tumor, The First Hospital of Qinhuangdao, No. 258, Wenhua Road, Haigang District, Qinhuangdao, 066000, Hebei Province, China, sqg1980@tom.com.

RESUMEN / SUMMARY: - This study aimed to analyze the expression, clinical significance of proto-oncogene in non small cell lung cancer (NSCLC), and the biological effect in its cell line by siRNA targeting wild-type p53-induced phosphatase 1 (Wip1). Immunohistochemistry and reverse transcription polymerase chain reaction (RT-PCR) were, respectively, used to analyze Wip1 protein expression in 75 cases of NSCLC and normal tissues to study the relationship between Wip1 expression and clinical parameters. Wip1 siRNA was transiently transfected into papillary NSCLC H1299 cell by liposome-mediated method and was detected by RT-PCR and Western blot. MTT assay, cell apoptosis, and cell cycle were also conducted as to the influence of the downregulated expression of Wip1 that might be found on H1299 cells biological effect. The positive rates of Wip1 protein was 69.3 % in NSCLC tissues but 16.0 % expressed in normal tissues (P < 0.05). The relative content of Wip1 mRNA was 0.785 +/- 0.062 and 0.147 +/- 0.020 in NSCLC tissues and normal tissues, respectively, with significant differences between the two types (P < 0.05). There were no significant differences between Wip1 expression and sex, age, tumor size, and pathological types (P > 0.05). However, there were significant differences between Wip1 expression and lymph node metastasis, clinical stages, and tumor differentiation (P < 0.05). Individuals

with positive and negative levels of Wip1 expression showed were statistically significant differences in the 5-year overall survival rate ($P < 0.05$). RT-PCR and Western blot showed that H1299 cell transfected Wip1 siRNA had a lower relative expressive content than normal cell ($P < 0.05$). MTT assay, cell apoptosis, and cell cycles demonstrated that H1299 cell transfected Wip1 siRNA had a lower survival fraction, higher cell apoptosis, more percentage of the G0/G1 phases, and lower cells in the S phases ($P < 0.05$). Wip1 protein and mRNA were increased in NSCLC, specifically in lymph node metastasis, clinical stages, and tumor differentiation. Wip1 may be involved in the biological processes of NSCLC cell proliferation, cell apoptosis, and cell cycle.

[192]

TÍTULO / TITLE: - Combination of ascorbate/epigallocatechin-3-gallate/gemcitabine synergistically induces cell cycle deregulation and apoptosis in mesothelioma cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Toxicol Appl Pharmacol. 2013 Nov 4. pii: S0041-008X(13)00473-0. doi: 10.1016/j.taap.2013.10.025.

●● Enlace al texto completo (gratis o de pago) [1016/j.taap.2013.10.025](#)

AUTORES / AUTHORS: - Martinotti S; Ranzato E; Parodi M; Vitale M; Burlando B

INSTITUCIÓN / INSTITUTION: - Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "Amedeo Avogadro", viale T. Michel 11, 15121 Alessandria, Italy.

RESUMEN / SUMMARY: - Malignant mesothelioma (MMe) is a poor-prognosis tumor in need of innovative therapies. In a previous in vivo study, we showed synergistic anti-MMe properties of the ascorbate/epigallocatechin-3-gallate/gemcitabine combination. We have now focused on the mechanism of action, showing the induction of apoptosis and cell cycle arrest through measurements of caspase 3, intracellular Ca^{2+} , annexin V, and DNA content. StellArray PCR technology and Western immunoblotting revealed DAPK2-dependent apoptosis, upregulation of cell cycle promoters, downregulation of cell cycle checkpoints and repression of NFkappaB expression. The complex of data indicates that the mixture is synergistic in inducing cell cycle deregulation and non-inflammatory apoptosis, suggesting its possible use in MMe treatment.

[193]

TÍTULO / TITLE: - A combination of pterostilbene with autophagy inhibitors exerts efficient apoptotic characteristics in both chemosensitive and chemoresistant lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Toxicol Sci. 2013 Oct 23.

●● Enlace al texto completo (gratis o de pago) [1093/toxsci/kft238](#)

AUTORES / AUTHORS: - Hsieh MJ; Lin CW; Yang SF; Sheu GT; Yu YY; Chen MK; Chiou HL

INSTITUCIÓN / INSTITUTION: - Cancer Research Center, Changhua Christian Hospital, Changhua 500, Taiwan.

RESUMEN / SUMMARY: - The emergence of multidrug resistance (MDR), meaning that cancer cells develop simultaneous resistance to different drugs, has limited the clinical

efficacy and application of chemotherapy. Pterostilbene, a naturally occurring phytoalexin exerts a variety of pharmacologic activities, including antioxidation, cancer prevention and cytotoxicity to various cancer cells. In this study, results approved the capability of pterostilbene to effectively inhibit the cell growth of docetaxel-induced multidrug resistance human lung cancer cells lines and such inhibition is through an induction of cell cycle arrest and apoptosis. Meanwhile, the observation of the formation of acidic vesicular organelles and LC3-II production revealed an induction of autophagy at an early stage by pterostilbene, which was triggered by an inhibition of the AKT and JNK and an activation of the ERK1/2 pathway. Furthermore, an inhibition of autophagy by pretreatment with 3-methyladenine, bafilomycin A1 or Beclin 1 siRNA was able to enhance pterostilbene-triggered apoptosis. In conclusion, this study demonstrate that pterostilbene causes autophagy and apoptosis in lung cancer cells. Furthermore, a combination of pterostilbene with autophagy inhibitors may strengthen the efficiency of proapoptotic chemotherapeutic strategies in both chemosensitive and chemoresistant lung cancer cells, which may be of great value for the clinical management of lung cancer patients with multidrug resistance.

[194]

TÍTULO / TITLE: - Effect of metformin on residual cells after chemotherapy in a human lung adenocarcinoma cell line.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Dec;43(6):1846-54. doi: 10.3892/ijo.2013.2120. Epub 2013 Oct 3.

●● [Enlace al texto completo \(gratis o de pago\) 3892/ijo.2013.2120](#)

AUTORES / AUTHORS: - Kitazono S; Takiguchi Y; Ashinuma H; Saito-Kitazono M; Kitamura A; Chiba T; Sakaida E; Sekine I; Tada Y; Kurosu K; Sakao S; Tanabe N; Iwama A; Yokosuka O; Tatsumi K

INSTITUCIÓN / INSTITUTION: - Department of Respiriology, Graduate School of Medicine, Chiba University, Chuo-ku, Chiba 260-8670, Japan.

RESUMEN / SUMMARY: - Cancer chemotherapy, including molecular targeted therapy, has major limitations because it does not kill all the cancer cells; the residual cells survive until they acquire chemoresistance. In the present study, the combined effects of metformin and gefitinib were examined in vivo in a mouse xenograft model, inoculated with a human lung adenocarcinoma cell line that possesses an activating epidermal growth factor receptor mutation. The mechanism of the interaction was further elucidated in vitro. Metformin did not suppress the growth of already established tumors, nor did metformin augment tumor shrinkage by gefitinib. However, metformin significantly suppressed the regrowth of the tumor after effective treatment with gefitinib, suggesting the specific effect of metformin on the residual cells. Cytotoxicity of metformin was characterized by the absence of apoptosis induction and unremarkable cell cycle shift in vitro. The residual cell population after treatment with gefitinib was characterized by enriched cells with high expression of CD133 and CD24. Metformin was still effective on this specific cell population. Targeting residual cells after chemotherapy may represent an effective novel strategy for the treatment of cancer. Elucidating the mechanism of metformin cytotoxicity provides insights into future development of anticancer therapeutics.

[195]

TÍTULO / TITLE: - Neighbourhood socioeconomic status and individual lung cancer risk: Evaluating long-term exposure measures and mediating mechanisms.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Soc Sci Med. 2013 Nov;97:95-103. doi: 10.1016/j.socscimed.2013.08.005. Epub 2013 Aug 24.

- [Enlace al texto completo \(gratuito o de pago\)](#)

[1016/j.socscimed.2013.08.005](#)

AUTORES / AUTHORS: - Hystad P; Carpiano RM; Demers PA; Johnson KC; Brauer M

INSTITUCIÓN / INSTITUTION: - School of Population and Public Health, University of British Columbia, 2206 East Mall, Vancouver, BC, Canada V6T 1Z3. Electronic address: phystad@gmail.com.

RESUMEN / SUMMARY: - Neighbourhood socioeconomic status (SES) has been associated with numerous chronic diseases, yet little information exists on its association with lung cancer incidence. This outcome presents two key empirical challenges: a long latency period that requires study participants' residential histories and long-term neighbourhood characteristics; and adequate data on many risk factors to test hypothesized mediating pathways between neighbourhood SES and lung cancer incidence. Analysing data on urban participants of a large Canadian population-based lung cancer case-control study, we investigate three issues pertaining to these challenges. First, we examine whether there is an association between long-term neighbourhood SES, derived from 20 years of residential histories and five national censuses, and lung cancer incidence. Second, we determine how this long-term neighbourhood SES association changes when using neighbourhood SES measures based on different latency periods or at time of study entry. Third, we estimate the extent to which long-term neighbourhood SES is mediated by a range of individual-level smoking behaviours, other health behaviours, and environmental and occupational exposures. Results of hierarchical logistic regression models indicate significantly higher odds of lung cancer cases residing in the most compared to the least deprived quintile of the long-term neighbourhood SES index (OR: 1.46; 95% CI: 1.13-1.89) after adjustment for individual SES. This association remained significant (OR: 1.38; 1.01-1.88) after adjusting for smoking behaviour and other known and suspected lung cancer risk factors. Important differences were observed between long-term and study entry neighbourhood SES measures, with the latter attenuating effect estimates by over 50 percent. Smoking behaviour was the strongest partial mediating pathway of the long-term neighbourhood SES effect. This research is the first to examine the effects of long-term neighbourhood SES on lung cancer risk and more research is needed to further identify specific, modifiable pathways by which neighbourhood context may influence lung cancer risk.

[196]

TÍTULO / TITLE: - Repeat Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy May Offer Survival Benefit for Intraperitoneal Mesothelioma: A Single Institution Experience.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Surg Oncol. 2013 Oct 25.

●● Enlace al texto completo (gratis o de pago) [1245/s10434-013-3341-7](https://doi.org/10.1245/s10434-013-3341-7)

AUTORES / AUTHORS: - Wong J; Koch AL; Deneve JL; Fulp W; Tanvetyanon T; Dessureault S

INSTITUCIÓN / INSTITUTION: - Department of Gastrointestinal Oncology, Moffitt Cancer Center, Tampa, FL, USA, joyce.wong02@gmail.com.

RESUMEN / SUMMARY: - INTRODUCTION: Cytoreduction with heated intraperitoneal chemotherapy (HIPEC) has demonstrated improved overall survival (OS) in malignant peritoneal mesothelioma (MPM). The role of repeated HIPEC for MPM is less clear. METHODS: An institutional review board-approved database of MPM patients was analyzed for clinical factors and outcomes. RESULTS: From June 2004 to March 2012, 29 patients underwent surgical treatment for mesothelioma. HIPEC was aborted in 3 and completed in 26; 8 underwent additional repeat HIPEC. The majority was male (62 %), median age 66 years. There was no significant difference in surgery duration, blood loss, or hospital-stay-duration between initial and repeat HIPEC. Cisplatin was the chemotherapy used. Complications occurred in 17 (65 %) initial and 6 (50 %) repeat HIPEC, with wound complications being most common. Reoperation was less common (4 % initial and 25 % repeat), and perioperative death was rare (4 % initial, 0 % repeat). Fourteen (54 %) initial and seven (58 %) repeat HIPEC patients received adjuvant chemotherapy. Median time from HIPEC to initiation of chemotherapy was not different between initial and repeat HIPEC (8.8 and 4.6 months, respectively, $p = 0.68$). Median treatment-free time (time from initial to repeat HIPEC or chemotherapy) also was not different between initial and repeat HIPEC (8.8 and 6.3 months, respectively, $p = 0.92$). Median OS for the cohort was 41.2 months. Patients who underwent repeat HIPEC had improved median OS (80 months) versus single HIPEC (27.2 months; $p = 0.007$). A lower peritoneal carcinoma index and complete cytoreduction were associated positively with OS. CONCLUSIONS: Cytoreduction and HIPEC for MPM are associated with longer OS. Patients who are candidates for repeat HIPEC may derive an even greater OS advantage.

[197]

TÍTULO / TITLE: - Aflatoxin G1-induced oxidative stress causes DNA damage and triggers apoptosis through MAPK signaling pathway in A549 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Food Chem Toxicol. 2013 Dec;62:661-9. doi: 10.1016/j.fct.2013.09.030. Epub 2013 Sep 30.

●● Enlace al texto completo (gratis o de pago) [1016/j.fct.2013.09.030](https://doi.org/10.1016/j.fct.2013.09.030)

AUTORES / AUTHORS: - Shen H; Liu J; Wang Y; Lian H; Wang J; Xing L; Yan X; Wang J; Zhang X

INSTITUCIÓN / INSTITUTION: - Lab of Pathology, Hebei Medical University, Shijiazhuang, China.

RESUMEN / SUMMARY: - Our previous studies showed that Aflatoxin G1 (AFG1) could induce lung adenocarcinoma, and that the cancer cells originated from alveolar type II cells (AT-II cells). Recently, we found AFG1 induced structural impairment in rat AT-II cells, which may account for an early event in lung tumorigenesis. However, the mechanism of AFG1-induced AT-II cell damage remains unclear. DNA damage and apoptosis induced by oxidative stress are well accepted causes of cell damage. Thus, we explore whether AFG1 activates the reactive oxygen species

(ROS)/MAPK/apoptosis pathway to cause cell damage in human AT-II cells like the cell line (A549). We found AFG1 induced oxidative stress by increasing ROS generation and caused DNA double-strand breaks (DSBs) by up-regulating gammaH2AX expression. AFG1 also triggered apoptosis in A549 cells by regulating Fas/FasL, caspase-8, Bax, Bcl-2, and activating caspase-3. Pre-treatment with antioxidant n-acetyl-l-cysteine (NAC) reduced ROS generation and DNA DSBs, inhibited apoptosis, and increased cell viability in AFG1-treated cells. Furthermore, we found AFG1 activated ROS-mediated JNK and p38 pathways to induce cell apoptosis in A549 cells. In conclusion, our results indicate that AFG1 induces oxidative DNA damage and triggers apoptosis through ROS-mediated JNK and p38 signaling pathways in A549 cells, which may contribute to AFG1-induced AT-II cell damage.

[198]

TÍTULO / TITLE: - Correlation of dose computed using different algorithms with local control following stereotactic ablative radiotherapy (SABR)-based treatment of non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Nov 11. pii: S0167-8140(13)00520-3. doi: 10.1016/j.radonc.2013.10.012.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.radonc.2013.10.012](#)

AUTORES / AUTHORS: - Chetty IJ; Devpura S; Liu D; Chen D; Li H; Wen NW; Kumar S; Fraser C; Siddiqui MS; Ajlouni M; Movsas B

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Henry Ford Hospital, Detroit, USA. Electronic address: ichetty1@hfhs.org.

RESUMEN / SUMMARY: - **PURPOSE:** To retrospectively compute dose distributions for lung cancer patients treated with SABR, and to correlate dose distributions with outcome using a tumor control probability (TCP) model. **METHODS:** Treatment plans for 133 NSCLC patients treated using 12Gy/fxnx4 (BED=106Gy), and planned using a pencil-beam (1D-equivalent-path-length, EPL-1D) algorithm were retrospectively re-calculated using model-based algorithms (including convolution/superposition, Monte Carlo). 4D imaging was performed to manage motion. TCP was computed using the Marsden model and associations between dose and outcome were inferred. **RESULTS:** Mean D95 reductions of 20% (max.=33%) were noted with model-based algorithms (relative to EPL-1D) for the smallest tumors (PTV<20cm³), corresponding to actual delivered D95 BEDs of approximately 60-85Gy. For larger tumors (PTV>100cm³), D95 reductions were approximately 10% (BED>100Gy). Mean lung doses (MLDs) were 15% lower for model-based algorithms for PTVs<20cm³. No correlation between tumor size and 2-year local control rate was observed clinically, consistent with TCP calculations, both of which were approximately 90% across all PTV bins. **CONCLUSION:** Results suggest that similar control rates might be achieved for smaller tumors using lower BEDs relative to larger tumors. However, more studies with larger patient cohorts are necessary to confirm this possible finding.

[199]

TÍTULO / TITLE: - Highly efficient tumor transduction and antitumor efficacy in experimental human malignant mesothelioma using replicating gibbon ape leukemia virus.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Gene Ther. 2013 Nov 8. doi: 10.1038/cgt.2013.67.

●● Enlace al texto completo (gratis o de pago) [1038/cgt.2013.67](#)

AUTORES / AUTHORS: - Kubo S; Takagi-Kimura M; Logg CR; Kasahara N

INSTITUCIÓN / INSTITUTION: - Department of Genetics, Hyogo College of Medicine, Nishinomiya, Japan.

RESUMEN / SUMMARY: - Retroviral replicating vectors (RRVs) have been shown to achieve efficient tumor transduction and enhanced therapeutic benefit in a wide variety of cancer models. Here we evaluated two different RRVs derived from amphotropic murine leukemia virus (AMLV) and gibbon ape leukemia virus (GALV), in human malignant mesothelioma cells. In vitro, both RRVs expressing the green fluorescent protein gene efficiently replicated in most mesothelioma cell lines tested, but not in normal mesothelial cells. Notably, in ACC-MESO-1 mesothelioma cells that were not permissive for AMLV-RRV, the GALV-RRV could spread efficiently in culture and in mice with subcutaneous xenografts by in vivo fluorescence imaging. Next, GALV-RRV expressing the cytosine deaminase prodrug activator gene showed efficient killing of ACC-MESO-1 cells in a prodrug 5-fluorocytosine dose-dependent manner, compared with AMLV-RRV. GALV-RRV-mediated prodrug activator gene therapy achieved significant inhibition of subcutaneous ACC-MESO-1 tumor growth in nude mice. Quantitative reverse transcription PCR demonstrated that ACC-MESO-1 cells express higher PiT-1 (GALV receptor) and lower PiT-2 (AMLV receptor) compared with normal mesothelial cells and other mesothelioma cells, presumably accounting for the distinctive finding that GALV-RRV replicates much more robustly than AMLV-RRV in these cells. These data indicate the potential utility of GALV-RRV-mediated prodrug activator gene therapy in the treatment of mesothelioma. Cancer Gene Therapy advance online publication, 8 November 2013; doi:10.1038/cgt.2013.67.

[200]

TÍTULO / TITLE: - A randomized, phase II study of vandetanib maintenance for advanced or metastatic non-small-cell lung cancer following first-line platinum-doublet chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):455-60. doi: 10.1016/j.lungcan.2013.08.027. Epub 2013 Sep 8.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.08.027](#)

AUTORES / AUTHORS: - Ahn JS; Lee KH; Sun JM; Park K; Kang ES; Cho EK; Lee DH; Kim SW; Lee GW; Kang JH; Lee JS; Lee JW; Ahn MJ

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Samsung Medical Center, Sungkyunkwan University, 50 Irwon-dong, Gangnam-gu, Seoul 135-710, Republic of Korea.

RESUMEN / SUMMARY: - BACKGROUND: This randomized, phase II study investigated whether benefit could be obtained by giving vandetanib, an oral inhibitor of vascular endothelial and epithelial growth factor receptor, as a maintenance treatment in non-small cell lung cancer (NSCLC). METHODS: Patients were randomly assigned

to either vandetanib or placebo after completion of 4 cycles of first-line chemotherapy. A progression-free survival (PFS) rate at 3 months was selected as the primary endpoint. We set a maximum PFS rate at 3 months to 30% (null hypothesis), and a minimum PFS rate at 3 months to 50% (alternative hypothesis). RESULTS: At the interim analysis, 9 of 24 patients in the vandetanib arm were progression-free at 3 months, whereas 7 of 24 in the placebo arm were progression-free. The placebo arm was closed at the first stage. The vandetanib arm proceeded to the second stage, and recruited a total of 75 patients. At the second stage, 28 out of 63 evaluable patients receiving vandetanib achieved PFS at 3 months. The alternative hypothesis that the PFS rate at 3 months is at least 50% was accepted. The median PFS was 2.7 months (95% CI, 1.9-4.4 months) in the vandetanib arm and 1.7 months (95% CI, 0.9-2.6 months) in the placebo arm. The most common adverse events in patients receiving vandetanib were rash (77.3%) and diarrhea (60.0%). CONCLUSIONS: Maintenance therapy with vandetanib for patients with NSCLC after standard platinum doublet chemotherapy is well tolerated and may prolong PFS compared with placebo, and needs additional investigation.

[201]

TÍTULO / TITLE: - Clinical indications and results after chest wall resection for recurrent mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Dec;146(6):1373-80. doi: 10.1016/j.jtcvs.2013.07.012. Epub 2013 Oct 8.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.07.012](#)

AUTORES / AUTHORS: - Burt BM; Ali SO; Dasilva MC; Yeap BY; Richards WG; Baldini EH; Sugarbaker DJ

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, Stanford University Medical School, Stanford, Calif.

RESUMEN / SUMMARY: - OBJECTIVE: The ipsilateral hemithorax is the most common site of recurrence after surgical resection for malignant pleural mesothelioma. Salvage treatment has generally been ineffective. We reviewed the outcomes after resection of isolated ipsilateral chest recurrence after cytoreductive surgery in patients with malignant pleural mesothelioma. METHODS: Patients with malignant pleural mesothelioma who underwent initial surgical resection at our institution from 1988 to 2011 and were subsequently treated for localized recurrence with an additional chest resection were identified and their data retrospectively reviewed. RESULTS: A total of 1142 patients underwent either extrapleural pneumonectomy (n = 794) or pleurectomy/decortication (n = 348). Of the patients who returned for follow-up, 47 (4.1%) had chest wall recurrence amenable to resection. The location of recurrence was predominantly incisional (49%) and/or costophrenic (38%). The median time to recurrence after either extrapleural pneumonectomy or pleurectomy/decortication was 16.1 months (range, 2.7-58.2). No 30-day mortality was found for chest wall resection, and the median length of stay in the hospital was 3 days (range, 0-12). The median overall survival duration after chest wall resection correlated positively with the time to recurrence (epithelial: median, 8.9, 17.2, and 35.8 months for a time to recurrence of <12, 12 to <24, and ≥24 months, respectively; biphasic: median, 2.7 and 15.9 months for a time to recurrence of <10 and ≥10 months, respectively). CONCLUSIONS:

Chest wall resection is a safe and effective therapeutic option in the management of localized chest wall recurrence of malignant pleural mesothelioma. The time to recurrence appears to be predictive of the expected survival benefit in both epithelial and biphasic malignant pleural mesothelioma.

[202]

TÍTULO / TITLE: - Foxm1 transcription factor is required for the initiation of lung tumorigenesis by oncogenic Kras

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Nov 11. doi: 10.1038/onc.2013.475.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.475](#)

AUTORES / AUTHORS: - Wang IC; Ustiyani V; Zhang Y; Cai Y; Kalin TV; Kalinichenko VV

INSTITUCIÓN / INSTITUTION: - 1] Division of Pulmonary Biology, Perinatal Institute of Cincinnati Children's Hospital Research Foundation, Cincinnati, OH, USA [2] Department of Life Sciences, National Tsing Hua University, Hsinchu, Taiwan [3] Institute of Biotechnology, National Tsing Hua University, Hsinchu, Taiwan.

RESUMEN / SUMMARY: - Lung cancer is the leading cause of deaths in cancer patients in the United States. Identification of new molecular targets is clearly needed to improve therapeutic outcomes of this devastating human disease. Activating mutations in K-Ras oncogene and increased expression of FOXM1 protein are associated with poor prognosis in patients with non-small-cell lung cancer. Transgenic expression of activated KrasG12D in mouse respiratory epithelium is sufficient to induce lung adenocarcinomas; however, transcriptional mechanisms regulated by K-Ras during the initiation of lung cancer remain poorly understood. Foxm1 transcription factor, a downstream target of K-Ras, stimulates cellular proliferation during embryogenesis, organ repair and tumor growth, but its role in tumor initiation is unknown. In the present study, we used transgenic mice expressing KrasG12D under control of Sftpc promoter to demonstrate that Foxm1 was induced in type II epithelial cells before the formation of lung tumors. Conditional deletion of Foxm1 from KrasG12D-expressing respiratory epithelium prevented the initiation of lung tumors in vivo. The loss of Foxm1 inhibited expression of K-Ras target genes critical for the nuclear factor-kappaB (NF-kappaB) and c-Jun N-terminal kinase (JNK) pathways, including Ikbkb, Nfkb1, Nfkb2, Rela, Jnk1, N-Myc, Pttg1 and Cdkn2a. Transgenic overexpression of activated FOXM1 mutant was sufficient to induce expression of these genes in alveolar type II cells. FOXM1 directly bound to promoter regions of Ikbkb, Nfkb2, N-Myc, Pttg1 and Cdkn2a, indicating that these genes are direct FOXM1 targets. FOXM1 is required for K-Ras-mediated lung tumorigenesis by activating genes critical for the NF-kappaB and JNK pathways. Oncogene advance online publication, 11 November 2013; doi:10.1038/onc.2013.475.

[203]

TÍTULO / TITLE: - Low-Dose Hypersensitivity and Bystander Effect are Not Mutually Exclusive in A549 Lung Carcinoma Cells after Irradiation with Charged Particles.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiat Res. 2013 Nov;180(5):491-8. doi: 10.1667/RR13358.1. Epub 2013 Oct 14.

●● Enlace al texto completo (gratis o de pago) [1667/RR13358.1](https://doi.org/10.1667/RR13358.1)

AUTORES / AUTHORS: - Heuskin AC; Wera AC; Riquier H; Michiels C; Lucas S

INSTITUCIÓN / INSTITUTION: - a NAMur Research Institute for Life Sciences (NARILIS), Research Center for the Physics of Matter and Radiation (PMR), University of Namur:

RESUMEN / SUMMARY: - The purpose of this study was to measure survival fraction of A549 lung carcinoma cells irradiated with charged particles of various LET and to determine mechanisms responsible for enhanced cell killing in the low-dose region. A549 cells were irradiated with a broadbeam of either 10 and 25 keV/mum protons or 100 keV/mum alpha particles and then processed for clonogenic assays and phospho-histone H3 staining. The survival fraction of unirradiated A549 cells co-cultured with irradiated cells was also evaluated. A549 cells were shown to exhibit low-dose hypersensitivity (HRS) for both protons and alpha particles. The dose threshold at which HRS occurs decreased with increasing linear energy transfer (LET), whereas alphas, the initial survival curve slope, increased with increasing LET. In addition, the enhanced cell killing observed after irradiation with alpha particles was partly attributed to the bystander effect, due to the low proportion of hit cells at very low doses. Co-culture experiments suggest a gap junction-mediated bystander signal. Our results indicate that HRS is likely to be dependent on LET, and that a bystander effect and low-dose hypersensitivity may co-exist within a given cell line.

[204]

TÍTULO / TITLE: - Variance of TNFAIP8 expression between tumor tissues and tumor-infiltrating CD4+ and CD8+ T cells in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 19.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1307-9](https://doi.org/10.1007/s13277-013-1307-9)

AUTORES / AUTHORS: - Wang L; Song Y; Men X

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Jinan No.4 People's Hospital, 50 Shifan Road, Jinan, Shandong Province, 250031, China.

RESUMEN / SUMMARY: - Tumor necrosis factor alpha-induced protein 8 (TNFAIP8) has been recently documented in various malignancies, but its role in non-small cell lung cancer (NSCLC) remains uncertain. In the current study, we investigated the level of TNFAIP8 in NSCLC tissues, adjacent noncancerous lung tissues, healthy lung tissues, CD4+ T cells, and CD8+ T cells by real-time reverse transcription PCR (RT-PCR) and Western blot analysis. Results revealed that the mRNA level of TNFAIP8 was significantly increased in cancer tissue than in healthy lung tissue from donors ($p < 0.001$). Interestingly, adjacent noncancerous lung tissues also showed higher mRNA level of TNFAIP8 than healthy lung tissue from donors ($p < 0.01$). Similarly, protein level of TNFAIP8 was elevated in NSCLC tissues and adjacent noncancerous lung tissues. We further analyzed TNFAIP8 expression in CD4+ T cells and CD8+ T cells. Data demonstrated that both mRNA level and protein level were significantly decreased in tumor-infiltrating CD4+ and CD8+ T cells than in peripheral CD4+ and CD8+ T cells. Moreover, patients with advanced stages presented lower protein expression of TNFAIP8 in tumor-infiltrating CD8+ T cells than patients with primary

stages ($p < 0.05$). These results provide evidence that TNFAIP8 plays critical roles in NSCLC and may be used as a therapeutic target for the disease.

[205]

TÍTULO / TITLE: - Resveratrol enhances ionizing radiation-induced premature senescence in lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Dec;43(6):1999-2006. doi: 10.3892/ijo.2013.2141. Epub 2013 Oct 17.

●● [Enlace al texto completo \(gratis o de pago\) 3892/ijo.2013.2141](#)

AUTORES / AUTHORS: - Luo H; Wang L; Schulte BA; Yang A; Tang S; Wang GY

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC 29425, USA.

RESUMEN / SUMMARY: - Radiotherapy is used in >50% of patients during the course of cancer treatment both as a curative modality and for palliation. However, radioresistance is a major obstacle to the success of radiation therapy and contributes significantly to tumor recurrence and treatment failure, highlighting the need for the development of novel radiosensitizers that can be used to overcome tumor radioresistance and, thus, improve the efficacy of radiotherapy. Previous studies indicated that resveratrol (RV) may sensitize tumor cells to chemotherapy and ionizing radiation (IR). However, the mechanisms by which RV increases the radiation sensitivity of cancer cells have not been well characterized. Here, we show that RV treatment enhances IR-induced cell killing in non-small cell lung cancer (NSCLC) cells through an apoptosis-independent mechanism. Further studies revealed that the percentage of senescence-associated beta-galactosidase (SA-beta-gal)-positive senescent cells was markedly higher in cells treated with IR in combination with RV compared with cells treated either with IR or RV alone, suggesting that RV treatment enhances IR-induced premature senescence in lung cancer cells. Comet assays demonstrate that RV and IR combined treatment causes more DNA double-strand breaks (DSBs) than IR or RV treatment alone. DCF-DA staining and flow cytometric analyses demonstrate that RV and IR combined treatment leads to a significant increase in ROS production in irradiated NSCLC cells. Furthermore, our investigation shows that inhibition of ROS production by N-acetyl-cysteine attenuates RV-induced radiosensitization in lung cancer cells. Collectively, these results demonstrate that RV-induced radiosensitization is associated with significant increase of ROS production, DNA-DSBs and senescence induction in irradiated NSCLC cells, suggesting that RV treatment may sensitize lung cancer cells to radiotherapy via enhancing IR-induced premature senescence.

[206]

TÍTULO / TITLE: - Proteomic and redox-proteomic study on the role of glutathione reductase in human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Electrophoresis. 2013 Oct 1. doi: 10.1002/elps.201300250.

●● [Enlace al texto completo \(gratis o de pago\) 1002/elps.201300250](#)

AUTORES / AUTHORS: - Fan CY; Chou HC; Lo YW; Wen YF; Tsai YC; Huang H; Chan HL

INSTITUCIÓN / INSTITUTION: - Institute of Bioinformatics and Structural Biology & Department of Medical Sciences, National Tsing Hua University, Hsinchu, Taiwan.

RESUMEN / SUMMARY: - Glutathione reductase (GR), a cytosolic protein, plays a vital role in maintaining a correct redox status in cells. However, comprehensive investigations of GR-modulated cellular responses, including protein level alteration and redox regulation, have yet to be performed. In this study, we cultured a human lung adenocarcinoma line transfected with empty pLKO.1 vector as a control, CL1-0shControl, and its GR-knockdown derivative, CL1-0shDeltaGR, to evaluate differential protein level alteration and redox regulation of these 2 cell lines. We identified 34 spots that exhibited marked changes in intensities, and 13 proteins showing significant changes in thiol reactivity, in response to GR-depletion. Several proteins involved in redox regulation, calcium signaling, cytoskeleton regulation, and protein folding showed significant changes in expression, whereas proteins involved in redox regulation, protein folding, and glycolysis displayed changes in thiol reactivity. Interestingly, GR knockdown induces peroxiredoxin-1 overexpression in the air-exposed tissue and high oxygen consuming tissue such as cornea and liver, but not in the low oxygen consuming tissues such as breast and uterine. In summary, we used a comprehensive lung adenocarcinoma-based proteomic approach for identifying GR-modulated protein expression alteration and redox modification. Based on our research, this is the first comprehensive proteomic and redox-proteomic analysis used to investigate the role of GR in a mammalian cell model. This article is protected by copyright. All rights reserved.

[207]

TÍTULO / TITLE: - Thymoquinone inhibits microtubule polymerization by tubulin binding and causes mitotic arrest following apoptosis in A549 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochimie. 2013 Oct 7. pii: S0300-9084(13)00346-5. doi: 10.1016/j.biochi.2013.09.025.

●● Enlace al texto completo (gratis o de pago) [1016/j.biochi.2013.09.025](#)

AUTORES / AUTHORS: - Acharya BR; Chatterjee A; Ganguli A; Bhattacharya S; Chakrabarti G

INSTITUCIÓN / INSTITUTION: - Department of Biotechnology and Dr. B.C. Guha Centre for Genetic Engineering and Biotechnology, University of Calcutta, 35 Ballygunge Circular Road, Kolkata, WB 700019, India.

RESUMEN / SUMMARY: - Microtubule-Targeting agents (MTA) are indispensable for cancer therapeutics. We here report thymoquinone (TQ) as a new MTA that already has been appreciated for its anticancer effects. TQ induced G2/M cell cycle arrest in human non-small lung epithelial cells (A549) and majority of arrested cells were in mitosis. TQ depolymerized the microtubule (MT) network and disrupted mitotic spindle organization of A549 cells. MT depolymerization by TQ was followed by apoptosis and subsequent loss in cell viability (IC50 value of approximately 10 μ M). Interestingly, TQ didn't affect the MT network of normal HUVEC cells at and below the IC50 concentration for A549 cells. TQ also inhibited tubulin polymerization in cell-free system with an IC50 of 27 μ M and bound to tubulin heterodimers at a single site with

a dissociation constant of 1.19 μM at 25 degrees C. Binding of TQ to tubulin quenched the tryptophan fluorescence of protein in a time-dependent manner. The TQ-tubulin binding kinetics was biphasic in nature and equilibrated in 30 min. TQ competed with colchicine for tubulin binding with a K_i of 1.9 μM as determined by modified Dixon plot analysis, this suggests TQ may bind tubulin at or near the colchicine binding site and in silico modeling study supported that. Our results establish a novel antimitotic mechanism of TQ by its direct binding to tubulin-MT network in A549 cells.

[208]

TÍTULO / TITLE: - Association of CYP3A4, CYP3A5 polymorphisms with lung cancer risk in Bangladeshi population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1230-0](#)

AUTORES / AUTHORS: - Islam MS; Mostofa AG; Ahmed MU; Sayeed MS; Hassan MR; Hasnat A

INSTITUCIÓN / INSTITUTION: - Department of Pharmacy, Noakhali Science and Technology University, Sonapur, Noakhali, 3814, Bangladesh.

RESUMEN / SUMMARY: - The rate of direct smoking, second hand smoking, and smokeless tobacco users as well as the amount of environmental pollutant like polycyclic aromatic hydrocarbons is increasing in Bangladesh. Therefore, the prevalence of lung cancer is increasing day by day. To the best of our knowledge, no pharmacogenetic study of CYP3A4, CYP3A5 genes has been reported on Bangladeshi population relating those with lung cancer. The present study was conducted to determine the association of CYP3A4, CYP3A5 gene polymorphisms and tobacco smoking in the development of lung cancer in Bangladeshi population. A case-control study was carried out on 106 lung cancer patients and 116 controls to investigate three allelic variants-CYP3A4*1B, CYP3A5*3, and CYP3A5*6 using Polymerase Chain Reaction Restriction Fragment Length Polymorphism. Risk of lung cancer was estimated as odds ratio (OR) and 95 % confidence interval (CI) using unconditional logistic regression models. The variant allele frequencies for CYP3A4*1B (*1A/*1B + *1B/*1B) were 2.83 % and 0.86 % and that of CYP3A5*3 (*1A/*3 + *3/*3) were 88.68 % and 85.34 % in cases and controls, respectively. Individual carrying at least one variant allele of CYP3A4*1B (CYP3A4*1A/1B + *1B/1B) has a 3.35 times more risk (OR = 3.35, 95 % CI = 0.34-32.71, $p = 0.271$) for developing lung cancer whereas individual carrying at least one variant allele of CYP3A5 (CYP3A5*1A/3 + *3/3) has a 1.26 times more risk (OR = 1.35, 95 % CI = 0.61-2.97) and both are statistically non-significant ($p > 0.05$). CYP3A5*6 was absent in the study population. No association of lung cancer with the mentioned polymorphisms was found both in heavy and light smokers. In the cases of all three major types of lung cancer-squamous cell carcinoma, adenocarcinoma, and small cell carcinoma-significantly strong relationships ($p < 0.05$) have been found. To confirm the association of lung cancer with the mentioned polymorphisms, large number volunteers (patients and controls) will be required.

[209]

TÍTULO / TITLE: - A Case-Control Study of Long-Term Exposure to Ambient Volatile Organic Compounds and Lung Cancer in Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Epidemiol. 2013 Nov 27.

●● Enlace al texto completo (gratis o de pago) [1093/aje/kwt289](#)

AUTORES / AUTHORS: - Villeneuve PJ; Jerrett M; Brenner D; Su J; Chen H; McLaughlin JR

RESUMEN / SUMMARY: - Few studies have investigated associations between nonoccupational exposure to ambient volatile organic compounds and lung cancer. We conducted a case-control study of 445 incident lung cancers and 948 controls (523 hospital, 425 general population) in Toronto, Ontario, Canada, between 1997 and 2002. Participants provided information on several risk factors, including tobacco use, secondhand exposure to cigarette smoke, obesity, and family history of cancer. Exposure to benzene, hydrocarbons, and nitrogen dioxide was estimated using land-use regression models. Exposures were linked to residential addresses to estimate exposure at the time of interview, 10 years before interview, and across past residences (time-weighted average). Logistic regression was used to estimate adjusted odds ratios. Analyses involving the population-based controls found that an interquartile-range increase in the time-weighted average benzene concentration (0.15 microg/m³) across previous residences was associated with lung cancer (odds ratio = 1.84, 95% confidence interval: 1.26, 2.68). Similarly, an interquartile-range increase in the time-weighted average nitrogen dioxide concentration (4.8 ppb) yielded an odds ratio of 1.59 (95% confidence interval: 1.19, 2.12). Our study suggests that long-term exposure to ambient volatile organic compounds and nitrogen dioxide at relatively low concentrations is associated with lung cancer. Further work is needed to evaluate joint relationships between these pollutants, smoking, and lung cancer.

[210]

TÍTULO / TITLE: - Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 15;19(22):6322-8. doi: 10.1158/1078-0432.CCR-13-1975. Epub 2013 Sep 27.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-1975](#)

AUTORES / AUTHORS: - Cardnell RJ; Feng Y; Diao L; Fan YH; Masrourpour F; Wang J; Shen Y; Mills GB; Minna JD; Heymach JV; Byers LA

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: Department of Thoracic/Head and Neck Medical Oncology; Bioinformatics and Computational Biology; Systems Biology, UT MD Anderson Cancer Center, Houston; Hamon Center for Therapeutic Oncology Research and the Simmons Comprehensive Cancer Center, UT Southwestern, Dallas, Texas; and Biomarin Pharmaceuticals Inc., Novato, California.

RESUMEN / SUMMARY: - PURPOSE: Small cell lung carcinoma (SCLC) is an aggressive malignancy affecting nearly 30,000 people annually in the United States. We have previously identified elevated PARP1 levels in SCLC and demonstrated in vitro sensitivity to the PARP inhibitors AZD 2281 and AG014699. Here, we evaluate activity of a novel, potent PARP inhibitor, BMN 673, and identify markers of response

as a basis for developing predictive markers for clinical application. EXPERIMENTAL DESIGN: Inhibition of SCLC proliferation by BMN 673 was assayed in vitro and effects on tumor growth were measured in SCLC xenograft models. Protein expression and pathway activation was assessed by reverse phase protein array and western blot analysis. PARP inhibition was confirmed using a PAR ELISA. RESULTS: We demonstrate striking, single agent activity of BMN 673 in SCLC cell lines and xenografts, with single agent BMN 673 exhibiting in vivo activity similar to cisplatin. Sensitivity to BMN 673 was associated with elevated baseline expression levels of several DNA repair proteins, whereas greater drug resistance was observed in SCLC models with baseline activation of the PI3K/mTOR pathway. Furthermore, we developed and confirmed these data with a novel "DNA repair score" consisting of a group of 17 DNA repair proteins. CONCLUSIONS: Elevated expression of multiple DNA repair proteins, as well as a corresponding "DNA repair protein score," predict response to BMN 673 in in vitro SCLC models. These observations complement recent work in which PI3K inhibition sensitizes breast cancer models to PARP inhibition, suggesting cooperation between DNA repair and PI3K pathways. Clin Cancer Res; 19(22); 6322-8. ©2013 AACR.

[211]

TÍTULO / TITLE: - Targeting Small Cell Lung Cancer Harboring PIK3CA Mutation with a Selective Oral PI3K Inhibitor PF-4989216.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 15.

●● [Enlace al texto completo \(gratis o de pago\) 1158/1078-0432.CCR-13-](#)

[1663](#)

AUTORES / AUTHORS: - Walls M; Baxi SM; Mehta PP; Liu KK; Zhu J; Estrella H; Li C; Zientek M; Zong Q; Smeal T; Yin MJ

INSTITUCIÓN / INSTITUTION: - Research, Pfizer Inc.

RESUMEN / SUMMARY: - PURPOSE: Constitutive activation of PI3K occurs frequently in many human tumors via either gene mutation in the p110alpha catalytic subunit of PI3K or functional loss of tumor suppressor PTEN. Small cell lung cancer (SCLC) patients have very poor prognosis and survival rates such that an effective targeted therapy is in strong demand for these patients. In this study, we characterized the highly selective oral PI3K inhibitor, PF-4989216, in preclinical SCLC models to investigate whether targeting the PI3K pathway is an effective targeted therapy option for SCLCs that harbor a PIK3CA mutation. EXPERIMENTAL DESIGN: A panel of SCLC lines with PIK3CA mutation or PTEN loss were treated with PF-4989216 in several in vitro assays including: PI3K pathway signaling, cell viability, apoptosis, cell cycle progression, and cell transformation. SCLC lines that were sensitive in vitro to PF-4989216 were further evaluated by in vivo animal studies to determine the pharmacokinetic/pharmacodynamic relationship and tumor growth inhibition by PF-4989216 treatment. RESULTS: PF-4989216 inhibited PI3K downstream signaling and subsequently led to apoptosis induction, and inhibition in cell viability, transformation, and xenograft tumor growth in SCLCs harboring PIK3CA mutation. In SCLCs with PTEN loss, PF-4989216 also inhibited PI3K signaling but did not induce BIM-mediated apoptosis nor was there any effect in cell viability or transformation. These results implicate differential tumorigenesis and apoptosis mechanisms in SCLCs harboring

PIK3CA mutation versus PTEN loss. CONCLUSION: Our results suggest that PF-4989216 is a potential cancer drug candidate for SCLC patients with PIK3CA mutation but not PTEN loss.

[212]

TÍTULO / TITLE: - Inhibition of p38 MAPK-dependent MutS homologue-2 (MSH2) expression by metformin enhances gefitinib-induced cytotoxicity in human squamous lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):397-406. doi: 10.1016/j.lungcan.2013.09.011. Epub 2013 Sep 25.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.011](#)

AUTORES / AUTHORS: - Ko JC; Chiu HC; Wo TY; Huang YJ; Tseng SC; Huang YC; Chen HJ; Syu JJ; Chen CY; Jian YT; Jian YJ; Lin YW

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, National Taiwan University Hospital, Hsin-Chu Branch, Taiwan; Department of Nursing, Yuanpei University, Hsinchu, Taiwan; Institute of Technology Law, National Chiao Tung University, Hsinchu, Taiwan.

RESUMEN / SUMMARY: - OBJECTIVES: Gefitinib, a quinazoline-derived tyrosine kinase inhibitor, has anti-tumor activity in vivo and in vitro. Human MutS homologue-2 (MSH2) plays a central role in promoting genetic stability by correcting DNA replication errors. The present study investigated the effects of p38 mitogen-activated protein kinase (MAPK) signal on gefitinib-induced MSH2 expression in two human non-small cell lung squamous cancer cell lines. MATERIALS AND METHODS: After the gefitinib treatment, the expressions of MSH2 mRNA were determined by real-time PCR and RT-PCR analysis. Protein levels of MSH2, phospho-MKK3/6, phospho-p38 MAPK were determined by Western blot analysis. We used specific MSH2, and p38 MAPK small interfering RNA to examine the role of p38 MAPK-MSH2 signal in regulating the chemosensitivity of gefitinib. Cell viability was assessed by MTS assay, trypan blue exclusion, and colony-forming ability assay. RESULTS: Exposure of gefitinib increased MSH2 protein and mRNA levels, which was accompanied by MKK3/6-p38 MAPK activation in H520 and H1703 cells. Moreover, blocking p38 MAPK activation by SB202190 significantly decreased gefitinib-induced MSH2 expression by increasing mRNA and protein instability. In contrast, enhancing p38 activation using constitutively active MKK6 (MKK6E) increased MSH2 protein and mRNA levels. Specific inhibition of MSH2 expression by siRNA enhanced gefitinib-induced cytotoxicity. Metformin, an anti-diabetic drug, might reduce cancer risk. In human lung squamous cancer cells, metformin decreased gefitinib-induced MSH2 expression and augmented the cytotoxic effect and growth inhibition by gefitinib. Transient expression of MKK6E or HA-p38 MAPK vector could abrogate metformin and gefitinib-induced synergistic cytotoxic effect in H520 and H1703 cells. CONCLUSION: Together, down-regulation of MSH2 expression can be a possible strategy to enhance the sensitivity of gefitinib to human lung squamous cancer cells.

[213]

TÍTULO / TITLE: - DPMA, a deoxypodophyllotoxin derivative, induces apoptosis and anti-angiogenesis in non-small cell lung cancer A549 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Bioorg Med Chem Lett. 2013 Dec 15;23(24):6650-5. doi: 10.1016/j.bmcl.2013.10.048. Epub 2013 Oct 31.

●● Enlace al texto completo (gratis o de pago) [1016/j.bmcl.2013.10.048](#)

AUTORES / AUTHORS: - Sang CY; Xu XH; Qin WW; Liu JF; Hui L; Chen SW

INSTITUCIÓN / INSTITUTION: - School of Pharmacy, Lanzhou University, Lanzhou 730000, PR China.

RESUMEN / SUMMARY: - We found that the deoxypodophyllotoxin derivative, 2,6-dimethoxy-4-(6-oxo-(5R,5aR,6,8,8aR,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl)phenyl (®-1-amino-4-(methylthio)-1-oxobutan-2-yl)carbamate (DPMA), exhibited superior cytotoxicity compared with etoposide. In this study, we investigated the mechanism of action of DPMA. DPMA exhibited anti-proliferative activity and induced apoptosis in A549 cells in a dose- and time-dependant manner. DPMA inhibited microtubule formation and induced expression of Bax, cleaved caspase-3, p53 and ROS, and inhibited Bcl-2 expression. DPMA also affected cyclinB1, cdc2 and p-cdc2 expression, inducing cell cycle arrest. DPMA also inhibited tube formation of VEGF-induced human umbilical vein endothelial cells. These studies demonstrate that DPMA inhibits p53/cdc2/Bax signaling, thereby inhibiting cell growth/angiogenesis and inducing apoptosis.

[214]

TÍTULO / TITLE: - Oleifolioside B-mediated autophagy promotes apoptosis in A549 human non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Dec;43(6):1943-50. doi: 10.3892/ijo.2013.2143. Epub 2013 Oct 17.

●● Enlace al texto completo (gratis o de pago) [3892/ijo.2013.2143](#)

AUTORES / AUTHORS: - Jin CY; Yu HY; Park C; Han MH; Hong SH; Kim KS; Lee YC; Chang YC; Cheong J; Moon SK; Kim GY; Moon HI; Kim WJ; Lee JH; Choi YH

INSTITUCIÓN / INSTITUTION: - School of Pharmaceutical Science, Zhengzhou University, Henan 450001, P.R. China.

RESUMEN / SUMMARY: - The biochemical mechanisms of cell death by oleifolioside B (OB), a cycloartane-type triterpene glycoside isolated from *Dendropanax morbifera* Leveille, were investigated in A549 human lung carcinoma cells. Our data indicated that exposure to OB led to caspase activation and typical features of apoptosis; however, apoptotic cell death was not prevented by z-VAD-fmk, a pan-caspase inhibitor, demonstrating that OB-induced apoptosis was independent of caspase activation. Subsequently, we found that OB increased autophagy, as indicated by an increase in monodansylcadaverine fluorescent dye-labeled autophagosome formation and in the levels of the autophagic form of microtubule-associated protein 1 light chain 3 and Atg3, an autophagy-specific gene, which is associated with inhibiting phosphonuclear factor erythroid 2-related factor 2 (Nrf2) expression. However, pretreatment with bafilomycin A1, an autophagy inhibitor, attenuated OB-induced apoptosis and dephosphorylation of Nrf2. The data suggest that OB-induced autophagy functions as a death mechanism in A549 cells and OB has potential as a novel anticancer agent

capable of targeting apoptotic and autophagic cell death and the Nrf2 signaling pathway.

[215]

TÍTULO / TITLE: - PX-12 inhibits the growth of A549 lung cancer cells via G2/M phase arrest and ROS-dependent apoptosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2014 Jan;44(1):301-8. doi: 10.3892/ijo.2013.2152. Epub 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [3892/ijo.2013.2152](#)

AUTORES / AUTHORS: - You BR; Shin HR; Park WH

INSTITUCIÓN / INSTITUTION: - Department of Physiology, Medical School, Research Institute for Endocrine Sciences, Chonbuk National University, Jeonju 561-180, Republic of Korea.

RESUMEN / SUMMARY: - PX-12 (1-methylpropyl 2-imidazolyl disulfide) is an inhibitor of thioredoxin (Trx-1), which has antitumor effects. However, little is known about the toxicological effect of PX-12 on cancer cells. We investigated the anti-growth effects of PX-12 on A549 lung cancer cells in relation to reactive oxygen species (ROS) and glutathione (GSH) levels. Based on MTT assays, PX-12 inhibited the growth of A549 cells with an IC50 of approximately 20 microM at 72 h. DNA flow cytometric analysis indicated that PX-12 significantly induced the G2/M phase arrest of the cell cycle in A549 cells. This agent also induced apoptotic cell death, as demonstrated by Annexin V-FITC staining cells and the loss of mitochondrial membrane potential MMP (psim). In addition, the administration of Bax siRNA attenuated PX-12-induced A549 cell death. All the tested caspase inhibitors, especially Z-VAD significantly prevented apoptosis induced by PX-12. With respect to ROS and GSH levels, PX-12 increased ROS levels including O2*⁻ in A549 cells and induced GSH depletion. N-acetyl cysteine (NAC) markedly reduced ROS levels in PX-12-treated A549 cells. NAC also prevented apoptotic cell death and GSH depletion induced by PX-12. This is the first report to show that PX-12 inhibits the growth of A549 cells via G2/M phase arrest, and Bax-mediated and ROS-dependent apoptosis.

[216]

TÍTULO / TITLE: - Better survival after lung cancer surgery in high-volume hospitals.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Thorax. 2013 Oct 30. doi: 10.1136/thoraxjnl-2013-204661.

●● Enlace al texto completo (gratis o de pago) [1136/thoraxjnl-2013-204661](#)

AUTORES / AUTHORS: - Sartipy U

[217]

TÍTULO / TITLE: - Piperine induces apoptosis of lung cancer A549 cells via p53-dependent mitochondrial signaling pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 24.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1433-4](#)

AUTORES / AUTHORS: - Lin Y; Xu J; Liao H; Li L; Pan L

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, 306 Hospital of PLA, Beijing, 100101, China.

RESUMEN / SUMMARY: - The aim of this study was to evaluate the cytotoxic and apoptotic effects of piperine on human lung cancer A549 cells and to explore its mechanisms. Piperine was found to exert the greatest cytotoxic effect against A549 cells in a dose-dependent manner, whereas it showed no effect on WI38 human lung fibroblasts. This cell growth-inhibitory effect might be attributed to cell DNA damage and cytotoxic effects. Besides, piperine had the ability to cause cell cycle arrest in G2/M phase and to activate caspase-3 and caspase-9 cascades in A549 cells. Furthermore, piperine-induced apoptosis could be blocked by the broad caspase inhibitor z-VAD-fmk in majority. In addition, piperine treatment decreased Bcl-2 protein expression, but increased Bax protein expression in A549 cells, which were positively correlated with an elevated expression of p53 compared to control. Taken together, these results suggested that piperine could induce p53-mediated cell cycle arrest and apoptosis via activation of caspase-3 and caspase-9 cascades, as well as increasing the Bax/Bcl-2 ratio. Thus, piperine could be developed as an effective antitumor agent in the prevention and treatment of lung cancer without toxicity to the host.

[218]

TÍTULO / TITLE: - 50 years ago in the journal of pediatrics: cigarettes, school children, and lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Pediatr. 2013 Nov;163(5):1371. doi: 10.1016/j.jpeds.2013.04.064.

●● Enlace al texto completo (gratis o de pago) 1016/j.jpeds.2013.04.064

AUTORES / AUTHORS: - Fisher PG

INSTITUCIÓN / INSTITUTION: - Departments of Neurology, Pediatrics, and Human Biology, Stanford University, Lucile Packard Children's Hospital, Palo Alto, California.

[219]

TÍTULO / TITLE: - Total Lesion Glycolysis in Early-Stage Non-Small Cell Lung Cancer: Proposal for an Alternative Dimensionless Volume-Based Parameter.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Surg. 2013 Oct 28.

●● Enlace al texto completo (gratis o de pago)

1097/SLA.0000000000000292

AUTORES / AUTHORS: - Laffon E; Marthan R

INSTITUCIÓN / INSTITUTION: - University Bordeaux, Centre de Recherche, Cardio-Thoracique de Bordeaux, INSERM, U-1045 and CHU de Bordeaux - F-33000, Bordeaux, France, elaffon@u-bordeaux2.fr.

[220]

TÍTULO / TITLE: - Novel pandemic influenza A (H1N1) virus infection modulates apoptotic pathways that impact its replication in A549 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Microbes Infect. 2013 Nov 18. pii: S1286-4579(13)00224-4. doi: 10.1016/j.micinf.2013.11.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.micinf.2013.11.003](#)

AUTORES / AUTHORS: - Wang X; Tan J; Zoueva O; Zhao J; Ye Z; Hewlett I

INSTITUCIÓN / INSTITUTION: - Lab of Molecular Virology, Division of Emerging and Transfusion Transmitted Diseases, Bethesda, MD 20892, USA. Electronic address: xue.wang@fda.hhs.gov.

RESUMEN / SUMMARY: - It is not well-known whether apoptosis signaling affects influenza virus infection and reproduction in human lung epithelial cells. Using A549 cell line, we studied the relationship of some apoptosis-associated molecules with novel pandemic influenza A (H1N1) virus, A/California/04/2009. Infected cells displayed upregulated Fas ligand, activated FADD and caspase-8, and downregulated FLIP in the extrinsic apoptotic pathway. p53 expression increased and Bcl-XL expression decreased in the intrinsic pathway. Expression of pre-apoptotic molecules (FasL, FADD, and p53) increased virus replication, while inhibition of activity of FADD, caspase-8 and caspase-3, and expression of anti-apoptotic proteins (FLIP and Bcl-XL) decreased virus replication. p38, ERK and JNK from MAPK pathways were activated in infected cells, and inhibition with their inhibitors diminished virus replication. In the p38 superfamily, p38alpha expression increased viral RNA production, while expression of p38beta and p38gamma decreased. These data indicated that influenza virus induces apoptotic signaling pathways, which benefit virus replication.

[221]

TÍTULO / TITLE: - An optimization algorithm for 3D real-time lung tumor tracking during arc therapy using kV projection images.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Phys. 2013 Oct;40(10):101710. doi: 10.1118/1.4821545.

●● Enlace al texto completo (gratis o de pago) [1118/1.4821545](#)

AUTORES / AUTHORS: - Zhuang L; Liang J; Yan D; Zhang T; Marina O; Ionascu D

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, William Beaumont Hospital, 3601 West Thirteen Mile Road, Royal Oak, Michigan 48073.

RESUMEN / SUMMARY: - **PURPOSE:** To develop a real-time markerless 3D tumor tracking using kilovoltage (kV) cone-beam CT (CBCT) projection images during volumetric modulated arc therapy (VMAT) treatment of lung tumors. **METHODS:** The authors have developed a method to identify the position of lung tumors during VMAT treatment, where the current mean 3D position is detected and subsequently the real time 3D position is obtained. The mean position is evaluated by iteratively minimizing an observation error function between the tumor coordinate detected in the imaging plane and the coordinate of the corresponding projection of the estimated mean position. The 3D trajectory is reconstructed using the same optimization formalism, where an observation error function is minimized for tumor positions confined within a predefined amplitude bin as determined from the superior-inferior tumor motion. Dynamic phantom experiments were performed and image data acquired during patient treatment were analyzed to characterize the reconstruction ability of the proposed method. **RESULTS:** The proposed algorithm needs to acquire kV projection data until a certain gantry angle is passed through, termed the black-out angle, before

accurate estimation mean 3D tumor position is possible. The black-out angle for the mean position method is approximately 20 degrees , while for the 3D trajectory reconstruction an additional approximately 15 degrees is required. The mean 3D position and 3D trajectory reconstruction are accurate within +/- 0.5 mm.

CONCLUSIONS: The authors present a real-time tracking framework to locate lung tumors during VMAT treatment using an optimization algorithm applied to CBCT kV projection images taken concomitantly with the treatment delivery. The authors' technique does not introduce significant additional dose and can be used for real-time treatment monitoring.

[222]

TÍTULO / TITLE: - Part I-mechanism of adaptation: high nitric oxide adapted A549 cells show enhanced DNA damage response and activation of antiapoptotic pathways.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 16.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1318-6](#)

AUTORES / AUTHORS: - Aqil M; Elseth KM; Vesper BJ; Deliu Z; Aydogan B; Xue J; Radosevich JA

INSTITUCIÓN / INSTITUTION: - Department of Oral Medicine and Diagnostic Sciences, College of Dentistry, University of Illinois at Chicago, 801 S. Paulina St., Chicago, IL, 60612, USA.

RESUMEN / SUMMARY: - Our previous studies demonstrate that A549, a human lung adenocarcinoma line, could be adapted to the free radical nitric oxide (NO[Symbol: see text]). NO[Symbol: see text] has been shown to be overexpressed in human tumors. The original cell line, A549 (parent), and the newly adapted A549-HNO (which has a more aggressive phenotype) serves as a useful model system to study the role of NO[Symbol: see text] in tumor biology. It is well known that DNA damage response (DDR) is altered in cancer cells and NO[Symbol: see text] is known to cause DNA damage. Modulations in molecular mechanisms involved in DNA damage response in A549-HNO cells can provide better insights into the enhanced growth behavior of these cells. Thus, here, we carried out a series of time course experiments by treating A549 and A549-HNO cells with NO[Symbol: see text] donor and examining levels of proteins involved in the DDR pathway. We observed induced expression of key components of DDR pathway in A549-HNO cells. The HNO cells showed sustained expression of key proteins involved in both nonhomologous end joining (NHEJ) and homologous recombination pathways, whereas parent cells only expressed low levels of NHEJ pathway proteins. Further with prolonged NO[Symbol: see text] exposure, ATR, Chk1, and p53 were activated and upregulated in HNO cells. Activation of p53 results in inhibition of apoptosis through induced Mcl1 expression. It also leads to cell cycle modulation. Interestingly, several reports show that cancer stem cells have enhanced expression of proteins involved in DNA damage response and also activated an antiapoptotic response. Our results here suggest that our HNO adapted A549 cells have increased activation of DNA damage response pathway proteins which can lead to better DNA repair function. Enhanced DDR leads to activation of antiapoptosis response and modulation in the cell cycle which may lead to better survival of these cells under harsh conditions. Thus, our present investigation further supports the hypothesis that HNO exposure leads to survival of these cells.

[223]

TÍTULO / TITLE: - PLGA nanoparticles containing SN-38 for reversing multiple drug resistance of A549/DDP cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Control Release. 2013 Nov 28;172(1):e67. doi: 10.1016/j.jconrel.2013.08.138.

●● Enlace al texto completo (gratis o de pago) [1016/j.jconrel.2013.08.138](#)

AUTORES / AUTHORS: - Wang Y; Guo M; Lu Y; Ding L; Yu S

INSTITUCIÓN / INSTITUTION: - Jiangsu Key Laboratory for Supramolecular Medicinal Materials and Applications, College of Life Sciences, Nanjing Normal University, Nanjing 210046, China.

[224]

TÍTULO / TITLE: - HSP-90 inhibitor ganetespib is synergistic with doxorubicin in small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Oct 28. doi: 10.1038/onc.2013.439.

●● Enlace al texto completo (gratis o de pago) [1038/onc.2013.439](#)

AUTORES / AUTHORS: - Lai CH; Park KS; Lee DH; Alberobello AT; Raffeld M; Pierobon M; Pin E; Petricoin Iii EF; Wang Y; Giaccone G

INSTITUCIÓN / INSTITUTION: - 1] Medical Oncology Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA [2].

RESUMEN / SUMMARY: - Small cell lung cancer (SCLC) at advanced stage is considered an incurable disease. Despite good response to initial chemotherapy, the responses in SCLC patients with metastatic disease are of short duration and resistance inevitably occurs. Although several target-specific drugs have altered the paradigm of treatment for many other cancers, we have yet to witness a revolution of the same magnitude in SCLC treatment. Anthracyclines, such as doxorubicin, have definite activity in this disease, and ganetespib has shown promising activity in preclinical models but underwhelming activity as a single agent in SCLC patients. Using SCLC cell lines, we demonstrated that ganetespib (IC₅₀: 31 nM) was much more potent than 17-allylamino-17-demethoxygeldanamycin (17-AAG), a geldanamycin derivative (IC₅₀: 16 μM). Ganetespib inhibited SCLC cell growth via induction of persistent G₂/M arrest and Caspase 3-dependent cell death. MTS assay revealed that ganetespib synergized with both doxorubicin and etoposide, two topoisomerase II inhibitors commonly used in SCLC chemotherapy. Expression of receptor-interacting serine/threonine-protein kinase 1 (RIP1), a protein that may function as a pro-survival scaffold protein or a pro-death kinase in TNFR1-activated cells, was induced by doxorubicin and downregulated by ganetespib. Depletion of RIP1 by either RIP1 small interfering RNA (siRNA) or ganetespib sensitized doxorubicin-induced cell death, suggesting that RIP1 may promote survival in doxorubicin-treated cells and that ganetespib may synergize with doxorubicin in part through the downregulation of RIP1. In comparison to ganetespib or doxorubicin alone, the ganetespib+doxorubicin combination caused significantly more growth regression and death of human SCLC xenografts in immunocompromised mice. We conclude that ganetespib and

doxorubicin combination exhibits significant synergy and is efficacious in inhibiting SCLC growth in vitro and in mouse xenograft models. Our preclinical study suggests that ganetespib and doxorubicin combination therapy may be an effective strategy for SCLC treatment, which warrants clinical testing. Oncogene advance online publication, 28 October 2013; doi:10.1038/onc.2013.439.

[225]

TÍTULO / TITLE: - Protumorigenic effects of mir-145 loss in malignant pleural mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncogene. 2013 Nov 18. doi: 10.1038/onc.2013.476.

●● [Enlace al texto completo \(gratis o de pago\) 1038/onc.2013.476](#)

AUTORES / AUTHORS: - Cioce M; Ganci F; Canu V; Sacconi A; Mori F; Canino C; Korita E; Casini B; Alessandrini G; Cambria A; Carosi MA; Blandino R; Panebianco V; Facciolo F; Visca P; Volinia S; Muti P; Strano S; Croce CM; Pass HI; Blandino G

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, NYU Langone Medical Center, New York, NY, USA.

RESUMEN / SUMMARY: - We identified a discrete number of microRNAs differentially expressed in benign or malignant mesothelial tissues. We focused on mir-145 whose levels were significantly downregulated in malignant mesothelial tissues and malignant pleural mesothelioma (MPM) cell lines as compared to benign tissues (pleura, peritoneum or cysts). We show that promoter hyper-methylation caused very low levels in MPM cell lines and specimens. Treatment of MPM cell lines with mir-145 agonists negatively modulated some protumorigenic properties of MPM cells, such as clonogenicity, cell migration and resistance to pemetrexed treatment. The main effector mechanism of the clonogenic death induced by mir-145 was that of accelerated senescence. We found that mir-145 targeted OCT4 via specific binding to its 3'-UTR. Increased intracellular levels of mir-145 decreased the levels of OCT4 and its target gene ZEB1, thereby counteracting the increase of OCT4 induced by pemetrexed treatment which is known to favor the development of chemoresistant cells. In line with this, reintroduction of OCT4 into mimic-145 treated cells counteracted the effects on clonogenicity and replicative senescence. This further supports the relevance of the mir-145-OCT4 interaction for the survival of MPM cells. The potential use of mir-145 expression levels to classify benign vs malignant mesothelial tissues and the differences between pemetrexed-induced senescence and that induced by the re-expression of mir-145 are discussed. Oncogene advance online publication, 18 November 2013; doi:10.1038/onc.2013.476.

[226]

TÍTULO / TITLE: - SPOCK1 is a novel transforming growth factor-beta target gene that regulates lung cancer cell epithelial-mesenchymal transition.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Nov 1;440(4):792-7. doi: 10.1016/j.bbrc.2013.10.024. Epub 2013 Oct 14.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.bbrc.2013.10.024](#)

AUTORES / AUTHORS: - Miao L; Wang Y; Xia H; Yao C; Cai H; Song Y

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Nanjing Drum Tower Hospital Affiliated to Medical School of Nanjing University, Nanjing 210008, China.

RESUMEN / SUMMARY: - Lung cancer is the leading cause of cancer related death worldwide and the prognosis is still poor with 5-year survival of approximately 15%. Metastasis is the leading cause of death by cancer. Recent researches have demonstrated that epithelial-to-mesenchymal transition (EMT) plays a key role in the early process of metastasis of cancer cells. Here, we identified that SPARC/osteonectin, cwcv and kazal-like domains proteoglycan 1 (SPOCK1) is a novel transforming growth factor-beta1 (TGF-beta) target gene that regulates lung cancer cell EMT. TGF-beta has been reported as a major inducer of EMT. We observed that the expression of SPOCK1 in lung cancer tumor tissues is significantly higher than matched normal lung tissues. Moreover, the expression of SPOCK1 was also significantly higher in metastasis tumor tissues than non-metastasis tumor tissues. Levels of SPOCK1 mRNA were increased among patients with shorter disease-free survival times, indicating the potential role of SPOCK1 in lung cancer progression and metastasis. Silencing SPOCK1 expression with endoribonuclease-prepared small interfering RNA (esiRNA) in lung cells inhibits lung cancer cell growth, colony formation and invasion in vitro. Interestingly, ectopic expression of SPOCK1 in epithelial lung cancer cells induced EMT with increased expression of the mesenchymal marker Vimentin and decreased expression of epithelial marker E-cadherin. We also found that the expression of SPOCK1 was increased under treatment of TGF-beta, indicating that SPOCK1 is a novel downstream target of TGF-beta. Taken together, our study showed that SPOCK1 is a novel metastasis related biomarker in lung cancer and may be new diagnostic and therapeutic target for lung cancer.

[227]

TÍTULO / TITLE: - MicroRNA-31 inhibits cisplatin-induced apoptosis in non-small cell lung cancer cells by regulating the drug transporter ABCB9.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Lett. 2013 Oct 4. pii: S0304-3835(13)00703-9. doi: 10.1016/j.canlet.2013.09.034.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.09.034](#)

AUTORES / AUTHORS: - Dong Z; Zhong Z; Yang L; Wang S; Gong Z

INSTITUCIÓN / INSTITUTION: - Institute of Biochemistry and Molecular Biology, Zhejiang Provincial Key Laboratory of Pathophysiology, Ningbo University School of Medicine, Ningbo, China.

RESUMEN / SUMMARY: - Alterations in microRNA (miRNA) expression have been found to be involved in tumor growth and response to chemotherapy. However, the possible role of miR-31 in cisplatin (DDP) resistance in non-small cell lung cancer (NSCLC) remains unclear. In this study, we identified a DDP-sensitive and a DDP-resistant cell line from four candidate human NSCLC cell lines. Notably, we found that miR-31 was significantly upregulated in the DDP-resistant cell line compared with its level in the DDP-sensitive cell line. As a result, miR-31 overexpression induced DDP resistance in the DDP-sensitive cell line, and miR-31 knockdown rescued DDP sensitivity in the DDP-resistant cell line. Interestingly, miR-31 was inversely correlated with the expression of the drug resistance gene ABCB9. The luciferase activity assay

showed that miR-31 directly targets the 3'UTR of ABCB9, which is known to play a crucial role in drug resistance. Mechanistically, we showed that miR-31 confers DDP-induced apoptosis and that inhibition of ABCB9 is required for DDP resistance. The data demonstrate that miR-31 exerts an anti-apoptotic effect most likely through the inhibition of ABCB9 and thus provide a novel strategy involving the use of miR-31 as a potential target in NSCLC chemotherapy.

[228]

TÍTULO / TITLE: - Loss of an EGFR-amplified chromosome 7 as a novel mechanism of acquired resistance to EGFR-TKIs in EGFR-mutated NSCLC cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 16. pii: S0169-5002(13)00446-7. doi: 10.1016/j.lungcan.2013.10.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.003](#)

AUTORES / AUTHORS: - Furugaki K; Iwai T; Moriya Y; Harada N; Fujimoto-Ouchi K

INSTITUCIÓN / INSTITUTION: - Product Research Department, Kamakura Research Laboratories, Chugai Pharmaceutical Co., Ltd., Japan.

RESUMEN / SUMMARY: - Epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) show notable effects against non-small cell lung cancers (NSCLCs) harboring EGFR-activating mutations. However, almost all patients eventually acquire resistance to EGFR-TKIs. In this study, we established novel erlotinib resistant NSCLC cells and examined their resistant mechanisms. Resistant cells were established in 14, 3, and 0 wells exposed to 0.1, 1, and 10µM erlotinib, respectively. The IC50 values of these cells were 47- to 1209-fold higher than that of the parent cells. No secondary T790M mutation was detected in any resistant cells. However, in 13/17 resistant cells, EGFR copy number was reduced less than approximately one-eighth of parent cells, and in one resistant cell (B10), >99.99% of the population was EGFR-unamplified cells. Most (97.5%) parent cells showed EGFR amplification, but 2.5% of the population comprised EGFR-unamplified cells. An EGFR-unamplified clone (4D8) isolated from parent cells in erlotinib-free normal medium also showed erlotinib resistance comparable to the resistant B10 cells. Loss of an EGFR-amplified chromosome 7 (EGFR-ampch7) was observed in 4D8 and B10 cells. EGFR-unamplified cells were constantly maintained as a minor population of the parent cells under normal cell culture conditions. In conclusion, loss of an EGFR-ampch7 causes acquired resistance in EGFR-mutated HCC827 cells exposed to a relatively low concentration of erlotinib, but a high concentration prevents the emergence of resistance.

[229]

TÍTULO / TITLE: - Autophagy sensitivity of neuroendocrine lung tumor cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Dec;43(6):2031-8. doi: 10.3892/ijo.2013.2136. Epub 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [3892/ijo.2013.2136](#)

AUTORES / AUTHORS: - Hong SK; Kim JH; Starenki D; Park JI

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Medical College of Wisconsin, Milwaukee, WI 53226, USA.

RESUMEN / SUMMARY: - Neuroendocrine (NE) phenotypes characterize a spectrum of lung tumors, including low-grade typical and intermediate-grade atypical carcinoid, high-grade large-cell NE carcinoma and small cell lung carcinoma. Currently, no effective treatments are available to cure NE lung tumors, demanding identification of biological features specific to these tumors. Here, we report that autophagy has an important role for NE lung tumor cell proliferation and survival. We found that the expression levels of the autophagy marker LC3 are relatively high in a panel of lung tumor cell lines expressing high levels of neuron-specific enolase (NSE), a key NE marker in lung tumors. In response to bafilomycin A1 and chloroquine, NE lung tumor cells exhibited cytotoxicity whereas non-NE lung tumor cells exhibited cytostasis, indicating a distinct role of autophagy for NE lung tumor cell survival. Intriguingly, in certain NE lung tumor cell lines, the levels of processed LC3 (LC3-II) were inversely correlated with AKT activity. When AKT activity was inhibited using AKTi or MK2206, the levels of LC3-II and SQSTM1/p62 were increased. In contrast, torin 1, rapamycin or mTOR knockdown increased p62 levels, suggesting that these two pathways have opposing effects on autophagy in certain NE lung tumors. Moreover, inhibition of one pathway resulted in reduced activity of the other, suggesting that these two pathways crosstalk in the tumors. These results suggest that NE lung tumor cells share a common feature of autophagy and are more sensitive to autophagy inhibition than non-NE lung tumor cells.

[230]

TÍTULO / TITLE: - Isothermally Sensitive Detection of Serum Circulating miRNAs for Lung Cancer Diagnosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anal Chem. 2013 Dec 3;85(23):11174-9. doi: 10.1021/ac403462f. Epub 2013 Nov 13.

●● Enlace al texto completo (gratis o de pago) [1021/ac403462f](#)

AUTORES / AUTHORS: - Li Y; Liang L; Zhang CY

INSTITUCIÓN / INSTITUTION: - Single-Molecule Detection and Imaging Laboratory, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, Guangdong 518055, China.

RESUMEN / SUMMARY: - Tumor-derived miRNAs in serum are emerging as the new noninvasive biomarkers for the diagnosis of human cancers, especially at their early stage. An ideal method with high sensitivity, excellent selectivity, a simple procedure, and small amounts of starting materials is imperative for the detection of clinic circulating miRNAs. Here, we develop a new method for isothermally sensitive detection of serum miRNAs using hairpin probe-based rolling circle amplification (HP-RCA). This method exhibits ultrahigh sensitivity toward lung cancer-related miR-486-5p with a detection limit of as low as 10 fM and a large dynamic range of 6 orders of magnitude, and it can even discriminate miR-486-5p from both miRNAs with high sequence homology and its precursors (pre-miRNAs). More importantly, this method can directly and accurately distinguish the expression of serum miR-486-5p among six nonsmall-cell lung carcinoma (NSCLC) patients and six healthy persons, holding a great potential for further applications in the clinical diagnosis of lung cancers.

[231]

TÍTULO / TITLE: - Carving of non-asbestiform tremolite and the risk of lung cancer: a follow-up mortality study in a historical nephrite processing cohort.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Occup Environ Med. 2013 Dec;70(12):852-7. doi: 10.1136/oemed-2013-101404. Epub 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [1136/oemed-2013-101404](#)

AUTORES / AUTHORS: - Yang HY; Shie RH; Chen PC

INSTITUCIÓN / INSTITUTION: - Department of Occupational Medicine, Buddhist Tzu Chi General Hospital, Hualien, Taiwan.

RESUMEN / SUMMARY: - **OBJECTIVES:** The health risks associated with exposure to non-asbestiform asbestos minerals, including nephrite, are unclear. In 1965 nephrite processing began in the town of Fengtian in Taiwan, and the majority of inhabitants were involved in the industry from 1970 until 1980. The objectives of this study were to examine lung cancer deaths and assess the carcinogenic effects of nephrite carving. **METHODS:** We studied mortality due to lung cancer (ICD-9 code 162 for cancers of the trachea, bronchus and lung) from 1979 to 2011. We calculated the standardised mortality ratio (SMR) for lung cancer using the age- and sex-specific cancer mortality rates in eastern Taiwan as the standard rates. Air samples, bulk samples and a surface sample were analysed. **RESULTS:** Nephrite is a non-asbestiform asbestos mineral composed of microcrystalline tremolite. During nephrite processing, in personal air samples the average concentration of elongated mineral particles with the morphological characteristics of asbestos fibres was 1.4 f/cm³, with rough grinding generating the highest concentrations (4.7 f/cm³). Transmission electron microscopy (TEM) confirmed that the air samples contained intact asbestiform tremolite fibres. The ambient air samples and the wipe sample indicated paraoccupational contamination. The crude mortality rates for lung cancer were higher in Fengtian than in Taiwan for all age groups and both genders. The SMR for lung cancer was 1.28 (95% CI 1.12 to 1.45). **CONCLUSIONS:** Nephrite carving may increase the risk of lung cancer. Appropriate medical monitoring is warranted for workers who are exposed to similar materials.

[232]

TÍTULO / TITLE: - Plumbagin induces apoptotic and autophagic cell death through inhibition of the PI3K/Akt/mTOR pathway in human non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Lett. 2013 Nov 23. pii: S0304-3835(13)00803-3. doi: 10.1016/j.canlet.2013.11.001.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.11.001](#)

AUTORES / AUTHORS: - Li YC; He SM; He ZX; Li M; Yang Y; Pang JX; Zhang X; Chow K; Zhou Q; Duan W; Zhou ZW; Yang T; Huang GH; Liu A; Qiu JX; Liu JP; Zhou SF

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Xiaolan Hospital, Southern Medical University, Zhongshan, Guangdong 528415, China; Department of Pharmaceutical Science, College of Pharmacy, University of South Florida, Tampa, FL 33612, USA.

RESUMEN / SUMMARY: - Plumbagin (PLB) has shown anti-cancer activity but the mechanism is unclear. This study has found that PLB has a potent pro-apoptotic and pro-autophagic effect on A549 and H23 cells. PLB arrests cells in G2/M phase, and increases the intracellular level of reactive oxygen species in both cell lines. PLB dose-dependently induces autophagy through inhibition of PI3K/Akt/mTOR pathway as indicated by reduced the phosphorylation of Akt and mTOR. Inhibition or induction of autophagy enhances PLB-induced apoptosis. There is crosstalk between PLB-induced apoptosis and autophagy. These findings indicate that PLB initiates both apoptosis and autophagy in NSCLC cells through coordinated pathways.

[233]

TÍTULO / TITLE: - Programmed death ligand-1 expression in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lab Invest. 2013 Nov 11. doi: 10.1038/labinvest.2013.130.

●● Enlace al texto completo (gratis o de pago) [1038/labinvest.2013.130](#)

AUTORES / AUTHORS: - Velcheti V; Schalper KA; Carvajal DE; Anagnostou VK; Syrigos KN; Szol M; Herbst RS; Gettinger SN; Chen L; Rimm DL

INSTITUCIÓN / INSTITUTION: - Solid Tumor, Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA.

RESUMEN / SUMMARY: - Recent strategies targeting the interaction of the programmed cell death ligand-1 (PD-L1, B7-H1, CD274) with its receptor, PD-1, resulted in promising activity in early phase clinical trials. In this study, we used various antibodies and in situ mRNA hybridization to measure PD-L1 in non-small cell lung cancer (NSCLC) using a quantitative fluorescence (QIF) approach to determine the frequency of expression and prognostic value in two independent populations. A control tissue microarray (TMA) was constructed using PD-L1-transfected cells, normal human placenta and known PD-L1-positive NSCLC cases. Only one of four antibodies against PD-L1 (5H1) validated for specificity on this TMA. In situ PD-L1 mRNA using the RNAscope method was similarly validated. Two cohorts of NSCLC cases in TMAs including 340 cases from hospitals in Greece and 204 cases from Yale University were assessed. Tumors showed PD-L1 protein expression in 36% (Greek) and 25% (Yale) of the cases. PD-L1 expression was significantly associated with tumor-infiltrating lymphocytes in both cohorts. Patients with PD-L1 (both protein and mRNA) expression above the detection threshold showed statistically significant better outcome in both series (log-rank P=0.036 and P=0.027). Multivariate analysis showed that PD-L1 expression was significantly associated with better outcome independent of histology. Measurement of PD-L1 requires specific conditions and some commercial antibodies show lack of specificity. Expression of PD-L1 protein or mRNA is associated with better outcome. Further studies are required to determine the value of this marker in prognosis and prediction of response to treatments targeting this pathway. Laboratory Investigation advance online publication, 11 November 2013; doi:10.1038/labinvest.2013.130.

[234]

TÍTULO / TITLE: - A comparison of amplitude-based and phase-based positron emission tomography gating algorithms for segmentation of internal target volumes of tumors subject to respiratory motion.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Radiat Oncol Biol Phys. 2013 Nov 1;87(3):562-9. doi: 10.1016/j.ijrobp.2013.06.2042.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijrobp.2013.06.2042](#)

AUTORES / AUTHORS: - Jani SS; Robinson CG; Dahlbom M; White BM; Thomas DH; Gaudio S; Low DA; Lamb JM

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, David Geffen School of Medicine, University of California, Los Angeles, California. Electronic address: sjani@mednet.ucla.edu.

RESUMEN / SUMMARY: - PURPOSE: To quantitatively compare the accuracy of tumor volume segmentation in amplitude-based and phase-based respiratory gating algorithms in respiratory-correlated positron emission tomography (PET). METHODS AND MATERIALS: List-mode fluorodeoxyglucose-PET data was acquired for 10 patients with a total of 12 fluorodeoxyglucose-avid tumors and 9 lymph nodes. Additionally, a phantom experiment was performed in which 4 plastic butyrate spheres with inner diameters ranging from 1 to 4 cm were imaged as they underwent 1-dimensional motion based on 2 measured patient breathing trajectories. PET list-mode data were gated into 8 bins using 2 amplitude-based (equal amplitude bins [A1] and equal counts per bin [A2]) and 2 temporal phase-based gating algorithms. Gated images were segmented using a commercially available gradient-based technique and a fixed 40% threshold of maximum uptake. Internal target volumes (ITVs) were generated by taking the union of all 8 contours per gated image. Segmented phantom ITVs were compared with their respective ground-truth ITVs, defined as the volume subtended by the tumor model positions covering 99% of breathing amplitude. Superior-inferior distances between sphere centroids in the end-inhale and end-exhale phases were also calculated. RESULTS: Tumor ITVs from amplitude-based methods were significantly larger than those from temporal-based techniques ($P=.002$). For lymph nodes, A2 resulted in ITVs that were significantly larger than either of the temporal-based techniques ($P<.0323$). A1 produced the largest and most accurate ITVs for spheres with diameters of ≥ 2 cm ($P=.002$). No significant difference was shown between algorithms in the 1-cm sphere data set. For phantom spheres, amplitude-based methods recovered an average of 9.5% more motion displacement than temporal-based methods under regular breathing conditions and an average of 45.7% more in the presence of baseline drift ($P<.001$). CONCLUSIONS: Target volumes in images generated from amplitude-based gating are larger and more accurate, at levels that are potentially clinically significant, compared with those from temporal phase-based gating.

[235]

TÍTULO / TITLE: - Fulvestrant increases gefitinib sensitivity in non-small cell lung cancer cells by upregulating let-7c expression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Pharmacother. 2013 Nov 7. pii: S0753-3322(13)00123-6. doi: 10.1016/j.biopha.2013.10.007.

●● Enlace al texto completo (gratis o de pago) 1016/j.biopha.2013.10.007

AUTORES / AUTHORS: - Shen H; Liu J; Wang R; Qian X; Xu R; Xu T; Li Q; Wang L; Shi Z; Zheng J; Chen Q; Shu Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

RESUMEN / SUMMARY: - Patients with non-small cell lung cancer (NSCLC) who have activating epidermal growth factor receptor (EGFR) mutations benefit from treatment with EGFR-tyrosine kinase inhibitors (EGFR-TKIs), namely, gefitinib and erlotinib. However, these patients eventually develop resistance to EGFR-TKIs. About 50% of this acquired resistance may be the result of a secondary mutation in the EGFR gene, such as the one corresponding to T790M. In our previous study, we found that combined treatment with fulvestrant and gefitinib decreases the proliferation of H1975 NSCLC cells, compared to treatment with either fulvestrant or gefitinib alone; however, the molecular mechanism for the improved effects of the combination treatment are still unknown. In this study, we confirmed that fulvestrant increases the gefitinib sensitivity of H1975 cells and found that let-7c was most upregulated in the fulvestrant-treated cells. Our data revealed that let-7c increases gefitinib sensitivity by repressing RAS and inactivating the phosphoinositide 3-kinase (PI3K)/AKT and mitogen-activated extracellular signal-regulated kinase (MEK)/extracellular signal-regulated kinase (ERK) signaling pathways. Taken together, our findings suggest that let-7c plays an important role in fulvestrant-induced upregulation of gefitinib sensitivity in H1975 cells.

[236]

TÍTULO / TITLE: - Number of Lymph Nodes Associated With Maximal Reduction of Long-Term Mortality Risk in Pathologic Node-Negative Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Surg. 2013 Nov 20. pii: S0003-4975(13)02145-0. doi: 10.1016/j.athoracsur.2013.09.058.

●● Enlace al texto completo (gratis o de pago)

1016/j.athoracsur.2013.09.058

AUTORES / AUTHORS: - Osarogiagbon RU; Ogbata O; Yu X

INSTITUCIÓN / INSTITUTION: - Thoracic Oncology Research Group, Baptist Cancer Center, Memphis, Tennessee. Electronic address: rosarogi@bmg.md.

RESUMEN / SUMMARY: - BACKGROUND: Forty-four percent of patients with pathologic node negative (pN0) non-small cell lung cancer (NSCLC) die within 5 years of curative-intent surgical procedures. Heterogeneity in pathologic nodal examination practice raises concerns about the accuracy of nodal staging in these patients. We hypothesized a reciprocal relationship between the number of lymph nodes examined and the probability of missed lymph node metastasis and sought to identify the number of lymph nodes associated with the lowest mortality risk in pN0 NSCLC. METHODS: We analyzed resections for first primary pN0 NSCLC in the United States Surveillance, Epidemiology, and End Results (SEER) database from 1998 to 2009, with survival updated to December 31, 2009. RESULTS: In 24,650 eligible patients, there was a significant sequential reduction in mortality risk with examination of more lymph nodes. The lowest mortality risk occurred in those with 18 to 21 lymph nodes examined. The hazard ratio for all-cause mortality was 0.65 and the 95% confidence interval (CI) was 0.57 to 0.73; for lung cancer-specific mortality, hazard ratio was 0.62 and CI was 0.53

to 0.73 ($p < 0.001$ for both). The median number of lymph nodes examined was only 6.
CONCLUSIONS: Lymph node evaluation falls far short of optimal in patients with resected pN0 NSCLC, raising the odds of underestimation of long-term mortality risk and failure to identify candidates for postoperative adjuvant therapy. This represents a major quality gap for which corrective intervention is warranted.

[237]

TÍTULO / TITLE: - Flavonol isolated from ethanolic leaf extract of *Thuja occidentalis* arrests the cell cycle at G2-M and induces ROS-independent apoptosis in A549 cells, targeting nuclear DNA.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cell Prolif. 2013 Nov 23. doi: 10.1111/cpr.12079.

●● [Enlace al texto completo \(gratis o de pago\) 1111/cpr.12079](#)

AUTORES / AUTHORS: - Mukherjee A; Sikdar S; Bishayee K; Boujedaini N; Khuda-Bukhsh AR

INSTITUCIÓN / INSTITUTION: - Department of Zoology, Cytogenetics and Molecular Biology Laboratory, University of Kalyani, Kalyani, West Bengal, 741235, India.

RESUMEN / SUMMARY: - OBJECTIVES: The K-ras gene mutation commonly found in lung adenocarcinomas contributes to their non-invasive expansion. Our main objective here was to develop a chemopreventive agent against K-ras-mutated lung adenocarcinoma cell line like-A549. MATERIALS AND METHODS: We isolated flavonol from ethanolic leaf extract of *Thuja occidentalis*, and evaluated its apoptotic potentials on A549 cells. They were treated with 1-10 $\mu\text{g/ml}$ of flavonol and viability was tested retaining normal lung cells L-132 as control. We performed assays such as TUNEL, annexin V, cell-cycle and mitochondrial membrane potentials, by FACS analysis. ROS-mediated oxidative stress and drug-DNA interactions were analysed along with gene expression studies for p53, Bax-Bcl2, cytochrome c, the caspase cascade genes and PARP. RESULTS: Flavonol reduced A549 cell viability in a dose- and time-dependent manner (IC_{50} value = $7.6 \pm 0.05 \mu\text{g/ml}$ following 48 h incubation) sparing normal L-132 cells. It effected G2-M phase cell cycle arrest and apoptosis, as indicated by progressive increase in the sub-G1, annexin V and TUNEL-positive cell populations. Apoptotic effects appeared to be mitochondria-dependent, caspase-3-mediated, but ROS-independent. Analysis of circular dichroism data revealed that flavonol intercalated with nuclear DNA. In vivo studies on non small cell lung carcinoma (NSCLC)-induced mice confirmed anti-cancer potential of flavonol. CONCLUSION: Flavonol-induced apoptosis apparently resulted from intercalation of cells' nuclear DNA. Flavonol inhibited growth of induced lung tumours in the mice, indicating its potential as an effective agent against NSCLC.

[238]

TÍTULO / TITLE: - Identification of CD90 as a marker for lung cancer stem cells in A549 and H446 cell lines.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2733-40. doi: 10.3892/or.2013.2784. Epub 2013 Oct 3.

●● [Enlace al texto completo \(gratis o de pago\) 3892/or.2013.2784](#)

AUTORES / AUTHORS: - Yan X; Luo H; Zhou X; Zhu B; Wang Y; Bian X

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, The First Affiliated Hospital of Third Military Medical University, Chongqing 400038, P.R. China.

RESUMEN / SUMMARY: - Accumulating evidence supports that cancer stem cells (CSCs) are responsible for tumor initiation, progression, distal metastasis and even drug resistance. Although CD90 has been identified as a marker for several types of stem cells, such as liver CSCs, the potential role of CD90 as a marker for lung CSCs has yet to be fully characterized. Our previous study demonstrated that the lung cancer stem-like cells isolated from A549 tumor spheres, which were cultured in serum-free conditioned medium, had stronger proliferation and self-renewal abilities, and expressed higher levels of the stem cell markers Sox2 and Oct4 as compared to A549 adherent cells. In the present study, we identified CD90 as a novel surface marker of CSCs in lung cancer cells. Furthermore, we isolated CD90+ CSCs from lung cancer cell lines A549 and H446. Our results revealed that the CD90+ cells, but not the CD90- cells, from lung cancer cells displayed higher tumorigenic capacity. These findings suggest that CD90 could be a potential marker of lung CSCs and thus provide new insight into further therapeutic strategies of lung cancer.

[239]

TÍTULO / TITLE: - Expression of RRM1 and RRM2 as a novel prognostic marker in advanced non-small cell lung cancer receiving chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 24.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s13277-013-1255-4](#)

AUTORES / AUTHORS: - Wang L; Meng L; Wang XW; Ma GY; Chen JH

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, 250021, China.

RESUMEN / SUMMARY: - The aim of this study was to examine the prognostic value of BRCA1, RRM1, and RRM2 in patients with non-small cell lung cancer (NSCLC) who received adjuvant chemotherapy. A total of 418 patients who underwent curative pulmonary resection were obtained between January 2007 and November 2009. The relative cDNA quantification for BRCA1, RRM1, and RRM2 was conducted using a fluorescence-based, real-time detection method, and beta-actin was used as a reference gene. The low expression of RRM1 and RRM2 significantly increased the platinum-based chemotherapy response (For RRM1: odds ratio (OR) = 2.09, 95 % confidence interval (CI) = 1.38-3.18; For RRM2: OR = 1.64, 95 % CI = 1.09-2.48). The univariate analysis indicated that low expression of RRM1 attained a longer time to progression and overall survival time, with HR (95 % CI) of 0.50 (0.33-0.77) and 0.60 (0.39-0.92), respectively. Similarly, low expression of RRM2 had a longer time to progression and overall survival, with HR (95 % CI) of 0.57 (0.38-0.86) and 0.47 (0.31-0.71), respectively. In conclusion, low expression of RRM1 and RRM2 could be used to predict the treatment response to platinum-based chemotherapy and survival in NSCLC. The RRM1 and RRM2 could substantially contribute to the future design of individualized cancer treatment in NSCLC patients.

[240]

TÍTULO / TITLE: - Gemcitabine sensitizes lung cancer cells to Fas/FasL system-mediated killing.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Immunology. 2013 Oct 15. doi: 10.1111/imm.12190.

●● Enlace al texto completo (gratis o de pago) [1111/imm.12190](#)

AUTORES / AUTHORS: - Siena L; Pace E; Ferraro M; Sano CD; Melis M; Profita M; Spatafora M; Gjomarkaj M

INSTITUCIÓN / INSTITUTION: - Istituto di Biomedicina e Immunologia Molecolare, Consiglio Nazionale delle Ricerche, Palermo, Italy.

RESUMEN / SUMMARY: - Gemcitabine is a chemotherapy agent commonly used in the treatment of NSCLC which has been demonstrated to induce apoptosis in NSCLC cells by increasing functionally active Fas expression. The aim of this study was to evaluate the Fas/FasL system involvement in gemcitabine-induced lung cancer cell killing. NSCLC H292 cells were cultured in presence or absence of gemcitabine. FasL mRNA and protein were evaluated by real-time PCR, and by western blot and flow cytometry, respectively. Apoptosis of FasL expressing cells was evaluated by flow cytometry, and caspase-8 and-3 activation by western blot and by a colorimetric assay. Cytotoxicity of LAK cells and malignant pleural fluid (PF) lymphocytes against H292 cells was analyzed in presence or absence of the neutralizing anti-Fas ZB4 antibody, by flow cytometry. Gemcitabine increased FasL mRNA and total protein expression, the percentage of H292 cells bearing membrane-bound FasL (mFasL) and of mFasL positive apoptotic H292 cells, as well as caspase-8 and-3 cleavage. Moreover, gemcitabine increased CH11-induced caspase-8 and-3 cleavage and proteolytic activity. Cytotoxicity of LAK cells and PF lymphocytes was increased against gemcitabine-treated H292 cells and was partially inhibited by ZB4 antibody. These results demonstrate that gemcitabine: 1) induces an up-regulation of FasL in lung cancer cells triggering cell apoptosis via an autocrine/paracrine loop; 2) induces a Fas-dependent apoptosis mediated by caspase-8 and-3 activation; 3) enhances the sensitivity of lung cancer cells to cytotoxic activity of LAK cells and malignant PF lymphocytes, partially via Fas/FasL pathway. Our data strongly suggest an active involvement of Fas/FasL system in gemcitabine-induced lung cancer cell killing. This article is protected by copyright. All rights reserved.

[241]

TÍTULO / TITLE: - Copy number variation at 6q13 is associated with lung cancer risk in a Han Chinese population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Lung Res. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [3109/01902148.2013.822946](#)

AUTORES / AUTHORS: - Hu XY; Bai XM; Qiao X; Zhu YQ

INSTITUCIÓN / INSTITUTION: - 1Department of Respiratory Medicine, The First People's Hospital, Wujiang, Jiangsu, China.

RESUMEN / SUMMARY: - ABSTRACT Copy number variations (CNVs), a major source of human genetic polymorphism, have been suggested to have an important role in genetic susceptibility to common diseases such as cancer, immune diseases, and neurological disorders. Lung cancer is a multifactorial tumor closely associated with genetic background. Previous genome-wide association studies have identified single

nucleotide polymorphisms (SNPs) that are associated with lung cancer susceptibility. This study examined the CNVR2966.1 at 6q13 and its association with lung cancer susceptibility. The CNVR2966.1 was found to be a 10,379 bp nucleotides deletion/insertion within the uniform boundaries chromosome 6: 74,648,791-74,659,169. The risk of lung cancer observed in 503 cases and 623 controls was significantly associated with copy number of CNVR2966.1, with the odds ratio (OR) being 1.38 [95% confidence interval (CI) = 1.05-1.79; P = .007] for one copy genotype compared with two copies genotype. These results suggest that CNVR2966.1 is associated with lung cancer risk.

[242]

TÍTULO / TITLE: - Inhibition of miR-92b suppresses nonsmall cell lung cancer cells growth and motility by targeting RECK.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cell Biochem. 2013 Oct 27.

●● Enlace al texto completo (gratis o de pago) [1007/s11010-013-1882-5](#)

AUTORES / AUTHORS: - Lei L; Huang Y; Gong W

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Xiangyang Central Hospital, Xiangyang, 441021, China.

RESUMEN / SUMMARY: - microRNAs play critical roles in the progression and metastasis of nonsmall cell lung cancer (NSCLC). miR-92b acts as an oncogene in some malignancies; however, its role in NSCLC remains poorly understood. Here, we found that miR-92b was significantly increased in human NSCLC tissues and cell lines. Inhibition of miR-92b remarkably suppressed cell proliferation, migration, and invasion of NSCLC cells. Reversion-inducing-cysteine-rich protein with kazal motifs (RECK) was identified to be a target of miR-92b. Expression of miR-92b was negatively correlated with RECK in NSCLC tissues. Collectively, miR-92b might promote NSCLC cell growth and motility partially by inhibiting RECK.

[243]

TÍTULO / TITLE: - The Clinical Staging of Lung Cancer Through Imaging: A Radiologist's Guide to the Revised Staging System and Rationale for the Changes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiol Clin North Am. 2014 Jan;52(1):69-83. doi: 10.1016/j.rcl.2013.08.007. Epub 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago) [1016/j.rcl.2013.08.007](#)

AUTORES / AUTHORS: - Kligerman S

INSTITUCIÓN / INSTITUTION: - Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201, USA. Electronic address: skligerman@umm.edu.

RESUMEN / SUMMARY: - In 2009, the International Union Against Cancer and the American Joint Committee on Cancer accepted a revised staging system for the staging of lung cancer. Changes to the staging system were made to correlate patient survival more accurately with characteristics of the primary tumor (T) and presence or extent of nodal (N) and metastatic disease (M). Many changes were made to the staging system, most notably within the tumor (T) and metastases (M) designations.

There are many ways to clinical stage lung cancer, but PET-CT remains one of the most accurate noninvasive methods.

[244]

TÍTULO / TITLE: - Combination of liquiritin, isoliquiritin and isoliquirigenin induce apoptotic cell death through upregulating p53 and p21 in the A549 non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):298-304. doi: 10.3892/or.2013.2849. Epub 2013 Nov 14.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2849](#)

AUTORES / AUTHORS: - Zhou Y; Ho WS

INSTITUCIÓN / INSTITUTION: - School of Life Sciences, The Chinese University of Hong Kong, Shatin, Hong Kong, SAR, P.R. China.

RESUMEN / SUMMARY: - Liquiritin, isoliquiritin and isoliquirigenin are the active polyphenols present in *Glycyrrhiza uralensis* which has been used for the treatment of cancer and its complications. The present study was conducted to evaluate the cytotoxicity and antitumor activity of liquiritin, isoliquiritin and isoliquirigenin on human non-small lung cancer cells including apoptosis-induction, inhibition of apoptotic pathways and to explore the underlying mechanism. Lactate dehydrogenase assays, FITC Annexin V staining assay were performed to evaluate cellular cytotoxicity and apoptosis activity. The results showed that pretreatment with these polyphenols induced apoptosis in A549 cells. Liquiritin, isoliquiritin and isoliquirigenin significantly increased cytotoxicity of, and upregulated p53 and p21 and downregulated the apoptotic pathways. Furthermore, it inhibited cell cycle at the G2/M phase. Western blot analysis showed it significantly decreased the protein expression of PCNA, MDM2, p-GSK-3beta, p-Akt, p-c-Raf, p-PTEN, caspase-3, pro-caspase-8, pro-caspase-9 and PARP, Bcl-2 in a concentration-dependent manner while the protein expression of p53, p21 and Bax was increased. In addition, Akt pathway was downregulated. These findings suggest that liquiritin, isoliquiritin and isoliquirigenin inhibited the p53-dependent pathway and showed crosstalk between Akt activities. These active polyphenols can be an alternative agent for the treatment of lung cancer.

[245]

TÍTULO / TITLE: - Catechin-7-O-xyloside induces apoptosis via endoplasmic reticulum stress and mitochondrial dysfunction in human non-small cell lung carcinoma H1299 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):314-20. doi: 10.3892/or.2013.2840. Epub 2013 Nov 8.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2840](#)

AUTORES / AUTHORS: - Yoon JW; Lee JS; Kim BM; Ahn J; Yang KM

INSTITUCIÓN / INSTITUTION: - Department of Food Science and Engineering, Ewha Womans University, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - The medicinal plant *Ulmus davidiana* var. *japonica* has significant potential as a cancer chemoprevention agent. Catechin-7-O-xyloside

(C7Ox) was purified from ultrafine *U. davidiana* var. *japonica* ethanol extract. In the present study, we investigated the apoptotic effect of C7Ox in the non-small cell lung cancer (NSCLC) cell line H1299. C7Ox treatment induced cell death and decreased plasma membrane integrity, an event typical of apoptosis. C7Ox-induced apoptosis was associated with the proteolytic activation of caspase-6, cleavage of poly(ADP-ribose) polymerase (PARP) and loss of mitochondrial membrane potential. C7Ox also induced the endoplasmic reticulum (ER) stress-regulated pro-apoptotic transcription factor CHOP. The suppression of CHOP expression significantly decreased C7Ox-induced cell death, LDH leakage and caspase-6 activation. Antitumor effects, evaluated based on protracted tumor regression, were observed when nude-mice bearing H1299 xenografts were treated with C7Ox. C7Ox-induced tumor regression was accompanied by enhanced expression of CHOP mRNA. Our data suggest that C7Ox can trigger mitochondrial-mediated apoptosis, and that ER stress is critical for C7Ox-induced apoptosis in H1299 NSCLC cells.

[246]

TÍTULO / TITLE: - Suppression of proliferation and migration in highly-metastatic lung cancer cells as well as tumor growth by a new synthesized compound TBrC and its molecular mechanisms of action.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cytotechnology. 2013 Oct 17.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s10616-013-9641-8](#)

AUTORES / AUTHORS: - Ji D; Wang Y; Zhang H; Chen L; Liu X; Sun F; Liu K; Yao J; Zhang G

INSTITUCIÓN / INSTITUTION: - Laboratory of Molecular Pharmacology, School of Pharmacy, Yantai University, No. 30, Qing Quan Lu, Lai Shan Qu, Yantai, 264005, Shandong Province, China.

RESUMEN / SUMMARY: - To develop new anticancer agents has been considered as a useful and necessary strategy to suppress highly-metastatic lung cancer, the leading cause of cancer-related deaths in the world. In this study, we synthesized a new compound ethyl 6-bromocoumarin-3-carboxyl L-theanine (TBrC) and studied the anticancer activity of TBrC and its molecular mechanisms of action. Our results show that TBrC remarkably inhibits the proliferation and migration in highly-metastatic lung cancer cells by inducing apoptosis and cell cycle arrest as well as regulating related protein expressions. Further study indicated that TBrC not only enhances the protein levels of Bax, cytosolic cytochrome c, caspase-3 and PARP-1 but also reduces the protein expressions of Bcl-2, cyclin D1, VEGFR1 and NF-kappaB as well as inhibits the phosphorylation and expressions of VEGFR2 and Akt in the cancer cells. More importantly, TBrC displays strong suppression of highly-metastatic tumor growth and reduces the tumor weight by 61.6 % in tumor-bearing mice without toxicity to the mice. Our results suggest that TBrC suppresses the proliferation and migration of lung cancer cells via VEGFR-Akt-NF-kappaB signaling pathways; TBrC may have a wide therapeutic and/or adjuvant therapeutic application in the treatment of lung cancer.

[247]

TÍTULO / TITLE: - Tumor invasiveness as defined by the newly proposed IASLC/ATS/ERS classification has prognostic significance for pathologic stage IA lung adenocarcinoma and can be predicted by radiologic parameters.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Oct 13. pii: S0022-5223(13)00997-5. doi: 10.1016/j.jtcvs.2013.08.058.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.08.058](#)

AUTORES / AUTHORS: - Takahashi M; Shigematsu Y; Ohta M; Tokumasu H; Matsukura T; Hirai T

INSTITUCIÓN / INSTITUTION: - Department of Chest Surgery, Fukui Red Cross Hospital, Fukui, Japan. Electronic address: mt10947@yahoo.co.jp.

RESUMEN / SUMMARY: - OBJECTIVES: The International Association for the Study of Lung Cancer, American Thoracic Society, and European Respiratory Society (IASLC/ATS/ERS) have collaborated to propose a new pathologic classification of lung adenocarcinoma. In this classification, noninvasiveness and invasiveness have been newly defined for lung adenocarcinoma. The aims of this study were to validate the prognostic significance of tumor invasiveness as defined by the new IASLC/ATS/ERS classification and to assess the relationship between pathologic invasiveness and radiologic findings in pathologic stage IA lung adenocarcinoma. METHODS: We retrospectively reviewed 123 consecutive patients with pathologic stage IA lung adenocarcinoma. Pathologic data were classified according to the new IASLC/ATS/ERS classification. The following radiologic parameters were assessed using thin-section computed tomography: the ground-glass opacity ratio, tumor disappearance rate, and consolidation diameter. RESULTS: There were 54 noninvasive and 69 invasive adenocarcinomas. Five-year overall survival rates for noninvasive adenocarcinoma and invasive adenocarcinoma were 100% and 78.4%, respectively; this difference was statistically significant ($P < .01$), indicating the prognostic value of this classification. Receiver operating characteristic curves of the ground-glass opacity ratio, tumor disappearance rate, and consolidation diameter identified the optimal cut-off values for predicting the presence of invasive tumors as 50%, 75%, and 10 mm, respectively. CONCLUSIONS: We found that by using the new IASLC/ATS/ERS classification, histologic subtypes of pathologic stage IA lung adenocarcinoma with prognostic value could be identified. Tumor invasiveness of lung adenocarcinoma as defined by this classification can be predicted by evaluating the ground-glass opacity ratio, tumor disappearance rate, and consolidation diameter on thin-section computed tomography.

[248]

TÍTULO / TITLE: - Urinary metabolites of a polycyclic aromatic hydrocarbon and volatile organic compounds in relation to lung cancer development in lifelong never smokers in the Shanghai Cohort Study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Carcinogenesis. 2013 Nov 25.

●● Enlace al texto completo (gratis o de pago) [1093/carcin/bgt352](#)

AUTORES / AUTHORS: - Yuan JM; Butler LM; Gao YT; Murphy SE; Carmella SG; Wang R; Nelson HH; Hecht SS

INSTITUCIÓN / INSTITUTION: - Cancer Control and Population Sciences, University of Pittsburgh Cancer Institute, Pittsburgh, PA 15232, USA.

RESUMEN / SUMMARY: - Exposures to polycyclic aromatic hydrocarbons (PAHs) from various environmental and occupational sources are considered a primary risk factor for lung cancer among lifelong never smokers, based largely on results from epidemiologic studies utilizing self-reported exposure information. Prospective, biomarker-based human studies on the role of PAH and other airborne carcinogens in the development of lung cancer among lifelong non-smokers have been lacking. We prospectively investigated levels of urinary metabolites of a PAH and volatile organic compounds in relation to lung cancer risk in a nested case-control study of 82 cases and 83 controls among lifelong never smokers of the Shanghai Cohort Study, a prospective cohort of 18 244 Chinese men aged 45-64 years at enrollment. We quantified three PAH metabolites: r-1,t-2,3,c-4-tetrahydroxy-1,2,3,4-tetrahydrophenanthrene (PheT), 3-hydroxyphenanthrene (3-OH-Phe) and total hydroxyphenanthrenes (total OH-Phe, the sum of 1-, 2-, 3- and 4-OH-Phe), as well as metabolites of the volatile organic compounds acrolein (3-hydroxypropyl mercapturic acid), benzene (S-phenyl mercapturic acid), crotonaldehyde (3-hydroxy-1-methylpropylmercapturic acid) and ethylene oxide (2-hydroxyethyl mercapturic acid). Urinary cotinine was also quantified to confirm non-smoking status. Compared with the lowest quartile, odds ratios (95% confidence intervals) for lung cancer risk for the highest quartile levels of PheT, 3-OH-Phe and total OH-Phe were 2.98 (1.13-7.87), 3.10 (1.12-7.75) and 2.59 (1.01-6.65) (all P trend < 0.05), respectively. None of the metabolites of the volatile organic compounds were associated with overall lung cancer risk. This study demonstrates a potentially important role of exposure to PAH in the development of lung cancer among lifelong never smokers.

[249]

TÍTULO / TITLE: - Diversin increases the proliferation and invasion ability of non-small-cell lung cancer cells via JNK pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Lett. 2013 Nov 15. pii: S0304-3835(13)00798-2. doi: 10.1016/j.canlet.2013.10.033.

●● Enlace al texto completo (gratis o de pago) 1016/j.canlet.2013.10.033

AUTORES / AUTHORS: - Luan L; Zhao Y; Xu Z; Jiang G; Zhang X; Fan C; Liu D; Zhao H; Xu K; Wang M; Yu X; Wang E

INSTITUCIÓN / INSTITUTION: - Department of Pathology, First Affiliated Hospital and College of Basic Medical Sciences, China Medical University, Shenyang, China; Department of Pathology, Fengtian Hospital Affiliated To Shenyang Medical College, Shenyang, China.

RESUMEN / SUMMARY: - The expression and significance of Diversin in human tumors remains unclear. We found that Diversin was overexpressed in NSCLC, and exhibited direct correlation to poor differentiation, advanced TNM stage, lymph node metastasis and survival time. Overexpression of Diversin lead to a significant increase in proliferation and invasion of NSCLC cells, possibly through activation of JNK, cyclin B and MMP9, and the effects were blocked by JNK inhibitor. These results suggest Diversin is overexpressed in NSCLC and predict poor prognosis. Diversin may promote cell proliferation and invasion through JNK pathway.

[250]

TÍTULO / TITLE: - Luteolin attenuates TGF-beta1-induced epithelial-mesenchymal transition of lung cancer cells by interfering in the PI3K/Akt-NF-kappaB-Snail pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Life Sci. 2013 Dec 5;93(24):924-33. doi: 10.1016/j.lfs.2013.10.004. Epub 2013 Oct 17.

●● Enlace al texto completo (gratis o de pago) [1016/j.lfs.2013.10.004](#)

AUTORES / AUTHORS: - Chen KC; Chen CY; Lin CJ; Yang TY; Chen TH; Wu LC; Wu CC

INSTITUCIÓN / INSTITUTION: - Division of Chest Medicine, Department of Internal Medicine, Taichung Veterans General Hospital, Taichung, Taiwan, ROC.

RESUMEN / SUMMARY: - AIMS: Luteolin is a natural flavonoid that possesses a variety of pharmacological activities, such as anti-inflammatory and anti-cancer abilities. Whether luteolin regulates the transformation ability of lung cancer cells remains unclear. The current study aims to uncover the effects and underlying mechanisms of luteolin in regulation of and epithelial-mesenchymal transition of lung cancer cells. MAIN METHODS: The lung adenocarcinoma A549 cells were used in this experiment; the cells were pretreated with luteolin followed by administration with TGF-beta1. The expression levels of various cadherin and related upstream regulatory modules were examined. KEY FINDINGS: Pretreatment of luteolin prevented the morphological change and downregulation of E-cadherin of A549 cells induced by TGF-beta1. In addition, the activation of PI3K-Akt-IkappaBa-NF-kappaB-Snail pathway which leads to the decline of E-cadherin induced by TGF-beta1 was also attenuated under the pretreatment of luteolin. SIGNIFICANCE: We provide the mechanisms about how luteolin attenuated the epithelial-mesenchymal transition of A549 lung cancer cells induced by TGF-beta1. This finding will strengthen the anti-cancer effects of flavonoid compounds via the regulation of migration/invasion and EMT ability of various cancer cells.

[251]

TÍTULO / TITLE: - Crizotinib: A Review of Its Use in the Treatment of Anaplastic Lymphoma Kinase-Positive, Advanced Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Drugs. 2013 Nov 28.

●● Enlace al texto completo (gratis o de pago) [1007/s40265-013-0142-z](#)

AUTORES / AUTHORS: - Frampton JE

INSTITUCIÓN / INSTITUTION: - Adis, 41 Centorian Drive, Private Bag 65901, Mairangi Bay, North Shore, 0754, Auckland, New Zealand, demail@springer.com.

RESUMEN / SUMMARY: - Crizotinib (Xalkori®) is an orally active, small molecule inhibitor of multiple receptor tyrosine kinases, including anaplastic lymphoma kinase (ALK), c-Met/hepatocyte growth factor receptor and c-ros oncogene 1. In the EU, crizotinib has been conditionally approved for the treatment of adults with previously treated, ALK-positive, advanced non-small cell lung cancer (NSCLC). This approval has been based on objective response rate and tolerability data from two ongoing phase I/II studies (PROFILE 1001 and PROFILE 1005); these results have been

substantiated and extended by findings from an ongoing phase III study (PROFILE 1007) in patients with ALK-positive, advanced NSCLC who had received one prior platinum-based regimen. Those treated with crizotinib experienced significant improvements in progression-free survival, objective response rate, lung cancer symptoms and global quality of life, as compared with those treated with standard second-line chemotherapy (pemetrexed or docetaxel). The relative survival benefit with crizotinib is unclear, however, as the data are still immature and likely to be confounded by the high cross-over rate among chemotherapy recipients. Crizotinib treatment was generally well tolerated in the three PROFILE studies, with liver transaminase elevations and neutropenia being the most common grade 3 or 4 adverse events. Crizotinib is the standard of care in terms of the treatment of patients with ALK-positive, advanced NSCLC; while the current EU approval is for second (or subsequent)-line use only, the first-line use of the drug is being evaluated in ongoing phase III studies. Key issues relating to the use of crizotinib in clinical practice include identifying the small subset of eligible patients, the almost inevitable development of resistance and the high cost of treatment.

[252]

TÍTULO / TITLE: - The CIK cells stimulated with combination of IL-2 and IL-15 provide an improved cytotoxic capacity against human lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 9.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s13277-013-1265-2](#)

AUTORES / AUTHORS: - Wei C; Wang W; Pang W; Meng M; Jiang L; Xue S; Xie Y; Li R; Hou Z

INSTITUCIÓN / INSTITUTION: - Yan'an Affiliated Hospital of Kunming Medical University, No. 245 East of Renmin Road, Kunming, 650051, Yunan, People's Republic of China.

RESUMEN / SUMMARY: - Generation of cytokine-induced killer (CIK) cells is an emerging approach in adoptive donor lymphocyte infusion for patients with a wide range of tumors. However, our previous in vitro studies have shown that the killing efficacy of CIK cells against lung cancer was lower than other tumor cells, while the underlying mechanisms are not clear. We explored the feasibility to improve CIK cells mediated cytotoxicity against lung cancer. Interleukin (IL)-15 is a pleiotropic cytokine that stimulates cytolytic activity and cytokine secretion of NK cells, which may enhance the cytotoxic activity of CIK cells. In this study, we intended to stimulate the CIK cells by IL-2 in combination with IL-15 in cell expansion to achieve enhanced cytotoxicity against lung cancer cells. The different phenotypes of IL-2 or combination of IL-2 and IL-15 stimulated cytokine-induced killer cells were determined, and the improved cytotoxicity of IL-2 and IL-15 induced CIK cells against lung adenocarcinoma were evaluated both in vitro and in vivo. CIK cells stimulated with both IL-2 and IL-15 has shown greater proliferative potential than CIK cells treated with IL-2 alone. IL-15 induction also has driven the expansion of CD3+CD56+ subset and significantly enhanced cytotoxicity against tumor cells. Further analysis has demonstrated that CIKIL-2&IL-15 injected mice models have shown significant tumor regression and lower expression level of CyclinD1 in tumor tissue. This study has provided preclinical

evidences that CIKIL-2&IL-15 with enhanced cytotoxicity may offer alternative treatment option for patients with lung cancer.

[253]

TÍTULO / TITLE: - Part II-mechanism of adaptation: A549 cells adapt to high concentration of nitric oxide through bypass of cell cycle checkpoints.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 17.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1319-5](#)

AUTORES / AUTHORS: - Aqil M; Deliu Z; Elseth KM; Shen G; Xue J; Radosevich JA

INSTITUCIÓN / INSTITUTION: - Department of Oral Medicine and Diagnostic Sciences, College of Dentistry, University of Illinois at Chicago, 801 S. Paulina St., Chicago, IL, 60612, USA.

RESUMEN / SUMMARY: - Previous work has shown enhanced survival capacity in high nitric oxide (HNO)-adapted tumor cells. In Part I of this series of manuscripts, we have shown that A549-HNO cells demonstrate an improved growth profile under UV and X-ray radiation treatment. These cells exhibit increased expression of proteins involved in DNA damage recognition and repair pathway, both the non-homologous end joining pathway and homologous recombination. These include Ku80, DNA-PK, XLF ligase and MRN complex proteins. Further, the A549-HNO cells show high levels of ATM, ATR, Chk1 and Chk2, and phospho-p53. Activation of these molecules may lead to cell cycle arrest and apoptosis due to DNA damage. This is observed in parent A549 cells in response to NO donor treatment; however, the A549-HNO cells proliferate and inhibit apoptosis. Cell cycle analysis showed slowed progression through S phase which will allow time for DNA repair. Thus, to better understand the increased growth rate in A549-HNO when compared to the parent cell line A549, we studied molecular mechanisms involved in cell cycle regulation in A549-HNO cells. During the initial time period of NO donor treatment, we observe high levels of cyclin/Cdk complexes involved in regulating various stages of the cell cycle. This would lead to bypass of G1-S and G2-M checkpoints. The HNO cells also show much higher expression of Cdc25A. Cdc25A activates Cdk molecules involved in different phases of the cell cycle. In addition, there is enhanced phosphorylation of the Rb protein in HNO cells. This leads to inactivation of Rb/E2F checkpoint regulating G1-S transition. This may lead to faster progression in S phase. Thus, all of these perturbations in HNO cells lead to accelerated cell cycle progression and a higher growth rate. We also assessed expression of cell cycle inhibitors in HNO cells. Interestingly, the HNO cells show a significant decline in p21CIP1 at initial time points, but with prolonged exposure, the levels were much higher than those of the parent cells. This suggests an initial bypass of cell cycle checkpoints as p21CIP1 can inhibit the activity of all cyclin/Cdk complexes. p21CIP1 is also known to inhibit p53-induced apoptosis. This could be important during later phases of the cell cycle to allow time for repair of damaged DNA and thus better survival of HNO cells.

[254]

TÍTULO / TITLE: - Level of plasmacytoid dendritic cells is increased in non-small cell lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 18.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1297-7](#)

AUTORES / AUTHORS: - Shi W; Li X; Porter JL; Ostrodi DH; Yang B; Li J; Wang Y; Zhang J; Bai L; Jiao S

INSTITUCIÓN / INSTITUTION: - Department of Oncology, PLA General Hospital, 28 Fuxing Road, Haidian District, Beijing, 100853, China.

RESUMEN / SUMMARY: - In non-small cell lung carcinoma (NSCLC), the immune system fails to eradicate established tumors partly due to the induction of immune tolerance within the tumor microenvironment. Plasmacytoid dendritic cells (pDCs) play critical roles in regulating the immune system. In this study, we investigated pDCs in the peripheral blood of NSCLC. CD4 + CD123 + BDCA2+ pDCs were tested from peripheral blood mononuclear cells in 52 NSCLC patients and 52 healthy controls by flow cytometry. Results revealed that proportion of pDCs was significantly increased in cases than in controls (0.52 +/- 0.07 % versus 0.21 +/- 0.02 %, p < 0.001), whereas myeloid dendritic cells (mDCs) did not present any obvious difference between patients and healthy donors (0.25 +/- 0.04 % versus 0.18 +/- 0.02 %, p = 0.120). We further studied pDCs in NSCLC patients with different clinical stages. Data showed that cases with higher stages (III/IV) had elevated level of pDCs than those with lower stages (I/II) (0.65 +/- 0.09 % versus 0.25 +/- 0.07 %, p = 0.006). In addition, the amount of pDCs was identified to be associated with squamous cell carcinoma, one of the major subtypes of NSCLC. Interestingly, we observed that smoking patients presented significantly elevated pDCs than those non-smokers (0.63 +/- 0.09 % versus 0.22 +/- 0.05 %, p = 0.008). These data suggested that pDCs may be closely involved in the pathogenesis of NSCLC and may predict the progression of the disease.

[255]

TÍTULO / TITLE: - Inhibition of c-Met promoted apoptosis, autophagy and loss of the mitochondrial transmembrane potential in oridonin-induced A549 lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Pharm Pharmacol. 2013 Nov;65(11):1622-42. doi: 10.1111/jphp.12140. Epub 2013 Sep 15.

●● Enlace al texto completo (gratis o de pago) [1111/jphp.12140](#)

AUTORES / AUTHORS: - Liu Y; Liu JH; Chai K; Tashiro S; Onodera S; Ikejima T

INSTITUCIÓN / INSTITUTION: - Faculty of Life Science and Technology, Kunming University of Science and Technology, Kunming, China; China-Japan Research Institute of Medical and Pharmaceutical Sciences, Shenyang Pharmaceutical University, Shenyang, China.

RESUMEN / SUMMARY: - OBJECTIVE: Herein, inhibition of hepatocyte growth factor receptor, c-Met, significantly increased cytochrome c release and Bax/Bcl-2 ratio, indicating that c-Met played an anti-apoptotic role. The following experiments are to elucidate this anti-apoptotic mechanism, then the effect of c-Met on autophagy has also been discussed. METHODS: Investigated was the influence of c-Met on apoptosis, autophagy and loss of mitochondrial transmembrane potential (Deltapsim), and the relevant proteins were examined. KEY FINDINGS: First, we found that activation of extracellular signal-regulated kinase (ERK), p53 was promoted by c-Met interference. Subsequent studies indicated that ERK was the upstream effector of p53, and this

ERK-p53 pathway mediated release of cytochrome c and up-regulation of Bax/Bcl-2 ratio. Secondly, the inhibition of c-Met augmented oridonin-induced loss of mitochondrial transmembrane potential (Deltapsim), resulting apoptosis. Finally, the inhibition of c-Met increased oridonin-induced A549 cell autophagy accompanied by Beclin-1 activation and conversion from microtubule-associated protein light chain 3 (LC3)-I to LC3-II. Activation of ERK-p53 was also detected in autophagy process and could be augmented by inhibition of c-Met. Moreover, suppression of autophagy by 3-methyladenine (3-MA) or small interfering RNA against Beclin-1 or Atg5 decreased oridonin-induced apoptosis. Inhibition of apoptosis by pan-caspase inhibitor (z-VAD-fmk) decreased oridonin-induced autophagy as well and Loss of Deltapsim also occurred during autophagic process. CONCLUSION: Thus, inhibiting c-Met enhanced oridonin-induced apoptosis, autophagy and loss of Deltapsim in A549 cells.

[256]

TÍTULO / TITLE: - Invited review DNA copy number changes as diagnostic tools for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Thorax. 2013 Nov 4. doi: 10.1136/thoraxjnl-2013-204681.

●● [Enlace al texto completo \(gratis o de pago\) 1136/thoraxjnl-2013-204681](#)

AUTORES / AUTHORS: - Bowcock AM

RESUMEN / SUMMARY: - Lung cancer usually presents as advanced stage disease and there is a need for early diagnosis so that appropriate treatments can be provided prior to tumour progression. Copy number variation is frequently detected in tumours and can contribute to tumour progression. This is because regions harbouring DNA imbalance can contain genes encoding critical proteins whose altered dosage contributes to the neoplastic process. Three copy number variations (CNVs) from chromosomes 3p26-p11.1 (loss), 3q26.2-29 (gain) and 6q25.3-24.3 (loss) have previously been described in individuals presenting with endobronchial squamous metaplasia. These CNVs were predictors of cancer diagnosed within 44 months with 97% accuracy. An evaluation of this CNV-based classifier with an independent set of 12 samples (10 men and 2 women), each with a carcinoma in situ or invasive carcinoma at the same site at follow-up demonstrated 92% prediction accuracy. The negative predictive value of this classifier was 89%. The gain at 3q26.2-q29 contributed the most to the classification, being present in virtually all lesions. This region harbours the PIK3CA gene and evaluation of the number of copies of this gene gave very similar results to those from array comparative genomic hybridisation. This type of test can be performed on sputum or bronchial brushings. Larger cohorts now need to be examined to confirm this finding and to possibly refine the regions of CNV. This type of approach paves the way for future molecular analyses to assist in selecting subjects with endobronchial squamous metaplastic or dysplastic lesions who might benefit from more aggressive therapeutic intervention or surveillance.

[257]

TÍTULO / TITLE: - Activity of the Monocarboxylate Transporter 1 inhibitor AZD3965 in Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 25.

●● Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-2270](https://doi.org/10.1158/1078-0432.CCR-13-2270)

AUTORES / AUTHORS: - Polanski R; Hodgkinson C; Fusi A; Nonaka D; Priest L; Kelly P; Trapani F; Bishop P; White A; Critchlow SE; Smith PD; Blackhall FH; Dive C; Morrow CJ

INSTITUCIÓN / INSTITUTION: - Clinical and Experimental Pharmacology Group, CRUK Manchester Institute, University of Manchester.

RESUMEN / SUMMARY: - PURPOSE: The monocarboxylate transporter 1 (MCT1) inhibitor AZD3965 is undergoing Phase I evaluation in the UK. AZD3965 is proposed, via lactate transport modulation, to kill tumor cells reliant on glycolysis. We investigated the therapeutic potential of AZD3965 in small cell lung cancer (SCLC) seeking rationale for clinical testing in this disease and putative predictive biomarkers for trial use. EXPERIMENTAL DESIGN: AZD3965 sensitivity was determined for 7 SCLC cell lines, in normoxia and hypoxia, and for a tumor xenograft model. Proof of mechanism was sought via changes in intracellular/tumor lactate. Expression of MCT1 and related transporter MCT4 were assessed by western blot. Drug resistance was investigated via MCT4 siRNAi and overexpression. The expression and clinical significance of MCT1 and MCT4 were explored in a tissue microarray from 78 SCLC patients. RESULTS: AZD3965 sensitivity varied in vitro and was highest in hypoxia. Resistance in hypoxia was associated with increased MCT4 expression. In vivo, AZD3965 reduced tumor growth and increased intra-tumor lactate. In the tissue microarray, high MCT1 expression was associated with worse prognosis (p=0.014). MCT1 and hypoxia marker CA IX expression in the absence of MCT4 was observed in 21% of SCLC tumors. CONCLUSIONS: This study provides a rationale to test AZD3965 in SCLC patients. Our results suggest that patients with tumors expressing MCT1 and lacking in MCT4 are most likely to respond.

[258]

TÍTULO / TITLE: - Prognostic value of fibroblast growth factor receptor 1 gene locus amplification in resected lung squamous cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1371-7. doi: 10.1097/JTO.0b013e3182a46fe9.

●● Enlace al texto completo (gratis o de pago) [1097/JTO.0b013e3182a46fe9](https://doi.org/10.1097/JTO.0b013e3182a46fe9)

AUTORES / AUTHORS: - Craddock KJ; Ludkovski O; Sykes J; Shepherd FA; Tsao MS
INSTITUCIÓN / INSTITUTION: - *Departments of Pathology, daggerOntario Cancer Institute, double daggerDepartment of Biostatistics, section signDivision of Medical Oncology and Hematology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; and paragraph signDepartments of Laboratory Medicine and Pathobiology, ||Medicine, University of Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - INTRODUCTION: Fibroblast growth factor receptor 1 (FGFR1) gene amplification was recently reported as a recurrent abnormality in 10% to 20% of primary lung squamous cell carcinomas (SqCCs), and has attracted significant interest as a potential therapeutic target. Limited data are available for its prognostic impact in early-stage SqCC. METHODS: Tissue microarrays containing 135 primary lung SqCCs and 58 matching lymph node metastases were tested by

interphase fluorescence in situ hybridization for DNA copy number (CN) abnormalities at the 8p12 region including FGFR1. RESULTS: FGFR1 amplification was found in 18.2% (22 of 121 evaluable) of primary SqCC, using a definition of average copies of FGFR1 per cell of 5.0 or more. Concordance rate between primaries and matching lymph node metastases was 97.7% (43 of 44; 7 amplified and 37 nonamplified), with the only discordant case showing CN at approximately the dichotomous cutoff. Similarly, concordance between two separate lymph node metastases in each of 10 patients was 100% (1 amplified and 9 nonamplified). Using various CN cutoffs, we found no statistically significant association between FGFR1 CN abnormalities and patient age, sex, tumor grade, stage, smoking status, disease-free survival, cause-specific survival, or overall survival. CONCLUSION: FGFR1 amplification is not prognostic in resected lung squamous cell carcinoma patients.

[259]

TÍTULO / TITLE: - Tumor-suppressive microRNA-449a induces growth arrest and senescence by targeting E2F3 in human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Lett. 2013 Nov 6. pii: S0304-3835(13)00786-6. doi: 10.1016/j.canlet.2013.10.031.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.10.031](#)

AUTORES / AUTHORS: - Ren XS; Yin MH; Zhang X; Wang Z; Feng SP; Wang GX; Luo YJ; Liang PZ; Yang XQ; He JX; Zhang BL

INSTITUCIÓN / INSTITUTION: - The State Key Laboratory of Respiratory, Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou 510530, China; University of Science and Technology of China, Hefei 230026, China.

RESUMEN / SUMMARY: - MicroRNA-449a (miR-449a) was significantly downregulated in 156 lung cancer tissues ($p < 0.001$). We found that the low expression of miR-449a was highly correlated with cancer recurrence and survival of lung cancer patients. The transient introduction of miR-449a caused cell cycle arrest and cell senescence in A549 and 95D cells. Further studies revealed that E2F3 was a direct target of miR-449a in lung cancer cells. miR-449a also suppressed tumor formation in vivo in nude mice. These results suggest that miR-449a plays an important role in lung cancer tumorigenesis and that miR-449a might predict cancer recurrence and survival of lung cancer patients.

[260]

TÍTULO / TITLE: - Invited Commentary: Epidemiologic Studies of the Impact of Air Pollution on Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Epidemiol. 2013 Nov 27.

●● Enlace al texto completo (gratis o de pago) [1093/aje/kwt290](#)

AUTORES / AUTHORS: - Hart JE

RESUMEN / SUMMARY: - In this issue of the Journal, Villeneuve et al. (Am J Epidemiol. 0000;000(00):000-000) present epidemiologic evidence supporting the literature on the adverse effects of air pollution on risk of lung cancer. They found that ambient exposure to volatile organic compounds, especially when measured at longer time

scales, was associated with increased odds of lung cancer in citizens of Toronto, Ontario, Canada, between 1997 and 2002. Specifically, in fully adjusted models, they observed that an interquartile-range increase in benzene concentration was associated with an odds ratio of 1.51 (95% confidence interval: 1.13, 2.01) using exposure at the time of interview. The odds ratio increased to 1.84 (95% confidence interval: 1.26, 2.68) when time-weighted exposure at all previous addresses was considered. They obtained similar results for exposure to nitrogen dioxide. These findings add weight to the substantial (and rapidly growing) body of literature on the relation of air pollution with lung cancer risk, as well as illustrate important aspects of the effects of different exposure assessment choices and potential sources of key interest.

[261]

TÍTULO / TITLE: - Prognostic impact of the mean platelet volume/platelet count ratio in terms of survival in advanced non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Sep 2. pii: S0169-5002(13)00385-1. doi: 10.1016/j.lungcan.2013.08.020.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.08.020](#)

AUTORES / AUTHORS: - Inagaki N; Kibata K; Tamaki T; Shimizu T; Nomura S

INSTITUCIÓN / INSTITUTION: - First Department of Internal Medicine, Kansai Medical University, 10-15 Fumizono-cho, Moriguchi-City, Osaka 570-8507, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Mean platelet volume (MPV) is a platelet volume index. Classically, MPV was recognized as a hallmark of platelet activation. Recent studies have revealed that the MPV and MPV/platelet count (PC) ratio can predict long-term mortality in patients with ischemic cardio-vascular disease. In addition, these indices were correlated with the pathophysiological characteristics of patients with various disorders, including malignant tumors. PATIENTS AND METHODS: We retrospectively analyzed various hematological indices of patients with advanced non-small cell lung cancer (NSCLC). The aim of this study was to evaluate the contribution of platelet volume indices to survival in these patients. RESULTS: A total of 268 patients were enrolled in the study. The median age of the patients was 68 years (range: 31-87 years). We compared various hematological indices between the NSCLC group and an age- and sex-matched comparator group. MPV was significantly decreased in the NSCLC group compared to the comparator group. In contrast, the PC was significantly increased in the NSCLC group. Consequently, the MPV/PC ratio was also decreased in the NSCLC group (0.397 vs. 0.501). In receiver operating characteristics (ROC) curve analysis, the MPV/PC ratio was associated with a sensitivity of 62.3% and a specificity of 74.6% at a cutoff value of 0.408730 (area under the curve [AUC], 0.72492). Univariate analysis revealed that overall survival (OS) was significantly shorter in the group with a low MPV/PC ratio than in the other group (median survival time [MST]: 10.3 months vs. 14.5 months, log-rank, P=0.0245). Multivariate analysis confirmed that a low MPV/PC ratio was an independent unfavorable predictive factor for OS (hazard ratio [HR]: 1.668, 95% confidence interval [CI]: 1.235-2.271, P=0.0008). CONCLUSION: These data clearly demonstrate that the MPV/PC ratio was closely associated with survival in patients with advanced NSCLC.

[262]

TÍTULO / TITLE: - Rubus idaeus L. reverses epithelial-to-mesenchymal transition and suppresses cell invasion and protease activities by targeting ERK1/2 and FAK pathways in human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Food Chem Toxicol. 2013 Dec;62:908-18. doi: 10.1016/j.fct.2013.10.021. Epub 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) [1016/j.fct.2013.10.021](#)

AUTORES / AUTHORS: - Hsieh YS; Chu SC; Hsu LS; Chen KS; Lai MT; Yeh CH; Chen PN

INSTITUCIÓN / INSTITUTION: - Clinical Laboratory, Chung Shan Medical University Hospital, No. 110, Section 1, Jianguo N. Road, Taichung, Taiwan; Institute of Biochemistry and Biotechnology, Chung Shan Medical University, No. 110, Section 1, Jianguo N. Road, Taichung, Taiwan.

RESUMEN / SUMMARY: - Epithelial to mesenchymal transition (EMT) has been considered essential for cancer metastasis, a multistep complicated process including local invasion, intravasation, extravasation, and proliferation at distant sites. Herein we provided molecular evidence associated with the antimetastatic effect of Rubus idaeus L. extracts (RIE) by showing a nearly complete inhibition on the invasion ($p < 0.001$) of highly metastatic A549 cells via reduced activities of matrix metalloproteinase-2 (MMP-2) and urokinase-type plasminogen activator (u-PA). We performed Western blot to find that RIE could induce up-regulation of epithelial marker such as E-cadherin and alpha-catenin and inhibit the mesenchymal markers such as N-cadherin, fibronectin, snail-1, and vimentin. Selective snail-1 inhibition by snail-1-specific-siRNA also showed increased E-cadherin expression in A549 cells suggesting a possible involvement of snail-1 inhibition in RIE-caused increase in E-cadherin level. RIE also inhibited p-FAK, p-paxillin and AP-1 by Western blot analysis, indicating the anti-EMT effect of RIE in human lung carcinoma. Importantly, an in vivo BALB/c nude mice xenograft model showed that RIE treatment reduced tumor growth by oral gavage, and RIE represent promising candidates for future phytochemical-based mechanistic pathway-targeted cancer prevention strategies.

[263]

TÍTULO / TITLE: - Resveratrol contributes to chemosensitivity of malignant mesothelioma cells with activation of p53.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Food Chem Toxicol. 2013 Nov 14;63C:153-160. doi: 10.1016/j.fct.2013.11.004.

●● Enlace al texto completo (gratis o de pago) [1016/j.fct.2013.11.004](#)

AUTORES / AUTHORS: - Lee YJ; Park IS; Lee YJ; Shim JH; Cho MK; Nam HS; Park JW; Oh MH; Lee SH

INSTITUCIÓN / INSTITUTION: - Soonchunhyung Environmental Health Center for Asbestos, College of Medicine, Soonchunhyang University, Cheonan Hospital, Cheonan 330-930, Republic of Korea; Division of Molecular Cancer Research, Soonchunhyang Medical Research Institute, Soonchunhyang University, Cheonan 330-930, Republic of Korea.

RESUMEN / SUMMARY: - Resveratrol is a naturally occurring polyphenolic phytoalexin with chemopreventive properties. We previously reported a synergistic anti-proliferative effect of resveratrol and clofarabine against malignant mesothelioma (MM) cells. Here, we further investigated molecular mechanisms involved in the synergistic interaction of these compounds in MM MSTO-211H cells. Resveratrol, in combination with clofarabine, time-dependently induced a strong cytotoxic effect with the nuclear accumulation of phospho-p53 (p-p53) in MSTO-211H cells, but not in normal mesothelial MeT-5A cells. Combination treatment up-regulated the levels of p-p53, cleaved caspase-3, and cleaved PARP proteins. Gene silencing with p53-targeting siRNA attenuated the sensitivity of cells to the combined treatment of two compounds. Analyses of p53 DNA binding assay, p53 reporter gene assay, and RTP-CR toward p53-regulated genes, including Bax, PUMA, Noxa and p21, demonstrated that induced p-p53 is transcriptionally active. These results were further confirmed by the siRNA-mediated knockdown of p53 gene. Combination treatment significantly caused the accumulation of cells at G1 phase with the increases in the sub-G0/G1 peak, DNA ladder, nuclear fragmentation, and caspase-3/7 activity. Taken together, these results demonstrate that resveratrol and clofarabine synergistically elicit apoptotic signal via a p53-dependent pathway, and provide a scientific rationale for clinical evaluation of resveratrol as a promising chemopotentiator in MM.

[264]

TÍTULO / TITLE: - Targeting epithelial to mesenchymal transition with Met inhibitors reverts chemoresistance in small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Cancer Res. 2013 Nov 27.

- Enlace al texto completo (gratis o de pago) [1158/1078-0432.CCR-13-1330](#)

AUTORES / AUTHORS: - Canadas I; Rojo F; Taus A; Arpi O; Arumi-Uria M; Pijuan L; Menendez S; Zazo S; Domine M; Salido M; Mojal S; Garcia de Herreros A; Rovira A; Albanell J; Arriola E

INSTITUCIÓN / INSTITUTION: - CANCER RESEARCH PROGRAM, IMIM.

RESUMEN / SUMMARY: - PURPOSE: Met receptor phosphorylation is associated with poor prognosis in human SCLC. The aim of our work was to investigate the effects of hepatocyte growth factor (HGF)/Met mediated epithelial mesenchymal transition in SCLC and to evaluate the role of Met inhibition in mesenchymal/chemorefractory SCLC models. Experimental design: SCLC models of HGF-induced EMT were evaluated in vitro and in vivo (subcutaneous xenografts in BALB/c nude mice) for chemosensitivity and response to Met inhibition with PF-2341066 (Crizotinib). Human SCLC samples at diagnosis (N:87) and relapse (N:5) were evaluated by immunohistochemistry and immunofluorescence for EMT markers and Met status and correlated these with patient outcome. RESULTS: We identified that the activation of the Met receptor through HGF induced expression of mesenchymal markers, an aggressive phenotype and chemoresistance. Blockade of this process with the Met inhibitor resensitized cells to chemotherapy in vitro and in vivo. Moreover, mesenchymal markers in human SCLC specimens were associated with Met activation, predicted worse survival and were upregulated in chemorefractory disease. CONCLUSION: These results provide novel evidence on an important role of Met-dependent EMT in the adverse clinical behavior

of SCLC and supports clinical trials of Met inhibitors and chemotherapy in this fatal disease.

[265]

TÍTULO / TITLE: - Vibration response imaging versus perfusion scan in lung cancer surgery evaluation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Oct 27. pii: S0022-5223(13)01063-5. doi: 10.1016/j.jtcvs.2013.08.066.

●● Enlace al texto completo (gratis o de pago) 1016/j.jtcvs.2013.08.066

AUTORES / AUTHORS: - Marina N; Rodriguez-Trigo G; Jimenez U; Morales B; Lopez de Santa Maria E; Pijoan JI; Galdiz JB

INSTITUCIÓN / INSTITUTION: - Department of Pulmonology, Cruces University Hospital, Basque Country, España. Electronic address: nuria.marinamalanda@osakidetza.net.

RESUMEN / SUMMARY: - OBJECTIVE: Ventilation/perfusion scan is a standard procedure in high-risk surgical patients to predict pulmonary function after surgery. Vibration response imaging is a technique that could be used in these patients. The objective of our study was to compare this imaging technique with the usual scanning technique for predicting postoperative forced expiratory volume. METHODS: We assessed 48 patients with lung cancer who were candidates for lung resection. Forced spirometry, vibration response imaging, and ventilation/perfusion scan were performed in patients before surgery, and spirometry was performed after intervention. RESULTS: We included 48 patients (43 men; mean age, 64 years) undergoing lung cancer surgery (32 lobectomies/16 pneumonectomies). On comparison of both techniques, for pneumonectomy, we found a concordance of 0.84 (95% confidence interval, 0.76-0.92) and Bland-Altman limits of agreement of -0.33 to +0.45, with an average difference of 0.064. By comparing postoperative spirometry with vibration response imaging, we found a concordance of 0.66 (95% confidence interval, 0.38-0.93) and Bland-Altman limits of agreement of -0.60 to +0.33, with an average difference of -0.13. CONCLUSIONS: The 2 techniques presented good concordance values. Vibration response imaging shows non-negligible confidence intervals. Vibration response imaging may be useful in preoperative algorithms in patients before lung cancer surgery.

[266]

TÍTULO / TITLE: - CHK1 levels correlate with sensitization to pemetrexed by CHK1 inhibitors in non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):477-84. doi: 10.1016/j.lungcan.2013.09.010. Epub 2013 Sep 23.

●● Enlace al texto completo (gratis o de pago) 1016/j.lungcan.2013.09.010

AUTORES / AUTHORS: - Grabauskiene S; Bergeron EJ; Chen G; Chang AC; Lin J; Thomas DG; Giordano TJ; Beer DG; Morgan MA; Reddy RM

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Section of Thoracic Surgery, University of Michigan Medical School, Ann Arbor, MI 48109, USA.

RESUMEN / SUMMARY: - OBJECTIVE: Overexpression of checkpoint kinase 1 (CHK1) is associated with poorer patient outcome and therapeutic resistance in multiple tumor models. Inhibition of CHK1 has been proposed as a strategy to increase the effectiveness of chemotherapeutic agents, especially in p53-deficient tumors. In this study, we evaluated the effects of a novel CHK1 inhibitor, MK-8776, in combination with pemetrexed (PMX) on cell proliferation and survival in a panel of p53 mutant non-small cell lung cancer (NSCLC) cell lines. METHODS: We examined CHK1 expression in 442 resected lung adenocarcinoma specimens using Affymetrix U133A gene expression arrays. We correlated CHK1 mRNA expression with patient survival, tumor differentiation and genomic complexity. We evaluated CHK1 levels in NSCLC cell lines and identified four p53 mutant cell lines with variable CHK1 expression (H1993, H23, H1437 and H1299) based on publicly available gene expression data. We confirmed differential CHK1 mRNA and CHK1 protein levels by qRT-PCR, ELISA, Western Blot analysis (WB) and immunohistochemistry. We examined cell line sensitization to PMX in response to CHK1 inhibition with MK-8776 using WST-1 and clonogenic survival assays. RESULTS: We found that elevated CHK1 expression in primary lung adenocarcinomas correlates with poor tumor differentiation and significantly worse patient survival. Tumors with elevated CHK1 mRNA levels have a higher number of gene mutations and DNA copy number gain or amplifications. CHK1 inhibition by MK-8776 enhances sensitivity of NSCLC cell lines to PMX. CHK1 mRNA and protein expression are variable among NSCLC cell lines, and cells expressing higher levels of CHK1 protein are more sensitive to the CHK1 inhibition by MK-8776 as compared to low CHK1 expressing cells. CONCLUSIONS: These findings suggest that CHK1 levels may not only serve as a biomarker of poor prognosis in surgically-resected lung adenocarcinomas, but could also be a predictive marker for CHK1 inhibitor sensitivity, pending in vivo and clinical confirmation.

[267]

TÍTULO / TITLE: - Venom present in sea anemone (*Heteractis magnifica*) induces apoptosis in non-small-cell lung cancer A549 cells through activation of mitochondria-mediated pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - *Biotechnol Lett.* 2013 Nov 5.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s10529-013-1402-4](#)

AUTORES / AUTHORS: - Ramezanpour M; da Silva KB; Sanderson BJ

INSTITUCIÓN / INSTITUTION: - Department of Medical Biotechnology, School of Medicine, Flinders University of South Australia, Bedford Park, SA, 5042, Australia, rame0010@flinders.edu.au.

RESUMEN / SUMMARY: - Lung cancer is a major cause of cancer deaths throughout the world and the complexity of apoptosis resistance in lung cancer is apparent. Venom from *Heteractis magnifica* caused dose-dependent decreases in survival of the human non-small-cell lung cancer cell line, as determined by the MTT and Crystal Violet assays. The *H. magnifica* venom induced cell cycle arrest and induced apoptosis of A549 cells, as confirmed by annexin V/propidium iodide staining. The venom-induced apoptosis in A549 cells was characterized by cleavage of caspase-3 and a reduction in the mitochondrial membrane potential. Interestingly, crude extracts from *H. magnifica* had less effect on the survival of non-cancer cell lines. In the non-cancer

cells, the mechanism via which cell death occurred was through necrosis not apoptosis. These findings are important for future work using *H. magnifica* venom for pharmaceutical development to treat human lung cancer.

[268]

TÍTULO / TITLE: - A systems pharmacology approach to improve drug therapy in NSCLC: Establishing a CESAR network.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Pharmacol Ther. 2013 Nov 11.

●● Enlace al texto completo (gratis o de pago) [5414/CPXCES13EA07](#)

AUTORES / AUTHORS: - Kalayda GV; Michaelis M; Cinatl Jr J; Mader RM; Frohlich H; Sarin N; Melin J; Engel F; Jager W; Frotschl R; Jaehde U; Kloft C; Ritter CA

[269]

TÍTULO / TITLE: - The use of hollow mesoporous silica nanospheres to encapsulate bortezomib and improve efficacy for non-small cell lung cancer therapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomaterials. 2014 Jan;35(1):316-26. doi: 10.1016/j.biomaterials.2013.09.098. Epub 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago)

[1016/j.biomaterials.2013.09.098](#)

AUTORES / AUTHORS: - Shen J; Song G; An M; Li X; Wu N; Ruan K; Hu J; Hu R

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Molecular Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 320 Yue-yang Road, Shanghai 200031, China; University of Chinese Academy of Sciences, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 320 Yue-yang Road, Shanghai 200031, China; Shanghai Key Laboratory of Molecular Andrology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 320 Yue-yang Road, Shanghai 200031, China.

RESUMEN / SUMMARY: - Bortezomib (BTZ) is the first clinically approved proteasome inhibitor for treating multiple human malignancies. However, the poor water-solubility and low stability of BTZ and the emergence of tumor resistance have severely restrained its therapeutic efficacy. Herein, we report the application of hollow mesoporous silica nanospheres (HMSNs) in encapsulating BTZ for drug delivery. In vitro cell viability assay on human NSCLC H1299 cells, the half-maximum inhibiting concentration (IC₅₀) of HMSNs-BTZ was 42% of that for free BTZ in 48 h treatments. In vivo tumor-suppression assay further indicated that HMSNs-BTZ (0.3 mg/kg) showed approximately 1.5 folds stronger anti-tumor activity than free BTZ. Furthermore, we report that more potent induction of cell cycle arrest and apoptotic cell death, along with promoted activation of Caspase 3 and autophagy might mechanistically underlie the improved anti-tumor efficacy of HMSNs-BTZ. Finally, the tumor-suppressing effect of HMSNs-BTZ was enhanced in the presence of wild-type p53 signaling, suggesting a potential enhancement in clinical efficacy with combined p53 gene therapy and BTZ-based chemotherapy. Therefore, the HMSNs-based nanoparticles are emerging as a promising platform to deliver therapeutic agents for

beneficial clinical outcomes through lowering doses and frequency of drug administration and reducing potential side effects.

[270]

TÍTULO / TITLE: - Extract of Bryophyllum laetivirens reverses etoposide resistance in human lung A549 cancer cells by downregulation of NF-kappaB.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):161-8. doi: 10.3892/or.2013.2844. Epub 2013 Nov 12.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2844](#)

AUTORES / AUTHORS: - Kaewpiboon C; Srisuttee R; Malilas W; Moon J; Kaowinn S; Cho IR; Johnston RN; Assavalapsakul W; Chung YH

INSTITUCIÓN / INSTITUTION: - Program in Biotechnology, Chulalongkorn University, Bangkok 10330, Thailand.

RESUMEN / SUMMARY: - Since multidrug resistance (MDR) is one of the main reasons for failure in cancer treatment, its suppression may increase the efficacy of cancer therapy. In the present study we attempted to identify a new and effective anticancer drug against MDR cancer cells. We first found that lung cancer A549 cells resistant to etoposide (A549RT-eto) exhibit upregulation of NF-kappaB and SIRT1 in comparison to A549 parental cells. During a search for anticancer drug candidates from medicinal plant sources, we found that an extract fraction (F14) of Bryophyllum laetivirens leaves downregulated expression of NF-kappaB and SIRT1, sensitizing the levels of A549RT-eto cells to apoptosis through downregulation of P-glycoprotein (P-gp), which is encoded by the MDR1 gene. To address whether NF-kappaB is involved in resistance to etoposide through P-gp, we treated A549RT-eto cells with Bay11-7802, an inhibitor of NF-kappaB. We then observed that Bay11-7802 treatment reduced P-gp expression levels, and furthermore combined treatment with the F14 extract and Bay11-7802 accelerated apoptosis through a decrease in P-gp levels, suggesting that NF-kappaB is involved in MDR. To address whether upregulation of SIRT1 is involved in resistance to etoposide through P-gp, we treated A549RT-eto cells with SIRT1 siRNA or nicotinamide (NAM), an inhibitor of SIRT1. we found that suppression of SIRT1 did not reduce P-gp levels. furthermore, the combined treatment with the F14 extract, and SIRT1 siRNA or NAM did not accelerate apoptosis, indicating that SIRT1 is not involved in the regulation of P-gp levels in A549RT-eto cells. Taken together, we suggest that upregulation of NF-kappaB determines etoposide resistance through P-gp expression in human A549 lung cancer cells. We herein demonstrated that B. laetivirens extract reverses etoposide resistance in human A549 lung cancer cells through downregulation of NF-kappaB.

[271]

TÍTULO / TITLE: - Antiproliferative activity of Pt(IV)-bis(carboxylato) conjugates on malignant pleural mesothelioma cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Inorg Biochem. 2013 Dec;129:52-7. doi: 10.1016/j.jinorgbio.2013.09.003. Epub 2013 Sep 13.

●● Enlace al texto completo (gratis o de pago) [1016/j.jinorgbio.2013.09.003](#)

AUTORES / AUTHORS: - Alessio M; Zanellato I; Bonarrigo I; Gabano E; Ravera M; Osella D

INSTITUCIÓN / INSTITUTION: - Dipartimento di Scienze e Innovazione Tecnologica, Università del Piemonte Orientale "Amedeo Avogadro", Viale T. Michel 11, 15121 Alessandria, Italy.

RESUMEN / SUMMARY: - The bifunctional Pt(IV) conjugate cis,cis,trans-diamminedichloridobis(valproato)platinum(IV), based on the cisplatin square-plane with two axial valproato (2-propylpentanoate, VPA) ligands, has been re-synthesized with a modified procedure and its biological activity was compared with that of its isomer cis,cis,trans-diamminedichloridobis(n-octanoato)platinum(IV). Both complexes showed a striking cytotoxic effect (in the micro or sub-micromolar range) on various human carcinoma cell lines (namely ovarian, colon, breast and lung cancer), and, in particular, on cells derived from malignant pleural mesothelioma. This remarkable activity is due to the action of the cisplatin metabolite only, generated by the intracellular Pt(IV)-->Pt(II) reduction, which concentration is greatly increased by the enhanced cellular accumulation of the original, highly lipophilic Pt(IV)-bis(carboxylato) complexes. The two axial VPA ligands are released in a too low concentration to act as histone deacetylase inhibitor (HDACI), as VPA works in the millimolar range, so that no synergism can be claimed. Moreover, n-octanoic acid is substantially deprived of any HDACI propensity.

[272]

TÍTULO / TITLE: - miR-205 promotes the growth, metastasis and chemoresistance of NSCLC cells by targeting PTEN.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2897-902. doi: 10.3892/or.2013.2755. Epub 2013 Sep 30.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2755](#)

AUTORES / AUTHORS: - Lei L; Huang Y; Gong W

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Xiangyang Central Hospital, Xiangyang 441021, P.R. China.

RESUMEN / SUMMARY: - Non-small cell lung cancer (NSCLC) is one of the most common causes of cancer-related mortality worldwide. microRNAs (miRNAs) play critical roles in carcinogenesis. miR-205 has been shown to be upregulated in NSCLC. In the present study, we identified the promotive effects of miR-205 on various significant biological properties of NSCLC cells, and confirmed the regulation of PTEN by miR-205. The expression of miR-205 was examined by quantitative real-time PCR both in NSCLC cell lines and tissues. The effect of miR-205 on PTEN expression was assessed in NSCLC cell lines with miR-205 mimics/inhibitor to elevate/decrease miR-205 expression. Furthermore, the roles of miR-205 in regulating the biological properties of NSCLC cells, including growth, invasion and chemoresistance, were assayed using miR-205 mimic/inhibitor-transfected cells. The 3'-untranslated region (3'-UTR) of PTEN combined with miR-205 and this was confirmed by luciferase reporter assay and western blotting. miR-205 expression was increased in NSCLC cell lines as well as in tissues. Overexpression of miR-205 promoted growth, migration and invasion, and enhanced the chemoresistance of NSCLC cells. Luciferase activity and western blotting demonstrated that miR-205 negatively regulated PTEN at a

posttranscriptional level. However, miR-205 knockdown suppressed these processes in A549 cells and increased the expression of PTEN protein. Furthermore, overexpression of PTEN exhibited effects identical with those of the miR-205 inhibitor in NSCLC cells. Our results demonstrated that miR-205 is involved in the tumorigenesis of NSCLC through modulation of the PTEN signaling pathway.

[273]

TÍTULO / TITLE: - Inhibition of ZNF746 suppresses invasion and epithelial to mesenchymal transition in H460 non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):73-8. doi: 10.3892/or.2013.2801. Epub 2013 Oct 22.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2801](#)

AUTORES / AUTHORS: - Kim B; Sohn EJ; Jung JH; Shin EA; You OH; Im J; Kim SH

INSTITUCIÓN / INSTITUTION: - College of Oriental Medicine, Kyung Hee University, Dongdaemun-gu, Seoul 130-701, Republic of Korea.

RESUMEN / SUMMARY: - Although ZNF746, also known as Parkin-interacting substrate (PARIS), has been reported to suppress peroxisome proliferator-activated receptor gamma coactivator-1alpha (PGC-1alpha) and its target gene NRF-1 leading to the neurodegeneration in Parkinson's disease, its function in tumorigenesis has yet to be investigated. Thus, in the present study, the role of ZNF746 in the invasion and epithelial to mesenchymal transition (EMT) in H460 non-small cell lung cancer (NSCLC) cells was investigated. Invasion assay showed that inhibition of ZNF746 using siRNA transfection inhibited the invasion of H460 NSCLC cells using Boyden chamber. Quantitative PCR (qPCR) analysis revealed that the silencing of ZNF746 attenuated the expression of matrix metalloproteinase (MMP)1, MMP2 and MMP9, but not MMP7, in H460 NSCLC cells. Immunoblotting assay revealed that the expression of E-cadherin and beta-catenin of epithelial phenotype was upregulated, while Slug was downregulated in ZNF746 siRNA-transfected H460 NSCLC cells. Accordingly, the mRNA expression of E-cadherin was upregulated while vimentin or Slug, Twist, ZEB as EMT key transcriptional factors were suppressed in ZNF746 siRNA-transfected H460 NSCLC cells. Also, mRNA expression of transcriptional marker Nanog and Octamer-binding transcription factor 4 (OCT4), known to enhance malignancy and metastasis in lung adenocarcinoma, was suppressed in ZNF746 siRNA-transfected H460 NSCLC cells. Notably, the endogenous expression of ZNF746 was induced in parallel with Twist at the protein level during hypoxia. Overall, our findings suggest that inhibition of ZNF746 suppresses the invasion and EMT molecules in H460 NSCLC cells and ZNF746 may be an important target molecule in lung tumorigenesis.

[274]

TÍTULO / TITLE: - Transitioning from video-assisted thoracic surgical lobectomy to robotics for lung cancer: Are there outcomes advantages?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Cardiovasc Surg. 2013 Nov 16. pii: S0022-5223(13)01164-1. doi: 10.1016/j.jtcvs.2013.10.002.

●● Enlace al texto completo (gratis o de pago) [1016/j.jtcvs.2013.10.002](#)

AUTORES / AUTHORS: - Lee BE; Korst RJ; Kletsman E; Rutledge JR

INSTITUCIÓN / INSTITUTION: - Daniel and Gloria Blumenthal Cancer Center, Paramus, NJ; Division of Thoracic Surgery, Department of Surgery, The Valley Hospital/Valley Health System, Ridgewood, NJ. Electronic address: leebe@valleyhealth.com.

RESUMEN / SUMMARY: - **OBJECTIVES:** To determine if there are advantages to transitioning to robotics by a surgeon who is already proficient in performing video-assisted thoracic surgical (VATS) lobectomy. **METHODS:** A single surgeon proficient in VATS lobectomy initiated a robotic lobectomy program, and a retrospective review was conducted of his patients undergoing minimally invasive lobectomy (robotics or VATS) for lung cancer between 2011 and 2012. Data collected included patient/tumor characteristics, morbidity, mortality, operative times, and length of hospital stay. **RESULTS:** Over a 24-month period, a total of 69 patients underwent minimally invasive lobectomy (35 robotic, 34 VATS). Patients in each group were similar in age and clinical stage. Robotic upper lobectomy operative times were longer than VATS (172 vs 134 minutes; $P = .001$), with no significant difference in lower lobectomies noted (140 vs 123 minutes; $P = .1$). Median length of stay was 3 days in both groups, and the median number of lymph nodes harvested was 18 (robotic) versus 16 (VATS; $P = .42$). Morbidity and mortality for robotic versus VATS were 11% versus 18% ($P = .46$) and 0% versus 3% ($P = .49$), respectively. **CONCLUSIONS:** There does not seem to be a significant advantage for an established VATS lobectomy surgeon to transition to robotics based on clinical outcomes. The learning curve for robotic upper lobectomies seems to be more significant than that for lower lobectomies.

[275]

TÍTULO / TITLE: - Villeneuve et al. Respond to “Impact of Air Pollution on Lung Cancer”

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Epidemiol. 2013 Nov 27.

●● [Enlace al texto completo \(gratis o de pago\) 1093/aje/kwt291](#)

AUTORES / AUTHORS: - Villeneuve PJ; Jerrett M; Brenner D; Su J; Chen H; McLaughlin JR

[276]

TÍTULO / TITLE: - Clinical Significance of Erlotinib Monotherapy for Gefitinib-resistant Non-small Cell Lung Cancer with EGFR Mutations.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):5083-9.

AUTORES / AUTHORS: - Koyama N; Uchida Y

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary Medicine, Clinical Department of Internal Medicine, Jichi Medical University Saitama Medical Center, 1-847 Amanuma-cho, Omiya-ku, Saitama-shi, Saitama, 330-8503, Japan. nkoyama@jichi.ac.jp.

RESUMEN / SUMMARY: - **BACKGROUND:** The efficacy of the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI) erlotinib is difficult to be accurately assessed in patients with non-small cell lung cancer (NSCLC) because it is commonly employed after failure of another EGFR-TKI, gefitinib. **PATIENTS AND METHODS:** Medical records from 104 patients with NSCLC treated with erlotinib were retrospectively reviewed. **RESULTS:** There were no significant differences in erlotinib

efficacy between EGFR-mutated NSCLC with gefitinib resistance and NSCLC with wild-type EGFR. A therapeutic response of disease control (DC) and the onset of skin rash prolonged the progression-free survival (PFS), whereas the onset of interstitial lung disease shortened both PFS and overall survival (OS). The DC group also experienced prolonged OS. CONCLUSION: Erlotinib may be a therapeutic option for EGFR-mutated NSCLC with gefitinib resistance, as well as for NSCLC with wild-type EGFR. Therapeutic response of DC and the onset of the described adverse events may be practical predictors of survival in erlotinib treatment.

[277]

TÍTULO / TITLE: - Phosphorylated Akt expression is a prognostic marker in early-stage non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Pathol. 2013 Nov 21. doi: 10.1136/jclinpath-2013-201870.

●● [Enlace al texto completo \(gratis o de pago\) 1136/jclinpath-2013-201870](#)

AUTORES / AUTHORS: - Yip PY; Cooper WA; Kohonen-Corish MR; Lin BP; McCaughan BC; Boyer MJ; Kench JG; Horvath LG

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Sydney Cancer Centre, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia.

RESUMEN / SUMMARY: - AIMS: To determine the prognostic significance of pAkt expression in order to identify high-risk stage IB patients with non-small cell lung cancer (NSCLC) in an exploratory study. METHODS: We identified 471 consecutive patients with stage IB primary NSCLC according to the American Joint Commission on Cancer 6th edition tumour-node-metastasis (TNM) staging system, who underwent surgical resection between 1990 and 2008. Patients who received neoadjuvant or adjuvant treatments were excluded. Pathology reports were reviewed, and pathological characteristics were extracted. Expression of phosphorylated Akt (pAkt) in both cytoplasmic and nuclear locations was assessed by immunohistochemistry, and clinicopathological factors were analysed against 10-year overall survival using Kaplan-Meier and Cox proportional hazards model. RESULTS: 455 (96.6%) cancers were adequate for pAkt immunohistochemical analysis. The prevalence of pAkt expression in the cytoplasm and nucleus of the cancers was 60.7% and 43.7%, respectively. Patients whose cancers expressed higher levels of cytoplasmic pAkt had a trend towards longer overall survival than those with lower levels ($p=0.06$). Conversely, patients whose cancers expressed higher levels of nuclear pAkt had a poorer prognosis than those with lower levels of expression ($p=0.02$). Combined low cytoplasmic/high nuclear expression of pAkt was an independent predictor of overall survival (HR=2.86 (95% CI 1.35 to 6.04); $p=0.006$) when modelled with age (HR=1.05 (95% CI 1.03 to 1.07); $p<0.001$), extent of operation (HR=2.11 (95% CI 1.48 to 3.01); $p<0.001$), visceral pleural invasion (HR=1.63 (95% CI 1.24 to 2.15); $p<0.001$), gender, tumour size, histopathological type and grade ($p>0.05$). CONCLUSIONS: Level of expression of pAkt in the cytoplasm and nucleus is an independent prognostic factor that may help to select patients with high-risk disease.

[278]

TÍTULO / TITLE: - Role of fibulin-3 in lung cancer: In vivo and in vitro analyses.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2014 Jan;31(1):79-86. doi: 10.3892/or.2013.2799. Epub 2013 Oct 18.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2799](#)

AUTORES / AUTHORS: - Xu S; Yang Y; Sun YB; Wang HY; Sun CB; Zhang X

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, The First Hospital of China Medical University, Shenyang, Liaoning, P.R. China.

RESUMEN / SUMMARY: - Lung cancer was the most commonly diagnosed cancer in 2008 worldwide. The level of fibulin-3 expression was found to be decreased in many cancer types due to aberrant promoter methylation and is correlated with poor survival of patients. However, the role of fibulin-3 and which form of fibulin-3 is expressed in lung cancer cells remain unclear. Therefore, pathologic and functional studies were carried out to determine the role of fibulin-3 in suppressing lung cancer both in vivo and in vitro. In the present study, we found that the levels of fibulin-3 mRNA and protein were lower in cancer tissues than in normal tissues. Downregulation of fibulin-3 mRNA in tumor tissues was associated with an increase in fibulin-3 promoter methylation. Circulating fibulin-3 was significantly associated with tumor progression, survival rate of lung cancer patients, and the number of circulating tumor cells (CTCs). To examine the effects of exogenous expression of fibulin-3 in vitro, lung cancer A549 cells were transfected with the pEGFP-C1-fibulin-3 expression vector. Relative to the untreated cells, fibulin-3-expressing cells exhibited lower proliferation and mobility as determined by MTT and Transwell assays, respectively. To conclude, our results suggest that fibulin-3 negatively modulates the invasiveness of lung cancer cells via regulation of p38-MAPK and MMP-2/9.

[279]

TÍTULO / TITLE: - Synergistic effects of pemetrexed and amrubicin in non-small cell lung cancer cell lines: Potential for combination therapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Lett. 2013 Oct 15. pii: S0304-3835(13)00673-3. doi: 10.1016/j.canlet.2013.09.019.

●● Enlace al texto completo (gratis o de pago) [1016/j.canlet.2013.09.019](#)

AUTORES / AUTHORS: - Hatakeyama Y; Kobayashi K; Nagano T; Tamura D; Yamamoto M; Tachihara M; Kotani Y; Nishimura Y

INSTITUCIÓN / INSTITUTION: - Division of Respiratory Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan.

RESUMEN / SUMMARY: - The purpose is to examine the synergistic effect of pemetrexed (PEM) and amrubicin (AMR) on the proliferation of lung cancer cell lines. In vitro, dose-dependent synergistic effects of concurrent PEM and AMR, which is an active metabolite of AMR were observed in A549 and H460 cells. In real-time RT-qPCR analysis and western blotting, expression of the target enzymes of PEM were suppressed in cells treated with amrubicinol alone. In vivo, AMR/PEM treatment also showed synergistic antitumor activity both in A549-bearing and H520-bearing mice. PEM and AMR work synergistically to inhibit the proliferation of several different lung cancer cell lines.

[280]

TÍTULO / TITLE: - Primary non-small cell lung cancer response upon treatment with denosumab.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):506-8. doi: 10.1016/j.lungcan.2013.08.030. Epub 2013 Sep 8.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.08.030](#)

AUTORES / AUTHORS: - Curioni-Fontecedro A; Husmann L; Soldini D; Stahel RA

INSTITUCIÓN / INSTITUTION: - Department of Oncology, University Hospital Zurich, Zurich, Switzerland. Electronic address: alessandra.curioni@usz.ch.

RESUMEN / SUMMARY: - Here we report the case of a patient with metastatic adenocarcinoma of the lung harboring an ALK gene translocation. In this patient a response of the primary tumor and metastases has been detected upon treatment with denosumab. A possible link between ALK and RANK is postulated.

[281]

TÍTULO / TITLE: - Rib fractures after radiofrequency and microwave ablation of lung tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiology. 2013 Dec;269(3):946. doi: 10.1148/radiol.13131612.

●● Enlace al texto completo (gratis o de pago) [1148/radiol.13131612](#)

AUTORES / AUTHORS: - Yamakado K; Takaki H; Nakatsuka A

INSTITUCIÓN / INSTITUTION: - Department of Interventional Radiology, Mie University Hospital, 2-174 Edobashi Tsu, Mie 514-8507, Japan.

[282]

TÍTULO / TITLE: - Diagnosis and treatment of benign multicystic peritoneal mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Oct 21;19(39):6689-92. doi: 10.3748/wjg.v19.i39.6689.

●● Enlace al texto completo (gratis o de pago) [3748/wjg.v19.i39.6689](#)

AUTORES / AUTHORS: - Wang TB; Dai WG; Liu DW; Shi HP; Dong WG

INSTITUCIÓN / INSTITUTION: - Tian-Bao Wang, Wei-Gang Dai, Han-Ping Shi, Wen-Guang Dong, Department of Surgery, the First Affiliated Hospital, Sun Yat-sen University, Guangzhou 510080, Guangdong Province, China.

RESUMEN / SUMMARY: - Benign multicystic peritoneal mesothelioma (BMPM) is a rare cystic mesothelial lesion that occurs predominantly in reproductive aged women. A 56-year-old Caucasian male was admitted to our surgical department with a chief complaint of a painful mass in his right lower abdomen for almost 2 years. The physical examination revealed a palpable painful mass. Computed tomography demonstrated an irregular, cystic tumor in his right lower abdomen. There was no obvious capsule or internal septations. No enhancement after intravenous

administration of contrast was noted. An exploratory laparotomy was performed, and a multicystic tumor and adherent to the caecum was noted. The walls of the cysts were thin and smooth, filled with clear fluid, and very friable. An en bloc resection of the tumor, including appendix and caecum, was performed. Histological examination revealed multiple cysts lined with flattened simple epithelial cells, and the capsule walls of the cysts were composed of fibrous tissue. Immunohistochemical analysis documented positive expression of mesothelial cells and calretinin. The final diagnosis was BMPM. The patient was well at 6-mo follow-up. BMPM is exceedingly rare lesion. A complete resection of the tumor is required. The diagnosis of BMPM is based on pathological analysis.

[283]

TÍTULO / TITLE: - CYP2C19 genotype-based phase I studies of a c-Met inhibitor tivantinib in combination with erlotinib, in advanced/metastatic non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 26;109(11):2803-9. doi: 10.1038/bjc.2013.588. Epub 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.588](#)

AUTORES / AUTHORS: - Yamamoto N; Murakami H; Hayashi H; Fujisaka Y; Hirashima T; Takeda K; Satouchi M; Miyoshi K; Akinaga S; Takahashi T; Nakagawa K

INSTITUCIÓN / INSTITUTION: - Division of Thoracic Oncology, Shizuoka Cancer Center, 1007, Shimonagakubo, Nagaizumi-cho, Sunto-gun, Shizuoka 411-8777, Japan.

RESUMEN / SUMMARY: - Background:A previous clinical study in non-small cell lung cancer (NSCLC) patients in Western countries suggested the potential for combination of a first-in-class non-ATP-competitive c-Met inhibitor tivantinib with an epidermal growth factor receptor-tyrosine kinase inhibitor erlotinib. Polymorphisms of CYP2C19, the key metabolic enzyme for tivantinib, should be addressed to translate the previous Western study to Asian population, because higher incidence of poor metabolisers (PMs) is reported in Asian population.Methods:Japanese patients with advanced/metastatic NSCLC received tivantinib in combination with erlotinib to evaluate safety and pharmacokinetics. Doses of tivantinib were escalated separately for extensive metabolisers (EMs) and PMs.Results:Tivantinib, when combined with erlotinib, was well tolerated up to 360 mg BID for EMs and 240 mg BID for PMs, respectively. Among 25 patients (16 EMs and 9 PMs), the adverse events (AEs) related to tivantinib and/or erlotinib (>20%, any grade) were rash, diarrhoea, dry skin and nausea. Grade ≥ 3 AEs were leukopenia, anaemia and neutropenia. No dose-limiting toxicity was observed. Pharmacokinetics profile of tivantinib was not clearly different between the combination and monotherapy. Three partial response and three long-term stable disease (≥ 24 weeks) were reported.Conclusion:Two doses of tivantinib in combination with erlotinib were recommended based on CYP2C19 genotype: 360 mg BID for EMs and 240 mg BID for PMs.

[284]

TÍTULO / TITLE: - Respiratory epithelial adenomatoid hamartoma: a poorly recognized entity with mast cell recruitment and frequently associated with nasal polyposis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Surg Pathol. 2013 Nov;37(11):1678-85. doi: 10.1097/PAS.0000000000000092.

●● Enlace al texto completo (gratis o de pago)

[1097/PAS.0000000000000092](#)

AUTORES / AUTHORS: - Gauchotte G; Marie B; Gallet P; Nguyen DT; Grandhaye M; Jankowski R; Vignaud JM

INSTITUCIÓN / INSTITUTION: - Departments of *Pathology section signRadiology parallelCentre de Ressources Biologiques double daggerDepartment of Otolaryngology - Head and Neck Surgery, CHU daggerINSERM U954, Medical Faculty of Nancy, Universite de Lorraine, Nancy, France.

RESUMEN / SUMMARY: - Respiratory epithelial adenomatoid hamartoma (REAH) is regarded as a rare tumor of the nasal cavity. The mechanisms driving the development of REAH are unknown, and its nature as a benign tumor, hamartoma, or reactive inflammatory process is still open to discussion. A total of 150 consecutive patients operated on for nasal polyposis (NP) were extensively checked for the diagnosis of REAH. The profile of REAH occurring in association with NP was compared with solitary REAH in a series of 19 cases. The possible role of tryptase-producing mast cells (MC) and of metalloproteinases MMP2 and MMP9 in REAH development was investigated by immunohistochemistry. REAH lesions were identified in 35% of patients who had surgery for NP (53/150). The distribution of the lesions suggested that REAH originated in the olfactory cleft. Solitary REAH occurred about 20 times less frequently than those observed in an NP context but shared the same microscopic characteristics. Tryptase-producing MCs were recruited at high density in REAH (135/10 hpf), compared with inflammatory polyps (45/10 hpf; $P < 0.00005$) and hypertrophied turbinates (51/10 hpf; $P < 0.0005$). REAH also showed constant MMP9 expression and to a lesser degree MMP2 expression in epithelial cells. If solitary REAH is a relatively rare lesion, we demonstrated that an exhaustive sampling allows the detection of a high proportion of NP-associated REAH, sharing the same clinical and histologic characteristics with solitary REAH. Tryptase-producing MCs, possibly in association with MMP expression, may play a central role in REAH formation.

[285]

TÍTULO / TITLE: - EGFR Autophosphorylation but Not Protein Score Correlates With Histologic and Molecular Subtypes in Lung Adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Diagn Mol Pathol. 2013 Dec;22(4):204-9. doi: 10.1097/PDM.0b013e3182936957.

●● Enlace al texto completo (gratis o de pago)

[1097/PDM.0b013e3182936957](#)

AUTORES / AUTHORS: - Moldvay J; Barbai T; Bogos K; Pjurko V; Fillinger J; Popper HH; Timar J

INSTITUCIÓN / INSTITUTION: - *Department of Pulmonology dagger2nd Department of Pathology, Semmelweis University double daggerNational Koranyi Institute of Pulmonology parallelHAS-SU Molecular Oncology Research Group, Budapest,

Hungary section sign Department of Pathology, Medical University of Graz, Graz, Austria.

RESUMEN / SUMMARY: - Established clinicopathologic characteristics of non-small cell lung cancer patients define a subgroup responding better to EGFR-TK inhibitors: adenocarcinoma histology, ethnicity, sex, smoking status, presence of activating EGFR mutation, and/or K-RAS wild type. However, EGFR mutation does not automatically lead to increased activity of the protein influenced by several factors. As adenocarcinoma can be further divided into histologic subclasses, we compared adenocarcinomas without lepidic growth pattern (NLAC) to those characterized by pure or predominant lepidic growth (LAC) for EGFR protein expression and autophosphorylation activity (Y1173), as determined by immunohistochemistry. This pretarget therapy cohort comprised a total of 110 surgically operated patients of stage I non-small cell lung cancer: 49 NLAC and 61 LAC variants. The LAC group had a significantly better prognosis and the incidence of phospho-EGFR-positive tumors was significantly higher compared with NLAC. Patient sex did not influence EGFR activity, but the incidence of pEGFR-positive tumors was significantly lower among smoker patients. There was no statistically significant difference in EGFR or KRAS mutation frequencies between the 2 groups. In NLAC, pEGFR-positive tumors occurred exclusively among EGFR-mutant/K-RAS wild-type tumors. On the contrary, in LAC tumors, pEGFR-positive tumors were similarly frequent in the EGFR or K-RAS mutant groups indicating an interesting feedback activation of EGFR signaling in K-RAS mutant tumors. Our data also indicate that EGFR mutation leads to EGFR autophosphorylation only in a small fraction of adenocarcinoma patients, which might have clinical significance.

[286]

TÍTULO / TITLE: - Differential expression and activation of Epidermal Growth Factor Receptor 1 (EGFR1), ERK, AKT, STAT3, and TWIST1 in nonsmall cell lung cancer (NSCLC).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Lung Res. 2013 Nov;39(9):387-98. doi: 10.3109/01902148.2013.831960. Epub 2013 Oct 11.

●● [Enlace al texto completo \(gratis o de pago\) 3109/01902148.2013.831960](#)

AUTORES / AUTHORS: - Gorgisen G; Ozes D; Pehlivanoglu S; Erdogan A; Dertsiz L; Ozbilim G; Ozbudak IH; Savas B; Ozes ON

INSTITUCIÓN / INSTITUTION: - 1Faculty of Medicine, Department of Medical Biology and Genetics, Akdeniz University , Antalya , Turkey.

RESUMEN / SUMMARY: - ABSTRACT Lung cancer is the leading cause of death of both men and women across the world. Overexpression and activating mutations of the epidermal growth factor receptor-1 (EGFR1) are frequently observed and associated with poor prognosis. To inhibit the function of EGFR1, multiple antibodies and small-molecule tyrosine kinase inhibitors (TKI) that target EGFR1 have been developed. Even though some patients respond to these TKI, subsequent studies reveal that this is not the case for all nonsmall cell lung cancer (NSCLC) patients. In this study, we determine whether activation and expression levels of EGFR1, ERK, AKT, STAT3, and TWIST1 are dependent on the activating mutations of EGFR1. Protein lysates and DNA have been isolated from tumor and corresponding normal tissues of 16 NSCLC

patients. Genomic-DNA is used to sequence the exons 18, 19, and 21 of EGFR1, and exon 2 of k-RAS. Protein lysates were used to determine the expression or phosphorylation levels of EGFR, STAT3, ERK, AKT, and TWIST1. Our results revealed that 16 tumor samples of NSCLC patients showed no mutation in any of the indicated exons of EGFR1 and k-RAS albeit significant levels of activation or expression of the above-mentioned oncogenes. In NSCLC patients, the tumor micro-environment can be as important as the activating mutations of EGFR1. TK therapy may also be considered for patients who show high levels of activation of EGFR1 even in the absence of activating mutations.

[287]

TÍTULO / TITLE: - Secretory leukocyte protease inhibitor modulates urethane-induced lung carcinogenesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Carcinogenesis. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) [1093/carcin/bgt382](#)

AUTORES / AUTHORS: - Treda CJ; Fukuhara T; Suzuki T; Nakamura A; Zaini J; Kikuchi T; Ebina M; Nukiwa T

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Tohoku University Graduate School of Medicine 2-1 Seiryomachi, Aoba-ku, Sendai 980-8575, Japan.

RESUMEN / SUMMARY: - Secretory leukocyte protease inhibitor (SLPI), 11.7-kDa serine protease inhibitor, is produced primarily in the respiratory tract, but it is often elevated in lung, head/neck, and ovarian cancers. SLPI expression in relation to cancer progression, metastasis, and invasion has been studied extensively in non-small cell lung cancer. However, the role of SLPI during the early stages of carcinogenesis remains unknown. We hypothesized that SLPI is required from the initiation and promotion to the progression of lung carcinogenesis. A skin allograft model using SLPI-knockout mice and shRNA-treated cells was used to demonstrate that SLPI expression in tumor cells is crucial for tumor formation. Moreover, lung tumorigenesis induced by urethane, a chemical lung carcinogen, was significantly suppressed in SLPI-knockout mice in association with decreased NF-kappaB activity. SLPI deficiency also resulted in decreased cell numbers and decreased production of inflammatory cytokines in bronchoalveolar lavage fluids. The suppression of NF-kappaB activation in SLPI-knockout mice was associated with lower expression of NF-kappaB-related survival genes and DNA repair genes. Our findings demonstrate that SLPI plays an important role from the initial stages of lung carcinogenesis to the progression of lung cancer in an NF-kappaB-dependent manner.

[288]

TÍTULO / TITLE: - NF-kappaB activation was involved in reactive oxygen species-mediated apoptosis and autophagy in 1-oxo-2,3-dihydro-1H-benz[e][1,2-b:4,5-b']indole-11(13H)-en-12,8alpha-lactone-treated human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Arch Pharm Res. 2013 Nov 6.

●● Enlace al texto completo (gratis o de pago) [1007/s12272-013-0270-8](#)

AUTORES / AUTHORS: - Liu S; Wu D; Li L; Sun X; Xie W; Li X

INSTITUCIÓN / INSTITUTION: - School of Ocean, Shandong University, Weihai, 264209, People's Republic of China.

RESUMEN / SUMMARY: - 1-oxoeudesm-11(13)-eno-12,8alpha-lactone (OEL), a novel eudesmane-type sesquiterpene compound, has been shown to inhibit the growth of some cancer cell lines and induce significant apoptosis. Here, we investigated the anti-cancer activities of OEL in human lung cancer cells. Our studies demonstrated that OEL induced both apoptosis and autophagy in A549 and H460 cells. OEL-induced autophagy was assessed by appearance of autophagic vacuoles, formation of acidic vesicular organelles, conversion of LC3-I to LC3-II, recruitment of LC3-II to the autophagosomes, and activation of autophagy genes. Furthermore, administration of autophagic inhibitor 3-methyladenine augments OEL-induced apoptotic cell death. The induction of autophagy and apoptosis by OEL links to NF-kappaB activation and the generation of reactive oxygen species (ROS). Interruption of NF-kappaB activation by specific inhibitor promotes apoptosis, but decreases autophagy. ROS antioxidants (N-acetylcysteine) attenuated both OEL-induced autophagy and apoptosis. Further experiments confirmed that OEL-induced activation of ROS was increased by NF-kappaB inhibitor whereas NF-kappaB activation was not affected by ROS inhibition. These findings suggest that OEL-elicited autophagic response plays a protective role that impedes cell death, and inhibition of autophagy could be an adjunctive strategy for enhancing the chemotherapeutic effect of OEL as an antitumor agent.

[289]

TÍTULO / TITLE: - Superior anti-tumor protection and therapeutic efficacy of vaccination with dendritic cell/tumor cell fusion hybrids for murine Lewis lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Autoimmunity. 2013 Nov 5.

●● Enlace al texto completo (gratis o de pago) [3109/08916934.2013.850080](#)

AUTORES / AUTHORS: - Chen X; Liu Z; Huang Y; Li R; Zhang H; Dong S; Ge C; Zhang Z; Wang Y; Wang Y; Xue Y; Li Z; Song X

INSTITUCIÓN / INSTITUTION: - Department of Cancer Biotherapy Center and.

RESUMEN / SUMMARY: - Abstract Background: The development of protocols for the ex vivo generation of dendritic cells (DCs) has led to intensive research into their potential use in immunotherapy in the treatment of cancer. In this study, we examined the efficacy of dendritic cell-tumor cell fusion hybrid vaccines in eliciting an immune response against Lewis lung carcinoma (LLC) cells, as compared to other types of tumor vaccines. In addition, we also tested whether the efficacy of the vaccines was affected by the route of administration. Four different tumor vaccines were compared: (1) HC (hybrid cell), consisting of DC/LLC hybrids; (2) DC+LLC (DCs pulsed with apoptotic LLCs); (3) DC without antigen loading/pulsing; (4) LLC (apoptotic/irradiated tumor cells). We also compared four different routes of administration for each vaccine: (1) Preimmunization; (2) Vaccination therapy; (3) Adoptive immunotherapy; (4) Vaccination therapy combined with adoptive immunotherapy. Anti-tumor immunity was assessed in vivo and the CTL (cytotoxic T lymphocyte) response as well as the expression of key cytokines, IFN-gamma and IL-10 were further evaluated using in vitro assays. Results: Our data demonstrate that vaccination with HC hybrids provides more effective anti-tumor protective immunity and significantly greater therapeutic immunity than vaccination with DC+LLC, DC or LLC. Most remarkably, vaccination

therapy with HC hybrids was more successful than combination (vaccination + adoptive) therapy for the induction of anti-tumor responses. Splenocytes harvested from mice immunized with HC hybrids demonstrated the greatest cytotoxic T lymphocyte (CTL) activity and their production of IFN-gamma was high, while their production of IL-10 was very low. Conclusions: Our results suggest that vaccination therapy with DC-tumor cell fusion hybrids provides more effective protection against lung cancer.

[290]

TÍTULO / TITLE: - Phase II study of concurrent thoracic radiotherapy in combination with weekly paclitaxel plus carboplatin in locally advanced non-small cell lung cancer: LOGIK0401.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Dec;72(6):1353-9. doi: 10.1007/s00280-013-2335-2. Epub 2013 Oct 29.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00280-013-2335-2](#)

AUTORES / AUTHORS: - Takayama K; Inoue K; Tokunaga S; Matsumoto T; Oshima T; Kawasaki M; Imanaga T; Kuba M; Takeshita M; Harada T; Shioyama Y; Nakanishi Y

INSTITUCIÓN / INSTITUTION: - Research Institute for Diseases of the Chest, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashiku, Fukuoka, 812-8582, Japan, koichi-t@kokyu.med.kyushu-u.ac.jp.

RESUMEN / SUMMARY: - OBJECTIVES: Concurrent chemoradiotherapy for regionally advanced stage III non-small cell lung cancer is the standard treatment method. However, the clinical implications of consolidation chemotherapy following chemoradiation have been unclear. Therefore, we conducted a phase II study of concurrent weekly carboplatin plus paclitaxel treatment in combination with radiotherapy followed by vinorelbine monotherapy. The primary endpoint was the 1-year survival rate. PATIENTS AND METHODS: Chemonaive PS 0-1 patients with stage IIIA/B NSCLC were enrolled. During the concurrent chemoradiation phase, patients were treated with weekly paclitaxel 40 mg/m² plus carboplatin AUC 2. The primary tumor and involved nodes received 60 Gy in 2-Gy fractions over 6 weeks. During the consolidation phase, vinorelbine 25 mg/m² on days 1 and 8 was repeated for three cycles. RESULTS: A total of 40 eligible patients (72.5 % male; median age, 63 years; range 29-74 years) were analyzed for efficacy. Squamous cell carcinoma was the most common histology (47.5 %), and more patients had clinical stage IIIB (55 %) cancer. The average radiation dose was 56.5 Gy, and the average number of carboplatin plus paclitaxel cycles was 4.93. Seventeen patients proceeded to the consolidation chemotherapy phase, and 14 completed three cycles of vinorelbine monotherapy. The objective response rate was 75.0 %, including 1 patient who achieved a complete response. Progression-free survival and overall survival (OS) were 46 weeks [95 % confidence interval (CI) 31-64 weeks] and 110 weeks (95 % CI 90-184 weeks), respectively. The OS rate at 1 and 2 years was 85.0 % (95 % CI 69.6-93.0 %) and 53.9 % (95 % CI 37.1-68.0 %), respectively. CONCLUSION: Concurrent chemoradiation with weekly carboplatin and paclitaxel followed by vinorelbine consolidation is effective for stage III non-small cell lung cancer and shows a generally mild toxicity profile.

[291]

TÍTULO / TITLE: - Carboplatin-containing regimens as front-line treatment for advanced non-small-cell lung cancer in two groups of elderly.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Chemother. 2013 Jul 17.

●● Enlace al texto completo (gratis o de pago)

[1179/1973947813Y.0000000112](#)

AUTORES / AUTHORS: - Giuliani J; Piacentini P; Greco F; Mercanti A; Trolese A; Furini L; Durante E; Moratello G; Tognetto M; Bonetti A

RESUMEN / SUMMARY: - **OBJECTIVES:** We evaluated the impact of a carboplatin-based doublet in two groups of elderly patients with advanced non-small cell lung cancers (NSCLC). **MATERIALS AND METHODS:** A retrospective analysis of all consecutive elderly patients (≥ 70 year old) with advanced NSCLC who received a carboplatin-based doublet as front-line therapy at our medical oncology unit was performed. **RESULTS:** In the study, 57 consecutive elderly patients with advanced NSCLC were included. Carboplatin was combined with vinorelbine in 41 patients (71.9%) and with gemcitabine in 16 patients (28.1%). Overall, a total of 227 cycles were administered to 57 patients ? 142 cycles were administered to patients in group 1 and 85 cycles were given to patients in group 2 ? median number of administered cycles per patient was 4 (range 1-6). Of the patients, 35 (62%, group 1) were 'young-old' (70-74-year old) and 20 (38%, group 2) were 'old-old' (75-82-year old). Toxicity was mild in both subgroups (grade 3-4 neutropenia in 17.1% of group 1 and in 9.1% of group 2). At the univariate analysis, the median overall survival (OS) was 10.07 months ($P=0.789$, 95% CI: 8.49-11.64), 10.1 months in group 1 and 9.8 months in group 2. **CONCLUSIONS:** This evaluation shows the safety and efficacy of a carboplatin-based doublet given as firstline chemotherapy in elderly advanced NSCLC patients. The combination with vinorelbine or gemcitabine is associated with a very good toxicity profile that does not seem to have a detrimental effect on efficacy.

[292]

TÍTULO / TITLE: - Prognostic value of epidermal growth factor receptor mutations in resected lung adenocarcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2014 Jan;31(1):771. doi: 10.1007/s12032-013-0771-9. Epub 2013 Nov 19.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0771-9](#)

AUTORES / AUTHORS: - Liu WS; Zhao LJ; Pang QS; Yuan ZY; Li B; Wang P

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Cancer Prevention and Therapy, Department of Radiation Oncology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, 300060, China.

RESUMEN / SUMMARY: - The purpose of this study was to evaluate the association between epidermal growth factor receptor (EGFR) mutations and prognosis in patients with completely resected lung adenocarcinoma. A total of 131 patients were included in this study. EGFR mutation status in exons 18-21 of the tyrosine kinase-binding domain was detected using nested PCR amplification of individual exon. The chi (2) test was used to analyze the associations between EGFR mutations and the different variables.

The log-rank test and Cox regression model were used to evaluate the factors influencing disease-free survival (DFS) and overall survival (OS). EGFR mutations in 18-21 exons were detected in 58 of the 131 patients (44.3 %). Smoking status (P = 0.029), N stage (P = 0.021), and pathologic stage (P = 0.048) were significantly associated with EGFR mutations. The median DFS in mutant EGFR and wild-type EGFR groups was 36.6 and 25.7 months, respectively (P = 0.533). No significant correlation was observed between EGFR mutations and OS (P = 0.564). However, patients with exon 19 mutation tended to have longer DFS than those with exon 21 mutation (46.2 vs. 21.9 months, P = 0.056), and the 1-, 2-, and 3-year OS rates were significantly higher in patients with exon 19 mutation compared to patients with exon 21 mutation (100, 96.7, 93.3 vs. 91.3, 82.6, 60.9 %, respectively, P = 0.01). Our data demonstrated that EGFR mutations do not have significant prognostic value in primary resected lung adenocarcinomas, but patients with exon 19 mutation tended to have better prognostic value compared to patients with exon 21 mutation.

[293]

TÍTULO / TITLE: - Phase II study of low-dose paclitaxel with timed thoracic radiotherapy followed by adjuvant gemcitabine and carboplatin in unresectable stage III non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Sep 25. pii: S0169-5002(13)00432-7. doi: 10.1016/j.lungcan.2013.09.007.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.007](#)

AUTORES / AUTHORS: - Zhang J; Gay HA; Russo S; Parent T; Aljumaily R; Walker PR

INSTITUCIÓN / INSTITUTION: - Leo Jenkins Cancer Center, Division of Hematology Oncology, Department of Internal Medicine, Brody School of Medicine, East Carolina University, Greenville, NC, United States; Department of Medicine, Section of Hematology Oncology, Baylor College of Medicine, Houston, TX, United States.

RESUMEN / SUMMARY: - **OBJECTIVES:** The purpose of the proposed study is to evaluate the effectiveness and safety of low-dose paclitaxel with timed thoracic radiotherapy (TTR) for local control by inducing maximum radiosensitization through G2-M phase cell cycle arrest, followed by full dose adjuvant chemotherapy with gemcitabine and carboplatin for eradication of possible micrometastasis in unresectable stage III non-small cell lung cancer (NSCLC). **MATERIALS AND METHODS:** This is a single-center, non-randomized prospective phase II study. Patients with unresectable stage III NSCLC were treated with paclitaxel 15mg/m² IV, followed by TTR 6h later on Monday/Wednesday/Friday, and TTR only on Tuesday/Thursday mornings (total 55Gy). Full dose adjuvant chemotherapy consisted of intravenous carboplatin (AUC 5) on day 1, gemcitabine 1000mg/m² on days 1 and 8, every 21 days for 4 cycles. The primary endpoint was overall survival (OS). Secondary endpoints were overall response rate (ORR), and toxicities. **RESULTS:** Twenty-seven patients were eligible for the study. Patient characteristics were: 19 males (70%); median age 67 years (range 39-82); 15 (56%) stage IIIB; 89% with ECOG performance status \geq 1. Three-year OS was 16.7% in all patients, and 27.3% in patients received three or more cycles of adjuvant chemotherapy, respectively. ORR was 63%. Grade 3 toxicities during paclitaxel plus concurrent TTR phase were radiation esophagitis (11%) and radiation pneumonitis (4%), no grade 4 toxicities occurred. One grade 5

hemoptysis. Grade $\frac{3}{4}$ toxicities during adjuvant gemcitabine/carboplatin were pneumonitis (22%), anemia (30%), neutropenia (22%), and thrombocytopenia (33%), one grade 5 neutropenic fever. CONCLUSION: Low-dose paclitaxel with concurrent TTR is an effective chemoradiotherapy regimen in unresectable stage III NSCLC. Improved survival benefit was observed in patients who have received three or more cycles of full dose adjuvant chemotherapy, yet, gemcitabine related radiation pneumonitis and hematological toxicities limited adjuvant chemotherapy delivery.

[294]

TÍTULO / TITLE: - The impact of personalized medicine on survival: Comparisons of results in metastatic breast, colorectal and non-small-cell lung cancers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Treat Rev. 2013 Sep 25. pii: S0305-7372(13)00201-6. doi: 10.1016/j.ctrv.2013.09.012.

●● Enlace al texto completo (gratis o de pago) [1016/j.ctrv.2013.09.012](#)

AUTORES / AUTHORS: - Rossi A; Torri V; Garassino MC; Porcu L; Galetta D

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology, S.G. Moscati Hospital, Avellino, Italy.

RESUMEN / SUMMARY: - Breast, colorectal and lung cancers represent the three most incident forms of cancer worldwide. Among these three “big killers”, lung cancer is considered the one with the worst prognosis due to its high mortality even in early stages. Due to their more favorable prognosis, breast and colorectal cancers might appear to have benefited from major advances. Most oncologists who are faced with metastatic non-small cell lung cancer (NSCLC) find the reported results very frustrating when compared with those for metastatic breast (MBC) and colorectal cancers (MCRC). The aim of this analysis was to quantify and compare the relative magnitude of overall survival (OS) improvements in the first-line approaches in metastatic NSCLC, MBC and MCRC through the analysis of the main landmark meta-analyses and randomized clinical trials (RCTs) of commercially available drugs. Five items were considered and analyzed for each cancer. Moreover we evaluated the real clinical impact of the results reported by each item on the entire population; for each “big killer” an overall hazard ratio (HR) was estimated: 0.88 (95%+ CI: 0.72-1.07) for MBC, 0.94 (95%+ CI: 0.82-1.07) for MCRC, and about 0.80 (95%+ CI: 0.73-0.90) for advanced NSCLC. We showed that, in the last decades, these three tumors had important and constant OS improvements reached step by step. The relative magnitude of OS improvement seems higher in metastatic NSCLC than MBC and MCRC.

[295]

TÍTULO / TITLE: - Contemplating Genetic Feedback Regarding Lung Cancer Susceptibility.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Behav Med. 2013 Nov 13.

●● Enlace al texto completo (gratis o de pago) [1007/s12160-013-9561-z](#)

AUTORES / AUTHORS: - Shepperd JA; Novell CA; O'Neill SC; Docherty SL; Sanderson SC; McBride CM; Lipkus IM

INSTITUCIÓN / INSTITUTION: - Department of Psychology, University of Florida, PO Box 112250, Gainesville, FL, 32611-2250, USA, shepperd@ufl.edu.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: We examined three theoretical models (self-enhancement theory, consistency theory, and a combined model) for understanding how expectations and test result favorability influence smokers' desire for a retest following hypothetical genetic test results. METHOD: College smokers (N = 128) read a brochure describing a biomarker for lung cancer (the GSTM1 gene) then reported whether they thought they had the gene (indicating lower lung cancer risk) or were missing the gene (indicating higher lung cancer risk). Participants then reported whether they would get retested if they received favorable GSTM1 results versus unfavorable GSTM1 results. RESULTS: Participants were most likely to want a retest, suggesting rejection of the results, if they expected favorable news yet received unfavorable news. CONCLUSION: The findings supported the combined model such that smokers expressed greatest interest in a retest when they imagined genetic risk feedback that challenges both enhancement and consistency motives.

[296]

TÍTULO / TITLE: - Quantitative assessment of the influence of common variations (rs8034191 and rs1051730) at 15q25 and lung cancer risk.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 20.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s13277-013-1369-8](#)

AUTORES / AUTHORS: - Hu B; Huang Y; Yu RH; Mao HJ; Guan C; Zhao J

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Shanghai Xuhui District Center Hospital, Shanghai, 200031, People's Republic of China.

RESUMEN / SUMMARY: - Several genome-wide association studies on lung cancer (LC) have reported similar findings of a new susceptibility locus, 15q25. After that, a number of studies reported that rs8034191 and rs1051730 polymorphisms at chromosome 15q25 have been implicated in LC risk. However, studies have yielded contradictory results. To derive a more precise estimation of the relationship, a meta-analysis of 43,742 LC cases and 58,967 controls from 17 published case-control studies was performed. Overall, significantly elevated LC risk was associated with rs8034191-C (OR = 1.26, 95 % CI 1.22-1.31, P < 10⁻⁵) and rs105173-A variant (OR = 1.28, 95 % CI 1.20-1.36, P < 10⁻⁵) when all studies were pooled into the meta-analysis. In the subgroup analysis by ethnicity, significantly increased risks were found for rs8034191 and rs105173 polymorphisms among Caucasians and African American, while no significant associations were observed for the two polymorphisms in East Asians. In addition, we found that rs8034191 and rs105173 confer risk, for both adenocarcinoma and squamous cell carcinoma when stratified by histological types of LC. Furthermore, our results on stratified analysis according to smoking status showed an increased LC risk in ever-smokers, while no associations were detected among never-smokers for the two polymorphisms. In conclusion, this meta-analysis demonstrated that the two common variations (rs8034191 and rs1051730) at 15q25 are a risk factor associated with increased LC susceptibility, but these associations vary in different ethnic populations.

[297]

TÍTULO / TITLE: - Preclinical evaluation of 4-[3,5-bis(2-chlorobenzylidene)-4-oxo-piperidine-1-yl]-4-oxo-2-butenoic acid, in a mouse model of lung cancer xenograft.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Pharmacol. 2013 Dec;170(7):1436-48. doi: 10.1111/bph.12406.

●● Enlace al texto completo (gratis o de pago) [1111/bph.12406](#)

AUTORES / AUTHORS: - Yadav VR; Sahoo K; Awasthi V

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: 4-[3,5-Bis(2-chlorobenzylidene)-4-oxo-piperidine-1-yl]-4-oxo-2-butenoic acid CLEFMA is a new anti-cancer molecule. Here, we investigated changes in apoptosis and inflammatory markers during CLEFMA-induced tumour suppression. EXPERIMENTAL APPROACH: Lung adenocarcinoma H441 and A549, and normal lung fibroblast CCL151 cell lines were used, along with a xenograft model of H441 cells implanted in mice. Tumour tissues were analysed by immunoblotting, immunohistochemistry and/or biochemical assays. The ex vivo results were confirmed by performing selected assays in cultured cells. KEY RESULTS: CLEFMA-induced cell death was associated with cleavage of caspases 3/9 and PARP. In vivo, CLEFMA treatment resulted in a dose-dependent suppression of tumour growth and (18) F-fluorodeoxyglucose uptake in tumours, along with a reduction in the expression of the proliferation marker Ki-67. In tumour tissue homogenates, the anti-apoptotic markers (cellular inhibitor of apoptosis protein-1 (cIAP1), Bcl-xL, Bcl-2, and survivin) were inhibited and the pro-apoptotic Bax and BID were up-regulated. Further, CLEFMA decreased translocation of phospho-p65-NF-kappaB into the nucleus. In vitro, it inhibited the DNA-binding and transcriptional activity of NF-kappaB. It also reduced the expression of COX-2 in tumours and significantly depressed serum TNF-alpha and IL-6 levels. These effects of CLEFMA were accompanied by a reduced transcription and/or translation of the invasion markers VEGF, MMP9, MMP10, Cyclin D1 and ICAM-1. CONCLUSIONS AND IMPLICATIONS: Overall, CLEFMA inhibited growth of lung cancer xenografts and this tumour suppression was associated with NF-kappaB-regulated anti-inflammatory and anti-metastatic effects.

[298]

TÍTULO / TITLE: - Combining clinical and analytical parameters improves prediction of malignant pleural effusion.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Dec;191(6):633-43. doi: 10.1007/s00408-013-9512-2. Epub 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago) [1007/s00408-013-9512-2](#)

AUTORES / AUTHORS: - Valdes L; San-Jose E; Ferreiro L; Gonzalez-Barcala FJ; Golpe A; Alvarez-Dobano JM; Toubes ME; Rodriguez-Nunez N; Rabade C; Lama A; Gude F

INSTITUCIÓN / INSTITUTION: - Servicio de Neumología, Complejo Hospitalario Clínico-Universitario de Santiago, Travesía da Choupana s/n, 15706, Santiago de Compostela, España, luis.valdes.cuadrado@sergas.es.

RESUMEN / SUMMARY: - PURPOSE: The usefulness of a panel of tumour markers and clinical-radiological criteria for diagnosing malignant pleural effusion (MPE) is not clearly stated. Our purpose was to assess the performance of those parameters in the diagnosis of MPE. METHODS: Consecutive patients with exudative PE were enrolled and divided into two groups: MPE and non-MPE. Logistic regression analysis was used to estimate the probability of MPE. Four prognostic models were considered: (1) clinical-radiological variables; (2) analytical variables; (3) combination of clinical and analytical variables; and (4) simpler model removing some analytical variables. Calibration and discrimination (receiver operating characteristics curves and AUC) were performed. RESULTS: A total of 491 pleural exudates were included: tuberculous (n = 72), malignant (n = 211), parapneumonic (n = 115), empyemas (n = 32), or miscellaneous (n = 61). The AUC obtained with Model 1 (absence of chest pain and fever and radiological images compatible with malignancy), Model 2 (CEA, NSE, CYFRA 21-1, and TPS), Model 3 (sum of the variables of models 1 and 2), and Model 4 (the variables of model 1 plus CEA) were 0.918, 0.832, 0.952 (all with a P < 0.05), and 0.939 (P < 0.01 compared to models 1 and 2), respectively. The correct classification rate for Models 1, 2, 3, and 4, was 87.2, 79.5, 88.4, and 87.6 %, respectively. CONCLUSIONS: All models analysed had a good diagnostic yield for MPE, being greater in those that combined radiological and analytical criteria. Although Model 3 obtained a higher yield, the simplest model (Model 4) is very attractive due to its simplicity of use in daily practice.

[299]

TÍTULO / TITLE: - Higher risk of mortality from lung cancer in Taiwanese people with diabetes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Diabetes Res Clin Pract. 2013 Nov 2. pii: S0168-8227(13)00361-6. doi: 10.1016/j.diabres.2013.10.019.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.diabres.2013.10.019](#)

AUTORES / AUTHORS: - Tseng CH

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, National Taiwan University College of Medicine, Taipei, Taiwan; Division of Endocrinology and Metabolism, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan; Division of Environmental Health and Occupational Medicine of the National Health Research Institutes, Taipei, Taiwan. Electronic address: ccktsh@ms6.hinet.net.

RESUMEN / SUMMARY: - BACKGROUND: The association between diabetes and lung cancer is rarely studied in the Asian populations. This study investigated lung cancer mortality trends, mortality rate ratios between people with diabetes and the general population, and associated risk factors in people with diabetes in Taiwan. METHODS: Age-standardized trends from 1995 to 2006 were evaluated, followed by calculation of age-sex-specific average mortality rates within the 12-year period in the general population. A total of 113,347 men and 131,573 women with diabetes, aged ≥ 25 years and recruited in 1995-1998 were followed to 2006. Age-sex-specific mortality rate

ratios between people with diabetes and the general population were calculated. Cox regression evaluated the risk factors in the people with diabetes. RESULTS: A steady age-standardized trend was observed for either sex. A total of 1580 men and 931 women with diabetes died of lung cancer. Mortality rate ratios showed a significantly higher risk in patients with diabetes: 1.16 (1.04-1.30), 1.42 (1.33-1.53), 1.79 (1.61-1.99) and 4.37 (3.75-5.09) for ≥ 75 , 65-74, 55-64 and 25-54 years old, respectively, for men; and 1.35 (1.18-1.54), 1.41 (1.27-1.57), 1.88 (1.66-2.13) and 3.57 (2.95-4.33), respectively, for women. Age and smoking were significantly associated with lung cancer mortality in the people with diabetes, but sex, diabetes type and insulin use were not. Diabetes duration was significant when those who died of lung cancer within 5 years of diabetes diagnosis were excluded from analysis. CONCLUSIONS: People with diabetes have a higher risk of lung cancer mortality and this was most remarkable in the youngest age.

[300]

TÍTULO / TITLE: - Exposure-Response Estimates for Diesel Engine Exhaust and Lung Cancer Mortality Based on Data from Three Occupational Cohorts.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Environ Health Perspect. 2013 Nov 22.

●● [Enlace al texto completo \(gratis o de pago\) 1289/ehp.1306880](#)

AUTORES / AUTHORS: - Vermeulen R; Silverman DT; Garshick E; Vlaanderen J; Portengen L; Steenland K

INSTITUCIÓN / INSTITUTION: - Division of Environmental Epidemiology, Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands.

RESUMEN / SUMMARY: - BACKGROUND: Diesel engine exhaust (DEE) has recently been classified as a known human carcinogen. OBJECTIVE: To derive a meta-exposure-response curve (ERC) for DEE and lung cancer mortality and estimate lifetime excess risks (ELRs) of lung cancer mortality based on assumed occupational and environmental exposure scenarios. METHODS: We conducted a meta-regression of lung cancer mortality and cumulative exposure to elemental carbon (EC), a proxy measure of DEE, based on relative risk (RR) estimates reported by three large occupational cohort studies (including two studies of workers in the trucking industry and one study of miners). Based on the derived risk function, we calculated ELRs for several lifetime occupational and environmental exposure scenarios, and also calculated the fractions of annual lung cancer deaths attributable to DEE. RESULTS: We estimated a lnRR of 0.00098 (95% CI: 0.00055, 0.0014) for lung cancer mortality with each 1- $\mu\text{g}/\text{m}^3$ -year increase in cumulative EC based on a linear meta-regression model. Corresponding lnRRs for the individual studies ranged from 0.00061 to 0.0012. Estimated numbers of excess lung cancer deaths through age 80 for lifetime occupational exposures of 1, 10, and 25 $\mu\text{g}/\text{m}^3$ EC were 17, 200, and 689 per 10,000, respectively. For lifetime environmental exposure to 0.8 $\mu\text{g}/\text{m}^3$ EC, we estimated 21 excess lung cancer deaths per 10,000. Based on broad assumptions regarding past occupational and environmental exposures we estimate that approximately 6% of annual lung cancer deaths may be due to DEE exposure. CONCLUSIONS: Combined data from three US occupational cohort studies suggest that DEE at levels common in the workplace and in outdoor air appear to pose substantial excess lifetime risks of lung cancer, above usually acceptable limits in the

US and Europe, which are generally set at 1/1,000 and 1/100,000 based on lifetime exposure for the occupational and general population, respectively.

[301]

TÍTULO / TITLE: - Alveolar epithelial cells (A549) exposed at the air-liquid interface to diesel exhaust: First study in TNO's powertrain test center.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Toxicol In Vitro. 2013 Dec;27(8):2342-9. doi: 10.1016/j.tiv.2013.10.007. Epub 2013 Oct 23.

●● Enlace al texto completo (gratis o de pago) 1016/j.tiv.2013.10.007

AUTORES / AUTHORS: - Kooter IM; Alblas MJ; Jedynska AD; Steenhof M; Houtzager MM; Ras Mv

INSTITUCIÓN / INSTITUTION: - The Netherlands Organisation for Applied Scientific Research, TNO, P.O. Box 80015, 3508 TA Utrecht, The Netherlands. Electronic address: ingeborg.kooter@tno.nl.

RESUMEN / SUMMARY: - Air-liquid interface (ALI) exposures enable in vitro testing of mixtures of gases and particles such as diesel exhaust (DE). The main objective of this study was to investigate the feasibility of exposing human lung epithelial cells at the ALI to complete DE generated by a heavy-duty truck in the state-of-the-art TNO powertrain test center. A549 cells were exposed at the air-liquid interface to DE generated by a heavy-duty Euro III truck for 1.5h. The truck was tested at a speed of approximately 70kmh(-1) to simulate free-flowing traffic on a motorway. Twenty-four hours after exposure, cells were analyzed for markers of oxidative stress (GSH and HO-1), cytotoxicity (LDH and Alamar Blue assay) and inflammation (IL-8). DE exposure resulted in an increased oxidative stress response (significantly increased HO-1 levels and significantly reduced GSH/GSSH ratio), and a decreased cell viability (significantly decreased Alamar Blue levels and slightly increased LDH levels). However, the pro-inflammatory response seemed to decrease (decrease in IL-8). The results presented here demonstrate that we are able to successfully expose A549 cells at ALI to complete DE generated by a heavy-duty truck in TNO's powertrain test center and show oxidative stress and cytotoxicity responses due to DE exposure.

[302]

TÍTULO / TITLE: - NEDD9 promotes lung cancer metastasis through epithelial-mesenchymal transition.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Cancer. 2013 Oct 31. doi: 10.1002/ijc.28568.

●● Enlace al texto completo (gratis o de pago) 1002/ijc.28568

AUTORES / AUTHORS: - Jin Y; Li F; Zheng C; Wang Y; Fang Z; Guo C; Wang X; Liu H; Deng L; Li C; Wang H; Chen H; Feng Y; Ji H

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Cell Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, People's Republic of China.

RESUMEN / SUMMARY: - Metastasis is the major cause for high mortality of lung cancer with the underlying mechanisms poorly understood. The scaffolding protein neural precursor cell expressed, developmentally down-regulated 9 (NEDD9) has been

identified as a pro-metastasis gene in several types of cancers including melanoma and breast cancer. However, the exact role and related mechanism of NEDD9 in regulating lung cancer metastasis still remain largely unknown. Here, we demonstrate that NEDD9 knockdown significantly inhibits migration, invasion and metastasis of lung cancer cells in vitro and in vivo. The pro-metastasis role of Nedd9 in lung cancer is further supported by studies in mice models of spontaneous cancer metastasis. Moreover, we find that NEDD9 promotes lung cancer cell migration and invasion through the induction of epithelial-mesenchymal transition (EMT) potentially via focal adhesion kinase activation. More importantly, NEDD9 expression inversely correlates with E-cadherin expression in human lung cancer specimens, consistent with the findings from in vitro studies. Taken together, this study highlights that NEDD9 is an important mediator promotes lung cancer metastasis via EMT.

[303]

TÍTULO / TITLE: - Ex utero Intrapartum Treatment to Resection of a Bronchogenic Cyst Causing Airway Compression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Fetal Diagn Ther. 2013 Nov 21.

●● Enlace al texto completo (gratis o de pago) [1159/000355661](#)

AUTORES / AUTHORS: - Chatterjee D; Hawkins JL; Somme S; Galan HL; Prager JD; Crombleholme TM

INSTITUCIÓN / INSTITUTION: - Department of Anesthesiology, Colorado Fetal Care Center, Colorado Institute for Maternal and Fetal Health, University of Colorado School of Medicine, Aurora, Colo., USA.

RESUMEN / SUMMARY: - We present a case report of a 28-year-old primigravida with a singleton pregnancy complicated by a fetal bronchogenic cyst compressing the left mainstem bronchus with resultant hyperinflation of the entire left lung and rightward mediastinal shift. An ex utero intrapartum treatment to resection of the fetal bronchogenic cyst via a fetal thoracotomy was performed at 36 weeks' gestational age, circumventing a potentially complicated neonatal airway emergency at birth. © 2013 S. Karger AG, Basel.

[304]

TÍTULO / TITLE: - Autoantibodies against p16 protein-derived peptides may be a potential biomarker for non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Oct 13.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1271-4](#)

AUTORES / AUTHORS: - Zhang C; Ye L; Guan S; Jin S; Wang W; Sun S; Lee KH; Wei J; Liu B

INSTITUCIÓN / INSTITUTION: - Department of Radiobiology, School of Public Health, Jilin University, Changchun, 130021, China.

RESUMEN / SUMMARY: - Overexpression of tumor-associated antigens (TAAs) has been reported in many types of cancer and may trigger secretion of their autoantibodies. The present work was thus designed to test whether circulating antibody to p16 protein-derived antigens was altered in lung cancer. Two hundred

seventy-one patients with non-small cell lung cancer (NSCLC) and 226 control subjects matched in age, gender, and smoking history were recruited in this study. The levels of circulating anti-p16 IgA and IgG antibodies were tested using an enzyme-linked immunosorbent assay (ELISA) developed in-house with linear peptide antigens derived from p16 protein. Student's t test showed that patients with NSCLC had a significant higher level of anti-p16 IgG antibody than control subjects ($t = 2.74$, $P = 0.0063$) but did not have a significant increase in IgA antibody levels ($t = 1.92$, $P = 0.056$). The sensitivity against >90 % specificity was 19.7 % for the IgG assay with an inter-assay deviation of 11.6 %, and 10.3 % for the IgA assay with an inter-assay deviation of 14.7 %. Based on a cut-off value determined by the 99th percentile of control IgG levels, the anti-p16 IgG positivity was 6.7 % in patients with NSCLC compared to 0.88 % in control subjects ($\chi^2 = 10.58$, $P = 0.001$, $OR = 7.97$, 95 % CI 1.84-34.85). Circulating anti-p16 IgG levels were increased with stages of NSCLC, and patients with stage IV NSCLC had the highest IgG level among all four stages ($t = 2.42$, $P = 0.016$, compared with the control group). Pearson correlation analysis showed a significant correlation between circulating levels of IgA and IgG in the patient group ($r = -0.2$, $df = 236$, $P = 0.0021$) but not in the control group ($r = -0.1$, $df = 205$, $P = 0.146$). Circulating IgG antibody to p16 protein may be a potential biomarker with prognostic values for lung cancer.

[305]

TÍTULO / TITLE: - Applicability of the linear-quadratic formalism for modeling local tumor control probability in high dose per fraction stereotactic body radiotherapy for early stage non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Oct;109(1):13-20. doi: 10.1016/j.radonc.2013.09.005. Epub 2013 Oct 30.

•• Enlace al texto completo (gratis o de pago) [1016/j.radonc.2013.09.005](#)

AUTORES / AUTHORS: - Guckenberger M; Klement RJ; Allgauer M; Appold S; Dieckmann K; Ernst I; Ganswindt U; Holy R; Nestle U; Nevinny-Stickel M; Semrau S; Sterzing F; Wittig A; Andratschke N; Flentje M

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Würzburg, Germany. Electronic address: guckenberger_m@klinik.uni-wuerzburg.de.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: To compare the linear-quadratic (LQ) and the LQ-L formalism (linear cell survival curve beyond a threshold dose dT) for modeling local tumor control probability (TCP) in stereotactic body radiotherapy (SBRT) for stage I non-small cell lung cancer (NSCLC). MATERIALS AND METHODS: This study is based on 395 patients from 13 German and Austrian centers treated with SBRT for stage I NSCLC. The median number of SBRT fractions was 3 (range 1-8) and median single fraction dose was 12.5Gy (2.9-33Gy); dose was prescribed to the median 65% PTV encompassing isodose (60-100%). Assuming an alpha/beta-value of 10Gy, we modeled TCP as a sigmoid-shaped function of the biologically effective dose (BED). Models were compared using maximum likelihood ratio tests as well as Bayes factors (BFs). RESULTS: There was strong evidence for a dose-response relationship in the total patient cohort (BFs>20), which was lacking in single-fraction SBRT (BFs<3). Using the PTV encompassing dose or maximum (isocentric) dose, our data indicated a LQ-L transition dose (dT) at 11Gy (68% CI 8-

14Gy) or 22Gy (14-42Gy), respectively. However, the fit of the LQ-L models was not significantly better than a fit without the dT parameter ($p=0.07$, $BF=2.1$ and $p=0.86$, $BF=0.8$, respectively). Generally, isocentric doses resulted in much better dose-response relationships than PTV encompassing doses ($BFs>20$). CONCLUSION: Our data suggest accurate modeling of local tumor control in fractionated SBRT for stage I NSCLC with the traditional LQ formalism.

[306]

TÍTULO / TITLE: - The evolving genomic classification of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Pathol. 2013 Sep 30. doi: 10.1002/path.4275.

- Enlace al texto completo (gratis o de pago) [1002/path.4275](#)

AUTORES / AUTHORS: - Shames DS; Wistuba II

INSTITUCIÓN / INSTITUTION: - Genentech Inc., South San Francisco, California, USA.

RESUMEN / SUMMARY: - EGFR gene mutations and ALK gene fusions are well-characterised molecular targets in NSCLC. Activating alterations in a variety of potential oncogenic driver genes have also been identified in NSCLC, including ROS1, RET, MET, HER2 and BRAF. Together with EGFR and ALK, these mutations account for ~20% of NSCLCs. The identification of these oncogenic drivers has led to the design of rationally targeted therapies that have produced superior clinical outcomes in tumours harbouring these mutations. Many patients, however, have de novo or acquired resistance to these therapies. In addition, most NSCLCs are genetically complex tumours harbouring multiple potential activating events. For these patients, disease subsets are likely to be defined by combination strategies involving a number of targeted agents. These targets include FGFR1, PTEN, MET, MEK, PD-1/PD-L1 and NaPi2b. In light of the myriad new biomarkers and targeted agents, multiplex testing strategies will be invaluable in identifying the appropriate patients for each therapy and enabling targeted agents to be channelled to the patients most likely to gain benefit. The challenge now is how best to interpret the results of these genomic tests, in the context of other clinical data, to optimise treatment choices in NSCLC.

[307]

TÍTULO / TITLE: - E5501: phase II study of topotecan sequenced with etoposide/cisplatin, and irinotecan/cisplatin sequenced with etoposide for extensive-stage small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Nov 28.

- Enlace al texto completo (gratis o de pago) [1007/s00280-013-2338-z](#)

AUTORES / AUTHORS: - Owonikoko TK; Aisner J; Wang XV; Dahlberg SE; Rubin EH; Ramalingam SS; Gounder M; Rausch PG; Axelrod RS; Schiller JH

INSTITUCIÓN / INSTITUTION: - Emory University, Atlanta, GA, USA.

RESUMEN / SUMMARY: - PURPOSE: Sequence-dependent improved efficacy of topoisomerase I followed by topoisomerase 2 inhibitors was assessed in a randomized phase II study in extensive-stage small-cell lung cancer (SCLC). METHODS: Patients with previously untreated extensive-stage SCLC with measurable disease, ECOG performance status of 0-3 and stable brain metastases were eligible. Arm A consisted

of topotecan (0.75 mg/m²) on days 1, 2 and 3, etoposide (70 mg/m²) and cisplatin (20 mg/m²) (PET) on days 8, 9 and 10 in a 3-week cycle. Arm B consisted of irinotecan (50 mg/m²) and cisplatin (20 mg/m²) on days 1 and 8 followed by etoposide (85 mg/m² PO bid) on days 3 and 10 (PIE) in a 3-week cycle. RESULTS: We enrolled 140 patients and randomized 66 eligible patients to each arm. Only 54.5 % of all patients completed the planned maximum 6 cycles. There were grade \geq 3 treatment-related adverse events in approximately 70 % of the patients on both arms including 6 treatment-related grade 5 events. The overall response rates (CR + PR) were 69.7 % (90 % CI 59.1-78.9, 95 % CI 57.1-80.4 %) for arm A and 57.6 % (90 % CI 46.7-67.9, 95 % CI 44.8-69.7 %) for arm B. The median progression-free survival and overall survival were 6.4 months (95 % CI 5.4-7.5 months) and 11.9 months (95 % CI 9.6-13.7 months) for arm A and 6.0 months (95 % CI 5.4-7.0 months) and 11.0 months (95 % CI 8.6-13.1 months) for arm B. CONCLUSION: Sequential administration of topoisomerase inhibitors did not improve on the historical efficacy of standard platinum-doublet chemotherapy for extensive-stage SCLC.

[308]

TÍTULO / TITLE: - Combretastatin A-4 induces p53 mitochondrial-relocalisation independent-apoptosis in non-small lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cell Biol Int. 2013 Oct 23. doi: 10.1002/cbin.10199.

●● [Enlace al texto completo \(gratis o de pago\) 1002/cbin.10199](#)

AUTORES / AUTHORS: - Mendez-Callejas GM; Leone S; Tanzarella C; Antoccia A

INSTITUCIÓN / INSTITUTION: - Departament of Science University 'Roma Tre', V.le G. Marconi 446, 00146, Rome, Italy; Universidad de Ciencias Aplicadas y Ambientales, Calle 222, 55-37, Bogota, Colombia.

RESUMEN / SUMMARY: - Combretastatin A-4 (CA-4) is one of the most effective agents used in chemotherapy. Nevertheless, the contribution of p53 and Bim proteins in the CA-4-induced apoptosis in non-small lung cancer cells (NSCLC) remains unresolved, specifically on involving of p53 in the mitochondrial pathway activation by a transcription-independent mechanism. In this context, the p53-null H1299 and wt-p53 H460 NSCLC cells, in the absence and presence of pifithrin-micro (PFTmicro), an inhibitor of p53 mitochondrial-translocation, were treated with CA-4 and different cellular endpoints were analysed. In contrast to previous observations in H460 cells, CA-4 failed in the activation of an apoptotic response in H1299 cells, thus indicating an involvement of p53 in the cell death induced by the drug. We found that CA-4 led to p53 cellular re-localisation in H460 cells; in particular, p53 was released from the microtubular network and accumulated at mitochondria where it interacts with Bim protein and other proteins of the Bcl-2 (B-cell leukaemia-2) family, leading to cytochrome c release, alteration in the mitochondrial membrane polarisation, cell cycle arrest at the G2/M-phase, and cell death. Interestingly, the cytosolic and the mitochondrial accumulation of protein Bim was strictly dependent on p53 status. The extent of cell death was not reduced in H460 after combined treatment of PFTmicro with CA-4. Overall, the data support a model of CA-4-induced apoptosis in NSCLC, for which the expression of p53 protein is essential, but its mitochondrial function, linked to p53-transcription independent apoptosis pathway, is negligible.

[309]

TÍTULO / TITLE: - Phase II study of oral S-1 and cisplatin with concurrent radiotherapy for locally advanced non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):449-54. doi: 10.1016/j.lungcan.2013.09.004. Epub 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.004](#)

AUTORES / AUTHORS: - Kaira K; Tomizawa Y; Yoshino R; Yoshii A; Matsuura M; Iwasaki Y; Koga Y; Ono A; Nishioka M; Kamide Y; Hisada T; Ishizuka T; Shirai K; Ebara T; Saitoh J; Nakano T; Sunaga N

INSTITUCIÓN / INSTITUTION: - Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Showa-machi, Maebashi, Gunma 371-8511, Japan. Electronic address: kkaira1970@yahoo.co.jp.

RESUMEN / SUMMARY: - **PURPOSE:** To determine the efficacy and safety of oral S-1 in combination with cisplatin and thoracic radiotherapy in patients with unresectable stage III non-small-cell lung cancer (NSCLC). **METHODS AND MATERIALS:** S-1 (50mg/m²) was administered orally twice daily for 14 days, with cisplatin (40mg/m²) on days 1 and 8 of each cycle every 3 weeks, for 2-4 cycles. Thoracic radiation therapy was administered in 2Gy fractions five times weekly for a total dose of 60Gy. The primary endpoint was the response rate, and secondary endpoints included progression-free survival, overall survival and safety. **RESULTS:** Forty-one patients were enrolled in this study. The objective response rate was 87.8% (95% CI: 77.8-97.8%). The median progression-free survival was 467 days (15.4 months), and the median survival time was 904 days (29.7 months). The overall survival rates at 1- and 2-years were 85.7% and 52.9%, respectively. Hematological toxicities included grade 3 neutropenia (17%) and grade 3 leukopenia (27%). No grade 3 febrile neutropenia was detected, and grade 3 non-hematological toxicities were also mild. A grade 3 gastrointestinal hemorrhage was observed in one patient. **CONCLUSIONS:** The combination of oral S-1 plus cisplatin with concurrent radiotherapy is a promising treatment with a high efficacy and lower toxicity in patients with locally advanced NSCLC.

[310]

TÍTULO / TITLE: - Antineoplastic and immunomodulatory effect of polyphenolic components of *Achyranthes aspera* (PCA) extract on urethane induced lung cancer in vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Biol Rep. 2013 Nov 5.

●● Enlace al texto completo (gratis o de pago) [1007/s11033-013-2850-6](#)

AUTORES / AUTHORS: - Narayan C; Kumar A

INSTITUCIÓN / INSTITUTION: - School of Biotechnology, Faculty of Science, Banaras Hindu University, Varanasi, 221 005, UP, India.

RESUMEN / SUMMARY: - Polyphenolic compounds of *Achyranthes aspera* (PCA) extract is evaluated for anti-cancerous and cytokine based immunomodulatory effects. The PCA extract contains known components of phenolic acid and flavonoids such as mixture of quinic acid, chlorogenic acid, kaempferol, quercetin and chrysin along with

many unknown components. PCA has been orally feed to urethane (ethyl carbamate) primed lung cancerous mice at a dosage of 100 mg/kg body weight for 30 consecutive days. 100 mg powder of *A. aspera* contains 2.4 mg phenolic acid and 1.1 mg flavonoid (2:1 ratio). Enhanced activities and expression of antioxidant enzymes GST, GR, CAT, SOD, while down regulated expression and activation of LDH enzymes in PCA feed urethane primed lung cancerous tissues as compared to PCA non-feed urethane primed lung cancerous tissues were observed. PCA feed urethane primed lung tissues showed down regulated expression of pro-inflammatory cytokines IL-1beta, IL-6 and TNF-alpha along with TFs, NF-kappaB and Stat3 while the expression of pro-apoptotic proteins Bax and p53 were enhanced in PCA feed urethane primed lung tissues. FTIR and CD spectroscopy data revealed that PCA resisted the urethane mediated conformational changes of DNA which is evident by the shift in guanine and thymine bands in FTIR from 1,708 to 1,711 cm⁻¹ and 1,675 to 1,671 cm⁻¹, respectively in PCA feed urethane primed lung cancerous tissues DNA in comparison to urethane primed lung cancerous tissues DNA. The present study suggests that PCA components have synergistic anti-cancerous and cytokine based immunomodulatory role and DNA conformation restoring effects. However, more research is required to show the effects of each component separately and in combination for effective therapeutic use to cure and prevent lung cancer including other cancers.

[311]

TÍTULO / TITLE: - The difference in relationship between 18F-FDG uptake and clinicopathological factors on thyroid, esophageal, and lung cancers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nucl Med Commun. 2014 Jan;35(1):36-43. doi: 10.1097/MNM.000000000000019.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/MNM.000000000000019](#)

AUTORES / AUTHORS: - Kaida H; Kawahara A; Hayakawa M; Hattori S; Kurata S; Fujimoto K; Azuma K; Hirose Y; Takamori S; Hiromatsu Y; Nakashima T; Fujita H; Kage M; Hayabuchi N; Ishibashi M

INSTITUCIÓN / INSTITUTION: - aDivision of Nuclear Medicine, PET Center, and Department of Radiology, Kurume University School of Medicine bDepartment of Diagnostic Pathology, Kurume University Hospital cBiostatistics Center dDivision of Respiriology, Neurology, and Rheumatology, Department of Internal Medicine eDepartment of Surgery fDivision of Endocrinology, Department of Internal Medicine gDepartment of Otolaryngology and Facial Maxillary Surgery, Kurume University School of Medicine, Kurume, Fukuoka, Japan.

RESUMEN / SUMMARY: - **OBJECTIVES:** The aim of this study was to reveal the differences in clinicopathological factors affecting maximum standardized uptake value (SUV_{max}) between esophageal squamous cell carcinoma (ESCC), non-small-cell lung cancer (NSCLC), and papillary thyroid cancer (PTC). **METHODS:** This study consisted of 119 patients with ESCC (n=43), PTC (n=40), or NSCLC (n=36). We investigated the correlations between SUV_{max} and clinicopathological factors by using Spearman's correlation coefficient and the Kruskal-Wallis test. Multiple regression analysis was used to investigate which clinicopathological factors significantly affected SUV_{max} in each cancer type. **RESULTS:** The SUV_{max} correlated with glucose transporter-1

(GLUT-1) expression in NSCLC ($r=0.536$, $P=0.007$) and ESCC ($r=0.597$, $P<0.001$) but not in PTC. The SUVmax correlated with Ki-67 expression in NSCLC ($r=0.381$, $P=0.022$) and PTC ($r=0.374$, $P=0.017$) but not in ESCC. A high SUVmax was correlated with a higher pathological T stage (p-T stage) in NSCLC ($r=0.536$) and ESCC ($r=0.597$, both $P<0.001$) but not in PTC. An elevated SUVmax was significantly associated with pathological lymph node status (p-N) in NSCLC, but not in ESCC and PTC. In multiple regression analysis, p-T stage and GLUT-1 expression were statistically significant factors in ESCC, and p-T stage was a statistically significant factor in NSCLC. In PTC, Ki-67 showed a statistically significant association with SUVmax. CONCLUSION: SUVmax in NSCLC depended on the tumor invasion area; SUVmax in ESCC depended on tumor depth and GLUT-1 expression; and SUVmax in PTC might be associated with cell proliferation. The biological factors affecting SUVmax differ according to tumor type.

[312]

TÍTULO / TITLE: - Electricians' chrysotile asbestos exposure from electrical products and risks of mesothelioma and lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Regul Toxicol Pharmacol. 2013 Nov 1. pii: S0273-2300(13)00184-0. doi: 10.1016/j.yrtph.2013.10.008.

•• Enlace al texto completo (gratis o de pago) [1016/j.yrtph.2013.10.008](#)

AUTORES / AUTHORS: - Goodman JE; Peterson MK; Bailey LA; Kerper LE; Dodge DG

INSTITUCIÓN / INSTITUTION: - Gradient, 20 University Rd., Cambridge, MA 02138, United States. Electronic address: jgoodman@gradientcorp.com.

RESUMEN / SUMMARY: - Both mechanistic and epidemiology studies indicate chrysotile asbestos has a threshold below which it does not cause mesothelioma or lung cancer. We conducted a critical review to determine whether electricians are at increased risk for these cancers and, if so, whether their exposure to chrysotile in electrical products could be responsible. We found that most, but not all, epidemiology studies indicate electricians are at increased risk for both cancers. Studies that evaluated electricians' exposure to asbestos during normal work tasks have generally reported low concentrations in air; an experimental study showed that grinding or drilling products containing encapsulated chrysotile resulted in exposures to chrysotile fibers far below the OSHA PEL and the cancer no observed adverse effect level (NOAEL). Studies of other craftsmen who often work in the vicinity of electricians, such as insulators, reported asbestos (including amphibole) exposures that were relatively high. Overall, the evidence does not indicate that exposure to chrysotile in electrical products causes mesothelioma or lung cancer in electricians. Rather, the most likely cause of lung cancer in electricians is smoking, and the most likely cause of mesothelioma is exposure to amphibole asbestos as a result of renovation/demolition work or working in the proximity of other skilled craftsmen.

[313]

TÍTULO / TITLE: - Changing Rates for Liver and Lung Cancers in Qidong, China.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chem Res Toxicol. 2013 Nov 20.

- Enlace al texto completo (gratis o de pago) [1021/tx400313j](#)

AUTORES / AUTHORS: - Chen JG; Kensler TW

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, Qidong Liver Cancer Institute, Qidong, 226200, Jiangsu, China.

RESUMEN / SUMMARY: - Residents of Qidong, China are undergoing a rapid fluctuation in cancer incidence rates at many organ sites, reflecting a dynamic interplay of socio-behavioral, economic, and environmental factors. This Perspective On Statistical Trends examines the China age-standardized incidence rates (CASR), as tracked by the Qidong Cancer Registry for the past 40 years, for the two leading cancer killers in Qidong, liver and lung. Both cancer types are strongly influenced by environmental factors. The CASR for liver cancer has dropped nearly 50% in the last 4 decades, in part from access to deep-well drinking water in the 1970s with consequent diminished exposure to tumor promoting microcystins produced by blue-green algae. There have also been substantive reductions in exposures to dietary aflatoxins, as economic reform in the mid-1980s fostered a wholesale change in dietary staple from maize to rice. In men, lung cancer CASR has trebled over this period, likely driven by a high prevalence of smokers (approximately 65%) and an ever increasing smoking frequency in this population. Qidong women, by contrast, rarely smoke and have exhibited a flat CASR until the past decade where lung cancer rates have now doubled. This upturn may reflect an increasing burden of indoor and outdoor air pollution.

[314]

TÍTULO / TITLE: - Lung adenocarcinoma expression profile: one more layer of heterogeneity.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur Respir J. 2013 Nov;42(5):1180-2. doi: 10.1183/09031936.00087213.

- Enlace al texto completo (gratis o de pago) [1183/09031936.00087213](#)

AUTORES / AUTHORS: - Brambilla E

INSTITUCIÓN / INSTITUTION: - Institute Albert Bonniot, University Joseph Fourier, and Dept of Pathology, Grenoble University Hospital, Grenoble, France.

[315]

TÍTULO / TITLE: - Prognostic value of mitochondrial DNA content and G10398A polymorphism in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):3006-12. doi: 10.3892/or.2013.2783. Epub 2013 Oct 3.

- Enlace al texto completo (gratis o de pago) [3892/or.2013.2783](#)

AUTORES / AUTHORS: - Xu H; He W; Jiang HG; Zhao H; Peng XH; Wei YH; Wei JN; Xie CH; Liang C; Zhong YH; Zhang G; Deng D; Zhou YF; Zhou FX

INSTITUCIÓN / INSTITUTION: - Department of Radiation and Medical Oncology, Zhongnan Hospital of Wuhan University, Hubei Key Laboratory of Tumor Biological Behaviors and Hubei Cancer Clinical Study Center, Wuchang, Wuhan, Hubei 430071, P.R. China.

RESUMEN / SUMMARY: - Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer-related mortality worldwide. Mitochondrial dysfunction has been postulated to render cancer cells resistant to apoptosis based on the Warburg hypothesis. However, few studies have investigated the prognostic value of mitochondrial DNA (mtDNA) content and G10398A polymorphism in NSCLC patients. mtDNA copy number and G10398A polymorphism in 128 NSCLC tissue samples were assessed by real-time PCR (RT-PCR) and PCR-RFLP respectively, and their relationship to prognosis were analyzed by survival analysis and Cox proportional hazards model. In vitro, an mtDNA deletion A549 rho(0) cell model was utilized to assess the function of mtDNA on radiosensitivity. Cell cycle distribution and reactive oxygen species (ROS) were analyzed to elucidate the potential mechanisms. For the whole group, the median follow-up time and overall survival time were 22.5 and 23.4 months, respectively. Patients with high mtDNA content had a marginally longer survival time than patients with low mtDNA content (P=0.053). Moreover, patients with high mtDNA content plus 10398G had a significantly longer overall survival time compared with those having low mtDNA content plus 10398A (47 vs. 27 months, P<0.05). In addition, multivariate analysis showed that stage and low mtDNA content plus 10398A were the two most independent prognostic factors. In vitro, the A549 rho(0) cells showed more resistance to radiation than rho(+) cells. Following radiation, rho(0) cells showed delayed G2 arrest and lower ROS level as compared to rho(+) cells. In conclusion, the present study suggests that in patients with NSCLC, low mtDNA content plus 10398A could be a marker of poor prognosis which is associated with resistance to anticancer treatment caused by low mtDNA content plus 10398A polymorphism resulting in mitochondrial dysfunction.

[316]

TÍTULO / TITLE: - Interleukin-32 contributes to invasion and metastasis of primary lung adenocarcinoma via NF-kappaB induced matrix metalloproteinases 2 and 9 expression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cytokine. 2014 Jan;65(1):24-32. doi: 10.1016/j.cyto.2013.09.017. Epub 2013 Oct 18.

●● Enlace al texto completo (gratis o de pago) 1016/j.cyto.2013.09.017

AUTORES / AUTHORS: - Zeng Q; Li S; Zhou Y; Ou W; Cai X; Zhang L; Huang W; Huang L; Wang Q

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

RESUMEN / SUMMARY: - Interleukin (IL)-32 is a novel proinflammatory cytokine, which has been shown to play an important role in tumor growth and metastasis. Here, we discovered that IL-32 was aberrantly over-expressed in lung adenocarcinoma tissues and cell lines. Positive expression of IL-32 significantly correlated with the clinical staging, and lymph node and distant metastases. High expression of IL-32 was an independent indicator of poor prognosis in lung adenocarcinoma patients. Moreover, IL-32-facilitated cell migration and invasion in vitro was mediated through transactivation of the nuclear transcription factor (NF)-kappaB signaling pathway and subsequent upregulation of matrix metalloproteinase (MMP)-2 and MMP9 expression. These studies demonstrate that IL-32 plays a role in the tumor-associated inflammatory

microenvironment and that overexpression of IL-32 contributes to invasion and metastasis in primary lung adenocarcinoma, suggesting that it may have clinical utility as a prognostic biomarker and potential target for immunotherapy in lung adenocarcinoma.

[317]

TÍTULO / TITLE: - Allelic imbalance in 1p, 7q, 9p, 11p, 12q and 16q regions in non-small cell lung carcinoma and its clinical association: a pilot study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Biol Rep. 2013 Dec;40(12):6671-84. doi: 10.1007/s11033-013-2782-1. Epub 2013 Oct 4.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s11033-013-2782-1](#)

AUTORES / AUTHORS: - Czarnecka KH; Migdalska-Sek M; Antczak A; Pastuszek-Lewandoska D; Kordiak J; Nawrot E; Domanska D; Kaleta D; Gorski P; Brzezianska EB

INSTITUCIÓN / INSTITUTION: - Department of Molecular Bases of Medicine, Medical University of Lodz, Pomorska Str. 251, 92-213, Lodz, Poland.

RESUMEN / SUMMARY: - In lung cancer pathogenesis, genetic instability, i.e., loss of heterozygosity (LOH) and microsatellite instability (MSI) is a frequent molecular event, occurring at an early stage of cancerogenesis. The presence of LOH/MSI in non-small cell lung carcinoma (NSCLC) was found in many chromosomal regions, but exclusive of 3p their diagnostic value remains controversial. In this study we focused on other than 3p regions-1p31.2, 7q32.2, 9p21.3, 11p15.5, 12q23.2 and 16q22-the loci of many oncogenes and tumour suppressor genes. To analyze the potential role of LOH/MSI involved in NSCLC pathogenesis we allelotyped a panel of 13 microsatellite markers in a group of 56 cancer specimens. Our data demonstrate the presence of allelic loss for all (13) analyzed markers. Total LOH/MSI frequency in NSCLC was the highest for chromosomal region 11p15.5 (25.84 %), followed by 9p21.3 and 1p31.2 (19.87 and 16.67 % respectively). A statistically significant increase of total LOH/MSI frequency was detected for the 11p15.5 region ($p = 0.0301$; χ^2 test). The associations of total LOH/MSI frequency: 1) increase in 11p15.5 region ($p = 0.047$; χ^2 test) and 2) decrease in 7q32.2 region ($p = 0.037$; χ^2 test) have been statistically significant in AJCC III (American Joint Committee on Cancer Staging). In Fractional Allele Loss (FAL) index analysis, the correlation with cigarette addiction has been statistically significant. The increased amount of cigarettes smoked (pack years) in a lifetime correlates with increasing FAL ($p = 0.024$; Kruskal-Wallis test). These results demonstrate that LOH/MSI alternation in studied chromosomal regions is strongly influenced by tobacco smoking but do not seem to be pivotal NSCLC diagnostic marker with prognostic impact.

[318]

TÍTULO / TITLE: - Chemoprevention with Acetylsalicylic Acid, Vitamin D and Calcium Reduces Risk of Carcinogen-induced Lung Tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):4767-70.

AUTORES / AUTHORS: - Pommergaard HC; Burcharth J; Rosenberg J; Raskov H

INSTITUCIÓN / INSTITUTION: - Herlev Hospital - University of Copenhagen, Department of Surgery, Herlev Ringvej 75 - DK-2730 Herlev, Denmark.
hcpommergaard@gmail.com.

RESUMEN / SUMMARY: - Background/Aim: Research has shown that chemoprevention may be effective against the development of lung cancer. The purpose of the present study was to evaluate the effect of oral chemoprevention in a mouse model of tobacco carcinogen-induced lung tumor. MATERIALS AND METHODS: A total of 60 A/J mice were randomized to a normal diet, a diet with low calcium, or a chemoprevention diet with acetylsalicylic acid, 1-alpha 25(OH)2-vitamin D3 and calcium. In addition to the diet, mice received carcinogens by oral gavage for ten weeks. RESULTS: The chemoprevention diet significantly reduced the number of animals with tumors [1 vs. 13, ($p < 0.001$)] and the median number (range) of tumors [0 (0-1) vs. 1 (0-4), ($p < 0.001$)] compared to controls. No signs of toxicity in relation to the diets were observed. CONCLUSION: The chemoprevention diet had a protective effect against tumor development in the mouse lungs.

[319]

TÍTULO / TITLE: - Stereotactic body radiation therapy for primary lung cancers >3 centimeters.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1396-401. doi: 10.1097/JTO.0b013e3182a47181.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/JTO.0b013e3182a47181](#)

AUTORES / AUTHORS: - Cuaron JJ; Yorke ED; Foster A; Hsu M; Zhang Z; Liu F; Jackson A; Mychalczak B; Rosenzweig KE; Wu AJ; Rimner A

INSTITUCIÓN / INSTITUTION: - *Memorial Sloan-Kettering Cancer Center, New York, New York; and daggerMt. Sinai Hospital, New York, New York.

RESUMEN / SUMMARY: - INTRODUCTION: A retrospective analysis of the outcomes of stereotactic body radiation therapy (SBRT) in the treatment of large (>3 cm) non-small-cell lung cancers (NSCLCs). METHODS: Between February 2007 and November 2011, 63 patients with T2-T4N0 NSCLC were treated with SBRT. Toxicity was graded per Common Terminology Criteria for Adverse Events, version 4.0. Local failure-free survival (LFFS), recurrence-free survival, and overall survival curves were estimated using the Kaplan-Meier method and univariate analysis was performed using Cox regression. RESULTS: Median follow-up was 16.9 months. One- and 2-year LFFS was 88.8% and 75.7%, 1- and 2-year recurrence-free survival was 59.0% and 41.6%, and 1- and 2-year overall survival was 77.1% and 57.6%, respectively. Planning target volume less than 106 cm was associated with a significantly higher 1- and 2-year LFFS ($p = 0.05$). Grade 2 or higher acute and late pulmonary toxicities occurred in 19.3% and 19.3% of patients, respectively, and were not associated with common dose-volume parameters; 22.8% of patients developed grade 2 or higher chest wall pain, which was significantly associated with chest wall V30 70 cm or more ($p = 0.03$). CONCLUSIONS: SBRT for larger NSCLC tumors achieves high LFFS with acceptable toxicity. LFFS was worse with planning target volume 106 cm or more. Grade 2 or higher chest wall pain was associated with chest wall V30 70 cm or more.

[320]

TÍTULO / TITLE: - PA28gamma emerges as a novel functional target of tumour suppressor microRNA-7 in non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Cancer. 2013 Nov 26. doi: 10.1038/bjc.2013.728.

●● Enlace al texto completo (gratis o de pago) [1038/bjc.2013.728](#)

AUTORES / AUTHORS: - Xiong S; Zheng Y; Jiang P; Liu R; Liu X; Qian J; Gu J; Chang L; Ge D; Chu Y

INSTITUCIÓN / INSTITUTION: - 1] Department of Immunology and Key Laboratory of Molecular Medicine of Ministry of Education, Shanghai Medical College, Fudan University, Shanghai, People's Republic of China [2] Biotherapy Research Center of Fudan University, Shanghai, People's Republic of China [3] Department of Hematology/Oncology, The Second Hospital of Anhui Medical University, Hefei, Anhui, People's Republic of China.

RESUMEN / SUMMARY: - Background:MicroRNA-7 (miR-7) has been reported to be a tumour suppressor gene. However, whether it has a role in the growth of non-small-cell lung cancer (NSCLC) and what is its target involved in the tumour growth is still under investigation.Methods:NSCLC tissue sample, NSCLC cell lines and tissue microarray were investigated in this study. Total RNA, miRNA and protein were used for RT-PCR and western blot analysis. Immunohistochemistry was performed in tissues microarray. Cell culture and intervention experiments were performed in vitro and in vivo. Bioinformatics prediction, western blot and luciferase assay were identified the target of miR-7.Results:In this study, we found that the expression of miR-7 was significantly downregulated not only in NSCLC cell lines, but also in human NSCLC tissues compared with the matched adjacent tissues. Restoration of its expression through miR-7 mimics in A549 and H1299 NSCLC cells inhibited cell proliferation, colony formation, and cell-cycle progression in vitro. More importantly, the tumorigenicity in nude mice was reduced after administration of miR-7 in vivo. In advance, through bioinformatic analysis, luciferase assay and western blot, we identified a novel target of miR-7, PA28gamma (a proteasome activator) to be enrolled in the regulation with tumour. PA28gamma mRNA and protein levels are markedly upregulated in NSCLC cell lines and tumour samples, exhibiting a strong inverse relation with that of miR-7. In addition, knockdown of PA28gamma induced similar effects as overexpression of miR-7 in NSCLC cells. Furthermore, miR-7 overexpression or silencing of PA28gamma reduced the cyclinD1 expression at mRNA and protein level in NSCLC cell lines.Conclusion:All these findings strongly imply that the overexpression of PA28gamma resulted from miR-7 downexpression in NSCLC has an important role in promoting cancer cell progress and consequently results in NSCLC growth. Thus, strategies targeting PA28gamma and/or miR-7 may become promising molecular therapies in NSCLC treatment.British Journal of Cancer advance online publication, 26 November 2013; doi:10.1038/bjc.2013.728 www.bjcancer.com.

[321]

TÍTULO / TITLE: - Comparison of exposure assessment methods in a lung cancer case-control study: performance of a lifelong task-based questionnaire for asbestos and PAHs.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Occup Environ Med. 2013 Dec;70(12):884-91. doi: 10.1136/oemed-2013-101467. Epub 2013 Sep 18.

●● [Enlace al texto completo \(gratis o de pago\) 1136/oemed-2013-101467](#)

AUTORES / AUTHORS: - Bourgard E; Wild P; Gonzalez M; Fevotte J; Penven E; Paris C

INSTITUCIÓN / INSTITUTION: - Departement Epidemiologie en Entreprise, Institut National de Recherche et de Securite (INRS), Vandoeuvre-les-Nancy, France.

RESUMEN / SUMMARY: - **OBJECTIVE:** To describe the performance of a lifelong task-based questionnaire (TBQ) in estimating exposures compared with other approaches in the context of a case-control study. **METHODS:** A sample of 93 subjects was randomly selected from a lung cancer case-control study corresponding to 497 jobs. For each job, exposure assessments for asbestos and polycyclic aromatic hydrocarbons (PAHs) were obtained by expertise (TBQ expertise) and by algorithm using the TBQ (TBQ algorithm) as well as by expert appraisals based on all available occupational data (REFERENCE expertise) considered to be the gold standard. Additionally, a Job Exposure Matrix (JEM)-based evaluation for asbestos was also obtained. On the 497 jobs, the various evaluations were contrasted using Cohen's kappa coefficient of agreement. Additionally, on the total case-control population, the asbestos dose-response relationship based on the TBQ algorithm was compared with the JEM-based assessment. **RESULTS:** Regarding asbestos, the TBQ-exposure estimates agreed well with the REFERENCE estimate (TBQ expertise: level-weighted kappa (lwk)=0.68; TBQ algorithm: lwk=0.61) but less so with the JEM estimate (TBQ expertise: lwk=0.31; TBQ algorithm: lwk=0.26). Regarding PAHs, the agreements between REFERENCE expertise and TBQ were less good (TBQ expertise: lwk=0.43; TBQ algorithm: lwk=0.36). In the case-control study analysis, the dose-response relationship between lung cancer and cumulative asbestos based on the JEM is less steep than with the TBQ-algorithm exposure assessment and statistically non-significant. **CONCLUSIONS:** Asbestos-exposure estimates based on the TBQ were consistent with the REFERENCE expertise and yielded a steeper dose-response relationship than the JEM. For PAHs, results were less clear.

[322]

TÍTULO / TITLE: - Signaling Pathways Modulating Dependence of Lung Cancer on Mutant Epidermal Growth Factor Receptor and Mechanisms of Intrinsic and Acquired Resistance to Tyrosine Kinase Inhibitors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Wannesson L; Viteri S; Costa C; Karachaliou N; Molina-Vila MA; Rosell R

INSTITUCIÓN / INSTITUTION: - Oncology Institute of Southern Switzerland, CH6500 Bellinzona, Switzerland. Luciano.Wannesson@eoc.ch.

RESUMEN / SUMMARY: - A new era in lung cancer targeted therapy arrived with the discovery of a subset of lung adenocarcinomas harboring activating mutations of the epidermal growth factor receptor (EGFR), whose tyrosine kinase activity can be selectively blocked by small molecule pharmaceuticals referred as tyrosine kinase inhibitors (TKIs). This was the starting point for a less toxic and more effective

treatment strategy for a disease that has historically presented as chemorefractory and highly lethal. In spite of this progress, only 80% of the patients treated with this class of compounds will obtain a clinical benefit, of variable magnitude and duration, with remaining patients being primarily refractory to the treatment. Moreover, responding tumors will eventually develop acquired resistance to TKIs and progress to more advanced stages. In this review we summarize the current knowledge with regard to the mechanisms leading to tumor regression and the modifiers of this primary response that determine significant variability in sensitivity of tumors harboring EGFR activating mutations, ranging from complete remission to primary refractoriness. We also analyze the mechanisms of secondary resistance and the strategies the scientific community is exploring in order to overcome these barriers.

[323]

TÍTULO / TITLE: - Signaling Intermediates (MAPK and PI3K) as Therapeutic Targets in NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Ciuffreda L; Incani UC; Steelman LS; Abrams SL; Falcone I; Curatolo AD; Chappell WH; Franklin RA; Vari S; Cognetti F; McCubrey JA; Milella M

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology A, Regina Elena National Cancer Institute, Via Elio Chianesi 53, 00144, Rome, Italy.

michelemilella@hotmail.com.

RESUMEN / SUMMARY: - The RAS/RAF/MEK/ ERK and the PI3K/AKT/mTOR pathways govern fundamental physiological processes, such as cell proliferation, differentiation, metabolism, cytoskeleton reorganization and cell death and survival. Constitutive activation of these signal transduction pathways is a required hallmark of cancer and dysregulation, on either genetic or epigenetic grounds, of these pathways has been implicated in the initiation, progression and metastatic spread of lung cancers. Targeting components of the MAPK and PI3K cascades is thus an attractive strategy in the development of novel therapeutic approaches to treat lung cancer, although the use of single pathway inhibitors has met with limited clinical success so far. Indeed, the presence of intra- and inter-pathway compensatory loops that re-activate the very same cascade, either upstream or downstream the point of pharmacological blockade, or activate the alternate pathway following the blockade of one signaling cascade has been demonstrated, potentially driving preclinical (and possibly clinical) resistance. Therefore, the blockade of both pathways with combinations of signaling inhibitors might result in a more efficient anti-tumor effect, and thus potentially overcome and/or delay clinical resistance, as compared with single agent. The current review aims at summarizing the current status of preclinical and clinical research with regard to pathway crosstalks between the MAPK and PI3K cascades in NSCLC and the rationale for combined therapeutic pathway targeting.

[324]

TÍTULO / TITLE: - Lung Cancer Screening: Review and Performance Comparison Under Different Risk Scenarios.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) 1007/s00408-013-9517-x

AUTORES / AUTHORS: - Tota JE; Ramanakumar AV; Franco EL

INSTITUCIÓN / INSTITUTION: - Department of Oncology, McGill University, 546 Pine Avenue West, Montreal, H2W1S6, QC, Canada, joseph.tota@mail.mcgill.ca.

RESUMEN / SUMMARY: - Lung cancer is currently one of the most common malignant diseases and is responsible for substantial mortality worldwide. Compared with never smokers, former smokers remain at relatively high risk for lung cancer, accounting for approximately half of all newly diagnosed cases in the US. Screening offers former smokers the best opportunity to reduce their risk of advanced stage lung cancer and there is now evidence that annual screening using low-dose computed tomography (LDCT) is effective in preventing mortality. Studies are being conducted to evaluate whether the benefits of LDCT screening outweigh its costs and potential harms and to determine the most appropriate workup for patients with screen-detected lung nodules. Program efficiency would be optimized by targeting high-risk current smokers, but low uptake among this group is a concern. Former smokers may be invited for screening; however, if fewer long-term current smokers and more former smokers with long quit duration elect to attend, this could have very adverse effects on cost and screening test parameters. To illustrate this point, we present three possible screening scenarios with lung cancer prevalence ranging from between 0.62 and 5.0 %. In summary, cost-effectiveness of lung cancer screening may be improved if linked to successful smoking cessation programs and if better approaches are developed to reach very high-risk patients, e.g., long-term current smokers or others based on more accurate risk prediction models.

[325]

TÍTULO / TITLE: - Mitochondria in Lewis lung carcinoma cells under the effect of magnetosensitive nanocomplex and radiofrequency hyperthermia.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Bull Exp Biol Med. 2013 Aug;155(4):484-7.

AUTORES / AUTHORS: - Orel VE; Grabovoy AN; Romanov AV; Kharkevich NA; Schepotin IB

INSTITUCIÓN / INSTITUTION: - National Cancer Institute, Kiev, Ukraine. v-orel@i.com.ua; v-orel@voliacable.com.

RESUMEN / SUMMARY: - Electron microscopic study of Lewis lung carcinoma cell mitochondria after intravenous injection of a magnetosensitive nanocomplex based on ferric oxide (Fe₃O₄) nanoparticles and doxorubicin followed by radiofrequency hyperthermia showed that a common increase of the electron density of the cytoplasm was paralleled by mitochondrial edema in comparison with organelles of animals receiving doxorubicin alone. These changes were accompanied by virtually total lysis of the cristae and sharp clarification of mitochondrial matrix, which was seen from appreciable increase in mitochondria image brightness. Morphometric analysis showed lesser perimeter, area, and mean radius of the tumor cell mitochondria in animals receiving the injection of magnetosensitive nanocomplex and exposed to radiofrequency hyperthermia in comparison with those injected with doxorubicin alone. Histograms of distribution of the perimeter, area, and mean radius of the mitochondria after combined exposure to the nanocomplex and hyperthermia showed bimodal

asymmetrical distribution. Injection of the magnetosensitive nanocomplex followed by radiosensitive hyperthermia led to more significant impairment of the tumor cell mitochondrial ultrastructure than doxorubicin alone.

[326]

TÍTULO / TITLE: - Clinical Application of Pharmacogenetics of non-small cell lung cancer (NSCLC): time to “work it out”?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Galvani E; Toffalorio F; Peters GJ; De Pas T; Giovannetti E

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology VU University Medical Center De Boelelaan 1117 1081 HV Amsterdam The Netherlands.

elisa.giovannetti@gmail.com.

RESUMEN / SUMMARY: - The disappointing results in long-term survival of patients affected by non-small cell lung cancer (NSCLC) may be attributed, at least in part, to the lack of knowledge on the way by which genetic characteristics in normal and neoplastic cells affect responsiveness as well as metabolism of chemotherapy and new targeted agents. This issue deserves further pharmacogenetics studies, in order to select patients who may benefit from treatments that best match the individual and tumor genetic profile, thus allowing maximum activity and minimal toxicity. Even if most meta-analyses in NSCLC yielded contradictory results, a number of potential biomarkers for sensitivity/resistance to conventional chemotherapeutic agents such as gemcitabine, platinum-compounds, pemetrexed and taxanes have been proposed. Similarly, recent studies suggested the role of key polymorphisms in the prediction of toxicity to EGFR-targeted agents. However, larger prospective randomized trials of customized therapy to validate these biomarkers are still needed. Other critical points include the standardization of technical procedures and additional investigation to unravel pivotal factors influencing genotype-phenotype relationships. From this perspective, functional studies to clarify pharmacokinetics/pharmacodynamics interactions are critical for the pharmacogenetic optimization of anti-cancer regimens. Finally, due to the development of high-throughput technologies to decipher genetic characteristics, the traditional pharmacogenetic approach relying only on candidate genes suspected of affecting drug response/metabolism can be implemented by whole exome analyses providing further lists of potential predictive alleles. The clinical implementation of such pharmacogenetics/genomics studies as well as of therapeutic drug monitoring could enable clinicians to personalize treatment to enhance efficacy and/or limit toxicity.

[327]

TÍTULO / TITLE: - Hepatocyte growth factor and HER2/neu downregulate expression of apoptosis-inducing factor in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Nov 25. doi: 10.3892/or.2013.2867.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2867](#)

AUTORES / AUTHORS: - Chiang YY; Chow KC; Lin TY; Chiang IP; Fang HY

INSTITUCIÓN / INSTITUTION: - Department of Dental Laboratory Technology, Central Taiwan University of Science and Technology, Taichung, Taiwan, R.O.C.

RESUMEN / SUMMARY: - Our previous study showed that patients with advanced stages of non-small cell lung cancer (NSCLC) were frequently detected with upregulation of hepatocyte growth factor (HGF). In vitro, HGF reduced expression of apoptosis-inducing factor (AIF) and cisplatin sensitivity in NSCLC cells. The effect of HGF was via HGF receptor (c-MET) and the downstream effector, focal adhesion kinase (FAK). In this study, we determined the prognostic value of AIF in NSCLC patients. AIF expression was determined by immunohistochemistry and immunoblotting. Our data show that AIF expression was associated with better prognosis. Expression of AIF inversely correlated with that of positive NSCLC markers, e.g., dihydrodiol dehydrogenase (DDH), c-MET, short oncostatin M receptor (OSMRs), matrix metalloproteinase (MMP)-1, and HER2/neu, which were closely associated with drug resistance, tumor recurrence, metastasis and poor prognosis. Noteworthy, silence of HER2/neu gene expression increases AIF level and drug sensitivity. Addition of HGF inhibits AIF expression in HER2/neu-silenced cells. These results suggested that both HGF and HER2/neu affect drug resistance by regulating AIF expression in NSCLC.

[328]

TÍTULO / TITLE: - Clinicopathologic analysis of ROS1-rearranged non-small-cell lung cancer and proposal of a diagnostic algorithm.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1445-50. doi: 10.1097/JTO.0b013e3182a4dd6e.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/JTO.0b013e3182a4dd6e](#)

AUTORES / AUTHORS: - Go H; Kim DW; Kim D; Keam B; Kim TM; Lee SH; Heo DS; Bang YJ; Chung DH

INSTITUCIÓN / INSTITUTION: - Departments of *Pathology and daggerInternal Medicine, Seoul National University Hospital, Seoul, Korea; and double daggerCancer Research Institute and section signDepartment of Biomedical Sciences, Seoul National University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - INTRODUCTION: We sought to evaluate the clinical and pathological characteristics of patients with non-small-cell lung cancer (NSCLC) that harbored a ROS1 rearrangement. METHODS: Four hundred fifty-one Korean patients with resected NSCLC (the resected group) were examined for ROS1 rearrangements using a tissue microarray and ROS1 fluorescence in situ hybridization and analyzed for clinical and pathological features. Sixty-four patients with advanced pulmonary adenocarcinoma with no known oncogenic aberrations (the advanced group) were also screened for ROS1 rearrangements. RESULTS: Of the 451 consecutive patients from the resected group, ROS1 rearrangements were detected in eight cases (1.8%). In the advanced group, an additional eight patients (12.5%) were identified as harboring ROS1 rearrangements. ROS1 rearrangement was detected exclusively in adenocarcinomas and occurred more frequently in women than in men. With the exception of one patient with an EGFR deletion mutation in exon 19, ROS1-positive adenocarcinomas in all patients revealed no alterations in ALK, EGFR, KRAS, or MET

genes. Most ROS1-rearranged tumors showed solid and papillary patterns.
CONCLUSIONS: ROS1 rearrangements were detected in 1.8% of patients with resected NSCLC and were detected exclusively in adenocarcinomas, which is similar to the frequency detected in non-Asian patients. We suggest that ROS1 screening in adenocarcinoma patients with no known oncogenic aberrations is an effective strategy to find ROS1 rearrangements in NSCLC.

[329]

TÍTULO / TITLE: - AHNAK is highly expressed and plays a key role in cell migration and invasion in mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Nov 20. doi: 10.3892/ijo.2013.2183.

●● [Enlace al texto completo \(gratis o de pago\) 3892/ijo.2013.2183](#)

AUTORES / AUTHORS: - Sudo H; Tsuji AB; Sugyo A; Abe M; Hino O; Saga T

INSTITUCIÓN / INSTITUTION: - Diagnostic Imaging Program, Molecular Imaging Center, National Institute of Radiological Sciences, Inage-ku, Chiba 2638555, Japan.

RESUMEN / SUMMARY: - The worldwide incidence of the highly aggressive tumor mesothelioma is expected to increase. Mesothelioma is classified into three main histological subtypes: epithelioid, sarcomatoid and biphasic. Although the pathological diagnostic markers for epithelioid are established, to date no adequate marker for sarcomatoid mesothelioma has been found. Thus, a reliable diagnostic marker of sarcomatoid mesothelioma is necessary. In this study, to identify an unknown protein with 120 kDa expressed only in the mesothelioma cell line 211H, we conducted proteomic analysis and found five candidate proteins. One such protein, AHNAK, was highly expressed in all seven mesothelioma cell lines (211H, H28, H226, H2052, H2452, MESO1 and MESO4), but not in the mesothelial cell line MeT-5A by RT-PCR and immunofluorescence staining. Furthermore, we confirmed high AHNAK expression not only in xenografts but also in human mesothelioma specimens including sarcomatoid, epithelioid and biphasic mesothelioma using immunohistochemical staining. These findings suggest that AHNAK has the potential to be a new marker for detecting mesothelioma. Since AHNAK is involved in cell migration and invasion in other metastatic tumor cells, we conducted migration and invasion assays in mesothelioma cell lines. The number of migrating cells in six of seven mesothelioma cell lines and the number of invading cells in all seven cell lines were significantly increased compared with those in MeT-5A. Knockdown of AHNAK significantly reduced the cell migration and invasion ability in all seven mesothelioma cell lines. These results support further clinical evaluation of the association of AHNAK and metastasis in mesothelioma.

[330]

TÍTULO / TITLE: - Reduced Fatalism and Increased Prevention Behavior After Two High-Profile Lung Cancer Events.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Health Commun. 2013 Nov 25.

●● [Enlace al texto completo \(gratis o de pago\) 1080/10810730.2013.821553](#)

AUTORES / AUTHORS: - Portnoy DB; Leach CR; Kaufman AR; Moser RP; Alfano CM

INSTITUCIÓN / INSTITUTION: - a Cancer Prevention Fellowship Program, Center for Cancer Training, and the Behavioral Research Program, Division of Cancer Control and Population Sciences , National Cancer Institute , Rockville , Maryland , USA.

RESUMEN / SUMMARY: - The positive impact of media coverage of high-profile cancer events on cancer prevention behaviors is well-established. However, less work has focused on potential adverse psychological reactions to such events, such as fatalism. Conducting 3 studies, the authors explored how the lung cancer death of Peter Jennings and diagnosis of Dana Reeve in 2005 related to fatalism. Analysis of a national media sample in Study 1 found that media coverage of these events often focused on reiterating the typical profile of those diagnosed with lung cancer; 38% of the media mentioned at least 1 known risk factor for lung cancer, most often smoking. Data from a nationally representative survey in Study 2 found that respondents reported lower lung cancer fatalism, after, compared with before, the events (OR = 0.16, 95% CI [0.03, 0.93]). A sustained increase in call volume to the national tobacco Quitline after these events was found in Study 3. These results suggest that there is a temporal association between high-profile cancer events, the subsequent media coverage, psychological outcomes, and cancer prevention behaviors. These results suggest that high-profile cancer events could be leveraged as an opportunity for large-scale public health communication campaigns through the dissemination of cancer prevention messages and services.

[331]

TÍTULO / TITLE: - Novel compound PS-101 exhibits selective inhibition in non-small-cell lung cancer cell by blocking the EGFR-driven antiapoptotic pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Pharmacol. 2013 Dec 15;86(12):1721-30. doi: 10.1016/j.bcp.2013.10.013. Epub 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) [1016/j.bcp.2013.10.013](#)

AUTORES / AUTHORS: - Zhang GH; Cai LJ; Wang YF; Zhou YH; An YF; Liu YC; Peng Y; Chen ZF; Liang H

INSTITUCIÓN / INSTITUTION: - State Key Laboratory Cultivation Base for the Chemistry and Molecular Engineering of Medicinal Resources, School of Chemistry & Pharmacy, Guangxi Normal University, Guilin 541004, China.

RESUMEN / SUMMARY: - This study investigated the anticancer effect of a novel compound PS-101 in human lung cancer cells. By phenotype screening, PS-101 exhibited highly selective inhibition in EGFR-overexpressed non-small cell lung cancer cells NCI-H460 and A549 while displaying no obvious toxicity to normal hepatic cell HL-7702, lung fibroblast cell WI-38, liver cancer cell BEL-7404 and gastric cancer cell MCG-803. A combination of cell viability assay, immunoblotting, and RNA interference revealed that PS-101 induced EGFR-dependent inhibition selectivity. Further studies showed that PS-101 caused cell cycle arrest at G1 phase, changed cell size, induced apoptosis and led to cell death by increasing the proportion of sub-G1 cells. Molecular mechanism studies suggested that blocking the EGFR-driven antiapoptotic pathway is essential for PS-101-induced apoptosis. The contribution of blocking the EGFR-driven antiapoptotic pathway was verified through examines abundance of likely candidate proteins and RNA interference. The root cause for increase in BAD and decrease in Bcl-2 which altogether initiated caspase-dependent apoptosis were predominantly due

to down-regulation the expression of EGFR after PS-101 treatment. PS-101 strongly down-regulated the EGFR expression to trigger proapoptotic protein BAD increase and antiapoptotic protein Bcl-2 decrease, which altogether activated effector caspase-3/9 to initiate cell apoptosis. Taken together, these results suggest that PS-101 may be a potential candidate for cancer therapy against human lung cancer.

[332]

TÍTULO / TITLE: - Novel compound 1,3-bis (3,5-dichlorophenyl) urea inhibits lung cancer progression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Pharmacol. 2013 Dec 15;86(12):1664-72. doi: 10.1016/j.bcp.2013.09.022. Epub 2013 Oct 4.

●● Enlace al texto completo (gratis o de pago) [1016/j.bcp.2013.09.022](#)

AUTORES / AUTHORS: - Singhal SS; Figarola J; Singhal J; Nagaprashantha L; Berz D; Rahbar S; Awasthi S

INSTITUCIÓN / INSTITUTION: - Departments of Diabetes & Metabolic Diseases Research, and Medical Oncology, Beckman Research Institute, City of Hope, Comprehensive Cancer Center, Duarte, CA 91010, USA. Electronic address: ssinghal@coh.org.

RESUMEN / SUMMARY: - The successful clinical management of lung cancer is limited by frequent loss-of-function mutations in p53 which cooperates with chronic oxidant-stress induced adaptations in mercapturic acid pathway (MAP) which in turn regulates critical intracellular signaling cascades that determine therapeutic refractoriness. Hence, we investigated the anti-cancer effects and mechanisms of action of a novel compound called 1,3-bis(3,5-dichlorophenyl) urea (COH-SR4) in lung cancer. Treatment with COH-SR4 effectively inhibited the survival and clonogenic potential along with inducing apoptosis in lung cancer cells. COH-SR4 treatment caused the inhibition of GST activity and G0/G1 cell cycle arrest and inhibited the expression of cell cycle regulatory proteins CDK2, CDK4, cyclin A, cyclin B1, cyclin E1, and p27. The COH-SR4 activated AMPK pathway and knock-down of AMPK partially reversed the cytotoxic effects of COH-SR4 in lung cancer. COH-SR4 treatment lead to regression of established xenografts of H358 lung cancer cells without any overt toxicity. The histopathology of resected tumor sections revealed an increase in pAMPK, a decrease in the nuclear proliferative marker Ki67 and angiogenesis marker CD31. Western-blot analyses of resected tumor lysates revealed a decrease in pAkt and anti-apoptotic protein Bcl2 along with an increase in pAMPK, pro-apoptotic protein Bax and cleaved PARP levels. Importantly, COH-SR4 lead to decrease in the mesenchymal marker vimentin and increase in the normal epithelial marker E-cadherin. The results from our in-vitro and in-vivo studies reveal that COH-SR4 represents a novel candidate with strong mechanistic relevance to target aggressive and drug-resistant lung tumors.

[333]

TÍTULO / TITLE: - Targets in Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Pharmacol. 2013 Sep 30. pii: S0006-2952(13)00619-9. doi: 10.1016/j.bcp.2013.09.014.

- Enlace al texto completo (gratis o de pago) 1016/j.bcp.2013.09.014

AUTORES / AUTHORS: - Teicher BA

INSTITUCIÓN / INSTITUTION: - National Cancer Institute, Bethesda MD. Electronic address: teicherba@mail.nih.gov.

RESUMEN / SUMMARY: - Recurrent small cell lung cancer is a recalcitrant malignancy. The application of genomic technologies has begun to elucidate the large number of genetic abnormalities in SCLC. Several cell surface receptors are known to be overexpressed by SCLC in clinic specimens and cell in culture including GPCRs such as the bradykinin receptor, the chemokine receptor CXCR4, the vasopressin receptor and the three bombesin receptors. The glucose transporter GLUT1, the tetraspanin family member PETA/CD151 and the immunoglobulin superfamily member ALCAM/CD166 are also overexpressed by SCLC. NCAM/CD56 is overexpressed by nearly all SCLC and is currently the target for an antibody drug conjugate in Phase II trial. Although SCLC is not considered a RTK driven disease, IGF1R and FGFRs are often overexpressed by SCLC. SCLC aberrantly expresses several developmental transcription factors including ASCL1, SOX2, 4, and 11, OCT4, NANOG, PAX5; however, overexpression of MYC may be a driver in SCLC. Like other cancers, SCLC expresses survival factors and uses aerobic glycolysis as a major source of ATP. The drawback of many potential targets overexpressed by SCLC is expression of the same proteins by normal tissues. We are slowly learning more about the molecular abnormalities that occur in SCLC; however, therapeutic impact from new findings remains a goal to work toward.

[334]

TÍTULO / TITLE: - The role of the tumor-microenvironment in lung cancer-metastasis and its relationship to potential therapeutic targets.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Treat Rev. 2013 Oct 15. pii: S0305-7372(13)00205-3. doi: 10.1016/j.ctrv.2013.10.001.

- Enlace al texto completo (gratis o de pago) 1016/j.ctrv.2013.10.001

AUTORES / AUTHORS: - Wood SL; Pernemalm M; Crosbie PA; Whetton AD

INSTITUCIÓN / INSTITUTION: - Faculty Institute of Cancer Sciences, University of Manchester, Manchester Academic Health Science Centre, Wolfson Molecular Imaging Centre, Manchester M20 3LJ, UK. Electronic address: steven.wood@manchester.ac.uk.

RESUMEN / SUMMARY: - Non-small cell lung cancer (NSCLC) accounts for >80% of lung cancer cases and currently has an overall five-year survival rate of only 15%. Patients presenting with advanced stage NSCLC die within 18-months of diagnosis. Metastatic spread accounts for >70% of these deaths. Thus elucidation of the mechanistic basis of NSCLC-metastasis has potential to impact on patient quality of life and survival. Research on NSCLC metastasis has recently expanded to include non-cancer cell components of tumors-the stromal cellular compartment and extra-cellular matrix components comprising the tumor-microenvironment. Metastasis (from initial primary tumor growth through angiogenesis, intravasation, survival in the bloodstream, extravasation and metastatic growth) is an inefficient process and few released cancer cells complete the entire process. Micro-environmental interactions assist each of these steps and discovery of the mechanisms by which tumor cells co-operate with the

micro-environment are uncovering key molecules providing either biomarkers or potential drug targets. The major sites of NSCLC metastasis are brain, bone, adrenal gland and the liver. The mechanistic basis of this tissue-tropism is beginning to be elucidated offering the potential to target stromal components of these tissues thus targeting therapy to the tissues affected. This review covers the principal steps involved in tumor metastasis. The role of cell-cell interactions, ECM remodeling and autocrine/paracrine signaling interactions between tumor cells and the surrounding stroma is discussed. The mechanistic basis of lung cancer metastasis to specific organs is also described. The signaling mechanisms outlined have potential to act as future drug targets minimizing lung cancer metastatic spread and morbidity.

[335]

TÍTULO / TITLE: - Epigenetic regulation of ANKRD18B in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Carcinog. 2013 Nov 19. doi: 10.1002/mc.22101.

●● [Enlace al texto completo \(gratis o de pago\) 1002/mc.22101](#)

AUTORES / AUTHORS: - Liu WB; Han F; Jiang X; Yin L; Chen HQ; Li YH; Liu Y; Cao J; Liu JY

INSTITUCIÓN / INSTITUTION: - Institute of Toxicology, College of Preventive Medicine, Third Military Medical University, Chongqing 400038, P.R. China.

RESUMEN / SUMMARY: - The identification of the key genetic and epigenetic changes underlying lung carcinogenesis would aid effective early diagnosis and targeted therapies for lung cancer. In this study, we screened a novel hypermethylated gene ankyrin repeat domain 18B (ANKRD18B), to determine whether it is regulated by DNA methylation and clarify its biological and clinical implications in lung cancer. Methylation status and expression level were analyzed by methylation-specific PCR, bisulfite genomic sequencing, and quantitative reverse transcription-polymerase chain reaction (qRT-PCR). We detected ANKRD18B hypermethylation in 52 of 98 (53.1%) primary lung cancer tissues and in nine of 10 (90%) cell lines, whereas no methylation was seen in 10 normal lung tissue samples. ANKRD18B methylation was more frequently observed in patients with poor differentiation ($P < 0.05$). Notably, 62 pairs of samples from patients whose tumor tissue showed hypermethylation of ANKRD18B exhibited the same aberrant methylation in 72.7% and 69.7% of their corresponding plasma and sputum samples, respectively; whereas no hypermethylation of ANKRD18B was detected in the sputum and plasma from patients whose tumor sample lacked this alteration. In addition, ANKRD18B mRNA expression was significantly decreased or silenced in lung cancer tissues and cell lines associated with hypermethylation of the ANKRD18B region. Demethylation agent 5-aza-2'-deoxycytidine significantly increased ANKRD18B mRNA expression in lung cancer cell lines. Furthermore, overexpression of ANKRD18B suppressed lung cancer cell growth. These results suggest that the expression of ANKRD18B is regulated by CpG island hypermethylation in lung cancer. Our findings confirm the importance of the identification of new markers of epigenetic dysregulation in cancer. © 2013 Wiley Periodicals, Inc.

[336]

TÍTULO / TITLE: - Immunohistochemical detection of ROS1 is useful for identifying ROS1 rearrangements in lung cancers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mod Pathol. 2013 Nov 1. doi: 10.1038/modpathol.2013.192.

●● Enlace al texto completo (gratis o de pago) [1038/modpathol.2013.192](#)

AUTORES / AUTHORS: - Yoshida A; Tsuta K; Wakai S; Arai Y; Asamura H; Shibata T; Furuta K; Kohno T; Kushima R

INSTITUCIÓN / INSTITUTION: - Division of Pathology and Clinical Laboratories, National Cancer Center Hospital, Tokyo, Japan.

RESUMEN / SUMMARY: - The recent discovery and characterization of an oncogenic ROS1 gene fusion in a subset of lung cancers has raised significant clinical interest because small molecule inhibitors may be effective to these tumors. As lung cancers with ROS1 rearrangements comprise only 1-3% of lung adenocarcinomas, patients with such tumors must be identified to gain optimal benefit from molecular therapy. Recently, immunohistochemical analyses using a novel anti-ROS1 rabbit monoclonal antibody (D4D6) have shown promise for accurate identification of ROS1-rearranged cancers. To validate this finding, we compared the immunostaining results of tissue microarrays (TMAs) containing 17 ROS1-rearranged and 253 ROS1-non-rearranged lung carcinomas. All 17 ROS1-rearranged cancers showed ROS1 immunoreactivity mostly in a diffuse and moderate-to-strong manner with an H-score range of 5-300 (median, 260). In contrast, 69% of ROS1-non-rearranged cancers lacked detectable immunoreactivity, whereas the remaining 31% showed reactivity mainly in a weak or focal manner. The H-score for the entire ROS1-non-rearranged group ranged from 0 to 240 (median, 0). The difference in H-score between the two cohorts was statistically significant, and the H-score cutoff (≥ 150) allowed optimal discrimination (94% sensitivity and 98% specificity). Similar but slightly less-specific performance was achieved using the extent of diffuse ($\geq 75\%$) staining or $\geq 2+$ staining intensity as cutoffs. CD74-ROS1 and EZR-ROS1 fusions were significantly associated with at least focal globular immunoreactivity and plasma membranous accentuation, respectively, and these patterns were specific to ROS1-rearranged cases. Although full-length ROS1 is expressed in some ROS1-non-rearranged cases, we showed that establishment of an optimal set of interpretative criteria makes ROS1 immunohistochemistry a valuable method to rapidly and accurately screen lung cancer patients for appropriate molecular therapy. Modern Pathology advance online publication, 1 November 2013; doi:10.1038/modpathol.2013.192.

[337]

TÍTULO / TITLE: - Effect of AZD1480 in an epidermal growth factor receptor-driven lung cancer model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 29. pii: S0169-5002(13)00455-8. doi: 10.1016/j.lungcan.2013.10.011.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.011](#)

AUTORES / AUTHORS: - Murakami T; Takigawa N; Ninomiya T; Ochi N; Yasugi M; Honda Y; Kubo T; Ichihara E; Hotta K; Tanimoto M; Kiura K

INSTITUCIÓN / INSTITUTION: - Department of Hematology, Oncology and Respiratory Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan.

RESUMEN / SUMMARY: - **OBJECTIVE:** STAT3 plays a vital role in inducing and maintaining a pro-carcinogenic inflammatory microenvironment and is reported to be a critical mediator of the oncogenic effects of EGFR mutations. STAT3 activation is mediated through JAK family kinases. We investigated the effect of the JAK1/2 inhibitor AZD1480 on lung tumors induced by an activating EGFR mutation. **MATERIALS AND METHODS:** Three EGFR tyrosine kinase inhibitor-resistant cell lines (RPC-9, PC-9/Van-R and PC-9/ER3) established from PC-9 harboring an EGFR exon19 deletion mutation were used. Growth inhibition was measured using an MTT assay. Effects of AZD1480 were also evaluated in the xenograft model and in the EGFR transgenic mice model. Protein expressions were assessed by immunoblotting and immunohistochemistry. Group differences were compared using Student's t-test. To evaluate the efficacy of AZD1480 on survival, AZD1480 or vehicle was administered orally from 7 weeks of age of the transgenic mice. Overall survival curves were calculated using the Kaplan-Meier method. **RESULTS:** The sensitivities of resistant and parent cells to AZD1480 were similar in vitro. AZD1480 (30 or 50mg/kg/day, per os) reduced angiogenesis and revealed significant tumor regression in a mouse xenograft model. Subsequently, the transgenic mice were treated with AZD1480 (30mg/kg/day) or vehicle alone. The numbers of lung tumors (long axis exceeding 1mm) in the AZD1480-treated group and control group were 0.37+/-0.18 and 2.25+/-0.53 (p<0.001), respectively. AZD1480 treatment suppressed pSTAT3, pJAK1, pJAK2 and angiogenesis. The median survival time in the AZD1480-treated group (217 days) was significantly greater than that in the control group (106 days) (log-rank test, p<0.0001). **CONCLUSION:** AZD1480 may be effective against lung tumors driven by an activating EGFR mutation.

[338]

TÍTULO / TITLE: - MET and ALK as Targets for the Treatment of NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Capelletti M; Gelsomino F; Tiseo M

INSTITUCIÓN / INSTITUTION: - Medical Oncology Unit University Hospital of Parma Via Gramsci 14 43100 Parma, Italy. mtiseo@ao.pr.it.

RESUMEN / SUMMARY: - Cell proliferation, survival, differentiation, migration and metabolism are some of the fundamental cellular processes tightly controlled by the activity of tyrosine-kinase receptors (RTKs). The aberrant signaling of RTKs contributes to cancer growth and survival and has become important target for therapeutic approaches. Well-characterized kinase molecular target in lung cancer, in particular in non-small cell lung cancer (NSCLC), is the activated epidermal growth factor receptor (EGFR) pathway. More recently, the oncogenic role of other two tyrosine-kinases, the hepatocyte growth factor receptor (MET) and the anaplastic lymphoma kinase (ALK), has been recognized. Many different therapeutic strategies have been investigated with the goal to inhibit these receptors, subsequent downstream signaling cascades and arrest tumor growth. This review will discuss the MET and ALK pathways, the different

strategies of their inhibition and the potential approaches to overcome acquired resistance to kinase inhibitors in these two genes.

[339]

TÍTULO / TITLE: - Irreversible EGFR Inhibitors in the Treatment of Advanced NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Maione P; Rossi A; Bareschino M; Sacco PC; Schettino C; Casaluce F; Sgambato A; Gridelli C

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology "S.G. Moscati" Hospital Contrada Amoretta - 83100 Avellino (Italy). pmaione@libero.it.

RESUMEN / SUMMARY: - The epidermal growth factor receptor (EGFR) is among the most important target in the treatment of advanced non-small cell lung cancer (NSCLC). Erlotinib and gefitinib, two small molecules, are reversible EGFR tyrosine kinase inhibitors (TKIs). Non-small cell lung cancers with EGFR mutations, are characterized by excellent responses when treated with the EGFR-TKIs gefitinib and erlotinib. However, all the patients with tumors harbouring EGFR mutations experience disease progression after a median of 10 to 14 months of treatment with gefitinib or erlotinib. A group of new generation EGFR-TKIs irreversibly inhibit EGFR-TK and represent one of the strategies that may potentially overcome the acquired resistance to gefitinib and erlotinib or achieve better outcomes than reversible inhibitors in the first-line treatment of EGFR mutant lung cancers. Afatinib (BIBW 2992) and PF299804 are the irreversible EGFR-TKIs with the most relevant data in the treatment of advanced NSCLC, as primary EGFR-targeted therapy and after resistance to reversible EGFR-TKIs. However, to date, the role of irreversible EGFR inhibitors remains to be defined.

[340]

TÍTULO / TITLE: - Clinical characteristics and HPV type in recurrent respiratory papillomatosis in Colombia.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Salud Publica Mex. 2013 Aug;55(4):416-20.

AUTORES / AUTHORS: - Cuello G; Sanchez GI; Jaramillo R; Quintero K; Baena A; O'Byrne A; Reyes AJ; Santamaria C; Reina JC; Munoz N

INSTITUCIÓN / INSTITUTION: - Centro Medico Imbanaco, Cali, Colombia.

RESUMEN / SUMMARY: - Objective. Describe factors associated with aggressive forms of recurrent respiratory papillomatosis (RRP). Materials and methods. One hundred eighty-nine RRP cases diagnosed between 1985 and 2009 were identified in pathological records. HPV was detected by the SPF-10 method with broad spectrum primers, (version 1). Results. 113 patients had only one surgery (less aggressive) and 76, two or more interventions (more aggressive). The likelihood of aggressive lesions decreased with increasing age at diagnosis and HPV-11 was associated with no significant increase in the risk of aggressiveness. Conclusions. The age at diagnosis was the main determinant of RRP aggressiveness.

[341]

TÍTULO / TITLE: - Prognostic nutritional index predicts outcomes of malignant pleural mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Clin Oncol. 2013 Dec;139(12):2117-23. doi: 10.1007/s00432-013-1523-0. Epub 2013 Oct 23.

●● Enlace al texto completo (gratis o de pago) [1007/s00432-013-1523-0](#)

AUTORES / AUTHORS: - Yao ZH; Tian GY; Wan YY; Kang YM; Guo HS; Liu QH; Lin DJ

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Shandong Provincial Hospital Affiliated to Shandong University, Shandong University, No. 324 Jingwuweiqi Road, Jinan, 250021, Shandong Province, People's Republic of China.

RESUMEN / SUMMARY: - PURPOSE: Nutritional status has been associated with long-time outcomes in cancer patients. We investigated whether the prognostic nutritional index (PNI), an indicator of nutritional status, affects overall survival in patients with malignant pleural mesothelioma (MPM). METHODS: We enrolled 121 patients with histologically confirmed MPM, who had successfully undergone biopsy by medical thoracoscopy in this study. Demographic, clinical and laboratory data were collected retrospectively. The PNI was calculated as $10 \times \text{serum albumin value (g/dl)} + 0.005 \times \text{total lymphocyte count (per mm}^3\text{)}$ in peripheral blood. Univariate and multivariate analyses were used to identify prognostic factors. RESULTS: Mean pretreatment PNI was 44.6. PNI was significantly associated with age ($P = 0.031$), smoking habits ($P = 0.039$) and weight loss ($P = 0.029$). Survival analysis showed PNI to be an independent prognostic factor in MPM. Patients with lower PNIs ($\text{PNI} < 44.6$) had greater risk of death than those with higher PNIs ($\text{PNI} \geq 44.6$; hazard ratio: 2.290; 95 % confidence interval: 1.415-3.706; $P = 0.001$). These analyses were adjusted for patient age, gender, smoking habits, dyspnea, chest pain, weight loss, primary site of tumor, histology, platinum-based systemic chemotherapy, hospital and stage. CONCLUSIONS: Pretreatment PNI is a novel independent prognostic factor in MPM.

[342]

TÍTULO / TITLE: - Targeted CT Image Screening and Its Effect on Lung Cancer Detection Rate.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chest. 2013 Oct;144(4):1419-20. doi: 10.1378/chest.13-1321.

●● Enlace al texto completo (gratis o de pago) [1378/chest.13-1321](#)

AUTORES / AUTHORS: - Young RP; Hopkins RJ

[343]

TÍTULO / TITLE: - Comparison of Multiplanar Reformatted CT Lung Tumor Measurements to Axial Tumor Measurement Alone: Impact on Maximal Tumor Dimension and T Stage.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - AJR Am J Roentgenol. 2013 Nov;201(5):959-63. doi: 10.2214/AJR.12.10033.

●● Enlace al texto completo (gratis o de pago) [2214/AJR.12.10033](#)

AUTORES / AUTHORS: - Ridge CA; Huang J; Cardoza S; Zabor EC; Moskowitz CS; Zakowski MF; Ginsberg MS

INSTITUCIÓN / INSTITUTION: - 1 Department of Radiology, Memorial Sloan-Kettering Cancer Center, Box 29, 1275 York Ave, New York, NY 10065.

RESUMEN / SUMMARY: - **OBJECTIVE.** The purpose of this study was to compare measurements of lung tumor size between axial and multiplanar reformatted CT images, as well as to establish whether the difference between these measurements leads to a change in T stage. **MATERIALS AND METHODS.** Patients with lung tumors who underwent chest CT up to 31 days before lung resection between December 2010 and March 2012 were included. Axial, sagittal, and coronal CT images were evaluated by two independent readers (1 and 2) who were blinded to clinical data. In 89 patients, lung tumors categorized as T1a (54%), T1b (19%), T2a (24%), or T2b (3%) were analyzed. The longest tumor diameter using multiplanar reformatted CT was compared and correlated with axial CT alone and pathologic T stage. Statistical analysis included a Wilcoxon rank sum test to evaluate differences between measurements, intraclass correlation coefficient (ICC), and kappa statistic to assess agreement. **RESULTS.** Prediction of T stage using axial CT alone compared with multiplanar reformatted CT agreed in 82% of patients for reader 1 (kappa = 0.660 [95% CI, 0.531-0.789]) and 80% of patients for reader 2 (kappa = 0.695 [95% CI, 0.572-0.818]). Prediction of T stage using multiplanar reformatted CT resulted in upstaging in 18% and 20% of patients (for readers 1 and 2, respectively). Interobserver agreement (ICC [95% CI]) was 0.900 (0.803-0.954) for axial, 0.874 (0.772-0.946) for sagittal, and 0.754 (0.556-0.921) for coronal planes. **CONCLUSION.** Radiologic measurement of lung tumor T stage was higher using multiplanar reformatted CT as compared with axial CT alone. When available, multiplanar reformatted CT should be used to measure tumor dimension and thus assign an accurate lung cancer T stage.

[344]

TÍTULO / TITLE: - MiR-92b regulates the cell growth, cisplatin chemosensitivity of A549 non small cell lung cancer cell line and target PTEN.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochem Biophys Res Commun. 2013 Nov 1;440(4):604-10. doi: 10.1016/j.bbrc.2013.09.111. Epub 2013 Oct 4.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.bbrc.2013.09.111](#)

AUTORES / AUTHORS: - Li Y; Li L; Guan Y; Liu X; Meng Q; Guo Q

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Shandong Cancer Hospital and Institute, Jinan University, Jinan, Shandong 250117, PR China.

RESUMEN / SUMMARY: - MicroRNAs (miRNAs) have emerged to play important roles in tumorigenesis and drug resistance of human cancer. Fewer studies were explored the roles of miR-92b on human lung cancer cell growth and resistance to cisplatin (CDDP). In this paper, we utilized real-time PCR to verify miR-92b was significantly up-regulated in non-small cell lung cancer (NSCLC) tissues compared to matched adjacent normal tissues. In vitro assay demonstrated that knock-down of miR-92b inhabits cell growth and sensitized the A549/CDDP cells to CDDP. Furthermore, we found miR-92b could directly target PTEN, a unique tumor suppressor gene, which was downregulated in lung cancer tissues compared to the matched adjacent normal tissues. These data indicate that the miR-92b play an oncogene roles by regulates cell

growth, cisplatin chemosensitivity phenotype, and could serve as a novel potential maker for NSCLC therapy.

[345]

TÍTULO / TITLE: - MicroRNAs in Non-Small Cell Lung Cancer: Current Status and Future Therapeutic Promises.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Cortinovis D; Monica V; Pietrantonio F; Ceresoli G; La Spina; Wannesson L

INSTITUCIÓN / INSTITUTION: - Oncology Unit, San Gerardo Hospital, Monza.

d.cortinovis@hsgerardo.org.

RESUMEN / SUMMARY: - A biological characterization of tumor tissue is mandatory in NSCLC patients to identify cases at high risk of recurrence and to drive current targeted therapies such as EGFR and ALK inhibitors. In addition, promising results have been reported on the utility of molecular parameters for the prediction of the efficacy of systemic cytotoxic therapy. MicroRNAs (miRNAs) are small single stranded non-coding RNA molecules, which regulate gene expression at the posttranscriptional level. Growing evidence suggests that miRNAs are expressed aberrantly in many human cancers and that they play a significant role in carcinogenesis and cancer progression. There is increasing evidence that miRNA profiling may become an accurate way to differentiate tumor subtypes, determine prognosis and response to therapy. This review aims to summarize the current literature on this rapidly evolving field.

[346]

TÍTULO / TITLE: - Prognostic Factors Associated With Interventional Bronchoscopy in Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Surg. 2013 Oct 2. pii: S0003-4975(13)01813-4. doi: 10.1016/j.athoracsur.2013.07.118.

●● Enlace al texto completo (gratis o de pago)

1016/j.athoracsur.2013.07.118

AUTORES / AUTHORS: - Guibert N; Mazieres J; Lepage B; Plat G; Didier A; Hermant C

INSTITUCIÓN / INSTITUTION: - Service de Pneumologie-Allergologie, Hopital Larrey, CHU de Toulouse, Université de Toulouse III (Paul Sabatier), Toulouse, France.

Electronic address: nicolas.guibert@hotmail.fr.

RESUMEN / SUMMARY: - BACKGROUND: Interventional bronchoscopy is an effective procedure for malignant central airway obstruction, although its indications are poorly defined and its benefits difficult to predict. The purpose of the study was to identify the patients' or the disease's characteristics that are correlated with survival to enable clinicians to identify the best indications. METHODS: We retrospectively studied the data from 204 patients treated between 2004 and 2010. We analyzed survival times according to the patients' or disease's characteristics, and identified homogeneous risks using classification and regression trees. RESULTS: Reduced survival was associated with a high American Society of Anesthesiologists score (13, 5.9, and 2.9

months for scores of 2, 3, and 4, respectively; $p = 0.0005$), nonsquamous cell histology (median survival, 6.3 months; $p = 0.007$), metastatic tumors (9.2 and 6.2 months for stage IIIA and IIIB, respectively, versus 3 months for stage IV; $p = 0.0002$), and for patients who had not received a specific treatment (median survival, 8.6 versus 3.2 months for untreated patients; $p < 0.0001$). Classification and regression trees segmentation identified five distinct groups of patients. Patients receiving a specific treatment for squamous cell carcinoma derived the best survival (median, 13 months; $p < 0.0001$), whereas patients with an American Society of Anesthesiologists score of 4 treated for large cell cancer or adenocarcinoma and metastatic patients who did not receive any specific treatment had the worst survival (0.8 months and 2.7 months, respectively; $p < 0.0001$). CONCLUSIONS: Interventional bronchoscopy is a safe and effective procedure that should be integrated into a multimodal therapy for selected patients.

[347]

TÍTULO / TITLE: - A further investigation of the centroid-to-centroid method for stereotactic lung radiotherapy: a phantom study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Phys. 2013 Oct;40(10):101704. doi: 10.1118/1.4820365.

●● [Enlace al texto completo \(gratis o de pago\) 1118/1.4820365](#)

AUTORES / AUTHORS: - Lu B; Samant S; Mittauer K; Lee S; Huang Y; Li J; Kahler D; Liu C

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, Florida 32610.

RESUMEN / SUMMARY: - PURPOSE: Our previous study [B. Lu et al., "A patient alignment solution for lung SBRT setups based on a deformable registration technique," Med. Phys. 39(12), 7379-7389 (2012)] proposed a deformable-registration-based patient setup strategy called the centroid-to-centroid (CTC) method, which can perform an accurate alignment of internal-target-volume (ITV) centroids between averaged four-dimensional computed tomography and cone-beam computed tomography (CBCT) images. Scenarios with variations between CBCT and simulation CT caused by irregular breathing and/or tumor change were not specifically considered in the patient study [B. Lu et al., "A patient alignment solution for lung SBRT setups based on a deformable registration technique," Med. Phys. 39(12), 7379-7389 (2012)] due to the lack of both a sufficiently large patient data sample and a method of tumor tracking. The aim of this study is to thoroughly investigate and compare the impacts of breathing pattern and tumor change on both the CTC and the translation-only (T-only) gray-value mode strategies by employing a four-dimensional (4D) lung phantom.

METHODS: A sophisticated anthropomorphic 4D phantom (CIRS Dynamic Thorax Phantom model 008) was employed to simulate all desired respiratory variations. The variation scenarios were classified into four groups: inspiration to expiration ratio (IE ratio) change, tumor trajectory change, tumor position change, tumor size change, and the combination of these changes. For each category the authors designed several scenarios to demonstrate the effects of different levels of breathing variation on both of the T-only and the CTC methods. Each scenario utilized 4DCT and CBCT scans. The ITV centroid alignment discrepancies for CTC and T-only were evaluated. The dose-volume-histograms (DVHs) of ITVs for two extreme cases were analyzed. RESULTS:

Except for some extreme cases in the combined group, the accuracy of the CTC registration was about 2 mm for all cases for both the single and the combined scenarios. The performance of the CTC method was insensitive to region-of-registration (ROR) size selections, as suggested by the comparable accuracy between 1 and 2 cm expansions of the ROR selections for the method. The T-only method was suitable for some single scenarios, such as trajectory variation, position variation, and size variation. However, for combined scenarios and/or a large variation in the IE ratio, the T-only method failed to produce reasonable registration results (within 3 mm). The discrepancy was close to, or even greater than, 1 cm. In addition, unlike the CTC method, the T-only method was sensitive to the ROR size selection. The DVH analysis suggested that a large ITV to PTV margin should be considered if a breathing pattern variation is observed. CONCLUSIONS: The phantom study demonstrated that the CTC method was reliable for scenarios in which breathing pattern variation was involved. The T-only gray value method worked for some scenarios, but not for scenarios that involved an IE ratio variation. For scenarios involving position variation, the T-only method worked only with a careful selection of the ROR, whereas the CTC method was independent of ROR size as long as the ITVs were included in the ROR. One indication of the dose consequence analysis was that a large ITV to PTV margin should be considered if a breathing pattern variation is observed.

[348]

TÍTULO / TITLE: - EGFR Mutation-Specific Immunohistochemical Antibodies in Lung Adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Histopathology. 2013 Nov 20. doi: 10.1111/his.12331.

●● Enlace al texto completo (gratis o de pago) [1111/his.12331](#)

AUTORES / AUTHORS: - Allo G; Bandarchi B; Yanagawa N; Wang A; Shih W; Xu J; Dalby M; Nitta H; To C; Liu N; Sykes J; Tsao MS

INSTITUCIÓN / INSTITUTION: - Department of Pathology, University Health Network, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada.

RESUMEN / SUMMARY: - AIMS: We investigated the sensitivity and specificity of two novel EGFR mutation-specific antibodies in the detection of the most common EGFR mutations in lung adenocarcinoma. METHODS AND RESULTS: 241 resected lung adenocarcinoma specimens and 6 resected post-neoadjuvant gefitinib adenocarcinomas were analyzed for EGFR mutation using mass spectrometry, fragment analysis and direct PCR sequencing platforms. Tissue arrays and/or full section of these cases were evaluated by immunohistochemistry by two novel antibodies (clones SP125 and SP111) and two previously reported antibodies (clones 43B2 and 6B6), specific for L858R or 15-nucleotide exon-19 deletion EGFR mutations, respectively. SP125 antibody detected EGFR L858R mutation with a sensitivity of 76% and positive predictive value of 73%. SP111 antibody stained the 15-nucleotide EGFR exon 19 deletions with sensitivity of 83% and a positive predictive value of 94%. Pre-treatment with gefitinib did not affect antibody performance. Full-section immunohistochemical staining detected heterogeneous mutant EGFR proteins expression in tumours, and revealed L858R mutation in the non-neoplastic bronchial

epithelium adjacent to EGFR L858R-carrying carcinomas in 3 of 16 (19%) cases.
CONCLUSIONS: Immunohistochemistry using EGFR mutant specific antibodies may be useful in shortening the diagnostic time of lung adenocarcinoma with most common EGFR mutations, especially in samples with low tumour cellularity. This article is protected by copyright. All rights reserved.

[349]

TÍTULO / TITLE: - Quality Gaps and Comparative Effectiveness in Lung Cancer Staging and Diagnosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chest. 2013 Oct 3. doi: 10.1378/chest.13-1599.

●● [Enlace al texto completo \(gratis o de pago\) 1378/chest.13-1599](#)

AUTORES / AUTHORS: - Ost DE; Niu J; Elting L; Buchholz TA; Giordano SH

RESUMEN / SUMMARY: - BACKGROUND: Guidelines recommend mediastinal lymph node sampling as the first invasive test in patients with suspected lung cancer with mediastinal lymphadenopathy without distant metastases, but there are no comparative effectiveness studies on how test sequencing impacts outcomes. Our objective was to compare practice patterns and outcomes of diagnostic strategies in patients with lung cancer. METHODS: Retrospective cohort of 15,316 lung cancer patients with regional spread without distant metastases in the SEER or Texas Cancer Registry Medicare-linked databases. If the first invasive test involved mediastinal sampling patients were classified as guideline consistent, otherwise they were classified as inconsistent. We used propensity matching to compare the number of tests performed and multivariate logistic regression to compare the frequency of complications. RESULTS: 21% of patients had guideline consistent diagnostic evaluations. Among patients with NSCLC, 44% never had mediastinal sampling. Patients that had guideline consistent care required fewer tests than patients with guideline inconsistent care ($p < 0.0001$), including thoracotomies (49% vs. 80%, $p < 0.001$) and CT-guided biopsies (9% vs. 63%, $p < 0.001$), although they had more transbronchial needle aspirations (37% vs. 4%, $p < 0.001$). The consequence was that patients with guideline consistent care had fewer pneumothoraxes (4.8% vs. 25.6%, $p < 0.0001$), chest tubes (0.7% vs. 4.9%, $p < 0.001$), hemorrhages (5.4% vs. 10.6%, $p < 0.001$) and respiratory failure events (5.3% vs. 10.5%, $p < 0.001$). CONCLUSIONS: Guideline consistent care with mediastinal sampling first resulted in fewer tests and complications. We found three quality gaps: failure to sample the mediastinum first, failure to sample the mediastinum at all in NSCLC patients, and overuse of thoracotomy.

[350]

TÍTULO / TITLE: - Determinants of Practice Patterns and Quality Gaps in Lung Cancer Staging and Diagnosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chest. 2013 Nov 7. doi: 10.1378/chest.13-1628.

●● [Enlace al texto completo \(gratis o de pago\) 1378/chest.13-1628](#)

AUTORES / AUTHORS: - Ost DE; Niu J; Elting L; Buchholz TA; Giordano SH

RESUMEN / SUMMARY: - BACKGROUND: Guidelines recommend mediastinal lymph node sampling as the first invasive diagnostic procedure in patients with suspected

lung cancer with mediastinal lymphadenopathy without distant metastases. METHODS: Retrospective cohort of 15,316 patients with lung cancer with regional spread without metastatic disease in the SEER or Texas Cancer Registry Medicare-linked databases. Patients were categorized based on the sequencing of invasive diagnostic tests performed: A) Evaluation consistent with guidelines, mediastinal sampling done first; B) Evaluation inconsistent with guidelines, NSCLC present, mediastinal sampling performed but not as part of the first invasive test; C) Evaluation inconsistent with guidelines, NSCLC present, mediastinal sampling never done; and D) Evaluation inconsistent with guidelines, small cell lung cancer. The primary outcome was whether guideline consistent care was delivered. Secondary outcomes included whether patients with NSCLC ever had mediastinal sampling and use of TBNA among pulmonologists. RESULTS: Only 21% of patients had a diagnostic evaluation consistent with guidelines. Only 56% of NSCLC patients had mediastinal sampling prior to treatment. There was significant regional variability in guideline consistent care (range 12%-29%). Guideline consistent care was associated with lower patient age, metropolitan areas, and if the physician ordering or performing the test was male, U.S. trained, had seen more lung cancer patients, and was a pulmonologist or thoracic surgeon who had graduated more recently. More recent pulmonary graduates were also more likely to perform transbronchial needle aspiration (p<0.001). CONCLUSION: Guideline consistent care varied regionally and was associated with physician level factors, suggesting that a lack of effective physician training may be contributing to the quality gaps observed.

[351]

TÍTULO / TITLE: - Osteopontin Combined With CD44v6, a Novel Prognostic Biomarker in Non-Small Cell Lung Cancer Undergoing Curative Resection.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Surg. 2013 Dec;96(6):1943-51. doi: 10.1016/j.athoracsur.2013.07.089. Epub 2013 Oct 3.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1016/j.athoracsur.2013.07.089](#)

AUTORES / AUTHORS: - Sun BS; Li Y; Zhang ZF; You J; Wang CL

INSTITUCIÓN / INSTITUTION: - Department of Lung Cancer, Tianjin Cancer Institute and Hospital, Tianjin Medical University, Tianjin Lung Cancer Center, Key Laboratory of Cancer Prevention and Therapy of Tianjin, Tianjin, China.

RESUMEN / SUMMARY: - BACKGROUND: Osteopontin (OPN) is identified as one of the leading genes that promote the metastasis of malignant tumor through binding to CD44v6 and integrin. The purpose of the current study was to assess the prognostic significance of OPN and CD44v6 in patients with non-small cell lung cancer (NSCLC). METHODS: Tissue microarray was used to detect the expression of OPN and CD44v6 in 159 NSCLC patients undergoing complete pulmonary resection in our hospital between 2003 and 2006. The correlations among OPN, CD44v6, and clinicopathologic data were analyzed using chi(2) testing analysis. The prognostic values of OPN and CD44v6 were evaluated by univariate Kaplan-Meier survival analysis and multivariate Cox proportional hazard model analysis. RESULTS: OPN and CD44v6 were both independent predictors for overall survival and disease-free survival. When OPN and CD44v6 were considered together, the predictive range was extended and the

sensitivity was improved, especially for those patients with stage I NSCLC. The 6-year overall survival and disease-free survival rates in OPN+ or CD44v6+ patients were 49.1% and 39.6%, respectively, which were significantly lower than those of OPN-/CD44v6- patients (64.4% and 47.7%, respectively), and were higher than those of OPN+/CD44v6+ patients (16.4% and 14.8%, respectively). Stratification into OPN+/CD44v6+, OPN+ or CD44v6+, or OPN-/CD44v6- groups, based on the expression OPN and CD44v6, could efficiently predicted outcomes ($p < 0.001$) of NSCLC patients. CONCLUSIONS: The combination of OPN and CD44v6 is a valuable independent predictor of tumor recurrence and survival in NSCLC patients.

[352]

TÍTULO / TITLE: - EIF2AK4 Mutations in Pulmonary Capillary Hemangiomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chest. 2013 Oct 17. doi: 10.1378/chest.13-2366.

●● Enlace al texto completo (gratis o de pago) [1378/chest.13-2366](#)

AUTORES / AUTHORS: - Best DH; Sumner KL; Austin ED; Chung WK; Brown LM; Borczuk AC; Rosenzweig EB; Bayrak-Toydemir P; Mao R; Cahill BC; Tazelaar HD; Leslie KO; Hemnes AR; Robbins IM; Elliott CG

RESUMEN / SUMMARY: - ABSTRACT BACKGROUND: Pulmonary capillary hemangiomas (PCH) is a rare disease of capillary proliferation of unknown cause and with a high mortality. Families with multiple affected individuals with PCH suggest a heritable cause although the genetic etiology remains unknown. METHODS: We used exome sequencing to identify a candidate gene for PCH in a family with two affected brothers. We then screened 11 unrelated patients with familial (n=1) or sporadic (n=10) PCH for mutations. RESULTS: Using exome sequencing, we identified compound mutations in Eukaryotic Translation Initiation Factor 2 Alpha Kinase 4 (EIF2AK4), in both affected brothers. Both parents and an unaffected sister were heterozygous carriers. In addition, we identified two EIF2AK4 mutations in each of 2 of 10 unrelated individuals with sporadic PCH. Eukaryotic Translation Initiation Factor 2 Alpha Kinase 4 belongs to a family of kinases that regulate angiogenesis in response to cellular stress. CONCLUSION: Mutations in EIF2AK4 are likely to cause autosomal recessive PCH in familial and some non-familial cases.

[353]

TÍTULO / TITLE: - Comprehensive Analysis of Oncogenic Mutations in Lung Squamous Cell Carcinoma with Minor Glandular Component.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chest. 2013 Oct 24. doi: 10.1378/chest.12-2679.

●● Enlace al texto completo (gratis o de pago) [1378/chest.12-2679](#)

AUTORES / AUTHORS: - Pan Y; Wang R; Ye T; Li C; Hu H; Yu Y; Zhang Y; Wang L; Luo X; Li H; Li Y; Shen L; Sun Y; Chen H

RESUMEN / SUMMARY: - BACKGROUND: The mutations in oncogenic genes, such as EGFR, ALK, BRAF, HER2, DDR2, RET and AKT1, defined subsets of non-small cell lung cancers (NSCLC) with potential sensitivity to targeted therapies. At present, the mutational spectrum, prevalence and clinicopathologic characteristics in squamous cell carcinomas with minor (<10%) glandular component (SQCC-mGC) are not well

established. METHODS: Three hundred and ten surgically resected lung squamous cell carcinoma (SQCC) specimens were collected. The histology of all cases was re-evaluated using hematoxylin-eosin (H&E) and immunohistochemistry (IHC) staining. EGFR, KRAS, HER2, BRAF, PIK3CA, AKT1 and DDR2 mutations, as well as ALK and RET rearrangements, were examined in 310 SQCCs by directed sequencing. RESULTS: Ninety-five SQCC-mGCs (30.6%) and 215 pure SQCCs (69.4%) were identified. Of the 95 SQCC-mGCs, 26 (27.4%; 95%CI, 18.7%-37.4%) were found to harbor known oncogenic mutations, including 10 with EGFR, 7 with KRAS, 3 with PIK3CA, 1 with BRAF, 1 with HER2, 1 each with EGFR/PIK3CA and KRAS/PIK3CA double mutations and 2 with EML4-ALK fusions. Ten of 215 pure SQCCs (4.7%; 95%CI, 2.3%-8.4%) harbored mutations, including 7 with PIK3CA, 1 each with AKT1, DDR2, and EGFR. No RET rearrangements were detected in SQCCs. SQCC-mGCs had a significantly higher rate of mutations in known oncogenic genes than that in pure SQCCs (27.4% vs. 4.7%, $p < 0.001$). All KRAS mutations occurred in SQCC-mGCs. CONCLUSIONS: Our results demonstrated that oncogenic mutations in EGFR, KRAS, BRAF, HER2 and ALK were extremely rare or absent in patients with pure SQCC, while SQCC-mGC had relatively high frequency of EGFR, ALK or KRAS mutations. Prospective identification of these known oncogenic mutations in SQCC-mGC before the initiation of treatment is an essential step to identify which patient could benefit from targeted therapies.

[354]

TÍTULO / TITLE: - Physical activity preferences of early-stage lung cancer survivors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Support Care Cancer. 2013 Oct 5.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00520-013-2002-5](#)

AUTORES / AUTHORS: - Philip EJ; Coups EJ; Feinstein MB; Park BJ; Wilson DJ; Ostroff JS

INSTITUCIÓN / INSTITUTION: - Department of Psychiatry and Behavioral Sciences, Memorial Sloan-Kettering Cancer Center, 641 Lexington Avenue, 7th Floor, New York, NY, 10022, USA, philipe@mskcc.org.

RESUMEN / SUMMARY: - PURPOSE: Engagement in physical activity can provide important benefits for cancer patients and survivors, including those diagnosed with lung cancer. Despite this, many survivors do not engage in recommended levels of physical activity and little is known about the obstacles encountered by lung cancer survivors. The current study examines the physical activity preferences of early-stage lung cancer survivors. METHOD: As part of a larger survey study, 175 non-small cell lung cancer survivors who were on average 3.6 years from surgical treatment responded to questions regarding their preferences for physical activity and physical activity advice. Demographic and medical characteristics were also collected. RESULTS: The majority of respondents (62 %) reported a desire to receive advice regarding physical activity, predominantly before treatment (68 %), in face-to-face interactions (95 %) with a physician (80 %), and within the context of a cancer care center (92 %). Approximately half of participants indicated they would be interested in an exercise program tailored to lung cancer survivors and most individuals (73 %) reported feeling capable of engaging in an exercise program. Differences in physical activity preferences emerged based on demographic and disease characteristics.

CONCLUSIONS: The majority of participants reported a desire for physical activity advice and a willingness to engage in physical activity. Important differences were found based on demographic and medical characteristics, which may warrant consideration in the development and dissemination of physical activity interventions for this cancer survivor population.

[355]

TÍTULO / TITLE: - The expression of BTG1 is downregulated in NSCLC and possibly associated with tumor metastasis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 22.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s13277-013-1379-6](#)

AUTORES / AUTHORS: - Sun GG; Lu YF; Cheng YJ; Hu WN

INSTITUCIÓN / INSTITUTION: - Department of Chemoradiotherapy, Tangshan People's Hospital, NO.65, Shengli Road, Lunan District, Tangshan, 063000, Hebei Province, China.

RESUMEN / SUMMARY: - This study aimed to analyze the expression, clinical significance of B cell translocation gene 1 (BTG1) in nonsmall cell lung cancer (NSCLC) and the biological effect in its cell line by BTG1 overexpression. Immunohistochemistry and western blot were used to analyze BTG1 protein expression in 82 cases of NSCLC and 38 cases of normal tissues to study the relationship between BTG1 expression and clinical factors. Recombinant lentiviral vector was constructed to overexpress EMP-1 and then infect NSCLC H1299 cell line. Quantitative real-time RT-PCR and western blot were used to detect the mRNA level and protein of BTG1. 3-[4,5-dimethylthiazol -2-yl]-2,5-diphenyltetrazolium bromide (MTT) assay, cell apoptosis, cell cycles, and migration and invasion assays were also conducted as to the influence of the upregulated expression of BTG1 that might be found on H1299 cells biological effect. The level of BTG1 protein expression was found to be significantly lower in NSCLC tissue than normal tissues ($P < 0.05$). Decreased expression of BTG1 was significantly correlated with lymph node metastasis, clinic stage, and histological grade of patients with NSCLC ($P < 0.05$). Meanwhile, loss of BTG1 expression correlated significantly with poor overall survival time by Kaplan-Meier analysis ($P < 0.05$). The result of biological function show that H1299 cell transfected BTG1 had a lower survival fraction; higher percentage of the G0/G1 phases; higher cell apoptosis; significant decrease in migration and invasion; and lower CyclinD1, Bcl-2, and MMP-9 protein expression compared with H1299 cell untransfected BTG1 ($P < 0.05$). BTG1 expression decreased in NSCLC and correlated significantly with lymph node metastasis; clinical stage; histological grade; poor overall survival; cell proliferation; cell cycles; cell apoptosis; and migration and invasion in NSCLC cell by regulating CyclinD1, Bcl-2, and MMP-9 protein expression, suggesting that BTG1 may play important roles as a negative regulator to NSCLC cell.

[356]

TÍTULO / TITLE: - Pleural effusion hyaluronic acid as a prognostic marker in pleural malignant mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):491-8. doi: 10.1016/j.lungcan.2013.09.016. Epub 2013 Oct 9.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.016](https://doi.org/10.1016/j.lungcan.2013.09.016)

AUTORES / AUTHORS: - Creaney J; Dick IM; Segal A; Musk AW; Robinson BW

INSTITUCIÓN / INSTITUTION: - National Centre for Asbestos Related Diseases, University of Western Australia, School of Medicine and Pharmacology, Nedlands, Western Australia, Australia; The Australian Mesothelioma Tissue Bank, Sir Charles Gairdner Hospital, Nedlands, Western Australia, Australia. Electronic address: jenette.creaney@uwa.edu.au.

RESUMEN / SUMMARY: - BACKGROUND: Malignant mesothelioma (MM), a primarily asbestos-induced tumour, has a poor prognosis, with over-all 5-year survival less than 5%. Tumour biomarkers are being intensely investigated in MM as aids to diagnosis and prognosis. Hyaluronic acid (HA) is produced in MM but its role in prognostication remains uncertain. MATERIALS AND METHODS: HA concentrations were determined in matching serum and pleural effusion of 96 MM patients, 26 lung cancer patients and 42 patients with benign effusions resulting from infectious, cardiac, renal, liver and rheumatoid diseases and compared to the current 'best practice' biomarker, mesothelin. Liver and kidney function were determined for each patient. Diagnostic accuracy was determined by area under the receiver operator characteristic curve (AUC) analysis following logistic regression modelling. Difference in survival between groups was determined by both log-rank test and Cox proportional hazards regression modelling. RESULTS: For effusion HA, the AUC (IQ range) was 0.89 (0.82-0.94) and for effusion mesothelin, it was 0.85 (0.78-0.90). Serum HA was not diagnostically useful. A combined measure of effusion HA, and serum and effusion mesothelin had an AUC of 0.92 (0.86-0.96), which was significantly higher than effusion mesothelin alone. Effusion HA had a biphasic distribution in MM patients, dichotomised at a concentration of 75mg/L. The median survival of MM patients with high effusion HA was 18.0 (13.7-22.4) months, significantly longer than those with low HA effusion levels (12.6 months (8.4-16.8), p=0.004). Serum HA, and effusion and serum mesothelin were not significant prognostic indicators. CONCLUSION: This study demonstrates that a combined biomarker panel has greater diagnostic accuracy than effusion mesothelin alone, and that significant prognostic information is provided by effusion HA.

[357]

TÍTULO / TITLE: - Multiphoton Microscopy: A Potential "Optical Biopsy" Tool for Real-Time Evaluation of Lung Tumors Without the Need for Exogenous Contrast Agents.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Arch Pathol Lab Med. 2013 Nov 7.

●● Enlace al texto completo (gratis o de pago) [5858/arpa.2013-0122-OA](https://doi.org/10.5858/arpa.2013-0122-OA)

AUTORES / AUTHORS: - Jain M; Narula N; Aggarwal A; Stiles B; Shevchuk MM; Sterling J; Salamoon B; Chandel V; Webb WW; Altorki NK; Mukherjee S

RESUMEN / SUMMARY: - Context .- Multiphoton microscopy (MPM) is an emerging, nonlinear, optical-biopsy technique, which can generate subcellular-resolution images from unprocessed and unstained tissue in real time. Objective .- To assess the potential of MPM for lung tumor diagnosis. Design .- Fresh sections from tumor and adjacent nonneoplastic lung were imaged with MPM and then compared with corresponding hematoxylin-eosin slides. Results .- Alveoli, bronchi, blood vessels,

pleura, smokers' macrophages, and lymphocytes were readily identified with MPM in nonneoplastic tissue. Atypical adenomatous hyperplasia (a preinvasive lesion) was identified in tissue adjacent to the tumor in one case. Of the 25 tumor specimens used for blinded pathologic diagnosis, 23 were diagnosable with MPM. Of these 23 cases, all but one adenocarcinomas (15 of 16; 94%) were correctly diagnosed on MPM, along with their histologic patterns. For squamous cell carcinoma, 4 of 7 specimens (57%) were correctly diagnosed. For the remaining 3 squamous cell carcinoma specimens, the solid pattern was correctly diagnosed in 2 additional cases (29%), but it was not possible to distinguish the squamous cell carcinoma from adenocarcinoma. The other squamous cell carcinoma specimen (1 of 7; 14%) was misdiagnosed as adenocarcinoma because of pseudogland formation. Invasive adenocarcinomas with acinar and solid pattern showed statistically significant increases in collagen. Interobserver agreement for collagen quantification (among 3 observers) was 80%.
Conclusions .- Our pilot study provides a proof of principle that MPM can differentiate neoplastic from nonneoplastic lung tissue and identify tumor subtypes. If confirmed in a future, larger study, we foresee real-time intraoperative applications of MPM, using miniaturized instruments for directing lung biopsies, assessing their adequacy for subsequent histopathologic analysis or banking, and evaluating surgical margins in limited lung resections.

[358]

TÍTULO / TITLE: - A panel of four immunohistochemical markers (CK7, CK20, TTF-1, and p63) allows accurate diagnosis of primary and metastatic lung carcinoma on biopsy specimens.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Virchows Arch. 2013 Dec;463(6):749-54. doi: 10.1007/s00428-013-1488-z. Epub 2013 Oct 15.

•• Enlace al texto completo (gratis o de pago) [1007/s00428-013-1488-z](#)

AUTORES / AUTHORS: - Montezuma D; Azevedo R; Lopes P; Vieira R; Cunha AL; Henrique R

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Portuguese Oncology Institute-Porto, Rua Dr. Antonio Bernardino Almeida, 4200-072, Porto, Portugal.

RESUMEN / SUMMARY: - Accurate classification of lung cancer, as well as the differentiation between primary and metastatic carcinoma to the lung, mostly performed on biopsy or fine needle aspiration specimens, is critical for decisions on therapy and for determining prognosis. The limited amount of biopsy material available for morphological assessment has stimulated attempts to improve diagnostic accuracy through the use of immunohistochemistry (IHC), but an optimal IHC diagnostic algorithm has not been firmly established. We evaluated, on a retrospective series of biopsy specimens, the performance of a four-antibody IHC panel for accurate subclassification of non-small cell lung carcinoma (NSCLC) and for identification of metastatic carcinoma. Tumor morphology was assessed and IHC for CK7, CK20, TTF-1, and p63 was performed according to a two-step algorithm. Matched resection specimens served as gold standard and were compared with the corresponding biopsy. Of 443 biopsy specimens studied, 325 were diagnosed as primary carcinoma of the lung, 198 (44.7 %) as adenocarcinoma, 9 (2 %) as possibly adenosquamous carcinoma, 127 (28.7 %) as squamous cell carcinoma, and 40 (9 %) as NSCLC not

further classifiable. Ten cases (2.3 %) were classified as adenocarcinoma of unknown origin and 58 (13 %) as metastasis. Importantly, of the primary lung adenocarcinomas, 35 (17.7 %) had been considered on clinical grounds as a metastasis from a previously diagnosed primary tumor. Of the 55 cases submitted to surgical resection in 47 (85.5 %) the biopsy diagnosis was confirmed, revealing substantial agreement (kappa value = 0.757). Our two-step approach allows for accurate subclassification of NSCLC and also to distinguish between primary lung adenocarcinoma and metastasis, notably of colorectal adenocarcinoma, with crucial implications for appropriate patient management.

[359]

TÍTULO / TITLE: - Lung cancer in pregnancy: Report of nine cases from an international collaborative study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):499-505. doi: 10.1016/j.lungcan.2013.09.002. Epub 2013 Sep 12.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.002](#)

AUTORES / AUTHORS: - Boussios S; Han SN; Fruscio R; Halaska MJ; Ottevanger PB; Peccatori FA; Koubkova L; Pavlidis N; Amant F

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Ioannina University Hospital, Stavros Niarchos Avenue, 45500 Ioannina, Greece.

RESUMEN / SUMMARY: - OBJECTIVE: Lung cancer is an uncommon diagnosis during pregnancy. The combination of smoking in young women, increased maternal age during pregnancy, and increasing incidence of lung cancer worldwide may cause an increase of pregnancy associated lung cancer. The aim of this study was to describe all cases of lung cancer during pregnancy, registered in the international Cancer in Pregnancy registration study (CIP study; www.cancerinpregnancy.org). MATERIALS AND METHODS: We present nine cases, all advanced lung cancer during the course of pregnancy. Collected data included demographic features of the study patients, cancer treatment, pregnancy outcome as well as maternal and fetal outcomes. RESULTS AND CONCLUSION: Nine pregnant patients from 4 European centres with a median age of 33 years old (range, 26-42) were included. The median gestational age at diagnosis was 17 weeks (range, 6-28). All patients presented with metastatic disease including bone, lung, brain, spinal cord, pleura, lymph nodes, adrenal and liver. Histopathology was compatible with adenocarcinoma in 4 patients, non-small cell lung cancer with unidentified subtype in 2 patients and squamous-cell, large-cell and a poorly differentiated carcinoma in 3 patients, respectively. Eight patients were treated with systemic therapy, five of them during gestation. No responses were seen. The maternal postpartum outcome was poor with less than one year survival following delivery. One patient experienced a spontaneous abortion and three pregnancies were terminated. Five infants were all born premature due to poor maternal status by cesarean section, with a median gestational age of 30 weeks (range 26-33). To summarize, lung cancer in pregnancy has a dismal maternal outcome in our series. We add nine new cases and discuss both therapeutic and prognostic results.

[360]

TÍTULO / TITLE: - A Comparison of Methods for EGFR Mutation Testing in Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Diagn Mol Pathol. 2013 Dec;22(4):190-5. doi: 10.1097/PDM.0b013e318294936c.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/PDM.0b013e318294936c](#)

AUTORES / AUTHORS: - Young EC; Owens MM; Adebisi I; Bedenham T; Butler R; Callaway J; Cranston T; Crosby C; Cree IA; Dutton L; Faulkes C; Faulkner C; Howard E; Knight J; Huang Y; Lavender L; Lazarou LP; Liu H; Mair D; Milano A; Sandell S; Skinner A; Wallace A; Williams M; Spivey V; Goodall J; Frampton J; Ellard S

INSTITUCIÓN / INSTITUTION: - *Molecular Genetics Department, Royal Devon and Exeter NHS Trust, Exeter daggerMolecular Genetics, Institute of Medical Genetics, Cardiff and Vale NHS Trust, Cardiff, Wales double daggerOxford Medical Genetics Laboratories, Oxford University Hospitals NHS Trust, Oxford section signWessex Regional Genetics Laboratory, Salisbury Health Care NHS Trust, Wiltshire parallelBristol Genetics Laboratory, Southmead Hospital, Bristol paragraph signDepartment of Pathology, Warwick Medical School, University Hospitals Coventry and Warwickshire, Coventry #Regional Molecular Genetics Service, Genetic Medicine (6th Floor), St Mary's Hospital, Manchester **Molecular Diagnostics, Royal Surrey County Hospital double daggerdouble daggerMolecular Diagnostics, The Institute of Cancer Research and Royal Marsden NHS Foundation Trust, Surrey daggerdaggerMolecular Malignancy Laboratory, Department of Histopathology, Addenbrooke's Hospital, Cambridge University Hospitals NHS Foundation Trust parallel parallelHorizon Discovery Ltd., Waterbeach, Cambridge section sign section signSheffield Diagnostic Genetics Service, Sheffield, UK.

RESUMEN / SUMMARY: - EGFR mutation testing of tumor samples is routinely performed to predict sensitivity to treatment with tyrosine kinase inhibitors for patients with non-small cell lung cancer. At least 9 different methodologies are employed in UK laboratories, and the aim of this study was to compare the sensitivity of different methods for the detection of EGFR mutations. Participating laboratories were sent coded samples with varying mutation loads (from 0% to 15%) to be tested for the p.Leu858Arg (p.L858R) missense mutation and c.2235_2249del exon 19 deletion. The p.L858R mutation and deletions within exon 19 of the EGFR gene account for approximately 90% of mutation-positive cases. The 11 laboratories used their standard testing method(s) and submitted 15 sets of results for the p.L858R samples and 10 for the exon 19 deletion. The p.Leu858Arg (p.L858R) mutation was detected at levels between 1% and 7.5% by Sanger sequencing, pyrosequencing, real-time polymerase chain reaction (PCR), amplification refractory mutation system, and capillary electrophoresis single-strand conformation analysis. The c.2235_2249del mutation was detected at 1% to 5% by fragment size analysis, Sanger sequencing or real-time PCR. A mutation was detected in 24/25 (96%) of the samples tested which contained 5% mutated DNA. The 1% sensitivity claimed for commercial real-time PCR-targeted EGFR tests was achieved and our results show greater sensitivity for the Sanger sequencing and pyrosequencing screening methods compared to the 10% to 20% detection levels cited on clinical diagnostic reports. We conclude that multiple methodologies are suitable for the detection of acquired EGFR mutations.

[361]

TÍTULO / TITLE: - Pre-clinical Validation of Orthotopically-implanted Pulmonary Tumor by Imaging with 18F-Fluorothymidine-Positron Emission Tomography/Computed Tomography.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):4741-9.

AUTORES / AUTHORS: - Fushiki H; Miyoshi S; Noda A; Murakami Y; Sasaki H; Jitsuoka M; Mitsuoka K; Matsunari I; Nishimura S

INSTITUCIÓN / INSTITUTION: - Astellas Pharma Inc., 21 Miyukigaoka, Tsukuba, Ibaraki, 305-8585 Japan. hiroshi.fushiki@astellas.com.

RESUMEN / SUMMARY: - The development of positron-emission tomography (PET) and X-ray computed tomography (CT) imaging has improved the detection of tumor burden and, in turn, pre-clinical drug development and clinical treatment. In pre-clinical drug development, clinically-relevant murine cancer models, such as orthotopic models of lung cancer, have provided an accurate representation of tumor burden in humans. However, evidence demonstrating the capability of imaging-guided evaluation of these clinically-relevant models is limited. Here, we combined (18)F-fluorothymidine (FLT)-PET/CT imaging and a murine model of human non-small cell lung cancer (NSCLC) to improve the accuracy of anticancer drug evaluation in pre-clinical studies. We found that FLT-PET/CT imaging enabled the progression of pulmonary tumors to be longitudinally monitored rather than FDG-PET/CT. Furthermore, in an efficacy study of a standard treatment of docetaxel in a murine lung cancer model, FLT-PET imaging detected the anticancer response earlier than volumetric analysis by CT imaging. We, thus, observed a relationship between the alteration of FLT signals and Ki-67 index in the pulmonary tumor during the period of chemotherapy. These results indicate that the combination of FLT-PET/CT imaging and an orthotopic NSCLC model is an effective strategy for evaluating clinical efficacy and potential of an anticancer agent during pre-clinical development.

[362]

TÍTULO / TITLE: - Dual ALK and EGFR inhibition targets a mechanism of acquired resistance to the tyrosine kinase inhibitor crizotinib in ALK rearranged lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 14. pii: S0169-5002(13)00448-0. doi: 10.1016/j.lungcan.2013.09.019.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.019](#)

AUTORES / AUTHORS: - Yamaguchi N; Lucena-Araujo AR; Nakayama S; de Figueiredo-Pontes LL; Gonzalez DA; Yasuda H; Kobayashi S; Costa DB

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Division of Hematology/Oncology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

RESUMEN / SUMMARY: - INTRODUCTION: The multitargeted tyrosine kinase inhibitor (TKI) crizotinib is active against ALK translocated non-small-cell lung cancer (NSCLC); however acquired resistance invariably develops over time. ALK mutations have previously been implicated in only a third of resistant tumors. We sought to evaluate alternative mechanisms of resistance and preclinical strategies to overcome these in a

cell line driven by EML4-ALK. METHODS: We selected the NSCLC cell line NCI-H3122 (H3122: EML4-ALK E13;A20) and derived resistant variants that were able to grow in the presence of 1µM crizotinib. These were analyzed for ALK mutations, sensitivity to crizotinib in combination with other TKIs, and for activation of alternative tyrosine kinases. RESULTS: All H3122 crizotinib resistant (CR) clones lacked amplification or mutations in the kinase domain of ALK. To evaluate if possible alternative kinases functioned as “bypass” tracks for downstream signaling activation in these resistance cells, we performed of phospho-receptor tyrosine kinase array that demonstrated that CR clones had higher phospho-EGFR signals than H3122 cells before and after exposure to crizotinib. A functional approach of dual ALK TKI (with crizotinib) with combinatory TKI inhibition was used as a secondary screen for possible targets. Crizotinib+erlotinib (reversible EGFR TKI) and crizotinib+afatinib (irreversible EGFR/ERBB2 TKI) were able to inhibit the growth of H3122 CR clones, confirming EGFR activation as a mechanism of resistance. The removal of crizotinib from the culture media re-sensitized CR cells to crizotinib. CONCLUSIONS: We identified activation of EGFR as a mechanism of resistance to crizotinib in preclinical models of ALK translocated NSCLC. If EGFR activation is confirmed as a predominant mechanism of ALK TKI-induced resistance in patient-derived tumors, the use of ALK plus EGFR TKIs could be explored for this important cohort of NSCLCs.

[363]

TÍTULO / TITLE: - Gender-dependent effects of gonadectomy on lung carcinogenesis by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in female and male A/J mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2632-8. doi: 10.3892/or.2013.2759. Epub 2013 Oct 1.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2759](#)

AUTORES / AUTHORS: - Ninomiya F; Yokohira M; Kishi S; Nakano Y; Yamakawa K; Inoue T; Kuno T; Imaida K

INSTITUCIÓN / INSTITUTION: - Onco-Pathology, Department of Pathology and Host-Defense, Faculty of Medicine, Kagawa University, Miki-cho, Kita-gun, Kagawa 761-0793, Japan.

RESUMEN / SUMMARY: - The present study was conducted to investigate the effects of gonadectomy on lung carcinogenesis in female and male mice, and to determine an association between sex hormone and lung carcinogenesis. Female and male A/J mice were divided into gonadectomized and unoperated control groups and all animals were treated intraperitoneally with 1 or 2 injections of 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) at the dose of 2 mg/mouse. The mice were sacrificed 18 or 56 weeks after surgery. Serum levels of estradiol in females and testosterone in males were confirmed to be decreased by gonadectomy. Lung white nodules were detected in all mice of all groups. In the control groups of 18- and 56-week studies, the multiplicities of lung nodules in females were significantly greater than in males. In males in the 56-week study, the multiplicity of macroscopical lung nodules, bronchiolo-alveolar hyperplasias, adenomas and tumors (adenomas and adenocarcinomas) showed significant increase with castration. In females in the 18-week study, the multiplicity of adenomas decreased significantly by ovariectomy. Based on the results of the present study, female A/J mice were confirmed to be more susceptible to NNK-induced lung

carcinogenesis than males. Furthermore, it was suggested that the process is inhibited by testosterone and accelerated by estradiol. These findings indicate the possibility that sex hormones play important roles in determining sex differences in lung carcinogenesis in the A/J mice initiated by NNK.

[364]

TÍTULO / TITLE: - Lesion Detection and Characterization With Context Driven Approximation in Thoracic FDG PET-CT Images of NSCLC Studies.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - IEEE Trans Med Imaging. 2013 Oct 16.

●● Enlace al texto completo (gratis o de pago) [1109/TMI.2013.2285931](#)

AUTORES / AUTHORS: - Song Y; Cai W; Huang H; Wang X; Zhou Y; Fulham M; Feng D

RESUMEN / SUMMARY: - We present a lesion detection and characterization method for 18F-fluorodeoxyglucose positron emission tomography - computed tomography (FDG PET-CT) images of the thorax in the evaluation of patients with primary non-small cell lung cancer (NSCLC) with regional nodal disease. Lesion detection can be difficult due to low contrast between lesions and normal anatomical structures. Lesion characterization is also challenging due to similar spatial characteristics between the lung tumors and abnormal lymph nodes. To tackle these problems, we propose a context driven approximation (CDA) method. There are two main components of our method. First, a sparse representation technique with region-level contexts was designed for lesion detection. To discriminate low-contrast data with sparse representation, we propose a reference consistency constraint and a spatial consistent constraint. Second, a multi-atlas technique with image-level contexts was designed to represent the spatial characteristics for lesion characterization. To accommodate inter-subject variation in a multi-atlas model, we propose an appearance constraint and a similarity constraint. The CDA method is effective with a simple feature set, and does not require parametric modeling of feature space separation. The experiments on a clinical FDG PET-CT dataset show promising performance improvement over the state-of-the-art.

[365]

TÍTULO / TITLE: - Follow-up after lung cancer resection: is intensified also justified?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur Respir J. 2013 Nov;42(5):1178-9. doi: 10.1183/09031936.00085513.

●● Enlace al texto completo (gratis o de pago) [1183/09031936.00085513](#)

AUTORES / AUTHORS: - Van Schil PE

INSTITUCIÓN / INSTITUTION: - Antwerp University Hospital, Edegem, Belgium.

[366]

TÍTULO / TITLE: - Do mutations of the enhancer of zeste homolog 2 gene exist in small-cell lung cancer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):e103. doi: 10.1097/JTO.0b013e3182a85814.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a85814](https://doi.org/10.1097/JTO.0b013e3182a85814)

AUTORES / AUTHORS: - Toyokawa G; Takenoyama M; Ichinose Y

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology National Kyushu Cancer Center Minami-ku, Fukuoka, Japan.

[367]

TÍTULO / TITLE: - Impact and Safety of Adjuvant Chemotherapy on Pulmonary Function in Early Stage Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Respiration. 2013 Oct 30.

●● Enlace al texto completo (gratis o de pago) [1159/000355361](https://doi.org/10.1159/000355361)

AUTORES / AUTHORS: - Kreuter M; Vansteenkiste J; Herth FJ; Fischer JR; Eberhardt W; Zuna I; Reinmuth N; Griesinger F; Thomas M

INSTITUCIÓN / INSTITUTION: - Pneumology and Respiratory Critical Care Medicine, Thoraxklinik, University of Heidelberg, Germany.

RESUMEN / SUMMARY: - Background: Pulmonary function may decline after induction chemotherapy and predict perioperative complications in non-small cell lung cancer (NSCLC). The influence of adjuvant chemotherapy is largely indeterminate. Objective: To assess whether adjuvant chemotherapy alters pulmonary function and impacts on treatment-related adverse events. Methods: In a trial on adjuvant chemotherapy (the TREAT trial), 132 patients with R0-resected NSCLC were randomised to 4 cycles of cisplatin-vinorelbine (CVb, n = 65) or cisplatin-pemetrexed (CPx, n = 67). Pulmonary function tests (forced expiratory volume in 1 s, FEV1, forced vital capacity, FVC, total lung capacity, TLC, diffusing capacity for carbon monoxide, DLCO, and blood gas analyses, BGA) were analysed before and 30 days after the last chemotherapy, and changes were calculated (Delta = mean differences). Results: Overall, FVC increased significantly (Delta +290 ml, n = 76; p < 0.0001), while TLC did not change (Delta +220 ml, n = 41; p = 0.174). For CPx, FEV1 increased significantly (Delta +150 ml, n = 47; p = 0.0017), but not for CVb (Delta +30 ml, n = 30). DLCO decreased only for CVb (-8%, n = 6) but not for CPx (-0.39%, n = 17; p = 0.58). BGA did not change (p = 0.99). In a Cox regression analysis, baseline pulmonary function did not influence treatment failure. Conclusions: Adjuvant chemotherapy seems not to result in a decrease of pulmonary function parameters. A significant FVC increase was probably due to ongoing postoperative improvement. Decline of DLCO was noted with CVb but not with CPx. Pulmonary function does not impact on treatment failure. © 2013 S. Karger AG, Basel.

[368]

TÍTULO / TITLE: - Pulmonologists and lung cancer: pivotal role in multidisciplinary approach.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur Respir J. 2013 Nov;42(5):1183-5. doi: 10.1183/09031936.00145813.

- Enlace al texto completo (gratis o de pago) [1183/09031936.00145813](https://doi.org/10.1183/09031936.00145813)

AUTORES / AUTHORS: - Gaga M; Sculier JP; Rabe KF

INSTITUCIÓN / INSTITUTION: - Athens Chest Hospital, Athens, Greece.

[369]

TÍTULO / TITLE: - Strategies for improving outcomes in NSCLC: A look to the future.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):375-82. doi: 10.1016/j.lungcan.2013.08.025. Epub 2013 Sep 8.

- Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.08.025](https://doi.org/10.1016/j.lungcan.2013.08.025)

AUTORES / AUTHORS: - Stahel R; Peters S; Baas P; Brambilla E; Cappuzzo F; De Ruyscher D; Eberhardt WE; Felip E; Fennell D; Marchetti A; Paz-Ares L; Adjei AA
INSTITUCIÓN / INSTITUTION: - Department of Oncology, University Hospital Zurich, Zurich, Switzerland. Electronic address: Rolf.stahel@usz.ch.

RESUMEN / SUMMARY: - Advances in the management of non-small cell lung cancer (NSCLC) over the past 30 years have led to small increases in 5-year survival rates across Europe, though further improvements may require new treatment strategies. In order to improve efficiency and reduce the cost of development, future trials for new targeted agents in NSCLC should aim to recruit patients on the basis of tumour biology rather than clinical characteristics. However, identification of predictive biomarkers is required to maximise the benefits of new approaches and expedite the drug development process. Nevertheless, the NSCLC landscape is changing rapidly, and recent improvements in our understanding of the molecular biology of the disease will help in the identification of novel targeted agents as well as assisting in the development of personalised strategies for the numerous small subsets of defined NSCLC. Progress in imaging and treatment delivery is also likely to improve outcomes for patients with the disease. This article outlines recent progress in the treatment of NSCLC, identifies current challenges and describes proposals for improving the future management of the disease. It is hoped that implementation of some of these strategies will go some way to improving the outlook for patients with NSCLC.

[370]

TÍTULO / TITLE: - The N2 paradox: similar outcomes of pre- and postoperatively identified single-zone N2a positive non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Cardiothorac Surg. 2013 Sep 29.

- Enlace al texto completo (gratis o de pago) [1093/ejcts/ezt478](https://doi.org/10.1093/ejcts/ezt478)

AUTORES / AUTHORS: - Tsitsias T; Boulemden A; Ang K; Nakas A; Waller DA

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Glenfield Hospital, Leicester, UK.

RESUMEN / SUMMARY: - OBJECTIVES: Resection of N2a non-small-cell lung cancer (NSCLC) diagnosed preoperatively is controversial but there is support for resection of unexpected N2 disease discovered at surgery. Since the seventh TNM edition, we have intentionally resected clinical N2a disease. To validate this policy, we determined prognostic factors associated with all resected N2 disease. METHODS: From a prospective database of 1131 consecutive patients undergoing elective resection for

primary lung cancer over a period of 8 years, we identified 68 patients (35 females (51.4%), mean age 66 years, standard deviation (SD) 9 years) who had pathological N2 disease. All patients had positron emission computed tomography (CT-PET) staging and selective mediastinoscopy. A Cox-regression analysis was performed to identify prognostic factors. RESULTS: At a median follow-up of 38.7 months (standard error 10, 95% confidence interval (CI) 19.0-58.4), the overall median survival was 22.2 months (95% CI 14.6-29.8) with 1-, 2- and 5-year survival rates of 63.3, 46.6 and 13.2%, respectively. Survival after resection of pN2 disease is adversely affected by the need for pneumonectomy, multizone pN2b involvement and by non-compliance with adjuvant chemotherapy. Pathological involvement of the subcarinal zone but no other zone appears to be associated with an adverse prognosis (hazard ratio (HR) 1.87, P = 0.063). Importantly, long-term survival is not different between those patients who have a negative preoperative PET-CT scan and yet are found to have pN2 after resection, and those who are single-zone cN2a positive before resection on PET-CT scan (HR 1.37, P = 0.335). CONCLUSIONS: Our results support a policy of intentionally resecting single-zone N2a NSCLC identified preoperatively as part of a multimodality therapy.

[371]

TÍTULO / TITLE: - Accelerated hypo-fractionated radiotherapy for non small cell lung cancer: Results from 4 UK centres.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiother Oncol. 2013 Oct;109(1):8-12. doi: 10.1016/j.radonc.2013.07.014. Epub 2013 Oct 3.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.radonc.2013.07.014](#)

AUTORES / AUTHORS: - Din OS; Harden SV; Hudson E; Mohammed N; Pemberton LS; Lester JF; Biswas D; Magee L; Tufail A; Carruthers R; Sheikh G; Gilligan D; Hatton MQ

INSTITUCIÓN / INSTITUTION: - Dept. of Clinical Oncology, Weston Park Hospital, Sheffield, UK.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: A variety of radiotherapy fractionations are used as potentially curative treatments for non-small cell lung cancer. In the UK, 55Gy in 20 fractions over 4weeks (55/20) is the most commonly used fractionation schedule, though it has not been validated in randomized phase III trials. This audit pooled together existing data from 4 UK centres to produce the largest published series for this schedule. MATERIALS AND METHODS: 4 UK centres contributed data (Cambridge, Cardiff, Glasgow and Sheffield). Case notes and radiotherapy records of radically treated patients between 1999 and 2007 were retrospectively reviewed. Basic patient demographics, tumour characteristics, radiotherapy and survival data were collected and analysed. RESULTS: 609 patients were identified of whom 98% received the prescribed dose of 55/20. The median age was 71.3years, 62% were male. 90% had histologically confirmed NSCLC, 49% had stage I disease. 27% had received chemotherapy (concurrent or sequential) with their radiotherapy. The median overall survival from time of diagnosis was 24.0months and 2year overall survival was 50%. CONCLUSION: These data show respectable results for patients treated with accelerated hypo-fractionated radiotherapy for NSCLC with

outcomes comparable to those reported for similar schedules and represent the largest published series to date for 55/20 regime.

[372]

TÍTULO / TITLE: - Transcriptional analysis of hnRNPA0, A1, A2, B1, and A3 in lung cancer cell lines in response to acidosis, hypoxia, and serum deprivation conditions.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Lung Res. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [3109/01902148.2013.856049](#)

AUTORES / AUTHORS: - Romero-Garcia S; Prado-Garcia H; Lopez-Gonzalez JS

INSTITUCIÓN / INSTITUTION: - Department of Chronic-Degenerative Diseases, National Institute of Respiratory Diseases "Ismael Cosío Villegas," Mexico City, Mexico.

RESUMEN / SUMMARY: - ABSTRACT The ribonucleoproteins (hnRNPs) have important roles in multiple aspects of nucleic acid metabolism and in the regulation of different cellular processes. Abnormal expression of hnRNPs has been reported in several types of cancer including lung, pancreatic, and gastric carcinomas. Heterogeneous tumor cell populations generate a tumor microenvironment that can present normoxic, hypoxic, or acidic regions. The analysis of hnRNP transcriptional responses considering the changing nature of the tumor microenvironment is important to understand tumor cell survival under stress conditions. We analyzed the transcriptional response of hnRNPA0, A1, A2, B1, and A3 in lung tumor cell lines under acidosis, hypoxia, and serum deprivation conditions. We used qRT-PCR to obtain a relative quantification of the hnRNPA/B transcript levels. We found that the hnRNPA2 transcript was the most abundant, followed by B1, A0, and A1. Expression of hnRNPA3 was the lowest, although its transcript levels were the most constant. hnRNPA/B transcript levels in lung tumor cell lines responded to changes in the microenvironment; however, hnRNPB1 transcript levels relative to hnRNPA2 expression did not change in all tested stress conditions, indicating that the alternative splicing between these isoforms was constant. hnRNPA1, A2, and B1 transcript levels were upregulated under serum deprivation conditions; possibly to promote a migration phenotype. Our data provide new insights into the transcriptional responses of ribonucleoproteins that might favor tumor cell survival and migration.

[373]

TÍTULO / TITLE: - Real-world healthcare resource utilization in a European non-small cell lung cancer population: the EPICLIN-Lung study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Med Res Opin. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1185/03007995.2013.860373](#)

AUTORES / AUTHORS: - Vergnenegre A; Carrato A; Thomas M; Jernigan C; Medina J; Cruciani G

INSTITUCIÓN / INSTITUTION: - Hopital le Cluzeau, Service de l'Information Medicale et de l'Evaluation (SIME), Limoges, France.

RESUMEN / SUMMARY: - Abstract Background: There is a lack of data on health resource assessment in non-small cell lung cancer (NSCLC) to inform clinical decision-

making. The Epidemiological Study to Describe NSCLC Clinical Management Pattern in Europe-Lung (EPICLIN-Lung) study provides information on healthcare resource utilization associated with different NSCLC treatment strategies in real-life clinical settings. Methods: This multinational, multicenter, non-interventional study (NCT00831909) was conducted in eight European countries in 2009-2010. Patients with confirmed NSCLC were enrolled and followed for 12 months or until death. Information was collected on patient and disease characteristics, diagnosis and treatment patterns. Healthcare resource utilization was described in relation to diagnostic patterns and treatment received. Results: Data were available for 3508 patients (median age = 65.0 years, male = 77.6%, Caucasian = 98.4%, adenocarcinoma = 43.8%, stage IV = 48.6%, 10.8% never smoked). The overall mean number of hospitalization days was 16.4 (standard deviation (SD) = 18.42). Patients were followed up for a mean of 245.8 (131.4) days. Most patients (96.0%) underwent imaging procedures, most commonly scanning (93.9%). Surgery was associated with a mean of 12.5 (9.33) hospitalization days, with lobectomy and extended procedures (20.3%) being the most common surgery types. Radiotherapy resulted in a mean of 11.6 (14.12) hospitalization days. The majority of radiotherapy was palliative (56.0%), which resulted in fewer (mean 9.5 [11.12]) hospitalization days. Administration of systemic treatment resulted in a mean of 6.5 (8.04) hospitalization days, 1.7 (3.59) visits for disease-related events, 2.3 (1.83) adverse events and 5.4 (5.86) blood-specific resources. The key limitations of this study are those inherent to its non-interventional nature and wide regional focus, and the lack of cost-effectiveness data. Conclusions: EPICLIN-Lung provides important, Europe-wide information on drivers of healthcare resource use in different treatment strategies for NSCLC.

[374]

TÍTULO / TITLE: - BAI3, CDX2 and VIL1: a panel of three antibodies to distinguish small cell from large cell neuroendocrine lung carcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Histopathology. 2013 Nov 25. doi: 10.1111/his.12278.

●● [Enlace al texto completo \(gratis o de pago\) 1111/his.12278](#)

AUTORES / AUTHORS: - Bari MF; Brown H; Nicholson AG; Kerr KM; Gosney JR; Wallace WA; Soomro I; Muller S; Peat D; Moore JD; Ward LA; Freidin MB; Lim E; Vatish M; Snead DR

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Dow International Medical College, Karachi, Pakistan; Department of Pathology, University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK; Divisions of Reproduction and Metabolic and Vascular Health, Warwick Medical School, Coventry, UK.

RESUMEN / SUMMARY: - AIMS: Discriminating small-cell lung carcinoma (SCLC) from large-cell neuroendocrine carcinoma (LCNEC) rests on morphological criteria, and reproducibility has been shown to be poor. We aimed to identify immunohistochemical markers to assist this diagnosis. METHODS AND RESULTS: Gene expression profiling on laser captured frozen tumour samples from eight SCLC and eight LCNEC tumours identified a total of 888 differentially expressed genes (DEGs), 23 of which were validated by qRT-PCR. Antibodies to four selected gene products were then evaluated as immunohistochemical markers on a cohort of 173 formalin-fixed paraffin-embedded (FFPE) SCLC/LCNEC tumour samples, including 26 indeterminate tumours without a

consensus diagnosis. Three markers, CDX2, VIL1 and BAI3, gave significantly different results in the two tumour types ($P < 0.0001$): CDX2 and VIL1 in combination (either marker positive) showed sensitivity and specificity of 81% for LCNEC while BAI3 showed 89% sensitivity and 75% specificity for SCLC. Of the 26 indeterminate tumours 15 (58%) showed an immunophenotype suggesting either SCLC or LCNEC, eight (31%) showed staining of both tumour types, and three (11%) were negative for all markers. CONCLUSION: A panel of three markers, BAI3, CDX2 and VIL1, is a useful adjunct in the diagnosis of these tumour types.

[375]

TÍTULO / TITLE: - Paclitaxel loaded self-assembled nanocarrier reduces multidrug resistance in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Control Release. 2013 Nov 28;172(1):e96. doi: 10.1016/j.jconrel.2013.08.194.

●● Enlace al texto completo (gratis o de pago) [1016/j.jconrel.2013.08.194](#)

AUTORES / AUTHORS: - Zhang Z; Bu H; Liu Z; Wang Y; Niu B; Li Y

INSTITUCIÓN / INSTITUTION: - Center for Drug Delivery, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China.

[376]

TÍTULO / TITLE: - The VEGF pathway in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Dec;72(6):1169-81. doi: 10.1007/s00280-013-2298-3. Epub 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago) [1007/s00280-013-2298-3](#)

AUTORES / AUTHORS: - Alevizakos M; Kaltsas S; Syrigos KN

INSTITUCIÓN / INSTITUTION: - Oncology Unit GPP, Sotiria General Hospital, Athens School of Medicine, Athens, Greece.

RESUMEN / SUMMARY: - INTRODUCTION: Lung cancer is a disease whose prognosis has remained poor in the last decades. Recent advances in the understanding of the molecular pathways behind this disease have revealed several mediators of important tumor functions. One of these functions is angiogenesis, which is considered essential for tumor growth and propagation, and a key mediator promoting this process is the vascular endothelial growth factor (VEGF). In lung cancer, VEGF plays a significant role in establishing a vascular supply within the tumor. Thus, a new class of drugs has emerged, targeting its pathway, which has offered substantial, albeit small, improvements in patient prognosis. AREAS COVERED: The VEGF pathway and its role in a multitude of different human cancers are presented at first. We then proceed by analyzing its importance in lung cancer and exploring the therapeutic benefits achieved by its targeting, which set new goals for the future. EXPERT OPINION: Today, the VEGF pathway remains an attractive target for anticancer treatment, and the way forward requires detection of predictive markers and efforts for a more complete angiogenic blockade.

[377]

TÍTULO / TITLE: - Differences in the prognostic implications of vascular invasion between lung adenocarcinoma and squamous cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):407-12. doi: 10.1016/j.lungcan.2013.09.001. Epub 2013 Sep 12.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.001](#)

AUTORES / AUTHORS: - Usui S; Minami Y; Shiozawa T; Iyama S; Satomi K; Sakashita S; Sato Y; Noguchi M

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennoudai, Tsukuba-shi, Ibaraki, 305-8575, Japan; Department of Thoracic Surgery, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennoudai, Tsukuba-shi, Ibaraki, 305-8575, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: Vascular invasion (VI) has been accepted as a universally important prognostic factor for patients with lung carcinoma. However, the clinical significance of VI in each of the histological subtypes has been unclear. The aim of the present study was to investigate differences in the clinicopathological implications of VI between adenocarcinoma and squamous cell carcinoma. METHOD: A total of 336 patients were evaluated, of whom 81 were diagnosed as having peripheral-type squamous cell carcinoma, and 255 as having adenocarcinoma. RESULT: Among the 336 patients, the five-year survival rates for those who were VI-positive and VI-negative were 38.4% and 76.3%, respectively, the difference being significant ($p < 0.0001$). Multivariate analysis identified VI as an independent prognostic factor (hazard ratio: 1.86). Although the difference in cancer-free survival between VI-positive and -negative patients was statistically significant for adenocarcinoma ($p < 0.0001$), it was not significant for squamous cell carcinoma ($p = 0.086$). For adenocarcinoma, the difference between the survival curves for VI-positive and -negative patients was significant for the subtypes with a predominant lepidic ($p < 0.0001$), papillary ($p = 0.0026$), and acinar ($p = 0.0060$) component, whereas that for the predominantly solid subtype was not significant ($p = 0.58$). Squamous cell carcinomas were then divided into two groups on the basis of the diameter of vessels that had been invaded by the cancer cells: large-vessel invasion (LVI; 1000µm or more) and small-vessel invasion (SVI; less than 1000µm). Although there was no difference in the survival curves between the LVI and SVI groups, the LVI group showed a significantly higher incidence of cavity formation and distant metastasis. CONCLUSION: We conclude that VI is a useful prognostic indicator in lung carcinoma, although the clinical implications of VI differ between adenocarcinoma and squamous cell carcinoma.

[378]

TÍTULO / TITLE: - Lung cancer screening.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chest. 2013 Nov 1;144(5):1737. doi: 10.1378/chest.13-1539.

●● Enlace al texto completo (gratis o de pago) [1378/chest.13-1539](#)

AUTORES / AUTHORS: - Lamb CR; McKee AB; McKee BJ; Campagna A; Hesketh PJ

[379]

TÍTULO / TITLE: - Gastric bronchogenic cyst histologically diagnosed after laparoscopic excision: report of a case.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int Surg. 2013 Oct-Dec;98(4):455-60. doi: 10.9738/INTSURG-D-12-00038.1.

●● Enlace al texto completo (gratis o de pago) [9738/INTSURG-D-12-00038.1](#)

AUTORES / AUTHORS: - Kurokawa T; Yamamoto M; Ueda T; Enomoto T; Inoue K; Uchida A; Kikuchi K; Ohkohchi N

INSTITUCIÓN / INSTITUTION: - 1 Department of Surgery, Tsukuba Medical Center Hospital, Tsukuba City, Japan.

RESUMEN / SUMMARY: - Abstract Abdominal computed tomography of a 71-year-old man revealed a 3-cm mass in gastric cardia. Although the mass was widely attached to the gastric wall, no clear contrast enhancement was observed. Abdominal magnetic resonance imaging revealed the mass to have homogenous high intensity on T2W1 images and isointensity on T1W1 images. On diffusion-weighted imaging, no high intensity was observed. However, the mass had a smooth surface and was widely attached to the gastric wall, consistent with computed tomography findings. A gastric submucosal tumor was suspected. Laparoscopic tumor resection was performed. Histopathologic diagnosis of the mass was a bronchogenic cyst derived from the respiratory primordium originating in the foregut of the primitive intestine. Such cysts are mostly found in the mediastinum or thoracic cavity; their occurrence on the gastric wall is extremely rare. Despite this, we think that bronchogenic cysts should be considered in the differential diagnosis of abdominal unilocular cystic diseases.

[380]

TÍTULO / TITLE: - Hsa-miR-132 Regulates Apoptosis in Non-Small Cell Lung Cancer Independent of Acetylcholinesterase.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Mol Neurosci. 2013 Oct 26.

●● Enlace al texto completo (gratis o de pago) [1007/s12031-013-0136-z](#)

AUTORES / AUTHORS: - Zhang B; Lu L; Zhang X; Ye W; Wu J; Xi Q; Zhang X

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Cell Biology, Institute of Biochemistry and Cell Biology, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, China.

RESUMEN / SUMMARY: - MiR-132 is enriched in the central nerve system and is thought to be involved in neuronal development, maturation and function, and to be associated with several neurological disorders including Alzheimer's disease. In addition to its documented neuronal functions, an emerging role for miR-132 in tumorigenesis has been suggested. Recently, hsa-miR-132 was shown to be modulated in different tumor types. However, its role in non-small cell lung cancer (NSCLC) remains unclear. Here, we show that hsa-miR-132 can initiate apoptosis in NSCLC cells to dramatically attenuate tumor formation in nude mice independent of its effect on the proliferation/apoptosis-associated gene, acetylcholinesterase (AChE). Interestingly, hsa-miR-132 has no pro-apoptotic effect in normal pulmonary trachea epithelium. Taken together, these results suggest that hsa-miR-132 represses NSCLC growth by inducing apoptosis independent of AChE.

[381]

TÍTULO / TITLE: - Procyanidin C1 from Cinnamomi Cortex inhibits TGF-beta-induced epithelial-to-mesenchymal transition in the A549 lung cancer cell line.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Oncol. 2013 Dec;43(6):1901-6. doi: 10.3892/ijo.2013.2139. Epub 2013 Oct 16.

●● Enlace al texto completo (gratis o de pago) [3892/ijo.2013.2139](#)

AUTORES / AUTHORS: - Kin R; Kato S; Kaneto N; Sakurai H; Hayakawa Y; Li F; Tanaka K; Saiki I; Yokoyama S

INSTITUCIÓN / INSTITUTION: - Division of Pathogenic Biochemistry, Institute of Natural Medicine, University of Toyama, Toyama 930-0194, Japan.

RESUMEN / SUMMARY: - Cancer metastasis is one of the most critical events in cancer patients, and the median overall survival of stage IIIb or IV patients with metastatic lung cancer in the TNM classification is only 8 or 5 months, respectively. We previously demonstrated that Juzentaihoto, a Japanese traditional medicine, can inhibit cancer metastasis through the activation of macrophages and T cells in mouse cancer metastatic models; however, the mechanism(s) through which Juzentaihoto directly affects tumor cells during the metastasis process and which herbal components from Juzentaihoto inhibit the metastatic potential have not been elucidated. In this study, we focused on the epithelial-to-mesenchymal transition (EMT), which plays an important role in the formation of cancer metastasis. We newly determined that only the Cinnamomi Cortex (CC) extract, one of 10 herbal components of Juzentaihoto, inhibits TGF-beta-induced EMT. Moreover, the contents of catechin trimer in CC extracts were significantly correlated with the efficacy of inhibiting TGF-beta-induced EMT. Finally, the structure of the catechin trimer from CC extract was chemically identified as procyanidin C1 and the compound showed inhibitory activity against TGF-beta-induced EMT. This illustrates that procyanidin C1 is the main active compound in the CC extract responsible for EMT inhibition and that procyanidin C1 could be useful as a lead compound to develop inhibitors of cancer metastasis and other diseases related to EMT.

[382]

TÍTULO / TITLE: - Methylation of P16 in exhaled breath condensate for diagnosis of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Sep 25. pii: S0169-5002(13)00433-9. doi: 10.1016/j.lungcan.2013.09.008.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.008](#)

AUTORES / AUTHORS: - Xiao P; Chen JR; Zhou F; Lu CX; Yang Q; Tao GH; Tao YJ; Chen JL

INSTITUCIÓN / INSTITUTION: - Department of Respiriology, Second Affiliated Hospital of Nantong University, Nantong 226001, China. Electronic address: kingfalcon@163.com.

RESUMEN / SUMMARY: - BACKGROUND: Non-small cell lung cancer is the most frequently cause of cancer-related death in the world. To explore the technical

feasibility, we detected aberrant promoter methylation of P16 in exhaled breath condensate which was a new, non-invasive tool for diagnosis and screening program of NSCLC. METHODS: We analyzed aberrant promoter methylation of P16 in 180 samples from 60 individuals, including 30 NSCLC patients (cancer tissues, adjacent normal lung tissues, blood plasma, and EBC), and 30 healthy controls (blood plasma and EBC) by fluorescent quantitative methylation-specific polymerase chain reaction (F-MSP). RESULTS: The positive rate of aberrant promoter methylation of P16 was 26 of 30 (86.66%) in tumor tissues, 15 of 30 (50%) in blood plasma, and 12 of 30 (40%) in EBC, we have not observed the positive methylation of P16 in the adjacent normal lung tissues, or in EBC or blood plasma from the healthy control group. CONCLUSION: We found that detected promoter methylation of P16 in EBC was feasible, it should be a useful biomarker for diagnosis of NSCLC, it has potential prospect that detected the gene molecular in EBC because of noninvasive, specificity, convenient and repeatable.

[383]

TÍTULO / TITLE: - The degree of microRNA-34b/c methylation in serum-circulating DNA is associated with malignant pleural mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):485-90. doi: 10.1016/j.lungcan.2013.09.017. Epub 2013 Oct 10.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.lungcan.2013.09.017](#)

AUTORES / AUTHORS: - Muraoka T; Soh J; Toyooka S; Aoe K; Fujimoto N; Hashida S; Maki Y; Tanaka N; Shien K; Furukawa M; Yamamoto H; Asano H; Tsukuda K; Kishimoto T; Otsuki T; Miyoshi S

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama University, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: Malignant pleural mesothelioma (MPM) is an aggressive tumor with a poor prognosis. microRNA-34b/c (miR-34b/c), which plays an important role in the pathogenesis of MPM, is frequently downregulated by DNA methylation in approximately 90% of MPM cases. In this study, we estimated the degree of miR-34b/c methylation in serum-circulating DNA using a digital methylation specific PCR assay (MSP). MATERIALS AND METHODS: A real-time MSP assay was performed using the SYBR Green method. The melting temperature TM of each PCR product was examined using a melting curve analysis. For a digital MSP assay, 40 wells were analyzed per sample. A total of 110 serum samples from 48 MPM cases, 21 benign asbestos pleurisy (BAP) cases, and 41 healthy volunteers (HVs) were examined. RESULTS: Positive range of T_m value for miR-34b/c methylation was defined as 77.71-78.79 degrees C which was the mean±3 standard deviations of 40 wells of a positive control. The number of miR-34b/c methylated wells was counted per sample according to this criterion. The number of miR-34b/c methylated wells in MPM cases was significantly higher than that in BAP cases (P=0.03) or HVs (P<0.001). Advanced MPM cases tended to have higher number of miR-34b/c methylated wells than early MPM cases. Receiver-operating characteristic (ROC) curve analysis revealed that three number of miR-34b/c methylated wells per sample was the best cut-off of positivity of MPM with a 67% of sensitivity and a 77% specificity for prediction. The area under the ROC curve was 0.77. CONCLUSIONS: Our digital MSP

assay can quantify miR-34b/c methylation in serum-circulating DNA. The degree of miR-34b/c methylation in serum-circulating DNA is associated with MPM, suggesting that this approach might be useful for the establishment of a new detection system for MPM.

[384]

TÍTULO / TITLE: - Quantification of serum SOX2 DNA with FQ-PCR potentially provides a diagnostic biomarker for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):737. doi: 10.1007/s12032-013-0737-y. Epub 2013 Oct 15.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0737-y](#)

AUTORES / AUTHORS: - Wu Y; Du X; Xue C; Li D; Zheng Q; Li X; Chen H

INSTITUCIÓN / INSTITUTION: - Clinical Laboratories, The First Affiliated Hospital of Chongqing Medical University, Chongqing, 400016, China.

RESUMEN / SUMMARY: - Sex-determining region Y-box 2 (SOX2), as a subunit of transcription and reprogramming factor, plays a critical role in the development and progression of many malignancies, including lung cancer through gene amplification. In the present study, we aimed to quantify the levels of serum SOX2 DNA, analyze its diagnostic value and compare it with existing clinical parameters in lung cancer, and purpose to provide a novel tumor marker for lung cancer. Serum DNA was extracted from 94 lung cancer patients, 10 benign lung diseases, and 30 healthy volunteers, and then the levels of SOX2 DNA were quantified using real-time fluorescent quantitative polymerase chain reaction (FQ-PCR). The data were analyzed by statistical software SPSS14.0. The present results show that serum SOX2 DNA level in lung cancer group was higher compared to the levels in benign lung diseases group ($u = 102.0$, $p < 0.001$) or healthy group ($u = 140.0$, $p < 0.001$), and it was closely associated with TNM stage, histopathological type, and tumor size ($p = 0.031$, $p = 0.012$, and $p = 0.010$, respectively). However, serum SOX2 DNA levels of lung cancer patients were not associated with age, gender, smoking status, lymph node metastasis, or tumor differentiation ($p > 0.05$). ROC curve showed a sensitivity of 78.9% and a specificity of 82.5% for the ability of serum SOX2 DNA to detect lung cancer at the cutoff value of 1,078.3 copies/ul. Furthermore, we assessed the associations of serum SOX2 levels with clinical existing lung tumor markers, such as squamous cell carcinoma antigen, cytokeratin fragment 21-1, and neuron-specific enolase. The sensitivity was increased from 24.9, 66.1, and 39.1 to 84.2, 92.8, and 87.5%, respectively, by the combination of serum SOX2 DNA. Taken together, quantification of serum SOX2 DNA by FQ-PCR may serve as a novel accessory diagnostic tool for the clinical screening and detection of lung cancer.

[385]

TÍTULO / TITLE: - Computed tomography screening for lung cancer: Results of ten years of annual screening and validation of cosmos prediction model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):426-30. doi: 10.1016/j.lungcan.2013.08.026. Epub 2013 Sep 8.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.08.026](https://doi.org/10.1016/j.lungcan.2013.08.026)

AUTORES / AUTHORS: - Veronesi G; Maisonneuve P; Rampinelli C; Bertolotti R; Petrella F; Spaggiari L; Bellomi M

INSTITUCIÓN / INSTITUTION: - Division of Thoracic Surgery, European Institute of Oncology, Milan, Italy. Electronic address: giulia.veronesi@ieo.it.

RESUMEN / SUMMARY: - INTRODUCTION: It is unclear how long low-dose computed tomographic (LDCT) screening should continue in populations at high risk of lung cancer. We assessed outcomes and the predictive ability of the COSMOS prediction model in volunteers screened for 10 years. MATERIALS AND METHODS: Smokers and former smokers (>20 pack-years), >50 years, were enrolled over one year (2000-2001), receiving annual LDCT for 10 years. The frequency of screening-detected lung cancers was compared with COSMOS and Bach risk model estimates. RESULTS: Among 1035 recruited volunteers (71% men, mean age 58 years) compliance was 65% at study end. Seventy-one (6.95%) lung cancers were diagnosed, 12 at baseline. Disease stage was: IA in 48 (66.6%); IB in 6; IIA in 5; IIB in 2; IIIA in 5; IIIB in 1; IV in 5; and limited small cell cancer in 3. Five- and ten-year survival were 64% and 57%, respectively, 84% and 65% for stage I. Ten (12.1%) received surgery for a benign lesion. The number of lung cancers detected during the first two screening rounds was close to that predicted by the COSMOS model, while the Bach model accurately predicted frequency from the third year on. CONCLUSIONS: Neither cancer frequency nor proportion at stage I decreased over 10 years, indicating that screening should not be discontinued. Most cancers were early stage, and overall survival was high. Only a limited number of invasive procedures for benign disease were performed. The Bach model - designed to predict symptomatic cancers - accurately predicted cancer frequency from the third year, suggesting that overdiagnosis is a minor problem in lung cancer screening. The COSMOS model - designed to estimate screening-detected lung cancers - accurately predicted cancer frequency at baseline and second screening round.

[386]

TÍTULO / TITLE: - Comparison of Once and Twice Daily Radiotherapy for Limited Stage Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Oct 27.

●● Enlace al texto completo (gratis o de pago) [1007/s00408-013-9518-9](https://doi.org/10.1007/s00408-013-9518-9)

AUTORES / AUTHORS: - Gazula A; Baldini EH; Chen A; Kozono D

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Dana-Farber Cancer Institute/Brigham and Women's Hospital, 450 Brookline Avenue, Boston, MA, 02215, USA, agazula@umich.edu.

RESUMEN / SUMMARY: - PURPOSE: This study was designed to review outcomes of once- (QD) versus twice-daily (BID) radiotherapy (RT) for limited stage small-cell lung cancer (L-SCLC) treated at Dana-Farber Cancer Institute/Brigham and Women's Hospital. METHODS: We reviewed records for all patients with L-SCLC treated with radical chemoradiotherapy at our institution between January 2005 and December 2010. Differences in patient, tumor, and treatment characteristics were assessed by Student's t test and Fisher exact test. Outcomes were compared using Kaplan-Meier estimates and Cox proportional hazards regression. RESULTS: Twenty patients

received QD RT to a median dose of 61.2 Gy, and 26 patients received BID RT to a dose of 45 Gy. Median follow-up was 2.8 years. Overall survival (OS) was similar in both groups. 5-year locoregional control (LC) for all patients was 67 %: 80 % for the QD group and 57 % for the BID group (log-rank, P = 0.16). Grade 2 or higher dermatitis and pneumonitis were significantly higher in the QD group (15 vs. 0 %, P = 0.0014 and 13 vs. 4 %, P = 0.048, respectively), whereas Grade 2 or higher esophagitis trended higher in the BID group (44 vs. 24 %, P = 0.076). CONCLUSIONS: Although there were no differences in OS with QD versus BID RT, there was a trend toward increased LC in the QD group. Dermatitis and pneumonitis were more common for QD RT, and esophagitis was somewhat more common for BID RT. Possible differences in toxicities depending on RT regimen may be worth further investigation, until results from CALGB 30610 become available.

[387]

TÍTULO / TITLE: - Lung cancer screening with CT: Evaluation of radiologists and different computer assisted detection software (CAD) as first and second readers for lung nodule detection at different dose levels.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Radiol. 2013 Dec;82(12):e873-8. doi: 10.1016/j.ejrad.2013.08.026. Epub 2013 Sep 25.

●● Enlace al texto completo (gratis o de pago) [1016/j.ejrad.2013.08.026](#)

AUTORES / AUTHORS: - Christe A; Leidolt L; Huber A; Steiger P; Szucs-Farkas Z; Roos JE; Heverhagen JT; Ebner L

INSTITUCIÓN / INSTITUTION: - Department of Diagnostic, Interventional und Pediatric Radiology, University Hospital, Inselspital, Bern, Switzerland. Electronic address: andreas.christe@insel.ch.

RESUMEN / SUMMARY: - OBJECTIVES: To find the best pairing of first and second reader at highest sensitivity for detecting lung nodules with CT at various dose levels. MATERIALS AND METHODS: An anthropomorphic lung phantom and artificial lung nodules were used to simulate screening CT-examination at standard dose (100mAs, 120kVp) and 8 different low dose levels, using 120, 100 and 80kVp combined with 100, 50 and 25mAs. At each dose level 40 phantoms were randomly filled with 75 solid and 25 ground glass nodules (5-12mm). Two radiologists and 3 different computer aided detection softwares (CAD) were paired to find the highest sensitivity. RESULTS: Sensitivities at standard dose were 92%, 90%, 84%, 79% and 73% for reader 1, 2, CAD1, CAD2, CAD3, respectively. Combined sensitivity for human readers 1 and 2 improved to 97%, (p1=0.063, p2=0.016). Highest sensitivities - between 97% and 99.0% - were achieved by combining any radiologist with any CAD at any dose level. Combining any two CADs, sensitivities between 85% and 88% were significantly lower than for radiologists combined with CAD (p<0.03). CONCLUSIONS: Combination of a human observer with any of the tested CAD systems provide optimal sensitivity for lung nodule detection even at reduced dose at 25mAs/80kVp.

[388]

TÍTULO / TITLE: - High rate of FGFR1 amplifications in brain metastases of squamous and non-squamous lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 17. pii: S0169-5002(13)00447-9. doi: 10.1016/j.lungcan.2013.10.004.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.004](#)

AUTORES / AUTHORS: - Preusser M; Berghoff AS; Berger W; Ilhan-Mutlu A; Dinhof C; Widhalm G; Dieckmann K; Wohrer A; Hackl M; von Deimling A; Streubel B; Birner P

INSTITUCIÓN / INSTITUTION: - Department of Medicine I, Medical University of Vienna, Vienna, Austria; Comprehensive Cancer Center Vienna, Central Nervous System Tumours Unit (CCC-CNS), Vienna, Austria.

RESUMEN / SUMMARY: - **OBJECTIVES:** FGFR1 amplifications are common in squamous cell carcinoma and rare in adenocarcinoma of the lung, but have not been investigated in brain metastases of non-small cell lung cancer (NSCLC). **MATERIALS AND METHODS:** We performed fluorescent in situ hybridization (FISH) for FGFR1 and immunohistochemistry for pAKT, PI3K, HIF1a and Ki67 in 175 NSCLC brain metastases and 11 matched primary tumors. ALK gene rearrangement status was available from a previous study. We performed statistical correlations of clinical, histopathological and molecular data. **RESULTS:** FGFR1 amplifications were found in a total of 30/175 (17%) brain metastases: 4/21 (19%) squamous cell carcinomas, 20/130 (15.3%) adenocarcinomas, 2/12 (16.6%) adenosquamous carcinomas, 4/9 (44.4%) large cell carcinomas and 0/3 neuroendocrine large cell carcinoma. FGFR1 gene status was identical between primary tumors and brain metastases in 9/11 evaluable cases. In 2/11 cases (1 adenosquamous and 1 large cell carcinoma), FGFR1 amplifications were present only in the brain metastasis and not in the primary tumor. Furthermore, we found a significant positive correlation of ALK and FGFR1 gene amplification status in brain metastases ($p < 0.001$, Chi square test). Patients with high-level FGFR1 amplifications had significantly higher number of visceral metastases ($p < 0.001$, Chi square test). **CONCLUSION:** Our findings argue for an enrichment of FGFR1 amplifications in brain metastases of adenocarcinomas (where they were 5-fold more frequent than reported for primary tumors) and possibly also of other non-squamous carcinomas, but not in squamous cell carcinomas of the lung. These results may be relevant for targeted therapy and prophylaxis of NSCLC brain metastases.

[389]

TÍTULO / TITLE: - Spontaneous rupture of a giant intrapericardial bronchogenic cyst.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Surg. 2013 Nov;96(5):e109-10. doi: 10.1016/j.athoracsur.2013.05.095.

●● Enlace al texto completo (gratis o de pago)

[1016/j.athoracsur.2013.05.095](#)

AUTORES / AUTHORS: - Lu Q; Yang E; Wang W; Wang X; Li X

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Tangdu Hospital, Fourth Military Medical University, Xi'an, China.

RESUMEN / SUMMARY: - Bronchogenic cysts arise from an abnormal budding of the ventral diverticulum of the foregut or the tracheobronchial tree during embryogenesis. They are rarely found intrapericardially. Herein, we report the case of a 43-year-old man who presented with a ruptured intrapericardial bronchogenic cyst (IBC), with aggravating symptoms of chest tightness and shortness of breath. The cyst was

completely resected, and the patient's postoperative recovery was uneventful. This is the first report with radiologic evidence of an IBC that ruptured, rapidly releasing cystic liquid into the pericardium and exacerbating the patient's symptoms. These results argue for the complete surgical excision of an IBC at the time of diagnosis, even if the patient is asymptomatic.

[390]

TÍTULO / TITLE: - Diagnosis and phylogenetic analysis of ovine pulmonary adenocarcinoma in China.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Virus Genes. 2013 Oct 23.

●● Enlace al texto completo (gratis o de pago) [1007/s11262-013-0988-x](#)

AUTORES / AUTHORS: - Zhang K; Kong H; Liu Y; Shang Y; Wu B; Liu X

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Veterinary Etiological Biology, National Foot-and-Mouth Disease Reference Laboratory, Lanzhou Veterinary Research Institute, Chinese Academy of Agricultural Sciences, Xujiaping No.1, Yanchangpu, Lanzhou, 730046, Gansu, People's Republic of China, zks009@126.com.

RESUMEN / SUMMARY: - Ovine pulmonary adenocarcinoma (OPA) is a lung tumor of sheep caused by jaagsiekte sheep retrovirus (JSRV). OPA is common in sheep, and it is most commonly observed in China. Without preventative vaccines and serological diagnostic tools for assay of OPA, identification of JSRV based on reverse transcription polymerase chain reaction (RT-PCR) is very important for prevention and control measures for OPA in practice management. In this study, the diagnosis of OPA was made from analysis of clinical signs, pathological observations, JSRV-like particle discovery, and RT-PCR of the target env gene. The phylogenetic analysis showed that the China Shandong (SD) strain studied in this article belonged to exogenous JSRV, and it was very similar to 92k3, which was isolated from sheep in the Kenya (Y18305). The current study reported a severe outbreak of OPA in Shandong Province, China. The observations could offer a comparative view of the env gene of JSRV.

[391]

TÍTULO / TITLE: - A comparison on expression of selected biomarkers between primary lung cancers and matched metastases.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):742. doi: 10.1007/s12032-013-0742-1. Epub 2013 Oct 8.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0742-1](#)

AUTORES / AUTHORS: - Gao D; Zhang T; Li S; Liu Q; Du J

INSTITUCIÓN / INSTITUTION: - Institute of Oncology, Provincial Hospital Affiliated to Shandong University, Shandong University, 324 Jingwu Road, Jinan, 250021, Shandong Province, People's Republic of China.

RESUMEN / SUMMARY: - Many biomarkers have been identified to be new targeted drugs for lung cancer treatment. Their clinical outcomes are determined by their status mainly evaluated from primary cancer tissues. However, metastasis is the leading cause of death in cancer patients. It is unclear whether their status in primary cancers

is similar to that in corresponding metastases. Therefore, we aimed to evaluate similarities or differences for the selected biomarker expression between primary lung cancers and matched metastases and to provide evidence for further using these targets in metastatic tumors from lung cancer. Eleven patients who had received resection of paired tissues of primary lung cancers and matched metastases were collected. The protein expression of VEGF, HIF-1alpha, Met, P53, TGF-beta1, Cox-2 and TNF-alpha between paired tumors was detected by immunohistochemistry. The results showed that there was no statistical significance between primary cancers and matched metastases for the expressions of the selected biomarkers. The p values were more than 0.05. The major concordance of the selected biomarkers existed between paired primary and metastatic tumors. However, there were still minor differences. Differences in metastases compared with primary tumors were observed in respective two cases for VEGF, HIF-1alpha and Met, respective one case for TGF-beta1, COX2 and TNFalpha and three cases for P53. In conclusion, there were major concordance and minor difference for each biomarker between primary lung tumors and corresponding metastases, which may have important implications for the understanding of current metastasis models and treatment of advanced lung cancers.

[392]

TÍTULO / TITLE: - Stratification of Malignant Pleural Mesothelioma Prognosis Using Recursive Partitioning Analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Oct 20.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00408-013-9516-y](#)

AUTORES / AUTHORS: - Suzuki H; Asami K; Hirashima T; Okamoto N; Yamadori T; Tamiya M; Morishita N; Shiroyama T; Takeoka S; Osa A; Azuma Y; Okishio K; Kawaguchi T; Atagi S; Kawase I

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Malignancy, Osaka Prefectural Medical Center for Respiratory and Allergic Diseases, 3-7-1 Habikino Habikino-shi, Osaka, 583-8588, Japan, suzukih@opho.jp.

RESUMEN / SUMMARY: - **PURPOSE:** Prognostic factors and complicated prognostic models have been proposed for malignant pleural mesothelioma (MPM). This study was designed to stratify MPM prognosis by using a simple model. **METHODS:** Patients diagnosed with MPM in the past 10 years (n = 122) were examined retrospectively. Data on the presence of chest pain, performance status (PS), asbestos exposure, smoking status, white blood cell count (WBC), haemoglobin (Hb) concentration, platelet count (PLT), lactate dehydrone (LD), histology, stage, and date of death or censored status were collected. After the factors were examined in the univariate analysis, recursive partitioning analysis was performed. **RESULTS:** Statistically significant factors related to survival were the type of histology, stage, PS, WBC, PLT, Hb concentration, and LD. Histology, stage, PS, and Hb concentration were used in multivariate analysis. Stage and Hb concentration showed good statistical significance, whereas PS was borderline significant. The survival analyses were stratified into five groups by PS, stage, Hb concentration, and chest pain using recursive partitioning analysis. Group A comprised patients showing the most favourable prognoses (PS 0-2 and Hb concentration >12.1 g dL⁻¹ or PS 0-2 and Hb concentration ≤12.1 g dL⁻¹ without pain), and group B comprised the remaining patients. The median overall

survival in groups A and B was 563 days (95 % confidence interval [CI] 502-779) and 157 days (95 % CI 115-224), respectively (hazard ratio of 5.44 [3.46-8.53, P < 0.0001]). CONCLUSIONS: The MPM patients with PS 0-2 and Hb concentration >12.1 or <=12.1 g dL⁻¹ without chest pain had favourable prognoses.

[393]

TÍTULO / TITLE: - Digital PCR quantification of miRNAs in sputum for diagnosis of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Clin Oncol. 2013 Nov 27.

●● Enlace al texto completo (gratis o de pago) [1007/s00432-013-1555-5](#)

AUTORES / AUTHORS: - Li N; Ma J; Guarnera MA; Fang H; Cai L; Jiang F

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The University of Maryland Greenebaum Cancer Center, University of Maryland School of Medicine, 10 South Pine Street, MSTF 7th Floor, Baltimore, MD, 21201-1192, USA.

RESUMEN / SUMMARY: - PURPOSE: MicroRNAs (miRNAs) play important roles in the initiation and progression of lung cancer. Measuring miRNA expression levels in sputum could provide a potential approach for the diagnosis of lung cancer. The emerging digital PCR is a straightforward technique for precise, direct, and absolute quantification of nucleic acids. The objective of the study was to investigate whether digital PCR could be used to quantify miRNAs in sputum for lung cancer diagnosis. METHODS: We first determined and compared dynamic ranges of digital PCR and conventional quantitative reverse transcriptase PCR (qRT-PCR) for miRNA quantification using RNA isolated from sputum of five healthy individuals. We then used digital PCR to quantify copy number of two lung cancer-associated miRNAs (miR-31 and miR-210) in 35 lung cancer patients and 40 cancer-free controls. RESULTS: Copy number of the miRNAs measured by digital PCR displayed a linear response to input cDNA amount in a twofold dilution series over seven orders of magnitude. miRNA quantification determined by digital PCR assay was in good agreement with that obtained from qRT-PCR analysis in sputum. Furthermore, combined quantification of miR-31 and miR-210 copy number by using digital PCR in sputum of the cases and controls provided 65.71 % sensitivity and 85.00 % specificity for lung cancer diagnosis. CONCLUSION: As digital PCR becomes more established, it would be a robust tool for quantitative assessment of miRNA copy number in sputum for lung cancer diagnosis.

[394]

TÍTULO / TITLE: - Pulmonary tumors associated with the JC virus T-antigen in a transgenic mouse model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2603-8. doi: 10.3892/or.2013.2782. Epub 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2782](#)

AUTORES / AUTHORS: - Noguchi A; Kikuchi K; Ohtsu T; Yoshiwara M; Nakamura Y; Miyagi Y; Zheng H; Takano Y

INSTITUCIÓN / INSTITUTION: - Kanagawa Cancer Center Research Institute, Yokohama, Kanagawa 241-0815, Japan.

RESUMEN / SUMMARY: - Many attempts to demonstrate the oncogenic role of the JC virus (JCV) have been partially successful in producing brain tumors, either by direct inoculation of JCV into the brain or in transgenic models in rodents. We previously reported the presence of JCV DNA with a relatively high incidence in pulmonary and digestive organs. However, we could not prove the oncogenic role of JCV. We prepared a transgene composed of the K19 promoter, specific to bronchial epithelium with the JCV T-antigen and established transgenic (TG) mice. Pulmonary tumors were detected without any metastasis in 2 out of 15 (13.3%) 16-month-old K19/JCV T-antigen TG mice. Using immunohistochemistry (IHC), these tumors showed JCV T-antigen, p53 and CK 19 expression, but not expression of nuclear and cytoplasmic beta-catenin and insulin receptor substrate 1 (IRS1). IHC revealed the same expression pattern as in the bronchial epithelium of the TG mice. One tumor, which was examined with laser capture microdissection and molecular biological tools, demonstrated an EGFR mutation but not a K-ras mutation. We propose that the pulmonary tumors were derived from the JCV T-antigen in a TG mouse model. These findings shed light on pulmonary carcinogenesis.

[395]

TÍTULO / TITLE: - Biodurability/Retention of Libby Amphiboles in a Case of Mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ultrastruct Pathol. 2013 Oct 17.

●● [Enlace al texto completo \(gratis o de pago\) 3109/01913123.2013.821194](#)

AUTORES / AUTHORS: - Dodson RF; Mark EJ; Poye LW

INSTITUCIÓN / INSTITUTION: - Dodson Environmental Consulting, Inc. and ERI Environmental Consulting, Inc. , Tyler , Texas USA .

RESUMEN / SUMMARY: - Abstract Mesothelioma is considered a signal tumor for exposure to asbestos (fibrous materials) and can occur decades after first exposure. The present case study reports on tissue burden of fibrous dust in a person who used a vermiculite material (Zonolite) as an attic insulator some 50 years prior to her death. The exposure occurred in two construction/renovation projects in her private residences. She potentially had exposures to wall board/joint compounds during renovations. She additionally was reported to occasionally be involved in occupational activity, including drilling holes in presumed asbestos-containing electrical boxes. The tissue burden analysis revealed the presence of noncommercial amphibole asbestos fibers and consistent presence in the lung and lymph samples of Libby amphibole fibers. The findings of Libby amphibole fibers in human tissue can be attributed to exposure to Libby vermiculite. This study illustrates that analytical transmission electron microscopy can distinguish these structures from "asbestos" fibers. Further, the findings indicate that a population of these structures is biodurable and retained in the tissue years after first/last exposure.

[396]

TÍTULO / TITLE: - Chest CT findings of pleural tuberculosis: differential diagnosis of pleural tuberculosis and malignant pleural dissemination.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Radiol. 2013 Nov 26.

●● Enlace al texto completo (gratis o de pago) 1177/0284185113513894

AUTORES / AUTHORS: - Kim JS; Shim SS; Kim Y; Ryu YJ; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Mokdong Hospital, Ewha Womans University School of Medicine, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - **BACKGROUND:** The imaging features of pleural tuberculosis (PTB) can be similar to those of malignant pleural dissemination (MPD) with several case reports of CT findings in atypical presentations of PTB. **PURPOSE:** To describe the computed tomography (CT) features of PTB by comparing these imaging findings with those of MPD and to use the results to differentiate between the two diseases. **MATERIAL AND METHODS:** The study included 135 patients with PTB and 69 with MPD. The CT images were assessed in terms of the presence, extent, and contour of pleural thickening. Pleural nodules were analyzed in terms of number, size, and location. The CT findings of PTB and MPD were compared. **RESULTS:** The CT findings of PTB included circumferential pleural thickening (32.6%), mediastinal pleural involvement (31.9%), nodular thickening (8.9%), and pleural thickening >1 cm (2.2%). The CT features of MPD included nodular pleural thickening (56.5%), mediastinal pleural involvement (40.6%), circumferential thickening (23.2%), and pleural thickening >1 cm (7.2%). Comparing PTB and MPD, nodular pleural thickening was observed more frequently with MPD than PTB ($P < 0.001$). **CONCLUSION:** Nodular pleural thickening is observed in 8.9% of the patients with PTB on chest CT. Comparing PTB and MPD, nodular pleural thickening was the only finding significantly associated with MPD, particularly with nodules >10 mm.

[397]

TÍTULO / TITLE: - Conjunctival Metastasis as the Presenting Sign for Stage IV Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Optom Vis Sci. 2013 Nov 21.

●● Enlace al texto completo (gratis o de pago)

1097/OPX.0000000000000131

AUTORES / AUTHORS: - Chew R; Potter J; Dimattina A

INSTITUCIÓN / INSTITUTION: - *OD, FAAO Manchester Veteran's Administration Medical Center, Manchester, New Hampshire; New England College of Optometry, Boston, Massachusetts; and the Pennsylvania College of Optometry at Salus University, Philadelphia, Pennsylvania (all authors).

RESUMEN / SUMMARY: - **PURPOSE:** Lung cancer is the leading cause of cancer-related death in North America. It is often diagnosed at an advanced stage, leading to a poor prognosis. Symptoms of lung cancer often do not present until more advanced stages. Common sites of lung cancer metastasis are the bones, liver, and brain. The etiology of eye masses ranges from the relatively benign to those with tremendous risk of morbidity, and the differentiation is often difficult clinically. This case highlights the importance of more detailed workup, including biopsy, to determine the exact nature of the lesion. **CASE REPORT:** A 50-year-old white man was referred for evaluation of a "bump" on his right upper eyelid. He had noticed it for 1 month and noted enlargement during the past 2 weeks. He also reported that he had been smoking about one pack per day since 1969. External examination was remarkable for a 1.5-cm nodule pushing

up from under the right upper lid. When the lid was everted, there was a 0.9-cm red and black vascularized sessile lesion on the palpebral conjunctiva. The patient was referred to an oculoplastics specialist to rule out a malignant or metastatic conjunctival neoplasm. The oculoplastics service performed an excisional biopsy, and the pathologic examination showed a poorly differentiated and highly aggressive non-small-cell lung cancer (NSCLC). After systemic evaluation, he was diagnosed as having stage IV NSCLC, with metastases to the right eyelid, brain, liver, and right lung. He underwent multiple radiotherapy sessions. He died 5 months after our initial examination. CONCLUSIONS: Stage IV NSCLC is incurable, and its treatment is often palliative. Conjunctival metastasis of stage IV NSCLC is rare, and it is clinically difficult to differentiate eyelid tumors as benign or concerning by examination alone. This case highlights the importance of a thorough history, referral, proper imaging, and biopsy to diagnose a metastatic neoplasm in a patient at high risk for cancer.

[398]

TÍTULO / TITLE: - Differential expression of extracellular matrix constituents and cell adhesion molecules between malignant pleural mesothelioma and mesothelial hyperplasia.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1389-95. doi: 10.1097/JTO.0b013e3182a59f45.

●● Enlace al texto completo (gratis o de pago) [1097/JTO.0b013e3182a59f45](#)

AUTORES / AUTHORS: - Ali G; Borrelli N; Riccardo G; Proietti A; Pelliccioni S; Niccoli C; Boldrini L; Lucchi M; Mussi A; Fontanini G

INSTITUCIÓN / INSTITUTION: - *Unit of Pathological Anatomy, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy; daggerDepartment of Surgical, Medical, Molecular Pathology, and Critical Area, Division of Pathological Anatomy, University of Pisa, Pisa, Italy; double daggerUnit of Thoracic Surgery, Azienda Ospedaliera Universitaria Pisana, Pisa, Italy; and section signDepartment of Surgical, Medical, Molecular Pathology and Critical Area, Division of Thoracic Surgery, University of Pisa, Pisa, Italy.

RESUMEN / SUMMARY: - INTRODUCTION: Malignant pleural mesothelioma (MPM) is a highly aggressive neoplasm associated with asbestos exposure. Currently, the molecular mechanisms that induce MPM development are still unknown. The purpose of this study was to identify new molecular biomarkers for mesothelial carcinogenesis. METHODS: We analyzed a panel of 84 genes involved in extracellular matrix remodeling and cell adhesion by polymerase chain reaction (PCR) array in 15 samples of epithelioid mesothelioma and 10 samples of reactive mesothelial hyperplasia (MH; 3 of 25 samples were inadequate for mRNA analysis). To validate the differentially expressed genes identified by PCR array, we analyzed 27 more samples by immunohistochemistry, in addition to the 25 samples already studied. RESULTS: Twenty-five genes were differentially expressed in MPM and MH by PCR array. Of these we studied matrix metalloproteinase 7 (MMP7), MMP14, CD44, and integrin, alpha3 expression by immunohistochemistry in 26 epithelioid MPM and 26 MH samples from the entire series of 52 cases. We observed higher MMP14 and integrin, alpha3 expression in MPM samples compared with MH samples ($p = 0.000002$ and $p = 0.000002$, respectively). Conversely, CD44 expression was low in most (57.7%) mesothelioma samples but only in 11.5% of the MH samples ($p = 0.0013$). As regards

MMP7, we did not observe differential expression between MH and MPM samples.
CONCLUSIONS: We have extensively studied genes involved in cell adhesion and extracellular matrix remodeling in MPM and MH samples, gaining new insight into the pathophysiology of mesothelioma. Moreover, our data suggest that these factors could be potential biomarkers for MPM.

[399]

TÍTULO / TITLE: - Efficiency of the Therascreen® RGQ PCR kit for the detection of EGFR mutations in non-small cell lung carcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Chim Acta. 2013 Nov 21;429C:8-11. doi: 10.1016/j.cca.2013.11.014.

●● Enlace al texto completo (gratis o de pago) [1016/j.cca.2013.11.014](#)

AUTORES / AUTHORS: - Vallee A; Le Loupp AG; Denis MG

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, Nantes University Hospital, France.

RESUMEN / SUMMARY: - BACKGROUND: Activating mutations of the EGFR gene in lung carcinoma are associated with response to tyrosine kinase inhibitors. Therefore, a rapid, sensitive assay for mutation detection using routine pathological specimens is mandatory in clinical practice. METHODS: We have compared our in-house procedure to the Therascreen® EGFR RGQ PCR kit (Qiagen). This assay, based on allele-specific amplification, is approved in the United States, in Europe, Japan and China. RESULTS: We first selected a series of 209 that were representative of our routine practice during the last 2 years. Using our assays, EGFR mutations were detected in 36 (17.4%) of these patients (18 p.L858R mutations and 18 exon 19 deletions). All these alterations were also detected using the Therascreen® kit. In addition, this kit allowed us to detect 7 additional alterations: one exon 19 alteration (c.2239_2240TT>CC, p.L747P), 3 p.G719X mutations and 3 p.S768L mutations. In the second part of our study, we selected 81 samples that were identified as deleted for exon 19 using our assay. Eighteen different deletions were described following sequencing. All these samples were tested positive with the Therascreen® kit. CONCLUSION: The Therascreen® EGFR RGQ kit was found to be very powerful (sensitivity 100%; specificity 100%) for the detection of the most frequent EGFR alterations that are clearly associated with response to tyrosine kinase inhibitors.

[400]

TÍTULO / TITLE: - CARM1 and PRMT1 are dysregulated in lung cancer without hierarchical features.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biochimie. 2013 Nov 6. pii: S0300-9084(13)00392-1. doi: 10.1016/j.biochi.2013.10.021.

●● Enlace al texto completo (gratis o de pago) [1016/j.biochi.2013.10.021](#)

AUTORES / AUTHORS: - Elakoum R; Gauchotte G; Oussalah A; Wissler MP; Clement-Duchene C; Vignaud JM; Gueant JL; Namour F

INSTITUCIÓN / INSTITUTION: - INSERM NGERE UMR 954, Vandoeuvre F-54500, France.

RESUMEN / SUMMARY: - CARM1 and PRMT1 are 2 Protein Arginine Methyl Transferases (PRMT) dysregulated in cancer. CARM1 function is contradictory and depicted as facilitating proliferation or differentiation. PRMT1 is required for cell proliferation. CARM1 and PRMT1 cooperate for gene regulation. We report that CARM1 and PRMT1 are significantly overexpressed in 60 patients with Non-Small Cell Lung Carcinomas (NSCLC). CARM1 and PRMT1 correlated in healthy but not tumor tissue. Their levels of expression in tumor tissue were proportional to their levels of expression in the counterpart healthy tissue. Only CARM1 expression was found to be correlated with tumor differentiation and neither CARM1 nor PRMT1 expression was correlated with survival. Accordingly, CARM1 and PRMT1 are overexpressed in 2 NSCLC cell lines, A549 and H1299. Targeting PRMT1 with siRNA reduced proliferation, by decreasing cell growth and inhibiting soft agar colony formation, and promoted differentiation, by increasing the epithelial markers cytokeratin 7 and 8 and decreasing Neuromedin B receptor, which binds a mitogenic factor. siCARM1 yielded similar consequences but the conditions with siCARM1 reflected inhibition of both CARM1 and PRMT1. Together these results suggest that CARM1 and PRMT1 are involved in proliferation in lung cancer with no hierarchy of one protein over the other. The fact that CARM1 targeting suppresses PRMT1 in addition to CARM1 reinforces the functional importance of CARM1/PRMT1 interaction.

[401]

TÍTULO / TITLE: - Comment on: Functional MUC4 suppress epithelial-mesenchymal transition in lung adenocarcinoma metastasis. Gao L, Liu J, Zhang B, Zhang H, Wang D, Zhang T, Liu Y, Wang C. Tumour Biol. 2013, in press.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tumour Biol. 2013 Nov 17.

●● Enlace al texto completo (gratis o de pago) [1007/s13277-013-1390-y](#)

AUTORES / AUTHORS: - Jonckheere N; Van Seuning I

INSTITUCIÓN / INSTITUTION: - UMR837, Jean Pierre Aubert Research Center, Team #5 "Mucins, epithelial differentiation and carcinogenesis", Inserm, rue Polonovski, 59045, Lille Cedex, France, nicolas.jonckheere@inserm.fr.

RESUMEN / SUMMARY: - Gao and collaborators (Tumour Biol, 2013) have investigated the role of mucin 4 (MUC4) in lung cancer and have concluded that a loss of MUC4 results in epithelial mesenchymal transition via beta-catenin nuclear translocation and that MUC4 expression is correlated with a risk of lymph node metastasis in a cohort of 20 lung adenocarcinoma patients. This surprising analysis is contradictory to most of the scientific knowledge and literature regarding MUC4 contribution in epithelial cancers that is very hardly discussed in their manuscript.

[402]

TÍTULO / TITLE: - Association of c-Met phosphorylation with micropapillary pattern and small cluster invasion in pT1-size lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):413-9. doi: 10.1016/j.lungcan.2013.09.005. Epub 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.005](#)

AUTORES / AUTHORS: - Koga K; Hamasaki M; Kato F; Aoki M; Hayashi H; Iwasaki A; Kataoka H; Nabeshima K

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Fukuoka University Hospital and School of Medicine, 7-45-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan.

RESUMEN / SUMMARY: - Lung adenocarcinomas with micropapillary pattern (MPP) are associated with frequent nodal metastasis. However, little is known about the mechanisms that underlie MPP-associated nodal metastasis. We have previously reported that pT1 lung adenocarcinomas with MPP are significantly associated with small cluster invasion (SCI) and lymphatic involvement. SCI is defined as markedly resolved acinar-papillary tumor structures with single or small clusters of carcinoma cells invading stroma within fibrotic foci. In this study, we hypothesized that c-Met activation may be involved in the MPP-SCI sequence, given that the c-Met tyrosine-kinase receptor and its ligand hepatocyte growth factor (HGF), play important roles in tumor cell motility and invasion. We analyzed 125 pT1-size lung adenocarcinomas for immunohistochemical expression of phosphorylated c-Met and its correlation with MPP, SCI, lymphatic involvement and prognosis. SCI was significantly more frequent in the MPP-positive group ($P < 0.0001$) and associated with lymphatic involvement ($P < 0.0001$) and nodal metastasis ($P = 0.021$). c-Met protein was detected in all tumors by immunohistochemistry as membranous and cytoplasmic staining. Phospho-c-Met (pc-Met) was positive in 119/125 tumors (95%) and expressed at high levels in 27 cases (22%). A high level of pc-Met expression was significantly associated with MPP ($P = 0.01$) and SCI ($P = 0.0059$). Moreover, in tumors with MPP or SCI, those expressing high levels of pc-Met were significantly more associated with lymphatic involvement. In p-Stage IA lung adenocarcinomas ($n = 99$), patients in the high pc-Met expression group showed significantly worse survival than patient in the low expression group ($P = 0.0313$). These results suggest that activation of c-Met through phosphorylation may be involved in MPP and SCI.

[403]

TÍTULO / TITLE: - Integrated Glycoproteomics Demonstrates Fucosylated Serum Paraoxonase 1 Alterations in Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cell Proteomics. 2013 Oct 1.

●● [Enlace al texto completo \(gratis o de pago\) 1074/mcp.M113.028621](#)

AUTORES / AUTHORS: - Ahn JM; Sung HJ; Yoon YH; Kim BG; Yang WS; Lee C; Park HM; Kim BJ; Kim BG; Lee SY; An HJ; Cho JY

INSTITUCIÓN / INSTITUTION: - Seoul National University, Korea, Republic of;

RESUMEN / SUMMARY: - Small cell lung cancer (SCLC) is an aggressive type of lung cancer, and the detection of SCLCs at an early stage is necessary for successful therapy and for improving cancer survival rates. Fucosylation is one of the most common glycosylation based modifications. Increased levels of fucosylation have been reported in a number of pathological conditions including cancers. In this study, we aimed to identify and to validate the aberrant and selective fucosylated glycoproteins in the sera of SCLC patients. Fucosylated glycoproteins were enriched by Aleuria Aurantia Lectin (AAL) column after serum albumin and IgG depletion. In a narrow down and comparative data analysis of both label free proteomics and isobaric peptide tagging chemistry iTRAQ approaches, the fucosylated glycoproteins were identified as

up or down regulated in the sera of limited disease (LD) and extensive disease (ED) stage SCLC patients. Verification was performed by multiple reaction monitoring mass spectrometry to select reliable markers. Four fucosylated proteins APCS, C9, SERPINA4 and PON1 were selected and subsequently validated by hybrid AAL lectin ELISA (HLE) and Western blotting. Compared to Western blotting, the HLE analysis of these four proteins produced more optimal diagnostic values for SCLC. The PON1 protein levels were significantly reduced in the sera of SCLC patients, whereas the fucosylation levels of PON1 were significantly increased. Fucosylated PON1 exhibited an AUC of 0.91 for ED by HLE, whereas the PON1 protein levels produced an AUC of 0.82 by Western blot (WB). The glycan structural analysis of PON1 by MS/MS identified a biantennary fucosylated glycan modification consisting of a core + 2HexNAc + 1Fuc at increased levels in the sera of SCLC patients. In addition, the PON1 levels were decreased in the sera of the Lewis Lung Carcinoma (LLC) lung cancer mouse model that we examined. Our data suggest that fucosylated protein biomarkers, such as PON1, and their fucosylation levels and patterns can serve as diagnostic and prognostic serological markers for SCLC.

[404]

TÍTULO / TITLE: - Combining anti-Epidermal Growth Factor Receptor (EGFR) and Anti-Angiogenic Strategies in Advanced NSCLC: We Should have Known Better.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Di Maio M; Morabito A; Piccirillo MC; Daniele G; Giordano P; Costanzo R; Sandomenico C; Montanino A; Rocco G; Perrone F

INSTITUCIÓN / INSTITUTION: - Clinical Trials Unit National Cancer Institute - "G. Pascale" Foundation Via Mariano Semmola, 80131 Napoli, Italy. dimaio@libero.it.

RESUMEN / SUMMARY: - Drugs directed against Epidermal Growth Factor Receptor (EGFR), namely tyrosine kinase inhibitors erlotinib and gefitinib, and anti-angiogenic agents, namely the anti-Vascular Endothelial Growth Factor (VEGF) antibody bevacizumab, have independently demonstrated clinical benefit in the treatment of patients with advanced non-small cell lung cancer (NSCLC), and are currently approved for use in clinical practice. Pre-clinical studies have shown promising results with the combination of anti-EGFR and anti-angiogenesis drugs in different tumor models, including NSCLC. Several clinical trials have been conducted to verify if the combination of the two therapeutic strategies could improve the outcome in the setting of advanced NSCLC. The largest body of evidence has been produced testing the combination of erlotinib plus bevacizumab, or erlotinib plus a multi-targeted receptor tyrosine kinase inhibitor, namely sunitinib or sorafenib. Furthermore, several dual inhibitors, targeting both EGFR and VEGFR, have been tested in advanced NSCLC, with the greatest body of evidence produced with vandetanib. However, despite an intriguing pre-clinical background, the combination strategy has not yet produced clinically relevant results. Several phase III trials showed an improvement in progression-free survival, underlining some activity of targeting both pathways concurrently, but no trial has demonstrated an impact on overall survival to date. Unfortunately, the vast majority of trials conducted in this setting have been performed without any selection criteria based on molecular characteristics, compromising the chance of detecting a potentially relevant benefit in selected subgroup of patients. In

recent years, the important interaction between the efficacy of EGFR inhibitors and the presence of EGFR activating mutations in tumor cells has been repeatedly demonstrated. On the other hand, we still have no clear idea about predictive factors of efficacy for bevacizumab and other anti-angiogenic drugs. This is probably the real challenge to optimize the use of these drugs and to fully evaluate the real clinical potential of a combination strategy.

[405]

TÍTULO / TITLE: - Lung cancer: What are the links with oxidative stress, physical activity and nutrition.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Dec;82(3):383-9. doi: 10.1016/j.lungcan.2013.09.009. Epub 2013 Sep 23.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.09.009](#)

AUTORES / AUTHORS: - Filaire E; Dupuis C; Galvaing G; Aubreton S; Laurent H; Richard R; Filaire M

INSTITUCIÓN / INSTITUTION: - Laboratoire CIAMS, EA4532, Université Paris-Sud, Université Orleans, UFRSTAPS, 2 allée du Château, 45067 Orleans, France.

RESUMEN / SUMMARY: - Oxidative stress appears to play an essential role as a secondary messenger in the normal regulation of a variety of physiological processes, such as apoptosis, survival, and proliferative signaling pathways. Oxidative stress also plays important roles in the pathogenesis of many diseases, including aging, degenerative disease, and cancer. Among cancers, lung cancer is the leading cause of cancer in the Western world. Lung cancer is the commonest fatal cancer whose risk is dependent on the number of cigarettes smoked per day as well as the number of years smoking, some components of cigarette smoke inducing oxidative stress by transmitting or generating oxidative stress. It can be subdivided into two broad categories, small cell lung cancer and non-small-cell lung cancer, the latter is the most common type. Distinct measures of primary and secondary prevention have been investigated to reduce the risk of morbidity and mortality caused by lung cancer. Among them, it seems that physical activity and nutrition have some beneficial effects. However, physical activity can have different influences on carcinogenesis, depending on energy supply, strength and frequency of exercise loads as well as the degree of exercise-mediated oxidative stress. Micronutrient supplementation seems to have a positive impact in lung surgery, particularly as an antioxidant, even if the role of micronutrients in lung cancer remains controversial. The purpose of this review is to examine lung cancer in relation to oxidative stress, physical activity, and nutrition.

[406]

TÍTULO / TITLE: - CDKN2A/p16 inactivation mechanisms and their relationship to smoke exposure and molecular features in non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1378-88. doi: 10.1097/JTO.0b013e3182a46c0c.

●● Enlace al texto completo (gratis o de pago) [1097/JTO.0b013e3182a46c0c](#)

AUTORES / AUTHORS: - Tam KW; Zhang W; Soh J; Stastny V; Chen M; Sun H; Thu K; Rios JJ; Yang C; Marconett CN; Selamat SA; Laird-Offringa IA; Taguchi A; Hanash S; Shames D; Ma X; Zhang MQ; Lam WL; Gazdar A

INSTITUCIÓN / INSTITUTION: - *Hamon Center for Therapeutic Oncology Research and daggerDivision of Biostatistics, University of Texas Southwestern Medical Center, Dallas, Texas; double daggerDepartment of Integrative Oncology, British Columbia Cancer Agency Research Centre, Vancouver, B.C., Canada; section signTexas Scottish Rite Hospital for Children, Dallas, Texas; ||Department of Surgery, Biochemistry, and Molecular Biology, Keck School of Medicine, USC/Norris Comprehensive Cancer Center, Los Angeles, California; paragraph signPublic Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, Washington; #Oncology Biomarker Development, Genentech Inc., South San Francisco, California; **Department of Molecular and Cell Biology, Center for Systems Biology, University of Texas at Dallas, Dallas, Texas; and daggerdaggerDepartment of Pathology, University of Texas Southwestern Medical Center, Dallas, Texas.

RESUMEN / SUMMARY: - INTRODUCTION: CDKN2A (p16) inactivation is common in lung cancer and occurs via homozygous deletions, methylation of promoter region, or point mutations. Although p16 promoter methylation has been linked to KRAS mutation and smoking, the associations between p16 inactivation mechanisms and other common genetic mutations and smoking status are still controversial or unknown. METHODS: We determined all three p16 inactivation mechanisms with the use of multiple methodologies for genomic status, methylation, RNA, and protein expression, and correlated them with EGFR, KRAS, STK11 mutations and smoking status in 40 cell lines and 45 tumor samples of primary non-small-cell lung carcinoma. We also performed meta-analyses to investigate the impact of smoke exposure on p16 inactivation. RESULTS: p16 inactivation was the major mechanism of RB pathway perturbation in non-small-cell lung carcinoma, with homozygous deletion being the most frequent method, followed by methylation and the rarer point mutations. Inactivating mechanisms were tightly correlated with loss of mRNA and protein expression. p16 inactivation occurred at comparable frequencies regardless of mutational status of EGFR, KRAS, and STK11, however, the major inactivation mechanism of p16 varied. p16 methylation was linked to KRAS mutation but was mutually exclusive with EGFR mutation. Cell lines and tumor samples demonstrated similar results. Our meta-analyses confirmed a modest positive association between p16 promoter methylation and smoking. CONCLUSION: Our results confirm that all the inactivation mechanisms are truly associated with loss of gene product and identify specific associations between p16 inactivation mechanisms and other genetic changes and smoking status.

[407]

TÍTULO / TITLE: - Leser-Trelat syndrome in malignant mesothelioma and pulmonary adenocarcinoma: is the EGFR pathway part of the syndrome?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Virchows Arch. 2013 Nov 14.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s00428-013-1503-4](#)

AUTORES / AUTHORS: - Jepsen RK; Skov AG; Skov BG

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Rigshospitalet, Blegdamsvej 9, 2100, Copenhagen, Denmark, rke.doc@gmail.com.

RESUMEN / SUMMARY: - The syndrome of Leser-Trelat (LT) is characterized by the sudden appearance of multiple seborrheic keratoses (SKs) in association with internal occult malignancy. Usually, the syndrome has been associated with adenocarcinoma, most frequently of the gastrointestinal tract and breast. The pathogenesis is unclear but might be explained by circulating tumor-associated growth factors. We present two thoracic malignancies associated with LT: adenocarcinoma of the lung (ACL) and pleural malignant mesothelioma (MM). Both malignant tumors expressed high levels of epidermal growth factor receptors (EGFR) detected by immunohistochemistry (IHC), with membranous staining on the majority of malignant cells corresponding to maximum IHC scores of 290 and 300, respectively, for the MM and the ACL. SKs revealed a universal membranous staining throughout the entire epithelium with no difference in EGFR expression between the two cases and two controls with no malignant history. By fluorescence in situ hybridization, no amplification of the EGFR gene in malignant tumors as well as in SK lesions was observed. Further investigations are needed to see whether tumor-associated EGFR ligands/EGFR autocrine loops in malignant cells expressing high levels of EGFR protein on the surface might play a role for the development of SKs, as well as for the growth of malignant tumors in LT.

[408]

TÍTULO / TITLE: - The Feasibility and Efficacy of Stereotactic Body Radiotherapy for Centrally-located Lung Tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Nov;33(11):4959-64.

AUTORES / AUTHORS: - Takahashi W; Yamashita H; Omori M; Kitaguchi M; Shibata-Kobayashi S; Sakumi A; Nakagawa K

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Tokyo Hospital, 7-3-1, Hongo, Bunkyo-ku, Tokyo, 113-8655 Japan. yamachan07291973@yahoo.co.jp.

RESUMEN / SUMMARY: - Aim: To investigate the toxicity and outcome of stereotactic body radiotherapy (SBRT) for centrally-located lung tumors. PATIENTS AND METHODS: A retrospective review was conducted in 45 consecutive patients with centrally-located lung tumors who underwent SBRT. The incidence rate of adverse events (AEs) and outcome after SBRT for primary (32 patients), metastatic and recurrent (13 patients) lung tumors were evaluated. RESULTS: The median follow-up period was 21.2 months. Except for one patient who had grade 4 gastrointestinal toxicity, no patient exhibited any grade 4-5 AE. The 2-year overall survival of patients with primary non-small cell lung cancer (NSCLC) was significantly better than that of those with metastatic and recurrent tumors of 69.4% vs. 46.9% (p=0.04). The local control rates at two years, for patients in the NSCLC and the metastatic/recurrent groups were 70.9% and 100%, respectively (p=0.98). CONCLUSION: SBRT provided effective treatment for centrally-located lung tumors with tolerable toxicity.

[409]

TÍTULO / TITLE: - Lung cancer screening with low-dose computed tomography.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiol Clin North Am. 2014 Jan;52(1):27-46. doi: 10.1016/j.rcl.2013.08.006.

●● Enlace al texto completo (gratis o de pago) [1016/j.rcl.2013.08.006](https://doi.org/10.1016/j.rcl.2013.08.006)

AUTORES / AUTHORS: - Chiles C

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Wake Forest University Health Sciences Center, Medical Center Boulevard, Winston-Salem, NC 27157, USA. Electronic address: cchiles@wakehealth.edu.

RESUMEN / SUMMARY: - Current guidelines endorse low-dose computed tomography (LDCT) screening for smokers and former smokers aged 55 to 74, with at least a 30-pack-year smoking history. Adherence to published algorithms for nodule follow-up is strongly encouraged. Future directions for screening research include risk stratification for selection of the screening population and improvements in the diagnostic follow-up for indeterminate pulmonary nodules. Screening for lung cancer with LDCT has revealed that there are indolent lung cancers that may not be fatal. More research is necessary if the risk-benefit ratio in lung cancer screening is to be maximized.

[410]

TÍTULO / TITLE: - RASSF3 downregulation increases malignant phenotypes of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung Cancer. 2013 Oct 31. pii: S0169-5002(13)00458-3. doi: 10.1016/j.lungcan.2013.10.014.

●● Enlace al texto completo (gratis o de pago) [1016/j.lungcan.2013.10.014](https://doi.org/10.1016/j.lungcan.2013.10.014)

AUTORES / AUTHORS: - Fukatsu A; Ishiguro F; Tanaka I; Kudo T; Nakagawa K; Shinjo K; Kondo Y; Fujii M; Hasegawa Y; Tomizawa K; Mitsudomi T; Osada H; Hata Y; Sekido Y

INSTITUCIÓN / INSTITUTION: - Division of Molecular Oncology, Aichi Cancer Center Research Institute, 1-1 Kanokoden, Chikusa-ku, Nagoya 464-8681, Japan; Department of Respiratory Medicine, Graduate School of Medicine, Nagoya University, Nagoya 466-8550, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Ras-Association Family1A (RASSF1A) is a well-established tumor suppressor. Ten RASSF homologues comprise this family, and each member is considered a tumor suppressor. RASSF3 is one of the RASSF family members, but its function has not yet been clarified. Recently, we found that RASSF3 interacts with MDM2 and facilitates its ubiquitination, which induces apoptosis through p53 stabilization. However, the role of RASSF3 in human malignancies remains largely unknown. PATIENTS AND METHODS: Ninety-five non-small cell lung cancer (NSCLC) patients from Nagoya University Hospital and 45 NSCLC patients from Aichi Cancer Center Hospital underwent pulmonary resection at each hospital, and lung cancer and corresponding non-cancerous lung tissues were collected. The expression levels of RASSF3 were analyzed using quantitative real-time reverse transcription PCR. We performed statistical analysis to investigate the correlation with RASSF3 expression and the clinicopathological characteristics. We also transfected RASSF3-siRNA into NSCLC cells, and performed motility assays to evaluate the influence on migration ability. RESULTS: RASSF3 expression levels were downregulated in 125 of a total 140 NSCLCs. In a multivariate logistic regression analysis, the low RASSF3 expression group below the median value was independently correlated with progressive

phenotypes (lymph node metastasis and pleural invasion), non-adenocarcinoma histology and wild-type epidermal growth factor receptor (EGFR) status. In motility assays, RASSF3-knockdown NSCLC cells increased the migration rate compared to the control cells. CONCLUSIONS: We found that the expression levels of RASSF3 were frequently downregulated in NSCLCs. Downregulation of RASSF3 strongly correlated with the progressive phenotypes of NSCLCs and EGFR wild-type status. In vitro studies also suggested that RASSF3 downregulation increases migration ability of lung cancer cells. Together, our findings indicate RASSF3 is a candidate tumor suppressor gene of NSCLCs.

[411]

TÍTULO / TITLE: - Utilization of p40 (DeltaNp63) with p63 and Cytokeratin 5/6 Immunohistochemistry in Non-Small Cell Lung Carcinoma Fine-Needle Aspiration Biopsy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Cytol. 2013;57(6):619-24. doi: 10.1159/000354213. Epub 2013 Oct 1.

●● Enlace al texto completo (gratis o de pago) [1159/000354213](#)

AUTORES / AUTHORS: - Collins BT; Wang JF; Bernadt CT

INSTITUCIÓN / INSTITUTION: - Department of Pathology and Immunology, Washington University in St. Louis School of Medicine, St. Louis, Mo., USA.

RESUMEN / SUMMARY: - Objective: Specific subclassification of pulmonary non-small cell carcinoma (NSCCA) is clinically necessary, and the aim of this study is to examine the utilization of p40 (DeltaNp63) in fine-needle aspiration (FNA) biopsy for lung NSCCA. Study Design: Database files of the Washington University Medical Center were searched. Patients who underwent endobronchial ultrasound and CT FNA of a primary lung neoplasia were selected and immunohistochemistry (IHC) was performed. A panel of markers was utilized, including p40, p63, cytokeratin (CK) 5/6, thyroid transcription factor, and napsin. Results: One hundred patients were identified and comprised 38 squamous cell carcinomas (SCCA), 46 adenocarcinomas (AdCA), and 16 NSCCA. For SCCA, p40 was positive in 34/38 cases (89%) and negative in 4/38 cases (11%); p63 was positive in 33/38 cases (87%) and negative in 5/38 cases (13%); CK5/6 was positive in 38/38 cases. For AdCA cases, p40 was negative, p63 was positive in 2 cases (5%) and CK5/6 was negative in 43/46 cases (92%). Conclusion: For NSCCA, p40 had 89% sensitivity and 100% specificity compared to p63 with 86% sensitivity and 96% specificity and CK5/6 with 100% sensitivity and 96% specificity. In the evaluation of FNA biopsy for pulmonary NSCCA, p40 is a useful IHC marker for neoplastic subclassification, with better specificity in comparison to p63. © 2013 S. Karger AG, Basel.

[412]

TÍTULO / TITLE: - Cone beam CT verification for active breathing control (ABC)-gated radiotherapy for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Oncol. 2013 Nov 25.

●● Enlace al texto completo (gratis o de pago) [3109/0284186X.2013.861610](#)

AUTORES / AUTHORS: - Yeoh KW; McNair HA; McDonald F; Hawkins M; Hansen VN; Ramos M; Fragkandrea I; Bothwell S; Herbert T; Taylor H; Helyer S; Ashley S; Brada M

INSTITUCIÓN / INSTITUTION: - Radiotherapy Department, Royal Marsden NHS Foundation Trust and Institute of Cancer Research , Sutton, Surrey , UK.

[413]

TÍTULO / TITLE: - Histo-cytological diagnostic accuracy in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cytopathology. 2013 Nov 20. doi: 10.1111/cyt.12117.

●● Enlace al texto completo (gratis o de pago) [1111/cyt.12117](#)

AUTORES / AUTHORS: - Proietti A; Boldrini L; Ali G; Servadio A; Lupi C; Sensi E; Miccoli M; Ribechini A; Chella A; Lucchi M; Leocata P; Mussi A; Fontanini G

INSTITUCIÓN / INSTITUTION: - Department of Surgical, Medical, Molecular Pathology and Critical Area, Division of Pathological Anatomy, University of Pisa, Pisa, Italy.

RESUMEN / SUMMARY: - OBJECTIVE: The majority of patients with lung cancer are treated on the basis of a diagnosis made from the analysis of a small tumour biopsy or a cytological sample and histotype is becoming a critical variable in clinical workup as it has led to the introduction of newer biologically targeted therapies. Consequently, simply classifying cancers as small cell lung cancers or non-small cell lung cancers is no longer sufficient. METHODS: From 2009 to 2011, a review of the histo-cytological database was conducted to identify all small biopsy and cytology specimens collected for diagnostic purposes in patients with a thoracic lesion. In total, 941 patients were studied by examining exfoliative and/or aspirative cytological samples. To establish the accuracy of these methods, cytological and biopsy diagnoses were compared with each other and with subsequent resection specimens when available. Moreover, during the diagnostic workup, we examined a validated panel of immunohistochemical markers. RESULTS: The diagnostic concordance of pre-operative diagnoses with surgical samples was high in both cytology and biopsy samples [$\kappa = 0.71$, confidence interval (CI) = 0.6-0.81; $P < 0.0001$ and $\kappa = 0.61$, CI = 0.41-0.82; $P < 0.0001$ respectively; good agreement] but concordance between cytology and biopsy was moderate ($\kappa = 0.5$, CI = 0.43-0.54; $P < 0.0001$). Immunohistochemistry-aided diagnoses were definitive for histotype in 92.8% of both cytology (206/222) and biopsy (155/167) specimens. CONCLUSION: We found that lung cancer diagnosis and subtyping of cytology and biopsy samples are highly feasible and concordant; thus, the diagnostic approach to lung cancer does not require more invasive procedures.

[414]

TÍTULO / TITLE: - In-depth bioinformatic analysis of lung cancer-associated microRNA targets.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Rep. 2013 Dec;30(6):2945-56. doi: 10.3892/or.2013.2762. Epub 2013 Oct 1.

●● Enlace al texto completo (gratis o de pago) [3892/or.2013.2762](#)

AUTORES / AUTHORS: - Zhang H; Yang H; Zhang R; Zhang C; Zhang J; Li D

INSTITUCIÓN / INSTITUTION: - Jiangsu Engineering Research Center for microRNA Biology and Biotechnology, State Key Laboratory of Pharmaceutical Biotechnology, School of Life Sciences, Nanjing University, Nanjing, Jiangsu 210093, P.R. China.

RESUMEN / SUMMARY: - Lung cancer (LC) is the leading cause of cancer-related mortality worldwide. However, few studies of its specific mechanisms useful for diagnosis or treatment exist. microRNAs (miRNAs) present one mechanism through which genes with diverse functions on multiple pathways can be simultaneously regulated at the post-transcriptional level. However, LC-associated pathways targeted by LC-related miRNAs (LC-miRNAs) remain completely unknown. In the present study, we investigated 8 LC-miRNAs previously identified as regulators in three molecular subtypes of LC. The results showed that LC-miRNAs may post-transcriptionally function mainly through manipulating the expression of nucleic acid binding proteins and transcription factors, and target genes for the LC-miRNAs were most prominently predicted to function in regulation of transcription. Our analysis also highlighted the potential of these LC-miRNAs to regulate the cell differentiation, proliferation, endocytosis and migration signaling logically required to cause an LC cell mainly through five canonical pathways (PI3K-Akt signaling pathway, pathways in cancer, MAPK signaling pathway, HTLV-I infection and focal adhesion). These findings may form a useful basis for potential future development of novel LC therapeutic treatments.

[415]

TÍTULO / TITLE: - H2AX a Promising Biomarker for Lung Cancer: A Review.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Invest. 2013 Nov;31(9):582-99. doi: 10.3109/07357907.2013.849721.

●● Enlace al texto completo (gratis o de pago) [3109/07357907.2013.849721](#)

AUTORES / AUTHORS: - Matthaios D; Hountis P; Karakitsos P; Bouros D; Kakolyris S

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Democritus University of Thrace, Alexandroupolis, Greece, 1.

RESUMEN / SUMMARY: - Histone's H2A variant (H2AX) phosphorylation is an early indicator of DNA double-strand breaks formation and DNA damage response. Thus, it may act as a novel biomarker to monitor genotoxic events that can drive cancer development and tumor progression. This review will focus on the possible applications of H2AX as a key regulator of DNA damage response in lung cancer and as a biomarker of: sensitivity of lung tumors to chemotherapy and radiotherapy, treatment with PARP inhibitors, bystander effect, multistep lung carcinogenesis, environmental smoking, and chemical genotoxicity, chemoprevention, prognosis, and also as therapeutic targets in lung cancers.

[416]

TÍTULO / TITLE: - The mediastinal staging accuracy of 18F-Fluorodeoxyglycose Positron Emission Tomography/Computed Tomography in non-small cell lung cancer with variable time intervals to surgery.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ulster Med J. 2013 May;82(2):75-81.

AUTORES / AUTHORS: - Booth K; Hanna GG; McGonigle N; McManus KG; McGuigan J; O'Sullivan J; Lynch T; McAleese J

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Royal Victoria Hospital, Belfast.

RESUMEN / SUMMARY: - BACKGROUND: PET/CT scanning can determine suitability for curative therapy and inform decision making when considering radical therapy in patients with non-small cell lung cancer (NSCLC). Metastases to central mediastinal lymph nodes (N2) may alter such management decisions. We report a 2 year retrospective series assessing N2 lymph node staging accuracy with PET/CT compared to pathological analysis at surgery. METHODS: Patients with NSCLC attending our centre (excluding those who had induction chemotherapy) who had staging PET/CT scans and pathological nodal sampling between June 2006 and June 2008 were analysed. For each lymph node assessed pathologically, the corresponding PET/CT status was determined. 64 patients with 200 N2 lymph nodes were analysed. RESULTS: Sensitivity of PET/CT scans for identifying involved N2 lymph nodes was 39%, specificity 96% and overall accuracy 90%. For individual lymph node analysis, logistic regression demonstrated a significant linear association between PET/CT sensitivity and time from scanning to surgery ($p=0.031$) but not for specificity and accuracy. Those scanned <9 weeks before pathological sampling were significantly more sensitive (64% >9 weeks, 0% ≥ 9 weeks, $p=0.013$) and more accurate (94% <9 weeks, 81% ≥ 9 weeks, $p=0.007$). Differences in specificity were not seen (97% <9 weeks, 91% ≥ 9 weeks, $p=0.228$). No significant difference in specificity was found at any time point. CONCLUSIONS: We recommend that if a PET/CT scan is older than 9 weeks, and management would be altered by the presence of N2 nodes, re-staging of the mediastinum should be undertaken.

[417]

TÍTULO / TITLE: - Small cell carcinoma of the thyroid gland with a solid brain metastasis detected by F-18-FDG PET/CT.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Endocrine. 2013 Oct 22.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s12020-013-0084-y](#)

AUTORES / AUTHORS: - Treglia G; Salvatori M; Giovanella L

INSTITUCIÓN / INSTITUTION: - Department of Nuclear Medicine, Thyroid Center and PET/CT Centre, Oncology Institute of Southern Switzerland, Via Ospedale, 12, 6500, Bellinzona, Switzerland, giorgiomednuc@libero.it.

[418]

TÍTULO / TITLE: - The presence of air bronchogram is a novel predictor of negative nodal involvement in radiologically pure-solid lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Cardiothorac Surg. 2013 Oct 17.

●● [Enlace al texto completo \(gratis o de pago\) 1093/ejcts/ezt467](#)

AUTORES / AUTHORS: - Hattori A; Suzuki K; Maeyashiki T; Fukui M; Kitamura Y; Matsunaga T; Miyasaka Y; Takamochi K; Oh S

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Juntendo University School of Medicine, Tokyo, Japan.

RESUMEN / SUMMARY: - OBJECTIVES: Phase III trials regarding the feasibility of segmentectomy for lung cancer ≤ 2 cm in size are now underway in Japan and the USA. However, despite their small size, lung cancers that show a pure-solid appearance on thin-section computed tomography (CT) are considered to be invasive with a high frequency of nodal involvement. METHODS: Between 2008 and 2011, 556 clinical Stage IA lung cancer patients underwent pulmonary resection. For all patients, the findings obtained by preoperative thin-section CT were reviewed and the maximum standardized uptake value (SUVmax) on positron emission tomography was recorded. Several clinicopathological features were investigated to identify predictors of nodal metastasis using multivariate analyses. RESULTS: One hundred and eighty-four clinical Stage IA lung cancer patients showed a pure-solid appearance on thin-section CT. Among them, air bronchogram was found radiologically in 58 (32%) patients. Nodal involvement was observed in 10 (17%) patients with air bronchogram, compared with 43 (34%) without air bronchogram, in clinical Stage IA pure-solid lung cancer. A multivariate analysis revealed that air bronchogram, clinical T1a and SUVmax were significant predictors of postoperative nodal involvement ($P < 0.01$, <0.01 , and 0.03 , respectively). Furthermore, nodal metastasis was never seen in patients with clinical T1a pure-solid lung cancers who had both air bronchogram and low SUVmax. CONCLUSIONS: The presence of air bronchogram was a novel predictor of negative nodal involvement in clinical Stage IA pure-solid lung cancer. Segmentectomy with thorough lymph node dissection is a feasible option for these patients despite a pure-solid appearance.

[419]

TÍTULO / TITLE: - The overdiagnosis theory in lung cancer screening: Does it make any sense?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Surg Oncol. 2013 Nov 19. doi: 10.1002/jso.23491.

●● [Enlace al texto completo \(gratis o de pago\) 1002/jso.23491](#)

AUTORES / AUTHORS: - Kussman RS

[420]

TÍTULO / TITLE: - Biological correlation of (1)(8)F-FDG uptake on PET in pulmonary neuroendocrine tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Oct;33(10):4219-28.

AUTORES / AUTHORS: - Kaira K; Murakami H; Endo M; Ohde Y; Naito T; Kondo H; Nakajima T; Yamamoto N; Takahashi T

INSTITUCIÓN / INSTITUTION: - Division of Thoracic Oncology, Shizuoka Cancer Center, 1007 Shimonagakubo Nagaizumi-cho Sunto-gun, Shizuoka, 411-8777, Japan. kkaira1970@yahoo.co.jp.

RESUMEN / SUMMARY: - BACKGROUND: It is widely recognized that pulmonary neuroendocrine tumors (PNET) include a spectrum that ranges from low-grade typical carcinoid (TC) and atypical carcinoid (AC) to high-grade large cell neuroendocrine

carcinoma (LCNEC) and small cell lung carcinoma (SCLC). However, little is known about the usefulness of 2-[(18)F]-fluoro-2-deoxy-D-glucose ((18)F-FDG) positron-emission tomography (PET) in such tumors. We therefore, conducted a study including the analysis of the underlying biology of (18)F-FDG uptake. MATERIALS AND METHODS: Thirty-four patients with early-stage PNETs who underwent (18)F-FDG PET before treatment were included in this study. Tumor sections were stained by immunohistochemistry for glucose transporter-1 (Glut1 and Glut3), hypoxia-inducible factor-1 alpha (HIF-1alpha), hexokinase-I, vascular endothelial growth factor (VEGF), microvessel density (MVD) determined by CD34 and (Akt)/mammalian target of rapamycin (mTOR) signaling pathway. RESULTS: (18)F-FDG uptake correlated significantly with Glut1, HIF-1alpha, VEGF and CD34 expression. Uptake of (18)F-FDG tended to increase from low-grade to high-grade PNETs. Tumor metabolic activity was a useful marker for predicting postoperative prognosis in patients with early-stage PNETs. CONCLUSION: The amount of (18)F-FDG uptake is determined by the presence of glucose metabolism, hypoxia and angiogenesis.

[421]

TÍTULO / TITLE: - Effects of SRC and STAT3 upon gap junctional, intercellular communication in lung cancer lines.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Res. 2013 Oct;33(10):4401-10.

AUTORES / AUTHORS: - Geletu M; Guy S; Raptis L

INSTITUCIÓN / INSTITUTION: - Department of Biomedical and Molecular Sciences, Botterell Hall, Room 713, Queen's University, Kingston, Ontario, Canada K7L 3N6. raptisl@queensu.ca.

RESUMEN / SUMMARY: - BACKGROUND: We have previously demonstrated a positive correlation between SRC and its effector signal transducer and activator of transcription-3 (STAT3), and a reverse relation between SRC and gap junctional communication (GJIC) in seven non-small cell lung cancer (NSCLC) lines. Since a number of oncogenes besides SRC can affect GJIC, here we examined the actual contribution of the SRC/STAT3 axis to GJIC suppression. MATERIALS AND METHODS: SRC and STAT3 activity levels were examined in SK-LuCi-6, LC-T, QU-DB, SW-1573, BH-E, Calu-6, FR-E, SK-MES, H1299, BEN, WT-E, A549 and SHP-77 cells by western blott analysis, probing with antibodies specific for SRC-tyr418 or STAT3-tyr705. GJIC was examined by in situ electroporation. RESULTS: Confluence of all cultured NSCLC cells tested induces a dramatic increase in STAT3 activity, which is independent of SRC action. In addition, the LC-T line had high STAT3-705, despite the fact that SRC-418 expression was low, indicating that other, SRC-independent factors must be responsible for STAT3 activation and GJIC suppression in these cells; however, BH-E and SHP-77 cells with low GJIC, both SRC-418 and STAT3-705 expression were low, indicating that GJIC suppression can be independent of the SRC/STAT3 axis altogether. Our results also show that STAT3 inhibition does not restore GJIC in any of the examined lines, while in the non-transformed rat F111 fibroblast line which has extensive GJIC, STAT3 inhibition actually eliminated junctional permeability. CONCLUSION: Our results indicate a further level of complexity in the relationship between SRC, STAT3 and GJIC in NSCLC than what

has been previously demonstrated. In addition, STAT3 is actually required for, rather than suppressing GJIC.

[422]

TÍTULO / TITLE: - Elevated circulating levels of tissue factor-positive microvesicles are associated with distant metastasis in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Clin Oncol. 2013 Oct 30.

●● Enlace al texto completo (gratis o de pago) [1007/s00432-013-1544-8](#)

AUTORES / AUTHORS: - Tseng JC; Chang LC; Jiang BY; Liu YC; Chen HJ; Yu CT; Hua CC

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Chang Gung Memory Hospital, Keelung, Taiwan, ROC.

RESUMEN / SUMMARY: - PURPOSE: Microvesicles (MV) in the blood stream are associated with distant metastasis in cancer. Platelet or endothelial cell-related MV actively participate in thrombogenesis, which is an important step in cancer metastasis. This study investigated the correlations between MV levels of platelet-poor plasma and distant metastasis in lung cancer. METHODS: Platelet-poor plasma from 44 treatment-naive lung cancer (23 with distant metastasis) and 19 normal subjects was used to determine the levels of glycoprotein Ibeta (CD42) + platelet MV (PMV), P-selectin (CD62P) + PMV, VE-cadherin (CD144) + endothelial MV (EMV), tissue factor (CD142) + MV, thrombin-antithrombin complex and vascular endothelial growth factor (VEGF). RESULTS: The level of CD142 + MV was significant (odds ratio 5.86, 95 % confidence interval 1.31-38.3) in predicting distant metastasis in lung cancer, and a cutoff value of 2.668 (after logarithm transformation) in the ROC curve had a specificity of 90 % and a sensitivity of 59 %. The presence of distant metastasis showed a significant correlation between CD144 + EMV and VEGF, but not between CD144 + EMV and CD42 + PMV or CD62P + PMV in lung cancer subjects. CONCLUSIONS: The finding of CD142 + MV in platelet-poor plasma may be useful for suggesting distant metastasis in lung cancer. In addition to thrombogenesis, interaction between VE-cadherin and VEGF may be needed for successful metastasis in lung cancer.

[423]

TÍTULO / TITLE: - Sternal mass presenting as a first manifestation of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Med Sci. 2013 Nov;346(5):420. doi: 10.1097/01.MAJ.0000437742.25864.7b.

●● Enlace al texto completo (gratis o de pago)

[1097/01.MAJ.0000437742.25864.7b](#)

AUTORES / AUTHORS: - Marcos PJ; Rodriguez-Lorenzo A

INSTITUCIÓN / INSTITUTION: - *Servicio de Neumología, Complejo Hospitalario Universitario A Coruña, Xubias de arriba 84, 15006 A Coruña, España (E-mail: pedro.jorge.marcos.rodriquez@sergas.es).

[424]

TÍTULO / TITLE: - Application of high-resolution CT imaging data to lung cancer drug development: measuring progress: workshop IX.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1352-5. doi: 10.1097/01.JTO.0000435803.93490.04.

●● Enlace al texto completo (gratis o de pago)

1097/01.JTO.0000435803.93490.04

AUTORES / AUTHORS: - Mulshine JL; Avila R; Yankelevitz D; Baer TM; Estepar RS; Fenton L; Aldige CR

INSTITUCIÓN / INSTITUTION: - *Rush University, Chicago, Illinois; daggerKitware, Inc., Clifton Park, New York; double daggerMount Sinai School of Medicine, New York, New York; section signStanford University, Palo Alto, California; ||Brigham and Women's Hospital-Harvard Medical School, Boston Massachusetts; paragraph signLung Cancer Alliance, Washington, DC; and #Prevent Cancer Foundation, Alexandria, Virginia.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the leading cause of cancer death and a major public health challenge across the entire world. Computed tomography (CT) imaging of the lung is a rapidly improving medical imaging technique. Spiral CT has been reported to not only improve the early detection of lung cancer in screening high-risk tobacco-exposed populations but also to assist in the clinical assessment of new agents for therapy in lung cancer. METHODS: The Prevent Cancer Foundation has sponsored a series of workshops to accelerate progress in using quantitative imaging to advance lung cancer research progress, of which this report summarizes the Ninth Workshop. The defining strategy of this forum to support innovation in quantitative research for early lung cancer management was to enable software validations by assembling collections of high-quality images for which long-term clinical follow-up is known. An additional approach was to define a process for high-quality and economical national implementation of lung cancer screening. Representatives from the Quantitative Imaging Biomarker Alliance, the International Association for the Study of Lung Cancer, the Lung Cancer Alliance, and other organizations outlined their efforts in this regard. A major opportunity exists to advance the dialogue on the use of quantitative imaging tools to cross-fertilize and accelerate image-processing research across lung cancer and chronic obstructive pulmonary disease (COPD). CONCLUSION: The use of high-resolution CT imaging provides a window into a much earlier stage of COPD as well as coronary artery disease, both being tobacco-induced diseases. Progress in this area was reviewed and opportunities for enhanced collaborative progress defined. Key sessions reviewed emerging developments with imaging technology and the infrastructure to support the storage and distribution of these high-content modalities. Cooperation among diverse collaborators is essential to enable the rapid organic evolution of this field, so that improved outcomes with lung cancer, artery disease, and COPD can be obtained.

[425]

TÍTULO / TITLE: - Primary Pulmonary Synovial Sarcoma: A Rare Primary Pulmonary Tumor.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lung. 2013 Oct 30.

●● Enlace al texto completo (gratis o de pago) [1007/s00408-013-9521-1](https://doi.org/10.1007/s00408-013-9521-1)

AUTORES / AUTHORS: - Falkenstern-Ge RF; Kimmich M; Grabner A; Horn H; Friedel G; Ott G; Kohlhauf M

INSTITUCIÓN / INSTITUTION: - Division of Pulmonology, Klinik Schillerhoehe, Center for Pulmonology and Thoracic Surgery, Teaching Hospital of the University of Tuebingen, Solitude Str. 18, 70839, Stuttgart-Gerlingen, Germany, rogerfalkenstern@yahoo.de.

RESUMEN / SUMMARY: - INTRODUCTION: Pulmonary sarcomas overall are very uncommon and comprise only 0.5 % of all primary lung malignancies. The diagnosis is established only after sarcoma-like primary lung malignancies and a metastatic extrathoracic sarcoma have been excluded. Synovial sarcoma accounts for ~8 % of soft-tissue sarcomas. Synovial sarcoma arising from the pleura has rarely been reported. METHODS: We report a case of a 58-year-old woman who complained of right-sided chest pain and shortness of breath. Chest CT scan revealed a large heterogeneous mass, occupying most of the right hemithorax. Histologic diagnosis was supplemented by interphase cytogenetic (FISH) analysis. RESULTS: Computed tomography guided Tru-cut biopsy was suspicious for a sarcomatous or fibrous malignancy. However, intraoperative frozen-section diagnostics confirmed the diagnosis of a sarcoma. Immunohistochemistry showed that tumor cells expressed epithelial membrane antigen, CD99 and BCL2. Based on immunohistochemistry, the diagnosis of synovial sarcoma was suspected and was confirmed by FISH analysis. The patient was treated with right upper bilobectomy. Due to R1-resection status, postsurgical systemic chemotherapy was administered. CONCLUSIONS: Primary pulmonary synovial sarcoma is a rare primary lung tumor. Due to extensive size of the tumor with pleural and mediastinal invasion only a R1-resection status could be achieved by thoracic surgery.

[426]

TÍTULO / TITLE: - Evaluation of nestin in lung adenocarcinoma: relation to VEGF and Bcl-2.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomarkers. 2013 Nov 28.

●● Enlace al texto completo (gratis o de pago) [3109/1354750X.2013.863975](https://doi.org/10.1007/s1009-1354750X-2013-863975)

AUTORES / AUTHORS: - Ahmed MB; Nabih ES; Louka ML; Abdel Motaleb FI; El Sayed MA; Elwakiel HM

INSTITUCIÓN / INSTITUTION: - Department of Medical Biochemistry and.

RESUMEN / SUMMARY: - Abstract Context: Nestin is a marker of multipotent precursor cells that is up regulated in cancer. Objective: To explore its diagnostic role and its relationship to vascular endothelial growth factor (VEGF) and Bcl-2 in lung adenocarcinoma. Materials and methods: Evaluation of nestin expression in lung biopsies by real-time PCR and serum VEGF and Bcl-2 by ELISA in 27 adenocarcinoma patients and 15 control subjects. Results: Nestin was significantly higher in lung adenocarcinoma patients especially with advanced grade and stage and it was significantly correlated to VEGF and Bcl-2. Conclusion: Nestin can be considered as a potential diagnostic marker in lung adenocarcinoma.

[427]

TÍTULO / TITLE: - Plasma and EBC microRNAs as early biomarkers of non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomarkers. 2013 Dec;18(8):679-86. doi: 10.3109/1354750X.2013.845610. Epub 2013 Oct 8.

●● Enlace al texto completo (gratis o de pago) [3109/1354750X.2013.845610](#)

AUTORES / AUTHORS: - Mozzoni P; Banda I; Goldoni M; Corradi M; Tiseo M; Acampa O; Balestra V; Ampollini L; Casalini A; Carbognani P; Mutti A

INSTITUCIÓN / INSTITUTION: - Department of Clinical and Experimental Medicine, University of Parma , Parma , Italy .

RESUMEN / SUMMARY: - Abstract Lung cancer is a major cause of death in Western countries. Current screening methods are invasive and still lead to a high percentage of false positives. There is, therefore, a need to find biomarkers that increase the probability of detecting lung cancer early. MicroRNAs (miRNAs) are stable molecules in blood plasma and exhaled breath condensate (EBC). We quantified miRNA-21 and miRNA-486 expression from plasma and EBC samples from patients with a diagnosis of non-small-cell lung cancer (NSCLC) and controls. miRNA-21 was significantly higher in plasma and in EBC of the NSCLC patients and miRNA-486 was significantly lower. This difference indicates a significantly improved diagnostic value, and suggests that these miRNAs could be clinically used as a first-line screening test in high-risk subjects.

[428]

TÍTULO / TITLE: - Anterior cingulotomy improves malignant mesothelioma pain and dyspnoea.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Br J Neurosurg. 2013 Nov 7.

●● Enlace al texto completo (gratis o de pago) [3109/02688697.2013.857006](#)

AUTORES / AUTHORS: - Pereira EA; Paranathala M; Hyam JA; Green AL; Aziz TZ

INSTITUCIÓN / INSTITUTION: - Oxford Functional Neurosurgery and Experimental Neurology Group, Nuffield Department of Surgical Sciences, University of Oxford , Oxford , UK and Department of Neurological Surgery, The West Wing, John Radcliffe Hospital , Oxford , UK.

RESUMEN / SUMMARY: - Background. Bilateral anterior cingulotomy is a palliative procedure occasionally used for cancer pain, and human studies suggest anterior cingulate cortex is active in dyspnoeic states. Objectives. A case of debilitating thoracic wall pain due to malignant mesothelioma relieved by bilateral anterior cingulotomy is described and changes in dyspnoea investigated. Results. Improvements in pain, dyspnoea and the extent to which either symptom bothered the patient was seen for 2 months after surgery before disease progression led to death 5 months after surgery. Quality of life improvements were also seen for 2 months after surgery and pain relief was sustained from surgery to death. Arterial blood gas and lung function tests were unchanged by surgery, suggesting a reduction in pain and dyspnoea awareness by cingulotomy. Conclusions. Bilateral anterior cingulotomy effectively relieved both pain and dyspnoea. The role of the anterior cingulate cortex in pain and autonomic control

of respiration is discussed alongside the evidence for this palliative procedure for cancer pain.

[429]

TÍTULO / TITLE: - Lung cancer classification using neural networks for CT images.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Comput Methods Programs Biomed. 2014 Jan;113(1):202-9. doi: 10.1016/j.cmpb.2013.10.011. Epub 2013 Oct 18.

●● Enlace al texto completo (gratis o de pago) [1016/j.cmpb.2013.10.011](#)

AUTORES / AUTHORS: - Kuruvilla J; Gunavathi K

INSTITUCIÓN / INSTITUTION: - ECE Department, PSG College of Technology, Coimbatore 641004, India. Electronic address: jinsa_k@yahoo.com.

RESUMEN / SUMMARY: - Early detection of cancer is the most promising way to enhance a patient's chance for survival. This paper presents a computer aided classification method in computed tomography (CT) images of lungs developed using artificial neural network. The entire lung is segmented from the CT images and the parameters are calculated from the segmented image. The statistical parameters like mean, standard deviation, skewness, kurtosis, fifth central moment and sixth central moment are used for classification. The classification process is done by feed forward and feed forward back propagation neural networks. Compared to feed forward networks the feed forward back propagation network gives better classification. The parameter skewness gives the maximum classification accuracy. Among the already available thirteen training functions of back propagation neural network, the Traingdx function gives the maximum classification accuracy of 91.1%. Two new training functions are proposed in this paper. The results show that the proposed training function 1 gives an accuracy of 93.3%, specificity of 100% and sensitivity of 91.4% and a mean square error of 0.998. The proposed training function 2 gives a classification accuracy of 93.3% and minimum mean square error of 0.0942.

[430]

TÍTULO / TITLE: - Across The Universe Of K-Ras Mutations In Non-Small-Cell-Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Piva S; Ganzinelli M; Garassino MC; Caiola E; Farina G; Broggin M; Marabese M

INSTITUCIÓN / INSTITUTION: - Lab of Molecular Pharmacology, Oncology Department, IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Via G. La Masa 19 20156 Milan, Italy. massimo.broggin@marionegri.it.

RESUMEN / SUMMARY: - RAS family proteins are important signaling molecules that regulate cell growth, survival and differentiation by coupling receptor activation to downstream effector pathways. Three distinct genes encode for the three different proteins H-, K-, and N- RAS. These proteins share high sequence homology, particularly at the N-Terminal domain. Among them, K-RAS is the one most frequently mutated in human cancer. The majority of the mutations present in K-RAS are at codon 12 (from 80 to 100%) followed by codon 13 and 61. In all cases, aminoacid change

leads to a constitutively activated protein. K-RAS mutations have a role in tumor development as well as in tumor progression and resistance. Despite the various studies which have been published, the prognostic and predictive role of K-RAS mutations is still under debate. Keeping in mind that the glycine present at position 12 can be substituted by valine, aspartic acid or cysteine, it could well be that each different substitution plays a different role in K-RAS-dependent processes. The present article focuses on the molecular and biological characteristics of K-RAS protein, its role in NSCLC tumor development and progression. We also present an overview of the preclinical models both in vitro and in vivo available to determine the role of K-RAS in tumor progression and response to treatment and on the recent results obtained in this field. Finally, we have considered the impact of K-RAS mutations in clinical practice, analyzing the different recent trials that have taken into consideration K-RAS.

[431]

TÍTULO / TITLE: - Synchronous metastatic pulmonary adenocarcinoma with small cell lymphoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Leuk Lymphoma. 2013 Nov 14.

●● Enlace al texto completo (gratis o de pago) [3109/10428194.2013.850166](#)

AUTORES / AUTHORS: - Gajendra S; Gogia A; Tanwar P; Sahoo MK; Bhethanabhotla S; Durgapal P; Gupta R

INSTITUCIÓN / INSTITUTION: - Laboratory Oncology Unit.

[432]

TÍTULO / TITLE: - EZH2 regulates cancer cell migration through repressing TIMP-3 in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Oncol. 2013 Dec;30(4):713. doi: 10.1007/s12032-013-0713-6. Epub 2013 Oct 17.

●● Enlace al texto completo (gratis o de pago) [1007/s12032-013-0713-6](#)

AUTORES / AUTHORS: - Xu C; Hou Z; Zhan P; Zhao W; Chang C; Zou J; Hu H; Zhang Y; Yao X; Yu L; Yan J

INSTITUCIÓN / INSTITUTION: - First Department of Respiratory Medicine, Nanjing Chest Hospital, Nanjing, 210029, Jiangsu, China.

RESUMEN / SUMMARY: - Histone methylations play important roles in human cancer metastasis. Enhancer of zeste homolog 2 (EZH2) is a key component of the polycomb repressor complex 2, which is responsible for histone H3K27 methylation. EZH2 is overexpressed in lung cancer and epigenetically silences tumor suppressor genes. Here, we showed that EZH2 was up-regulated in lung cancer and had a positive correlation with pathologic stage, nodal involvement in lung cancer patients. Moreover, overexpression of EZH2 was correlated with reduced tissue inhibitor of metalloproteinase-3 (TIMP-3) expression, which was shown to be negatively associated with tumor metastasis. Of note, overall survival time of patients with high EZH2/low TIMP-3 expression was significantly shorter than that of patients with low EZH2/high TIMP-3 (P = 0.031). RNA interfering and pharmacologic inhibition of EZH2 reduced histone H3 lysine 27 tri-methylation level and increased TIMP-3 expression

level. Knockdown of EZH2 by siRNA significantly reduced A549 cancer cell migration. In contrast, reduction of TIMP-3 in A549 cells partially rescued EZH2 deficiency-induced loss of cell migration capacity. Taken together, our findings indicate that EZH2 accelerates cancer cell migration, in part, via the repression of TIMP-3 expression, suggesting a potential mechanism by which EZH2 promotes lung cancer progression and metastasis.

[433]

TÍTULO / TITLE: - Small-cell lung cancer exhibiting spontaneous regression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Intern Med. 2013;52(19):2249-52. Epub 2012 Mar 1.

AUTORES / AUTHORS: - Iwakami S; Fujii M; Ishiwata T; Iwakami N; Hara M; Ihara H; Wada R; Tsutsumi T; Seyama K; Takahashi K

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Juntendo University Shizuoka Hospital, Japan.

RESUMEN / SUMMARY: - A 56-year-old woman was admitted to our hospital because a chest X-ray and thoracic computed tomography (CT) scan revealed a heterogeneous tumor in the middle mediastinum during a visit to a nearby clinic for a consultation regarding a persistent cough and body weight loss. However, the tumor spontaneously decreased on thoracic CT performed on admission. Subsequently, a biopsy of the tumor using video-assisted thoracoscopy was performed. The pathological findings disclosed the tumor to be small-cell lung cancer with infiltration of CD8-positive T-cells exhibiting spontaneous regression. Cell-mediated immunity, including CD8-positive T-cells, may have relevance to the spontaneous regression of malignant tumors.

[434]

TÍTULO / TITLE: - Lung adenocarcinoma presenting with diffuse multiloculated cystic lesions.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Intern Med. 2013;52(20):2375.

AUTORES / AUTHORS: - Kushima H; Ishii H; Yokoyama A; Kadota J

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Oita University Hospital, Japan.

[435]

TÍTULO / TITLE: - Whole-genome sequencing analysis identifies a distinctive mutational spectrum in an arsenic-related lung tumor.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1451-5. doi: 10.1097/JTO.0b013e3182a4dd8e.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/JTO.0b013e3182a4dd8e](#)

AUTORES / AUTHORS: - Martinez VD; Thu KL; Vucic EA; Hubaux R; Adonis M; Gil L; MacAulay C; Lam S; Lam WL

INSTITUCIÓN / INSTITUTION: - *Department of Integrative Oncology, BC Cancer Agency, Vancouver, Canada; and daggerProgram of Cell and Molecular Biology, Faculty of Medicine, University of Chile, Santiago, Chile.

RESUMEN / SUMMARY: - INTRODUCTION: Arsenic exposure is a significant cause of lung cancer in North America and worldwide. Arsenic-related tumors are structurally indistinguishable from those induced by other carcinogens. Because carcinogens, like tobacco, induce distinctive mutational signatures, we sought to characterize the mutational signature of an arsenic-related lung tumor from a never smoker with the use of whole-genome sequencing. METHODS: Tumor and lung tissues were obtained from a never smoker with lung squamous cell carcinoma (LUSC), without familiar history of lung cancer and chronically exposed to high levels of arsenic-contaminated drinking water. The Illumina HiSeq-2000 platform was used to sequence each genome at approximately 30-fold haploid coverage. The mutational signature was compared with those observed in previously characterized lung tumors. RESULTS: The arsenic-related tumor exhibited alterations common in LUSC, such as the increased number of copies at 3q26 (SOX2 locus). However, the arsenic-related genome not only harbored a lower number of point mutations, but also had a remarkably high fraction of T>G/A>C mutations and low fraction of C>A/G>T transversions, which is uncharacteristic of LUSCs. Furthermore, at the gene level, we identified a rare G>C mutation in TP53, which is uncommon in lung tumors in general (<0.2%) but has been observed in other arsenic-related malignancies. CONCLUSIONS: We generated the first whole-genome sequence of an LUSC from a never-smoker patient chronically exposed to arsenic, and identified a distinct mutational spectrum associated with arsenic exposure, providing novel evidence supporting the hypothesis that arsenic-induced lung tumors arise through molecular mechanisms that differ from those of the common lung cancer.

[436]

TÍTULO / TITLE: - Moderately Differentiated Peripheral Adenocarcinoma Lung With Cilia.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Surg Pathol. 2013 Nov 26.

●● [Enlace al texto completo \(gratis o de pago\) 1177/1066896913510027](#)

AUTORES / AUTHORS: - Nair AR; Samvedam S; Madathipat U; Raman KT

RESUMEN / SUMMARY: - We report an extremely rare case in which cilia were identifiable on light microscopic examination in cells of a moderately differentiated peripheral adenocarcinoma in the lung. The cells were positive for cytokeratin 7, and the cilia were highlighted by epithelial membrane antigen staining. The prognostic significance of these extremely well-differentiated ciliated tumor cells will be known only with long-term follow-up of the patient and analysis of more such tumors.

[437]

TÍTULO / TITLE: - Ewing's Sarcoma/Primitive Neuroectodermal Tumor With Neuroendocrine Differentiation: Report of an Unusual Lung Tumor.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Surg Pathol. 2013 Oct 17.

●● [Enlace al texto completo \(gratis o de pago\) 1177/1066896913502227](#)

AUTORES / AUTHORS: - Barroca H; Souto Moura C; Lopes JM; Lisboa S; Teixeira MR; Damasceno M; Bastos P; Sobrinho Simoes M

RESUMEN / SUMMARY: - Ewing's sarcoma/primitive neuroectodermal tumor (PNET) has been the subject of recent reports describing morphologic variants (adamantinoma-like, large cell, spindle cell, sclerosing, clear cell, and vascular-like) of the most classic form, as well as cases displaying unusual morphologic differentiation and atypical immunohistochemical features. We report a case of an uncommon lung tumor in a 20-year-old female, morphologically and molecularly consistent with an Ewing's sarcoma/PNET tumor with foci of squamous differentiation, and peculiar expression of vimentin, high-molecular-weight keratins, p63, synaptophysin, and chromogranin. This case raises a challenging differential diagnostic problem with therapeutic implications: Should the patient be treated following the protocols for Ewing's sarcoma/PNET tumors or as for lung carcinoma with neuroendocrine features? The patient we report here was treated with neoadjuvant chemotherapy for Ewing's sarcoma/PNET according to Euro Ewing 99 study protocol followed by surgery and has no evidence of disease 15 months after the initial diagnosis. This highlights the importance of achieving the correct diagnosis of these atypical tumors using all clinical, morphological, and ancillary methods available to allow for their correct and timely treatment.

[438]

TÍTULO / TITLE: - Lung Adenocarcinoma Metastasis to Frontal Sinus Mimicking Pott's Puffy Tumor.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Craniofac Surg. 2013 Nov;24(6):e538-9. doi: 10.1097/SCS.0b013e318285d98a.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/SCS.0b013e318285d98a](#)

AUTORES / AUTHORS: - Koktekir E; Koktekir BE; Recber F; Akdemir G

INSTITUCIÓN / INSTITUTION: - From the *Departments of Neurosurgery and daggerOphthalmology, Faculty of Medicine, Selcuk University, Konya, Turkey.

RESUMEN / SUMMARY: - Metastasis of the lung adenocarcinoma to the paranasal sinuses is a rare clinical entity. We present a 75-year-old male patient who presented with swelling of the forehead and left upper eyelid with proptosis in left eye due to metastasis from lung adenocarcinoma. It appears as a puffy swelling of the forehead like a Pott's puffy tumor. Pott's puffy tumor is a subperiosteal abscess of the frontal bone associated with osteomyelitis and usually occurs as a complication of sinusitis or trauma.

[439]

TÍTULO / TITLE: - Anti-Angiogenic Drugs and Biomarkers in Non-Small-Cell Lung Cancer: A 'Hard Days Night'

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Pilotto S; Bonomi M; Massari F; Milella M; Ciuffreda L; Brunelli M; Fassan M; Chilosi M; Scarpa A; Tortora G; Bria E

INSTITUCIÓN / INSTITUTION: - Medical Oncology dU, Policlinico 'G.B. Rossi', University of Verona, P.zza L.A. Scuro 1, 37134, Verona, Italy. emiliobria@yahoo.it.

RESUMEN / SUMMARY: - The discovery of specific molecular alterations (i.e. EGFR activating mutations, EML4/ALK translocation, ROS1 rearrangements) in a selected population of patients affected by non small cell lung cancer (NSCLC) translated into effective treatments for this small but well defined fraction of patients, driven by the use of predictive biomarkers of efficacy for targeted agents. Unfortunately, the same reliable predictive biomarkers are lacking for anti-angiogenic drugs. Angiogenesis plays a major role in the progression of NSCLC, however, anti-angiogenic agents provided a minimal, although significant, clinical benefit in unselected populations, burdened by a not negligible toxicities. In this context, no validated angiogenic factor or other molecular biomarker of angiogenesis can reliably predict clinical outcome, sensitivity, early response or resistance to any of the investigated anti-angiogenic therapies currently used. Moreover, the available clinical data are prevalently retrospective, underpowered, and, in many cases, contradictory, thus underscoring that the understanding of the complex architecture of angiogenic signaling is still incomplete. We here review the currently available studies on the effect of anti-angiogenic drugs in NSCLC, with a particular focus on bio-molecular factors that are regarded as potential predictors of treatment efficacy.

[440]

TÍTULO / TITLE: - IL-27 inhibits epithelial-mesenchymal transition and angiogenic factor production in a STAT1-dominant pathway in human non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Exp Clin Cancer Res. 2013 Nov 25;32(1):97.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1756-9966-32-97](#)

AUTORES / AUTHORS: - Kachroo P; Lee MH; Zhang L; Baratelli F; Lee G; Srivastava MK; Wang G; Walser TC; Krysan K; Sharma S; Dubinett SM; Lee JM

RESUMEN / SUMMARY: - **BACKGROUND:** Interleukin-27 signaling is mediated by the JAK-STAT pathway via activation of STAT1 and STAT3, which have tumor suppressive and oncogenic activities, respectively. Epithelial—mesenchymal transition (EMT) and angiogenesis are key processes in carcinogenesis. Although IL-27 has been shown to have potent anti-tumor activity in various cancer models, the role of IL-27 in EMT and angiogenesis is poorly understood. In this study, we investigated the role of IL-27 in regulating EMT and angiogenesis through modulation of the STAT pathways in human non-small cell lung carcinoma (NSCLC) cells. **METHODS:** STAT activation following IL-27 exposure was measured in human NSCLC cell lines. Expression of epithelial (E-cadherin, gamma-catenin) and mesenchymal (N-cadherin, vimentin) markers were assessed by Western blot analysis. Production of pro-angiogenic factors (VEGF, IL-8/CXCL8, CXCL5) were examined by ELISA. Cell motility was examined by an in vitro scratch and transwell migration assays. Selective inhibitors of STAT1 (STAT1 siRNAs) and STAT3 (Stattic) were used to determine whether both STAT1 and STAT3 are required for IL-27 mediated inhibition of EMT and secretion of angiogenic factors. **RESULTS:** Our results demonstrate that IL-27 stimulation in NSCLC resulted in 1) STAT1 and STAT3 activation in a JAK-dependent manner, 2) development of epithelial phenotypes, including a decrease in the expression of a transcriptional repressor for E-cadherin (SNAIL), and mesenchymal marker (vimentin) with a reciprocal increase in

the expression of epithelial markers, 3) inhibition of cell migration, and 4) reduced production of pro-angiogenic factors. STAT1 inhibition in IL-27--treated cells reversed the IL-27 effect with resultant increased expression of Snail, vimentin and the pro-angiogenic factors. The inhibition of STAT3 activation had no effect on the development of the epithelial phenotype. CONCLUSION: IL-27 induces mesenchymal to epithelial transition and inhibits the production of pro-angiogenic factors in a STAT1-dominant pathway. These findings highlight the importance of STAT1 in repressing lung carcinogenesis and describe a new anti-tumor mechanism of IL-27.

[441]

TÍTULO / TITLE: - Mitochondrial targeting of alpha-tocopheryl succinate enhances its anti-mesothelioma efficacy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Redox Rep. 2013 Nov 12.

●● Enlace al texto completo (gratis o de pago)

[1179/1351000213Y.0000000064](#)

AUTORES / AUTHORS: - Kovarova J; Bajzikova M; Vondrusova M; Stursa J; Goodwin J; Nguyen M; Zobalova R; Pesdar EA; Truksa J; Tomasetti M; Dong LF; Neuzil J

RESUMEN / SUMMARY: - : Malignant mesothelioma (MM) is a fatal neoplastic disease with no therapeutic option. Therefore, the search for novel therapies is of paramount importance. METHODS: Since mitochondrial targeting of alpha-tocopheryl succinate (alpha-TOS) by its tagging with triphenylphosphonium enhances its cytotoxic effects to cancer cells, we tested its effect on MM cells and experimental mesotheliomas. RESULTS: Mitochondrially targeted vitamin E succinate (MitoVES) was more efficient in killing MM cells than alpha-TOS with IC50 lower by up to two orders of magnitude. Mitochondrial association of MitoVES in MM cells was documented using its fluorescently tagged analogue. MitoVES caused apoptosis in MM cells by mitochondrial destabilization, resulting in the loss of mitochondrial membrane potential, generation of reactive oxygen species, and destabilization of respiratory supercomplexes. The role of the mitochondrial complex II in the activity of MitoVES was confirmed by the finding that MM cells with suppressed succinate quinone reductase were resistant to MitoVES. MitoVES suppressed mesothelioma growth in nude mice with high efficacy. DISCUSSION: MitoVES is more efficient in killing MM cells and suppressing experimental mesotheliomas compared with the non-targeted alpha-TOS, giving it a potential clinical benefit.

[442]

TÍTULO / TITLE: - Overdiagnosis in lung cancer screening with low-dose computed tomography.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):e101-2. doi: 10.1097/JTO.0b013e3182a476d4.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a476d4](#)

AUTORES / AUTHORS: - Takiguchi Y; Sekine I; Iwasawa S

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology Graduate School of Medicine Chiba University Chiba, Japan.

[443]

TÍTULO / TITLE: - CT screening for lung cancer: countdown to implementation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lancet Oncol. 2013 Dec;14(13):e591-600. doi: 10.1016/S1470-2045(13)70293-6.

●● Enlace al texto completo (gratis o de pago) [1016/S1470-2045\(13\)70293-6](#)

AUTORES / AUTHORS: - Field JK; Hansell DM; Duffy SW; Baldwin DR

INSTITUCIÓN / INSTITUTION: - Roy Castle Lung Cancer Research Programme, University of Liverpool Cancer Research Centre, Liverpool, UK. Electronic address: J.K.Field@liv.ac.uk.

RESUMEN / SUMMARY: - Implementation of lung cancer CT screening is currently the subject of a major policy decision within the USA. Findings of the US National Lung Screening Trial showed a 20% reduction in lung cancer mortality and a 6.7% decrease in all-cause mortality; subsequently, five US professional and clinical organisations and the US Preventive Services Task Force recommended that screening should be implemented. Should national health services in Europe follow suit? The European community awaits mortality and cost-effectiveness data from the NELSON trial in 2015-16 and pooled findings of European trials. In the intervening years, a recommendation is proposed that a demonstration trial is done in the UK. In this Review, we summarise the existing evidence and identify questions that remain to be answered before the implementation of international lung cancer screening programmes.

[444]

TÍTULO / TITLE: - Pulmonary atelectasis after stereotactic ablative radiotherapy for a central lung tumor.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):e94-5. doi: 10.1097/JTO.0b013e3182a00911.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a00911](#)

AUTORES / AUTHORS: - Senti S; Ullmann EF; Senan S

INSTITUCIÓN / INSTITUTION: - *Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands; and daggerDepartment of Pulmonology, Rijnstate Ziekenhuis, Arnhem, The Netherlands.

[445]

TÍTULO / TITLE: - PARP inhibitors: an interesting pathway also for Non-Small Cell Lung Cancer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Levra MG; Olausson KA; Novello S; Soria JC

INSTITUCIÓN / INSTITUTION: - Department of Oncology University of Torino, Regione Gonzole 10, 10043 Orbassano (TO), Italy. silvia.novello@unito.it.

RESUMEN / SUMMARY: - Treatment of lung cancer is improving, also based on the identification of molecular characteristics of the tumor, of which some already constitute promising targets. One of the molecular characteristics thought to play an important role in lung cancer is DNA repair dysfunctionality. Deregulated expression of DNA repair proteins, such as PARP, has been studied in lung cancer as a possible biomarker and clinically useful target, but the literature remains relatively poor. Pharmacological inactivation of PARP has allowed the identification of a synthetic lethality with a second DNA repair protein such as BRCA1, but has also shown the potential to sensitize tumors to commonly used cytotoxic agents. The current manuscript reviews data regarding PARP in the context of DNA repair and its different pathways, as well as the clinical data generated until now with PARP inhibitors. A deeper understanding of the DNA damage response in lung malignancies, and particularly a clarification of the crosstalk between DNA repair functionality and genetic stability, is key to optimize the development of PARP inhibitors in the setting of NSCLC.

[446]

TÍTULO / TITLE: - Approaching the Increasing Complexity of Non-Small Cell Lung Cancer Taxonomy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Pharm Des. 2013 Nov 5.

AUTORES / AUTHORS: - Maugeri-Sacca M; Bartucci M; Pagliuca A; Patrizii M; Signore M; De Maria R

INSTITUCIÓN / INSTITUTION: - National Cancer Institute, via E. Chianesi, n. 53, 00144, Rome, Italy. maugeri.marcello@gmail.com.

RESUMEN / SUMMARY: - The advent of molecular targeted agents is changing the treatment of solid tumors. In non-small-cell lung cancer compounds directed against oncogenic proteins offer novel therapeutic opportunities for a fraction of patients whose tumors harbor specific genetic defects. With the increased level of resolution achieved by high-throughput technologies, the taxonomy of lung cancer is rapidly changing. For instance, by cataloguing genetic abnormalities in squamous cell lung cancer the Cancer Genome Atlas Network revealed the existence of multiple molecular entities, each one characterized by specific molecular abnormalities, and by a different spectrum of activated/inactivated molecular networks. Although this increased complexity could be perceived as a further drawback in effective anticancer therapy, on the other hand the combined interrogation of genomic and proteomic data is expected to provide the whole molecular map of each tumor, and to determine the information flow in the explored biological system. In particular, novel genetic and proteomic approaches are offering the opportunity for matching specific genetic defects and aberrant protein-protein interactions with active pathway-targeted inhibitors. Moreover, the isolation and characterization of a cellular pool endowed with stem-like traits, and able to recapitulate the parental disease in animals, is enabling investigators to recreate the individual patient tumor in the laboratory. In this article, we discuss how novel technologies and cellular and animal models, applied to lung cancer research, hold the potential to foster a new wave of biomarker-driven clinical trials.

[447]

TÍTULO / TITLE: - Adequacy of lymph node transbronchial needle aspirates using convex probe endobronchial ultrasound for multiple tumor genotyping techniques in non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1438-44. doi: 10.1097/JTO.0b013e3182a471a9.

●● [Enlace al texto completo \(gratis o de pago\)](#)

[1097/JTO.0b013e3182a471a9](#)

AUTORES / AUTHORS: - Folch E; Yamaguchi N; VanderLaan PA; Kocher ON; Boucher DH; Goldstein MA; Huberman MS; Kent MS; Gangadharan SP; Costa DB; Majid A

INSTITUCIÓN / INSTITUTION: - Departments of *Surgery, daggerMedicine, double daggerPathology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts.

RESUMEN / SUMMARY: - INTRODUCTION: Adequate tumor acquisition is essential to identify somatic molecular alterations in non-small-cell lung cancer (NSCLC), such as epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) translocations. The success and failure rates for tumor genotyping of tissue obtained from fine-needle aspirates of nodal tissue using a convex probe endobronchial ultrasound (CP-EBUS) and other diagnostic modalities in routine NSCLC care have not been described. METHODS: Clinicopathologic data, tumor genotype success and failure rates were retrospectively compiled and analyzed from 207 patient-tumor samples sent for routine tumor genotype in clinical practice, including 42 patient-tumor samples obtained from hilar or mediastinal lymph nodes using CP-EBUS. RESULTS: The median age of the patients was 65 years, 62.3% were women, 77.8% were white, 26.6% were never smokers, 73.9% had advanced NSCLC, and 84.1% had adenocarcinoma histology. Tumor tissue was obtained from CP-EBUS-derived hilar or mediastinal nodes in 42 cases (20.2% of total). In this latter cohort, the overall success rate for EGFR mutation analysis was 95.2%, for Kirsten rat sarcoma viral oncogene homolog (KRAS) mutation 90.5%, and for ALK fluorescence in situ hybridization 90.5%. In the complete 207 tumors, the success rate for EGFR was 92.3%, for KRAS 91.8%, and for ALK 89.9%. The failure rates were not significantly different when comparing CP-EBUS-derived nodal tissue versus all other samples or versus surgical biopsies of mediastinal nodes, but were significantly lower than image-guided percutaneous transthoracic core-needle biopsies. CONCLUSIONS: The success rate of multiple tumor genomic analyses techniques for EGFR, KRAS, and ALK gene abnormalities using routine lung cancer tissue samples obtained from hilar or mediastinal lymph nodes by means of CP-EBUS exceeds 90%, and this method of tissue acquisition is not inferior to other specimen types. Tumor genotype techniques are feasible in most CP-EBUS-derived samples and therefore further expansion of routine tumor genotype for the care of patients with NSCLC may be possible using targeted sample acquisition through CP-EBUS.

[448]

TÍTULO / TITLE: - Transesophageal ultrasonography for lung cancer staging: learning curves of pulmonologists.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1402-8. doi: 10.1097/JTO.0b013e3182a46bf1.

●● Enlace al texto completo (gratis o de pago) [1097/JTO.0b013e3182a46bf1](#)

AUTORES / AUTHORS: - Konge L; Annema J; Vilmann P; Clementsen P; Ringsted C

INSTITUCIÓN / INSTITUTION: - *Centre for Clinical Education, University of Copenhagen and the Capital Region of Denmark, Copenhagen, Denmark; daggerPulmonology Department, Leiden University Medical Center, Leiden, The Netherlands, and Pulmonology Department, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands; double daggerDepartment of Surgical Gastroenterology, Copenhagen University Hospital, Herlev, Denmark; section signDepartment of Pulmonology, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark; and ||The Wilson Centre, University of Toronto and University Health Network, Toronto, Canada.

RESUMEN / SUMMARY: - INTRODUCTION: Accurate mediastinal nodal staging is essential for patients with resectable non-small-cell lung cancer and is achieved by combined endobronchial ultrasound and transesophageal endoscopic ultrasound (EUS). Training requirements for EUS-guided fine-needle aspiration (FNA) for lung cancer staging are unknown. METHODS: Pulmonologists from Denmark and The Netherlands were enrolled in a dedicated, supervised training program. They performed standardized EUS-FNA procedures for mediastinal nodal analysis and their performances were assessed by EUS experts using a validated EUS assessment tool. Data were collected prospectively and used to plot learning curves and relate these to procedures performed by experienced investigators. RESULTS: Four participants performed 91 EUS-FNA procedures (range, 19-24). The performances of the participants improved significantly and became more consistent, but were still highly variable even in the latter part of the learning curves. Only two of the participants reached the mean score of experienced operators-after 17 and 23 procedures, respectively. CONCLUSIONS: Pulmonologists with knowledge of lung cancer staging and experience in bronchoscopy quickly improved their performance of EUS-FNA. However, acquisition of skills varies between individuals, and certification should be based on assessment of performance of multiple cases. Twenty procedures were not enough to secure consistent and competent performance of all trainees.

[449]

TÍTULO / TITLE: - PET/CT findings for bone marrow carcinosis because of lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Oncol. 2013 Nov;8(11):1456-7. doi: 10.1097/JTO.0b013e3182a47524.

●● Enlace al texto completo (gratis o de pago)

[1097/JTO.0b013e3182a47524](#)

AUTORES / AUTHORS: - Watanabe K; Shinkai M; Nagai K; Yamaguchi N; Ishigatsubo Y; Kaneko T

INSTITUCIÓN / INSTITUTION: - *Respiratory Disease Center, Yokohama City University Medical Center, Yokohama, Kanagawa, Japan; and daggerDepartment of Internal

[450]

TÍTULO / TITLE: - Elderly Subset Analysis of Randomized Phase III Study Comparing Pemetrexed Plus Carboplatin with Docetaxel Plus Carboplatin as First-Line Treatment for Patients with Locally Advanced or Metastatic Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Drugs R D. 2013 Nov 26.

- [Enlace al texto completo \(gratis o de pago\) 1007/s40268-013-0032-6](#)

AUTORES / AUTHORS: - Pereira JR; Cheng R; Orlando M; Kim JH; Barraclough H

INSTITUCIÓN / INSTITUTION: - Instituto Brasileiro Cancerologia Toracica, Sao Paulo, Brazil.

RESUMEN / SUMMARY: - BACKGROUND: Many physicians consider platinum-doublet chemotherapy inappropriate for elderly patients, regardless of their medical fitness. OBJECTIVE: This was a retrospective subgroup analysis of data from a multicenter, randomized, phase III clinical trial evaluating pemetrexed + carboplatin versus docetaxel + carboplatin in elderly chemo-naive patients with advanced, nonsquamous non-small cell lung cancer (NSCLC). METHODS: Data from elderly patients (aged ≥ 65 years and ≥ 70 years) were evaluated using the same statistical methods as those used in patients aged < 70 years and qualified intent-to-treat (Q-ITT) populations. The primary objective of the clinical trial was comparison of pemetrexed + carboplatin with docetaxel + carboplatin in terms of survival without grade 3 or 4 toxicity in chemo-naive NSCLC patients. RESULTS: The ≥ 65 - and ≥ 70 -year age groups had 68 and 37 patients, respectively. Among patients aged ≥ 65 years, the adjusted hazard ratio (HR) for survival without grade 3-4 toxicity (HR 0.40, 95 % confidence interval [CI] 0.23-0.70) favored pemetrexed + carboplatin; this was similar to the HRs in patients aged ≥ 70 years (HR 0.43, 95 % CI 0.20-0.92), patients aged < 70 years (HR 0.44, 95 % CI 0.32-0.62), and the Q-ITT population (HR 0.45, 95 % CI 0.34-0.61). The median values for overall survival (OS) and progression-free survival (PFS) were similar across all age-group subsets and the Q-ITT population. The HRs for OS and PFS were similar for all age-group subsets, except for the ≥ 70 -year age group, which favored pemetrexed + carboplatin to a greater extent. The toxicity profile was similar across age groups, with the exception of diarrhea, mucosal inflammation, and grade 3-4 neutropenia and leukopenia, which were slightly more common in elderly patients in both treatment arms. Between-arm differences in the toxicity profiles for the ≥ 65 -, ≥ 70 - and < 70 -year age subgroups were similar to those in the Q-ITT population. There were no on-study deaths or unexpected toxicities. CONCLUSION: The benefits of pemetrexed + carboplatin were maintained, and toxicity was manageable in both elderly subgroups. The favorable risk-benefit profile of pemetrexed + carboplatin makes it an appropriate first-line treatment option for elderly patients with advanced nonsquamous NSCLC.

[451]

TÍTULO / TITLE: - A randomized phase III trial of postoperative adjuvant therapy for completely resected stage IA-IIIa lung cancer using an antiangiogenetic agent: irsogladine maleate.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Minerva Chir. 2013 Dec;68(6):587-97.

AUTORES / AUTHORS: - Sagawa M; Shibuya J; Takahashi S; Endo C; Abiko M; Suzuki H; Matsumura Y; Sakuma T; Sato N; Deguchi H; Nakamura Y; Hasumi T; Kondo T

INSTITUCIÓN / INSTITUTION: - Japanese Northern East Area Thoracic Surgery Study Group (JNETS) - sagawam@kanazawa-med.ac.jp.

RESUMEN / SUMMARY: - Aim: Although angiogenesis plays an important role in the invasion and metastasis of solid tumors, very few anti-angiogenetic drugs have been developed. Reexamining the anti-angiogenetic effects of existing drugs such as Thalidomide is another possible strategy for drug discovery. Irsogladine maleate (IM) is a drug invented to treat gastric ulcers; however, several reports have shown that IM also exerts anti-angiogenetic effects in vitro, in vivo and in humans. In order to elucidate whether treatment with IM would improve the prognoses of patients with resected lung cancer, we conducted a randomized trial. Methods: In the control group, uracil-tegafur (250 mg/m²/day) was administered for two years to patients with resected stage IB - IIIa lung cancer, and no adjuvant therapy was administered to those with stage IA disease. In the study group, IM (4 mg/body/day) was additionally administered for two years. Results: No significant differences were observed in the major prognostic factors among 305 eligible patients between the study and control groups. Adverse effects were minimal. The overall survival of the patients in the study and control groups were not statistically different. When the analysis was stratified by regimen, among the patients with resected stage IA disease, disease-specific survival in the study group was slightly higher than that in the control group; however, the difference was not significant (p=0.07). Conclusion: Although it could not be proven that IM improves the prognoses of resected lung cancer patients, IM might have some effect on resected stage IA disease, and another trial should be conducted.

[452]

TÍTULO / TITLE: - "EXHALE": exercise as a strategy for rehabilitation in advanced stage lung cancer patients: a randomized clinical trial comparing the effects of 12 weeks supervised exercise intervention versus usual care for advanced stage lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 14;13:477. doi: 10.1186/1471-2407-13-477.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-477](#)

AUTORES / AUTHORS: - Quist M; Langer SW; Rorth M; Christensen KB; Adamsen L

INSTITUCIÓN / INSTITUTION: - The University Hospitals Centre for Health Research (UCSF), Copenhagen, Denmark. morten.quist@regionh.dk.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the leading cause of cancer death in North America and Western Europe. Patients with lung cancer in general have reduced physical capacity, functional capacity, poor quality of life and increased levels of anxiety and depression. Intervention studies indicate that physical training can address these issues. However, there is a lack of decisive evidence regarding the

effect of physical exercise in patients with advanced lung cancer. The aim of this study is to evaluate the effects of a twelve weeks, twice weekly program consisting of: supervised, structured training in a group of advanced lung cancer patients (cardiovascular and strength training, relaxation). METHODS/DESIGN: A randomized controlled trial will test the effects of the exercise intervention in 216 patients with advanced lung cancer (non-small cell lung cancer (NSCLC) stage IIIb - IV and small cell lung cancer (SCLC) extensive disease (ED)). Primary outcome is maximal oxygen uptake (VO₂peak). Secondary outcomes are muscle strength (1RM), functional capacity (6MWD), lung capacity (Fev₁) and patient reported outcome (including anxiety, depression (HADS) and quality of life (HRQOL)). DISCUSSION: The present randomized controlled study will provide data on the effectiveness of a supervised exercise intervention in patients receiving systemic therapy for advanced lung cancer. It is hoped that the intervention can improve physical capacity and functional level, during rehabilitation of cancer patients with complex symptom burden and help them to maintain independent function for as long as possible. TRIAL REGISTRATION: <http://ClinicalTrials.gov>, NCT01881906.

[453]

TÍTULO / TITLE: - Stigma among patients with lung cancer: a patient-reported measurement model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Psychooncology. 2013 Oct 3. doi: 10.1002/pon.3371.

●● [Enlace al texto completo \(gratis o de pago\) 1002/pon.3371](#)

AUTORES / AUTHORS: - Hamann HA; Ostroff JS; Marks EG; Gerber DE; Schiller JH; Lee SJ

INSTITUCIÓN / INSTITUTION: - Harold C. Simmons Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; Department of Psychiatry, UT Southwestern Medical Center, Dallas, TX, USA; Department of Clinical Sciences, UT Southwestern Medical Center, Dallas, TX, USA.

RESUMEN / SUMMARY: - BACKGROUND: Although stigma may have negative psychosocial and behavioral outcomes for patients with lung cancer, its measurement has been limited. A conceptual model of lung cancer stigma and a patient-reported outcome measure are needed to mitigate these sequelae. This study identified key stigma-related themes to provide a blueprint for item development through a thematic analysis of semi-structured interviews and focus groups with lung cancer patients. METHODS: Participants were recruited from two outpatient oncology clinics and included (i) 42 lung cancer patients who participated in individual interviews and (ii) 5 focus groups (inclusive of 23 new lung cancer patients). Never smokers, long-term quitters, recent quitters, and current smokers participated. Individual interviews facilitated theme development and a conceptual model of lung cancer stigma, whereas subsequent focus groups provided feedback on the conceptual model. Qualitative data analyses included iterative coding and validation with existing theory. RESULTS: Two main thematic elements emerged from interviews with lung cancer patients: perceived (felt) stigma and internalized (self) stigma. Discussions of perceived stigma were pervasive, whereas those of internalized stigma were more commonly endorsed among current and recently quit smokers. Participants also discussed maladaptive (e.g., decreased disclosure) and adaptive (e.g., increased advocacy) stigma-related consequences. CONCLUSIONS: Results indicate widespread acknowledgment of

perceived stigma among lung cancer patients but varying degrees of internalized stigma and associated consequences. Next steps for patient-reported outcome measure development are item consolidation, item development, expert input, and cognitive interviews before field testing and psychometric analysis. Future work should address stigma-related consequences and interventions for reducing lung cancer stigma. Copyright © 2013 John Wiley & Sons, Ltd.

[454]

TÍTULO / TITLE: - Survival outcomes in patients with advanced non-small cell lung cancer treated with erlotinib: expanded access programme data from Belgium (the TRUST study).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Cancer Care (Engl). 2013 Oct 24. doi: 10.1111/ecc.12146.

●● Enlace al texto completo (gratis o de pago) [1111/ecc.12146](#)

AUTORES / AUTHORS: - Van Meerbeeck J; Galdermans D; Bustin F; De Vos L; Lechat I; Abraham I

INSTITUCIÓN / INSTITUTION: - Thoracic Oncology, Ghent University Hospital, Gent, Belgium.

RESUMEN / SUMMARY: - Erlotinib has been shown to prolong progression-free (PFS) and overall survival (OS) in patients with advanced non-small cell lung cancer (NSCLC). We report here on effectiveness data on the subsample of 261 patients from 40 centres in Belgium involved in the TRUST study. Median age was 63 years. Most (69.0%) were male and current/former smokers (84.7%); with Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1 (74.3%), stage IV disease (75.1%) and adenocarcinoma by histology (54.0%). Erlotinib was administered mainly as second- (47.1%) or third-line treatment (48.3%). Response rate was 6.5%; disease control rate 58.3%. Median PFS was 2.2 months. Better PS ($P = 0.0384$), stage IIIB disease ($P = 0.0018$) and presence of rash ($P < 0.0001$) were associated with longer PFS. OS rates at 1, 2 and 3 years were 26.4%, 10.9% and 6.4% respectively. Median OS was 5.9 months. Female gender ($P = 0.007$), better PS ($P < 0.0001$), stage IIIB disease ($P = 0.0355$) and presence of rash ($P < 0.0001$) were associated with longer OS. The findings confirm the therapeutic benefit of erlotinib in a broad range of patients in a sample from a country with a historically high lung cancer morbidity and mortality burden. Several determinants of PFS and OS are identified.

[455]

TÍTULO / TITLE: - Treatment Receipt and Outcomes among Lung Cancer Patients with Depression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Oncol (R Coll Radiol). 2013 Sep 27. pii: S0936-6555(13)00336-1. doi: 10.1016/j.clon.2013.09.001.

●● Enlace al texto completo (gratis o de pago) [1016/j.clon.2013.09.001](#)

AUTORES / AUTHORS: - Sullivan DR; Ganzini L; Duckart JP; Lopez-Chavez A; Deffebach ME; Thielke SM; Slatore CG

INSTITUCIÓN / INSTITUTION: - Health Services Research & Development, Portland Veterans Affairs Medical Center, Portland, OR, USA; Division of Pulmonary & Critical Care Medicine, Department of Medicine, Oregon Health & Science University, Portland, OR, USA. Electronic address: sullivad@ohsu.edu.

RESUMEN / SUMMARY: - AIMS: Among lung cancer patients, depression has been associated with increased mortality, although the mechanisms are unknown. We evaluated the association of depression with mortality and receipt of cancer therapies among depressed veterans with lung cancer. MATERIALS AND METHODS: A retrospective, cohort study of lung cancer patients in the Veterans Affairs-Northwest Health Network from 1995 to 2010. Depression was defined by ICD-9 coding within 24 months before lung cancer diagnosis. Multivariable Cox proportional analysis and logistic regression were used. RESULTS: In total, 3869 lung cancer patients were evaluated; 14% had a diagnosis of depression. A diagnosis of depression was associated with increased mortality among all stage lung cancer patients (hazard ratio = 1.14, 95% confidence interval: 1.03-1.27, P = 0.01). Among early-stage (I and II) non-small cell lung cancer (NSCLC) patients, the hazard ratio was 1.37 (95% confidence interval: 1.12-1.68, P = 0.003). There was no association of depression diagnosis with surgery (odds ratio = 0.83, 95% confidence interval: 0.56-1.22, P = 0.34) among early-stage NSCLC patients. A depression diagnosis was not associated with mortality (hazard ratio = 1.02, 95% confidence interval: 0.89-1.16, P = 0.78) or chemotherapy (odds ratio = 1.07, 95% confidence interval: 0.83-1.39, P = 0.59) or radiation (odds ratio = 1.04, 95% confidence interval: 0.81-1.34, P = 0.75) receipt among advanced-stage (III and IV) NSCLC patients. Increased utilisation of health services for depression was associated with increased mortality among depressed patients. CONCLUSIONS: Depression is associated with increased mortality in lung cancer patients and this association is higher among those with increased measures of depression care utilisation. Differences in lung cancer treatment receipt are probably not responsible for the observed mortality differences between depressed and non-depressed patients. Clinicians should recognise the significant effect of depression on lung cancer survival.

[456]

TÍTULO / TITLE: - EGFR and KRAS mutations, and ALK fusions: current developments and personalized therapies for patients with advanced non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pharmacogenomics. 2013 Nov;14(14):1765-77. doi: 10.2217/pgs.13.177.

●● Enlace al texto completo (gratis o de pago) [2217/pgs.13.177](#)

AUTORES / AUTHORS: - de Mello RA; Madureira P; Carvalho LS; Araujo A; O'Brien M; Popat S

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Portuguese Oncology Institute, Rua Dr Antonio Bernardino de Almeida, 4200-072, Porto, Portugal.

RESUMEN / SUMMARY: - Personalized therapy has significantly developed in lung cancer treatment over recent years. VEGF and EGF play a major role in non-small-cell lung cancer (NSCLC) tumor angiogenesis and aggressiveness. EGFR mutation as well as KRAS and ALK rearrangements are important biomarkers in the field owing to potential targeted therapies involved in clinical practice: erlotinib, gefitinib, cetuximab

and crizotinib. More recently, regulation of tumor immunity through CTLA4 and PD1/L1 has emerged as a promising field in NSCLC management. This review will focus on the current and future biomarkers in the advanced NSCLC field and also address potential related targeted therapies for these patients.

[457]

TÍTULO / TITLE: - A Multicenter Blinded Study Evaluating EGFR and KRAS Mutation Testing Methods in the Clinical Non-Small Cell Lung Cancer Setting-IFCT/ERMETIC2 Project Part 1: Comparison of Testing Methods in 20 French Molecular Genetic National Cancer Institute Platforms.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Mol Diagn. 2013 Oct 30. pii: S1525-1578(13)00213-4. doi: 10.1016/j.jmoldx.2013.07.009.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.jmoldx.2013.07.009](#)

AUTORES / AUTHORS: - Beau-Faller M; Blons H; Domerg C; Gajda D; Richard N; Escande F; Solassol J; Denis MG; Cayre A; Nanni-Metellus I; Olschwang S; Lizard S; Piard F; Pretet JL; de Fraipont F; Bieche I; de Cremoux P; Rouquette I; Bringuier PP; Mosser J; Legrain M; Voegeli AC; Saulnier P; Morin F; Pignon JP; Zalcmán G; Cadranel J

INSTITUCIÓN / INSTITUTION: - Department of Molecular Biology, Strasbourg University Hospital, EA 3430, Strasbourg University, Strasbourg, France; Intergroupe Francophone de Cancerologie Thoracique, Paris, France. Electronic address: michele.faller@chru-strasbourg.fr.

RESUMEN / SUMMARY: - Epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors have limited use as first-line treatment for mutated EGFR metastatic non-small cell lung cancer. The French National Cancer Institute has installed molecular genetics platforms implementing EGFR and KRAS testing. However, there is considerable uncertainty as to which detection methods should be applied for routine diagnosis. This study aimed to compare the EGFR and KRAS genotyping methods developed by the IFCT/ERMETIC2 network platforms in two blind panels: 25 samples of serial dilutions of cell line DNA (20 centers) and 74 FFPE lung tumor samples (10 centers). The best threshold of mutation detection on cell lines was obtained using allele-specific amplification-based technologies. Nonamplifiable tissue samples were significantly less common when using alternative testing versus direct sequencing [15%; 95% confidence interval (CI), 14%-16% versus 40%; 95% CI, 39%-42%; $P < 0.001$]. Mutated cases increased from 42% (95% CI, 31%-54%) to 53% (95% CI, 41%-64%), with three supplementary EGFR mutations (p.G179A at exon 18 and p.L858R and p.L861Q at exon 21) and five supplementary KRAS mutations, when using alternative testing instead of direct sequencing. False-positive results were observed when using a PCR-based sizing assay, high-resolution melting, or pyrosequencing. Concordance analysis returned good kappa test scores for EGFR exon 19 and KRAS analysis when comparing sequencing with alternative methods and revealed no difference between alternative techniques themselves.

[458]

TÍTULO / TITLE: - Treatment of lung cancer in the elderly patient.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):802-9. doi: 10.1055/s-0033-1358560. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358560](#)

AUTORES / AUTHORS: - Weiss J; Langer C

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA.

RESUMEN / SUMMARY: - The median age of presentation with lung cancer is 71, making the elderly the dominant subgroup. Although some elderly patients are frail, others have great physiological reserve. Geriatric assessment can clarify the specific strengths and weaknesses of older patients, improving management. This assessment should, at the minimum, encompass performance status, comorbidity, medications, level of independence in activities of daily living and instrumental activities of daily living, cognitive assessment, nutrition assessment, and assessment of social support. The fit elderly with localized disease should be offered curative resection; video-assisted thoracic surgery may be preferred over thoracotomy. Fit septuagenarians with node positive or > 4 cm primary tumors should then be considered for adjuvant chemotherapy. For less fit patients, the data on stereotactic radiosurgery indicate that it presents a viable treatment option. Data on stage III disease are limited but suggest that chemoradiotherapy, particularly when the chemotherapy is administered on a weekly schedule, is feasible in fit older patients. For the older patients with metastatic cancer, abundant tissue should be obtained at diagnosis to allow for comprehensive molecular characterization with the hopes of rendering the patient eligible for targeted therapy. When such a targeted therapy is not available, there is duration of life and quality of life benefit to the administration of cytotoxic chemotherapy. The standard of care for older patients with Eastern Cooperative Oncology Group (ECOG) performance status 0 to 2 is a platinum-based doublet. Prospective data on second-line therapy after failure of first-line therapy are limited but suggest a benefit to treatment.

[459]

TÍTULO / TITLE: - Tumor necrosis factor-alpha gene promoter -308 and -238 polymorphisms in patients with lung cancer as a second primary tumor.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Sci Monit. 2013 Oct 11;19:846-51. doi: 10.12659/MSM.889554.

●● Enlace al texto completo (gratis o de pago) [12659/MSM.889554](#)

AUTORES / AUTHORS: - Flego V; Ristic S; Devic Pavlic S; Matanic Lender D; Bulat-Kardum L; Kapovic M; Radojic Badovinac A

INSTITUCIÓN / INSTITUTION: - Department of Pulmonology, Clinical Hospital Centre Rijeka, Rijeka, Croatia.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the most common second primary cancer. We investigated whether the TNF-alpha-308 and TNF-alpha-238 polymorphisms were associated with the susceptibility and severity of lung cancer as the second primary cancer (LC2). MATERIAL/METHODS: This study included 104 patients from the group LC2. The control subjects included 2 groups. The first control group (LC1) comprised 201 unrelated patients with lung cancer as a first primary cancer. The second control group (HC) comprised 230 healthy blood donors, matched

for sex and age to the study group. RESULTS: The frequencies of the TNF-alpha-238 polymorphism GG genotype and the G allele were higher in the LC2 group than in the LC1 group, but the differences did not reach significance ($p=0.054$ and $p=0.057$, respectively). Similar differences were found in the TNF-alpha-238 polymorphism GG genotype and G allele between the LC2 group and the HC group ($p=0.054$ and $p=0.057$, respectively). In terms of the different types of lung cancer, patients with a second primary NSCLC (non-small cell lung cancer) more frequently had TNF-alpha-238 polymorphism GG genotypes and G alleles than patients with a first primary NSCLC (the differences approached statistical significance: $p=0.060$, $p=0.064$, respectively). All (100%) patients of group LC2 ($n=104$) had the GG genotype and the G allele. GG genotype was exclusive and no A allele was found in group LC2. CONCLUSIONS: TNF-alpha-238 polymorphism GG genotype and the G allele could have a promotional effect on the development of NSCLC in the group of patients with LC2.

[460]

TÍTULO / TITLE: - Small molecule antagonist of the bone morphogenetic protein type I receptors suppresses growth and expression of Id1 and Id3 in lung cancer cells expressing Oct4 or nestin.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cancer. 2013 Oct 26;12(1):129.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1476-4598-12-129](#)

AUTORES / AUTHORS: - Langenfeld E; Deen M; Zachariah E; Langenfeld J

RESUMEN / SUMMARY: - BACKGROUND: Bone morphogenetic proteins (BMP) are embryonic morphogens that are aberrantly expressed in lung cancer. BMPs mediate cell fate decisions and self-renewal of stem cells, through transcription regulation of inhibitor of differentiation protein/DNA binding proteins (Id1-3). Inhibition of BMP signaling decreases growth and induces cell death of lung cancer cells lines by downregulating the expression of Id proteins. It is not known whether the BMP signaling cascade regulates growth and the expression of Id proteins of lung cancer cells expressing the stem cell markers Oct4 and/or nestin. METHODS: Lung cancer cells expressing Oct4 or nestin were isolated from lung cancer cell lines by stably transfecting the Oct4 promoter or nestin promoter expression vectors that induce expression of the green fluorescent protein reporter. RESULTS: Our studies suggest that lung cancer cells expressing Oct4 or nestin are different cell populations. Microarray and quantitative RT-PCR demonstrated that the expression of specific stem cell markers were different between isolated Oct4 and nestin cells. Both the Oct4 and nestin populations were more tumorigenic than controls but histologically they were quite different. The isolated Oct4 and nestin cells also responded differently to inhibition of BMP signaling. Blockade of BMP signaling with the BMP receptor antagonist DMH2 caused significant growth inhibition of both the Oct4 and nestin cell populations but only increased cell death in the nestin population. DMH2 also induced the expression of nestin in the Oct4 population but not in the nestin cells. We also show that BMP signaling is an important regulator of Id1 and Id3 in both the Oct4 and nestin cell populations. Furthermore, we show that NeuN is frequently expressed in NSCLC and provide evidence suggesting that Oct4 cells give rise to cancer cells expressing nestin and/or NeuN. CONCLUSION: These studies show that although biologically

different, BMP signaling is growth promoting in cancer cells expressing Oct4 or nestin. Inhibition of BMP signaling decreases expression of Id proteins and suppresses growth of cancer cells expressing Oct4 or Nestin. Small molecule antagonists of the BMP type I receptors represent potential novel drugs to target the population of cancer cells expressing stem cell markers.

[461]

TÍTULO / TITLE: - Home administration of maintenance pemetrexed for patients with advanced non-squamous non-small cell lung cancer: rationale, practicalities and phase II feasibility study design.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Health Qual Life Outcomes. 2013 Oct 3;11(1):163. doi: 10.1186/1477-7525-11-163.

●● Enlace al texto completo (gratis o de pago) [1186/1477-7525-11-163](#)

AUTORES / AUTHORS: - Lal R; Bourayou N; Hillerdal G; Nicolson M; Vikstrom A; Lorenzo M; D'yachkova Y; Barriga S; Visseren-Grul C

INSTITUCIÓN / INSTITUTION: - Eli Lilly, Neuilly sur Seine, France.

bourayou_nawel@lilly.com.

RESUMEN / SUMMARY: - BACKGROUND: Home-based care in oncology is mainly reserved for patients at the end of life. Regulations regarding home delivery of cytotoxics differ across Europe, with a notable lack of practice guidelines in most countries. This has led to a lack of data addressing the feasibility of home-based administration of cytotoxic chemotherapy. In advanced non-squamous non-small cell lung cancer, pemetrexed is approved as maintenance therapy after first-line chemotherapy. In this setting, patients have the potential to be treated long-term with maintenance therapy, which, in the absence of unacceptable toxicity, is continued until disease progression. The favourable safety profile of pemetrexed and the ease of its administration by 10-minute intravenous infusion every 3 weeks make this drug a suitable candidate for administration in a home setting. METHODS: Literature and regulations relevant to the home-based delivery of cytotoxic therapy were reviewed, and a phase II feasibility study of home administration of pemetrexed maintenance therapy was designed. At least 50 patients with advanced non-squamous non-small cell lung cancer, Eastern Cooperative Oncology Group performance status 0-1 and no progressive disease after four cycles of platinum-based first-line therapy are required to allow investigation of the feasibility of home-based administration of pemetrexed maintenance therapy (500 mg/m² every 3 weeks until progressive disease or unacceptable toxicity). Feasibility is being assessed as adherence to the home-based administration process (primary endpoint), patient safety, impact on patients' quality of life, patient and physician satisfaction with home care, and healthcare resource use and costs. Enrolment of patients from the UK and Sweden, where home-based care is relatively well developed, commenced in December 2011. DISCUSSION: This feasibility study addresses an important aspect of maintenance therapy, that is, patient comfort during protracted home-based chemotherapy. The study design requires unusual methodology and specific logistics to address outcomes relevant to the home-delivery approach. This article presents a study design that offers a novel and reproducible model for home-based chemotherapy, and provides an up-to-date

overview of the literature regarding this type of treatment. TRIAL REGISTRATION: ClinicalTrials.gov: NCT01473563.

[462]

TÍTULO / TITLE: - TLR4 signaling pathway in mouse Lewis lung cancer cells promotes the expression of TGF-beta1 and IL-10 and tumor cells migration.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Mater Eng. 2014;24(1):869-75. doi: 10.3233/BME-130879.

●● Enlace al texto completo (gratis o de pago) [3233/BME-130879](#)

AUTORES / AUTHORS: - Li C; Li H; Jiang K; Li J; Gai X

INSTITUCIÓN / INSTITUTION: - Department of Immunology, Basic Medical College of Beihua University, Jilin 132013, China.

RESUMEN / SUMMARY: - The signaling pathways that trigger tumor cell escape from immune surveillance are not understood completely. Toll-like receptors (TLRs) are considered to be expressed in both immune cells and tumor cells. By detecting TLRs expression in mouse Lewis lung cancer (LLC) before and after co-culture with mouse lymphocytes, the authors concluded that LLC cells constitutively expressed TLR1, TLR2, TLR3, TLR4, TLR5, TLR6 and TLR9. Meanwhile, TLR4 expression in LLC cells was the strongest after co-culture with mouse lymphocytes. To investigate the possible roles of TLR4 signaling pathway in LLC, the concentrations of TGF-beta1 and IL-10 protein in LLC cells supernatant were detected by ELISA, and the migration of LLC cells were detected by transwell assay after lipopolysaccharide (LPS) stimulation. TLR4 protein expression in LLC cells was also detected after LPS stimulation by FCM. The results indicated that both levels of TGF-beta1 and IL-10 protein were significantly increased after LPS stimulation and reached to a maximum at 24 h and 10 mug/mL of LPS. The migrated LLC cells with LPS stimulation were significantly increased and reached to a maximum at 10 mug/mL of LPS. The expression of TLR4 protein was significantly enhanced after 10 mug/mL of LPS stimulation. These results suggest that the activation of TLR4 signaling pathway in lung cancer cells may be involved in tumor escape and progression by promoting the expression of TGF-beta1 and IL-10 and tumor cells migration.

[463]

TÍTULO / TITLE: - Octanal-induced inflammatory responses in cells relevant for lung toxicity: Expression and release of cytokines in A549 human alveolar cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Hum Exp Toxicol. 2013 Oct 15.

●● Enlace al texto completo (gratis o de pago) [1177/0960327113506722](#)

AUTORES / AUTHORS: - Song MK; Lee HS; Choi HS; Shin CY; Kim YJ; Park YK; Ryu JC

INSTITUCIÓN / INSTITUTION: - 1Center for Integrated Risk Research, Cellular and Molecular Toxicology Laboratory, Korea Institute of Science and Technology, Cheongryang, Seoul, Korea.

RESUMEN / SUMMARY: - Inhalation is an important route of aldehyde exposure, and lung is one of the main targets of aldehyde toxicity. Octanal is distributed ubiquitously

in the environment and is a component of indoor air pollutants. We investigated whether octanal exposure enhances the inflammatory response in the human respiratory system by increasing the expression and release of cytokines and chemokines. The effect of octanal in transcriptomic modulation was assessed in the human alveolar epithelial cell line A549 using oligonucleotide arrays. We identified a set of genes differentially expressed upon octanal exposure that may be useful for monitoring octanal pulmonary toxicity. These genes were classified according to the Gene Ontology functional category and Kyoto Encyclopedia of Genes and Genomes analysis to explore the biological processes related to octanal-induced pulmonary toxicity. The results show that octanal affects the expression of several chemokines and inflammatory cytokines and increases the levels of interleukin 6 (IL-6) and IL-8 released. In conclusion, octanal exposure modulates the expression of cytokines and chemokines important in the development of lung injury and disease. This suggests that inflammation contributes to octanal-induced lung damage and that the inflammatory genes expressed should be studied in detail, thereby laying the groundwork for future biomonitoring studies.

[464]

TÍTULO / TITLE: - Serum Anti-CCNY Autoantibody Is an Independent Prognosis Indicator for Postoperative Patients with Early-Stage Nonsmall-Cell Lung Carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Dis Markers. 2013;35(5):317-25. doi: 10.1155/2013/935943. Epub 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [1155/2013/935943](#)

AUTORES / AUTHORS: - Ma L; Yue W; Teng Y; Zhang L; Gu M; Wang Y

INSTITUCIÓN / INSTITUTION: - Department of Cellular & Molecular Biology, Beijing TB and Thoracic Tumor Research Institution/Beijing Chest Hospital, Capital Medical University, 97 Beimeichang, Tongzhou, Beijing 101149, China.

RESUMEN / SUMMARY: - Cyclin Y (CCNY) is a novel cyclin and almost nothing is known about its role in human cancers. To investigate the clinical significance of serum anti-CCNY autoantibodies in nonsmall-cell lung carcinoma (NSCLC), the serum levels of CCNY protein in 264 patients with NSCLC, 103 patients with tuberculosis, and 89 healthy controls were analyzed by immunohistochemistry. The result shows that, compared with normal lung tissues, the NSCLC tissues contained higher levels of CCNY protein. The levels of anti-CCNY autoantibodies were higher in the sera of the patients with NSCLC than in the sera of the healthy controls ($P < 0.001$) or the patients with tuberculosis ($P = 0.027$). Moreover, in a Cox regression analysis, anti-CCNY autoantibody was an independent factor that predicted poor prognosis for postoperative patients with early-stage NSCLC ($P = 0.026$) as well as for those with distant metastasis ($P = 0.012$). Our data indicated that Anti-CCNY autoantibody may be useful as a latent tumor marker to facilitate diagnosis and may represent a novel prognostic indicator for patients with early stage NSCLC.

[465]

TÍTULO / TITLE: - FHIT, EGFR, and MSH2: Possible Etiopathologic, Prognostic, and Predictive Role in Non-Small Cell Lung Carcinoma in Egyptian Patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Appl Immunohistochem Mol Morphol. 2013 Oct 31.

●● Enlace al texto completo (gratis o de pago) [1097/PAI.0b013e3182988fa5](#)

AUTORES / AUTHORS: - Younes SF; Aiad HA; Asaad NY; Natkunam Y; Mokhtar NM

INSTITUCIÓN / INSTITUTION: - *Department of Pathology, Faculty of Medicine, Menoufia University, Menoufia double daggerDepartment of Pathology, National Cancer Institute, Cairo University, Giza, Egypt daggerDepartment of Pathology, School of Medicine, Stanford University, Stanford, CA.

RESUMEN / SUMMARY: - The high incidence and mortality of lung carcinoma in Egypt necessitates studying the factors that may be implicated in non-small cell lung carcinoma (NSCLC) pathogenesis and could affect patient management. The aim was to study FHIT, epidermal growth factor receptor (EGFR), and MSH2 protein expression in Egyptian patients with NSCLC. Immunohistochemical staining for FHIT, EGFR, and MSH2 was performed on 64 specimens from NSCLC patients and correlated with prognostic parameters, response to therapy, and overall survival. FHIT loss was observed in 64% of NSCLC patients and was significantly associated with SCC (P=0.003) and poor tumor grade (P=0.043). EGFR overexpression was observed in 47% of NSCLC patients and was significantly associated with SCC (P=0.002). MSH2 was reduced in 23.4% of NSCLC patients and was significantly associated with adenocarcinoma (P=0.024). In a univariate analysis, a significant relationship was seen between the poor overall survival in NSCLC patients and high T-stage (P=0.029), presence of metastasis (P=0.014), advanced-stage grouping (P=0.004), and FHIT loss (P=0.033). Further, FHIT loss was significantly related to disease progression in patients treated with chemotherapy (P=0.038). We conclude that all 3 markers play a role in the development of NSCLC in Egyptian patients. We suggest that FHIT loss be used as a predictor for progression in chemotherapy-treated NSCLC patients.

[466]

TÍTULO / TITLE: - Levels of circulating microparticles in lung cancer patients and possible prognostic value.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Dis Markers. 2013;35(5):301-10. doi: 10.1155/2013/715472. Epub 2013 Sep 15.

●● Enlace al texto completo (gratis o de pago) [1155/2013/715472](#)

AUTORES / AUTHORS: - Tseng CC; Wang CC; Chang HC; Tsai TH; Chang LT; Huang KT; Leu S; Yen CH; Liu SF; Chen CH; Yang CT; Yip HK; Lin MC

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Kaohsiung 83301, Taiwan.

RESUMEN / SUMMARY: - Background. Endothelial-derived microparticles (EDMPs) and platelet-derived microparticles (PDMPs) have been reported to be increasing in various diseases including malignant diseases. Here, we investigated whether these MPs may be useful biomarkers for predicting lung cancer (LC) disease status, cell type, or metastasis. Methods and Results. One hundred and thirty LC patients were prospectively enrolled into the study between April 2011 and February 2012. Flow cytometric analysis demonstrated that the circulating levels of platelet-derived activated MPs (PDac-MPs), platelet-derived apoptotic MPs (PDAp-MPs), endothelial-

derived activated MPs (EDAc-MPs), and endothelial-derived apoptotic MPs (EDAp-MPs) were significantly higher in LC patients than in 30 age- and gender-matched normal control subjects (all $P < 0.05$). Additionally, circulating level of PDAc-MPs was significantly lower ($P = 0.031$), whereas the circulating levels of the other three biomarkers did not differ (all $P > 0.1$) in early stage versus late stage LC patients. Furthermore, the circulating levels of the four types of MPs did not differ among patients with different disease statuses (i.e., disease controlled, disease progression, and disease without treatment, i.e., fresh case) (all $P > 0.2$) or between patients with or without LC metastasis (all $P > 0.5$). Moreover, only the circulating level of EDAp-MPs was significantly associated with the different cell types (i.e., squamous cell carcinoma, adenocarcinoma, and small cell carcinoma) of LC ($P = 0.045$). Conclusion. Circulating MP levels are significantly increased in LC patients as compared with normal subjects. Among the MPs, only an increased level of EDAp-MPs was significantly associated with different LC cell types.

[467]

TÍTULO / TITLE: - A Phase II Study of Pemetrexed in Chemotherapy-naive Elderly Patients Aged ≥ 75 years with Advanced Non-squamous Non-small-cell Lung Cancer (HANSHIN Oncology Group 003).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Jpn J Clin Oncol. 2013 Dec;43(12):1184-9. doi: 10.1093/jjco/hyt159. Epub 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [1093/jjco/hyt159](#)

AUTORES / AUTHORS: - Hattori Y; Iwasaku M; Satouchi M; Nishiyama A; Korogi Y; Otsuka K; Fujita S; Katakami N; Mori M; Nishino K; Morita S; Negoro S

INSTITUCIÓN / INSTITUTION: - *Department of Thoracic Oncology, Hyogo Cancer Center, 13-70 Kitaoji-cho, Akashi-shi, Hyogo 673-8558, Japan.

satouchi@hp.pref.hyogo.jp.

RESUMEN / SUMMARY: - OBJECTIVE: Pemetrexed has relatively mild toxicity and possibly can be administered long term to patients with non-small-cell lung cancer. We conducted a Phase II trial to evaluate the efficacy and safety of pemetrexed in chemotherapy-naive elderly patients with advanced non-squamous non-small-cell lung cancer. METHODS: In this multicenter Phase II trial, we recruited elderly patients with non-squamous non-small-cell lung cancer. Patients with previously untreated Stage IIIB or IV non-squamous non-small-cell lung cancer, ≥ 75 years, Eastern Cooperative Oncology Group performance status 0-1 and adequate organ functions were eligible. Patients received pemetrexed (500 mg/m²) intravenously on Day 1 every 3 weeks until disease progression. The primary endpoint was objective response rate.

RESULTS: Forty-seven patients were enrolled from August 2009 to July 2011, and 46 patients were eligible. The median age was 79 years (range 75-91 years), 57% were males, 37% had never smoked, 87% had adenocarcinoma, 74% had Stage IV and 33% had epidermal growth factor receptor tyrosine kinase-activating mutation. The median number of cycles was 4 (1-20). The objective response rate was 13.3% (95% confidence interval; 5.1-26.8%), the disease control rate was 66.7% (95% confidence interval 51.0-80.0%), the median progression-free survival was 4.9 months (95% confidence interval 3.0-6.1 months) and the median overall survival was 18.2 months (95% confidence interval 13.2-23.5 months). One Grade 5 infection (pneumonia) was

observed. CONCLUSIONS: This study did not meet the primary endpoint. Pemetrexed monotherapy is not recommended in chemotherapy-naive elderly patients aged ≥ 75 years with advanced non-squamous non-small-cell lung cancer.

[468]

TÍTULO / TITLE: - Lung cancer: let's try for prevention and cure.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med J Aust. 2013 Nov 18;199(10):639-40.

●● [Enlace al texto completo \(gratis o de pago\) 5694/mja13.11278](#) [pii]

AUTORES / AUTHORS: - Olver IN

INSTITUCIÓN / INSTITUTION: - Cancer Council Australia, Sydney, NSW, Australia.

ian.olver@cancer.org.au.

[469]

TÍTULO / TITLE: - Assessment of nutritional status in patients with primary lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tunis Med. 2013 Oct;91(10):600-4.

AUTORES / AUTHORS: - Chermiti Ben Abdallah F; Ben Said H; Chamkhi N; Ferchichi M; Chtourou A; Taktak S; Ben Kheder A

RESUMEN / SUMMARY: - Background: Lung cancer is the leading cause of cancer-related mortality worldwide. Malnutrition is a common problem among patients with cancer, affecting up to 85% of patients with certain cancers and represents a risk factor for poor prognosis. aim: evaluate nutritional status in patients with lung cancer before and during treatment using nutritional risk index. methods: it's a prospective study conducted in pneumology IV department in Abderahman Mami hospital, from January to May 2011. 30 male patients with a lung cancer were included. Nutritional status was assessed before and during treatment based on anthropometric measures, biological markers and nutritional risk index (NRI). results: Mean age of patients was 58 +/- 12 years, ranging from 19 to 82 years. 29 patients had non small cell lung cancer and one patient had small cell cancer. Malnutrition was noted in 14 patients (47%) before treatment according to the NRI. It was noted in 23 patients (77%) after three cycles of chemotherapy with severe malnutrition in 8 patients. Relationship between body mass index (BMI) and the NRI was linear, but NRI tends to evaluate more objectively risk of malnutrition in patients with lung cancer. Conclusion: Nutritional assessment in patient with lung cancer should be performed systematically, early and repeatedly. Several markers can be used such as BMI and NRI. Nutritional support will reduce morbidity and improve quality of life in patients with lung cancer.

[470]

TÍTULO / TITLE: - Reappraisal of Short-term Low-volume Hydration in Cisplatin-based Chemotherapy: Results of a Prospective Feasibility Study in Advanced Lung Cancer in the Okayama Lung Cancer Study Group Trial 1002.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Jpn J Clin Oncol. 2013 Nov;43(11):1115-23. doi: 10.1093/jjco/hyt128. Epub 2013 Sep 29.

●● Enlace al texto completo (gratis o de pago) [1093/jico/hyt128](#)

AUTORES / AUTHORS: - Hotta K; Takigawa N; Hisamoto-Sato A; Ichihara E; Kudo K; Uchida K; Yanase-Nakamura K; Tanaka H; Kato Y; Tabata M; Tanimoto M; Kiura K

INSTITUCIÓN / INSTITUTION: - *Department of Respiratory Medicine, Okayama University Hospital, 2-5-1 Shikata-cho, Kita-ku, Okayama, 700-8558, Japan.
khotta@md.okayama-u.ac.jp.

RESUMEN / SUMMARY: - OBJECTIVE: Cisplatin can induce severe renal toxicity. However, the degree and pattern of hydration that is most efficient at preventing it have scarcely been formally evaluated. We here performed a prospective feasibility study of cisplatin-based chemotherapy with short-term low-volume hydration in advanced lung cancer. METHODS: Chemo-naive patients with advanced lung cancer and reserving renal function who were suitable for cisplatin use (≥ 60 mg/m²) on Day 1) were eligible for this study. Two-and-a-half-liter hydration within approximately 4.5 h was investigated. The primary end point was the proportion of patients who underwent cisplatin-based chemotherapy without any Grade 2 or more renal toxicity in the first cycle. RESULTS: A total of 46 patients were registered, all of whom were evaluable for renal toxicity. The median baseline creatinine score was 0.70 mg/dl and the median cisplatin dose on Day 1 was 80 mg/m². In the first cycle, none of the patients developed Grade 2 or more creatinine toxicity, which met the primary endpoint. Four patients (9%) had Grade 1 toxicity, with a median worst creatinine score of 1.19 mg/dl, but it disappeared rapidly. Creatinine toxicity was influenced by several clinical factors, including the performance status. Ten patients (22%) needed extra hydration during the first cycle, mainly due to gastrointestinal toxicity. However, all 10 were able to undergo further cycles of treatment. Thirty-two (86%) of the 37 patients who were assumed to be able to undergo further treatment at our institute received it in an outpatient setting. CONCLUSIONS: This study demonstrated prospectively the feasibility of short-term low-volume hydration.

[471]

TÍTULO / TITLE: - Salvage Therapy beyond Targeted Therapy in Lung Adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):837-44. doi: 10.1055/s-0033-1358553. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358553](#)

AUTORES / AUTHORS: - Ho JC; Tam TC; Lam SK

INSTITUCIÓN / INSTITUTION: - Division of Respiratory Medicine, Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong SAR, China.

RESUMEN / SUMMARY: - Targeted therapy in lung adenocarcinoma has evolved rapidly over the last few years, especially in the application of epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) tyrosine kinase inhibitors (TKIs). Although many patients with advanced EGFR-mutated or ALK-rearranged lung adenocarcinoma do benefit from treatment with a specific TKI, the duration of disease control is notoriously short. Different patterns of disease progression have been recognized that may require distinct treatment approaches. Isolated progressive disease in the central nervous system requires additional local therapy (radiotherapy or

surgery) and an exploratory pulsatile regimen of TKI. Oligoprogressive disease at extracranial sites, representing resistant tumor clones in isolated lesions, requires local ablative therapy (radiotherapy or surgery) and continuation of the existing TKI. Multifocal progressive disease is a key therapeutic challenge to overcome because of widespread acquired resistance due to heterogeneous mechanisms. It is now known that EGFR TKI-acquired resistance is mostly (50-60%) due to a single resistance mutation in exon 20 (T790M) and occasionally (5-10%) due to c-MET amplification. On the contrary, the acquired resistance mechanisms to ALK TKI appear more diverse. Specific therapeutic strategies are being developed to overcome various acquired resistance mechanisms and may further improve the overall prognosis of advanced lung adenocarcinoma with actionable driver mutations.

[472]

TÍTULO / TITLE: - Gemcitabine and vinorelbine as second-line or beyond treatment in patients with malignant pleural mesothelioma pretreated with platinum plus pemetrexed chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Oncol. 2013 Oct 26.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s10147-013-0619-5](#)

AUTORES / AUTHORS: - Toyokawa G; Takenoyama M; Hirai F; Toyozawa R; Inamasu E; Kojo M; Morodomi Y; Shiraishi Y; Takenaka T; Yamaguchi M; Shimokawa M; Seto T; Ichinose Y

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology, National Kyushu Cancer Center, 3-1-1 Notame, Minami-ku, Fukuoka, 811-1395, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Malignant pleural mesothelioma (MPM) is an aggressive neoplasm that responds poorly to chemotherapy. Although treatment with pemetrexed in combination with cisplatin serves as first-line chemotherapy for MPM, the optimal second-line and beyond therapy has not yet been fully examined. METHODS: Between March 2008 and October 2011, 17 consecutive Japanese patients pretreated with at least one regimen of platinum plus pemetrexed chemotherapy received gemcitabine and vinorelbine. Responses, survival time, and toxicity were retrospectively evaluated. RESULTS: Response [partial response (PR) + complete response (CR)] and disease control [stable disease (SD) + PR + CR] rates were 18 and 82 %, respectively. The median progression-free survival (PFS) after combination chemotherapy was 6.0 months, whereas the median overall survival (OS) was 11.2 months. Grade 3 or 4 neutropenia and anemia were observed in 41 and 29 % of patients, respectively, and one patient experienced febrile neutropenia. Grade 3 or 4 nonhematologic toxicities included constipation (6 %) and phlebitis (6 %). CONCLUSION: Combination chemotherapy using gemcitabine with vinorelbine was shown to have moderate activity in Japanese MPM patients pretreated with platinum plus pemetrexed chemotherapy. A further multicenter phase II trial is warranted to confirm the efficacy and safety of this combination treatment.

[473]

TÍTULO / TITLE: - Lung cancer in women: differences in epidemiology, biology, histology, and treatment outcomes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):792-801. doi: 10.1055/s-0033-1358550. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358550](#)

AUTORES / AUTHORS: - Rivera MP

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

RESUMEN / SUMMARY: - Lung cancer is a major health problem for both men and women, not only because of the high incidence rate but, more alarming, the high mortality rate. The prevalence of lung cancer in women has been increasing worldwide. In the United States, lung cancer is currently the leading cause of cancer death in women, and this may well be the case in European countries in just a few years. The most important risk factors for the development of lung cancer in both men and women is cigarette smoking. Smoking among women has increased significantly since the 1960s, and, unfortunately, the risk of death from cigarette smoking continues to increase among women. Although epidemiological data remain controversial regarding the increased risk of lung cancer from tobacco exposure in women, there is little controversy surrounding the fact that the biology of lung cancer differs between the sexes. This paper summarizes the explanations for the sex differences in lung cancer, including differences in molecular abnormalities, growth factor receptors, hormonal influences, cytochrome P-450 enzymes, and DNA repair capacity, as well as differences in the histology of lung cancer and treatment outcomes in women.

[474]

TÍTULO / TITLE: - Antiangiogenic agents and chemotherapy in advanced non-small cell lung cancer: a clinical perspective.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Expert Rev Anticancer Ther. 2013 Oct;13(10):1193-206. doi: 10.1586/14737140.2013.845093.

●● Enlace al texto completo (gratis o de pago) [1586/14737140.2013.845093](#)

AUTORES / AUTHORS: - Girard N

INSTITUCIÓN / INSTITUTION: - Department of Respiratory medicine, Thoracic Oncology, Louis Pradel Hospital, Hospices Civils de Lyon, Claude Bernard University, Lyon, France +33 47 235 7652 +33 47 235 7653 nicolas.girard@chu-lyon.fr.

RESUMEN / SUMMARY: - Antiangiogenic agents represent a major advance in the management of patients with advanced non-small-cell lung cancer receiving chemotherapy. While bevacizumab has been available for first-line treatment, other drugs, such as nintedanib, recently demonstrated significant activity in the second-line setting. This review covers most recent results with antiangiogenic treatments, focusing on data relevant for routine clinical practice; recent results potentially leading to new agents approval are discussed. While biomarkers are still awaited to better-select patients for these approaches, the development of antiangiogenic agents represent a model for implementation in thoracic oncology, while highlighting the promise of a better outcome for patients with advanced lung cancer.

[475]

TÍTULO / TITLE: - Genetic amplification of in gastric and lung cancer and its potential as a novel therapeutic target.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Biol Ther. 2013 Nov 19;15(1).

AUTORES / AUTHORS: - Li J; Han S; Qian Z; Su X; Fan S; Fu J; Jie Liu Y; Yin X; Gao Z; Zhang J; Yu DH; Ji Q

INSTITUCIÓN / INSTITUTION: - Innovation Center China; Asia & Emerging Market iMed; AstraZeneca Innovation Medicines and Early Development; Shanghai, PR China.

RESUMEN / SUMMARY: - Protein phosphatase methylesterase 1 (PPME1) is a protein phosphatase 2A (PP2A)-specific methyl esterase that negatively regulates PP2A through demethylation at its carboxy terminal leucine 309 residue. Emerging evidence shows that the upregulation of PPME1 is associated with poor prognosis in glioblastoma patients. By performing an array comparative genomic hybridization analysis to detect copy number changes, we have been the first to identify PPME1 gene amplification in 3.8% (5/131) of Chinese gastric cancer (GC) samples and 3.1% (4/124) of Chinese lung cancer (LC) samples. This PPME1 gene amplification was confirmed by fluorescence in situ hybridization analysis and is correlated with elevated protein expression, as determined by immunohistochemistry analysis. To further investigate the role of PPME1 amplification in tumor growth, short-hairpin RNA-mediated gene silencing was employed. A knockdown of PPME1 expression resulted in a significant inhibition of cell proliferation and induction of cell apoptosis in PPME1-amplified human cancer cell lines SNU668 (GC) and Oka-C1 (LC), but not in nonamplified MKN1 (GC) and HCC95 (LC) cells. The PPME1 gene knockdown also led to a consistent decrease in PP2A demethylation at leucine 309, which was correlated with the downregulation of cellular Erk and AKT phosphorylation. Our data indicate that PPME1 could be an attractive therapeutic target for a subset of GCs and LCs.

[476]

TÍTULO / TITLE: - Tailored therapy in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Can Respir J. 2013 Sep-Oct;20(5):367-8.

AUTORES / AUTHORS: - Rakovich G; Tremblay L

RESUMEN / SUMMARY: - Historically, all non-small cell lung cancers were essentially grouped together and considered to be a single disease. However, it is now recognized that non-small cell lung cancer actually comprises a genetically diverse group of tumours. This, in turn, affords a new opportunity for the development of effective treatments tailored to individual tumours and patients. Advances in molecular biology have made possible the development of drugs against specific molecular targets on cancer cells, most notably the tyrosine kinase inhibitors. The relevant literature and current practice guidelines are discussed. In addition, other related areas of active investigation, including tumour vaccines and pharmacogenetics, are briefly reviewed.

[477]

TÍTULO / TITLE: - Should we screen for lung cancer in Australia?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med J Aust. 2013 Nov 4;199(9):585-6.

●● Enlace al texto completo (gratis o de pago) [5694/mja13.11110](#) [pii]

AUTORES / AUTHORS: - Marshall HM; Fong KM; Bowman RV

INSTITUCIÓN / INSTITUTION: - University of Queensland Thoracic Research Centre, Brisbane, QLD, Australia. henry_marshall@health.qld.gov.au.

[478]

TÍTULO / TITLE: - Lung cancer in Victoria: are we making progress?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med J Aust. 2013 Nov 18;199(10):674-9.

●● Enlace al texto completo (gratis o de pago) [5694/mja13.10331](#) [pii]

AUTORES / AUTHORS: - Mitchell PL; Thursfield VJ; Ball DL; Richardson GE; Irving LB; Torn-Broers Y; Giles GG; Wright GM

INSTITUCIÓN / INSTITUTION: - Olivia Newton-John Cancer and Wellness Centre, Austin Health, Melbourne, VIC, Australia. paul.mitchell@austin.org.au.

RESUMEN / SUMMARY: - OBJECTIVES: To identify areas to improve patient management in lung cancer, which remains the greatest cause of death from cancer in Australia. DESIGN AND SETTING: Retrospective survey of all cases of lung cancer reported to the Victorian Cancer Registry from 1 January to 30 June 2003 and followed up for 5 years. MAIN OUTCOME MEASURES: Patient and disease characteristics, investigations, staging, treatment, cause of death, survival. RESULTS: 841 patients were included. Smoking data were available for 799, of whom 63 (7.9%) had never smoked. Of 655 non-small cell lung cancer (NSCLC) cases, 198 (30.2%) were treated with curative intent, 125 (19.1%) by surgery and 73 (11.1%) by radiotherapy with or without chemotherapy. Only 7 (6.9%) of surgical patients with complete R0 resection had adjuvant chemotherapy. Of 101 small cell lung cancer (SCLC) cases, a third had limited stage disease which was mostly treated with curative intent by chemotherapy with or without radiotherapy. Patients whose cases were discussed at a multidisciplinary meeting (MDM) were significantly more likely to receive anticancer treatment and had longer survival; on multivariate analysis, MDM discussion was an independent prognostic factor. Compared with a similar survey 10 years earlier, the median age of patients diagnosed with lung cancer had increased by almost 3 years, the proportion of affected men decreased and adenocarcinoma was more frequent, while 10% of patients continued to have no pathologically confirmed diagnosis and 26% continued to receive no anticancer treatment. The number of patients with NSCLC who went on to a definitive surgical procedure fell with no detriment to survival, which likely reflected better staging with the introduction of positron emission tomography scanning. CONCLUSIONS: Opportunities to improve patient management included increasing the proportion with a pathologically confirmed diagnosis and greater use of postsurgical adjuvant chemotherapy. A high proportion of patients received no treatment, with underuse of chemotherapy and radiotherapy. Critically, the low rate of case discussions at MDMs needs to increase. However, effective strategies are required to identify cases early, as over two-thirds currently present with incurable disease.

[479]

TÍTULO / TITLE: - Should we screen for lung cancer in Australia?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med J Aust. 2013 Nov 4;199(9):586.

●● Enlace al texto completo (gratis o de pago) [5694/mja13.11158](#) [pii]

AUTORES / AUTHORS: - Hew M; Stirling RG; Abramson MJ

INSTITUCIÓN / INSTITUTION: - The Alfred, Melbourne, VIC, Australia.

m.hew@alfred.org.au.

[480]

TÍTULO / TITLE: - Should we screen for lung cancer in Australia?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med J Aust. 2013 Nov 4;199(9):586.

●● Enlace al texto completo (gratis o de pago) [5694/mja13.11144](#) [pii]

AUTORES / AUTHORS: - Mitchell PL; John T

INSTITUCIÓN / INSTITUTION: - North-Eastern Melbourne Integrated Cancer Service, Austin Health, Melbourne, VIC, Australia. paul.mitchell@austin.org.au.

[481]

TÍTULO / TITLE: - Cathepsin B as a potential prognostic and therapeutic marker for human lung squamous cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cancer. 2013 Oct 20;12(1):125.

●● Enlace al texto completo (gratis o de pago) [1186/1476-4598-12-125](#)

AUTORES / AUTHORS: - Gong F; Peng X; Luo C; Shen G; Zhao C; Zou L; Li L; Sang Y; Zhao Y; Zhao X

RESUMEN / SUMMARY: - BACKGROUND: The lung squamous cell carcinoma survival rate is very poor despite multimodal treatment. It is urgent to discover novel candidate biomarkers for prognostic assessment and therapeutic targets to lung squamous cell carcinoma (SCC). RESULTS: Herein a two-dimensional gel electrophoresis and ESI-Q-TOF MS/MS-based proteomic approach was used to identify differentially expressed proteins between lung SCC and adjacent normal tissues. 31 proteins with significant alteration were identified. These proteins were mainly involved in metabolism, calcium ion binding, signal transduction and so on. Cathepsin B (CTSB) was one of the most significantly altered proteins and was confirmed by western blotting. Immunohistochemistry showed the correlation between higher CTSB expression and lower survival rate. No statistically significant difference between CTSB-shRNA treated group and the controls was observed in tumor volume, tumor weight, proliferation and apoptosis. However, the CTSB-shRNA significantly inhibited tumor metastases and prolonged survival in LL/2 metastatic model. Moreover, CTSB, Shh and Ptch were up-regulated in patients with metastatic lung SCC, suggesting that hedgehog signaling might be activated in metastatic lung SCC which could affect the expression of CTSB that influence the invasive activity of lung SCC. CONCLUSIONS: These data suggested that CTSB might serve as a prognostic and therapeutic marker for lung SCC.

[482]

TÍTULO / TITLE: - Comparative evaluation of CT-based and respiratory-gated PET/CT-based planning target volume (PTV) in the definition of radiation treatment planning in lung cancer: preliminary results.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Nucl Med Mol Imaging. 2013 Nov 1.

●● Enlace al texto completo (gratis o de pago) [1007/s00259-013-2594-5](#)

AUTORES / AUTHORS: - Guerra L; Meregalli S; Zorz A; Niespolo R; De Ponti E; Elisei F; Morzenti S; Brenna S; Crespi A; Gardani G; Messa C

INSTITUCIÓN / INSTITUTION: - Nuclear Medicine, San Gerardo Hospital, Monza, Italy, l.querra@hsgerardo.org.

RESUMEN / SUMMARY: - PURPOSE: The aim of this study was to compare planning target volume (PTV) defined on respiratory-gated positron emission tomography (PET)/CT (RG-PET/CT) to PTV based on ungated free-breathing CT and to evaluate if RG-PET/CT can be useful to personalize PTV by tailoring the target volume to the lesion motion in lung cancer patients. METHODS: Thirteen lung cancer patients (six men, mean age 70.0 years, 1 small cell lung cancer, 12 non-small cell lung cancer) who were candidates for radiation therapy were prospectively enrolled and submitted to RG-PET/CT. Ungated free-breathing CT images obtained during a PET/CT study were visually contoured by the radiation oncologist to define standard clinical target volumes (CTV1). Standard PTV (PTV1) resulted from CTV1 with the addition of 1-cm expansion of margins in all directions. RG-PET/CT images were contoured by the nuclear medicine physician and radiation oncologist according to a standardized institutional protocol for contouring gated images. Each CT and PET image of the patient's respiratory cycle phases was contoured to obtain the RG-CT-based CTV (CTV2) and the RG-PET/CT-based CTV (CTV3), respectively. RG-CT-based and RG-PET/CT-based PTV (PTV2 and PTV3, respectively) were then derived from gated CTVs with a margin expansion of 7-8 mm in head to feet direction and 5 mm in anterior to posterior and left to right direction. The portions of gated PTV2 and PTV3 geometrically not encompassed in PTV1 (PTV2 out PTV1 and PTV3 out PTV1) were also calculated. RESULTS: Mean +/- SD CTV1, CTV2 and CTV3 were 30.5 +/- 33.2, 43.1 +/- 43.2 and 44.8 +/- 45.2 ml, respectively. CTV1 was significantly smaller than CTV2 and CTV3 (p = 0.017 and 0.009 with Student's t test, respectively). No significant difference was found between CTV2 and CTV3. Mean +/- SD of PTV1, PTV2 and PTV3 were 118.7 +/- 94.1, 93.8 +/- 80.2 and 97.0 +/- 83.9 ml, respectively. PTV1 was significantly larger than PTV2 and PTV3 (p = 0.038 and 0.043 with Student's t test, respectively). No significant difference was found between PTV2 and PTV3. Mean +/- SD values of PTV2 out PTV1 and PTV3 out PTV1 were 12.8 +/- 25.4 and 14.3 +/- 25.9 ml, respectively. The percentage values of PTV2 out PTV1 and PTV3 out PTV1 were not lower than 10 % of PTV1 in 6/13 cases (46.2 %) and than 20 % in 3/13 cases (23.1 %). CONCLUSION: Our preliminary data showed that RG-PET/CT in lung cancer can affect not only the volume of PTV but also its shape, as demonstrated by the assessment of gated PTVs outside standard PTV. The use of a gating technique is thus crucial for better delineating PTV by tailoring the target volume to the lesion motion in lung cancer patients.

[483]

TÍTULO / TITLE: - Integrated Chinese-western therapy versus western therapy alone on survival rate in patients with non-small-cell lung cancer at middle-late stage.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Tradit Chin Med. 2013 Aug;33(4):433-8.

AUTORES / AUTHORS: - Lin G; Li Y; Chen S; Jiang H

INSTITUCIÓN / INSTITUTION: - Xiangya Hospital, Xiangya Medical College Zhongnan University, Changsha 410008, China. lingq1977@126.com

RESUMEN / SUMMARY: - OBJECTIVE: To compare the effects of integrated Chinese-Western therapy versus Western therapy alone on the survival rate of patients with non-small-cell lung cancer (NSCLC) at middle-late stage and to evaluate prognostic factors. METHODS: We selected 98 inpatients with middle-late stage NSCLC diagnosed from March 2009 to March 2011 and randomly divided them into two groups, with 49 cases in each group, and the clinical data were analyzed retrospectively. The control group was treated by the combined methods of Western Medicine, including chemotherapy, supportive treatment and symptomatic treatment. The observation group was treated by injection and prescriptions of Chinese medicine based on Traditional Chinese Medicine syndrome differentiation and by the same combined methods of western treatment used in the control group. After treatment, the survival rates of the patients were compared by the stage of cancer and evaluation of 24 prognostic factors analyzed by a Cox regression model, and the clinical data were statistically analyzed. RESULTS: The survival rates of all patients were over 90.0% at 1 and 3 months after treatment with no significant differences between the two groups ($P > 0.05$); In the observation group the survival rates at 6 months and 1 year were 93.4% and 42.8%, respectively, being superior to 85.6% and 18.3% in the control group ($P < 0.05$). The median survival time in the observation group was superior to the control group ($P < 0.05$); The effects of 24 prognostic factors were significantly better in the observation group than in the control group ($P < 0.05$). CONCLUSION: Integrated Chinese-western therapy can significantly improve the survival rate in patients with middle-late stage NSCLC and improve prognostic factors compared with western therapy alone.

[484]

TÍTULO / TITLE: - NOB1 in Non-small-cell Lung Cancer: Expression Profile and Clinical Significance.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pathol Oncol Res. 2013 Nov 23.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s12253-013-9717-y](#)

AUTORES / AUTHORS: - Liu K; Gu MM; Chen HL; You QS

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, Affiliated Hospital of Nantong University, Xi Si Road 20#, Nantong City, Jiangsu Province, 226001, People's Republic of China.

RESUMEN / SUMMARY: - Nin one binding (NOB1) gene has been reported up-regulated in several types of cancer. The aim of this study was to investigate the expression profile of NOB1 in non-small-cell lung cancer (NSCLC) and assess the clinical significance. qRT-PCR was used in the detection of NOB1 mRNA expression both in NSCLC tissue and in adjacent normal lung tissue. Western blot analysis and immunohistochemistry were used in the detection of NOB1 protein expression. The

clinicopathological implications of NOB1 were analyzed statistically. It was confirmed by RT-qPCR that expression of NOB1 mRNA in NSCLC cells was higher than in human lung cells ($P < 0.05$), and NOB1 mRNA was also over-expressed in NSCLC tissue when compared with adjacent tissue and normal lung tissue ($P < 0.05$). Western blot analysis showed that NOB1 protein was significantly increased in NSCLC cell lines compared with human lung cell line. Western blot analysis and immunohistochemistry showed that NOB1 protein was significantly increased in NSCLC tissue compared with adjacent tissue and normal lung tissue ($P < 0.05$). There were significant associations between NOB1 expression and TNM stage, lymph node metastasis, and histopathological grade ($P < 0.05$), but not gender, age, smoke, or tumor diameter ($P > 0.05$). Our results suggest that enhanced expression of NOB1 gene plays an important role in the occurrence and development of NSCLC. NOB1 may be a potential therapeutic target in NSCLC.

[485]

TÍTULO / TITLE: - Disparities in mental health outcomes among lung cancer survivors associated with ruralness of residence.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Psychooncology. 2013 Nov 11. doi: 10.1002/pon.3440.

●● [Enlace al texto completo \(gratis o de pago\) 1002/pon.3440](#)

AUTORES / AUTHORS: - Andrykowski MA; Steffens RF; Bush HM; Tucker TC

INSTITUCIÓN / INSTITUTION: - Department of Behavioral Science, University of Kentucky College of Medicine, Lexington, KY, USA.

RESUMEN / SUMMARY: - **OBJECTIVE:** Healthy People 2020 identifies elimination of health disparities as a key aim. Rural residence is associated with disparities in cancer screening, physical morbidity, and survival. The present study aimed to identify potential disparities in mental health (MH) outcomes (e.g., anxiety and depression symptoms, distress) in lung cancer (LC) survivors associated with ruralness of residence. **METHODS:** Lung cancer survivors (LC group; $n = 193$; mean age = 63.1 years; mean time since diagnosis = 15.6 months) were recruited from the population-based SEER Kentucky Cancer Registry. LC survivors completed a telephone interview and questionnaire assessing MH outcomes. U.S. Department of Agriculture Rural-Urban Continuum Codes were used to identify Rural ($n = 117$) and Urban ($n = 76$) LC survivors. A healthy comparison (HC) group was recruited ($n = 152$) and completed a questionnaire assessing MH outcomes. **RESULTS:** Across six MH indices, Rural LC survivors reported poorer MH relative to Urban LC survivors with a mean effect size (ES) of 0.43 SD in unadjusted analyses and 0.29 SD in analyses adjusted for education and physical comorbidity. Comparison of the LC and HC groups revealed significant Ruralness x Group interactions for five of six MH indices. The Rural LC group reported poorer MH than the Rural HC group with a mean ES of 0.51 SD. The MH of Urban LC and HC groups did not differ (mean ES = 0.00 SD). **CONCLUSIONS:** Rural residence is a risk factor for poorer MH outcomes for LC survivors. The MH of Rural LC survivors may be more negatively impacted by cancer diagnosis and treatment than the MH of Urban LC survivors. Copyright © 2013 John Wiley & Sons, Ltd.

[486]

TÍTULO / TITLE: - Dimethylaminoparthenolide (DMAPT), A Water Soluble Parthenolide, Suppresses Lung Tumorigenesis in Vitro and in Vivo and Downregulates the STAT3 Signaling Pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Cancer Drug Targets. 2013 Nov 4.

AUTORES / AUTHORS: - Song JM; Qian X; Upadhyayya P; Hong KH; Kassie F

INSTITUCIÓN / INSTITUTION: - Masonic Cancer Center, 2Institue for Therapeutics Discovery and Development, 3College of Veterinary Medicine, University of Minnesota, Minnesota, USA. kassi012@umn.edu.

RESUMEN / SUMMARY: - Lung cancer is the most fatal cancer and development of agents that suppress lung tumorigenesis is a crucial strategy to reduce mortality related to this disease. In the present study, we showed, using an in vitro model of lung tumorigenesis, that dimethylamino-parthenolide (DMAPT), a water soluble parthenolide analog, selectively inhibited the growth and survival of premalignant and malignant cells with minimal effects on parental immortalized cells. These effects were paralleled by suppression of pSTAT3, Mcl-1 and cyclin D1 and PARP cleavage, suggesting that that the anti-proliferative and apoptotic effects of DMAPT could be mediated, at least in part, via suppression of the STAT3 signaling pathway. Moreover, in tobacco smoke carcinogen-induced lung tumor bioassay in mice, intranasal instillation of low doses of DMAPT significantly reduced the overall lung tumor multiplicity by 39%. Interestingly, the drug was specifically effective (62% reduction) against bigger lung tumors (> 2 mm), which have a higher potential to develop into lung adenocarcinoma. Western immunoblotting analyses of mouse lung tissues indicated significantly lower level of pSTAT3 and Mcl-1 in the carcinogen plus DMAPT group relative to the group treated with the carcinogen only. Given the evidence that STAT3 is activated in more than half of lung cancers and it regulates genes involved in cell proliferation, survival and angiogenesis, DMAPT is a promising agent for lung cancer chemoprevention in subjects who are at high risk of developing this devastating disease.

[487]

TÍTULO / TITLE: - miR-137 impairs the proliferative and migratory capacity of human non-small cell lung cancer cells by targeting paxillin.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Hum Cell. 2013 Nov 17.

●● Enlace al texto completo (gratis o de pago) [1007/s13577-013-0085-4](#)

AUTORES / AUTHORS: - Bi Y; Han Y; Bi H; Gao F; Wang X

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, The Affiliated Hospital of Binzhou Medical University, Binzhou, 256603, Shandong, People's Republic of China.

RESUMEN / SUMMARY: - Human lung cancer is the leading cause of cancer motility worldwide, with nearly 1.4 million deaths each year, among which non-small cell lung cancer (NSCLC) accounts for almost 85 % of this disease. The discovery of microRNAs (miRNAs) provides a new avenue for NSCLC diagnostic and treatment regimens. Currently, a large number of miRNAs have been reported to be associated with the progression of NSCLC, among which serum miR-137 has been examined to be down-regulated in NSCLC patients. However, the function of miR-137 on NSCLC

cells migration and invasion and the relative mechanisms were less known. Here, we found that ectopic expression of miR-137 could inhibit cell proliferation, induce cell apoptosis, and suppress cell migration and invasion in NSCLC cell line A549. Moreover, we found that paxillin (PXN) was a target gene of miR-137 in NSCLC cells and restored expression of PXN abolished the miR-137-mediated suppression of cell migration and invasion. Taken together, our results showed that miR-137 acted as a tumor suppressor in NSCLC by targeting PXN, and it may provide novel diagnostic and therapeutic options for human NSCLC clinical operation in future.

[488]

TÍTULO / TITLE: - Subtoxic and toxic concentrations of benzene and toluene induce Nrf2-mediated antioxidative stress response and affect the central carbon metabolism in lung epithelial cells A549.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Proteomics. 2013 Nov;13(21):3211-21. doi: 10.1002/pmic.201300126. Epub 2013 Oct 16.

●● Enlace al texto completo (gratis o de pago) [1002/pmic.201300126](#)

AUTORES / AUTHORS: - Murugesan K; Baumann S; Wissenbach DK; Kliemt S; Kalkhof S; Otto W; Mogel I; Kohajda T; von Bergen M; Tomm JM

INSTITUCIÓN / INSTITUTION: - Helmholtz Centre for Environmental Research, Department of Proteomics, Leipzig, Germany.

RESUMEN / SUMMARY: - Since people in industrialized countries spend most of their time indoors, the effects of indoor contaminants such as volatile organic compounds become more and more relevant. Benzene and toluene are among the most abundant compounds in the highly heterogeneous group of indoor volatile organic compounds. In order to understand their effects on lung epithelial cells (A549) representing lung's first line of defense, we chose a global proteome and a targeted metabolome approach in order to detect adverse outcome pathways caused by exposure to benzene and toluene. Using a DIGE approach, 93 of 469 detected protein spots were found to be differentially expressed after exposure to benzene, and 79 of these spots were identified by MS. Pathway analysis revealed an enrichment of proteins involved in Nrf2-mediated and oxidative stress response glycolysis/gluconeogenesis. The occurrence of oxidative stress at nonacute toxic concentrations of benzene and toluene was confirmed by the upregulation of the stress related proteins NQO1 and SOD1. The changes in metabolism were validated by ion chromatography MS/MS analysis revealing significant changes of glucose-6-phosphate, fructose-6-phosphate, 3-phosphoglycerate, and NADPH. The molecular alterations identified as a result of benzene and toluene exposure demonstrate the detrimental effect of nonacute toxic concentrations on lung epithelial cells. The data provided here will allow for a targeted validation in in vivo models.

[489]

TÍTULO / TITLE: - IGFBP2/FAK Pathway Is Causally Associated with Dasatinib Resistance in Non-Small Cell Lung Cancer Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 22.

- Enlace al texto completo (gratuito o de pago) [1158/1535-7163.MCT-13-0233](#)

AUTORES / AUTHORS: - Lu H; Wang L; Gao W; Meng J; Dai B; Wu S; Minna J; Roth JA; Hofstetter WL; Swisher SG; Fang B

INSTITUCIÓN / INSTITUTION: - Authors' Affiliations: 1Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, Texas; 2The 8th Department of Internal Medicine, The Third Affiliated Hospital of Harbin Medical University, Harbin, China; and 3Hamon Center for Therapeutic Oncology, The Harold C. Simmons Comprehensive Cancer Center, University of Texas Southwestern Medical Center, Dallas, Texas.

RESUMEN / SUMMARY: - Insulin-like growth factor (IGF)-binding protein-2 (IGFBP2) expression is increased in various types of cancers, including in a subset of patients with lung cancer. Because IGFBP2 is involved in signal transduction of some critical cancer-related pathways, we analyzed the association between IGFBP2 and response to pathway-targeted agents in seven human non-small cell lung cancer (NSCLC) cell lines. Western blot analysis and ELISA showed that four of the seven NSCLC cell lines analyzed expressed high levels of IGFBP2, whereas the remaining three had barely detectable IGFBP2. Susceptibilities of those seven cell lines to nine anticancer agents targeting to IGF1R, Src, FAK, MEK, and AKT were determined by a dose-dependent cell viability assay. The results showed that high IGFBP2 levels were associated with resistance to dasatinib and, to a lesser degree, to sacaratinib, but not to other agents. Ectopic IGFBP2 overexpression or knockdown revealed that changing IGFBP2 expression levels reversed dasatinib susceptibility phenotype, suggesting a causal relationship between IGFBP2 expression and dasatinib resistance. Molecular characterization revealed that focal adhesion kinase (FAK) activation was associated with increased IGFBP2 expression and partially contributed to IGFBP2-mediated dasatinib resistance. Treatment with a combination of dasatinib and FAK inhibitor led to enhanced antitumor activity in IGFBP2-overexpressing and dasatinib-resistant NSCLC cells in vitro and in vivo. Our results showed that the IGFBP2/FAK pathway is causally associated with dasatinib resistance and may be used as biomarkers for identification of dasatinib responders among patients with lung cancer. Simultaneous targeting on Src and FAK will likely improve the therapeutic efficacy of dasatinib for treatment of lung cancer. Mol Cancer Ther; 12(12); 1-10. ©2013 AACR.

[490]

TÍTULO / TITLE: - MiR-134/487b/655 Cluster Regulates TGF-beta-induced Epithelial-Mesenchymal Transition and Drug Resistance to Gefitinib by Targeting MAGI2 in Lung Adenocarcinoma Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cancer Ther. 2013 Nov 20.

- Enlace al texto completo (gratuito o de pago) [1158/1535-7163.MCT-13-](#)

[0448](#)

AUTORES / AUTHORS: - Kitamura K; Seike M; Okano T; Matsuda K; Miyanaga A; Mizutani H; Noro R; Minegishi Y; Kubota K; Gemma A

INSTITUCIÓN / INSTITUTION: - 1epartment of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School.

RESUMEN / SUMMARY: - Epithelial-mesenchymal transition (EMT) has recently been recognized as a key element of cell invasion, migration, metastasis, and drug resistance in several types of cancer, including non-small cell lung cancer (NSCLC). Our aim was to clarify microRNA (miRNA) -related mechanisms underlying EMT followed by acquired resistance to epidermal growth factor receptor tyrosine-kinase inhibitor (EGFR-TKI) in NSCLC. MiRNA expression profiles were examined before and after transforming growth factor-beta1 (TGF-beta1) exposure in four human adenocarcinoma cell lines with or without EMT. Correlation between expressions of EMT-related miRNAs and resistance to EGFR-TKI gefitinib was evaluated. MiRNA array and quantitative RT-PCR revealed that TGF-beta1 significantly induced overexpression of miR-134, miR-487b, and miR-655, which belong to the same cluster located on chromosome 14q32, in lung adenocarcinoma cells with EMT. MAGI2 (membrane-associated guanylate kinase, WW and PDZ domain-containing protein 2), a predicted target of these miRNAs and a scaffold protein required for PTEN (phosphatase and tensin homolog), was diminished in A549 cells with EMT after the TGF-beta1 stimulation. Overexpression of miR-134 and miR-487b promoted the EMT phenomenon and affected the drug resistance to gefitinib, whereas knockdown of these miRNAs inhibited the EMT process and reversed TGF-beta1-induced resistance to gefitinib. Our study demonstrated that the miR-134/487b/655 cluster contributed to the TGF-beta1-induced EMT phenomenon and affected the resistance to gefitinib by directly targeting MAGI2, whose suppression subsequently caused loss of PTEN stability in lung cancer cells. The miR-134/miR-487b/miR-655 cluster may be new therapeutic targets in advanced lung adenocarcinoma patients, depending on the EMT phenomenon.

[491]

TÍTULO / TITLE: - Outcomes: wedge resection versus lobectomy for non-small cell lung cancer at the Cancer Centre of Southeastern Ontario 1998-2009.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Can J Surg. 2013 Dec;56(6):E165-70.

●● [Enlace al texto completo \(gratis o de pago\) 1503/cjs.006311](#) [pii]

AUTORES / AUTHORS: - McGuire AL; Hopman WM; Petsikas D; Reid K

INSTITUCIÓN / INSTITUTION: - From the Division of Thoracic Surgery, the Ottawa Hospital, Ottawa, Ont.

RESUMEN / SUMMARY: - BACKGROUND: Sublobar resection for non-small cell lung cancer (NSCLC) remains controversial owing to concern about local recurrence and long-term survival outcomes. We sought to determine the efficacy of wedge resection as an oncological procedure. METHODS: We analyzed the outcomes of all patients with NSCLC undergoing surgical resection at the Cancer Centre of Southeastern Ontario between 1998 and 2009. The standard of care for patients with adequate cardiopulmonary reserve was lobectomy. Wedge resection was performed for patients with inadequate reserve to tolerate lobectomy. Predictors of recurrence and survival were assessed. Appropriate statistical analyses involved the chi(2) test, an independent samples t test and Kaplan-Meier estimates of survival. Outcomes were stratified for tumour size and American Joint Committee on Cancer seventh edition TNM stage for non-small cell lung cancer. RESULTS: A total of 423 patients underwent surgical resection during our study period: wedge resection in 71 patients and

lobectomy in 352. The mean age of patients was 64 years. Mean follow-up for cancer survivors was 39 months. There was no significant difference between wedge resection and lobectomy for rate of tumour recurrence, mortality or disease-free survival in patients with stage IA tumours less than 2 cm in diameter. CONCLUSION: Wedge resection with lymph node sampling is an adequate oncological procedure for non-small cell lung cancer in properly selected patients, specifically, those with stage IA tumours less than 2 cm in diameter.

[492]

TÍTULO / TITLE: - Pathways Enrichment Analysis for Differentially Expressed Genes in Squamous Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pathol Oncol Res. 2013 Oct 10.

●● Enlace al texto completo (gratis o de pago) [1007/s12253-013-9685-2](#)

AUTORES / AUTHORS: - Qian L; Luo Q; Zhao X; Huang J

INSTITUCIÓN / INSTITUTION: - Shanghai Lung Cancer Center, Shanghai Chest Hospital, Shanghai JiaoTong University, NO.241 Huaihai Road, Shanghai, 200030, China.

RESUMEN / SUMMARY: - Squamous lung cancer (SQLC) is a common type of lung cancer, but its oncogenesis mechanism is not so clear. The aim of this study was to screen the potential pathways changed in SQLC and elucidate the mechanism of it. Published microarray data of GSE3268 series was downloaded from Gene Expression Omnibus (GEO). Significance analysis of microarrays was performed using software R, and differentially expressed genes (DEGs) were harvested. The functions and pathways of DEGs were mapped in Gene Ontology and KEGG pathway database, respectively. A total of 2961 genes were filtered as DEGs between normal and SQLC cells. Cell cycle and metabolism were the mainly changed functions of SQLC cells. Meanwhile genes such as MCM, RFC, FEN1, and POLD may induce SQLC through DNA replication pathway, and genes such as PTTG1, CCNB1, CDC6, and PCNA may be involved in SQLC through cell cycle pathway. It is demonstrated that pathway analysis is useful in the identification of target genes in SQLC.

[493]

TÍTULO / TITLE: - Radiation risk of lung cancer screening.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):738-47. doi: 10.1055/s-0033-1358615. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358615](#)

AUTORES / AUTHORS: - Frank L; Christodoulou E; Kazerooni EA

INSTITUCIÓN / INSTITUTION: - Department of Radiology, University of Michigan, Health System, Taubman Center, Ann Arbor, Michigan.

RESUMEN / SUMMARY: - Lung cancer screening with low dose computed tomography (CT) is the only method ever proven to reduce lung cancer-specific mortality in high-risk current and former cigarette smokers. Radiation exposure from annual screening CT examinations and subsequent CT and nuclear medicine testing to further evaluate positive screening CTs is sometimes raised as a reason to avoid screening and is

often misunderstood. With all testing, there are potential benefits and risks. As we sit on the brink of widespread adoption of lung cancer screening CT, we aim to explain why the risks associated with radiation exposure from lung cancer screening are very low and should not be used to avoid screening or dissuade individuals who qualify for screening CT to participate in a lung cancer screening program.

[494]

TÍTULO / TITLE: - Small cell carcinoma of the urinary bladder: a contemporary review with a special focus on bladder-sparing treatments.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Expert Rev Anticancer Ther. 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [1586/14737140.2013.851605](#)

AUTORES / AUTHORS: - Koga F; Yokoyama M; Fukushima H

INSTITUCIÓN / INSTITUTION: - Tokyo Metropolitan Cancer and Infectious diseases Center Komagome Hospital, Urology, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo, 113-8677 Japan.

RESUMEN / SUMMARY: - Small cell carcinoma of the urinary bladder (SCCUB) is a rare and aggressive disease. To date, no standard treatment has been proposed due to the lack of prospective studies resulting from the rarity of this disease. Recently published studies of relatively large patient cohorts, however, have shed some light on the management of SCCUB patients. In this article, the authors review the epidemiology, pathogenesis, diagnosis and treatment (based on disease stage), and they then discuss the optimal therapeutic strategy for SCCUB patients, particularly for those with limited, locoregional disease. The authors conclude that multidisciplinary approaches are needed for the optimal management of this aggressive disease. The authors also discuss bladder-sparing approaches for SCCUB patients, compared to those for conventional bladder urothelial carcinoma patients.

[495]

TÍTULO / TITLE: - Personalizing therapy in advanced non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):822-36. doi: 10.1055/s-0033-1358552. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358552](#)

AUTORES / AUTHORS: - Villaruz LC; Burns TF; Ramfidis VS; Socinski MA

INSTITUCIÓN / INSTITUTION: - Lung and Thoracic Malignancies Program, University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania.

RESUMEN / SUMMARY: - The recognition that non-small cell lung cancer (NSCLC) is not a single disease entity, but rather a collection of distinct molecularly driven neoplasms, has permanently shifted the therapeutic landscape of NSCLC to a personalized approach. This personalization of NSCLC therapy is typified by the dramatic response rates seen in EGFR mutant NSCLC when treated with targeted tyrosine kinase inhibitor therapy and in ALK translocation-driven NSCLC when treated with ALK inhibitors. Targeted therapeutic approaches in NSCLC necessitate consideration of more invasive biopsy techniques aimed at providing sufficient tissue for both histological determination and molecular profiling in all patients with stage IV

disease both at the time of diagnosis and at the time of disease progression. Comprehensive genotyping efforts have identified oncogenic drivers in 62% lung adenocarcinomas and an increasing proportion of squamous cell carcinomas of the lung. The identification of these oncogenic drivers and the triage of patients to clinical trials evaluating novel targeted therapeutic approaches will increasingly mold a landscape of personalized lung cancer therapy where each genotype has an associated targeted therapy. This review outlines the state of personalized lung cancer therapy as it pertains to individual NSCLC genotypes.

[496]

TÍTULO / TITLE: - Comparison of the Diagnostic Accuracy of the MSLN Gene Products, Mesothelin and Megakaryocyte Potentiating Factor, as Biomarkers for Mesothelioma in Pleural Effusions and Serum.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Dis Markers. 2013;35(2):119-27. doi: 10.1155/2013/874212. Epub 2013 Aug 6.

●● [Enlace al texto completo \(gratis o de pago\) 1155/2013/874212](#)

AUTORES / AUTHORS: - Creaney J; Sneddon S; Dick IM; Dare H; Boudville N; Musk AW; Skates SJ; Robinson BW

INSTITUCIÓN / INSTITUTION: - National Centre for Asbestos Related Diseases, School of Medicine and Pharmacology, University of Western Australia and Australian Mesothelioma Tissue Bank, Sir Charles Gairdner Hospital, Perth, WA 6009, Australia.

RESUMEN / SUMMARY: - The MSLN gene products, soluble mesothelin and megakaryocyte potentiating factor (MPF), are being investigated as biomarkers for the asbestos-related cancer malignant mesothelioma (MM). Pleural fluid biomarkers of MM can be elevated when serum levels remain normal. The aim of this study was to determine if this was true for MPF and to compare levels of mesothelin. Biomarker concentrations were compared in 66 MM patients, 39 patients with other malignancies, 37 with benign disease, 18 asbestos-exposed healthy individuals, and 53 patients with chronic kidney disease. In pleural effusions, MPF and soluble mesothelin concentrations were both significantly elevated in MM patients relative to controls. No significant difference between the area under the receiver operator curve (AUC) for MPF (0.945 +/- 0.02) and mesothelin (0.928 +/- 0.03) when distinguishing MM from all other causes of effusion was observed. MPF and mesothelin serum concentrations were highly correlated and of equivalent diagnostic accuracy with AUCs of 0.813 +/- 0.04 and 0.829 +/- 0.03, respectively. Serum levels of both markers increased with decreasing kidney function. In conclusion, MPF is elevated in the pleural effusions of MM patients similar to that of mesothelin. Mesothelin and MPF convey equivalent diagnostic information for distinguishing MM from other diseases in pleural effusions as well as serum.

[497]

TÍTULO / TITLE: - Lung cancer screening with low-radiation dose computed tomography after liver transplantation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Transplant. 2013 Oct 29;18:587-92. doi: 10.12659/AOT.884021.

●● Enlace al texto completo (gratis o de pago) [12659/AOT.884021](https://doi.org/10.12659/AOT.884021)

AUTORES / AUTHORS: - Herrero JI; Bastarrika G; D'Avola D; Montes U; Pueyo J; Inarrairaegui M; Pardo F; Quiroga J; Zulueta J

INSTITUCIÓN / INSTITUTION: - Liver Unit, Clinica Universidad de Navarra, Pamplona, España and Centro de Investigación Biomedica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), España.

RESUMEN / SUMMARY: - Background The prognosis of non-cutaneous malignancies after liver transplantation is dismal, mainly because most cases are diagnosed at advanced stages. In the last decade, studies have shown the potential role of screening for lung cancer with low-radiation dose computed tomography. Material and Methods Fifty-nine liver transplant recipients with a cumulative dose of smoking greater than 10 pack-years were enrolled in a lung cancer screening program using yearly low-radiation dose computed tomography. Results Lung cancer was diagnosed in 7 patients (11.8%), 5 of which were in stage Ia at diagnosis. Patients with lung cancer were significantly older (median age 66 vs. 58 years), had a higher cumulative history of smoking, and had emphysema more frequently than patients without cancer. Conclusions Screening for lung cancer with low-radiation dose computed tomography in liver transplant recipients results in the diagnosis of lung cancer in early stages.

[498]

TÍTULO / TITLE: - Neurosurgical management of intracranial metastatic mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Can J Neurol Sci. 2013 Nov;40(6):878-80.

AUTORES / AUTHORS: - Westwick HJ; Jansen GH; Da Silva VF

[499]

TÍTULO / TITLE: - Successful pulmonary thrombectomy for malignant tumor thrombus after adrenal cancer resection.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Can J Cardiol. 2013 Nov;29(11):1532.e19-21. doi: 10.1016/j.cjca.2013.07.671. Epub 2013 Sep 27.

●● Enlace al texto completo (gratis o de pago) [1016/j.cjca.2013.07.671](https://doi.org/10.1016/j.cjca.2013.07.671)

AUTORES / AUTHORS: - Kimmaliardjuk DM; Morash C; Hudson C; Ruel M

INSTITUCIÓN / INSTITUTION: - Division of Cardiac Surgery, University of Ottawa Heart Institute, Ottawa, Ontario, Canada.

RESUMEN / SUMMARY: - A 28-year-old patient presented with a right adrenal mass compressing the right kidney and invading the inferior vena cava. The tumor was completely resected; however, on a transesophageal echocardiogram intraoperatively, a new pulmonary artery thrombus, measuring 1.4 x 1.8 cm, was detected. The patient was therefore taken to the operating room the next day. The thrombus was visualized and removed and measured 4 x 2 x 1 x 1 cm. The pathology report identified the mass as an adrenal tumor thrombus with malignant elements. To our knowledge, this is the first known case report of an adrenal tumor thrombus successfully resected at the level of the left pulmonary artery.

[500]

TÍTULO / TITLE: - Serum cytokine levels in patients with advanced non-small cell lung cancer: correlation with clinical outcome of erlotinib treatment.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chin Med J (Engl). 2013 Oct;126(20):3931-5.

AUTORES / AUTHORS: - Wang YS; Miao LY; Liu L; Cai HR; Ding JJ; Ren SX; Zhou CC; Schmid-Bindert G

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Nanjing Drum Tower Hospital Affiliated to Medical School of Nanjing University, Nanjing, Jiangsu 210008, China.

RESUMEN / SUMMARY: - BACKGROUND: Serum expression of cytokines may provide information about the clinical outcome of advanced non-small cell lung cancer (NSCLC) patients. This study aimed to investigate the relationship between serum cytokine levels and the clinical outcome of erlotinib treatment in a second or third line setting in patients with advanced NSCLC. METHODS: A total of 162 patients with advanced NSCLC who received erlotinib as either second or third line therapy were enrolled in this study. Blood samples were collected before the initiation of erlotinib treatment, and the levels of IL-1, IL-2R, IL-6, and tumor necrosis factor (TNF)-alpha were assessed by enzyme-linked immunosorbent assay (ELISA). Cutoff points were defined as the median levels of IL-1 (low (≥ 26.5 pg/ml) and high (> 26.5 pg/ml)), IL-2R (low ($= 115$ pmol/L) and high (> 15 pmol/L)), IL-6 (low (≤ 49.5 pg/ml) and high (> 49.5 pg/ml)), and TNF-alpha (low (≤ 48.5 pg/ml) and high (> 48.5 pg/ml)). Kaplan-Meier analysis was used to estimate the survival time, and Cox regression analyses were used to correlate cytokines and baseline clinical characteristics with clinical outcomes, including time to progression (TTP) and overall survival (OS). RESULTS: Between January 2007 and May 2011, 162 patients were enrolled. Their median age was 58 years. In this group, 109 were males and 53 were females, 74 were former or current smokers and 88 were non-smokers. A total of 122 patients had adenocarcinoma, 27 had squamous cell carcinoma, and 13 had tumors with other types of histology. And 139 patients had an Eastern cooperative oncology group (ECOG) performance status of 0-1, while 23 scored at 2-3. Expression of IL-1, IL-2R, and IL-6 was not significantly associated with age, gender, ECOG performance status, smoking status, or histology and stage of tumor. Only TNF-alpha was associated with smoking status ($P = 0.045$). Survival analysis showed that patients with low levels of either IL-6 or TNF-alpha had a statistically longer TTP and OS than patients with high expression ($P < 0.05$). These cytokines remained significant upon multivariate analysis ($P < 0.05$). CONCLUSION: IL-6 or TNF-alpha may serve as potential predictive biomarker for the efficacy of erlotinib.

[501]

TÍTULO / TITLE: - Impact of the IASLC/ATS/ERS classification in pN0 pulmonary adenocarcinomas: A study with radiological-pathological comparisons and survival analyses.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pathol Res Pract. 2013 Oct 19. pii: S0344-0338(13)00329-4. doi: 10.1016/j.prp.2013.09.016.

●● Enlace al texto completo (gratis o de pago) 1016/j.prp.2013.09.016

AUTORES / AUTHORS: - Ambrosini-Spaltro A; Ruiu A; Seebacher C; Vattemi E; Gentile L; Feil B; Zaraca F; Carella R

INSTITUCIÓN / INSTITUTION: - Pathology Unit, Central Hospital, Bolzano, Italy. Electronic address: andrea.ambrosinispaltro@asbz.it.

RESUMEN / SUMMARY: - The aim of this study was: (1) to compare the new pathological findings as detected by the IASLC/ATS/ERS classification with the traditional radiological features in pulmonary pN0 adenocarcinomas, (2) to evaluate their prognostic significance on overall survival (OS). A total of 42 surgically resected pN0 pulmonary adenocarcinomas were analyzed. On CT scans, the following radiological data were recorded: sphericity, predominant margins, cavitation and bronchogram, attenuation and percentage of ground glass opacity (GGO). On pathological examination, tumors were categorized according to the IASLC/ATS/ERS classification; Sica score and grade, pathological stage, tumor major axis, pleural invasion, vascular and lymphatic invasion, peritumoral lymphoid infiltration, and cytological features were also determined. Clinical follow up was available in 37 cases (range 1-117 months). Radiologically, 31 solid and 11 semisolid tumors were found. Morphologically, 2 minimally invasive and 40 invasive adenocarcinomas were diagnosed. In radiological-pathological comparisons, (1) the acinar pattern was higher in tumors with solid attenuation and low GGO ($p=0.018$); (2) the lepidic pattern was more elevated in tumors with high GGO ($p=0.012$). In multivariate survival analyses with stage, predominant margins on CT scans ($p=0.036$) and Sica score ($p=0.028$) significantly affected OS. This study confirms the validity of the new classification of pulmonary adenocarcinomas in radiological-pathological comparisons and underlines the importance of both radiological and pathological findings in correctly identifying their prognostic features.

[502]

TÍTULO / TITLE: - Predictive value of optical coherence tomography on the outcome of lung adenocarcinoma with choroidal metastases.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Arch Soc Esp Oftalmol. 2013 May 11. pii: S0365-6691(13)00061-0. doi: 10.1016/j.oftal.2013.01.013.

●● Enlace al texto completo (gratis o de pago) 1016/j.oftal.2013.01.013

AUTORES / AUTHORS: - Garcia-Fernandez M; Burgueno-Montanes C

INSTITUCIÓN / INSTITUTION: - Servicio de Oftalmología, Hospital Universitario Central de Asturias, Oviedo, España. Electronic address: migarci@hotmail.es.

RESUMEN / SUMMARY: - CLINICAL CASE: A 59 year-old male, with the diagnosis of lung adenocarcinoma stage iv, following palliative systemic chemotherapy treatment. He was referred to our department due to bilateral blurred vision. In the eye-fundus we observed: bilateral choroidal metastases with macular involvement, and in optical coherence tomography (OCT): neurosensory detachment in both eyes. This neurosensory detachment showed improvement with chemotherapy before the clinical and radiologic improvement. DISCUSSION: OCT could be a great tool in order to

predict the response to systemic treatment in cases of lung adenocarcinoma associated with choroidal metastases.

[503]

TÍTULO / TITLE: - Pathology quiz: oncocytic cyst of the ventricular fold.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Middle East J Anesthesiol. 2013 Jun;22(2):213-5.

AUTORES / AUTHORS: - Hamdan AL; Homsy MT; Turfe Z; Boulos F

INSTITUCIÓN / INSTITUTION: - Hamdan Voice Unit, Department of Otolaryngology-Head & Neck Surgery, American University of Beirut Medical Center, P.O. Box: 110236 Beirut, Lebanon. ah77@aub.edu.lb

[504]

TÍTULO / TITLE: - Simultaneous detection of multiple microRNAs for expression profiles of microRNAs in lung cancer cell lines by capillary electrophoresis with dual laser-induced fluorescence.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Chromatogr A. 2013 Nov 8;1315:195-9. doi: 10.1016/j.chroma.2013.09.048. Epub 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) 1016/j.chroma.2013.09.048

AUTORES / AUTHORS: - Ban E; Chae DK; Song EJ

INSTITUCIÓN / INSTITUTION: - Molecular Recognition Research Center, Korea Institute of Science and Technology, Seoul 136-791, Republic of Korea.

RESUMEN / SUMMARY: - MicroRNAs (miRNAs) are small, endogenous, single-stranded, noncoding RNAs. Circulating miRNAs are being considered as promising disease biomarkers. Indeed, single miRNAs have been associated with a wide variety of disease conditions and can target multiple mRNAs; therefore, several miRNAs may be simultaneously involved in disease progression and development. In this study, we developed a capillary electrophoresis with dual laser-induced fluorescence (CE with dual LIF) method using two color laser excitations for simultaneous determination of multiple miRNAs. Target miRNAs were hybridized with 6-FAM- or Cy5-labeled DNA probes for simultaneous determination of multiple miRNAs at excitation wavelengths of 488 and 635 nm. The hybridized miRNAs were separated using CE with dual LIF and detected within 13 min at excitation wavelengths of 488 and 635 nm without any interference or crosstalk. Additionally, the proposed approach was used successfully to detect and evaluate levels of several endogenous miRNAs from lung cancer cell lines. These results showed the potential of CE with dual LIF for fast, specific, simultaneous analysis of multiple miRNAs in cell extracts, biofluids, and tissues.

[505]

TÍTULO / TITLE: - Transglottic basaloid squamous cell carcinoma of the larynx.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Middle East J Anesthesiol. 2013 Jun;22(2):229-32.

AUTORES / AUTHORS: - Hamdan AL; Moukarbel R; Tawil A; Kaspar H; Natout M

INSTITUCIÓN / INSTITUTION: - Department of Otolaryngology/Head & Neck Surgery, American University of Beirut Medical Center-Lebanon. alhamdan@svclb.com

RESUMEN / SUMMARY: - OBJECTIVE: To report a rare case of Transglottic Basaloid Squamous cell carcinoma of the larynx and review the pathologic features of these lesions. CASE REPORT: A 64 year old male, heavy smoker and alcohol abuser, presented with a 6 month history of hoarseness. Laryngoscopy revealed a right transglottic lesion involving the epiglottis, aryepiglottic fold, ventricle and true vocal fold. Microscopically, the tumor was characterized by infiltrating solid sheets of basaloid cells showing palisading pattern along the edges. In areas of solid growth, tumor cells displayed scant cytoplasm, and hyperchromatic nuclei. A portion of the tumor abutting the thyroid cartilage showed squamous differentiation. An island of tumor cells with comedonecrosis was also noted. Immunohistochemical staining for a number of markers was performed. CONCLUSION: Basaloid squamous cell carcinoma displays a biphasic histology. The stage of the disease at presentation is invariably advanced with metastatic lymphadenopathy in two thirds of the patients.

[506]

TÍTULO / TITLE: - Treatment of Elderly Patients Affected by Lung Cancer: Why to Treat, when to Treat and what we Know.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Agents Med Chem. 2013 Nov;13(9):1378-82.

AUTORES / AUTHORS: - Bearz A; Berretta M; Lleshi A; Berto E; Tirelli U

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, National Cancer Institute of Aviano, via Franco Gallini 2, 33081 Aviano (PN), Italy. abearz@cro.it.

RESUMEN / SUMMARY: - In the recent years many advances have been achieved in the field of the treatment of lung cancer; with the development of novel therapeutic pathways due to the knowledge of oncologic drivers involved in the carcinogenesis of the lung, as well as the involvement of new radiotherapeutic and surgical techniques. Nevertheless, the standard treatment for elderly is still debated, mainly because of an underrepresentation of elderly patients in clinical trials. Herein we try to summarize the main guidelines for the treatment of lung cancer, with particular attention for the elderly patients, what we know and what has changed.

[507]

TÍTULO / TITLE: - A case of peritoneal mesothelioma masquerading as a urachal mass.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - ANZ J Surg. 2013 Oct 28. doi: 10.1111/ans.12226.

●● [Enlace al texto completo \(gratis o de pago\) 1111/ans.12226](#)

AUTORES / AUTHORS: - Huynh K; Krantz J; Ahmadi N; Indrajit B; Khadra M

INSTITUCIÓN / INSTITUTION: - Nepean Urological Research Centre, Nepean Hospital, University of Sydney, Kingswood, New South Wales, Australia.

[508]

TÍTULO / TITLE: - Malignant tumor of Brenner : one case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tunis Med. 2013 Oct;91(10):612.

AUTORES / AUTHORS: - Mathlouthi N; Slimani O; Belgharbi A; Ben Temime R; Makhoulouf T; Attia L; Chachia A

[509]

TÍTULO / TITLE: - Clinical study on mannan peptide combined with TP regimen in treating patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4801-4.

AUTORES / AUTHORS: - Yan HA; Shen K; Huang XE

INSTITUCIÓN / INSTITUTION: - Tumor Department of Siyang People's Hospital, Suqian, China E-mail : huangxinen06@aliyun.com.

RESUMEN / SUMMARY: - PURPOSE: To investigate short-term response rate, quality of life and toxicities of mannan peptide combined with TP regimen in treating patients with non-small cell lung cancer (NSCLC). PATIENTS AND METHODS: Forty one patients with NSCLC were divided into an experimental group treated with TP regimen combined with mannan peptide (21 patients) and a control group treated with TP alone (20 patients). RESULTS: Response rates were 61.9% (13/21) for the experimental and 60% (12/20) for the control group ($p>0.05$). Regarding toxicity, white blood cell decreased more frequently in the control group (65%, 13/20) than in the experimental group (33.3%, 7/21) ($p<0.05$); nausea and vomiting also occurred more frequently in the control group (55%, 11/20 vs 23.8%, 5/21) ($p<0.05$). In terms of quality of life, this index was improved by 57.1% (12/21) and 25% (5/20) in experimental and control groups, respectively ($p<0.05$). CONCLUSIONS: Response rate of TP after combined with mannan peptide is mildly increased, while this combination alleviates bone marrow suppression as well as nausea and vomiting of TP, and improves quality of life when treating patients with NSCLC. However, this conclusion should be confirmed by randomized clinical trials.

[510]

TÍTULO / TITLE: - Effectiveness and cost-effectiveness of erlotinib versus gefitinib in first-line treatment of epidermal growth factor receptor-activating mutation-positive non-small-cell lung cancer patients in Hong Kong.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Hong Kong Med J. 2013 Nov 22. doi: 10.12809/hkmj133986.

●● [Enlace al texto completo \(gratis o de pago\) 12809/hkmj133986](#)

AUTORES / AUTHORS: - Lee VW; Schwander B; Lee VH

INSTITUCIÓN / INSTITUTION: - School of Pharmacy, The Chinese University of Hong Kong, Shatin, Hong Kong.

RESUMEN / SUMMARY: - OBJECTIVE. To compare the effectiveness and cost-effectiveness of erlotinib versus gefitinib as first-line treatment of epidermal growth factor receptor-activating mutation-positive non-small-cell lung cancer patients. DESIGN. Indirect treatment comparison and a cost-effectiveness assessment. SETTING. Hong Kong. PATIENTS. Those having epidermal growth factor receptor-activating mutation-positive non-small-cell lung cancer. INTERVENTIONS. Erlotinib versus gefitinib use was compared on the basis of four relevant Asian phase-III

randomised controlled trials: one for erlotinib (OPTIMAL) and three for gefitinib (IPASS; NEJGSG; WJTOG). The cost-effectiveness assessment model simulates the transition between the health states: progression-free survival, progression and death, over a life-time horizon. The World Health Organization criterion (incremental cost-effectiveness ratio <3 times of gross domestic product/capita: <US\$102 582; approximately <HK\$798 078) was used to rate cost-effectiveness. RESULTS. The best fit of study characteristics and prognostic patient characteristics were found between the OPTIMAL and IPASS trials. Comparing progression-free survival hazard ratios of erlotinib versus gefitinib using only these randomised controlled trials in an indirect treatment comparison resulted in a statistically significant progression-free survival difference in favour of erlotinib (indirect treatment comparison hazard ratio=0.33; 95% confidence interval, 0.19-0.58; P=0.0001). The cost-effectiveness assessment model showed that the cost per progression-free life year gained and per quality-adjusted life year gained was at acceptable values of US\$39 431 (approximately HK\$306 773) and US\$62 419 (approximately HK\$485 619) for erlotinib versus gefitinib, respectively. CONCLUSION. The indirect treatment comparison of OPTIMAL versus IPASS shows that erlotinib is significantly more efficacious than gefitinib. Furthermore, the cost-effectiveness assessment indicates that the incremental cost-effectiveness ratios are well within an acceptable range in relation to the survival benefits obtained. In conclusion, erlotinib is cost-effective compared to gefitinib for first-line epidermal growth factor receptor-activating mutation-positive non-small-cell lung cancer patients.

[511]

TÍTULO / TITLE: - Women and Lung Cancer: What is New?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Thorac Cardiovasc Surg. 2013 Summer;25(2):87-94.
doi: 10.1053/j.semtcvs.2013.05.002.

●● Enlace al texto completo (gratis o de pago) [1053/j.semtcvs.2013.05.002](#)

AUTORES / AUTHORS: - North CM; Christiani DC

INSTITUCIÓN / INSTITUTION: - Pulmonary and Critical Care Unit, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts.

RESUMEN / SUMMARY: - In the last 20 years, there has been an increased focus on gender differences in health and disease. The earliest studies of lung cancer enrolled mainly men, as the incidence of lung cancer among women was exceedingly low. As social patterns changed around World War II and women began to smoke more, the epidemiology of lung cancer has changed. The higher percentage of lung cancer in nonsmoking women as compared with nonsmoking men suggests that lung cancer behaves differently in women. Studies of lung cancer in women indicate that there are differences in risk factors, histology, pathophysiology, treatment outcomes, and prognosis as compared with men. The purpose of this review is to provide a concise summary of the literature on lung cancer as it pertains to women, with an emphasis on new areas of research and treatment options.

[512]

TÍTULO / TITLE: - Phase II study on Javanica oil emulsion injection (Yadanzi®) combined with chemotherapy in treating patients with advanced lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4791-4.

AUTORES / AUTHORS: - Lu YY; Huang XE; Cao J; Xu X; Wu XY; Liu J; Xiang J; Xu L

INSTITUCIÓN / INSTITUTION: - Department of Chemotherapy, the Affiliated Jiangsu Cancer Hospital of Nanjing Medical University and Jiangsu Institute of Cancer Research, Nanjing, China E-mail : huangxinen06 @aliyun.com, xulin_83@yahoo.cn.

RESUMEN / SUMMARY: - PURPOSE: To investigate the efficacy and safety of Javanica oil emulsion injection (Yadanzi®) combined with pemetrexed and platinum (PP) for treating patients with advanced lung cancer. PATIENTS AND METHODS: From June 2011 to June 2013, we recruited 58 patients with advanced lung cancer, and divided them into two groups. Twenty eight patients received Yadanzi® (from ZheJiang Jiuxu Pharmaceutical Co., Ltd.) together with PP chemotherapy (combined group), while the others were given only PP chemotherapy (control group). After two cycles of treatment, efficacy and safety of treatment were evaluated. RESULTS: The overall response rate [(CR+PR+SD)/(CR+PR+SD+PD)] of the combined group was higher than that of control group (89.7% vs. 86.2%, p>0.05). Regarding rate of life improvement, it was 82.8% in combined group, and 51.7% in the control group (p<0.05). In terms of side effects, leukopenia in combined group was less frequent than that in control group (p<0.05). More patients in the control group were found to suffer liver toxicity. CONCLUSIONS: Javanica oil emulsion injection combined with chemotherapy could be considered as a safe and effective regimen in treating patients with advanced lung adenocarcinoma. It can improve the quality of life and reduce the possibility of leukopenia. Further clinical trials with a large sample size should be conducted to confirm whether addition of Yadanzi® to chemotherapy could increase the response rate, reduce toxicity, enhance tolerability and improve quality of life for patients with advanced lung cancer.

[513]

TÍTULO / TITLE: - Suppression of NF-kappaB signaling and P-glycoprotein Function by Gambogic Acid Synergistically Potentiates Adriamycin -induced Apoptosis in Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Cancer Drug Targets. 2013 Nov 12.

AUTORES / AUTHORS: - Wang LH; Yang JY; Yang SN; Li Y; Ping GF; Hou Y; Cui W; Wang ZZ; Xiao W; Wu CF

INSTITUCIÓN / INSTITUTION: - 1Department of Pharmacology, Shenyang Pharmaceutical University, Shenyang, 110016, People's Republic of China. wucf@syphu.edu.cn.

RESUMEN / SUMMARY: - Gambogic acid (GA) has been approved by the Chinese Food and Drug Administration for the treatment of lung cancer in clinical trials. However, whether GA has chemosensitizing properties when combined with other chemotherapy agents in the treatment of lung cancer is not known. Here we investigated the effects of GA combined with adriamycin (ADM), a common chemotherapy agent, in regard to their activities and the possible mechanisms against lung cancer in vitro and in vivo. Cell viability results showed that sequential GA-ADM treatment was synergistic, while the reverse sequence and simultaneous treatments were antagonistic or additive, in lung cancer cells and ADM resistant cells, but not in

normal cells. The combined use of GA and ADM synergistically displayed apoptosis-inducing activities in lung cancer cells. Moreover, GA in combination with ADM could promote PARP cleavage, enhance caspases activation and decrease the expression of anti-apoptotic proteins in lung cancer cells. The combined use of GA and ADM decreased the expression of P-glycoprotein and increased the accumulation of ADM in lung cancer cells. Furthermore, it was found that, prior to ADM treatment, GA could inhibit NF-kappaB signaling pathways, of which have been validated to confer ADM resistance. The critical role of NF-kappaB was further confirmed by using PDTC, a NF-kappaB inhibitor, which significantly increased apoptosis induction by the combination of GA and ADM and inhibited ADM-induced ABCB1 upregulation. Importantly, our results indicated that the combination of GA and ADM exerted enhanced anti-tumor effects on A549 xenograft models through inhibiting NF-kappaB and P-glycoprotein, and attenuated ADM-induced cardiotoxicity. Collectively, these findings indicate that GA sensitizes lung cancer cells to ADM in vitro and in vivo, providing a rationale for the combined use of GA and ADM in lung cancer chemotherapy.

[514]

TÍTULO / TITLE: - Pharmacokinetic-pharmacodynamic modeling of the anticancer effect of erlotinib in a human non-small cell lung cancer xenograft mouse model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Pharmacol Sin. 2013 Nov 5;34(11):1427-36. doi: 10.1038/aps.2013.101. Epub 2013 Oct 7.

●● Enlace al texto completo (gratis o de pago) [1038/aps.2013.101](#)

AUTORES / AUTHORS: - Wu Q; Li MY; Li HQ; Deng CH; Li L; Zhou TY; Lu W

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutics, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing 100191, China.

RESUMEN / SUMMARY: - Aim: Erlotinib is used to treat non-small-cell lung cancer (NSCLC), which targets epidermal growth factor receptor (EGFR) tyrosine kinase. The aim of this study was to investigate the relationship between erlotinib plasma concentrations and phosphorylated EGFR (pEGFR) levels, as well as the relationship between pEGFR levels and tumor growth inhibition in a human non-small-cell lung cancer xenograft mouse model. Methods: Female BALB/c nude mice were implanted with the human NSCLC cell line SPC-A-1. The animals were given via gavage a single dose of erlotinib (4, 12.5, or 50 mg/kg). Pharmacokinetics of erlotinib was determined using LC-MS/MS. Tumor volume and pEGFR levels in tumor tissues were measured at different time points after erlotinib administration. The levels of pEGFR in tumor tissues was detected using Western blotting and ELISA assays. Results: The pharmacokinetics of erlotinib was described by a two-compartment model with first order extravascular absorption kinetics. There was a time delay of approximately 2 h between erlotinib plasma concentrations and pEGFR degradation. The time course of pEGFR degradation was reasonably fit by the indirect response model with a calculated IC50 value of 1.80 µg/mL. The relationship between pEGFR levels and tumor volume was characterized by the integrated model with a K_{bio} value of 0.507 cm³/week, which described the impact of pEGFR degradation on tumor growth. Conclusion: The pharmacokinetic/pharmacodynamic properties of erlotinib in a human tumor xenograft model were described by the indirect response model and integrated model, which will

be helpful in understanding the detailed processes of erlotinib activity and determining an appropriate dosing regimen in clinical studies.

[515]

TÍTULO / TITLE: - Novel medium-term carcinogenesis model for lung squamous cell carcinoma induced by N-nitroso-tris-chloroethylurea in mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Sci. 2013 Sep 21. doi: 10.1111/cas.12289.

●● Enlace al texto completo (gratis o de pago) [1111/cas.12289](#)

AUTORES / AUTHORS: - Tago Y; Yamano S; Wei M; Kakehashi A; Kitano M; Fujioka M; Ishii N; Wanibuchi H

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Osaka City University Graduate School of Medicine, Osaka, Japan.

RESUMEN / SUMMARY: - Targeted treatments for lung cancer based on pathological diagnoses are required to enhance therapeutic efficacy. There are few well-established animal models for lung squamous cell carcinoma although several highly reproducible mouse models for lung adenoma and adenocarcinoma are available. This study was carried out to establish a new lung squamous cell carcinoma mouse model. In the first experiment, female A/J mice were painted topically on back skin twice weekly with 75 μ L 0.013 M N-nitroso-tris-chloroethylurea for 2, 4, and 8 weeks (n = 15-20 per group) as initiation of lung lesions, and surviving mice were killed at 18 weeks. In the second experiment, mice were treated as above for 4 weeks and killed at 6, 12, or 18 weeks (n = 3 per group). Lung lobes were subjected to histopathological, immunohistochemical, immunoblotting, and ultrastructural analyses. In the case of treatment for 2, 4, and 8 weeks, incidences of lung squamous cell carcinoma were 25, 54, and 71%, respectively. Cytokeratin 5/6 and epidermal growth factor receptor were clearly expressed in dysplasia and squamous cell carcinoma. Desmosomes and tonofilaments developed in the squamous cell carcinoma. Considering the carcinogenesis model, we conclude that 2 or 4 weeks of N-nitroso-tris-chloroethylurea treatment may be suitable for investigating new chemicals for promotional or suppressive effects on lung squamous cell carcinoma.

[516]

TÍTULO / TITLE: - Tissue Acquisition and Specimen Processing in the Diagnosis of NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):787-91. doi: 10.1055/s-0033-1358555. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358555](#)

AUTORES / AUTHORS: - Akulian J; Yarmus L; Feller-Kopman D

INSTITUCIÓN / INSTITUTION: - Section of Interventional Pulmonology, Division of Pulmonary and Critical Care, University of North Carolina in Chapel Hill, Chapel Hill, North Carolina.

RESUMEN / SUMMARY: - The current management of non-small cell lung cancer (NSCLC) requires pathological differentiation between adenocarcinoma and squamous cell carcinoma using immunohistochemistry and morphological analysis. Additionally,

as novel therapies for specific genetic mutation and chromosomal rearrangement profiles in patients with adenocarcinoma are becoming more numerous and clinically available, adequate tissue acquisition and specimen processing have become crucial. Historically, tissue was obtained via mediastinoscopy or video-assisted thoracoscopy (VATS). However, 80% of patients with lung cancer are ultimately found to be nonsurgical candidates. More recently, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has been shown to be a safe and potentially superior modality to obtain tissue for diagnosis, staging, and molecular profiling. The preparation of tissue specimens has also been the subject of study as different methods have been shown to increase cellular yield. This is of particular importance as the number of clinically significant targetable mutations and chromosomal rearrangements continues to grow and the need for more tissue increases.

[517]

TÍTULO / TITLE: - Percutaneous lung tumor ablation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tech Vasc Interv Radiol. 2013 Dec;16(4):239-52. doi: 10.1053/j.tvir.2013.09.001.

●● Enlace al texto completo (gratis o de pago) [1053/j.tvir.2013.09.001](#)

AUTORES / AUTHORS: - Robert Sheu Y; Hong K

INSTITUCIÓN / INSTITUTION: - Department of Vascular and Interventional Radiology, Johns Hopkins University, Baltimore, MD.

RESUMEN / SUMMARY: - Percutaneous thermal ablation is a minimally invasive treatment for primary or secondary malignancies of the lung. Currently, 3 different modalities are available: radiofrequency, microwave, and cryoablation. Radiofrequency ablation remains to date the most developed although the other 2 modalities have their own distinct advantages. Percutaneous ablation can be used for treatment of stage 1 and 2 non-small cell lung carcinoma either alone or in combination with other therapies. Specifically, their noninvasive nature allows them to be used on patients who are otherwise deemed nonoperable. Percutaneous ablation can also be used to treat stage 3a non-small cell lung carcinoma in carefully selected patients. With nonlung primaries, percutaneous ablation can be used to control limited pulmonary metastasis, recurrences after alternative treatments, or to provide pain relief. Although the long-term data for percutaneous ablation is still being investigated, their noninvasive nature and efficacy will ensure their viability and evolution in the future. In this article we review the indications for percutaneous ablation, evaluation of the potential patient, an overview of the ablation options currently available, procedural details, potential complications, and expected results and follow-up.

[518]

TÍTULO / TITLE: - Surgical pathology of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):770-86. doi: 10.1055/s-0033-1358558. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358558](#)

AUTORES / AUTHORS: - Rezaei MK; Nolan NJ; Schwartz AM

INSTITUCIÓN / INSTITUTION: - The George Washington University Medical Center, Department of Pathology, Washington, DC.

RESUMEN / SUMMARY: - The diagnosis, treatment, and management of lung tumors represent a complex set of decision algorithms and require the cooperation and interaction of a team of experts and support systems. The surgical pathologist, an early, important member of the diagnostic team, uses clinical and radiological evidence to differentiate benign from malignant tumors and renders a unique diagnosis that provides both prognostic and treatment information. Using routine histopathologic criteria, histochemical and immunohistochemical stains, and molecular and genetic testing, surgical pathologists and cytopathologists may distinguish between small cell and other bronchogenic carcinomas, separate adenocarcinomas from squamous cell carcinomas, differentiate between pleural carcinomas and diffuse malignant mesotheliomas, and discriminate among the varieties of neuroendocrine carcinomas. Among adenocarcinomas, the pathological examination stratifies those tumors with absent or minimal central invasive cores that have an excellent prognosis from the more common adenocarcinomas with larger invasive components. These distinctions are necessary based on differences in tumor biology, response to therapy, and prognosis for these different histological types. Histopathologic analysis should attempt to provide a precise diagnosis and limit the usage of the term non-small cell carcinoma. The team approach also enables the optimal use of tumor tissue for diagnostic purposes as well as molecular genetic testing and the discovery of targetable sites for therapeutic management. Though low-stage tumors tend to be initially treated with surgical resection, more advanced stages will be approached with limited tissue acquisition, necessitating a strategy for best practices of scarce tissue resources. The awareness of diagnostic modalities and tissue handling by all members of the team ensures the best patient-centered care.

[519]

TÍTULO / TITLE: - The PFP/RAG2 double-knockout mouse in metastasis research: small-cell lung cancer and prostate cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Methods Mol Biol. 2014;1070:191-201. doi: 10.1007/978-1-4614-8244-4_14.

●● Enlace al texto completo (gratis o de pago) [1007/978-1-4614-8244-4_14](#)

AUTORES / AUTHORS: - Muller I; Ullrich S

INSTITUCIÓN / INSTITUTION: - Institute for Anatomy, Experimental Morphology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

RESUMEN / SUMMARY: - Patients with small-cell lung cancer (SCLC) and prostate cancer (PCa) as well as other solid tumors may have micro- or macro-metastatic spread at an early stage of the disease. SCLC and PCa xenograft transfer models in immunodeficient mice fail to model this metastatic spread in vivo. In both tumor types the depletion of NK cells found in immunodeficient mice results in an increased number of spontaneous metastases, mirroring the clinical situation where NK cell activity in patients is related to metastatic spread of the disease. As a result NK cell activity directly influences treatment options and mortality. Newly developed immunodeficient mouse strains lacking functional T- and B-cells (rag2 knockout) however presenting

functional NK cells (perforin knockout) are superior in producing spontaneous metastasis of SCLC and PCa cells compared to the system using SCID mice.

[520]

TÍTULO / TITLE: - Surgical Outcomes after Initial Surgery for Clinical Single-station N2 Non-small-cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Jpn J Clin Oncol. 2013 Nov 7.

●● Enlace al texto completo (gratis o de pago) [1093/jjco/hyt164](#)

AUTORES / AUTHORS: - Hishida T; Yoshida J; Ohe Y; Aokage K; Ishii G; Nagai K

INSTITUCIÓN / INSTITUTION: - 1Division of Thoracic Surgery, National Cancer Center Hospital East, Chiba.

RESUMEN / SUMMARY: - OBJECTIVE: Single-station N2 (Stage IIIA) non-small-cell lung cancer has been reported to have a relatively favorable prognosis after surgery. However, most previous studies examined surgical outcomes in N2 disease by pathologic nodal status but not by clinical nodal status. The objective of this study was to clarify the surgical outcomes in clinical single-station N2 non-small-cell lung cancer patients. METHODS: A total of 125 consecutive patients with clinical single-station N2 non-small-cell lung cancer were treated in our institution between 1992 and 2008. Among them, 97 (78%) patients underwent thoracotomy, and were included in this retrospective study. We defined clinical single-station N2 node as a node measuring 1-2 cm in a single mediastinal station observed on contrast-enhanced computed tomography. The median follow-up period was 5.9 years (range, 1.8-12.6). RESULTS: Eighty-eight (91%) patients underwent lung resection. Of them, 17 (19%) had true (pathologic) single-station N2 disease. Twenty-eight (32%) had pathologic multistation N2 and 43 (49%) had pN0-1 disease with favorable prognoses. The overall survival of the clinical single-station N2/pathologic N2 patients after initial surgery was unsatisfactory with a 5-year overall survival of 23.6%, but their prognoses were heterogeneous. True single-station pathologic N2 status (hazard ratio = 0.35, P = 0.008) and negative subcarinal node status (hazard ratio = 0.34, P = 0.022) were independent favorable prognostic factors after initial resection for clinical single-station N2/pathologic N2 patients. The patients with both factors revealed a relatively favorable 5-year overall survival of 43.8%. CONCLUSION: Clinical single-station N2 status does not always correspond with pathologic true N2 status. From a prognostic point of view, initial surgery for clinical single-station N2 patients is indicated if their true single-station N2 status and negative subcarinal involvement are preoperatively confirmed.

[521]

TÍTULO / TITLE: - ERCC1 expression does not predict survival and treatment response in advanced stage non-small cell lung cancer cases treated with platinum based chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4679-83.

AUTORES / AUTHORS: - Ozdemir O; Ozdemir P; Veral A; Uluer H; Ozhan MH

INSTITUCIÓN / INSTITUTION: - Department of Chest Diseases, Ege University Faculty of Medicine, Izmir, Turkey E-mail : ozer_ozdemir@yahoo.com.

RESUMEN / SUMMARY: - BACKGROUND: ERCC1 is considered as a promising molecular marker that may predict platinum based chemotherapy response in non small cell lung cancer patients. We therefore investigated whether its expression is indeed associated with clinical outcomes in advanced stage NSCLC patients. MATERIALS AND METHODS: Pretreatment tumor biopsy samples of 83 stage 3B and 4 non-small cell lung cancer patients treated with platinum based chemotherapy were retrospectively analyzed for immunohistochemical ERCC1 expression. None of the patients received curative surgery or radiotherapy. RESULTS: By calculating H- scores regarding the extent and intensity of immunohistochemical staining of tumor biopsy samples, ERCC1 expression was found to be positive in 50 patients (60.2%). ERCC1 positive and negative groups had no statistically significant differences regarding treatment response, progression free survival and overall survival (respectively $p=0.161$; $p=0.412$; $p=0.823$). CONCLUSIONS: In our study we found no association between ERCC1 expression and survival or treatment response. The study has some limitations, such as small sample size and retrospective analysis method. There is need of more knowledge for use of ERCC1 guided chemotherapy regimens in advanced stage NSCLC.

[522]

TÍTULO / TITLE: - Stereotactic Ablative Radiotherapy (SABR) for Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):845-54. doi: 10.1055/s-0033-1358554. Epub 2013 Nov 20.

●● [Enlace al texto completo \(gratis o de pago\) 1055/s-0033-1358554](#)

AUTORES / AUTHORS: - Iyengar P; Westover K; Timmerman RD

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, Texas.

RESUMEN / SUMMARY: - Stereotactic ablative radiotherapy (SABR), otherwise known as stereotactic body radiation therapy (SBRT), is an external beam treatment modality that offers the ability to deliver with high precision large doses of radiation over a limited number of fractions. SABR is currently a standard of care in the treatment of early-stage primary non-small cell lung cancers (NSCLCs) that are medically inoperable and for metastases in many anatomical locations. To date, local control and toxicity parameters with SABR for early-stage NSCLCs are comparable to those found in reports of experiences with surgical resection. It is increasingly apparent that some patients with borderline resectable lung primaries are also looking to SABR as a noninvasive means of therapy. However, randomized comparisons have not been completed to assess survival in operable patients. This review summarizes the advanced technology and radiation concepts that have helped clinicians optimize the use of stereotactic ablative therapies for lung cancer, with an emphasis on the rationale for future continued use of this advanced treatment modality.

[523]

TÍTULO / TITLE: - The use of single incision thoracoscopic pleurectomy in the management of malignant pleural effusion.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Chir Belg. 2013 Jul-Aug;113(4):270-4.

AUTORES / AUTHORS: - Kara M; Alzafer S; Okur E; Halezeroglu S

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Acibadem University School of Medicine, Turkey. murat19071966@gmail.com

RESUMEN / SUMMARY: - BACKGROUND: A number of procedures have been used in the management of malignant pleural effusion including repeated thoracentesis, tube thoracostomy, drainage with catheter, chemical pleurodesis, pleurectomy and pleuro-peritoneal shunt. However, the optimal method of management remains unclear. On the other hand, single incision thoracoscopic surgery has been defined as a less invasive method than the standard threeportal videothoracoscopy. We herein present our series of patients who underwent single incision thoracoscopic pleurectomy for malignant pleural effusion. PATIENTS AND METHODS: We performed a single incision thoracoscopic pleurectomy in a total of 19 consecutive patients, 11 (57.8%) male and 8 (42.2%) female with a mean age of 56.3 +/- 16.9 years who had malignant pleural effusions. We made a single 2-2.5 cm incision at the seventh or eighth intercostal spaces on the midaxillary line for the procedure. RESULTS: We performed a total of 23 single incision thoracoscopic total pleurectomies consisting of 11 (57.8%) right-sided, 4 (21.1%) left-sided and 4 (21.1%) bilateral procedures. The mean total postoperative drainage was 553 +/- 266 cc (Median; 470 cc), and the mean chest tube removal time was 2.3 +/- 0.4 days (Median; 2 days). We observed neither morbidity nor mortality. No patient required an additional port or a conversion to thoracotomy. Median follow-up was 83 days (range, 30 to 359 days). Pleural effusion recurred in two (8.6%) out of 23 procedures which resulted in a success rate as 91.4% for the procedure. CONCLUSION: Single incision thoracoscopic pleurectomy is a safe, less invasive and an effective method of pleurodesis with a low recurrence rate in patients with malignant pleural effusion.

[524]

TÍTULO / TITLE: - Carinal sleeve pneumonectomy for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Chir Belg. 2013 Jul-Aug;113(4):258-62.

AUTORES / AUTHORS: - Sanli M; Arslan E; Isik AF; Tuncozgun B; Elbeyli L

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Gaziantep University, Gaziantep, Turkey. sanli@gantep.edu.tr

RESUMEN / SUMMARY: - BACKGROUND: Here, we present our experience of 12 lung cancer cases operated with carinal sleeve pneumonectomy (CSP) from 2001 to 2011. METHODS: 12 cases who had undergone CSP in our department from 2001 to 2011 were retrospectively evaluated and presented by taking into account their demographical and clinical features, the surgical technique that was used, the complications that developed and the latest conditions of these patients. RESULTS: Of the 12 cases, 11 were male and 1 was female with a mean age of 58.6 years (40-71 years). 11 cases had right and 1 had left CSP. The etiology for resection was lung cancer in all cases. 10 cases had carinal invasion of the lung cancer, 1 had bronchopleural fistula developing after right pneumonectomy, 1 had distal tracheal

rupture due to intubation tube placed during pneumonectomy; these all resulted in performing CSP. Five patients developed complications during the postoperative period. Three cases developed recurrences/metastases during the follow-up. Nine patients died, 3 patients were alive and were followed-up by our department. For all the cases, the median survival was 9 months, the estimated survival rate of 2-years was 33%, and 5-year survival rate was 22%. Survival for 2-4 years was 71%. CONCLUSIONS: We think that with increasing surgical experience better results are obtained in these technically demanding procedures.

[525]

TÍTULO / TITLE: - Advances in surgical techniques in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):855-66. doi: 10.1055/s-0033-1358557. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358557](#)

AUTORES / AUTHORS: - Kim AW; Detterbeck FC

INSTITUCIÓN / INSTITUTION: - Section of Thoracic Surgery, Department of Surgery, Yale School of Medicine, New Haven, Connecticut.

RESUMEN / SUMMARY: - Thoracic surgery is a dynamic field, and many scientific, technological, technical, and organizational changes are occurring. A prominent example is the use of less invasive approaches to major resection of non-small cell lung cancer (NSCLC), both thoracoscopic and robotic. Sophisticated technology corroborated by clinical data has led to these approaches becoming accepted additions to the armamentarium. Additionally, improvements in perioperative pain management have also contributed to dramatically changing the experience of patients who undergo modern thoracic surgery. Lung cancer is being detected more often at an early stage. At the same time, advances in techniques, patient care, clinical science, and multidisciplinary treatment support an increased role for aggressive resection in the face of larger locally advanced tumors or for those with limited metastatic disease. These advances, conducted in the setting of multidisciplinary decision making, have resulted in real and palpable advancements for patients with lung cancer.

[526]

TÍTULO / TITLE: - MicroRNA-10b overexpression promotes non-small cell lung cancer cell proliferation and invasion.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Med Res. 2013 Nov 12;18:41. doi: 10.1186/2047-783X-18-41.

●● Enlace al texto completo (gratis o de pago) [1186/2047-783X-18-41](#)

AUTORES / AUTHORS: - Liu Y; Li M; Zhang G; Pang Z

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Affiliated Tumor Hospital, Xinjiang Medical University, Urumqi, Xinjiang 830011, China.
qq_zhang2@126.com.

RESUMEN / SUMMARY: - BACKGROUND: miRNAs are a class of small non-coding RNA molecules that play an important role in the pathogenesis of human diseases through negative regulation of gene expression. Although miRNA-10b (miR-10b) has

been implicated in other tumors, its role in non-small cell lung cancer (NSCLC) is still unknown. The aim of the present study was to investigate the role of miR-10b in NSCLC. METHODS: Expression of miR-10b was analyzed in NSCLC cell line A549 by qRT-PCR. Cell viability was evaluated using Cell Counting Kit (CCK)-8. Cell migration and invasion were evaluated by wound healing assay and transwell assays. Cell cycle and apoptosis analyses were performed. Western blotting was used to predicate the target of miR-10b. RESULTS: The A549 cell line transfected with the miR-10b exhibited significantly increased proliferation, migration, and invasion capacities when compared with the control cells ($P < 0.05$). Kruppel-like factor 4 (KLF4) may be indirectly targeted by miR-10b during the proliferation increasing of A549 cells. CONCLUSION: In this study, we found that miR-10b is a tumor enhancer in NSCLC. Thus, miR-10b may represent a potential therapeutic target for NSCLC intervention.

[527]

TÍTULO / TITLE: - Synthesis and antiproliferative activity of benzofuran-based analogs of cercosporamide against non-small cell lung cancer cell lines.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Med Chem. 2013 Nov;69:823-32. doi: 10.1016/j.ejmech.2013.09.013. Epub 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [1016/j.ejmech.2013.09.013](#)

AUTORES / AUTHORS: - Bazin MA; Boderio L; Tomasoni C; Rousseau B; Roussakis C; Marchand P

INSTITUCIÓN / INSTITUTION: - Universite de Nantes, Nantes Atlantique Universites, Laboratoire de Chimie Therapeutique, Cibles et Medicaments des Infections et du Cancer, IICiMed EA 1155, UFR des Sciences Pharmaceutiques et Biologiques, 1 rue Gaston Veil, 44035 Nantes, France.

RESUMEN / SUMMARY: - A novel series of 3-methyl-1-benzofuran derivatives were synthesized and screened in vitro for their antiproliferative activity against two human NSCLC cell lines (NSCLC-N6 mutant p53 and A549 wild type p53). Most promising compounds presented a structural analogy with the west part of cercosporamide, a natural product of biological interest. In particular, compounds 10, 12 and 31 showed cytotoxic activities at micromolar concentrations ($IC_{50} < 9.3 \mu M$) and compounds 13, 18 and 32 displayed moderate IC_{50} values (25-40 μM).

[528]

TÍTULO / TITLE: - Low frequency KRAS mutations in colorectal cancer patients and the presence of multiple mutations in oncogenic drivers in non-small cell lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Genet. 2013 Sep-Oct;206(9-10):330-9. doi: 10.1016/j.cancergen.2013.09.004. Epub 2013 Oct 2.

●● Enlace al texto completo (gratis o de pago)

[1016/j.cancergen.2013.09.004](#)

AUTORES / AUTHORS: - Jiang L; Huang J; Morehouse C; Zhu W; Korolevich S; Sui D; Ge X; Lehmann K; Liu Z; Kiefer C; Czapiga M; Su X; Brohawn P; Gu Y; Higgs BW; Yao Y

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China.

RESUMEN / SUMMARY: - Intratumor heterogeneity can confound the results of mutation analyses in oncogene genes using traditional methods thereby challenging the application of targeted cancer therapy strategies for patients. Ultradeep sequencing can detect low frequency and expanded clonal mutations in primary tumors to better inform treatment decisions. KRAS coding exons in 61 treatment-naive colorectal cancer (CRC) tumors and KRAS, EGFR, ALK, and MET in lung tumors from three Chinese non-small cell lung cancer (NSCLC) patients were sequenced using ultradeep sequencing methods. Forty-one percent of CRC patients (25/61) harbored mutations in the KRAS active domain, eight of which (13%) were not detected by Sanger sequencing. Three (of eight) had frequencies less than 10% and one patient harbored more than one mutation. Low frequency KRAS active (G12R) and EGFR kinase domain mutations (G719A) were identified in one NSCLC patient. A second NSCLC patient showed an EML4-ALK fusion with ALK, EGFR, and MET mutations. A third NSCLC patient harbored multiple low frequency mutations in KRAS, EGFR, and MET as well as ALK gene copy number increases. Within the same patient, multiple low frequency mutations occurred within a gene. A complex pattern of intrinsic low frequency driver mutations in well-known tumor oncogenes may exist prior to treatment, resulting in resistance to targeted therapies. Ultradeep sequencing can characterize intratumor heterogeneity and identify such mutations to ultimately affect treatment decisions.

[529]

TÍTULO / TITLE: - Small-cell lung cancer (SCLC) cell adhesion on E- and P-selectin under physiological flow conditions.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Methods Mol Biol. 2014;1070:47-56. doi: 10.1007/978-1-4614-8244-4_4.

- Enlace al texto completo (gratis o de pago) [1007/978-1-4614-8244-4_4](#)

AUTORES / AUTHORS: - Richter U

INSTITUCIÓN / INSTITUTION: - Institute for Anatomy II: Experimental Morphology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

RESUMEN / SUMMARY: - Hematogenous metastasis is still a poorly understood phenomenon. The rate-limiting step within the metastatic cascade is not yet clear although it may be estimated that the extravasation of circulating tumor cells is a step of crucial importance, as most tumor cells that are shed into circulation undergo apoptosis. The process of extravasation includes a cascade of consecutive steps, starting with adhesion of tumor cells circulating in the bloodstream to endothelial cells, mimicking leukocyte adhesion and transmigration. Endothelial cell selectin-leukocyte glycan interaction occurs when leukocytes adhere to endothelial cells under conditions of shear stress. As there are parallels between cancer cell endothelial interactions with leukocyte endothelial cell systems an experimental setup has been developed in which adhesion of small cell lung carcinoma adhesive properties can be analyzed under physiological shear stress conditions during their attachment to E- and P-selection.

[530]

TÍTULO / TITLE: - Immunotherapy in lung cancer: “b7-bombers” and other new developments.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):810-21. doi: 10.1055/s-0033-1358551. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358551](#)

AUTORES / AUTHORS: - Creelan BC; Antonia SJ

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida.

RESUMEN / SUMMARY: - Several recent immunotherapy agents have exhibited exceptional activity, and their eventual approval for use in lung cancer appears plausible. The immune checkpoint proteins, such as the B7 superfamily, are becoming increasingly relevant targets for therapeutic inhibition. Tumor vaccines hold the potential to deliver durable responses that are specific for tumor antigen, with favorable adverse effect profiles. Several vaccine trials are accruing more patients than any previous lung cancer trials and are designed to select a specific population based on a predefined, scientifically justified biomarker. These emerging immune treatments may hold great potential for the systemic treatment of lung cancers.

[531]

TÍTULO / TITLE: - Lung cancer screening.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):727-37. doi: 10.1055/s-0033-1358549. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358549](#)

AUTORES / AUTHORS: - Arenberg D

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary & Critical Care Medicine, Department of Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan.

RESUMEN / SUMMARY: - The National Lung Screening Trial demonstrated that lung cancer screening with three annual low-dose computed tomographic scans has the potential to reduce lung cancer-specific mortality by 20% in an older population of heavy smokers. This was a great achievement by the National Lung Screening Trial (NLST) investigators, but this should be viewed as an important first step in an unfinished process. Many major questions remain about how to best realize this mortality reduction in a practical real-world context. Screening for lung cancer will be most effective if it is accompanied by continued research into risk modeling, patient communication strategies, and biomarkers. For clinicians establishing a program of lung cancer screening, we encourage this to be done in a responsible fashion, adhering to practices specified in the design of the NLST, and with careful attention given to proper management of screen-detected abnormalities and maintenance of screening registries.

[532]

TÍTULO / TITLE: - Requirement for Interaction of PI3-Kinase p110alpha with RAS in Lung Tumor Maintenance.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Cell. 2013 Nov 11;24(5):617-30. doi: 10.1016/j.ccr.2013.09.012.

●● Enlace al texto completo (gratis o de pago) [1016/j.ccr.2013.09.012](#)

AUTORES / AUTHORS: - Castellano E; Sheridan C; Thin MZ; Nye E; Spencer-Dene B; Diefenbacher ME; Moore C; Kumar MS; Murillo MM; Gronroos E; Lassailly F; Stamp G; Downward J

INSTITUCIÓN / INSTITUTION: - Signal Transduction Laboratory, Cancer Research UK London Research Institute, 44 Lincoln's Inn Fields, London WC2A 3LY, UK.

RESUMEN / SUMMARY: - RAS proteins directly activate PI3-kinases. Mice bearing a germline mutation in the RAS binding domain of the p110alpha subunit of PI3-kinase are resistant to the development of RAS-driven tumors. However, it is unknown whether interaction of RAS with PI3-kinase is required in established tumors. The need for RAS interaction with p110alpha in the maintenance of mutant Kras-driven lung tumors was explored using an inducible mouse model. In established tumors, removal of the ability of p110alpha to interact with RAS causes long-term tumor stasis and partial regression. This is a tumor cell-autonomous effect, which is improved significantly by combination with MEK inhibition. Total removal of p110alpha expression or activity has comparable effects, albeit with greater toxicities.

[533]

TÍTULO / TITLE: - HER2 and lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Expert Rev Anticancer Ther. 2013 Oct;13(10):1219-28. doi: 10.1586/14737140.2013.846830.

●● Enlace al texto completo (gratis o de pago) [1586/14737140.2013.846830](#)

AUTORES / AUTHORS: - Landi L; Cappuzzo F

INSTITUCIÓN / INSTITUTION: - Medical Oncology Department, Istituto Toscano Tumori, Ospedale Civile, viale Alfieri 36, 57100 Livorno, Italy.

RESUMEN / SUMMARY: - In non-small-cell lung cancer (NSCLC), the identification of oncogenic driver mutations led to the definition of different clinical entities with different therapeutic opportunities, as demonstrated in patients harboring EGF receptor (EGFR) mutations or anaplastic lymphoma kinase translocations. Human EGFR2 (or HER2) has an established role as a prognostic and predictive factor in breast cancer. Although HER2 deregulation, including overexpression, amplification and mutation, has been described in NSCLC, its role as a therapy biomarker remains undefined. In the last few years, there has been a growing interest on HER2 mutation, with few anecdotal or retrospective studies suggesting a relevant role for this biomarker. This review discusses the prognostic and predictive impact of HER2 deregulation and the clinical implications of anti-HER2 strategies in NSCLC.

[534]

TÍTULO / TITLE: - Runx3 inactivation is a crucial early event in the development of lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Cell. 2013 Nov 11;24(5):603-16. doi: 10.1016/j.ccr.2013.10.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.ccr.2013.10.003](https://doi.org/10.1016/j.ccr.2013.10.003)

AUTORES / AUTHORS: - Lee YS; Lee JW; Jang JW; Chi XZ; Kim JH; Li YH; Kim MK; Kim DM; Choi BS; Kim EG; Chung JH; Lee OJ; Lee YM; Suh JW; Chuang LS; Ito Y; Bae SC

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, College of Medicine, Chungbuk National University, Cheongju 361-763, South Korea.

RESUMEN / SUMMARY: - Targeted inactivation of Runx3 in mouse lung induced mucinous and nonmucinous adenomas and markedly shortened latency of adenocarcinoma formation induced by oncogenic K-Ras. RUNX3 was frequently inactivated in K-RAS mutated human lung adenocarcinomas. A functional genetic screen of a fly mutant library and molecular analysis in cultured cell lines revealed that Runx3 forms a complex with BRD2 in a K-Ras-dependent manner in the early phase of the cell cycle; this complex induces expression of p14(ARF)/p19(Arf) and p21(WAF/CIP). When K-Ras was constitutively activated, the Runx3-BRD2 complex was stably maintained and expression of both p14(ARF) and p21(WAF/CIP) was prolonged. These results provide a missing link between oncogenic K-Ras and the p14(ARF)-p53 pathway, and may explain how cells defend against oncogenic K-Ras.

[535]

TÍTULO / TITLE: - Lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Semin Respir Crit Care Med. 2013 Dec;34(6):725-6. doi: 10.1055/s-0033-1358616. Epub 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1055/s-0033-1358616](https://doi.org/10.1055/s-0033-1358616)

AUTORES / AUTHORS: - Rivera MP

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of North Carolina in Chapel Hill, Chapel Hill, North Carolina.

[536]

TÍTULO / TITLE: - Pulmonary cryptococcosis and cryptococcal osteomyelitis mimicking primary and metastatic lung cancer in F-FDG PET/CT.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Infect Dis. 2013 Sep 25. pii: S1201-9712(13)00269-5. doi: 10.1016/j.ijid.2013.08.009.

●● Enlace al texto completo (gratis o de pago) [1016/j.ijid.2013.08.009](https://doi.org/10.1016/j.ijid.2013.08.009)

AUTORES / AUTHORS: - Wang J; Ju HZ; Yang MF

INSTITUCIÓN / INSTITUTION: - State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qinchun Road, Zhejiang Province, Hangzhou, China.

[537]

TÍTULO / TITLE: - What lies within: novel strategies in immunotherapy for non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncologist. 2013;18(11):1203-13. doi: 10.1634/theoncologist.2013-0171. Epub 2013 Oct 8.

●● [Enlace al texto completo \(gratis o de pago\) 1634/theoncologist.2013-0171](#)

AUTORES / AUTHORS: - Forde PM; Reiss KA; Zeidan AM; Brahmer JR

INSTITUCIÓN / INSTITUTION: - The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins University, Baltimore, Maryland, USA.

RESUMEN / SUMMARY: - Immunotherapy has become an increasingly important therapeutic strategy for those with cancer, with phase III studies demonstrating survival advantages in melanoma and castration-resistant prostate cancer. Non-small cell lung cancer (NSCLC) is a promising target for the next generation of immune-based strategies. In this article, we examine the current state of the art in lung cancer immunotherapy, including vaccines that specifically target lung tumor antigens and immune checkpoint antibodies such as anti-programmed death 1 (anti-PD-1). Both approaches harness innate immunity against tumors by suppressing tumor-induced immune paresis. Methods. To identify relevant clinical trials of immunotherapy in NSCLC, PubMed and Medline databases were searched using the terms “immunotherapy” and “NSCLC,” and several other therapy-specific search terms (e.g., PD-1, NSCLC). Additionally, abstracts presented at international lung cancer symposia, the American Society of Clinical Oncology annual meeting, and the European Society of Medical Oncology annual meeting between 2005 and 2013 were evaluated. Results. Large international phase III trials of NSCLC vaccines have completed accrual in both the adjuvant and metastatic disease settings. Results of the START study were disappointing, but results from other studies are still awaited. Immune checkpoint modulation has shown promise, with separate phase I studies of the anti-PD-1 antibody, nivolumab, and anti-PD-L1 antibody, MPDL3280A, demonstrating good tolerance and durable responses for certain patients with NSCLC who were heavily pretreated. Conclusions. Immune-based strategies have shown initial promise for early- and advanced-stage NSCLC. Validating these findings in randomized studies and discovering durable biomarkers of response represent the next challenges for investigation.

[538]

TÍTULO / TITLE: - Importance of systemic mediastinal lymphadenectomy in exact staging of bronchogenic carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Bratisl Lek Listy. 2013;114(10):569-72.

AUTORES / AUTHORS: - Hytych V; Taskova A; Horazdovsky P; Konopa Z; Demes R; Cermak J; Vrabcova A; Hoferka P; Pohnan R

RESUMEN / SUMMARY: - Constituent part of radical lung resection for lung cancer is a dissection of mediastinal lymph nodes. Lymphadenectomy is a standard procedure in an assessment of clinical stage of the disease. The aim of the study was to map metastasizing of bronchogenic non-small cell lung carcinoma into homolateral mediastinal lymph nodes and to assess the importance of mediastinal lymphadenectomy for exact staging and survival. Methods: Study of 31 patients with

lung resection and systematic mediastinal lymphadenectomy operated from August 2004 to January 2007, with pre-operative stage Ia to IIb (TNM classification) - according to CT without mediastinal lymph nodes invasion and with positive histological finding after systematic mediastinal lymphadenectomy. Results: Tumors in right upper lobe metastasized in 45.5 % into group 1 nodes (stages N1-N4) and group 3 nodes (stages N7) and in 9 % into group 4 nodes (stages N8-N9). Tumors of the right middle lobe metastasized in 100 % into group 3 nodes (stage N7). Tumors of the right lower lobe metastasized in 87.5 % into group 3 nodes (N7) and in 12.5 % into group 4 nodes (stages N8-N9). Tumors of the left upper lobe metastasized in 9.0 % in group 1 nodes (stages N1-N4), in 82 % into group 2 nodes (stages N5-N6) and in 9.0 % were found skip metastases into group 4 nodes (stages N8-N9). Tumors of the left lower lobe metastasized in 26.7 % in group 4 nodes, 46.6 % into group 3 nodes, in 20,0 % into group 2 nodes and in 6,7 % into group 1 nodes. Conclusion: Systematic mediastinal lymphadenectomy is crucial for determining the stage of the disease according to the TNM classification. Systematic lymphadenectomy is essential for the diagnosis of stage IIIa disease and setting of additional therapy that prolongs survival (Ref. 17).
Keywords: systematic lymphadenectomy, bronchogenic carcinoma, additional therapy, lung cancer.

[539]

TÍTULO / TITLE: - Safety and effectiveness of stereotactic body radiotherapy for a clinically diagnosed primary stage I lung cancer without pathological confirmation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Oncol. 2013 Nov 12.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s10147-013-0637-3](#)

AUTORES / AUTHORS: - Sakanaka K; Matsuo Y; Nagata Y; Maki S; Shibuya K; Norihisa Y; Narabayashi M; Ueki N; Mizowaki T; Hiraoka M

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology and Image-Applied Therapy, Graduate School of Medicine, Kyoto University, 54 Shogoin, Kawahara-cho, Sakyo-ku, Kyoto, Kyoto, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Pathological diagnosis fails in some pulmonary tumors, although they may be highly suspected to be primary lung cancer. We studied the outcome of stereotactic body radiotherapy for a clinically diagnosed primary stage I lung cancer without pathological confirmation. METHODS: The current study included 37 patients (39 lesions) treated with stereotactic body radiotherapy who were clinically diagnosed with primary stage I lung cancer between August 1998 and April 2009 at our hospital. Pulmonary tumors were highly suspected to be malignant from physical and imaging examinations. Biopsies were performed for 62 % of patients, although malignancy was not pathologically confirmed. In the other 38 % of patients, a biopsy was not feasible. Median age of the patients was 77 years. Median tumor diameter was 20 mm. A total median dose of 48 Gy was prescribed to the isocenter in four fractions. Median follow-up period was 39 months. RESULTS: The 3-year overall survival, local control, and regional-distant control were 74.2, 94.0, and 68.6 %, respectively. In patients with tumors ≤ 20 mm, overall survival and regional-distant control were significantly higher than in patients with tumors > 20 mm ($p \leq 0.001$), whereas no significant difference was observed regarding local control. No grade 3-5 adverse events possibly, probably, or definitely related to the treatment were

observed. CONCLUSIONS: Stereotactic body radiotherapy is safe and effective for a clinically diagnosed primary stage I lung cancer when pathological diagnosis is difficult even with repeat biopsies, or a biopsy is not feasible for reasons of the patient's health condition or wishes.

[540]

TÍTULO / TITLE: - Relationship between programmed death-ligand 1 and clinicopathological characteristics in non-small cell lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chin Med Sci J. 2013 Sep;28(3):147-51.

AUTORES / AUTHORS: - Chen YY; Wang LB; Zhu HL; Li XY; Zhu YP; Yin YL; Lu FZ; Wang ZL; Qu JM

RESUMEN / SUMMARY: - OBJECTIVE: To evaluate the correlation between programmed death-ligand 1 (PD-L1) expression in primary lung cancer cells, tumor associated macrophages (TAM) and patients' clinicopathological characteristics. METHODS: From 2008 to 2010, 208 non-small cell lung cancer patients who underwent surgery or CT-guided biopsy were recruited from Huadong Hospital, Fudan University. Immunohistochemistry staining was performed to evaluate the PD-L1 expression in both primary lung cancer cells and CD68 positive TAM. The relationship between PD-L1 expression and the clinical pathology was evaluated using chi(2) test. Spearman's rank correlations were used to determine the correlation between PD-L1 expression in tumor cells and macrophages. RESULTS: Positive PD-L1 expression in primary cancer cells was found in 136 (65.3%) patients, which were negatively correlated with lymph node metastasis (P=0.009) and smoking history (P=0.036). Besides, TAM with PD-L1 expression (found in 116 patients) was positively associated with smoking history (P=0.034), well-differentiation (P=0.029) and negative lymph node metastasis (P=0.0096). A correlation between PD-L1 expression in primary tumor cells and non-small cell lung cancer associated macrophages was found (r=0.228, P=0.021). CONCLUSION: PD-L1, secreted from TAM, might induce cancer cells apoptosis, and decrease lymph node metastasis.

[541]

TÍTULO / TITLE: - Are neutrophil/lymphocyte and platelet/lymphocyte rates in patients with non-small cell lung cancer associated with treatment response and prognosis?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5237-42.

AUTORES / AUTHORS: - Unal D; Eroglu C; Kurtul N; Oguz A; Tasdemir A

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Kayseri Education and Research Hospital, Kayseri, Turkey E-mail : dilekunaldr@gmail.com.

RESUMEN / SUMMARY: - Background: Inflammation is a critical component of tumor progression. Many cancers arise from sites of infection, chronic irritation, and inflammation. It is now becoming clear that the tumour microenvironment, which is largely orchestrated by inflammatory cells, is an essential participant in the neoplastic process, promoting proliferation, survival and migration. Platelets can release some growth factors such as platelet-derived growth factor, platelet factor 4, and thrombospondin. Such factors have been shown to promote hematogenous tumour

spread, tumor cell adhesion and invasion, and angiogenesis and to play an important role in tumor progression. In this study, we aimed to investigate effects of the pretreatment neutrophil to lymphocyte ratio (NLR) and the platelet to lymphocyte ratio (PLR) on survival and response to chemoradiotherapy in patients with non-small-cell lung cancer (NSCLC). Materials and Methods: Ninety-four patients with non-metastatic NSCLC were included and separated into two groups according to median value of NLR and PLR (low: <3.44 or high: ≥ 3.44 and low: <194 or high ≥ 194 , respectively). Results: Pretreatment high NLR and PLR were associated with significantly shorter disease-free and overall survival rates. Multivariate analysis revealed that the overall survival rates were significantly linked with PLR (OR: 1.87, CI: 1.20-2.91, p: 0.006) and response to chemoradiotherapy (OR: 1.80, CI: 1.14-2.81, p: 0.012) and the disease-free survival rates were significantly associated with NLR (OR: 1.81, CI: 1.16-2.82, p: 0.009) and response to chemoradiotherapy (OR: 2.30, CI: 1.45-3.66, p: 0.001). There was no significant difference between patients with high and low NLR in terms of response to chemoradiotherapy. Similarly, there was no significant influence of the PLR. Conclusions: Pretreatment NLR and PLR measurements can provide important prognostic results in patients with NSCLC and assessment of the two parameters together appears to better predict the prognosis in patients with NSCLC. The effect of inflammation, indicators of NLR and PLR, on survival seems independent of the response to chemoradiotherapy.

[542]

TÍTULO / TITLE: - Post-progression survival in patients with non-small cell lung cancer with clinically acquired resistance to gefitinib.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Korean Med Sci. 2013 Nov;28(11):1595-602. doi: 10.3346/jkms.2013.28.11.1595. Epub 2013 Oct 31.

●● Enlace al texto completo (gratis o de pago) [3346/jkms.2013.28.11.1595](#)

AUTORES / AUTHORS: - Kim H; Yun T; Lee YJ; Han JY; Kim HT; Lee GK

INSTITUCIÓN / INSTITUTION: - Department of Hemato-oncology, Pusan National University Hospital, Busan, Korea.

RESUMEN / SUMMARY: - Most patients with tyrosine kinase inhibitor (TKI)-sensitive non-small cell lung cancer (NSCLC) eventually develop acquired resistance to TKIs. Factors that affect TKI-sensitive patient survival after progression during TKI treatment remain unknown. We attempted to identify factors that affected post-progression survival. We retrospectively reviewed 81 advanced NSCLC patients with disease progression following tumor response and durable (≥ 6 months) disease stabilization with first-line or second-line gefitinib. Post-progression survival (PPS) and characteristics were investigated and compared in patients who did ($n = 16$) and did not ($n = 65$) resume TKIs. Most patients were female never-smokers with adenocarcinoma. Median overall PPS was 10.3 months (95% confidence interval [CI], 7.458-13.142). Age, gender, smoking history, histology, Eastern Cooperative Oncology Group performance status at gefitinib initiation, initial stage, and platinum-based chemotherapy after gefitinib were not significant predictors of PPS. Pemetrexed use after gefitinib significantly improved PPS (18.5 vs 8.6 months; hazard ratio [HR], 0.45; $P = 0.008$). Gefitinib reuse tended to lengthen PPS but was insignificant in multivariate analysis (27.4 vs 8.8 months; HR, 0.53; $P = 0.095$). NSCLC patients assumed to have

clinically acquired resistance to TKIs had relatively long PPS. TKIs reuse or pemetrexed use after progression with gefitinib may improve PPS.

[543]

TÍTULO / TITLE: - Identifying lung cancer patients who may be eligible for epidermal growth factor receptor (EGFR) mutation testing.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - N Z Med J. 2013 Aug 30;126(1381):49-56.

AUTORES / AUTHORS: - Hicks K; Wong C

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Taranaki Base Hospital, Weston, 4310, New Plymouth, New Zealand. karalynhicks@yahoo.com.

RESUMEN / SUMMARY: - AIM: To characterise patients with non-squamous, non-small cell lung cancer (NSCLC) diagnosed at Counties Manukau District Health Board (CMDHB; South Auckland, New Zealand) to estimate the number who may be eligible for EGFR mutation testing. METHODS: Retrospective review of clinical records of 206 patients diagnosed at CMDHB with primary lung cancer between 01/07/2011 and 30/06/2012 RESULTS: Of the 206 patients, 141 (68.4%) had non-squamous, non-small cell lung cancer (NSCLC). Of these 141 cases: 87 (62%) were adenocarcinomas; 73 (51.8%) were male; 78 (55.3%) were European, 16 (18.4%) were Pacific Islanders, 22 (15.4%) were Maori and 15 (10.7%) were Asian, with nine being from South East Asia; 28 (19.9%) had never smoked; 103 (73.0%) had advanced cancer (stage IIIA or more advanced); and 112 (79.4%) cases had an ECOG performance score of two or less. There were four patients with advanced adenocarcinoma who were South East Asian females and had never smoked, all of whom had an ECOG performance score of less than two. CONCLUSION: In a 1-year cohort of primary lung cancer patients, 68% had non-squamous, NSCLC and were potentially eligible for EGFR mutation testing. Patients with advanced stage, non-squamous NSCLC comprised half of all lung cancer patients.

[544]

TÍTULO / TITLE: - Polymorphisms in XPD Gene Could Predict Clinical Outcome of Platinum-Based Chemotherapy for Non-Small Cell Lung Cancer Patients: A Meta-Analysis of 24 Studies.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 15;8(11):e79864. doi: 10.1371/journal.pone.0079864.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0079864](#)

AUTORES / AUTHORS: - Qin Q; Zhang C; Yang X; Zhu H; Yang B; Cai J; Cheng H; Ma J; Lu J; Zhan L; Liu J; Liu Z; Xu L; Sun X

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, the First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China.

RESUMEN / SUMMARY: - OBJECTIVE: Xeroderma pigmentosum group D (XPD) is an essential gene involved in the nucleotide excision repair (NER) pathway. Two commonly studied single nucleotide polymorphisms (SNPs) of XPD (Lys751Gln, A>C, rs13181; Asp312Asn, G>A, rs1799793) are implicated in the modulation of DNA repair capacity, thus related to the responses to platinum-based chemotherapy. Here we

performed a meta-analysis to better evaluate the association between the two XPD SNPs and clinical outcome of platinum-based chemotherapy in non-small cell lung cancer (NSCLC) patients. METHODS: A comprehensive search of PubMed database was conducted to identify relevant articles. Primary outcomes included objective response (i.e., complete response + partial response vs. stable disease + progressive disease), progression-free survival (PFS) and overall survival (OS). The pooled and 95% confidence intervals (CIs) of ORs (odds ratios) and HRs (hazard ratios) were estimated using the fixed or random effect model. RESULTS: Twenty-four studies were eligible according to the inclusion criteria. None of the XPD Lys751Gln/Asp312Asn polymorphisms was associated with objective response, PFS or OS in NSCLC patients treated with platinum drugs. However, in stratified analysis by ethnicity, the XPD Lys751Gln (A>C) polymorphism was not significantly associated with increased response in Caucasians (OR = 1.35, 95%CI = 1.0-1.83, P = 0.122 for heterogeneity) but was associated with decreased PFS in Asians (HR = 1.39, 95%CI = 1.07-1.81, P = 0.879 for heterogeneity). Furthermore, a statistically significant difference existed in the estimates of effect between the two ethnicities (P = 0.014 for TR; P<0.001 for PFS). CONCLUSIONS: XPD Lys751Gln (A>C) may have inverse predictive and prognostic role in platinum-based treatment of NSCLC according to different ethnicities. Further studies are needed to validate our findings.

[545]

TÍTULO / TITLE: - Is Alcohol an independent risk factor for Oro-Pharyngeal and Pulmonary Carcinogenesis - An Acetaldehyde concentrations based Double Blinded Randomized Control Trial.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Int Oral Health. 2013 Aug;5(4):62-7. Epub 2013 Aug 28.

AUTORES / AUTHORS: - Dagli RJ; Kulkarni S; Duraiswamy P; Dagli NR; Khara NV; Khara BN

INSTITUCIÓN / INSTITUTION: - Department of Public Health Dentistry, Vyas Dental College & Hospital, Jodhpur, Rajasthan, India.

RESUMEN / SUMMARY: - Background: There is increasing evidence that a major part of the tumour-promoting action of alcohol is mediated via its first, toxic and carcinogenic metabolite acetaldehyde. Materials & Methods: The double blinded randomized control trial was designed for 82 male volunteers aged 20-29 years. Exclusion criteria were individual under antibiotic therapy, smokers, mutant Aldehyde Dehydrogenase deficient subject or any other systemic disease. Subjects were randomized in experimental (alcohol + soft drink) and control group (soft drink) from each pair of equal body weighted volunteers. The amount of alcohol consumed was calculated to be equivalent to 0.7 g alcohol/kilogram of body weight. Samples of breath for Acetaldehyde concentration (AC) were captured with the aid of a highly reproducible fuel cell gas-sampling device (PST-M1; Lions Laboratories, Cardiff, Wales). In Statistical analysis, mean AC was compared among both groups at different interval using paired t-test and Analysis of variance. Results: Mean acetaldehyde level was recorded higher ([Formula: see text]) among interventional group which can be produced from ethanol during metabolism or by oro-pharyngeal microbes. After 15 minutes of drink, the AC was [Formula: see text] in ethanol group compared to [Formula: see text] in soft-drink group. There was significant increase in AC after 1 hour ([Formula: see text]) which was [Formula: see text] in ethanol group compared to

[Formula: see text] in soft-drink group. Conclusion: Although acetaldehyde is metabolite of alcohol, its organ specific production with risk for oro-pharyngeal and pulmonary carcinogenesis makes alcohol an independent risk factor of carcinogenesis. How to cite this article: Dagli RJ, Kulkarni S, Duraiswamy P, Dagli NR, Khara NV, Khara BN. Is Alcohol an independent risk factor for Oro-Pharyngeal and Pulmonary Carcinogenesis - An Acetaldehyde concentrations based Double Blinded Randomized Control Trial. J Int Oral Health 2013; 5(4):62-67.

[546]

TÍTULO / TITLE: - Prognostic significance of circulating tumor cells in advanced non-small cell lung cancer patients treated with docetaxel and gemcitabine.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Transl Oncol. 2013 Nov 12.

●● Enlace al texto completo (gratis o de pago) [1007/s12094-013-1128-8](#)

AUTORES / AUTHORS: - Juan O; Vidal J; Gisbert R; Munoz J; Macia S; Gomez-Codina J

INSTITUCIÓN / INSTITUTION: - Medical Oncology Department, Hospital Universitari I Politecnic La Fe, Bulevar Sur s/n, 46026, Valencia, España, juan_osc@gva.es.

RESUMEN / SUMMARY: - PURPOSE: To evaluate the association in the change of circulating tumor cell (CTC) levels and clinical outcomes (PFS and OS) in patients with advanced non-small cell lung cancer (NSCLC) treated homogeneously with docetaxel and gemcitabine administered every 2 weeks. METHODS: We prospectively evaluated 37 patients for CTC levels at baseline and after 2 months of chemotherapy (before third cycle). Detection was carried out with the CellSearch system. RESULTS: Nine of the 37 patients (24 %) had ≥ 2 CTCs at the baseline determination. Median progression-free survival (PFS) was 4.3 months (95 % CI 2.5-8.3) for patients with CTC 0-1 as compared to 9.4 months (95 % CI 1.2-12.2) for those with CTC ≥ 2 ($p = 0.3506$). Median overall survival (OS) was 8.1 (95 % CI 2.8-16.3) and 12.2 (95 % CI 1.4-12.2) months for patients with 0-1 CTCs and ≥ 2 CTCs, respectively ($p = 0.7639$). Patients with a second CTC quantification were classified as: group 1, CTC = 0-1 at baseline and CTC = 0-1 after second chemotherapy cycle (18 patients); group 2, CTC ≥ 2 at baseline and CTC = 0-1 after second determination (5 patients). Median PFS was 7.7 and 9.9 months for group 1 and group 2, respectively ($p = 0.4467$). CONCLUSIONS: CTCs ≥ 2 at baseline were detected only in 24 % of this group of patients with advanced NSCLC and poor performance status. No significant differences in PFS and OS between patients with or without CTCs at baseline were observed.

[547]

TÍTULO / TITLE: - Phase II clinical trial of whole-brain irradiation plus three-dimensional conformal boost with concurrent topotecan for brain metastases from lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiat Oncol. 2013 Oct 14;8(1):238. doi: 10.1186/1748-717X-8-238.

●● Enlace al texto completo (gratis o de pago) [1186/1748-717X-8-238](#)

AUTORES / AUTHORS: - Ge XH; Lin Q; Ren XC; Liu YE; Chen XJ; Wang DY; Wang YQ; Cao B; Li ZG; Liu ML

INSTITUCIÓN / INSTITUTION: - Department of Oncology, North China Petroleum Bureau General Hospital of Hebei Medical University, 8 Huizhan Avenue, Renqiu, Hebei Province 062552, PR China. zyy_linqiang@hotmail.com.

RESUMEN / SUMMARY: - BACKGROUND: Patients with brain metastases from lung cancer have poor prognoses and short survival time, and they are often excluded from clinical trials. Whole-cranial irradiation is considered to be the standard treatment, but its efficacy is not satisfactory. The purpose of this phase II clinical trial was to evaluate the preliminary efficacy and safety of the treatment of whole-brain irradiation plus three-dimensional conformal boost combined with concurrent topotecan for the patients with brain metastases from lung cancer. METHODS: Patients with brain metastasis from lung cancer received concurrent chemotherapy and radiotherapy: conventional fractionated whole-brain irradiation, 2 fields/time, 1 fraction/day, 2 Gy/fraction, 5 times/week, and DT 40 Gy/20 fractions; for the patients with ≤ 3 lesions with diameter ≥ 2 cm, a three-dimensional (3-D) conformal localised boost was given to increase the dosage to 56-60 Gy; and during radiotherapy, concurrent chemotherapy with topotecan was given (the chemoradiotherapy group, CRT). The patients with brain metastasis from lung cancer during the same period who received radiotherapy only were selected as the controls (the radiotherapy-alone group, RT). RESULTS: From March 2009 to March 2012, both 38 patients were enrolled into two groups. The median progression-free survival(PFS) time, the 1- and 2-year PFS rates of CRT group and RT group were 6 months, 42.8%, 21.6% and 3 months, 11.6%, 8.7% ($\chi^2 = 6.02$, $p = 0.014$), respectively. The 1- and 2-year intracranial lesion control rates of CRT and RT were 75.9%, 65.2% and 41.6%, 31.2% ($\chi^2 = 3.892$, $p = 0.049$), respectively. The 1- and 2-year overall survival rates (OS) of CRT and RT were 50.8%, 37.9% and 40.4%, 16.5% ($\chi^2 = 1.811$, $p = 0.178$), respectively. The major side effects were myelosuppression and digestive toxicities, but no differences were observed between the two groups. CONCLUSION: Compared with radiotherapy alone, whole-brain irradiation plus 3-D conformal boost irradiation and concurrent topotecan chemotherapy significantly improved the PFS rate and the intracranial lesion control rate of patients with brain metastases from lung cancer, and no significant increases in side effects were observed. Based on these results, this treatment method is recommended for phase III clinical trial.

[548]

TÍTULO / TITLE: - Diaphragm motion and lung function prediction in patients operated for lung cancer - a pilot study on 27 patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cardiothorac Surg. 2013 Nov 18;8(1):213.

●● Enlace al texto completo (gratis o de pago) [1186/1749-8090-8-213](#)

AUTORES / AUTHORS: - Subotic DR; Stevic R; Gajic M; Vesovic R

RESUMEN / SUMMARY: - BACKGROUND: The influence of the diaphragm motion to the accuracy of postoperative lung function prediction after the lung resection is still debatable. METHODS: Prospective study that included 27 patients who underwent a lung resection for cancer. Diaphragm movements were assessed radiographically and by ultrasonography before the operation and postoperatively, with the lung fully expanded. The relationship between the diaphragm movements and differences between ppo FEV1 and measured postoperative FEV1, was analysed by expressing diaphragm movements as preoperative diaphragm amplitudes, preoperative-

postoperative amplitude differences or in relation to fixed intrathoracic distances. RESULTS: The mean difference between preoperative and postoperative diaphragm amplitudes of the diseased side was 2.42 +/- 1.25 cm and 2.11 +/- 2.04 cm when measured radiographically and by ultra sound respectively (p > 0.05). A significant positive correlation was found for the entire group only between the patients' height and the differences ppo FEV1 - actual FEV1: the prediction was more unprecise in taller patients. With the cut-off value of 550 ml for differences between ppo FEV1 and actual FEV1, a significant inverse correlation was found only if the preoperative ipsilateral diaphragm amplitude was presented as a percentage of the preoperative apex-base distance in inspiration. For right-sided tumours, the greater the difference between preoperative and postoperative ipsilateral diaphragm amplitudes, the greater discrepancy between predicted and actual postoperative FEV1. For left-sided tumours, inverse correlation existed if the preoperative diaphragm amplitude was presented as a percentage of the preoperative distance apex-base. CONCLUSION: Diaphragm movements influence the accuracy of the postoperative lung function prediction.

[549]

TÍTULO / TITLE: - A Phase II Trial of Saracatinib, an Inhibitor of src Kinases, in Previously-Treated Advanced Non-Small-Cell Lung Cancer: The Princess Margaret Hospital Phase II Consortium.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Oct 26. pii: S1525-7304(13)00178-2. doi: 10.1016/j.clcc.2013.08.001.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.08.001](#)

AUTORES / AUTHORS: - Laurie SA; Goss GD; Shepherd FA; Neil Reaume M; Nicholas G; Philip L; Wang L; Schwock J; Hirsh V; Oza A; Tsao MS; Wright JJ; Leigh NB

INSTITUCIÓN / INSTITUTION: - The Ottawa Hospital Cancer Centre, University of Ottawa, Ottawa, Ontario. Electronic address: slaurie@toh.on.ca.

RESUMEN / SUMMARY: - BACKGROUND: The src family of kinases may play a role in the malignant phenotype through effects on migration, motility, adhesion and proliferation. The activity of saracatinib, an orally available inhibitor of src kinases, was evaluated in patients with advanced, platinum-pretreated NSCLC. PATIENTS AND METHODS: Eligible patients with advanced NSCLC of any histologic subtype and who had obtained a best response to prior platinum-based chemotherapy of at least stable disease received saracatinib 175 mg orally daily in a 28 day cycle. The primary end point was the proportion of patients progression-free after 4 cycles (16 weeks) of therapy; 8 such patients of 32 evaluable were required to deem the therapy active. Immunohistochemistry for src expression was performed on archival tissue from enrolled patients. RESULTS: Thirty-seven patients received a median of 2 cycles (range, 1-14) each. Six of 31 evaluable patients were progression-free at 16 weeks. Two partial responses were observed, lasting 3.7 and 14.6 months; 1 responder had an EGFR exon 19 deletion. An additional 4 patients had stable disease for at least 4 cycles. The median progression-free and overall survival times were 1.8 and 7.6 months. No correlation between src protein expression and outcome was observed. CONCLUSIONS: There may be a subset of saracatinib-responsive NSCLC that is currently molecularly undefined. Further studies of this agent in a population preselected for target mutations that potentially relevant to src pathways, such as EGFR, should be considered.

[550]

TÍTULO / TITLE: - Five-year relative survival rate of lung cancer in the USA, Europe and Japan.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Jpn J Clin Oncol. 2013 Dec;43(12):1287-8. doi: 10.1093/jjco/hyt189.

●● Enlace al texto completo (gratis o de pago) [1093/jjco/hyt189](#)

AUTORES / AUTHORS: - Matsuda A; Katanoda K

[551]

TÍTULO / TITLE: - Brain metastasis from non-small cell lung cancer (NSCLC) : Prognostic importance of the number of involved extracranial organs.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Strahlenther Onkol. 2013 Oct 9.

●● Enlace al texto completo (gratis o de pago) [1007/s00066-013-0439-6](#)

AUTORES / AUTHORS: - Gerdan L; Segedin B; Nagy V; Khoa MT; Trang NT; Schild SE; Rades D

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Lubeck, Ratzeburger Allee 160, 23538, Lubeck, Germany.

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: This study investigated the potential prognostic value of the number of involved extracranial organs in patients with brain metastasis from non-small cell lung cancer (NSCLC). MATERIAL AND METHODS: A total of 472 patients who received whole-brain radiotherapy (WBRT) alone with 5 x 4 Gy or 10 x 3 Gy for brain metastasis from NSCLC were included in this retrospective study. In addition to the number of involved extracranial organs, 6 further potential prognostic factors were investigated including WBRT regimen, age, gender, Karnofsky Performance Score (KPS), number of brain metastases, and the interval from cancer diagnosis to WBRT. Subgroup analyses were performed for patients with metastatic involvement of one (lung vs. bone vs. other metastasis) and two (lung + bone vs. lung + lymph nodes vs. other combinations) extracranial organs. RESULTS: The survival rates at 6 months of the patients with involvement of 0, 1, 2, 3, and ≥ 4 extracranial organs were 52, 27, 17, 4, and 14 %, respectively ($p < 0.001$). On multivariate analysis, the number of involved extracranial organs remained significant (risk ratio 1.32; 95 % confidence interval 1.19-1.46; $p < 0.001$). Age < 65 years ($p = 0.004$), KPS ≥ 70 ($p < 0.001$), and only 1-3 brain metastases ($p = 0.022$) were also significantly associated with survival in the multivariate analysis. In the separate analyses of patients with involvement of one and two extracranial organs, survival was not significantly different based on the pattern of extracranial organ involvement. CONCLUSION: The number of involved extracranial organs is an independent prognostic factor of survival in patients with brain metastasis from NSCLC, irrespective of the pattern of extracranial organ involvement.

[552]

TÍTULO / TITLE: - Association between clinical pathology and multiple genes mRNA expression in Chinese patients with NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S98-S100. doi: 10.4103/0973-1482.119118.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119118](#)

AUTORES / AUTHORS: - Chen G; Jundong GU; Chen J; Liu Y; Song Z

INSTITUCIÓN / INSTITUTION: - Department of Lung Cancer Surgery, Tianjin Medical University General Hospital, Tianjin, 300052, China.

RESUMEN / SUMMARY: - Objective: The aim of this study was to evaluate whether there was an association between pathology type and ERCC1, BRCA1, RRM1, TUBB3, STMN1, TOP2A and epidermal growth factor receptor (EGFR) messenger ribonucleic acid (mRNA) expression level in Chinese patients with non-small cell lung carcinoma (NSCLC). Materials and Methods: mRNA expression level of these genes was analyzed in 181 cancer tissues by using xTAG-step liquid-chip array. The mRNA expression level of the seven genes was evaluated in association with the clinical pathology type. Results: The average mRNA expression level of the seven genes were ERCC1 (1.02 +/- 0.03), BRCA1 (0.15 +/- 0.04), RRM1 (0.19 +/- 0.05), TUBB3 (0.31 +/- 0.06), STMN1 (2.78 +/- 0.42), TOP2A (3.04 +/- 0.42) and EGFR (0.58 +/- 0.09), respectively in Chinese patients with NSCLC. The mRNA expression level of ERCC1, STMN1 and TOP2A genes were statistical different with different pathology type (p a < 0.05); STMN1 and TOP2A genes mRNA expression were much higher in squamous cell lung carcinoma than that in non-squamous cell lung carcinoma (p a < 0.05). And ERCC1 gene expression was much lower in squamous cell carcinoma than that in non-squamous cell carcinoma (p a < 0.05). Conclusion: mRNA expression level of STMN1, TOP2A and ERCC1 were correlated with the clinical pathology type.

[553]

TÍTULO / TITLE: - A study of the pleurodesis potential of talc, iodopovidone, doxacycline and silver nitrate in experimental and clinical conditions in patients with malignant pleural effusions.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Folia Med (Plovdiv). 2013 Apr-Jun;55(2):82-3.

AUTORES / AUTHORS: - Yankulov AD

INSTITUCIÓN / INSTITUTION: - Clinic of Thoracic and Abdominal Surgery, Department of Special Surgery, St. George University Hospital, Medical University, Plovdiv, Bulgaria.

[554]

TÍTULO / TITLE: - Serum BMP-2 Up-regulation as an Indicator of Poor Survival in Advanced Non-small Cell Lung Cancer Patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5293-9.

AUTORES / AUTHORS: - Fei ZH; Yao CY; Yang XL; Huang XE; Ma SL

INSTITUCIÓN / INSTITUTION: - The Second Clinical College, Zhejiang Chinese Medical University, Hangzhou, China E-mail : huangxinen06@aliyun.com, mashenglin@medmail.com.cn.

RESUMEN / SUMMARY: - Purpose: High levels of bone morphogenetic protein (BMPs) have been reported in patients with lung cancer. This study was conducted to assess

correlations between serum BMP-2 levels and prognostic outcome in patients with non-small-cell lung cancer (NSCLC). Methods: Blood samples from 84 patients with advanced NSCLC and 42 healthy controls were analyzed and quantitated for serum BMP-2 levels before and after two cycles of chemotherapy using a commercially available ELISA kit. Results: The median level of BMP-2 was 146.9 pg/ml in patients with NSCLC vs. 87.7 pg/ml in healthy controls ($P < 0.01$). A significant correlation was observed between pretreatment serum BMP-2 level and ECOG PS, disease stage and number of organs with metastases ($P < 0.05$). Serum BMP-2 level decreased significantly in patients who achieved objective response after two cycles of chemotherapy. Multivariate analysis showed that increased BMP-2 level and advanced clinical stage were significantly correlated with poor prognosis. Conclusion: Serum BMP-2 level is positively correlated with clinical stage, ECOG PS and metastatic burden and may serve as an independent negative predictor for prognosis. Decreased BMP-2 after chemotherapy could be a reliable marker for efficacy of treatment.

[555]

TÍTULO / TITLE: - Clinical Outcome With Platinum-Based Chemotherapy in Patients With Advanced Nonsquamous EGFR Wild-Type Non-Small-Cell Lung Cancer Segregated According to KRAS Mutation Status.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Oct 17. pii: S1525-7304(13)00179-4. doi: 10.1016/j.clcc.2013.08.002.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.08.002](#)

AUTORES / AUTHORS: - Metro G; Chiari R; Bennati C; Cenci M; Ricciuti B; Puma F; Flacco A; Rebonato A; Giannarelli D; Ludovini V; Bellezza G; Ferolla P; Minotti V; Crino L

INSTITUCIÓN / INSTITUTION: - Medical Oncology, Santa Maria della Misericordia Hospital, Azienda Ospedaliera di Perugia, Perugia, Italy. Electronic address: giulio.metro@yahoo.com.

RESUMEN / SUMMARY: - BACKGROUND: We hypothesized that KRAS mutations function as a marker of poor sensitivity to first-line platinum-based chemotherapy in patients with advanced nonsquamous EGFR wild-type (WT) non-small-cell lung cancer (NSCLC). PATIENTS AND METHODS: Consecutive advanced nonsquamous EGFR WT NSCLCs treated at the Medical Oncology of Perugia with simultaneous assessment of KRAS mutation status were eligible. Anaplastic lymphoma kinase (ALK) gene status was known in roughly half of the patients who had KRAS WT. RESULTS: Two hundred four patients were included. Among them, the 77 individuals carrying a KRAS-mutant phenotype experienced a significantly inferior outcome in terms of response rate ($P = .04$), disease control rate ($P = .05$), and progression-free survival (PFS) ($P = .05$) compared with the EGFR WT/KRAS WT population. The association between KRAS mutation and shorter PFS remained statistically significant at multivariate analysis (hazard ratio [HR], 1.45). In addition, patients with KRAS mutations reported a significantly shorter overall survival (OS) compared with patients with EGFR WT/KRAS WT/ALK negativity ($n = 64$) ($P = .02$). Among patients with KRAS mutations, those harboring a mutation at codon 13 ($n = 12$) performed worse than those with a mutation at codon 12 ($n = 62$) in terms of both PFS and OS ($P = .09$ for both). CONCLUSION: KRAS mutation appears to negatively affect sensitivity to first-

line platinum-based chemotherapy in patients with advanced nonsquamous EGFR WT NSCLC. Studies on larger case series are needed to address differences in clinical outcome according to the type of mutation.

[556]

TÍTULO / TITLE: - Timeliness of care and prognosis in patients with lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ir J Med Sci. 2013 Oct 4.

●● Enlace al texto completo (gratis o de pago) [1007/s11845-013-1025-8](#)

AUTORES / AUTHORS: - Gonzalez-Barcala FJ; Falagan JA; Garcia-Prim JM; Valdes L; Carreira JM; Puga A; Martin-Lancharro P; Garcia-Sanz MT; Anton-Sanmartin D; Canive-Gomez JC; Pose-Reino A; Lopez-Lopez R

INSTITUCIÓN / INSTITUTION: - Servicio de Neumología, Hospital Clínico-Universitario, C/Choupana SN, 15706, Santiago de Compostela, España,

francisco.javier.gonzalez.barcala@sergas.es.

RESUMEN / SUMMARY: - BACKGROUND: Timeliness of care is an important dimension of health care quality. The determining factors of less timely care and their influence on the survival of patients with lung cancer (LC) remain uncertain. AIMS: To analyse the delays in the diagnosis and treatment of LC in our health area, the factors associated with the timeliness of care and their possible relationship with the survival of these patients. METHODS: A retrospective study was conducted on all patients with a cytologically confirmed diagnosis of LC between 1 June 2005 and 31 May 2008. The time delays for consultation (specialist delay), diagnosis (diagnosis delay), and treatment (treatment delay), were analysed, as well as the factors associated with these delays and the influence of the timeliness of care on survival. RESULTS: A total of 307 cases were included (87 % males). The mean specialist delay was 53.6 days (median 35 days), diagnosis delay 31.5 days (median 18 days), treatment delay 23.5 days (median 14 days). The greater age of the patient and a more advanced stage were associated with a shorter specialist delay. Male sex, a more advanced stage, and poor general status were associated with a shorter treatment delay. The survival is longer in patients with a longer treatment delay. CONCLUSIONS: The delay in the diagnosis in our population seems to be excessively long. The greater the age, a more advanced tumour stage, male sex, and poor general health status are associated with shorter delays. A longer treatment delay is associated with a longer survival.

[557]

TÍTULO / TITLE: - Chemoprevention of lung cancer: prospects and disappointments in human clinical trials.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancers (Basel). 2013 Jan 24;5(1):131-48. doi: 10.3390/cancers5010131.

●● Enlace al texto completo (gratis o de pago) [3390/cancers5010131](#)

AUTORES / AUTHORS: - Greenberg AK; Tsay JC; Tchou-Wong KM; Jorgensen A; Rom WN

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary, Critical Care, and Sleep Medicine, Departments of Medicine and Environmental Medicine, New York University School of Medicine, New York, NY 10016, USA. alissa.greenberg@nyumc.org.

RESUMEN / SUMMARY: - Decreasing the risk of lung cancer, or preventing its development in high-risk individuals, would have a huge impact on public health. The most effective means to decrease lung cancer incidence is to eliminate exposure to carcinogens. However, with recent advances in the understanding of pulmonary carcinogenesis and the identification of intermediate biomarkers, the prospects for the field of chemoprevention research have improved dramatically. Here we review the most recent research in lung cancer chemoprevention-focusing on those agents that have been investigated in human clinical trials. These agents fall into three major categories. First, oxidative stress plays an important role in pulmonary carcinogenesis; and therefore, antioxidants (including vitamins, selenium, green tea extracts, and isothiocyanates) may be particularly effective in preventing the development of lung cancer. Second, inflammation is increasingly accepted as a crucial factor in carcinogenesis, and many investigators have focused on anti-inflammatory agents, such as glucocorticoids, NSAIDs, statins, and PPARgamma agonists. Finally, the PI3K/AKT/mTOR pathway is recognized to play a central role in tobacco-induced carcinogenesis, and inhibitors of this pathway, including myoinositol and metformin, are promising agents for lung cancer prevention. Successful chemoprevention will likely require targeting of multiple pathways to carcinogenesis-both to minimize toxicity and maximize efficacy.

[558]

TÍTULO / TITLE: - Immunotherapy for lung cancer: ongoing clinical trials.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Future Oncol. 2013 Oct 22.

- [Enlace al texto completo \(gratis o de pago\) 2217/fon.13.166](#)

AUTORES / AUTHORS: - Declerck S; Vansteenkiste J

INSTITUCIÓN / INSTITUTION: - Respiratory Oncology Unit (Department of Pulmonology) & Leuven Lung Cancer Group, University Hospital KU Leuven, Leuven, Belgium.

RESUMEN / SUMMARY: - Modulation of a patient's immune system so that it acts against lung cancer cells has not been successful in the past decades. Advances in our understanding of the immune response to tumors resulted in the development of different kinds of novel immunotherapeutic agents. This has resulted in the development of two major approaches. First, antigen-specific immunotherapy or cancer vaccination, with the MAGE-A3 vaccine in resected early-stage non-small-cell lung cancer (NSCLC), the L-BLP25 vaccine in locally advanced NSCLC after chemoradiotherapy and belagenpumatucel-L and the TG4010 vaccine in advanced-stage NSCLC. Second, non-antigen-specific immunotherapy or cancer immunomodulation is reviewed, including how monoclonal antibodies modulate the interaction between antigen-presenting cells, T-lymphocytes and tumor cells (e.g., antibodies against CTLA-4, or against PD-1 receptor or its ligands). Recent Phase II trials with these treatments have shown promising results of efficacy and tolerability, which has led to testing in several large Phase III trials. Some of these are fully recruited, while others are still ongoing, and important results are expected in the near future.

[559]

TÍTULO / TITLE: - The predictive value of 53BP1 and BRCA1 mRNA expression in advanced non-small-cell lung cancer patients treated with first-line platinum-based chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncotarget. 2013 Oct;4(10):1572-81.

AUTORES / AUTHORS: - Bonanno L; Costa C; Majem M; Sanchez JJ; Gimenez-Capitan A; Rodriguez I; Vergnenegre A; Massuti B; Favaretto A; Rugge M; Pallares C; Taron M; Rosell R

INSTITUCIÓN / INSTITUTION: - Second Medical Oncology Unit, Istituto Oncologico Veneto I.R.C.C.S, Via Gattamelata 64, Padova, Italia.

RESUMEN / SUMMARY: - Platinum-based chemotherapy is the standard first-line treatment for non-oncogene-addicted non-small cell lung cancers (NSCLCs) and the analysis of multiple DNA repair genes could improve current models for predicting chemosensitivity. We investigated the potential predictive role of components of the 53BP1 pathway in conjunction with BRCA1. The mRNA expression of BRCA1, MDC1, CASPASE3, UBC13, RNF8, 53BP1, PIAS4, UBC9 and MMSET was analyzed by real-time PCR in 115 advanced NSCLC patients treated with first-line platinum-based chemotherapy. Patients expressing low levels of both BRCA1 and 53BP1 obtained a median progression-free survival of 10.3 months and overall survival of 19.3 months, while among those with low BRCA1 and high 53BP1 progression-free survival was 5.9 months (P less than 0.0001) and overall survival was 8.2 months (P=0.001). The expression of 53BP1 refines BRCA1-based predictive modeling to identify patients most likely to benefit from platinum-based chemotherapy.

[560]

TÍTULO / TITLE: - Acquired Resistance to Targeted Therapies Against Oncogene-Driven Non-Small-Cell Lung Cancer: Approach to Subtyping Progressive Disease and Clinical Implications.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Oct 12. pii: S1525-7304(13)00220-9. doi: 10.1016/j.clcc.2013.10.001.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.clcc.2013.10.001](#)

AUTORES / AUTHORS: - Gandara DR; Li T; Lara PN; Kelly K; Riess JW; Redman MW; Mack PC

INSTITUCIÓN / INSTITUTION: - Division of Hematology and Oncology, University of California, Davis, Sacramento, CA. Electronic address: david.gandara@ucdmc.ucdavis.edu.

RESUMEN / SUMMARY: - In the emerging era of targeted therapy for advanced-stage non-small-cell lung cancer, it is becoming increasingly important to anticipate underlying driver oncogene alterations at the time of initial diagnosis and tumor-tissue acquisition, so that patients can be selected in a timely fashion for first-line tyrosine kinase inhibitor (TKI) therapy if their cancers are found to harbor tyrosine-kinase-activating mutations in the epidermal growth factor receptor gene or gain-of-function rearrangements in the anaplastic lymphoma kinase gene. However, despite the clear benefits of TKI therapy over chemotherapy in these settings, the eventual emergence of acquired resistance and progressive disease (PD) is universal. How to best approach oncogene-driven non-small-cell lung cancer at the time of acquired resistance to initial TKI therapy is an increasingly complex question because of

variability in mechanisms of resistance, extent of PD, and inter- and inpatient tumor heterogeneity. Here we propose an approach to subtyping PD in the setting of acquired resistance as well as subsequent clinical implications.

[561]

TÍTULO / TITLE: - Concomitant occurrence of EGFR (epidermal growth factor receptor) and KRAS (V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog) mutations in an ALK (anaplastic lymphoma kinase)-positive lung adenocarcinoma patient with acquired resistance to crizotinib: a case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Res Notes. 2013 Nov 26;6(1):489.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1756-0500-6-489](#)

AUTORES / AUTHORS: - Rossing HH; Grauslund M; Urbanska EM; Melchior LC; Rask CK; Costa JC; Skov BG; Sorensen JB; Santoni-Rugiu E

RESUMEN / SUMMARY: - BACKGROUND: Anaplastic lymphoma kinase-positive non-small cell lung carcinoma patients are generally highly responsive to the dual anaplastic lymphoma kinase and MET tyrosine kinase inhibitor crizotinib. However, they eventually acquire resistance to this drug, preventing the anaplastic lymphoma kinase inhibitors from having a prolonged beneficial effect. The molecular mechanisms responsible for crizotinib resistance are beginning to emerge, e.g., in some anaplastic lymphoma kinase-positive non-small cell lung carcinomas the development of secondary mutations in this gene has been described. However, the events behind crizotinib-resistance currently remain largely uncharacterized. Thus, we report on an anaplastic lymphoma kinase-positive non-small cell lung carcinoma patient with concomitant occurrence of epidermal growth factor receptor and V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog mutations upon development of crizotinib-resistance. CASE PRESENTATION: A 61-year-old Caucasian never-smoking male was diagnosed with anaplastic lymphoma kinase -positive pulmonary adenocarcinoma, stage T4N3M1b. Treatment with crizotinib initially resulted in complete objective response in the thorax and partial response in the abdomen, but after 8 months of therapy the patient acquired resistance and progressed. Biopsies from new metastases revealed development of epidermal growth factor receptor and V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog mutations concomitant with the original anaplastic lymphoma kinase gene rearrangement and without signs of anaplastic lymphoma kinase fusion gene amplification or secondary anaplastic lymphoma kinase mutations. CONCLUSION: To our knowledge, this is the first report of an anaplastic lymphoma kinase-positive pulmonary adenocarcinoma, which upon emergence of crizotinib resistance acquired 2 new somatic mutations in the epidermal growth factor receptor and V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog genes, respectively, concomitant with the original anaplastic lymphoma kinase rearrangement. Thus, these 3 driver mutations, usually considered mutually exclusive, may coexist in advanced non-small cell lung carcinoma that becomes resistant to crizotinib, presumably because heterogeneous tumor clones utilize epidermal growth factor receptor and/or V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog signaling to circumvent the inhibition of anaplastic lymphoma kinase-mediated signaling by crizotinib. The identification of new targetable somatic mutations by tumor re-biopsy may help clarify the mechanism behind the development of the acquired crizotinib resistance and pave the way for combined strategies involving multiple targeted therapies.

[562]

TÍTULO / TITLE: - Human leptin protein induces proliferation of A549 cells via inhibition of PKR-like ER kinase and activating transcription factor-6 mediated apoptosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Yonsei Med J. 2013 Nov;54(6):1407-15. doi: 10.3349/ymj.2013.54.6.1407.

●● Enlace al texto completo (gratis o de pago) [3349/ymj.2013.54.6.1407](#)

AUTORES / AUTHORS: - Lai Q; Sun Y

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, General Hospital of Zaozhuang Mining Group, Qi lian shan Road 12, Shandong, Zaozhuang 277000, China. laiqunzz@yeah.net.

RESUMEN / SUMMARY: - PURPOSE: To investigate the anti-apoptotic mechanism of leptin in non-small cell lung cancer. MATERIALS AND METHODS: The influences of leptin on apoptosis were investigated, analyzing the mechanism that triggers growth of A549 cells. The effects of leptin on cell proliferation were examined by XTT analysis. Leptin, C/EBP homologous protein (CHOP), phosphorylated-PKR-like ER kinase (p-Perk), inositol requiring proteins-1, spliced X-box transcription factor-1 (XBP1), cleaved activating transcription factor-6 (ATF6), eukaryotic translation initiation factor-2alpha, caspase-12 and CHOP protein were detected in four groups by western blot, and endoplasmic reticulum (ER) stress related mRNA were detected by reverse transcription PCR. RESULTS: The expression of leptin in A549 and leptin transfected cells inhibited cisplatin activated ER stress-associated mRNA transcription and protein activation. Two ER stress unfolded protein response pathways, PERK and ATF6, were involved, and XBP1 and tumor necrosis factor receptor-associated factor 2 (TRAF2) were increased significantly when treated with cisplatin in A549-siRNA against leptin cells. Furthermore, CHOP expression was inhibited upon leptin expression in A549, LPT-PeP and LPT-EX cells. CONCLUSION: Leptin serves as an important factor that promotes the growth of A549 cells through blocking ER stress-mediated pathways. This blocking is triggered by p-Perk and ATF6 via inhibition of CHOP expression.

[563]

TÍTULO / TITLE: - Plasminogen Activator Inhibitor Type 1 () A15T Gene Polymorphism Is Associated with Prognosis in Patients with Mutation Positive Pulmonary Adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tuberc Respir Dis (Seoul). 2013 Oct;75(4):140-149. Epub 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [4046/trd.2013.75.4.140](#)

AUTORES / AUTHORS: - Lim JE; Park MS; Kim EY; Jung JY; Kang YA; Kim YS; Kim SK; Shim HS; Cho BC; Chang J

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Hongik Hospital, Seoul, Korea.

RESUMEN / SUMMARY: - BACKGROUND: Plasminogen activator inhibitor type 1 (PAI-1), an important regulator of plasminogen activator system which controls degradation of extracellular membrane and progression of tumor cells, and PAI-1 gene polymorphic variants have been known as the prognostic biomarkers of non-small cell lung cancer

patients. Recently, experimental in vitro study revealed that transforming growth factor-beta1 initiated PAI-1 transcription through epithelial growth factor receptor (EGFR) signaling pathway. However, there is little clinical evidence on the association between PAI-1 A15T gene polymorphism and prognosis of Korean population with pulmonary adenocarcinoma and the influence of activating mutation of EGFR kinase domain. METHODS: We retrospectively reviewed the medical records of 171 patients who were diagnosed with pulmonary adenocarcinoma and undergone EGFR mutation analysis from 1995 through 2009. RESULTS: In all patients with pulmonary adenocarcinoma, there was no significant association between PAI-1 A15T polymorphic variants and prognosis for overall survival. However, further subgroup analysis showed that the group with AG/AA genotype had a shorter 3-year survival time than the group with GG genotype in patients with EGFR mutant-type pulmonary adenocarcinoma (mean survival time, 24.9 months vs. 32.5 months, respectively; $p=0.015$). In multivariate analysis of 3-year survival for patients with pulmonary adenocarcinoma harboring mutant-type EGFR, the AG/AA genotype carriers had poorer prognosis than the GG genotype carriers (hazard ratio, 7.729; 95% confidence interval, 1.414-42.250; $p=0.018$). CONCLUSION: According to our study of Korean population with pulmonary adenocarcinoma, AG/AA genotype of PAI-1 A15T would be a significant predictor of poor short-term survival in patients with pulmonary adenocarcinoma harboring mutant-type EGFR.

[564]

TÍTULO / TITLE: - LUNX mRNA-positive cells at different time points predict prognosis in patients with surgically resected nonsmall cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Transl Res. 2013 Oct 10. pii: S1931-5244(13)00303-4. doi: 10.1016/j.trsl.2013.09.010.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.trsl.2013.09.010](#)

AUTORES / AUTHORS: - Li J; Shi SB; Shi WL; Wang Y; Yu LC; Zhu LR; Ge LP

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, Department of Thoracic Surgery, and Center of Experimental Medicine, Affiliated Hospital of Jiangsu University, Zhenjiang, China. Electronic address: ljjian541226@163.com.

RESUMEN / SUMMARY: - LUNX is a lung-specific gene whose messenger ribonucleic acid (mRNA) expression is strictly limited to normal lung tissue and nonsmall cell lung cancer (NSCLC) tissue. The aim of this study was to investigate whether the detection of LUNX mRNA-positive circulating tumor cells (CTC)s in peripheral blood at different time points is useful for predicting disease recurrence, disease-free survival (DFS), and overall survival (OS) in NSCLC patients undergoing surgery. Serial blood samples from 68 patients with stage I-III NSCLC were examined by real-time quantitative polymerase chain reaction assay targeting LUNX mRNA before (T0) and after surgery (T1) and after the completion of adjuvant chemotherapy (T2). Results showed that LUNX mRNA-positive CTCs were detected in 40 of 68 NSCLC patients (58.8%) before surgery; the detection rates of LUNX mRNA-positive CTCs at T1 and T2 time points were 32.4% (22/68) and 33.3% (20/60), respectively. The detection of LUNX mRNA-positive CTC at 3 time points was associated with lymph node status and pathologic stage. During the follow-up period, patients with LUNX mRNA-positive CTC at 3 time points had a higher relapse rate and a shorter DFS and OS than those without. Multivariate analysis revealed that presence of LUNX mRNA-positive CTC at T1 and

T2 time points was an independent unfavorable factor for DFS and OS. In conclusion, detection of LUNX mRNA-positive CTC after surgery and the completion of adjuvant chemotherapy in patients with stage I-III NSCLC are highly predictive for DFS and OS. This technique could aid in the prediction of prognosis and design of tailored treatment.

[565]

TÍTULO / TITLE: - Clinical significance of preoperative neutrophil lymphocyte ratio versus platelet lymphocyte ratio in patients with small cell carcinoma of the esophagus.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - ScientificWorldJournal. 2013 Sep 5;2013:504365. doi: 10.1155/2013/504365.

●● Enlace al texto completo (gratis o de pago) [1155/2013/504365](#)

AUTORES / AUTHORS: - Feng JF; Huang Y; Zhao Q; Chen QX

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Zhejiang Cancer Hospital, No. 38 Guangji Road, Banshan Bridge, Hangzhou 310022, China.

RESUMEN / SUMMARY: - Recent studies have shown that the presence of systemic inflammation correlates with poor survival in various of cancers. The aim of this study was to determine the prognostic values of neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) in patients with small cell carcinoma of the esophagus (SCCE). Preoperative NLR and PLR were evaluated in 43 patients with SCCE from January 2001 to December 2010. The prognostic significance of both markers was then determined by both uni- and multivariate analytical methods. Receiver operating characteristic (ROC) curves were also plotted to verify the accuracy of NLR and PLR for survival prediction. Patients with PLR ≥ 150 had significantly poorer (relapse-free survival) RFS and (overall survival) OS compared to patients with PLR < 150 . However, RFS or OS did not differ according to NLR categories (< 3.5 and ≥ 3.5). The areas under the curve (AUC) indicated that PLR was superior to NLR as a predictive factor. The results of the present study conclude that PLR is superior to NLR as a predictive factor in patients with SCCE.

[566]

TÍTULO / TITLE: - The significant increase and dynamic changes of the myeloid-derived suppressor cells percentage with chemotherapy in advanced NSCLC patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Transl Oncol. 2013 Nov 6.

●● Enlace al texto completo (gratis o de pago) [1007/s12094-013-1125-y](#)

AUTORES / AUTHORS: - Wang S; Fu Y; Ma K; Liu C; Jiao X; Du W; Zhang H; Wu X

INSTITUCIÓN / INSTITUTION: - Department of Biotherapy and Laboratory of Biotherapy, The Fourth Affiliated Hospital of China Medical University, Shenyang, 110032, China, sywang66@yahoo.com.

RESUMEN / SUMMARY: - PURPOSE: To investigate the correlations between myeloid-derived suppressor cells (MDSCs) in the peripheral blood and cancer stage, immune function, and chemotherapy. METHODS: Percentages of MDSCs (CD11b+CD14-CD33+ cells) and lymphocyte subsets in peripheral blood mononuclear cells (PBMCs) of 94 patients with Non-small cell lung cancer (NSCLC) who were treated naive and 30 healthy individuals were measured. Changes of the MDSCs percentage were further detected in patients with advanced NSCLC treated with systemic chemotherapy.

Finally, coculture with CD8+ cells was developed to determine effect of MDSCs on IFN-gamma secretion of T lymphocytes. RESULTS: MDSCs percentage of 94 patients with NSCLC was significantly higher than that of 30 healthy subjects ($P < 0.05$), the percentages were increased with tumor progression, in patients with stage III and IV percentages were significantly higher than those in stage I and II patients ($P = 0.013$). The MDSCs percentage was negatively related to percentage of CD8+ cells in the peripheral blood ($r = -0.354$, $n = 38$, $P = 0.029$), and when they were cocultured, IFN-gamma secretion of CD8+ cells was significantly decreased ($P < 0.05$). In 20 patients with advanced NSCLC who received systemic chemotherapy, nine partial remission (PR) cases got MDSCs percentage significantly decreased ($P < 0.001$), three stable disease (SD) cases remained invariable ($P = 0.307$) and eight progressive disease (PD) cases got significantly increased ($P = 0.024$). CONCLUSION: The percentage of MDSCs in the patients was significantly higher than that of the healthy control subjects and it increased with tumor progression partially by inhibiting the CD8+ cell function. The dynamic changes of MDSCs percentage reflected the efficacy of systemic chemotherapy.

[567]

TÍTULO / TITLE: - Fluorodeoxyglucose positron-emission tomography ratio in non-small cell lung cancer patients treated with definitive radiotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiat Oncol J. 2013 Sep;31(3):111-7. doi: 10.3857/roj.2013.31.3.111. Epub 2013 Sep 30.

•• Enlace al texto completo (gratis o de pago) [3857/roj.2013.31.3.111](#)

AUTORES / AUTHORS: - Kang HC; Wu HG; Yu T; Kim HJ; Paeng JC

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Seoul National University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: To determine whether the maximum standardized uptake value (SUV) of [(18)F] fluorodeoxyglucose uptake by positron emission tomography (FDG PET) ratio of lymph node to primary tumor (mSUVR) could be a prognostic factor for node positive non-small cell lung cancer (NSCLC) patients treated with definitive radiotherapy (RT). MATERIALS AND METHODS: A total of 68 NSCLC T1-4, N1-3, M0 patients underwent FDG PET before RT. Optimal cutoff values of mSUVR were chosen based on overall survival (OS). Independent prognosticators were identified by Cox regression analysis. RESULTS: The most significant cutoff value for mSUVR was 0.9 with respect to OS. Two-year OS was 17% for patients with mSUVR > 0.9 and 49% for those with mSUVR ≤ 0.9 ($p = 0.01$). In a multivariate analysis, including age, performance status, stage, use of chemotherapy, and mSUVR, only performance status ($p = 0.05$) and mSUVR > 0.9 ($p = 0.05$) were significant predictors of OS. Two-year OS for patients with both good performance (Eastern Cooperative Oncology Group [ECOG] ≤ 1) and mSUVR ≤ 0.9 was significantly better than that for patients with either poor performance (ECOG > 1) or mSUVR > 0.9 , 23% (71% vs. 23%, $p = 0.04$). CONCLUSION: Our results suggested that the mSUVR was a strong prognostic factor among patients with lymph node positive NSCLC following RT. Addition of mSUVR to performance status identifies a subgroup at highest risk for death after RT.

[568]

TÍTULO / TITLE: - Safety of polyethylene glycol recombinant human granulocyte colony-stimulating factor in treating non-small cell lung cancer patients at I b stage.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Trop Med. 2013 Nov;6(11):912-5. doi: 10.1016/S1995-7645(13)60163-7.

●● Enlace al texto completo (gratis o de pago) [1016/S1995-7645\(13\)60163-7](#)

AUTORES / AUTHORS: - Yan B; Zhang W; Lu F; Chen ZL; Han BH; Jiang LY

INSTITUCIÓN / INSTITUTION: - Respiratory Department, Affiliated Chest Hospital of Shanghai Jiaotong University, Shanghai 200030, China.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate resistance and safety of HHPG-19K in treating non-small cell lung cancer patients. METHODS: A total of 30 cases were selected and randomly divided into 5 groups: three HHPG-19K groups of different dosage (60 mug/kg/day, 100 mug/kg/day, 200 mug/kg/day), positive control group (Filgrastim, namely G-CSF5 mug/kg/day) and negative control group. Safety indexes of 5 groups were observed and compared. RESULTS: All patients had adverse event (100%) in three HHPG-19K groups, and increased ALP, ALT and AST were main events. The degree was mild to moderate. There was no significant difference in the incidence of adverse event between dosage groups and positive control group no difference. But the incidence of negative control group was 13%, which was significantly lower than dosage groups and positive control group. CONCLUSIONS: non-small cell lung cancer patients have satisfactory tolerance to HHPG-19K, and have no resistance. Besides, dosage at 100 mu g/kg is the most safe.

[569]

TÍTULO / TITLE: - An extremely elderly patient with lung cancer who underwent surgery.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013;19(5):382-5. Epub 2013 Oct 3.

AUTORES / AUTHORS: - Watanabe Y; Yonechi A; Inoue T; Kanno R; Oishi A; Suzuki H
INSTITUCIÓN / INSTITUTION: - The First Department of surgery, Fukushima Medical University, Hikarigaoka, Fukushima, Japan.

RESUMEN / SUMMARY: - We report the case of an extremely elderly patient with long-term survival after surgical resection for lung cancer. A 93-year-old man was evaluated for an abnormal density on chest radiography. Chest computed tomography (CT) showed a nodular density of 2.5 x 2.5 cm in the left S4b segment. Lung cancer was diagnosed by bronchoscopy, and left posterolateral thoracotomy and S4 segmentectomy were performed. Group 1 lymph node dissection and sampling of the 6th lymph node were also performed. Pathological examination revealed poorly differentiated squamous cell carcinoma without any lymph node metastases. The tumor was staged as p-T1aN0M0 stage IA. No complications were encountered postoperatively, and the patient was discharged. He remains alive as of 5 years postoperatively without any recurrence.

[570]

TÍTULO / TITLE: - Age is a prognostic factor affecting survival in lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Nov;6(5):1507-1513. Epub 2013 Sep 6.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1566](http://dx.doi.org/10.3892/ol.2013.1566)

AUTORES / AUTHORS: - Tas F; Ciftci R; Kilic L; Karabulut S

INSTITUCIÓN / INSTITUTION: - Institute of Oncology, University of Istanbul, Capa, Istanbul 34390, Turkey.

RESUMEN / SUMMARY: - Despite all efforts at management, prognosis of advanced lung cancer is extremely poor, with a median survival time of ~1 year. The number of cancer patients aged >70 years is significantly increased among the cancer patient population. The aim of this study was to investigate the clinical importance of age in lung cancer. Data from 110 patients with histologically confirmed lung cancer, who were treated and followed up in the Institute of Oncology, University of Istanbul, were recorded from medical charts. There were 100 (91%) males with a median age of 59 years (range, 35-88 years). The majority of patients had non-small cell lung cancer (NSCLC; 84%) and metastatic stage (56%). The rate of positive response to chemotherapy was lower in elderly patients ($P=0.01$) and the incidence of anemia was higher compared with that in younger patients ($P=0.02$). The majority of mortalities occurred in elderly patients ($P=0.01$). The median survival time of elderly patients was significantly lower compared with that of younger patients (37.8 vs. 57 weeks; $P=0.009$). The 1-year survival rates in younger and elderly patients were 67.3 and 42.5%, respectively. In multivariate analysis, elderly patients also had significantly poorer survival ($P=0.023$). In the group of elderly patients, analyses revealed that significant prognostic factors, including stage of disease and serum lactate dehydrogenase (LDH) levels, were associated with survival. Elderly patients diagnosed with small cell lung cancer had a poorer outcome compared with those with NSCLC ($P=0.009$), and older patients with elevated serum LDH levels had a shorter survival time compared with those with normal levels ($P=0.042$). In conclusion, age is one of the major prognostic factors affecting survival in lung cancer patients; therefore, patients should be managed according to age in clinical practice.

[571]

TÍTULO / TITLE: - Expression and clinical significance of IGF-1, IGFBP-3, and IGFBP-7 in serum and lung cancer tissues from patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Oct 16;6:1437-44. doi: 10.2147/OTT.S51997.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S51997](http://dx.doi.org/10.2147/OTT.S51997)

AUTORES / AUTHORS: - Wang Z; Wang Z; Liang Z; Liu J; Shi W; Bai P; Lin X; Magaye R; Zhao J

INSTITUCIÓN / INSTITUTION: - Jinan University, Guangzhou, Guangdong, People's Republic of China ; The Affiliated Hospital of Guangdong Medical College, Zhanjiang, Guangdong, People's Republic of China.

RESUMEN / SUMMARY: - The expression and clinical significance of insulin-like growth factor 1 (IGF-1), insulin-like growth factor binding protein 3 (IGFBP-3), and insulin-like growth factor binding protein 7 (IGFBP-7) were investigated in serum and lung cancer tissues from 57 patients with non-small cell lung cancer (NSCLC). Lung cancer tissues at different pathologic stages (27 patients at stages I-II and 30 patients at stages III-IV), normal lung tissues from 17 patients with benign pulmonary disease, and serum samples from both lung cancer and benign pulmonary disease patients were collected

during surgery. Enzyme-linked immunosorbent assay and avidin-biotin-peroxidase complex immunohistochemical staining were used to detect IGF-1, IGFBP-3, and IGFBP-7 expression in serum and tissues, respectively. The results show that expression of IGF-1 in lung cancer tissues and serum from NSCLC patients were significantly higher than in the control ($P < 0.05$). However, expression of IGFBP-3 and IGFBP-7 in cancer tissues and serum from NSCLC patients was significantly lower than in the control ($P < 0.05$). These results suggest that upregulation of IGF-1 and downregulation of IGFBP-3 and IGFBP-7 may be potential diagnostic biomarkers for NSCLC.

[572]

TÍTULO / TITLE: - Variation of blood T lymphocyte subgroups in patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4671-3.

AUTORES / AUTHORS: - Wang WJ; Tao Z; Gu W; Sun LH

INSTITUCIÓN / INSTITUTION: - Department of Infectious Diseases, Nanjing First Hospital, Nanjing Medical University, Nanjing, China E-mail : tz1010@126.com.

RESUMEN / SUMMARY: - OBJECTIVES: To study variation in T lymphocyte subgroups and its clinical significance in non-small cell lung cancer (NSCLC). METHODS: Levels of CD3+ , CD4+ , CD8+ , CD4+/CD8+ , NK and Treg cells in peripheral blood of NSCLC cases and healthy adults were determined by flow cytometry. RESULTS: CD3+ , CD4+ and CD4+/CD8+ ratio and NK cells in NSCLCs were decreased significantly in comparison with the control group ($P < 0.01$), and decreased with increase in the clinical stage of NSCLC, while CD8+ cells demonstrated no significant change ($P > 0.05$). Treg cells were significantly more frequent than in the control group ($P < 0.01$), and increased with the clinical stage of NSCLC. CONCLUSION: The cellular immune function of the NSCLC patients is lowered. It is important to detect change of T lymphocyte subgroups by flow cytometry for the diagnosis, treatment and prognostic assessment of NSCLC patients.

[573]

TÍTULO / TITLE: - Anti scl-70 antibody positive systemic sclerosis in a patient with lung cancer: a paraneoplastic or a purely coincidental phenomenon?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Indian J Dermatol. 2013 Sep;58(5):400-1. doi: 10.4103/0019-5154.117326.

●● Enlace al texto completo (gratis o de pago) [4103/0019-5154.117326](https://doi.org/10.4103/0019-5154.117326)

AUTORES / AUTHORS: - Gangopadhyay A; Sen S; Naskar B; Chatterjee G

INSTITUCIÓN / INSTITUTION: - Department of Dermatology, IPGMER and SSKM Hospital, 240, AJC Bose Road, Kolkata, India. E-mail: dranu84@gmail.com.

[574]

TÍTULO / TITLE: - Three-Dimensional Pulmonary Model Using Rapid-Prototyping in Patient with Lung Cancer Requiring Segmentectomy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Nov 8.

AUTORES / AUTHORS: - Akiba T; Nakada T; Inagaki T

INSTITUCIÓN / INSTITUTION: - Department of Surgery, Jikei University Kashiwa Hospital, Chiba, Japan.

RESUMEN / SUMMARY: - Thoracoscopic pulmonary segmentectomy of the lung is sometime adopted for the lung cancer, but a problem with segmentectomy is variable anatomy. Recently, we are exploring the impact of three-dimensional models using rapid-prototyping technique. It is useful for decision making, surgical planning, and intraoperative orientation for surgical treatment in patient with lung cancer who underwent pulmonary segmentectomy. These newly created models allow us to clearly identify the surgical margin and the intersegmental plane, vessels, and bronchi related to the cancer in the posterior segment. To the best of our knowledge, there are few reports describing a pulmonary model so far.

[575]

TÍTULO / TITLE: - Comorbidity and survival of Danish lung cancer patients from 2000-2011: a population-based cohort study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Epidemiol. 2013 Nov 1;5(Suppl 1):31-8. doi: 10.2147/CLEP.S47473.

●● Enlace al texto completo (gratis o de pago) [2147/CLEP.S47473](#)

AUTORES / AUTHORS: - Deleuran T; Thomsen RW; Norgaard M; Jacobsen JB; Rasmussen TR; Sogaard M

INSTITUCIÓN / INSTITUTION: - Department of Clinical Epidemiology, Aarhus, Denmark ; Department of Medicine V, Hepatology and Gastroenterology, Aarhus, Denmark.

RESUMEN / SUMMARY: - **OBJECTIVE:** To examine lung cancer survival and the impact of comorbidity in the Central Denmark Region from 2000 to 2011. **METHODS:** We performed a population-based cohort study of lung cancer patients diagnosed during four 3-year calendar periods (2000-2002, 2003-2005, 2006-2008, and 2009-2011) in the Central Denmark Region. The Danish National Registry of Patients was used to identify 9,369 incident lung cancer patients, and to obtain data on their Charlson comorbidity index score, categorized as no (score = 0), medium (score = 1-2), or high (score \geq 3) level comorbidity. We calculated 1- and 5-year survival in different calendar time periods overall, and by age, sex, and level of comorbidity, and used Cox regression to compute mortality rate ratios (MRR) for each level of comorbidity versus no comorbidity in different calendar time periods. **RESULTS:** Overall 1-year survival increased from 31% in 2000-2002 to 37% in 2009-2011, while the 5-year survival increased from 10% in 2000-2002 to predicted 13% in 2009-2011 with the largest improvement observed for women and patients less than 80 years. The adjusted 1-year MRR in patients with high comorbidity compared with those without comorbidity was 1.23 (95% confidence interval [CI]: 1.05-1.46) in 2000-2002 and 1.35 (95% CI: 1.17-1.56) in 2009-2011. The corresponding adjusted 5-year MRRs were 1.21 (95% CI: 1.04-1.40) in 2000-2002 and 1.26 (95% CI: 1.11-1.42) in 2009-2011. **CONCLUSION:** Lung cancer patients' survival increased from 2000 to 2011 in the Central Denmark Region, most prominently for women under 80 years and patients with no, or medium level of comorbidity. Their prognosis remained nonetheless dismal

with overall 5-year survival of 13%, and comorbidity remained a negative prognostic factor.

[576]

TÍTULO / TITLE: - Serum proteomic study on EGFR-TKIs target treatment for patients with NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Oct 21;6:1481-91. doi: 10.2147/OTT.S51887.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S51887](#)

AUTORES / AUTHORS: - Wu X; Liang W; Hou X; Lin Z; Zhao H; Huang Y; Fang W; Zhao Y; Wu J; Yang Y; Xue C; Hu Z; Zhang J; Zhang J; Ma Y; Zhou T; Qin T; Zhang L

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Oncology in South China, Department of Medical Oncology, Sun Yat-sen University Cancer Center, Guangzhou, People's Republic of China.

RESUMEN / SUMMARY: - BACKGROUND: Although epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKIs) are widely used for EGFR mutated non-small-cell lung cancer (NSCLC) patients, tumor sample availability and heterogeneity of the tumor remain challenging for physicians' selection of these patients. Here, we developed a serum proteomic classifier based on matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF-MS) to predict the clinical outcome of patients treated with EGFR-TKIs. METHOD: A total of 68 patients were included in this study. All patients received EGFR-TKIs as second or third line treatment and blood samples were collected before treatment. Using magnetic bead assisted serum peptide capture coupled to MALDI-TOF-MS, pretreatment serum from 24 NSCLC patients was analyzed to develop a proteomic classifier (training set). In a blinded test set with 44 patients, each sample was classified into "good" or "poor" groups using this classifier. Survival analysis of each group was done based on this classification. RESULT: A 3-peptide proteomic classifier was developed from the training set. In the testing set, the classifier was able to distinguish patients of "good" or "poor" outcomes with 93% accuracy, sensitivity, and specificity. The overall survival and progression free survival of the predicted good group were found to be significantly longer than the poor group, not only in the whole population but also in certain subgroups, such as pathological adenocarcinoma and nonsmokers. With respect to the tumor samples available for EGFR mutation detection, all eight EGFR mutant tumors and three of the 12 wild type EGFR tumors were classified as good while nine of the 12 wild type EGFR tumors were classified as poor. CONCLUSION: The current study has shown that a proteomic classifier can predict the outcome of patients treated with EGFR-TKIs and may aid in patient selection in the absence of available tumor tissue. Further studies are necessary to confirm these findings.

[577]

TÍTULO / TITLE: - SIRT1 Expression Is Associated with the Chemotherapy Response and Prognosis of Patients with Advanced NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 5;8(11):e79162. doi: 10.1371/journal.pone.0079162.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079162](#)

AUTORES / AUTHORS: - Zhang T; Rong N; Chen J; Zou C; Jing H; Zhu X; Zhang W

INSTITUCIÓN / INSTITUTION: - Department of Cardiovascular Surgery, Provincial Hospital Affiliated to Shandong University, Shandong University, Jinan, Shandong Province, China.

RESUMEN / SUMMARY: - AIM: The role of Sirtuin 1 (SIRT 1) in carcinogenesis is controversial. This study was to explore the association between the SIRT1 expression and the clinical characteristics, the responsiveness to chemotherapy and prognosis in Non-small cell lung cancer (NSCLC). METHODS: We enrolled 295 patients with inoperable advanced stage of NSCLC, namely, stage III (A+B) and IV NSCLC. All patients had received platinum-based chemotherapy after diagnosis and the chemotherapy response were evaluated. All patients were followed up for overall survival (OS) and progression free survival (PFS). In vitro, H292 cells were transfected with SIRT1 small interfering RNA (siRNA). The cell biological behaviors and chemosensitivity to cisplatin treatment were studied. The in vivo tumorigenesis and metastasis assays were performed in nude mice. RESULTS: We found that the SIRT1 expressions were significantly associated with the tumor stage, tumor size and differentiation status. Patients with high SIRT 1 expressions had a significantly higher chance to be resistant to chemotherapy than those with low SIRT 1 expression. Patients with high expression of SIRT1 had significantly shorter OS and DFS than those with low expression. Cox analyses confirmed that the SIRT 1 expression was a strong predictor for a poor OS and PFS in NSCLC patients underwent Platinum-based chemotherapy. In vitro studies revealed that the reduced expression SIRT 1 by siRNA technique significantly inhibited cell proliferation, migration and invasion. More importantly, SIRT1 si-RNA significantly enhanced the chemosensitivity of H292 cells to cisplatin treatment. The in vivo tumorigenesis and metastasis assays showed that SIRT1 knockdown dramatically reduced the tumor volume and the metastatic ability in nude mice. CONCLUSION: Collectively, our data suggest that the SIRT1 expression may be a molecular marker associated with the NSCLC clinical features, treatment responsiveness and prognosis of advanced NSCLC.

[578]

TÍTULO / TITLE: - Therapeutic vaccines explored in patients with Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Anticancer Agents Med Chem. 2013 Nov 7.

AUTORES / AUTHORS: - Ma K; Tang YH

INSTITUCIÓN / INSTITUTION: - LSU Health Sciences Center, School of Medicine, 1501 Kings Hwy, P.O. Box 33932, Shreveport, LA 71130, USA. yahuitang2001@yahoo.fr.

RESUMEN / SUMMARY: - Traditional anti-cancer therapies (surgery, radiotherapy and chemotherapy) have limited effectiveness in curbing progression of advanced tumors. However, with advances in immunology and molecular biology in the last two decades, the prognosis of cancer immunotherapy has improved. An emerging therapy is the cancer vaccine as adjunctive therapy. The purpose of this paper is to review this therapeutic modality for non-small cell lung cancer.

[579]

TÍTULO / TITLE: - Improving care and quality of life for patients with lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nurs Stand. 2013 Oct 30;28(9):50-8. doi: 10.7748/ns2013.10.28.9.50.e8052.

- Enlace al texto completo (gratis o de pago)

[7748/ns2013.10.28.9.50.e8052](https://doi.org/10.7748/ns2013.10.28.9.50.e8052)

AUTORES / AUTHORS: - Bennett A; White J

INSTITUCIÓN / INSTITUTION: - Barnsley Hospital NHS Foundation Trust, South Yorkshire.

RESUMEN / SUMMARY: - Lung cancer is the most common cancer worldwide and is associated with significant morbidity and mortality. In recent years, there have been important developments in the techniques used to diagnose lung cancer and in the treatment options available, allowing more people to be given anti-cancer treatment with the aim of increasing survival rates. This article provides an overview of lung cancer, including epidemiology, risk factors, diagnosis and treatment. It aims to provide healthcare professionals with information to improve care delivery and patients' quality of life.

[580]

TÍTULO / TITLE: - Lung cancer mortality and exposure to polycyclic aromatic hydrocarbons in British coke oven workers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Public Health. 2013 Oct 16;13(1):962.

- Enlace al texto completo (gratis o de pago) [1186/1471-2458-13-962](https://doi.org/10.1186/1471-2458-13-962)

AUTORES / AUTHORS: - Miller BG; Doust E; Cherrie JW; Hurley JF

RESUMEN / SUMMARY: - BACKGROUND: Workers on coke oven plants may be exposed to potentially carcinogenic polycyclic aromatic hydrocarbons (PAHs), particularly during work on the ovens tops. Two cohorts, employees of National Smokeless Fuels (NSF) and the British Steel Corporation (BSC) totalling more than 6,600 British coke plant workers employed in 1967, had been followed up to mid-1987 for mortality. Previous analyses suggested an excess in lung cancer risk of around 25%, or less when compared with Social Class IV ('partly skilled'). Analyses based on internal comparisons within the cohorts identified statistical associations with estimates of individual exposures, up to the start of follow-up, to benzene-soluble materials (BSM), widely used as a metric for mixtures of PAHs. Some associations were also found with times spent in certain coke ovens jobs with specific exposure scenarios, but results were not consistent across the two cohorts and limitations in the exposure estimates were noted. The present study was designed to reanalyse the existing data on lung cancer mortality, incorporating revised and improved exposure estimates to BSM and to benzo[a]pyrene (B[a]P), including increments during the follow-up and a lag for latency. METHODS: Mean annual average concentrations of both BSM and B[a]P were estimated by analysis of variance (ANOVA) from concentration measurements at all NSF and six BSC plants, and summarised by job and plant, with a temporal trend (for the BSM only). These were combined with subjects' work histories, to produce exposure estimates in each year of follow-up, with a 10-year lag to allow for latency. Exposures to BSM and to B[a]P were sufficiently uncorrelated to permit analysis in relation to each variable separately. Lung cancer death risks during the follow-up were analysed in relation to the estimated time-dependent exposures, both continuous and grouped, using Cox regression models, with adjustment for age.

RESULTS: Changing the exposure estimates changed the estimated relative risks compared with earlier results, but the new analyses showed no significant trends with continuous measures of exposure to either BSM or B[a]P, nor with time spent on ovens tops. Analyses with grouped exposures showed mixed results. Across all BSC plants, the relative risk coefficient for working 5 or more years on ovens tops, where the exposures were highest, was 1.81, which was statistically significant. However, results for those with 0--5 years on ovens tops did not suggest a trend; the evidence for an underlying relationship was thus suggestive but not strong. CONCLUSIONS: The new results are in line with previous findings; they show some signs consistent with an effect of coke ovens work on lung cancer risk, especially on ovens tops, but the preponderant absence of significant results, and the inconsistencies between results for NSF and BSC, highlight how little evidence there is in these data of any effect.

[581]

TÍTULO / TITLE: - Survival analysis in advanced non small cell lung cancer treated with platinum based chemotherapy in combination with paclitaxel, gemcitabine and etoposide.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4661-6.

AUTORES / AUTHORS: - Natukula K; Jamil K; Pingali UR; Suresh Attili VS; Naidu Madireddy UR

INSTITUCIÓN / INSTITUTION: - Department of Genetics, Bhagwan Mahavir Medical Research Centre, Hyderabad, India E-mail : kaiser.jamil@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: The wide spectrum of clinical features in advanced stages of non-small cell lung cancer (NSCLC) probably contributes to disparities in outcomes because of different prognostic variables significant for stage IIIB/IV patients. Hence the aim of this study was to check for favorable response of patients to various chemotherapeutic combinations with respect to patient survival in stage IIIB and stage IV NSCLC disease. We selected those patients for our study who were receiving treatment with paclitaxel, gemcitabine or etoposide in combination with platinum based drugs. MATERIALS AND METHODS: Seventy-two patients who visited the hospital from June 2009 to November 2012 with confirmed diagnosis of lung cancer were included, and data were collected for follow up and classified according to treatment received with respect to patients' regimen and response, and overall survival. This study analyzed tumor variables that were associated with clinical outcome in advanced NSCLC patients who were undergoing first-line chemotherapy for stage IIIB/IV NSCLC. RESULTS: Comparative data on various parameters like age, gender, stage, histology, site of disease, metastatic site and chemo-regimens was analyzed; these parameters predicted variable significant improvement for overall survival ($p \geq 0.05$). One and two year survival rates were 20.8% and 15.3% . CONCLUSIONS: In this study we found slight improvement in survival rates in NSCLC and clinical outcomes with one combination (carboplatin+paclitaxel). Overall there were only marginal differences in survival rates for other chemo-regimens evaluated in this study.

[582]

TÍTULO / TITLE: - Genetic Variation in a MicroRNA-502 Minding Site in SET8 Gene Confers Clinical Outcome of Non-Small Cell Lung Cancer in a Chinese Population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 11;8(10):e77024. doi: 10.1371/journal.pone.0077024.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077024](#)

AUTORES / AUTHORS: - Xu J; Yin Z; Gao W; Liu L; Yin Y; Liu P; Shu Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

RESUMEN / SUMMARY: - BACKGROUND: Genetic variants may influence microRNA-target interaction through modulate their binding affinity, creating or destroying miRNA-binding sites. SET8, a member of the SET domain-containing methyltransferase, has been implicated in a variety array of biological processes. METHODS: Using Taqman assay, we genotyped a polymorphism rs16917496 T>C within the miR-502 binding site in the 3'-untranslated region of the SET8 gene in 576 non-small cell lung cancer (NSCLC) patients. Functions of rs16917496 were investigated using luciferase activity assay and validated by immunostaining. RESULTS: Log-rank test and cox regression indicated that the CC genotype was associated with a longer survival and a reduced risk of death for NSCLC [58.0 vs. 41.0 months, P = 0.031; hazard ratio = 0.44, 95% confidential interval: 0.26-0.74]. Further stepwise regression analysis suggested rs16917496 was an independently favorable factor for prognosis and the protective effect more prominent in never smokers, patients without diabetes and patients who received chemotherapy. A significant interaction was observed between rs16917496 and smoking status in relation to NSCLC survival (P<0.001). Luciferase activity assay showed a lower expression level for C allele as compared with T allele, and the miR-502 had an effect on modulation of SET8 gene in vitro. The CC genotype was associated with reduced SET8 protein expression based on immunostaining of 192 NSCLC tissue sample (P = 0.007). Lower levels of SET8 were associated with a non-significantly longer survival (55.0 vs. 43.1 months). CONCLUSION: Our data suggested that the rs16917496 T>C located at miR-502 binding site contributes to NSCLC survival by altering SET8 expression through modulating miRNA-target interaction.

[583]

TÍTULO / TITLE: - The application of gamma stereotactic body radiation therapy in stage I/II non-small-cell lung cancer. Promising and encouraging outcome.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Saudi Med J. 2013 Nov;34(11):1139-44.

AUTORES / AUTHORS: - Li HQ; Wang YJ; Li J; Li P; Wang X; Wu WZ; Xia TY

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Air Force General Hospital, Beijing, China.

RESUMEN / SUMMARY: - OBJECTIVE: To further evaluate the efficacy and toxicity of the gamma-ray stereotactic body radiation therapy (SBRT) in patients with stage I/II non-small-cell lung cancer (NSCLC). METHODS: Twenty-nine newly diagnosed patients with stage I/II NSCLC who had no previous treatments, underwent OUR-QGD type of the gamma-SBRT at the Radiation Oncology Department, People's Liberation Army Airforce General Hospital, Beijing, China from January 2007 to July 2010. All patients were immobilized by vacuum bag, and then a slow CT scan was performed

without any respiration gating. The total radiation dose of 50%, 60%, and 70% isodose line were prescribed in 50, 60, and 70 Grey (Gy) correspondingly, covering 100% of the planning target volume (PTV), 90% of the clinical target volume (CTV), and 80% of the gross target volume (GTV) in 10 fractions. The CT scans of the chest were required at one, 3, 6, 12, 18, and 24 months to evaluate the efficacy of the treatment. RESULTS: The median follow-up duration was 24 months, and the final follow-up rate is 96.6%. Local control rates of one and 2 years were all 93.1%. The progression-free survival rates versus overall survival rate of one year was 89.7% versus 96.6%, and 2 years was 86.1% versus 89.4%. Acute radiation reactions was diagnosed in 34.5%, and late radiation reactions in 37.9% of patients. CONCLUSION: The gamma-SBRT results in a good curative effects, and minimal toxicity in the treatment of stage I/II NSCLC.

[584]

TÍTULO / TITLE: - Novel Association Between CD74 Polymorphisms and Hematologic Toxicity in Patients With NSCLC After Platinum-Based Chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Nov 9. pii: S1525-7304(13)00183-6. doi: 10.1016/j.clcc.2013.08.006.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.08.006](#)

AUTORES / AUTHORS: - Tan X; Wu Q; Cai Y; Zhao X; Wang S; Gao Z; Yang Y; Li X; Qian J; Wang J; Su B; Chen H; Han B; Jiang G; Lu D

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Disease, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND: Platinum-based chemotherapy regimens can cause DNA damage. Macrophage migration inhibitory factor (MIF) plays an important role in the regulation of the cell cycle by either controlling the activity of the SKP1-Cullin/Cdc53-F-box protein ubiquitin ligase (SCF) complex or activating its receptor, CD74. PATIENTS AND METHODS: We used a pathway-based approach to investigate the association between genetic polymorphisms in MIF-pathway genes and the outcomes of platinum-based chemotherapy in advanced non-small-cell lung cancer (NSCLC). We used iSelect 24x1 HD BeadChip (Illumina, Inc, San Diego, CA) to genotype 32 tag and potentially functional single nucleotide polymorphisms (SNPs) of 8 selected genes and evaluated their associations with different outcomes for 1004 patients with advanced NSCLC treated with platinum-based chemotherapy. In particular, gastrointestinal toxicity and hematologic toxicity were analyzed for associations with specific genotypes, alleles, and haplotypes. RESULTS: Two polymorphisms of CD74, rs2748249 (C/A) and rs1560661 (A/G), were significantly associated with hematologic toxicity. Carrying an A allele in rs2748249 was associated with higher hematologic toxicity (odds ratio [OR], 1.72; 95% confidence interval [CI], 1.24-2.39; P = .001) and carrying a G allele in rs1560661 was associated with lower hematologic toxicity (OR, 0.42; 95% CI, 0.25-0.70; P = .00099) compared with the wild type. Haplotype analysis revealed that the patients with the CG haplotype (consisting of rs2748249 and rs1560661) had reduced hematologic toxicity compared with patients with other haplotypes (OR, 0.70; 95% CI, 0.56-0.87; P = .0013). The binding domain shared by 3 transcription factors (activator protein-2alpha [AP-2alpha], progesterone response A/B, and TFII-I) comprised the 2 SNPs that may be involved in the regulation of CD74-related B-cell survival. CONCLUSION: Our study is the first to suggest, to our

knowledge, that polymorphisms in CD74 might be a marker of lower hematologic toxicity for patients with advanced NSCLC receiving platinum-based chemotherapy.

[585]

TÍTULO / TITLE: - Computed tomography screening for lung cancer: where are we now?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - N C Med J. 2013 Sep-Oct;74(5):406-10.

AUTORES / AUTHORS: - Christensen JD; Tong BC

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Duke University Medical Center, Box 3808, Durham, NC 27710, USA. jared.christensen@duke.edu.

RESUMEN / SUMMARY: - Low-dose computed tomography (LDCT) screening has been shown to result in detection of earlier-stage lung cancers, with a 20% reduction in cancer-related deaths. LDCT screening offers significant potential benefits to selected patients; however, many questions remain, including questions about the applicability of lung cancer screening in clinical practice.

[586]

TÍTULO / TITLE: - Decreased SARI expression predicts poor prognosis of Chinese patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Sep 15;6(10):2056-63.

AUTORES / AUTHORS: - Zhou RJ; Shi Z; Zhou K; Wang HD; Zhang GQ; Li XT; Xu JP

INSTITUCIÓN / INSTITUTION: - Department of Emergency, Xinqiao Hospital, Third Military Medical University No. 183, Xinqiaozheng Rd, Chongqing 400037, China.

RESUMEN / SUMMARY: - SARI is associated with the risk for several cancers, and loss of SARI expression is frequently found in aggressive and metastatic cancer. Limited evidence shows that SARI is a tumor suppressor gene, but the role of SARI in non-small cell lung cancer (NSCLC) has not been previously reported. This study was to investigate the SARI expression profile in surgically resected lung cancer tissues of Chinese patients by immunohistochemistry and evaluate the relationship between SARI expression and prognosis of lung cancer patients. Furthermore, SARI gene was transfected into lung cancer cells (A549), and the growth curve and cell healing of lung cancer cells were determined, aiming to investigate the influence of SARI on the growth and migration of lung cancer cells in vitro. Results showed that 103 of 195 (52.82%) tissues were positive for SARI. When compared with normal tissues, SARI expression significantly reduced in 50.26% of NSCLC tissues. Patients with negative or reduced SARI expression were more likely to have advanced lung cancer and lymph node metastasis. In squamous carcinoma and adenocarcinoma patients, the SARI expression had no relation with the survival time; However in one-on-one analysis SARI expression in tumor cells and adjacent tissues, patients which tumor cells SARI express reduced than adjacent tissues, survival time was significantly shorter than those without reduction in SARI expression (Log Rank test, $p = 0.001$). After transfection by SARI gene, the proliferation and migration of A549 cells were obviously inhibited ($p < 0.001$). These results demonstrate that decreased SARI expression may predict a poor prognosis in NSCLC patients, and SARI may serve as a prognostic biomarker and potential therapeutic target for lung cancer.

[587]

TÍTULO / TITLE: - Altered miR-143 and miR-150 expressions in peripheral blood mononuclear cells for diagnosis of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chin Med J (Engl). 2013 Dec;126(23):4510-6.

AUTORES / AUTHORS: - Zeng XL; Zhang SY; Zheng JF; Yuan H; Wang Y

INSTITUCIÓN / INSTITUTION: - Department of Clinical Laboratory, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China.

RESUMEN / SUMMARY: - BACKGROUND: Sensitive and specific biomarkers for identifying early stage of non-small cell lung cancer (NSCLC) are urgently needed to improve the therapeutic outcome and reduce the mortality. Small non-coding microRNAs (miRNAs) are key components of cancer development and are considered as potential biomarkers for cancer diagnosis and for monitoring treatment. The aim of this study was to determine whether aberrant miRNA expression can be used as a marker in peripheral blood mononuclear cells (PBMC) for the diagnosis of NSCLC. METHODS: The levels of two mature miRNAs (miR-143 and miR-150) were detected by probe-based stem-loop quantitative reverse-transcriptase PCR (RT-qPCR) in PBMC of 64 patients with NSCLC and 26 healthy individuals, and the relationship between miR-143 and miR-150 levels and clinical and pathological factors was explored. RESULTS: All endogenous miRNAs were present in peripheral blood in a remarkably stable form and detected by RT-qPCR. MiR-143 expression in the PBMC specimens was significantly lower in NSCLC patients than in healthy individuals ($P < 0.0001$). MiR-150 expression in the PBMC specimens was not significantly different between NSCLC patients and healthy individuals ($P = 0.260$). MiR-150 expression was significantly higher in lung adenocarcinoma patients than in healthy individuals ($P = 0.001$). There was a very strong difference in the expression level of miR-150 between lung adenocarcinoma patients and lung squamous cell carcinoma patients ($P < 0.0001$). In receiver operating characteristic curve (ROC) analysis, low expression of miR-143 showed the area under the ROC (AUC) of 0.885 for distinguishing cancer patients from healthy subjects. High expression of miR-150 had an AUC of 0.834 for distinguishing lung adenocarcinoma patients from healthy subjects. High expression of miR-150 had an AUC of 0.951 for distinguishing lung adenocarcinoma from lung squamous cell carcinoma. The miR-150 level was significantly associated with distant metastasis ($P = 0.014$). CONCLUSIONS: It is indicated that there is a potential for using miR-143 as a novel diagnostic biomarker for NSCLC. Moreover, miR-150 can be a highly accurate marker for differentiating adenocarcinoma from squamous cell carcinoma.

[588]

TÍTULO / TITLE: - miR-30b and miR-30c expression predicted response to tyrosine kinase inhibitors as first line treatment in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chin Med J (Engl). 2013 Dec;126(23):4435-9.

AUTORES / AUTHORS: - Gu YF; Zhang H; Su D; Mo ML; Song P; Zhang F; Zhang SC

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Beijing Tuberculosis and Thoracic Tumor Research Institute/Beijing Chest Hospital, Capital Medical University, Beijing 101149, China.

RESUMEN / SUMMARY: - BACKGROUND: Aberrantly expressed microRNAs are a hallmark of cancer, and microRNA expression profiling is associated with tumor progression and response to chemotherapy, suggesting their potential application as prognostic and predictive biomarkers. The role of microRNAs in lung cancer remains elusive. It has been recently reported that epidermal growth factor receptor (EGFR) and hepatocyte growth factor receptor (MET) tyrosine kinase can regulate expression of specific microRNAs including miR-30b, miR-30c, miR-221, miR-222, miR-103 and miR-203, and induce tumorigenesis and gefitinib resistance in lung cancers. We intend to study the role of miR-30b and miR-30c expression in predicting response to tyrosine kinase inhibitors (TKIs) in non-small cell lung cancer (NSCLC). METHODS: We have therefore retrospectively examined expression of miR-30b miR-30c in 41 formalin fixed paraffin embedded tissue samples from NSCLC patients when TKIs were used as first line therapy. RESULTS: We found a significant correlation between expression of miR-30b and miR-30c. Furthermore, miR-30b and miR-30c expression correlated with short-term response. Kaplan-Meier analysis further revealed that the expression of miR-30b and miR-30c predicted progression free survival and the overall survival rate in the examined cohort. CONCLUSION: Our study identified miR-30b and miR-30c as useful prognostic predictors in NSCLC patients who underwent first line treatment with TKIs.

[589]

TÍTULO / TITLE: - Phase II study of whole brain radiotherapy with or without erlotinib in patients with multiple brain metastases from lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Drug Des Devel Ther. 2013 Oct 8;7:1179-86. doi: 10.2147/DDDT.S53011.

●● Enlace al texto completo (gratis o de pago) [2147/DDDT.S53011](#)

AUTORES / AUTHORS: - Zhuang H; Yuan Z; Wang J; Zhao L; Pang Q; Wang P

INSTITUCIÓN / INSTITUTION: - Department of Radiotherapy, Tianjin Medical University Cancer Institute and Hospital, Tianjin, People's Republic of China ; National Clinical Research Center of Cancer, Tianjin, People's Republic of China ; Tianjin Key Laboratory of Cancer Prevention and Therapy, Tianjin, People's Republic of China ; Tianjin Lung Cancer Center, Tianjin, People's Republic of China.

RESUMEN / SUMMARY: - The aim of this paper is to explore the efficacy of whole brain radiotherapy (WBRT) versus WBRT concurrent with erlotinib in patients with multiple brain metastases of lung adenocarcinoma. WBRT was administered at 30Gy/10f in both arms. In the combination arm, 150 mg erlotinib was given each day, starting the first day of radiotherapy and continuing for 1 month following the end of radiotherapy. Thereafter, pemetrexed or docetaxel monotherapy or the best supportive therapy was given to both arms. The intracranial objective response rate and the local progression-free survival (LPFS) were primary endpoints. Toxicity, progression-free survival (PFS) and overall survival (OS) were secondary endpoints. Thirty-one patients in the WBRT group and 23 patients in the combination group were enrolled from November 2009 to December 2011. In the WBRT and the combination arms, respectively, the objective

response rate was 54.84% and 95.65% (P = 0.001), the median local progression-free survival was 6.8 months and 10.6 months (P = 0.003), the median PFS was 5.2 months and 6.8 months (P = 0.009), and median OS was 8.9 months and 10.7 months (P = 0.020). In the combination group, there were no differences of LPFS, PFS, and OS between the epidermal growth factor receptor (EGFR) mutation patients and EGFR wild-type patients. No Grade 4 or higher side effects were observed in either group. A multivariate analysis indicated that erlotinib was the most important prognostic factor for a prolonged survival. Data showed that erlotinib in combination with WBRT had a tolerable toxicity profile and prolonged the LPFS, PFS, and OS of lung adenocarcinoma patients with multiple brain metastases compared with WBRT monotherapy.

[590]

TÍTULO / TITLE: - Is %DeltaSUVmax a Useful Indicator of Survival in Patients with Advanced Nonsmall-Cell Lung Cancer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - ScientificWorldJournal. 2013 Oct 9;2013:910957. doi: 10.1155/2013/910957.

●● Enlace al texto completo (gratis o de pago) [1155/2013/910957](#)

AUTORES / AUTHORS: - Cistaro A; Quartuccio N; Mojtahedi A; Fania P; Filosso PL; Cucinotta M; Campenni A; Ficola U; Baldari S

INSTITUCIÓN / INSTITUTION: - Positron Emission Tomography Centre, IRMET S.p.A., Euromedic, V.O. Vigliani 89, 10136 Turin, Italy ; PET Pediatric AIMN InterGroup, 10136 Turin, Italy ; Institute of Cognitive Sciences and Technologies, National Research Council, 00185 Rome, Italy.

RESUMEN / SUMMARY: - Purpose. To investigate the impact of the maximum standardized uptake value (SUVmax), size of primary lung lesion, and %DeltaSUVmax on outcome (overall survival (OS) and 2-year disease-free survival (2-year DFS)) of patients with advanced nonsmall-cell lung cancer (NSCLC). Materials and Methods. 86 stage III-IV NSCLC patients underwent 18 F-FDGPET/CT, before and after chemotherapy, and were classified into subgroups according to the response criteria of the European Organization for Research and Treatment of Cancer. SUVmax values and tumor size with the best prognostic significance were searched. Correlation between the SUVmax value and the initial response to therapy (best response) and the relationship between %DeltaSUVmax and OS were assessed. Results. In patients in PD (20/86), the average pretreatment SUVmax was 11.8 +/- 5.23, and the mean size of the primary lesion was 43.35 mm +/- 16.63. In SD, PR, and CR patients (66/86), the average pretreatment SUVmax was 12.7 +/- 8.05, and the mean size of the primary lesion was 41.6 mm +/- 21.15. Correlation was identified only for %DeltaSUVmax; patients with PD (DeltaSUVmax > +25%) showed a worse OS than patients with DeltaSUVmax < +25% (CR, PR, and SD) (P = 0.0235). Conclusions. In stage III-IV NSCLC, among the assessed factors, only %DeltaSUVmax may be considered as a useful prognostic factor.

[591]

TÍTULO / TITLE: - Perioperative blood transfusions and survival in patients with non-small cell lung cancer: a retrospective study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Anesthesiol. 2013 Nov 15;13(1):42.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2253-13-42](#)

AUTORES / AUTHORS: - Cata JP; Chukka V; Wang H; Feng L; Gottumukkala V; Martinez F; Vaporciyan AA

RESUMEN / SUMMARY: - BACKGROUND: Perioperative blood transfusions have been associated with poor clinical outcomes in the context of oncological surgery. Current literature is inconclusive whether blood transfusions are linked to shorter recurrence free and overall survival after lung cancer surgery. We hypothesize that blood transfusions in patients undergoing surgery for non-small cell lung cancer are associated with poor oncological survival. METHODS: After IRB approval, perioperative data from 636 patients who underwent lung cancer surgery was collected. Patients were evaluated for time to tumor recurrence and overall survival. RESULTS: 60 patients were transfused and 576 subjects were not. Patients who received transfusion were more likely to have more advanced disease ($p = 0.018$), and preoperative low hemoglobin concentrations ($p < 0.0001$) compared to non-transfused patients. In the multivariable Cox regression analysis, blood transfusion was associated with a significant reduction in recurrence free survival ($p = 0.025$), HR: 1.55 (95% CI: 1.06-2.27) and overall survival ($p = 0.0002$) HR: 2.04 (95% CI: 1.41-2.97). However, analysis after propensity score matching between the two groups revealed that the effect of blood transfusion was significant for reduction in overall survival ($p = 0.0356$), HR:1.838 (95% CI: 1.04-3.22) but not for recurrence free survival ($p = 0.1460$), HR:1.493 (95% CI: 0.87-2.56). CONCLUSIONS: Perioperative administration of red blood cells appears to be associated with a decreased overall survival but not recurrence free survival after lung cancer surgery. Our study has the limitations of a retrospective review. Hence, our results should be confirmed by a prospective randomized control trial.

[592]

TÍTULO / TITLE: - The burden of lung cancer in Tennessee—adopting a regional perspective.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tenn Med. 2013 Oct;106(9):33-5, 41.

AUTORES / AUTHORS: - Blackley D; Behringer B; Whiteside M

INSTITUCIÓN / INSTITUTION: - College of Public Health, East Tennessee State University, Johnson City, TN 37614-1700, USA. blackley@goldmail.etsu.edu

[593]

TÍTULO / TITLE: - Serum vascular endothelial growth factor-C levels: A possible diagnostic marker for lymph node metastasis in patients with primary non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):545-549. Epub 2013 Jun 4.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1373](#)

AUTORES / AUTHORS: - Zhang Y; Meng X; Zeng H; Guan Y; Zhang Q; Guo S; Liu X; Guo Q

INSTITUCIÓN / INSTITUTION: - Departments of Medical Oncology, Jinan, Shandong 250117, P.R. China.

RESUMEN / SUMMARY: - Accurate tumor staging is essential for selecting the appropriate treatment strategy for lung cancer. Computed tomography (CT), or positron emission tomography (PET), is the most commonly used non-invasive staging method of lymph node (LN) metastases (LNM), but this method remains unsatisfactory. The present study measured vascular endothelial growth factor (VEGF)-C levels in serum, tumor tissue and LNs to determine the correlation between serum VEGF-C and LNM, and also assessed the usefulness of serum VEGF-C as an additional diagnostic marker for identifying LNM. A total of 66 patients with non-small cell lung carcinoma (NSCLC) or benign tumors of the lung were included in this study, and circulating VEGF-C levels were assessed with enzyme-linked immunosorbent assays. RNA fractions extracted from the tumor tissues and LNs were subjected to quantitative polymerase chain reaction (qPCR) to assess the mRNA levels of VEGF-C. The VEGF-C levels in serum, tumor tissue and LNM were significantly higher compared with the control group ($P<0.05$). The VEGF-C levels of patients with LNM were significantly higher compared with those without LNM ($P<0.05$). The VEGF-C levels in the serum, tumor tissue and LNM were significantly correlated ($P<0.05$). With regard to the diagnosis of LNM using VEGF-C levels, the serum levels of VEGF-C reached a sensitivity of 65.0% and a specificity of 72.2% when a cutoff value of 655.65 pg/ml was applied. Serum VEGF-C levels may provide additional information for distinguishing between the absence and presence of LNM in patients with lung carcinoma. The evaluation of serum VEGF-C is complementary to accurate LN staging in NSCLC.

[594]

TÍTULO / TITLE: - eComment. Is surgery still worthwhile as compared to stereotactic ablative radiotherapy or CyberKnife in high-risk surgical patients with Stage I non-small-cell-lung cancer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Interact Cardiovasc Thorac Surg. 2013 Nov;17(5):853. doi: 10.1093/icvts/ivt400.

●● Enlace al texto completo (gratis o de pago) [1093/icvts/ivt400](#)

AUTORES / AUTHORS: - Scanagatta P

INSTITUCIÓN / INSTITUTION: - Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy.

[595]

TÍTULO / TITLE: - Increased red blood cell distribution width associates with cancer stage and prognosis in patients with lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 11;8(11):e80240. doi: 10.1371/journal.pone.0080240.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0080240](#)

AUTORES / AUTHORS: - Koma Y; Onishi A; Matsuoka H; Oda N; Yokota N; Matsumoto Y; Koyama M; Okada N; Nakashima N; Masuya D; Yoshimatsu H; Suzuki Y

INSTITUCIÓN / INSTITUTION: - Respiratory Center, Shinko Hospital, Kobe-city, Hyogo, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Red cell distribution width (RDW), one of many routinely examined parameters, shows the heterogeneity in erythrocyte size. We investigated the association of RDW levels with clinical parameters and prognosis of

lung cancer patients. METHODS: Clinical and laboratory data from 332 patients with lung cancer in a single institution were retrospectively studied by univariate analysis. Kaplan-Meier survival analysis and Cox proportional hazard models were used to examine the effect of RDW on survival. RESULTS: THE RDW LEVELS WERE DIVIDED INTO TWO GROUPS: high RDW ($\geq 15\%$), $n=73$ vs. low RDW, $n=259$ ($< 15\%$). Univariate analysis showed that there were significant associations of high RDW values with cancer stage, performance status, presence of other disease, white blood cell count, hemoglobin, mean corpuscular volume, platelet count, albumin level, C-reactive protein level, and cytokeratin 19 fragment level. Kruskal-Wallis tests revealed an association of RDW values with cancer stage in patients irrespective of comorbidity (patient with/without comorbidity: $p < 0.0001$, patient without comorbidity: $p < 0.0001$). Stages I-IV lung cancer patients with higher RDW values had poorer prognoses than those with lower RDW values (Wilcoxon test: $p = 0.002$). In particular, the survival rates of stage I and II patients ($n=141$) were lower in the high RDW group ($n=19$) than in the low RDW group ($n=122$) (Wilcoxon test: $p < 0.001$). Moreover, multivariate analysis showed higher RDW is a significant prognostic factor ($p = 0.040$). CONCLUSION: RDW is associated with several factors that reflect inflammation and malnutrition in lung cancer patients. Moreover, high levels of RDW are associated with poor survival. RDW might be used as a new and convenient marker to determine a patient's general condition and to predict the mortality risk of lung cancer patients.

[596]

TÍTULO / TITLE: - Chemical Constituents and Anticancer Activity of Curcuma zedoaria Roscoe Essential Oil against Non-Small Cell Lung Carcinoma Cells in Vitro and in Vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Agric Food Chem. 2013 Nov 27;61(47):11418-27. doi: 10.1021/jf4026184. Epub 2013 Nov 18.

•• Enlace al texto completo (gratis o de pago) [1021/jf4026184](#)

AUTORES / AUTHORS: - Chen CC; Chen Y; Hsi YT; Chang CS; Huang LF; Ho CT; Way TD; Kao JY

INSTITUCIÓN / INSTITUTION: - Institute of Biochemistry, College of Life Science, National Chung Hsing University, Taichung, Taiwan 402.

RESUMEN / SUMMARY: - In this study, we report that the essential oil obtained from Curcuma zedoaria Roscoe, known as zedoary, possesses efficient cytotoxic effects on non-small cell lung carcinoma (NSCLC) cells and causes cell apoptosis. Zedoary essential oil increased the sub-G1 population and the level of annexin-V binding and induced cleavage and activation of caspase-3, -8, and -9 and poly(ADP ribose) polymerase. Decreases in the levels of Bcl-2 and Bcl-xL and an increase in the Bax/Bcl-2 ratio were also observed following zedoary essential oil treatment. Notably, zedoary essential oil led to the release of AIF, endonuclease G, and cytochrome c into the cytosol and increased levels of p53 in H1299 cells. Our results indicate that zedoary essential oil slightly inhibited the phosphorylation of ERK1/2 and enhanced the phosphorylation of JNK1/2 and p38. Zedoary essential oil also inhibited AKT/NF-kappaB signaling pathways in H1299 cells. Moreover, intraperitoneal administration of zedoary essential oil significantly suppressed the growth of H1299 cells in vivo. In addition, potential active compounds were detected using gas chromatography and mass spectrometry. 8,9-Dehydro-9-formyl-cycloisolongifolene, 6-ethenyl-4,5,6,7-

tetrahydro-3,6-dimethyl-5-isopropenyl-trans-benzofuran, eucalyptol, and gamma-elemene were found in zedoary essential oil. In summary, our findings provide insight into the molecular mechanisms underlying zedoary essential oil-induced apoptosis in NSCLC cells that are worthy of further study.

[597]

TÍTULO / TITLE: - 20(S)-protopanaxadiol triggers mitochondrial-mediated apoptosis in human lung adenocarcinoma A549 cells via inhibiting the PI3K/Akt signaling pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Chin Med. 2013;41(5):1137-52. doi: 10.1142/S0192415X13500778.

●● Enlace al texto completo (gratis o de pago) [1142/S0192415X13500778](#)

AUTORES / AUTHORS: - Zhang YL; Zhang R; Xu HL; Yu XF; Qu SC; Sui DY

INSTITUCIÓN / INSTITUTION: - Department of Bioengineering, College of Chemistry, Chemical Engineering and Bioengineering, Donghua University, Shanghai 201620, China.

RESUMEN / SUMMARY: - 20(S)-Protopanaxadiol (PPD), an aglycone saponin ginsenoside isolated from *Panax quinquefolium* L, has been shown to inhibit the growth and proliferation in several cancer lines. However, the underlying molecular mechanisms remain poorly understood. In this study, we investigated the apoptosis-induced effects and the mechanism of 20(S)-PPD on human lung adenocarcinoma A549 cells. 20(S)-PPD showed a potent antiproliferative activity against A549 cells by triggering apoptosis. 20(S)-PPD-induced apoptosis was characterized by a dose-dependent loss of the mitochondrial membrane, release of cytochrome c, second mitochondria-derived activator of caspase (Smac) and apoptosis-inducing factor (AIF), activation of caspase-9/-3, and cleavage of poly (ADP-ribose) polymerase (PARP). Caspase-dependence was indicated by the ability of the pan-caspase inhibitor z-VAD-fmk to attenuate 20(S)-PPD-induced apoptosis. After treatment with 20(S)-PPD, the proportion of A549 cells at the G0/G1 phase increased, while cells at the S and G2/M phases decreased. Furthermore, 20(S)-PPD also triggered down-regulation of phosphorylated Akt (Ser473/Thr308) and glycogen synthase kinase 3beta (GSK 3beta). Knockdown of GSK 3beta with siRNA promoted the apoptotic effects of 20(S)-PPD. These results revealed an unexpected mechanism of action for this unique ginsenoside: triggering a mitochondrial-mediated, caspase-dependent apoptosis via down-regulation of the PI3K/Akt signaling pathway in A549 cells. Our findings encourage further studies of 20(S)-PPD as a promising chemopreventive agent against lung cancer.

[598]

TÍTULO / TITLE: - VATS lobectomy facilitates the delivery of adjuvant docetaxel-carboplatin chemotherapy in patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Dis. 2013 Oct;5(5):578-584.

●● Enlace al texto completo (gratis o de pago) [3978/j.issn.2072-1439.2012.02.05](#)

AUTORES / AUTHORS: - Zhi X; Gao W; Han B; Yang Y; Li H; Liu D; Wang C; Min G; Long H; Rigas JR; Carey M; Jahan T; Sammann A; Reza J; Wang D; Mann MJ; Jablons DM; He J

INSTITUCIÓN / INSTITUTION: - Beijing Lung Cancer Center, Capital Medical University, Beijing, China;

RESUMEN / SUMMARY: - BACKGROUND: To evaluate the safety and tolerability of docetaxel/carboplatin regimen in the post-operative setting of patients with non-small cell lung cancer (NSCLC). METHODS: Enrolment of 133 patients with stage Ib - IIIa NSCLC was undertaken in an open-label, single arm study to assess the safety and tolerability of docetaxel (75 mg/kg) and carboplatin (AUC 5.5) administered for 3 cycles after resection for curative intent. The primary endpoint of the study was safety, as reflected by a febrile neutropenia rate of <10%. Other endpoints assessed protocol compliance and the impact of minimally invasive surgical technique. RESULTS: Patient accrual was completed at 1 center in the US and 10 centers in China in <6 months. Febrile neutropenia complicated treatment in 12 patients (9.0%), below the predetermined safety threshold of 14 patients. Four VATS and 8 open thoracotomy patients experienced febrile neutropenia (P=0.26). Completion of the three-cycle adjuvant regimen was achieved in 86% (95% CI, 77-95%) of patients. Sixty-two of 66 VATS patients compared to 53 of 67 open thoracotomy patients received all three doses according to protocol (P<0.01). Thirteen serious adverse events (9.8%) and no deaths were attributed to the study regimen. CONCLUSIONS: In this rapidly accrued study, docetaxel and carboplatin were well-tolerated in the adjuvant treatment of NSCLC. Adjuvant treatment compliance was higher among patients undergoing a minimally invasive surgical approach. (ClinicalTrials.gov number NCT00883675).

[599]

TÍTULO / TITLE: - Regulatory expression of MMP-8/MMP-9 and inhibition of proliferation, migration and invasion in human lung cancer A549 cells in the presence of HGF variants.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Kaohsiung J Med Sci. 2013 Oct;29(10):530-9. doi: 10.1016/j.kjms.2013.01.011. Epub 2013 May 27.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.kjms.2013.01.011](#)

AUTORES / AUTHORS: - Ramanujam R; Lin YL; Liu JK; He S

INSTITUCIÓN / INSTITUTION: - Department of Biological Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan.

RESUMEN / SUMMARY: - Hepatocyte growth factor (HGF), a potent cytokine of mesenchymal origin, exhibits polytrophic physiological responses, including proliferation, migration, and invasion, in a wide variety of cells. Although it is known that inhibition of the responses by HGF variants was via signal transducers and activators of the transcription pathway, the mechanisms of action of the variants involved in the production of matrix metalloproteinases (MMPs) were not clearly understood. Thus, recombinant HGF variants, NK1, NK2, NK3, and NK4 were topically applied to assays for proliferation, migration, invasion, and expression of MMPs in the human lung cancer cell line A549 and compared to that of control medium and a glutathione-S-transferase control. Results showed that these recombinant HGF variants significantly inhibited proliferation, migration, and invasion of A549 at >4 nM, downregulated expression of MMP-9, and upregulated expression of MMP-8. The study clearly

suggests that binding of the HGF variants to the cell surface c-Met resulted in the downregulation of MMP-9, and upregulation of MMP-8 protein expressions might be key molecular signals against proliferation, migration, and invasion of A549 cells.

[600]

TÍTULO / TITLE: - Impact of age on functional exercise correlates in patients with advanced lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Sep 16;9:1277-83. doi: 10.2147/OTT.S50869.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S50869](#)

AUTORES / AUTHORS: - Wang LY; Wu HD; Chen KY; Hsieh CH; Lai CC

INSTITUCIÓN / INSTITUTION: - School and Graduate Institute of Physical Therapy, College of Medicine, National Taiwan University, Taiwan ; Physical Therapy Center, National Taiwan University Hospital, Taipei, Taiwan.

RESUMEN / SUMMARY: - BACKGROUND: The functional exercise capacity and its correlates in advanced cancer patients in stratified age groups were examined. MATERIALS AND METHODS: A total of 105 patients with advanced lung cancer were recruited prospectively and stratified into young (≤ 50 years), middle (51-65 years), and old (> 65 years) age groups. Respiratory performances, which included maximal inspiratory and expiratory pressure, forced expiratory volume in 1 second, and forced vital capacity were measured. The distance ambulated in a 6-minute walk test was used as an indicator for functional capacity. RESULTS: The young age group had lowest baseline pulmonary function and performed worse on the 6-minute walk test among the three age groups. The risk factors for poor functional capacity were female, lower percent predicted maximal expiratory pressure, worse dyspnea, and lower hemoglobin in the young age group; lower percent predicted forced expiratory volume in 1 second and forced vital capacity, and greater weight loss in the middle age group; and only worse dyspnea in the old age group. The above identified risk factors accounted for 73.6%, 58.5%, and 42.1% variance in 6-minute walk distance for the young, middle, and old age group, respectively. CONCLUSION: The impacts of these factors on functional exercise capacity should be carefully considered while designing exercise intervention according to age.

[601]

TÍTULO / TITLE: - P53 Arg72Pro and MDM2 SNP309 Polymorphisms Cooperate to Increase Lung Adenocarcinoma Risk in Chinese Female Non-smokers: A Case Control Study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5415-20.

AUTORES / AUTHORS: - Ren YW; Yin ZH; Wan Y; Guan P; Wu W; Li XL; Zhou BS

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology, School of Public Health, China Medical University, Shenyang 110001, PR China E-mail : bszhou@mail.cmu.edu.cn.

RESUMEN / SUMMARY: - Background: Cell cycle deregulation is a major component of carcinogenesis. The p53 tumor suppressor gene plays an important role in regulating cell cycle arrest, and mouse double minute 2 (MDM2) is a key regulator of p53 activity

and degradation. Abnormal expression of p53 and MDM2 occurs in various cancers including lung cancer. Methods: We investigated the distribution of the p53 Arg72Pro (rs1042522) and MDM2 SNP309 (rs2279744) genotypes in patients and healthy control subjects to assess whether these single nucleotide polymorphisms (SNPs) are associated with an increased risk of lung adenocarcinomas in Chinese female non-smokers. Genotypes of 764 patients and 983 healthy controls were determined using the TaqMan SNP genotyping assay. Results: The p53 Pro/Pro genotype (adjusted OR = 1.55, 95% CI = 1.17-2.06) significantly correlated with an increased risk of lung adenocarcinoma, compared with the Arg/Arg genotype. An increased risk was also noted for MDM2 GG genotype (adjusted OR = 1.68, 95% CI = 1.27-2.21) compared with the TT genotype. Combined p53 Pro/Pro and MDM2 GG genotypes (adjusted OR = 2.66, 95% CI = 1.54-4.60) had a supermultiplicative interaction with respect to lung adenocarcinoma risk. We also found that cooking oil fumes, fuel smoke, and passive smoking may increase the risk of lung adenocarcinomas in Chinese female non-smokers who carry p53 or MDM2 mutant alleles. Conclusions: P53 Arg72Pro and MDM2 SNP309 polymorphisms, either alone or in combination, are associated with an increased lung adenocarcinoma risk in Chinese female non-smokers.

[602]

TÍTULO / TITLE: - A Genetic Polymorphism in pre-miR-27a Confers Clinical Outcome of Non-Small Cell Lung Cancer in a Chinese Population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 6;8(11):e79135. doi: 10.1371/journal.pone.0079135.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0079135](#)

AUTORES / AUTHORS: - Xu J; Yin Z; Shen H; Gao W; Qian Y; Pei D; Liu L; Shu Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China.

RESUMEN / SUMMARY: - BACKGROUND: Recent evidence indicates that microRNAs (miRNAs) can function as tumor suppressors and oncogenes. Single nucleotide polymorphisms (SNPs) at miRNA genes can influence the maturation of miRNAs or miRNA-mediated transcriptional regulation. Our objective was to investigate the association of SNPs in deregulated miRNAs with clinical outcome in patients with non-small cell lung cancer (NSCLC) in a Chinese population. METHODS: Deregulated miRNAs in NSCLC and their SNPs were identified through public databases. A single SNP, rs895819 in pre-miR-27a, was found suitable for selection. TaqMan assays were performed for genotyping and to assess the effect on the overall survival (OS) and chemotherapy response in 576 NSCLC patients. RESULTS: Log-rank test and Cox regression analysis indicated that the G allele of rs895819 was associated with shorter survival and increased risk of death in NSCLC [dominant model: 22.0 vs. 46.0 months, $P < 0.001$; adjusted hazard ratio (HR) = 1.71, 95% confidential interval (CI): 1.12-2.26]. Further stepwise regression analysis suggested that this SNP was an independently unfavorable factor for the prognosis of NSCLC and the effect remained significant in subgroup analysis stratified by clinical parameters and treatment status. Moreover, multivariate logistic regression analysis showed that the subjects with AG/GG genotypes of rs895819 had significantly decreased response rate to platinum-based chemotherapy compared to those with the AA genotype. CONCLUSION: Our results

suggest that the pre-miR-27a rs895819 polymorphism may influence NSCLC patients' clinical outcome. Further large sample studies should be used to validate our findings.

[603]

TÍTULO / TITLE: - Ectopically expressed variant form of sperm mitochondria-associated cysteine-rich protein augments tumorigenicity of the stem cell population of lung adenocarcinoma cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 11;8(11):e69095. doi: 10.1371/journal.pone.0069095.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0069095](#)

AUTORES / AUTHORS: - Takahashi A; Hirohashi Y; Torigoe T; Tamura Y; Tsukahara T; Kanaseki T; Kochin V; Saijo H; Kubo T; Nakatsugawa M; Asanuma H; Hasegawa T; Kondo T; Sato N

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Sapporo Medical University School of Medicine, Chuo-ku, Sapporo, Japan ; Cancer Diagnosis Laboratory, Japan Science and Technology Agency Innovation Plaza Hokkaido, Japan Science and Technology Agency, Kita-Ku, Sapporo, Japan.

RESUMEN / SUMMARY: - Cancer stem-like cells (CSCs)/cancer-initiating cells (CICs) are defined as a small population of cancer cells that have self-renewal ability, differentiation ability and high tumor-initiating ability. CSCs/CICs are resistant to cancer therapies including chemotherapy and radiotherapy. Therefore, CSCs/CICs are thought to be responsible for cancer recurrence and distant metastasis after treatment. However, the molecular mechanisms of CSCs/CICs are still elusive. In this study, we isolated CSCs/CICs as side population (SP) cells from lung carcinoma, colon carcinoma and breast carcinoma cells and analyzed the molecular mechanisms of CSCs/CICs. cDNA micro-array screening and RT-PCR analysis revealed that sperm mitochondria-associated cysteine-rich protein (SMCP) is ectopically expressed in SP cells. 5'-Rapid amplification of cDNA end (RACE) analysis revealed that the SMCP transcript in SP cells was a variant form (termed vt2) which is composed from only one exon. SMCP vt2 was detected in only cancer cells, whereas the wild-type (vt1) form of SMCP was expressed in the testis. SMCP was shown to have a role in tumor initiation by SMCP overexpression and SMCP knockdown using siRNAs in lung cancer cells. Taken together, the initiation results indicate that an ectopically expressed variant form of SMCP has a role in tumor initiation of CSCs/CICs and that the variant form of SMCP might be a novel CSC/CIC marker and a potential and promising target of CSC/CIC-targeting therapy.

[604]

TÍTULO / TITLE: - Functional Genetic Polymorphisms in PP2A Subunit Genes Confer Increased Risks of Lung Cancer in Southern and Eastern Chinese.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 29;8(10):e77285. doi: 10.1371/journal.pone.0077285.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0077285](#)

AUTORES / AUTHORS: - Yang R; Yang L; Qiu F; Zhang L; Wang H; Yang X; Deng J; Fang W; Zhou Y; Lu J

INSTITUCIÓN / INSTITUTION: - The Institute for Chemical Carcinogenesis, The State Key Lab of Respiratory Disease, Guangzhou Medical University, Guangzhou, China.

RESUMEN / SUMMARY: - Protein phosphatase-2A (PP2A) is one of the major cellular serine-threonine phosphatases and functions as a tumor suppressor that negatively regulates the activity of some oncogenic kinases. Recent studies have reported that PP2A expression was suppressed during lung carcinogenesis, we there hypothesized that the single nucleotide polymorphisms (SNPs) in PP2A subunit genes may affect PP2A function and thus contribute to lung cancer susceptibility. In a two-stage case-control study with a total of 1559 lung cancer patients and 1679 controls, we genotyped eight putative functional SNPs and one identified functional SNP (i.e., rs11453459) in seven major PP2A subunits (i.e., PPP2R1A, PPP2R1B, PPP2CA, PPP2R2A, PPP2R2B, PPP2R5C, PPP2R5E) in southern and eastern Chinese. We found that rs11453459G (-G/GG) variant genotypes of PPP2R1A and the rs1255722AA variant genotype of PPP2R5E conferred increased risks of lung cancer (rs11453459, -G/GG vs. -: OR = 1.31, 95% CI = 1.13-1.51; rs1255722, AA vs. AG/GG: OR = 1.27, 95% CI = 1.07-1.51). After combined the two variants, the number of the adverse genotypes was positively associated with lung cancer risk in a dose-response manner (P trend = 5.63x10⁽⁻⁶⁾). Further functional assay showed that lung cancer tissues carrying rs1255722AA variant genotype had a significantly lower mRNA level of PPP2R5E compared with tissues carrying GG/GA genotypes. However, such effect was not observed for the other SNPs and other combinations. Our findings suggested that the two functional variants in PPP2R1A and PPP2R5E and their combination are associated with lung cancer risk in Chinese, which may be valuable biomarkers to predict risk of lung cancer.

[605]

TÍTULO / TITLE: - A regression model for risk difference estimation in population-based case—control studies clarifies gender differences in lung cancer risk of smokers and never smokers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Med Res Methodol. 2013 Nov 19;13(1):143.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1471-2288-13-143](#)

AUTORES / AUTHORS: - Kovalchik SA; De Matteis S; Landi MT; Caporaso NE; Varadhan R; Consonni D; Bergen AW; Katki HA; Wacholder S

RESUMEN / SUMMARY: - **BACKGROUND:** Additive risk models are necessary for understanding the joint effects of exposures on individual and population disease risk. Yet technical challenges have limited the consideration of additive risk models in case—control studies. **METHODS:** Using a flexible risk regression model that allows additive and multiplicative components to estimate absolute risks and risk differences, we report a new analysis of data from the population-based case—control Environment And Genetics in Lung cancer Etiology study, conducted in Northern Italy between 2002--2005. The analysis provides estimates of the gender-specific absolute risk (cumulative risk) for non-smoking- and smoking-associated lung cancer, adjusted for demographic, occupational, and smoking history variables. **RESULTS:** In the multiple-variable lexic regression, the adjusted 3-year absolute risk of lung cancer in never smokers was 4.6 per 100,000 persons higher in women than men. However, the absolute increase in 3-year risk of lung cancer for every 10 additional pack-years smoked was less for women than men, 13.6 versus 52.9 per 100,000 persons.

CONCLUSIONS: In a Northern Italian population, the absolute risk of lung cancer among never smokers is higher in women than men but among smokers is lower in women than men. Lexpit regression is a novel approach to additive-multiplicative risk modeling that can contribute to clearer interpretation of population-based case—control studies.

[606]

TÍTULO / TITLE: - Genetic Variants in MUC4 Gene Are Associated with Lung Cancer Risk in a Chinese Population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 21;8(10):e77723. doi: 10.1371/journal.pone.0077723.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0077723](#)

AUTORES / AUTHORS: - Zhang Z; Wang J; He J; Zheng Z; Zeng X; Zhang C; Ye J; Zhang Y; Zhong N; Lu W

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Respiratory Diseases, Guangzhou Institute of Respiratory Disease, The First Affiliated Hospital, Guangzhou Medical University, Guangzhou, Guangdong, China.

RESUMEN / SUMMARY: - Mucin MUC4, which is encoded by the MUC4 gene, plays an important role in epithelial cell proliferation and differentiation. Aberrant MUC4 overexpression is associated with invasive tumor proliferation and poor outcome in epithelial cancers. Collectively, the existing evidence suggests that MUC4 has tumor-promoter functions. In this study, we performed a case-control study of 1,048 incident lung cancer cases and 1,048 age- and sex frequency-matched cancer-free controls in a Chinese population to investigate the role of MUC4 gene polymorphism in lung cancer etiology. We identified nine SNPs that were significantly associated with increased lung cancer risk ($P = 0.0425$ for rs863582, 0.0333 for rs842226, 0.0294 for rs842225, 0.0010 for rs2550236, 0.0149 for rs2688515, 0.0191 for rs 2641773, 0.0058 for rs3096337, 0.0077 for rs859769, and 0.0059 for rs842461 in an additive model). Consistent with these single-locus analysis results, the haplotype analyses revealed an adverse effect of the haplotype “GGC” of rs3096337, rs859769, and rs842461 on lung cancer. Both the haplotype and diplotype “CTGAGC” of rs863582, rs842226, rs2550236, rs842225, and rs2688515 had an adverse effect on lung cancer, which is also consistent with the single-locus analysis. Moreover, we observed statistically significant interactions for rs863582 and rs842461 in heavy smokers. Our results suggest that MUC4 gene polymorphisms and their interaction with smoking may contribute to lung cancer etiology.

[607]

TÍTULO / TITLE: - Stage Migration in Planning PET/CT Scans in Patients Due to Receive Radiotherapy for Non-Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Oct 8. pii: S1525-7304(13)00181-2. doi: 10.1016/j.clcc.2013.08.004.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.clcc.2013.08.004](#)

AUTORES / AUTHORS: - Geiger GA; Kim MB; Xanthopoulos EP; Pryma DA; Grover S; Plastaras JP; Langer CJ; Simone CB 2nd; Rengan R

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Pennsylvania School of Medicine, Perelman Center for Advanced Medicine, Philadelphia, PA. Electronic address: geiger@uphs.upenn.edu.

RESUMEN / SUMMARY: - INTRODUCTION: This study examined rates of tumor progression in treatment-naive patients with non-small-cell lung cancer (NSCLC) as determined by repeat treatment-planning fluorine-18 (18F) fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT). METHODS AND MATERIALS: This study assessed patients who underwent PET/CT simulation for NSCLC stage II/III, radiation-naive, nonmetastatic NSCLC. It compared planning PET/CT with previous PET/CT images. Patients were analyzed for change in stage, treatment intent, or both. Progression was defined as a change in TNM status leading to upstaging, and standardized uptake value (SUV) velocity was defined as $[(SUV_{scan2} - SUV_{scan1}) / \text{interscan interval in days}]$. RESULTS: Of 149 consecutive patients examined between April 2009 and April 2011, 47 had prior PET/CT scans and were included. The median age was 68 years. New nodal disease or metastatic disease was identified in 24 (51%) of 47 patients. Fourteen (30%) had evidence of extrathoracic metastatic disease; the remaining 10 (21%) had new nodal disease that required substantial alteration of treatment fields. At a scan interval of 20 days, the rate of upstaging was 17%. SUV velocity was analyzed in the subset of patients who had their studies on the identical PET/CT scanner ($n = 14$). Nonupstaged patients had a mean SUV velocity of 0.074 units per day, compared with 0.11 units per day in patients that were upstaged by their second PET/CT scan ($P = .020$). CONCLUSION: Radiation treatment planning with hybrid PET/CT scans repeated within 120 days of an initial staging PET/CT scan identified significant upstaging in more than half of patients. For a subset of patients who underwent both scans on the same instrument, SUV velocity predicts upstaging, and the difference between those upstaged and those not was statistically significant.

[608]

TÍTULO / TITLE: - Prediction of 2 years-survival in patients with stage I and II non-small cell lung cancer utilizing (18)F-FDG PET/CT SUV quantification.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiol Oncol. 2013 Jul 30;47(3):219-23. doi: 10.2478/raon-2013-0023.

●● Enlace al texto completo (gratis o de pago) [2478/raon-2013-0023](#)

AUTORES / AUTHORS: - Cistaro A; Quartuccio N; Mojtahedi A; Fania P; Filosso PL; Campenni A; Ficola U; Baldari S

INSTITUCIÓN / INSTITUTION: - Positron Emission Tomography Centre IRMET S.p.A., Euromedic inc., Turin, Italy.

RESUMEN / SUMMARY: - BACKGROUND: The purpose of the study was to evaluate the correlation between the maximum standardized uptake value (SUV_{max}), size of primary lung lesion, disease-free survival (DFS) and overall survival (OS) in patients with stage I and II non-small cell lung cancer (NSCLC) in 2 years follow-up. PATIENTS AND METHODS: Forty-nine patients with stage I-II NSCLC were included in this study. Pre-surgical 2-deoxy-2-[18F]fluoro-D-glucose positron-emission tomography ((18)F-FDG PET/CT) study was performed for all patients. The relationship between SUV_{max}, tumour size and clinical outcome was measured. The cut-off value for SUV_{max} and tumour size with the best prognostic significance, probability of DFS and the

correlation between SUVmax and the response to therapy were calculated. RESULTS: There was a statistically significant correlation between SUVmax and DFS ($p = 0.029$). The optimal cut-offs were 9.00 for SUVmax ($p = 0.0013$) and 30mm for tumour size ($p = 0.0028$). Patients with SUVmax > 9 and primary lesion size > 30 mm had an expected 2years-DFS of 37.5%, while this rose to 90% if the tumour was <30 mm and/or SUVmax was <9 . CONCLUSIONS: In stage I-II, SUVmax and tumour size might be helpful to identify the subgroup of patients with high chance for recurrence.

[609]

TÍTULO / TITLE: - Decreased levels of serum cytokeratin 19 fragment CYFRA 21-1 predict objective response to chemotherapy in patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Ther Med. 2013 Aug;6(2):355-360. Epub 2013 Jun 20.

●● Enlace al texto completo (gratis o de pago) [3892/etm.2013.1171](#)

AUTORES / AUTHORS: - Pang L; Wang J; Jiang Y; Chen L

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Chinese PLA General Hospital, Beijing 100853;

RESUMEN / SUMMARY: - Diagnostic tools capable of predicting early responses to chemotherapy are required to improve the individual management of cancer patients. The present study aimed to evaluate the prognostic significance of the serum tumor markers CYFRA 21-1, carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), carbohydrate antigen (CA) 125, and CA 19-9 for predicting responses to different chemotherapy regimens in patients with non-small cell lung cancer (NSCLC). A total of 276 patients with postoperative stage I-IV NSCLC were retrospectively reviewed. The five tumor markers were measured before and after at least two cycles of chemotherapy using an electrochemiluminescent assay. Multivariate analysis revealed that performance status, age, postoperative stage and surgery were significantly associated with the response to chemotherapy. High baseline CYFRA 21-1 and CA 19-9 levels were associated with poor effectiveness of chemotherapy. Significant reductions in CYFRA 21-1 levels were associated with a positive response to various chemotherapy regimens. CEA, CA 125 and CA 19-9 expression was only associated with a positive response in patients receiving paclitaxel, docetaxel, pemetrexed and the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI). NSE expression was only associated with a positive response to gemcitabine. Receiver operating characteristic (ROC) curve analysis indicated that CYFRA 21-1 is the most sensitive of the tumor markers in predicting the response to chemotherapy. Serum CYFRA 21-1 is a useful surrogate marker for predicting the response to different chemotherapy regimens used to treat NSCLC and is a more sensitive marker than CEA, CA125, CA19-9 and NSE.

[610]

TÍTULO / TITLE: - High Coexpression of Both EGFR and IGF1R Correlates With Poor Patient Prognosis in Resected Non-Small-Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Nov 7. pii: S1525-7304(13)00182-4. doi: 10.1016/j.clcc.2013.08.005.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.08.005](#)

AUTORES / AUTHORS: - Gately K; Forde L; Cuffe S; Cummins R; Kay EW; Feuerhake F; O'Byrne KJ

INSTITUCIÓN / INSTITUTION: - Thoracic Oncology Research Group, Institute of Molecular Medicine, Trinity College Dublin, St. James's Hospital, Dublin, Ireland.
Electronic address: kgately@stjames.ie.

RESUMEN / SUMMARY: - BACKGROUND: Recent experimental and biomarker evidence indicates that the epidermal growth factor receptor (EGFR) and insulin-like growth factor receptor 1 (IGF1R) interact in the pathogenesis of malignant epithelial tumors, including lung cancer. This study examines the expression of both receptors and their prognostic significance in surgically resected non-small-cell lung cancer (NSCLC). METHODS: EGFR and IGF1R expression were evaluated in 184 patients with NSCLC (83 squamous cell carcinomas [SCCs], 83 adenocarcinomas [ADCs], and 18 other types) using immunohistochemical (IHC) analysis. Expression of both receptors was examined in matched fresh frozen normal and tumor tissues from 40 patients with NSCLC (20 SCCs and 20 ADCs) by Western blot analysis. RESULTS: High EGFR expression was detected in 51% of patients, and SCCs had higher EGFR expression than did non-SCCs (57.4% vs. 42.5%; $P = .028$). High IGF1R expression was observed in 53.8% of patients, with SCC having higher expression than non-SCC (62.6% vs. 37.3%; $P = .0004$). A significant association was shown between EGFR and IGF1R protein overexpression ($P < .005$). Patients with high expression of both receptors had a poorer overall survival (OS) ($P = .04$). Higher EGFR and IGF1R expression was detected in resected tumors relative to matched normal tissues ($P = .0004$ and $P = .0009$), with SCC having higher expression levels than ADC. CONCLUSION: Our findings indicate a close interrelationship between EGFR and IGF1R. Coexpression of both receptors correlates with poor survival. This subset of patients may benefit from treatments cotargeting EGFR and IGF1R.

[611]

TÍTULO / TITLE: - Resection of a Second Primary Lung Cancer in a Lobe Where Small-Cell Lung Cancer was Previously Treated with Chemoradiotherapy: Report of a Case.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Nov 8.

AUTORES / AUTHORS: - Tsukioka T; Yamamoto R; Takahama M; Nakajima R; Tei K; Okada S; Tada H

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Osaka City General Hospital, Osaka, Japan.

RESUMEN / SUMMARY: - There are few reports of resected cases of second primary lung cancer in post-treatment survivors of small-cell lung cancer. Here, we report a surgical case of a 62-year-old female with second primary lung adenocarcinoma after chemoradiotherapy against small-cell lung cancer. She had been treated for small-cell lung cancer 2 years earlier, and achieved complete response after the treatment. A new nodular lesion was detected at a different segment in the right lower lobe. We performed a right lower lobectomy accompanied with systemic mediastinal nodal dissection. Histopathological findings revealed that the new nodular lesion was a second primary lung adenocarcinoma. No metastatic tumor was seen in the dissected lymph node; the initial tumor had disappeared completely. The postoperative course was uneventful, and she was discharged on day 10 after the operation. Ten months after the operation, she was free of recurrent tumor.

[612]

TÍTULO / TITLE: - Combined germline variations of thrombophilic genes promote genesis of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5449-54.

AUTORES / AUTHORS: - Ozen F; Polat F; Arslan S; Ozdemir O

INSTITUCIÓN / INSTITUTION: - Department of Medical Genetics, Faculty of Medicine, Cumhuriyet University, Sivas, Turkey E-mail : ozdemir615@yahoo.com.

RESUMEN / SUMMARY: - Background: A large variety of familiar and non-familiar lung carcinomas (LC) are caused by long term exposure to chemical carcinogens that are present in tobacco smoke. We aimed to investigate the prevalence of 5 thrombophilic germ-line mutations in patients with lung carcinomas. Materials and Methods: A total of 52 LC patients and 212 healthy controls from same population were analyzed for FV Leiden, factor V H1299R (R2), PAI-1, MTHFR C677T, MTHFR A1298C, ACE I/D, and Apo E genes and compared. Results: Overall, heterozygous and/or homozygous point mutations in FV Leiden Apo E2, PAI-1 and MTHFR C677T genes were associated with LC in the current cohort. There was no meaningful association between LC and ACE I/D gene markers. Conclusions: The current results showed that LC is related to combined thrombophilic gene mutations and individuals with homozygosity of 4G in PAI-1 and MTHFR C677T genes and heterozygosity of FV Leiden, Apo E4 genes have a germ-line risk for LC tumorigenesis.

[613]

TÍTULO / TITLE: - Antibodies against benzo[a]pyrene in immunized mouse and in lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Oncol. 2013 Sep;35(3):207-10.

AUTORES / AUTHORS: - Ustinov VA; Matveeva VA; Kostyanko MA; Glushkov AN

INSTITUCIÓN / INSTITUTION: - Institute of Human Ecology of Siberian Branch of Russian Academy of Sciences, Kemerovo 650065, Russia.

RESUMEN / SUMMARY: - AIM: To evaluate the production of antibodies against benzo[a]pyrene (BP) (Ab1) and corresponding antiidiotypic antibodies (Ab2) in mice after immunization with BP-protein conjugate and in lung cancer patients. MATERIALS AND METHODS: The Ab1 and Ab2 levels were measured by non-competitive ELISA in blood serum of 10 mice immunized with BP-protein conjugate, and in blood serum of 288 healthy persons and 165 lung cancer patients. RESULTS: The Ab1 level of was 2-fold higher than Ab2 level in blood serum of BP-immunized mice. In lung cancer patients the Ab1 level was almost 3 times higher and the Ab2 level was by 30% higher than these indexes in healthy individuals. The Ab1/Ab2 ratio was 2 in BP-immunized mice and healthy individuals and 1 in lung cancer patients. CONCLUSION: Our data have shown that the Ab1/Ab2 ratio in lung cancer patients differ from that in healthy individuals and is close to the Ab1/Ab2 ratio in BP-immunized mouse.

[614]

TÍTULO / TITLE: - mutations in lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Sep;6(3):719-721. Epub 2013 Jun 26.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1427](#)

AUTORES / AUTHORS: - Sasaki H; Suzuki A; Shitara M; Okuda K; Hikosaka Y; Moriyama S; Yano M; Fujii Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Immunology and Surgery, Nagoya City University Graduate School of Medical Sciences, Nagoya, Aichi 467-8601, Japan.

RESUMEN / SUMMARY: - Kelch-like ECH-associated protein 1 (Keap1) inhibits nuclear factor erythroid 2-related 2 (NEF2L2; also named NRF2)-induced cytoprotection and has been hypothesized to represent a candidate tumor suppressor. We have previously reported the somatic mutations of the NRF2 gene (NFE2L2), however, the correlation between the Keap1 mutation and the clinicopathological features of lung cancer has not been well investigated. Therefore, in the present study, the Keap1 mutational status in non-small cell lung cancer (NSCLC) patients was investigated by reverse transcription PCR and direct sequencing. The study included 76 surgically-removed lung cancer cases from patients of the Nagoya City University Hospital in which the EGFR and NFE2L2 mutation status was already established. Keap1 mutations were identified in 2 (2.6%) adenocarcinoma patients with a history of heavy smoking. These mutations were identified to exist exclusively. The Keap1 mutation was only detected in patients with advanced adenocarcinoma (4.3%) and the completely exclusive status of this mutation and others, including EGFR, Kas, erbB2 and NRF2L2, is likely to improve the selection of personalized therapy for lung cancer.

[615]

TÍTULO / TITLE: - Role of quantitative and qualitative characteristics of free circulating DNA in the management of patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cell Oncol (Dordr). 2013 Dec;36(6):439-48. doi: 10.1007/s13402-013-0155-3. Epub 2013 Nov 1.

●● Enlace al texto completo (gratis o de pago) [1007/s13402-013-0155-3](#)

AUTORES / AUTHORS: - Ulivi P; Silvestrini R

INSTITUCIÓN / INSTITUTION: - Biosciences Laboratory, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Via Maroncelli 40, 47014, Meldola, FC, Italy, p.ulivi@irst.emr.it.

RESUMEN / SUMMARY: - BACKGROUND: The release of DNA into peripheral blood is a common event in cancer patients, occurring as a consequence of necrotic and apoptotic processes typical of tumor cells. However, free circulating DNA (fcDNA) is also present in patients with benign diseases and in healthy individuals. Both quantitative and qualitative aspects of fcDNA have been studied as potential biomarkers in a number of tumor types. In particular, quantitative analysis of fcDNA has been shown to play an important role in the diagnosis of non-small cell lung cancer (NSCLC), because of its ability to discriminate between healthy subjects and individuals with NSCLC. Additionally, fcDNA in cancer patients derives predominantly from tumor tissue and, as such, it can be used for the molecular characterization of the primary tumor. Targeted therapies in NSCLC have, in recent years, produced promising results, highlighting the importance of molecular profiling of the primary cancer lesions. Considering that little or no tumor material is available for at least

some of the patients, the possibility of using fcDNA for molecular analysis becomes increasingly important. In the present review we evaluated several quantitative and qualitative aspects of fcDNA that could be instrumental for the differential diagnosis of lung disease. CONCLUSIONS: There is ample evidence in the literature to support the possible use of peripheral blood-derived fcDNA in the early diagnosis and molecular characterization of lung cancer. This non-invasive method may also turn out to be valuable in monitoring drug response and in identifying induced mechanisms of drug resistance. Before it can be implemented in routine clinical practice, however, additional efforts are needed to standardize the methodology.

[616]

TÍTULO / TITLE: - EBUS-TBNA Provides Highest RNA Yield for Multiple Biomarker Testing from Routinely Obtained Small Biopsies in Non-Small Cell Lung Cancer Patients - A Comparative Study of Three Different Minimal Invasive Sampling Methods.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 29;8(10):e77948. doi: 10.1371/journal.pone.0077948.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077948](#)

AUTORES / AUTHORS: - Schmid-Bindert G; Wang Y; Jiang H; Sun H; Henzler T; Wang H; Pilz LR; Ren S; Zhou C

INSTITUCIÓN / INSTITUTION: - Department of Surgery, University Medical Center Mannheim, Medical Faculty Mannheim of Heidelberg University, Mannheim, Germany.

RESUMEN / SUMMARY: - BACKGROUND: Multiple biomarker testing is necessary to facilitate individualized treatment of lung cancer patients. More than 80% of lung cancers are diagnosed based on very small tumor samples. Often there is not enough tissue for molecular analysis. We compared three minimal invasive sampling methods with respect to RNA quantity for molecular testing. METHODS: 106 small biopsies were prospectively collected by three different methods forceps biopsy, endobronchial ultrasound (EBUS) guided transbronchial needle aspiration (TBNA), and CT-guided core biopsy. Samples were split into two halves. One part was formalin fixed and paraffin embedded for standard pathological evaluation. The other part was put in RNAlater for immediate RNA/DNA extraction. If the pathologist confirmed the diagnosis of non-small cell lung cancer(NSCLC), the following molecular markers were tested: EGFR mutation, ERCC1, RRM1 and BRCA1. RESULTS: Overall, RNA-extraction was possible in 101 out of 106 patients (95.3%). We found 49% adenocarcinomas, 38% squamouscarcinomas, and 14% non-otherwise-specified(NOS). The highest RNA yield came from endobronchial ultrasound guided needle aspiration, which was significantly higher than bronchoscopy (37.74+/-41.09 vs. 13.74+/-15.53 ng respectively, P = 0.005) and numerically higher than CT-core biopsy (37.74+/-41.09 vs. 28.72+/-44.27 ng respectively, P = 0.244). EGFR mutation testing was feasible in 100% of evaluable patients and its incidence was 40.8%, 7.9% and 14.3% in adenocarcinomas, squamouscarcinomas and NSCLC NOS subgroup respectively. There was no difference in the feasibility of molecular testing between the three sampling methods with feasibility rates for ERCC1, RRM1 and BRCA1 of 91%, 87% and 81% respectively. CONCLUSION: All three methods can provide sufficient tumor material for multiple biomarkers testing from routinely obtained small biopsies in lung cancer patients. In our study EBUS guided needle aspiration provided the highest amount of

tumor RNA compared to bronchoscopy or CT guided core biopsy. Thus EBUS should be considered as an acceptable option for tissue acquisition for molecular testing.

[617]

TÍTULO / TITLE: - Concomitant EGFR inhibitors combined with radiation for treatment of non-small cell lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4485-94.

AUTORES / AUTHORS: - Zheng DJ; Yu GH; Gao JF; Gu JD

INSTITUCIÓN / INSTITUTION: - Department of Clinical Oncology, Weifang People's Hospital, Weifang, China E-mail : jundonggu@aliyun.com.

RESUMEN / SUMMARY: - Epidermal growth factor receptor (EGFR) is considered to be one of the key driver genes in non-small cell lung cancer (NSCLC). Several clinical trials have shown great promise of EGFR tyrosine kinase inhibitors (TKIs) in the first-line treatment of NSCLC. Many advances have been made in the understanding of EGFR signal transduction network and the interaction between EGFR and tumor microenvironment in mediating cancer survival and development. The concomitant targeted therapy and radiation is a new strategy in the treatment of NSCLC. A number of preclinical studies have demonstrated synergistic anti-tumor activity in the combination of EGFR inhibitors and radiotherapy in vitro and in vivo. In the present review, we discuss the rationale of the combination of EGFR inhibitors and radiotherapy in the treatment of NSCLC.

[618]

TÍTULO / TITLE: - The Incidence of Hyponatraemia and Its Effect on the ECOG Performance Status among Lung Cancer Patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Clin Diagn Res. 2013 Aug;7(8):1678-82. doi: 10.7860/JCDR/2013/5900.3225. Epub 2013 Aug 1.

●● [Enlace al texto completo \(gratis o de pago\) 7860/JCDR/2013/5900.3225](#)

AUTORES / AUTHORS: - Sengupta A; Banerjee SN; Biswas NM; Jash D; Saha K; Maji A; Bandyopadhyaya A; Agarwal S

INSTITUCIÓN / INSTITUTION: - Associate Professor, Department of Pulmonary Medicine, N.R.S. Medical College , India .

RESUMEN / SUMMARY: - Context: Hyponatraemia is one of the common electrolytic disorders which are associated with lung cancer. Hyponatraemia may influence the ECOG performance status at presentation. Also, to the best of our knowledge, we found only limited Indian studies where the ECOG score was correlated with the serum sodium status in lung cancer patients on presentation. Aim: To assess the incidence of hyponatraemia among the patients of carcinoma of the lung before putting them into the specific treatment category for cancer and to check the effects on their ECOG performance status. Settings and Design: A cross-sectional, observational study was conducted on 116 consecutive patients of lung cancer during the period from November 2011 to October 2012. Material and Methods: The patients with a histologically proven diagnosis of lung cancer were grouped initially according to their ECOG performance statuses. The serum sodium value of each patient was measured and the hyponatraemic patients were given treatment according to the protocol. The

correlation of the ECOG performance status with the serum sodium of the lung cancer patients was measured. To check for any laboratory error in serum sodium, we selected (n = 58) age, sex and socioeconomic matched control patients. Results: At presentation 44.8% of the lung cancer patients showed hyponatraemia [52/116]. The ECOG score was significantly poor in the advanced clinical stages (ECOG \leq 2 Vs ECOG \geq 3 in NSCLC cases, $\chi^2(2) = 11.25$, $P = .0008$). The ECOG performance status score at admission showed a negative correlation with the serum sodium status which was measured on admission among all the patients (Pearson correlation coefficient = - 0.186). The clinical stage of the lung cancer also showed a positive correlation with the ECOG score at admission in our study (Pearson correlation coefficient = 0.295). Conclusion: Hyponatraemia is not an uncommon condition and it should be suspected and screened in each patient, as it may influence the ECOG performance status score, which serves as an important factor in the prognosis of lung cancer.

[619]

TÍTULO / TITLE: - Medical image. A rare “mimicker” of lung malignancy. Fibrosing mediastinitis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - N Z Med J. 2013 Nov 1;126(1385):87-8.

AUTORES / AUTHORS: - Cherian SV; Thampy E; Das SV

INSTITUCIÓN / INSTITUTION: - Dept of Pulmonary, Critical Care and Sleep Medicine, University of Texas Health Science Center at Houston, 6411 Fannin Street, Houston, Texas 77030, USA. sujithvcherian@gmail.com.

[620]

TÍTULO / TITLE: - The evaluation of efficacy and safety of sunitinib on EGFR-TKI pretreated advanced Non-small cell lung cancer patients in China.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Respir J. 2013 Oct 4. doi: 10.1111/crj.12059.

●● [Enlace al texto completo \(gratis o de pago\) 1111/crj.12059](#)

AUTORES / AUTHORS: - Liu YR; Zhu W; Zhang JL; Huang JQ; Zhao YZ; Zhang W; Han BH; Yao YH; Jiang LY

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, 200030, China.

RESUMEN / SUMMARY: - BACKGROUND: Sunitinib is an oral multi-targeted tyrosine kinase inhibitor (TKI) exhibiting antiangiogenic and antitumor effects OBJECTIVE: To evaluate the efficacy and potential toxicity of sunitinib therapy in advanced non-small cell lung cancer NSCLC patients in china METHODS: From January 2009 to August 2011, thirty patients with stage IV NSCLC, who were pretreated with the epidermal growth factor receptor (EGFR)-TKIs and then received sunitinib, were retrospectively reviewed. Univariate and multivariate Cox proportional hazard regression analysis was performed to determine the potential prognostic risk factors influencing NSCLC survival RESULTS: The median progression-free survival (PFS) and median overall survival (OS) of all 30 treated patients was 1.25 months (95% CI: 0.90-1.9 months) and 3.40 months (95% CI: 3.00-6.80 months), respectively. Cox regression analysis suggested that Eastern Cooperative Oncology Group (ECOG) performance status (PS) is predictive of both PFS ($p=0.001$) and OS ($p<0.001$). Common adverse events (AEs)

were reported involving hand-foot syndrome (53.3%), mucositis (40.0%), rash (36.7%) and diarrhea (33.3%). CONCLUSION: No sign of overall clinical benefits of sunitinib was detected in patients with pretreated EGFR-TKIs. Most patients suffered AEs from mild to moderate severity. ECOG PS is highly associated with PFS and OS rate. Further studies in NSCLC are required to determine whether sunitinib is beneficial nor not.

[621]

TÍTULO / TITLE: - Immunological effects of the TGFbeta-blocking antibody GC1008 in malignant pleural mesothelioma patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncoimmunology. 2013 Aug 1;2(8):e26218. Epub 2013 Aug 27.

●● Enlace al texto completo (gratis o de pago) [4161/onci.26218](#)

AUTORES / AUTHORS: - Stevenson JP; Kindler HL; Pappasavvas E; Sun J; Jacobs-Small M; Hull J; Schwed D; Ranganathan A; Newick K; Heitjan DF; Langer CJ; McPherson JM; Montaner LJ; Albelda SM

INSTITUCIÓN / INSTITUTION: - Penn Mesothelioma and Pleural Program; Perelman School of Medicine of the University of Pennsylvania; Philadelphia, PA USA.

RESUMEN / SUMMARY: - We evaluated a neutralizing anti-TGFbeta antibody (GC1008) in cancer patients with malignant pleura mesothelioma (MPM). The goal of this study was to assess immunoregulatory effects in relation to clinical safety and clinical response. Patients with progressive MPM and 1-2 prior systemic therapies received GC1008 at 3mg/kg IV over 90 min every 21 d as part of an open-label, two-center Phase II trial. Following TGFbeta blockade therapy, clinical safety and patient survival were monitored along with the effects of anti-TGFbeta antibodies on serum biomarkers and peripheral blood mononuclear cells (PBMC). Although designed as a larger trial, only 13 patients were enrolled when the manufacturer discontinued further development of the antibody for oncology indications. All participants tolerated therapy. Although partial or complete radiographic responses were not observed, three patients showed stable disease at 3 mo. GC1008 had no effect in the expression of NK, CD4+, or CD8+ T cell activating and inhibitory markers, other than a decrease in the expression of 2B4 and DNAM-1 on NK cells. However, serum from 5 patients showed new or enhanced levels of antibodies against MPM tumor lysates as measured by immunoblotting. Patients who produced anti-tumor antibodies had increased median overall survival (OS) (15 vs 7.5 mo, $p < 0.03$) compared with those who did not. To our knowledge, these data represent the first immune analysis of TGFbeta- blockade in human cancer patients.

[622]

TÍTULO / TITLE: - The effect of postoperative change in bronchial angle on postoperative pulmonary function after upper lobectomy in lung cancer patients.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Interact Cardiovasc Thorac Surg. 2013 Nov 14.

●● Enlace al texto completo (gratis o de pago) [1093/icvts/ivt463](#)

AUTORES / AUTHORS: - Seok Y; Cho S; Lee JY; Yang HC; Kim K; Jheon S

INSTITUCIÓN / INSTITUTION: - Department of Thoracic and Cardiovascular Surgery, Seoul National University Bundang Hospital, Seoungnam-si, South Korea.

RESUMEN / SUMMARY: - OBJECTIVES: Upper lobectomy inevitably leads to an upward displacement of the remaining lower lobe. Such displacement may result in bronchial angulation, thereby narrowing the airway. We hypothesized that the degree of displacement of the bronchus is associated with the degree of exacerbation of postoperative pulmonary dysfunction. This study investigated whether bronchial angulation affects postoperative pulmonary function. METHODS: Patients undergoing upper lobectomy for lung cancer were retrospectively evaluated. A check for the presence of dyspnoea, pulmonary function test, chest X-ray and chest computed tomography (CT) were performed at 3 and 12 months postoperatively in these patients. The angle formed by the main bronchus and the bronchus intermedius on the right side and that by the main bronchus and the lower lobar bronchus were measured using the coronal view of the chest CT. We analysed the relationship between the change in bronchial angle and pulmonary function. RESULTS: Ninety-nine patients were enrolled in this study. Among these patients, 50 underwent left upper lobectomy (LUL) and 49 underwent right upper lobectomy (RUL). Nine patients who underwent LUL showed worsening symptoms, and among them, 8 presented an increase in the angle. However, among the 9 patients with worsening symptoms after RUL, only 4 presented an increase in the angle. Decreased forced expiratory volume in 1 s (FEV1) from 3 to 12 months after surgery was observed in 16 patients in the LUL group and 14 in the RUL group. Exacerbation of pulmonary dysfunction was associated with an increase in the bronchial angle ($P = 0.04$ for LUL and $P = 0.02$ for RUL). The degree of angle change was also associated with the extent of FEV1 reduction ($P = 0.02$ for LUL and $P = 0.02$ for RUL). CONCLUSIONS: Although the change in the bronchial angle is a physiological condition, it can reduce postoperative pulmonary function. The measurement of the change in the angle using the coronal view of a chest CT is a useful screening tool for predicting the postoperative reduction in FEV1.

[623]

TÍTULO / TITLE: - Dosimetric errors during treatment of centrally located lung tumors with stereotactic body radiation therapy: Monte Carlo evaluation of tissue inhomogeneity corrections.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Dosim. 2013 Winter;38(4):436-41. doi: 10.1016/j.meddos.2013.06.002. Epub 2013 Oct 9.

●● Enlace al texto completo (gratis o de pago) [1016/j.meddos.2013.06.002](#)

AUTORES / AUTHORS: - Altunbas C; Kavanagh B; Dzingile W; Stuhr K; Gaspar L; Miften M

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Colorado School of Medicine, Aurora, CO. Electronic address: cem.altunbas@ucdenver.edu.

RESUMEN / SUMMARY: - Early experience with stereotactic body radiation therapy (SBRT) of centrally located lung tumors indicated increased rate of high-grade toxicity in the lungs. These clinical results were based on treatment plans that were computed using pencil beam-like algorithms and without tissue inhomogeneity corrections. In this study, we evaluated the dosimetric errors in plans with and without inhomogeneity corrections and with planning target volumes (PTVs) that were within the zone of the proximal bronchial tree (BT). For 10 patients, the PTV, lungs, and sections of the BT either inside or within 2cm of the PTV were delineated. Two treatment plans were

generated for each patient using the following dose-calculation methods: (1) pencil beam (PB) algorithm without inhomogeneity correction (IC) (PB - IC) and (2) PB with inhomogeneity correction (PB + IC). Both plans had identical beam geometry but different beam segment shapes and monitor units (MU) to achieve similar conformal dose coverage of PTV. To obtain the baseline dose distributions, each plan was recalculated using a Monte Carlo (MC) algorithm by keeping MUs the same in the respective plans. The median maximum dose to the proximal BT and PTV dose coverage in the PB + IC plans were overestimated by 8% and 11%, respectively. However, the median maximum dose to the proximal BT and PTV dose coverage in PB - IC plans were underestimated by 15% and 9%. Similar trends were observed in low-dose regions of the lung within the irradiated volume. Our study indicates that dosimetric bias introduced by unit tissue density plans cannot be characterized as underestimation or overestimation of dose without taking the tumor location into account. This issue should be considered when analyzing clinical toxicity data from early lung SBRT trials that utilized unit tissue density for dose calculations.

[624]

TÍTULO / TITLE: - The formulation and delivery of curcumin with solid lipid nanoparticles for the treatment of on non-small cell lung cancer both in vitro and in vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mater Sci Eng C Mater Biol Appl. 2013 Dec 1;33(8):4802-8. doi: 10.1016/j.msec.2013.07.047. Epub 2013 Aug 14.

●● Enlace al texto completo (gratis o de pago) [1016/j.msec.2013.07.047](#)

AUTORES / AUTHORS: - Wang P; Zhang L; Peng H; Li Y; Xiong J; Xu Z

INSTITUCIÓN / INSTITUTION: - First People's Hospital of Yunnan Province, Kunming, Yunnan 650031, China.

RESUMEN / SUMMARY: - Curcumin was determined to have anticancer potency on several kinds of carcinoma. However, its medical application was limited because of its poor bioavailability, unsatisfying dispersity and rapid metabolism in vivo. In this study, curcumin was delivered by solid lipid nanoparticles (SLN) for lung cancer treatment. The physicochemical characters of SLN-curcumin were detected by HPLC, TEM, Zeta potential analysis and FTIR, and the anticancer efficiency on lung cancer was determined both in vitro and in vivo. SLN-curcumin was synthesized by sol-gel method with the size ranged from 20 to 80 nm. After being loaded in SLN, the IC₅₀ of SLN-curcumin on A549 cells was 4 μM, only 1/20 of plain drug. The plasmid concentration of curcumin was highly increased in mice via i.p. after loaded with SLN. Furthermore, SLN-curcumin enhanced the targeting of curcumin to lung and tumor, which finally increased the inhibition efficiency of curcumin from 19.5% to 69.3%. The Flow Cytometry (FCM) analysis and immuno staining confirmed that the inhibition effect mostly came from apoptosis, but not necrosis. The tumor targeting and profound tumor inhibition effect of SLN-curcumin indicated its medical application on lung cancer treatment, and also provided a novel method for new anticancer agents' development.

[625]

TÍTULO / TITLE: - Casticin suppresses self-renewal and invasion of lung cancer stem-like cells from A549 cells through down-regulation of pAkt.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Biochim Biophys Sin (Shanghai). 2013 Nov 17.

●● Enlace al texto completo (gratis o de pago) 1093/abbs/gmt123

AUTORES / AUTHORS: - Liu F; Cao X; Liu Z; Guo H; Ren K; Quan M; Zhou Y; Xiang H; Cao J

INSTITUCIÓN / INSTITUTION: - College of Medicine, Hunan Normal University, Changsha 410013, China.

RESUMEN / SUMMARY: - A subpopulation of cancer stem cells is recognized as the cause of tumorigenesis and spreading. To investigate the effects of casticin (5,3'-dihydroxy-3,6,7,4'-tetramethoxyflavone), derived from Fructus Viticis Simplicifoliae, on lung cancer stem cells, we isolated and identified a subpopulation of lung cancer stem-like cells (LCSLCs) from non-small-cell lung carcinoma A549 cells with the features including self-renewal capacity and high invasiveness in vitro, elevated tumorigenic activity in vivo, and high expression of stemness markers CD133, CD44, and aldehyde dehydrogenase 1 (ALDH1), using serum-free suspension sphere-forming culture method. We then found that casticin could suppress the proliferation of LCSLCs in a concentration-dependent manner with an IC50 value of 0.4 μmol/L, being much stronger than that in parental A549 cells. In addition, casticin could suppress the self-renewal and invasion of LCSLCs concomitant with decreased CD133, CD44, and ALDH1 protein expression and reduced MMP-9 activity. Further experiments showed that casticin suppressed self-renewal and invasion at least partly through down-regulation of Akt phosphorylation. In conclusion, casticin suppressed the characteristics of LCSLCs, suggesting that casticin may be a candidate compound for curing lung cancer via eliminating cancer stem cells.

[626]

TÍTULO / TITLE: - Genotyping of Human Papillomavirus and TP53 Mutations at Exons 5 to 7 in Lung Cancer Patients from Iran.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Bioimpacts. 2013;3(3):135-40. doi: 10.5681/bi.2013.018. Epub 2013 Jun 10.

●● Enlace al texto completo (gratis o de pago) 5681/bi.2013.018

AUTORES / AUTHORS: - Jafari H; Gharemohammadlou R; Fakhrijou A; Ebrahimi A; Nejati-Koshki K; Nadri M; Sakhinia E

INSTITUCIÓN / INSTITUTION: - Department of Medical Genetics, School of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran.

RESUMEN / SUMMARY: - Introduction: There is a powerful relationship between high-risk human papillomaviruses and lung cancer. In fact, inactivation of p53 is the most common genetic abnormality in lung cancer. Indeed, the frequency of HPV types and TP53 mutations in squamous cell carcinoma of lung, among patients from the northwest of Iran has been evaluated in this article. Methodes: Fifty Paraffin embedded blocks of lung SCC were selected for detection of HPV DNA by Nested PCR, and then DNA was sequenced for HPV typing. Equal numbers of positive and negative samples for the HPV DNA were examined for the presence of mutations in exons 5-7 of the TP53 gene by PCR and direct sequencing. Results: Overtly 9 (18%) of 50 samples presented the HPV DNA: eight were HPV-18 and one was HPV-6. TP53 mutations were found in 5 samples (27.7%). Of these, 4 cases showed mutations in exon 5 and one case contained a mutation in exon 7. The most frequent mutation in exon 5 was the C to G transversion (c.409C>G), and also the T to A transversion (c.770T>A) in

exon 7. Conclusion: This study showed that HPV-18 is more likely to consequence in the development of lung cancer among some communities. Genetic alterations, alongside with environmental factors, all play a significant role in the pathogenesis of lung cancer.

[627]

TÍTULO / TITLE: - Inhibition of Hedgehog signaling sensitizes NSCLC cells to standard therapies through modulation of EMT-regulating miRNAs.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Hematol Oncol. 2013 Oct 7;6(1):77.

●● Enlace al texto completo (gratis o de pago) [1186/1756-8722-6-77](#)

AUTORES / AUTHORS: - Ahmad A; Maitah MY; Ginnebaugh KR; Li Y; Bao B; Gadgeel SM; Sarkar FH

RESUMEN / SUMMARY: - BACKGROUND: Epidermal growth factor receptor- tyrosine kinase inhibitors (EGFR-TKIs) benefit Non-small cell lung cancer (NSCLC) patients, and an EGFR-TKli erlotinib, is approved for patients with recurrent NSCLC. However, resistance to erlotinib is a major clinical problem. Earlier we have demonstrated the role of Hedgehog (Hh) signaling in Epithelial-to-Mesenchymal transition (EMT) of NSCLC cells, leading to increased proliferation and invasion. Here, we investigated the role of Hh signaling in erlotinib resistance of TGF-ss1-induced NSCLC cells that are reminiscent of EMT cells. METHODS: Hh signaling was inhibited by specific siRNA and by GDC-0449, a small molecule antagonist of G protein coupled receptor smoothed in the Hh pathway. Not all NSCLC patients are likely to benefit from EGFR-TKIs and, therefore, cisplatin was used to further demonstrate a role of inhibition of Hh signaling in sensitization of resistant EMT cells. Specific pre- and anti-miRNA preparations were used to study the mechanistic involvement of miRNAs in drug resistance mechanism. RESULTS: siRNA-mediated inhibition as well as pharmacological inhibition of Hh signaling abrogated resistance of NSCLC cells to erlotinib and cisplatin. It also resulted in re-sensitization of TGF-ss1-induced A549 (A549M) cells as well the mesenchymal phenotypic H1299 cells to erlotinib and cisplatin treatment with concomitant up-regulation of cancer stem cell (CSC) markers (Sox2, Nanog and EpCAM) and down-regulation of miR-200 and let-7 family miRNAs. Ectopic up-regulation of miRNAs, especially miR-200b and let-7c, significantly diminished the erlotinib resistance of A549M cells. Inhibition of Hh signaling by GDC-0449 in EMT cells resulted in the attenuation of CSC markers and up-regulation of miR-200b and let-7c, leading to sensitization of EMT cells to drug treatment, thus, confirming a connection between Hh signaling, miRNAs and drug resistance. CONCLUSIONS: We demonstrate that Hh pathway, through EMT-induction, leads to reduced sensitivity to EGFR-TKIs in NSCLCs. Therefore, targeting Hh pathway may lead to the reversal of EMT phenotype and improve the therapeutic efficacy of EGFR-TKIs in NSCLC patients.

[628]

TÍTULO / TITLE: - Effects of vinorelbine on cisplatin resistance reversal in human lung cancer A549/DDP cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4635-9.

AUTORES / AUTHORS: - Zhou YT; Li K; Tian H

INSTITUCIÓN / INSTITUTION: - Department of Thoracic, Qilu Hospital of Shandong University, Jinan, China E-mail : tianhuiy@sohu.com.

RESUMEN / SUMMARY: - Multi-drug resistance (MDR) is an essential aspect of human lung cancer chemotherapy failure. Recent studies have shown that vinorelbine is involved in underlying processes in human tumors, reversing the MDR in several types of cancer cells. However, the roles and potential mechanism are not fully clear. In this study, we explored effects of vinorelbine in multi-drug resistance reversal of human lung cancer A549/DDP cells. We found that vinorelbine increased drug sensitivity to cisplatin and intracellular accumulation of rhodamine-123, while decreasing expression of P-glycoprotein (P-gp), multi-drug resistance-associated protein (MRP1) and glutathione-S-transferase Pi (GST-Pi) in A549/DDP cells. At the same time, we also established downregulation of p-Akt and decreased transcriptional activation of NF-kappaB and twist after vinorelbine treatment. The results indicated that vinorelbine might be used as a potential therapeutic strategy in human lung cancer.

[629]

TÍTULO / TITLE: - Optimizing the antitumor selectivity of PVP-Hypericin re A549 cancer cells and HLF normal cells through pulsed blue light.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Photodiagnosis Photodyn Ther. 2013 Dec;10(4):591-9. doi: 10.1016/j.pdpdt.2013.06.005. Epub 2013 Aug 5.

●● Enlace al texto completo (gratis o de pago) 1016/j.pdpdt.2013.06.005

AUTORES / AUTHORS: - Penjweini R; Loew HG; Breit P; Kratky KW

INSTITUCIÓN / INSTITUTION: - University of Vienna, Faculty of Physics, Physics of Physiological Processes, Boltzmanng. 5, A-1090 Vienna, Austria; Hasselt University, Biomedical Research Institute, Agoralaan Building C, 3590 Diepenbeek, Belgium. Electronic address: rozhin.penjweini@uhasselt.be.

RESUMEN / SUMMARY: - Photodynamic therapy (PDT) is based on the preferential accumulation of photosensitizer in cancer cells with subsequent cytotoxicity mediated by singlet oxygen production after light excitation. As photosensitizers accumulate also in the surrounding non-cancer cells, the risk of damaging them by photosensitization is a limitation of PDT. Thus, minimizing the side-effects of PDT on normal cells is one of the challenging problems in medical practice. This paper studies the PDT side-effects of PVP-Hypericin (PVP: polyvinylpyrrolidone) photosensitizer excited with continuous or pulsed irradiation, on combined cell lines of human lung carcinoma epithelial cells (A549) and normal primary human lung fibroblast cells (HLF). In vitro PDTs are performed using pulsed or continuous irradiation with irradiance intensities $I^{(*)}=1.59, 6.34$ and 14.27mW/cm^2 . The LED pulse lengths L are 0.127, 1.29, 13, 54.5 and 131ms. Then fluorescence and phototoxicity of PVP-Hypericin in the A549 cancer cells are compared with those of HLF normal cells. Although, PVP-Hypericin accumulates more in A549 cancer cells, the results show that HLF cells produce dose-dependent photoreactions in the presence of photosensitizer. PVP-Hypericin induces the most optimized anticancer efficacy with moderate side-effects for $I^{(*)}=14.27\text{mW/cm}^2$ and $L=131\text{ms}$.

[630]

TÍTULO / TITLE: - Lung cancer: MET-negative patients-eclipsing benefits.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Dec;10(12):667. doi: 10.1038/nrclinonc.2013.194. Epub 2013 Oct 22.

●● Enlace al texto completo (gratis o de pago) [1038/nrclinonc.2013.194](#)

AUTORES / AUTHORS: - Hutchinson L

[631]

TÍTULO / TITLE: - FDG PET/CT is useful for detecting infiltration to the port site in patients with malignant pleural mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Gen Thorac Cardiovasc Surg. 2013 Nov 27.

●● Enlace al texto completo (gratis o de pago) [1007/s11748-013-0345-y](#)

AUTORES / AUTHORS: - Kawaguchi K; Taniguchi T; Usami N; Fukui T; Ishiguro F; Nakamura S; Yokoi K

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550, Japan, gucci@med.nagoya-u.ac.jp.

RESUMEN / SUMMARY: - OBJECTIVE: One reason for the poor outcomes of multimodality therapies, including macroscopic complete resection, in patients with malignant pleural mesothelioma (MPM) is the difficulty of correctly staging the disease, which can result in incomplete resection. The purpose of this study was to investigate the aspects of tumor infiltration to the port site and the usefulness of preoperative FDG PET/CT for diagnosing MPM. METHODS: Between June 2007 and May 2013, 21 patients who underwent surgical treatment with curative intent for MPM that had been previously diagnosed on a video-assisted thoracic surgery (VATS) biopsy were included in this study. RESULTS: There were 17 males and four females, with a mean age of 63 years. The accumulation of FDG at the port site was observed in all nine patients with tumor infiltration to the port site, whereas this feature was not noted in 15 patients without tumor extension to the port site. There were more positive lymph node cases in the infiltration group than in the non-infiltration group ($p = 0.02$). No significant differences in survival were observed between the patients with and without tumor infiltration to the port site. CONCLUSIONS: FDG PET/CT is useful for detecting tumor infiltration of MPM to the port site and may help to prevent local recurrence, especially port site relapse, following macroscopic complete resection. However, this condition is related to tumor aggressiveness; therefore, performing careful staging and determining the appropriate treatment strategy are required in such patients.

[632]

TÍTULO / TITLE: - The maximum standardized FDG uptake on PET-CT in patients with non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Multidiscip Respir Med. 2013 Oct 22;8(1):69.

●● Enlace al texto completo (gratis o de pago) [1186/2049-6958-8-69](#)

AUTORES / AUTHORS: - Ozgul MA; K Rk L G; Seyhan EC; Cetinkaya EA; Ozgul G; Yuksel M

RESUMEN / SUMMARY: - BACKGROUND: Non-small cell lung cancer (NSCLC) accounts for approximately 80% of new diagnoses of pulmonary carcinoma. This study investigated the correlation between 18 F-fluorodeoxyglucose uptake in computerized

tomography integrated positron emission tomography and tumor size, lymph node metastasis, and distant metastasis in patients with NSCLC. METHODS: The records of 151 NSCLC patients (139 male, 12 female; mean age 59.60 years) were evaluated retrospectively. RESULTS: Forty-one cases were adenocarcinomas; 45 squamous cell carcinomas; and 65 unspecified NSCLC. When the cases were categorized according to tumor size (group 1, ≤ 3 cm; group 2, > 3 and ≤ 5 cm; group 3, > 5 cm), the maximum standardized uptake value (SUVmax) was significantly lower in groups 1 and 2 compared with group 3 ($p = 0.006$ for each). Considering all cases, tumor SUVmax was not correlated with age, gender, or histopathological type. Lymph node metastases were pathologically proven in 24 cases: 24% of these were adenocarcinomas, 6% squamous cell carcinomas, and 16% unspecified NSCLC. Neither lymph node involvement nor distant metastases were correlated with tumor SUVmax, although lymph node size was positively correlated with lymph node SUVmax ($r = 0.775$; $p < 0.001$). CONCLUSIONS: SUVmax was significantly associated with tumor size, but not with distant metastases or lymph node involvement. Therefore, SUVmax on positron emission tomography is not predictive of the presence of metastases.

[633]

TÍTULO / TITLE: - Impact of physiotherapy on patients with advanced lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chron Respir Dis. 2013;10(4):223-32. doi: 10.1177/1479972313508965.

●● Enlace al texto completo (gratis o de pago) [1177/1479972313508965](#)

AUTORES / AUTHORS: - Ozalevli S

INSTITUCIÓN / INSTITUTION: - Dokuz Eylul University, School of Physical Therapy and Re-habilitation, Izmir, Turkey.

RESUMEN / SUMMARY: - Patients with lung cancer have high mortality and high morbidity. Lung cancer-related symptoms and problems such as dyspnea, fatigue, pain, and cachexia that begin in the early phase later result in poor physical functioning, psychosocial, and quality of life status. In addition, advancing age is associated with significant comorbidity. These patients may benefit from multidisciplinary therapy to reduce the perceived severity of dyspnea and fatigue and increase physical functioning and quality of life. Based on management of symptoms and problems such as dyspnea, physical inactivity, cancer-related fatigue, respiratory secretions, pain, and anxiety-depression of these patients, it is thought that physiotherapy techniques can be used on advanced lung cancer patients following a comprehensive evaluation. However, well-designed, prospective, and randomized-controlled trials are needed to prove the efficacy of physiotherapy and pulmonary rehabilitation in general for patients with advanced lung cancer.

[634]

TÍTULO / TITLE: - Lung cancer in women.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - South Med J. 2013 Oct;106(10):582-7. doi: 10.1097/SMJ.0000000000000004.

●● Enlace al texto completo (gratis o de pago)

[1097/SMJ.0000000000000004](#)

AUTORES / AUTHORS: - Graham PD; Thigpen SC; Geraci SA

INSTITUCIÓN / INSTITUTION: - From the G.V. (Sonny) Montgomery VA Medical Center, and the Department of Medicine, University of Mississippi School of Medicine, Jackson, and the Department of Medicine, Quillen College of Medicine, East Tennessee State University, Johnson City.

RESUMEN / SUMMARY: - Lung cancer is the deadliest cancer in women. In the last decade, the first measurable decline in disease-related mortality has occurred and in the last 5 years, the first decline in lung cancer incidence in women in the United States has been reported. Five-year survival rates are much higher in early-stage disease, making effective screening a priority. Data on screening with low-dose computed tomography are controversial; existing guidelines are not sex specific and recommend testing only for patients at high risk for the disease. Although cigarette smoking remains the predisposing factor that is most often associated with tumor development, the advent of molecularly targeted therapy and the growing evidence that susceptible targets are more prevalent in never-smoking women have brought more attention to this particular subpopulation. Studies of both surgery and systemic therapy suggest that not only never-smoking women but also women overall experience better outcomes than men. Identifying all of the factors contributing to these sex differences presents us with an opportunity to identify potentially a distinct tumor biology in women who would warrant a distinct personalized treatment approach.

[635]

TÍTULO / TITLE: - Expressions of CLDN1 and insulin-like growth factor 2 are associated with poor prognosis in stage N2 non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chin Med J (Engl). 2013;126(19):3668-74.

AUTORES / AUTHORS: - Zhang ZF; Pei BX; Wang AL; Zhang LM; Sun BS; Jiang RC; Wang CL

INSTITUCIÓN / INSTITUTION: - Department of Lung Cancer, Lung Cancer Center, Tianjin Medical University Cancer Institute & Hospital, National Clinical Research Center of Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin 300060, China (Email: zhangzhenfa1973@163.com).

RESUMEN / SUMMARY: - BACKGROUND: Patients with single station mediastinal lymph node (N2) non-small cell lung cancer (NSCLC) have a better prognosis than those with multilevel N2. The molecular factors which are involved in disease progression remain largely unknown. The purpose of this study was to investigate gene expression differences between single station and multilevel N2 NSCLC and to identify the crucial molecular factors which are associated with progress and prognosis of stage N2 NSCLC. METHODS: Gene expression analysis was performed using Agilent 4x44K Whole Human Genome Oligo Microarray on 10 freshfrozen lymph node tissue samples from single station N2 and paired multilevel N2 NSCLC patients. Real-time reverse transcription (RT)-PCR was used to validate the differential expression of 14 genes selected by cDNA microarray of which four were confirmed. Immunohistochemical staining for these validated genes was performed on formalin-fixed, paraffinembedded tissue samples from 130 cases of stage N2 NSCLC arranged in a high-density tissue microarray. RESULTS: We identified a 14 gene expression signature by comparative analysis of gene expression. Expression of these genes strongly differed between single station and multilevel N2 NSCLC. Four genes

(ADAM28, MUC4, CLDN1, and IGF2) correlated with the results of microarray and real-time RT-PCR analysis for the gene-expression data in samples from 56 NSCLC patients. Immunohistochemical staining for these genes in samples from 130 cases of stage N2 NSCLC demonstrated the expression of IGF2 and CLDN1 was negatively correlated with overall survival of stage N2 NSCLC. CONCLUSIONS: Our results suggest that the expression of CLDN1 and IGF2 indicate a poor prognosis in stage N2 NSCLC. Further, CLDN1 and IGF2 may provide potential targeting opportunities in future therapies.

[636]

TÍTULO / TITLE: - Increased serum S-TRAIL level in newly diagnosed stage-IV lung adenocarcinoma but not squamous cell carcinoma is correlated with age and smoking.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4819-22.

AUTORES / AUTHORS: - Kargi A; Bisgin A; Yalcin AD; Kargi AB; Sahin E; Gumuslu S

INSTITUCIÓN / INSTITUTION: - Division of Medical Oncology, Department of Internal Medicine, Antalya Training and Research Hospital, Antalya, Turkey E-mail : atilbisgin@yahoo.co.uk.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the leading cause of cancer mortality in the world. Many factors can protect against or facilitate its development. A TNF family member TRAIL, has a complex physiological role beyond that of merely activating the apoptotic pathway in cancer cells. Vitamin D is converted to its active form locally in the lung, and is also thought to play an important role in lung health. Our goal was to investigate the possible clinical significance of serum sTRAIL and 1,25-dihydroxyvitamin D(3) levels in patients with non-small cell lung cancer (NSCLC). MATERIALS AND METHODS: Totals of 18 consecutive adenocarcinoma and 22 squamous cell carcinoma patients with stage-IV non-small cell lung cancer referred to our institute were included in this study. There were 12 men and 6 women, with ages ranging from 38 to 97 (mean 60.5) years with adenocarcinoma, and 20 men and 2 women, with ages ranging from 46 to 80 (mean 65) years with squamous cell carcinoma. Serum levels of sTRAIL and 1,25-dihydroxyvitamin D(3) were measured in all samples at the time of diagnosis. RESULTS: sTRAIL levels in NSCLC patients were higher than in the control group. Although there was no correlation between patient survival and sTRAIL levels, the highest sTRAIL levels were correlated with age and cigarette smoking in the adenocarcinoma patients. sTRAIL level in healthy individuals were correlated with serum 1,25-dihydroxyvitamin D(3). CONCLUSIONS: Serum sTRAIL concentrations were increased in NSCLC patients, and correlated with age and smoking history, but not with overall survival.

[637]

TÍTULO / TITLE: - Minnelide: a novel therapeutic that promotes apoptosis in non-small cell lung carcinoma in vivo.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 15;8(10):e77411. doi: 10.1371/journal.pone.0077411.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0077411](#)

AUTORES / AUTHORS: - Rousalova I; Banerjee S; Sangwan V; Evenson K; McCauley JA; Kratzke R; Vickers SM; Saluja A; D’Cunha J

INSTITUCIÓN / INSTITUTION: - Division of Basic and Translational Research, Department of Surgery, University of Minnesota, Minneapolis, Minnesota, United States of America.

RESUMEN / SUMMARY: - BACKGROUND: Minnelide, a pro-drug of triptolide, has recently emerged as a potent anticancer agent. The precise mechanisms of its cytotoxic effects remain unclear. METHODS: Cell viability was studied using CCK8 assay. Cell proliferation was measured real-time on cultured cells using Electric Cell Substrate Impedance Sensing (ECIS). Apoptosis was assayed by Caspase activity on cultured lung cancer cells and TUNEL staining on tissue sections. Expression of pro-survival and anti-apoptotic genes (HSP70, BIRC5, BIRC4, BIRC2, UACA, APAF-1) was estimated by qRT-PCR. Effect of Minnelide on proliferative cells in the tissue was estimated by Ki-67 staining of animal tissue sections. RESULTS: In this study, we investigated in vitro and in vivo antitumor effects of triptolide/Minnelide in non-small cell lung carcinoma (NSCLC). Triptolide/Minnelide exhibited anti-proliferative effects and induced apoptosis in NSCLC cell lines and NSCLC mouse models. Triptolide/Minnelide significantly down-regulated the expression of pro-survival and anti-apoptotic genes (HSP70, BIRC5, BIRC4, BIRC2, UACA) and up-regulated pro-apoptotic APAF-1 gene, in part, via attenuating the NF-kappaB signaling activity. CONCLUSION: In conclusion, our results provide supporting mechanistic evidence for Minnelide as a potential in NSCLC.

[638]

TÍTULO / TITLE: - Lung cancer stem cells and low-intensity laser irradiation: a potential future therapy?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Stem Cell Res Ther. 2013 Oct 23;4(5):129.

●● [Enlace al texto completo \(gratis o de pago\) 1186/scrt340](#)

AUTORES / AUTHORS: - Crous AM; Abrahamse H

INSTITUCIÓN / INSTITUTION: - Laser Research Centre, Faculty of Health Sciences, University of Johannesburg, P.O, Box 17011, Doornfontein 2028, South Africa.

habrahamse@uj.ac.za.

RESUMEN / SUMMARY: - Lung cancer is notably a significant threat when considering worldwide cancer-related deaths. Despite significant advances in treatment modalities, death rates as a result of cancer relapse remain high. Relapse can occur as a result of metastasis. Cancer stem cells (CSCs) have been implicated as an important contributory factor in the development of metastasis. CSCs have the same characteristics as normal stem cells; that is, they can proliferate indefinitely and are capable of both self-renewal and differentiating into specialized cells. The molecular and cellular characteristics of stem cells and CSCs are coded for by cell-specific genes, which can be analyzed by using molecular assays setting the standard to work from. Low-intensity laser irradiation (LILI) has been applied in the treatment of numerous diseases and pathological conditions. LILI has been shown to stimulate proliferation of cells, capillary growth, and cellular metabolism as observed by adenosine triphosphate activation. It has been shown, by using different dosing levels of LILI, to either stimulate or inhibit cellular functions. One treatment strategy used on cancer cells is photodynamic therapy (PDT), in which cancer cells are treated with a

photosensitizer (PS) in combination with laser irradiation. PSs are non-toxic by themselves but, with light activation, cause reactive oxygen species generation, which causes cancer cell death. Cell-specific PSs are being developed for future cancer treatment. In this review, we look at the potential effects of LIL and PDT on lung CSCs.

[639]

TÍTULO / TITLE: - Surgical treatment and adjuvant therapies of recurrent respiratory papillomatosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Braz J Otorhinolaryngol. 2013 Sep-Oct;79(5):636-42. doi: 10.5935/1808-8694.20130114.

●● Enlace al texto completo (gratis o de pago) [5935/1808-8694.20130114](#)

AUTORES / AUTHORS: - Avelino MA; Zaiden TC; Gomes RO

INSTITUCIÓN / INSTITUTION: - UNIFESP, EPM.

RESUMEN / SUMMARY: - Recurrent respiratory papillomatosis or recurrent laryngeal papillomatosis is a disease of the larynx caused by human papilloma virus, characterized by verrucous epithelial lesions and usually recurring. In the literature there are several types of treatment, such as surgery to cold, laser and/or use of microdebrider, as of adjuvant therapies; all possible to decrease the permanent sequelae of the disease. **OBJECTIVE:** To review the literature regarding this disease with emphasis on surgical techniques and adjuvant therapies used today. **METHOD:** We used the literature review, through surveys based electronic data in the public domain, to search for articles between 1992-2012, using keywords: papilloma, human papilloma virus infection, larynx, therapeutic, papilloma virus vaccine. **RESULTS:** We surveyed 357 articles, of which 49 were used as the basis for this review. Scientific studies indicate a reduction of relapse in most adjuvant therapeutic presented. However, the survey showed different methodologies and samples, which did not allow to compare the types of treatment and adjuvant therapies. **CONCLUSION:** The choice of surgical technique varies among studies, but there is a trend to use the microdebrider. The newer adjuvant therapies, such as cidofovir, quadrivalent vaccine against human papilloma virus and bevacizumab, require further studies.

[640]

TÍTULO / TITLE: - Acute radiation pneumonitis after conformational radiotherapy for nonsmall cell lung cancer: clinical, dosimetric, and associated-treatment risk factors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Jul-Sep;9(3):447-51. doi: 10.4103/0973-1482.119339.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119339](#)

AUTORES / AUTHORS: - Leprieur EG; Fernandez D; Chatellier G; Klotz S; Giraud P; Durdux C

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Diseases, Hopital Ambroise Pare, 9 Avenue Charles-de-Gaulle 92100 Boulogne-Billancourt; University Versailles-Saint Quentin en Yvelines, 9 Boulevard d'Alembert, 78280 Guyancourt, France.

RESUMEN / SUMMARY: - **BACKGROUND:** Conformational thoracic radiotherapy (CTR) is a key-treatment in locally advanced nonsmall cell lung cancer (LA-NSCLC). Acute radiation pneumonitis (ARP) is one of the major complications. **AIMS:** To evaluate the

predictors of ARP after CTR in the treatment of LA-NSCLC. MATERIALS AND METHODS: A total of 47 consecutive patients (pts) were treated with CTR for LA-NSCLC and retrospectively analyzed. The mean total dose of radiation therapy (RT) was 65 Gy, with respiratory gating (RG) in 19 cases. Induction and concomitant chemotherapy was performed in 33 pts (70%) and 41 pts (87%), respectively. RESULTS: Eleven pts (23%) had an ARP resulting in death for one pt. In univariate analysis, age, sex, pretherapeutic value of forced expiratory volume (FEV), not-gated radiotherapy and type of concomitant chemotherapy did not appear as contributing factors in contrast to the administration of induction gemcitabine ($p = 0.03$). The occurrence of ARP was significantly associated with nontumor lung volumes irradiated to 13 Gy (V13, $p = 0.04$), 20 Gy (V20, $p = 0.02$), and 25 Gy (V25, $p = 0.006$), the mean lung dose ($p = 0.008$) and lung normal tissue complication probability (NTCP) ($p = 0.004$). In multivariate logistic regression analysis, the occurrence of ARP was significantly associated with age >75 years (odds ratio (OR) = 16.72, confidence interval (CI) 95% 1.77-157.87) and administration of induction gemcitabine (OR = 18.08, CI 95% 1.09-300.08). CONCLUSION: ARP is a common acute complication, requiring close posttreatment follow-up, particularly for elderly patients. The use of gemcitabine before radiation should be avoided. The benefits and risks of CTR must be carefully analyzed, according to the dosimetric parameters.

[641]

TÍTULO / TITLE: - The prognostic value of ERCC1 and RRM1 gene expression in completely resected non-small cell lung cancer: tumor recurrence and overall survival.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Manag Res. 2013 Oct 3;5:327-36. doi: 10.2147/CMAR.S52073.

●● Enlace al texto completo (gratis o de pago) [2147/CMAR.S52073](#)

AUTORES / AUTHORS: - Tantraworasin A; Saeteng S; Lertprasertsuke N; Arayawudhikul N; Kasemsarn C; Patumanond J

INSTITUCIÓN / INSTITUTION: - General Thoracic Unit, Department of Surgery, Faculty of Medicine, Chiang Mai University Hospital, Chiang Mai, Thailand.

RESUMEN / SUMMARY: - BACKGROUND: The roles of excision repair cross-complementing group 1 gene (ERCC1) expression and ribonucleotide reductase subunit M1 gene (RRM1) expression in completely resected non-small cell lung cancer (NSCLC) are still debatable. Previous studies have shown that both genes affected the overall survival and outcomes of patients who received platinum-based chemotherapy; however, some studies did not show this correlation. The aim of this study was to evaluate the prognostic values of ERCC1 and RRM1 gene expression in predicting tumor recurrence and overall survival in patients with completely resected NSCLC who received adjuvant chemotherapy and in those who did not. PATIENTS AND METHODS: A retrospective cohort study was conducted in 247 patients with completely resected NSCLC. All patients had been treated with anatomic resection (lobectomy or pneumonectomy) with systematic mediastinal lymphadenectomy between January 2002 and December 2011 at Chiang Mai University Hospital, Chiang Mai, Thailand. They were divided into two groups: recurrence and no recurrence. Protein expression of ERCC1 and RRM1 was determined by immunohistochemistry. Correlations between clinicopathologic variables, including ERCC1 and RRM1 expression and tumor recurrence, were analyzed. Univariate and multivariate Cox

proportional hazards regression analysis stratified by nodal involvement, tumor staging, intratumoral blood vessel invasion, intratumoral lymphatic invasion, and tumor necrosis was used to identify the prognostic roles of ERCC1 and RRM1. RESULTS: ERCC1 and RRM1 expression did not demonstrate prognostic value for tumor recurrence and overall survival in patients with completely resected NSCLC. In patients who did not receive adjuvant chemotherapy treatment, those with high ERCC1 and high RRM1 expression seemed to have greater potential for tumor recurrence and shorter overall survival than did those who had low ERCC1 and low RRM1 (hazard ratio [HR] =1.7, 95% confidence interval [CI] =0.6-4.3, P=0.292 and HR =1.6, 95% CI =0.5-4.5, P=0.411, respectively). In contrast, in patients who received adjuvant chemotherapy treatment, those with high ERCC1 and high RRM1 expression seemed to have benefited from adjuvant chemotherapy and showed good overall survival compared with those who had low ERCC1 and low RRM1 (HR =0.8, 95% CI = 0.4-1.8, P=0.612 and HR = 0.4, 95% CI = 0.1-2.4, P=0.325, respectively). Subgroup analysis in patients whose first-line metastatic chemotherapy failed demonstrated that ERCC1 expression and RRM1 expression were not prognostic factors for tumor recurrence and overall survival; however, patients who had high ERCC1 and high RRM1 expression seemed to have benefited from first-line chemotherapy treatment (HR =0.7, 95% CI =0.3-1.8, P=0.458). CONCLUSION: ERCC1 expression and RRM1 expression were not prognostic of tumor recurrence and overall survival in patients with completely resected NSCLC, either with or without adjuvant chemotherapy. Prospective studies that include a larger number of patients are needed for definite conclusions.

[642]

TÍTULO / TITLE: - Expression and clinical significance of the Trop-2 gene in advanced non-small cell lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):375-380. Epub 2013 May 29.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1368](#)

AUTORES / AUTHORS: - Jiang A; Gao X; Zhang D; Zhang L; Lu H

INSTITUCIÓN / INSTITUTION: - Departments of Respiratory Medicine, Taizhou People's Hospital Affiliated to Medical College of The Nantong University, Taizhou, Jiangsu 225300, P.R. China.

RESUMEN / SUMMARY: - The Trop-2 gene has been examined in various carcinomas and is reported to be significantly associated with prognosis. Little is known with regard to Trop-2 gene expression in advanced non-small cell lung carcinoma (NSCLC). The present study investigated the expression of Trop-2 and its association with the prognosis of advanced NSCLC. The clinical records of 87 patients with advanced NSCLC, consisting of 37 cases of squamous cell carcinoma (SCC) and 50 cases of adenocarcinoma (AdC), together with 17 tumor-adjacent normal tissues, were retrospectively evaluated. Trop-2 expression was measured using an immunohistochemical method and its association with clinicopathological data and prognosis was also evaluated. The expression of Trop-2 was significantly higher in the cancer tissues compared with the tumor-adjacent normal tissues, and significantly higher in SCC compared with AdC (P=0.018). In SCC, the overexpression of Trop-2 was only correlated with the histological grade of the tumor (P= 0.035) and no correlation was observed with gender, age, lymph node metastasis, TNM stage or Eastern Cooperative Oncology Group (ECOG) performance status (PS). In AdC, the

over-expression of Trop-2 was correlated with the histological grade, lymph node metastasis and TNM stage (P= 0.01, 0.024 and 0.015, respectively), while no correlation with gender, age or ECOG-PS was observed. The survival frequency was significantly higher in the Trop-2-negative patients compared with the Trop-2-positive patients [17.25 months (95% CI, 14.922-19.577) vs. 13.274 months (95% CI, 11.507-15.041); P= 0.008]. The survival time was significantly longer in the Trop-2-negative AdC patients [17.275 months (95% CI, 14.575-19.975) vs. 11.469 months (95% CI, 11.507-15.041); P= 0.002], but not in the SCC patients [17.167 months (95% CI, 12.428-21.906) vs. 14.647 months (95% CI, 12.062-17.232); P= 0.276]. The multivariate analysis revealed that Trop-2 expression [hazard ratio (HR) 2.381; P= 0.038], TNM stage (HR, 2.193; P= 0.03) and ECOG-PS (HR, 2.696; P= 0.007) were independent predictors for the survival outcome of patients with AdC. These results suggest that Trop-2 overexpression is closely correlated with an unfavorable prognosis in advanced NSCLC. Trop-2 is an independent prognostic marker and a potential new therapeutic target in advanced AdC.

[643]

TÍTULO / TITLE: - Protein kinase Cs in lung cancer: A promising target for therapies.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S74-9. doi: 10.4103/0973-1482.119102.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119102](#)

AUTORES / AUTHORS: - Fan C; Li Y; Jia J

INSTITUCIÓN / INSTITUTION: - People's Military Medical Press, Beijing, 100036, China.

RESUMEN / SUMMARY: - Lung cancer has been identified as one of the most deadly oncologies. The most influential causes for disease progression include smoking, genetic mutation and inflammatory lung diseases. Conventional therapies for lung cancer including chemo and radio-treatments often cause serious adverse effects. The advent of novel therapeutics that specifically target signalling pathways activated by genetic alterations has revolutionized the way patients with lung cancer are treated. These are comprised of various molecular targets on its carcinogen signalling pathways, among which the protein kinase C (PKC) family is a promising target. The 12 isotypes in the family demonstrate complex interactions. This inter-linked signalling loop has added complexity of developing effective therapies. An improved understanding of different molecules involved in these signalling pathways will provide several profound implications, ranging from preclinical work on the mechanisms to trial design. Therapies developed targeting individual/multiple PKCs combined with conventional strategies offer promising future combating cancer.

[644]

TÍTULO / TITLE: - Diagnosing malignant pleural effusions: how do we compare?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - N Z Med J. 2013 Aug 30;126(1381):42-8.

AUTORES / AUTHORS: - Lim MH; Garrett J; Mowlem L; Yap E

INSTITUCIÓN / INSTITUTION: - Auckland City Hospital, 2 Park Road, Grafton, Auckland 1023, New Zealand. lmhan88@hotmail.com.

RESUMEN / SUMMARY: - INTRODUCTION: Accurate and prompt diagnosis of malignant pleural effusion (MPE) is important as patients with suspected MPE often

wait for many days before the diagnosis is secure. AIMS: (1) To evaluate the diagnostic yield of pleural fluid cytology for patients admitted to Middlemore Hospital (MMH) in Auckland, New Zealand with MPE between 31 May 2010-1 June 2011. (2) To document the waiting time for cytology results to be made available and whether this contributed to length of stay. (3) To evaluate whether the volume of pleural fluid analysed contributed to diagnostic yield. METHODS: A retrospective audit of pleural fluid cytology results on 36 consecutive patients admitted to MMH with a pleural effusion which was subsequently proven to be due to malignancy. Data was obtained from hospital medical records and Web Eclair databases. RESULTS: 54.8% (17/31) of patients had positive pleural fluid cytology. Initial pleural fluid cytology was positive in 16 (51.6%). Only 4/15 patients with negative pleural fluid cytology had a repeat aspiration (1 was positive). Median cytology turnaround time was 6.72 days, range 2.23-43.06 days. Average length of stay (ALOS) was 7.78 days, range 1.11-20.8 days. Cytology turnaround times seem shorter for inpatients and when a diagnosis of cancer is unknown but the ALOS is longer if patients have negative initial cytology and when a diagnosis of cancer is uncertain. Samples >50mL appear to have a higher diagnostic yield compared to samples less than and equal to 50mL but this was not statistically significant (77.8% to 41.2%, p=0.08). CONCLUSION: Diagnostic yield from pleural fluid cytology at our hospital is comparable with other documented studies. ALOS appears to be influenced by a negative initial pleural fluid cytology and the uncertainty of diagnosis of cancer, not cytology turnaround time. The results suggest a more efficient diagnostic and treatment algorithm could be considered with emphasis on Day Stay investigation and treatment.

[645]

TÍTULO / TITLE: - Si-RNA mediated knockdown of CELF1 gene suppressed the proliferation of human lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Cell Int. 2013 Nov 15;13(1):115.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1475-2867-13-115](#)

AUTORES / AUTHORS: - Wu LN; Xue YJ; Zhang LJ; Ma XM; Chen JF

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the leading cause of cancer-related death in the world, with metastasis as the main reason for the mortality. CELF1 is an RNA-binding protein controlling the post-transcriptional regulation of genes related to cell survival. As yet, there is little knowledge of CELF1 expression and biological function in lung cancer. This study investigated the expression levels of CELF1 in lung cancer tissues and the biological function of CELF1 in lung cancer cells. METHODS: CELF1 mRNA expression was determined in lung cancer and normal tissues, and the relationship between the expression level of CELF1 and clinicopathological parameters was evaluated. The biological function of CELF1 in A549 and H1299 lung cancer cell lines growth was examined. RESULTS: The expression of CELF1 was higher in human lung cancer tissues compared with the normal lung tissue. Lentiviral-mediated transfection of CELF1 siRNA effectively silenced the expression of CELF1 in both A549 and H1299 cells. Moreover, CELF1 knockdown markedly reduced the survival rate of lung cancer cells. Colony formation assays revealed a reduction in the number and size of lung cancer cell colonies from CELF1 knockdown. CONCLUSION: These results indicated that CELF1 may have

significant roles in the progression of lung cancer, and suggested that siRNA mediated silencing of CELF1 could be an effective tool in lung cancer treatment.

[646]

TÍTULO / TITLE: - Long non-coding RNA MEG3 inhibits NSCLC cells proliferation and induces apoptosis by affecting p53 expression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 7;13:461. doi: 10.1186/1471-2407-13-461.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-461](#)

AUTORES / AUTHORS: - Lu KH; Li W; Liu XH; Sun M; Zhang ML; Wu WQ; Xie WP; Hou YY

INSTITUCIÓN / INSTITUTION: - Department of respiratory, First Affiliated Hospital, Nanjing Medical University, Nanjing, People's Republic of China. wxie@njmu.edu.cn.

RESUMEN / SUMMARY: - BACKGROUND: Long non-coding RNAs play an important role in tumorigenesis, hence, identification of cancer-associated lncRNAs and investigation of their biological functions and molecular mechanisms are important for understanding the development and progression of cancer. Recently, the downregulation of lncRNA MEG3 has been observed in various human cancers. However, its role in non-small cell lung cancer (NSCLC) is unknown. The aim of this study was to examine the expression pattern of MEG3 in NSCLC and to evaluate its biological role and clinical significance in tumor progression. METHODS: Expression of MEG3 was analyzed in 44 NSCLC tissues and 7 NSCLC cell lines by qRT-PCR. Over-expression approaches were used to investigate the biological functions of MEG3 in NSCLC cells. Bisulfite sequencing was used to investigate DNA methylation on MEG3 expression. The effect of MEG3 on proliferation was evaluated by MTT and colony formation assays, and cell apoptosis was evaluated by Hoechst staining and Flow-cytometric analysis. NSCLC cells transfected with pCDNA-MEG3 were injection into nude mice to study the effect of MEG3 on tumorigenesis in vivo . Protein levels of MEG3 targets were determined by western blot analysis. Differences between groups were tested for significance using Student's t-test (two-tailed). RESULTS: MEG3 expression was decreased in non-small cell lung cancer (NSCLC) tumor tissues compared with normal tissues, and associated with advanced pathologic stage, and tumor size. Moreover, patients with lower levels of MEG3 expression had a relatively poor prognosis. Overexpression of MEG3 decreased NSCLC cells proliferation and induced apoptosis in vitro and impeded tumorigenesis in vivo. MDM2 and p53 protein levels were affected by MEG3 over-expression in vitro. CONCLUSIONS: Our findings indicate that MEG3 is significantly down-regulated in NSCLC tissues that could be affected by DNA methylation, and regulates NSCLC cell proliferation and apoptosis, partially via the activation of p53. Thus, MEG3 may represent a new marker of poor prognosis and is a potential therapeutic target for NSCLC intervention.

[647]

TÍTULO / TITLE: - Lung Squamous Cell Carcinoma in Pulmonary Alveolar Proteinosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Nov 8.

AUTORES / AUTHORS: - Liu H; Wang Y; He W; Xu Q

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Shanghai Pulmonary Hospital, School of Medicine, Tongji University, Shanghai, China.

RESUMEN / SUMMARY: - Pulmonary alveolar proteinosis (PAP) is a rare pulmonary disease characterized by alveolar accumulation of surfactant. There are only four sporadic PAP case reports associated with lung cancers. These case reports describe only that lung cancer might develop subsequently or coincidentally with PAP. Here, we report a case of PAP associated with lung squamous cell carcinoma. This patient with PAP was a 57-year-old man, who had smoked one and a half pack of cigarettes per day for 30 years. In this case, PAP increased with lung cancer developing and disappeared after lung cancer resection. PAP may be the result of the lung squamous cell carcinoma developing in this case.

[648]

TÍTULO / TITLE: - RET fusion genes in Korean non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Korean Med Sci. 2013 Oct;28(10):1555-8. doi: 10.3346/jkms.2013.28.10.1555. Epub 2013 Sep 25.

●● Enlace al texto completo (gratis o de pago) [3346/jkms.2013.28.10.1555](#)

AUTORES / AUTHORS: - Yoo SS; Jin G; Jung HJ; Hong MJ; Choi JE; Jeon HS; Lee SY; Lim JO; Park JY

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea.

RESUMEN / SUMMARY: - Recently, rearranged during transfection (RET) fusions have been identified in approximately 1% of non-small cell lung cancer (NSCLC). To know the prevalence of RET fusion genes in Korean NSCLCs, we examined the RET fusion genes in 156 surgically resected NSCLCs using a reverse transcriptase polymerase chain reaction. Two KIF5B-RET fusions and one CCDC6-RET fusion were identified. All three patients were females and never smokers with adenocarcinomas. RET fusion genes were mutually exclusive from EGFR, KRAS mutations and EML4-ALK fusion. RET fusion genes occur 1.9% (3 of 156) of surgically treated NSCLC patients in Koreans.

[649]

TÍTULO / TITLE: - Cytoprotective effect of bioactive sea buckthorn extract on paraquat-exposed A549 cells via induction of Nrf2 and its downstream genes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2013 Dec;8(6):1852-60. doi: 10.3892/mmr.2013.1736. Epub 2013 Oct 16.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1736](#)

AUTORES / AUTHORS: - Podder B; Kim YS; Song HY

INSTITUCIÓN / INSTITUTION: - Department of Microbiology, College of Medicine, Soonchunhyang University, Cheonan, Chungnam 330-721, Republic of Korea.

RESUMEN / SUMMARY: - The extract of sea buckthorn (SBT) [*Hippophae rhamnoides* L. (Elaeagnaceae)], is used as a food supplement and traditional medicine in numerous countries. This study investigated the protective effects of the functional extract of SBT against paraquat (PQ)induced toxicity via antioxidant mechanisms in A549 cells. The

methanol extract of SBT (25200 microg/ml) was used to protect cells against PQ (200 microM)induced cell death. A viability assay was conducted using 3(4,5dimethylthioazol2ly)2,5diphenyltetrazolium bromide and lactate dehydrogenase (LDH). Total intracellular reactive oxygen species (ROS) were measured and plotted. For validation of the SBTinduced expression of nuclear factorE2related factor 2 (Nrf2) and its target genes, western blot analysis and qPCR were performed. The present study showed that pretreatment of A549 cells with SBT extract significantly attenuated PQ (200 microM)induced cellular toxicity. The maximum cytoprotective effect was identified using 200 microg/ml SBT extract; it began 24 h following exposure and was sustained up to 120 h (P<0.05). SBT extract significantly reduced LDH activity by 35.63% and ROS levels by 30.90% (P<0.05). Pretreatment with SBT extract activated Nrf2 mRNA and protein expression and its nuclear translocation. The SBT extract effectively induced Nrf2 target genes, such as NAD(P)H dehydrogenase quinone 1, glutathione peroxidase 1, glutathione reductase and catalase following treatment with PQ. Based on these results, it was hypothesized that SBT extract may be used as a potential therapeutic agent for the treatment of various oxidative stressrelated diseases.

[650]

TÍTULO / TITLE: - More efficient induction of antitumor T cell immunity by exosomes from CD40L gene-modified lung tumor cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2014 Jan;9(1):125-31. doi: 10.3892/mmr.2013.1759. Epub 2013 Oct 25.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1759](#)

AUTORES / AUTHORS: - Wang J; Wang L; Lin Z; Tao L; Chen M

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Hangzhou First People's Hospital, Hangzhou, Zhejiang 310006, P.R. China.

RESUMEN / SUMMARY: - The incidence of lung cancer increases annually. However, the effects of the present methods for the treatment of lung cancer are extremely poor. It has been reported that exosomes from heatstressed 3LL Lewis lung tumor cells effectively elicit systemic antitumor immunity. CD40 signaling is critical in the activation of dendritic cells (DCs), which are important in the induction of antitumor immunity. In the present study, exosomes from CD40 ligand genemodified 3LL tumor cells (CD40LEXO) were identified to be more immunogenic compared with controlEXO and lac Z-EXO. CD40LEXO induced a more mature phenotype of the DCs and promoted them to secrete high levels of interleukin12. CD40LEXOtreated DCs induced a greater proliferation of allogeneic T cells in the mixed lymphocyte reaction. Moreover, CD40LEXO induced robust tumor antigenspecific CD4+ T cell proliferation ex vivo. CD40LEXO were also extremely effective in the protective and therapeutic antitumor tests in vivo. These results indicate that CD40LEXO may be used as an efficient vaccine for lung cancer immunotherapy.

[651]

TÍTULO / TITLE: - No Association of XRCC1 and CLPTM1L Polymorphisms with Non-small Cell Lung Cancer in a Non-Smoking Han Chinese Population.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5171-4.

AUTORES / AUTHORS: - Sun Y; Zhang YJ; Kong XM

INSTITUCIÓN / INSTITUTION: - Departments of Chemotherapy, Zhejiang Cancer Hospital, Hangzhou, China E-mail : zhangyongjun770323 @163.com.

RESUMEN / SUMMARY: - Background: This study aimed to explore potential associations between single nucleotide polymorphisms (SNPs) of the x-ray repair cross-complementing group 1 (XRCC1) and cleft lip and palate transmembrane protein 1-like (CLPTM1L) and non-small cell lung cancer (NSCLC) susceptibility in non-smoker Chinese patients. Methods: A total of 200 NSCLC patients and 200 healthy controls with matched age and gender were recruited for genotyping of XRCC1 SNPs (rs2256507 and rs1001581) and CLPTM1L SNPs (rs401681 and rs4975616). Association of these SNPs with NSCLC risk was evaluated by computing the odds ratio (OR) and 95% confidence interval (CI) from multivariate unconditional logistic regression analyses with adjustment for gender and age. Results: The frequencies of genotype and allele in these four loci (rs2256507, rs1001581, rs401681, and rs4975616) were not significantly different between the cases and controls, or between either of the histological subgroups (adenocarcinoma and squamous cell carcinoma) and controls. Conclusions: Although these SNPs are associated with NSCLC risk in patients with a tobacco-smoking habit, this study demonstrated that XRCC1 and CLPTM1L gene SPNs are not linked with NSCLC risk in non-smoking patients, indicating that molecular mechanisms of NSCLC betwee tobacco smokers and non-smokers may be different. Future studies are needed to uncover the underlying molecular mechanisms for NSCLC in non-smokers.

[652]

TÍTULO / TITLE: - Evaluation of a curcumin analog as an anti-cancer agent inducing ER stress-mediated apoptosis in non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 24;13(1):494.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1471-2407-13-494](#)

AUTORES / AUTHORS: - Liu Z; Sun Y; Ren L; Huang Y; Cai Y; Weng Q; Shen X; Li X; Liang G; Wang Y

RESUMEN / SUMMARY: - BACKGROUND: Recent advances have highlighted the importance of the endoplasmic reticulum (ER) in cell death processes. Pharmacological interventions that effectively enhance tumor cell death through activating ER stress have attracted a great deal of attention for anti-cancer therapy. METHODS: A bio-evaluation on 113 curcumin analogs against four cancer cell lines was performed through MTT assay. Furthermore, real time cell assay and flow cytometer were used to evaluate the apoptotic induction of (1E,4E)-1,5-bis(5-bromo-2-ethoxyphenyl)penta-1,4-dien-3-one (B82). Western blot, RT-qPCR, and siRNA were then utilized to confirm whether B82-induced apoptosis is mediated through activating ER stress pathway. Finally, the in vivo anti-tumor effect of B82 was evaluated. RESULTS: B82 exhibited strong anti-tumor activity in non-small cell lung cancer (NSCLC) H460 cells. Treatment with B82 significantly induced apoptosis in H460 cells in vitro and inhibited H460 tumor growth in vivo. Further studies demonstrated that the B82-induced apoptosis is mediated by activating ER stress both in vitro and in vivo. CONCLUSIONS: A new monocarbonyl analog of curcumin, B82, exhibited anti-tumor

effects on H460 cells via an ER stress-mediated mechanism. B82 could be further explored as a potential anticancer agent for the treatment of NSCLC.

[653]

TÍTULO / TITLE: - The risk of schizophrenia and child psychiatric disorders in offspring of mothers with lung cancer and other types of cancer: a danish nationwide register study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 1;8(11):e79031. doi: 10.1371/journal.pone.0079031.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0079031](#)

AUTORES / AUTHORS: - Benros ME; Laursen TM; Dalton SO; Nordentoft M; Mortensen PB

INSTITUCIÓN / INSTITUTION: - National Centre for Register-Based Research, Aarhus University, Aarhus, Denmark ; Mental Health Centre Copenhagen, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark ; The Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, Aarhus, Denmark.

RESUMEN / SUMMARY: - BACKGROUND: Maternal immune responses and brain-reactive antibodies have been proposed as possible causal mechanisms for schizophrenia and some child psychiatric disorders. According to this hypothesis maternal antibodies may cross the placenta and interact with the developing CNS of the fetus causing future neurodevelopmental disorders. Therefore, we investigated if children of mothers with cancer might be at higher risk of developing psychiatric disorders, with particular focus on small-cell lung cancer, which is known to induce production of antibodies binding to CNS elements. METHODS: Nationwide population-based registers were linked, including the Danish Psychiatric Central Register and The Danish Cancer Registry. Data were analyzed as a cohort study using survival analysis techniques. Incidence rate ratios (IRRs) and accompanying 95% confidence intervals (CIs) were used as measures of relative risk. RESULTS: In general, parental cancer was not associated with schizophrenia in the offspring (IRR, 0.98; 95% CI, 0.95-1.01). Furthermore, we found no temporal associations with maternal cancer in general; neither around the pregnancy period. However, maternal small-cell lung cancer increased the risk of early-onset schizophrenia and maternal small-cell lung cancer diagnosed within 20 years after childbirth increased the risk of schizophrenia. Parental cancer was not associated with child psychiatric disorders (IRR, 1.01; 95% CI, 0.98-1.05) except for the smoking related cancers. There was a significantly increased risk of child psychiatric disorders in offspring of both mothers (IRR, 1.35; 95% CI, 1.16-1.58) and fathers (IRR, 1.47; 95% CI, 1.30-1.66) with lung cancer of all types. CONCLUSIONS: In general, parental cancer did not increase the risk of schizophrenia nor of child psychiatric disorders. However, maternal small-cell lung cancer increased the risk of schizophrenia in subgroups; and lung cancer in general increased the risk of child psychiatric disorders, which could be due to risk factors associated with parental smoking.

[654]

TÍTULO / TITLE: - Association between the Telomerase Reverse Transcriptase (TERT) rs2736098 Polymorphism and Cancer Risk: Evidence from a Case-Control Study of Non-Small-Cell Lung Cancer and a Meta-Analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 19;8(11):e76372. doi: 10.1371/journal.pone.0076372.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0076372](#)

AUTORES / AUTHORS: - Wu H; Qiao N; Wang Y; Jiang M; Wang S; Wang C; Hu L

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Qilu Hospital Affiliated to Shandong University, Jinan, Shandong Province, China.

RESUMEN / SUMMARY: - BACKGROUND: A common genetic variant, telomerase reverse transcriptase (TERT) rs2736098, was recently reported to be associated with lung cancer risk in Caucasians. In addition, many studies have investigated the role of this polymorphism in the etiology of cancer of various organs. Nevertheless, the results of related case-control studies remain inconsistent. METHODS: We hypothesized that the genetic risk variant identified in Caucasians may potentially influence the susceptibility to lung cancer in the Chinese population. To test this hypothesis, a case-control study including 539 non-small-cell lung cancer (NSCLC) cases and 627 cancer-free controls was conducted. Furthermore, to investigate the association between rs2736098 and cancer risk, a meta-analysis based on previously published studies and our case-control study was also performed. RESULTS: Multivariate logistic regression demonstrated that individuals carrying the A allele or the AA genotype exhibited a significantly elevated risk of NSCLC compared with those carrying the G allele or GG genotype (A vs. G: OR = 1.21, 95% CI = 1.02-1.43, P = 0.028; AA vs. GG: OR = 1.48, 95% CI = 1.05-2.09, P = 0.025). Additionally, this association was stronger among adenocarcinoma cases (AA vs. GG: OR = 1.67, 95% CI = 1.12-2.50, P = 0.013; A vs. G: OR = 1.28, 95% CI = 1.05-1.57, P = 0.016). In the meta-analysis, a borderline significant association between the rs2736098 polymorphism and overall cancer risk was observed (AA vs. GG: OR = 1.25, 95% CI = 1.07-1.46; AA vs. AG+GG: OR = 1.22, 95% CI = 1.06-1.41; additive model: OR = 1.10, 95% CI = 1.02-1.18), and further stratifications demonstrated a moderately increased risk for lung and bladder cancer, Asian ethnicity and hospital-based studies. CONCLUSIONS: Our results suggest that the rs2736098 polymorphism may contribute to the risk of lung cancer, especially adenocarcinoma, in the Chinese population. In addition, the current meta-analysis indicates that this genetic variant is only weakly associated with overall cancer risk. However, the rs2736098 polymorphism may affect individual susceptibility to lung and bladder cancer. Further studies are needed to validate our findings.

[655]

TÍTULO / TITLE: - Cigarette smoke extract induces the expression of GRP78 in A549 cells via the p38/MAPK pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2013 Dec;8(6):1683-8. doi: 10.3892/mmr.2013.1724. Epub 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1724](#)

AUTORES / AUTHORS: - He B; Luo B; Chen Q; Zhang L

INSTITUCIÓN / INSTITUTION: - Department of Geriatric Medicine, Xiangya Hospital of Central South University, Changsha, Hunan 410008, P.R. China.

RESUMEN / SUMMARY: - Apoptosis of alveolar epithelial cells has been implicated in the pathogenesis of chronic obstructive pulmonary disease. To determine the involvement of glucoseregulated protein 78 (GRP78) in the cigarette smoke extract

(CSE)induced apoptosis of alveolar epithelial cells and the potential mechanisms underlying this effect, A549 cells that originate from alveolar type II epithelial cells were exposed to various CSE conditions in the present study. GRP78 expression and its effect on the apoptosis of A549 cells were investigated using techniques such as RT-PCR, western blot analysis, gene knockdown by GRP78 siRNA interference and the terminal deoxynucleotidyl transferase dUTP nickend labeling assay. The activity of the p38/mitogenactivated protein kinase (MAPK) pathway and its involvement in GRP78 expression were also analyzed using SB203580, a p38/MAPK pathway inhibitor. It was demonstrated that GRP78 expression in the cells was significantly upregulated following CSE exposure and a 12h exposure of 5% CSE was the most efficient in inducing GRP78 expression. This CSEinduced GRP78 expression was significantly attenuated by GRP78 siRNA or by the use of SB203580. The downregulation of GRP78 expression by GRP78 siRNA also led to the increased expression of caspase-3 and an increased apoptotic index (AI, $P < 0.05$ vs. other groups). These results suggested that CSE induced GRP78 expression in A549 cells. This study demonstrated that upregulated GRP78 expression may be antiapoptotic effects and the p38/MAPK pathway was involved in the process of CSEinduced GRP78 expression in A549 cells.

[656]

TÍTULO / TITLE: - The Long Noncoding RNA HOTAIR Contributes to Cisplatin Resistance of Human Lung Adenocarcinoma Cells via downregulation of p21(WAF1/CIP1) Expression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 14;8(10):e77293. doi: 10.1371/journal.pone.0077293.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077293](#)

AUTORES / AUTHORS: - Liu Z; Sun M; Lu K; Liu J; Zhang M; Wu W; De W; Wang Z; Wang R

INSTITUCIÓN / INSTITUTION: - Department of Oncology, the Second Affiliated Hospital of Nanjing Medical University, Nanjing, P.R. China.

RESUMEN / SUMMARY: - HOTAIR, a long intervening non-coding RNA (lincRNA), associates with the Polycomb Repressive Complex 2 (PRC2) and is reported to reprogram chromatin organization and promote tumor progression. However, little is known about the roles of this gene in the development of chemoresistance phenotype of lung adenocarcinoma (LAD). Thus, we investigated the involvement of HOTAIR in the resistance of LAD cells to cisplatin. In this study, we show that HOTAIR expression was significantly upregulated in cisplatin-resistant A549/DDP cells compared with in parental A549 cells. Knockdown of HOTAIR by RNA interference could resensitize the responses of A549/DDP cells to cisplatin both in vitro and in vivo. In contrast, overexpression of HOTAIR could decrease the sensitivity of A549 and SPC-A1 cells to cisplatin. We also found that the siRNA/HOTAIR1-mediated chemosensitivity enhancement was associated with inhibition of cell proliferation, induction of G0/G1 cell-cycle arrest and apoptosis enhancement through regulation of p21(WAF1/CIP1) (p21) expression. Also, pcDNA/p21 or siRNA/p21 could mimic the effects of siRNA/HOTAIR1 or pcDNA/HOTAIR on the sensitivity of LAD cells to cisplatin. Importantly, siRNA/p21 or pcDNA/p21 could partially rescue the effects of siRNA/HOTAIR1 or pcDNA/HOTAIR on both p21 expression and cisplatin sensitivity in

LAD cells. Further, HOTAIR was observed to be significantly downregulated in cisplatin-responding LAD tissues, and its expression was inversely correlated with p21 mRNA expression. Taken together, our findings suggest that upregulation of HOTAIR contributes to the cisplatin resistance of LAD cells, at least in part, through the regulation of p21 expression.

[657]

TÍTULO / TITLE: - Right Native Lung Pneumonectomy Due to over Inflation Three Years after Left Single Lung Transplantation for Pulmonary Lymphangiomyomatosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Oct 3.

AUTORES / AUTHORS: - Liu F; Ruan Z; Wang S; Lin Q

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, The First People's Hospital Affiliated to Shanghai Jiao Tong University, Shanghai, China.

RESUMEN / SUMMARY: - Native lung hyperinflation (NLH) is one of the known complications after single lung transplantation (SLT). Generally, satisfactory results are achieved in patients undergoing SLT when simultaneous (or second stage) volume reduction of the contralateral native lung is performed. Contralateral native lung pneumonectomy after SLT is rarely reported. In this article, we report a case of a successful, right pneumonectomy of the native lung, 3 years after a left single lung transplant for pulmonary lymphangiomyomatosis (PLAM). The patient's pulmonary function and quality of life improved significantly after a right pneumonectomy of the native lung.

[658]

TÍTULO / TITLE: - Critical dose and toxicity index of organs at risk in radiotherapy: Analyzing the calculated effects of modified dose fractionation in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Dosim. 2013 Nov 13. pii: S0958-3947(13)00098-8. doi: 10.1016/j.meddos.2013.08.009.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.meddos.2013.08.009](#)

AUTORES / AUTHORS: - Pedicini P; Strigari L; Benassi M; Caivano R; Fiorentino A; Nappi A; Salvatore M; Storto G

INSTITUCIÓN / INSTITUTION: - Service of Medical Physics, I.R.C.C.S. Regional Cancer Hospital C.R.O.B, Rionero in Vulture, Italy. Electronic address: ppiern@libero.it.

RESUMEN / SUMMARY: - To increase the efficacy of radiotherapy for non-small cell lung cancer (NSCLC), many schemes of dose fractionation were assessed by a new "toxicity index" (I), which allows one to choose the fractionation schedules that produce less toxic treatments. Thirty-two patients affected by non resectable NSCLC were treated by standard 3-dimensional conformal radiotherapy (3DCRT) with a strategy of limited treated volume. Computed tomography datasets were employed to re plan by simultaneous integrated boost intensity-modulated radiotherapy (IMRT). The dose distributions from plans were used to test various schemes of dose fractionation, in 3DCRT as well as in IMRT, by transforming the dose-volume histogram (DVH) into a biological equivalent DVH (BDVH) and by varying the overall treatment time. The

BDVHs were obtained through the toxicity index, which was defined for each of the organs at risk (OAR) by a linear quadratic model keeping an equivalent radiobiological effect on the target volume. The less toxic fractionation consisted in a severe/moderate hyper fractionation for the volume including the primary tumor and lymph nodes, followed by a hypofractionation for the reduced volume of the primary tumor. The 3DCRT and IMRT resulted, respectively, in 4.7% and 4.3% of dose sparing for the spinal cord, without significant changes for the combined-lungs toxicity ($p < 0.001$). Schedules with reduced overall treatment time (accelerated fractionations) led to a 12.5% dose sparing for the spinal cord (7.5% in IMRT), 8.3% dose sparing for V20 in the combined lungs (5.5% in IMRT), and also significant dose sparing for all the other OARs ($p < 0.001$). The toxicity index allows to choose fractionation schedules with reduced toxicity for all the OARs and equivalent radiobiological effect for the tumor in 3DCRT, as well as in IMRT, treatments of NSCLC.

[659]

TÍTULO / TITLE: - A Novel Use of Gentamicin in the ROS-Mediated Sensitization of NCI-H460 Lung Cancer Cells to Various Anticancer Agents.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - ACS Chem Biol. 2013 Oct 17.

●● Enlace al texto completo (gratis o de pago) [1021/cb4007024](#)

AUTORES / AUTHORS: - Cuccarese MF; Singh A; Amiji M; O'Doherty GA

INSTITUCIÓN / INSTITUTION: - Department of Chemistry and Chemical Biology and double dagger Department of Pharmaceutical Sciences, Northeastern University, Boston, Massachusetts, United States.

RESUMEN / SUMMARY: - Aminoglycosides are broad-spectrum antibiotics that are used for the treatment of severe Gram-negative and Gram-positive bacterial infections. While bactericidal effects of aminoglycosides are due to binding to the 30S subunit of the bacterial ribosome, aminoglycosides can affect protein synthesis, intracellular calcium levels, and levels of reactive oxygen species (ROS) in eukaryotic cells. While aminoglycosides can be cytotoxic at high concentrations, our results show that at much lower doses, gentamicin can be implemented as a sensitizing agent for the NSCLC cell line NCI-H460, increasing the efficacy of camptothecin, digitoxin, and vinblastine in vitro. We have also established that this sensitization is reliant on the ROS response generated by gentamicin.

[660]

TÍTULO / TITLE: - Small-cell lung cancer with a rare epidermal growth factor receptor gene mutation showing "wax-and-wane" transformation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Nov 7;13(1):529.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-529](#)

AUTORES / AUTHORS: - Takagi Y; Nakahara Y; Hosomi Y; Hishima T

RESUMEN / SUMMARY: - BACKGROUND: Small-cell lung cancer with epidermal growth factor receptor (EGFR) gene mutation typically manifests as a transformation occurring after EGFR tyrosine kinase inhibitor therapy for adenocarcinoma with EGFR mutation, whereas primary small-cell lung cancer showing EGFR mutation is extremely rare. Second biopsy of EGFR-mutated tumor has been broadly recognized as necessary, but is not always performed in daily practice, mainly due to the

imbalance between the potential risk of the diagnostic procedure and the therapeutic impact of the biopsy result. CASE PRESENTATION: A 70-year-old woman who had never smoked was referred to our hospital with chief complaints of cough and back pain. Transbronchial lung biopsy from the primary tumor of the left upper lobe revealed combined small-cell lung cancer and adenocarcinoma, a subtype of small-cell lung cancer. EGFR L861Q mutation was detected in both small-cell lung cancer and adenocarcinoma components. Given the staging of cT2aN3M1b (Stage IV) and histological diagnosis, first-line chemotherapy with cisplatin plus irinotecan was initiated, and partial response was achieved. Seven months after initial diagnosis, the primary tumor enlarged again, and a second biopsy from the enlarged lesion detected only adenocarcinoma with the L861Q mutation. Erlotinib was started, but multiple brain metastases and enlarged mediastinal lymph nodes subsequently appeared. Whole-brain radiation therapy was performed, and endobronchial ultrasonography-guided transbronchial biopsy from the lymph node revealed reverse transformation to small-cell lung cancer with the L861Q mutation. Amrubicin therapy achieved partial response after two cycles, with the shrinkage lasting for eight months. Serum sialyl Lewis X antigen level increased when the adenocarcinoma component was dominant, whereas plasma pro-gastrin-releasing peptide level increased when the small-cell lung cancer component became dominant. CONCLUSIONS: Transformation of the tumor correlates with the difference between small-cell lung cancer and adenocarcinoma in sensitivity to therapies, so repeated biopsies are beneficial for choosing appropriate treatments. Noninvasively obtainable parameters such as tumor markers can support the need for biopsy.

[661]

TÍTULO / TITLE: - TGF-beta1 Downregulates COX-2 Expression Leading to Decrease of PGE2 Production in Human Lung Cancer A549 Cells, Which Is Involved in Fibrotic Response to TGF-beta1.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 2;8(10):e76346. doi: 10.1371/journal.pone.0076346.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0076346](#)

AUTORES / AUTHORS: - Takai E; Tsukimoto M; Kojima S

INSTITUCIÓN / INSTITUTION: - Department of Radiation Biosciences, Faculty of Pharmaceutical Sciences, Tokyo University of Science, Noda-shi, Chiba, Japan.

RESUMEN / SUMMARY: - Transforming growth factor-ss1 (TGF-beta1) is a multifunctional cytokine that is involved in various pathophysiological processes, including cancer progression and fibrotic disorders. Here, we show that treatment with TGF-beta1 (5 ng/mL) induced downregulation of cyclooxygenase-2 (COX-2), leading to reduced synthesis of prostaglandin E2 (PGE2), in human lung cancer A549 cells. Treatment of cells with specific inhibitors of COX-2 or PGE2 receptor resulted in growth inhibition, indicating that the COX-2/PGE2 pathway contributes to proliferation in an autocrine manner. TGF-beta1 treatment induced growth inhibition, which was attenuated by exogenous PGE2. TGF-beta1 is also a potent inducer of epithelial mesenchymal transition (EMT), a phenotype change in which epithelial cells differentiate into fibroblastoid cells. Supplementation with PGE2 or PGE2 receptor EP4 agonist PGE1-alcohol, as compared with EP1/3 agonist sulprostone, inhibited TGF-beta1-induced expression of fibronectin and collagen I (extracellular matrix

components). Exogenous PGE2 or PGE2 receptor agonists also suppressed actin remodeling induced by TGF-beta1. These results suggest that PGE2 has an anti-fibrotic effect. We conclude that TGF-beta1-induced downregulation of COX-2/PGE2 signaling is involved in facilitation of fibrotic EMT response in A549 cells.

[662]

TÍTULO / TITLE: - Paired diagnostic and pharmacodynamic analysis of rare non-small cell lung cancer cells enabled by the VerIFAST platform.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lab Chip. 2013 Nov 26;14(1):99-105. doi: 10.1039/c3lc50912e.

●● Enlace al texto completo (gratis o de pago) [1039/c3lc50912e](#)

AUTORES / AUTHORS: - Casavant BP; Strotman LN; Tokar JJ; Thiede SM; Traynor AM; Ferguson JS; Lang JM; Beebe DJ

INSTITUCIÓN / INSTITUTION: - Department of Biomedical Engineering, Wisconsin Institutes for Medical Research, University of Wisconsin-Madison, 1111 Highland Ave., Madison, WI, USA. djbeebe@wisc.edu.

RESUMEN / SUMMARY: - Lung cancer is the leading cause of cancer-related deaths in the United States and worldwide. This has led to major research initiatives focusing on improving early diagnosis rate, as well as the development of pharmacodynamic biomarkers. However, broad clinical integration of these approaches is limited due to the invasive nature of lung biopsies, needle aspirates and resections. Recently, an advance for sampling suspicious lung nodules to collect mini-bronchoalveolar lavage (mBAL) samples was shown to be diagnostically relevant but limited by standard cytology techniques leading to low sensitivity and specificity. In addition, a second non-invasive method that holds great promise is the collection of circulating tumor cells, a rare population of tumor cells that have shed into peripheral circulation from primary or metastatic tumor sites, from blood. Here, we utilize a recently published platform, VerIFAST, for the capture and proteomic analysis of rare cells, to isolate cells of interest from lung cancer patients using both mBAL and blood samples. The VerIFAST platform leverages surface tension at the microscale to pin aqueous and oil fluids in adjacent chambers to create a virtual filter between two aqueous fluids. In this manuscript, the VerIFAST was further enhanced to include oil pinning, which allowed on-device tumbling, further eliminating a laborious and time consuming step that could result in increased sample loss. Finally, we further developed the base assays used in standard histopathologic assays for diagnostic and pharmacodynamic analysis of these rare lung cancer cells. Specifically, we examined thyroid transcription factor-1 (TTF-1) signal intensity, in which loss is associated with more aggressive disease, and epidermal growth factor receptor (EGFR) signal intensity, which is a high value therapeutic target in lung cancer.

[663]

TÍTULO / TITLE: - Overall survival and toxicities regarding thoracic three-dimensional radiotherapy with concurrent chemotherapy for stage IV non-small cell lung cancer: results of a prospective single-center study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 12;13:474. doi: 10.1186/1471-2407-13-474.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-474](#)

AUTORES / AUTHORS: - Su SF; Hu YX; Ouyang WW; Lu B; Ma Z; Li QS; Li HQ; Geng YC

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Oncology, Affiliated Hospital of Guiyang Medical College, and Guizhou Cancer Hospital, 1 Beijing Road West, Guizhou, Guiyang, People's Republic of China. lbgymaaaa@sohu.com.

RESUMEN / SUMMARY: - BACKGROUND: The role of chemotherapy given concurrently with thoracic three-dimensional radiotherapy for stage IV non-small cell lung cancer (NSCLC) is not well defined. We performed this study to investigate overall survival and toxicity in patients with stage IV NSCLC treated with this modality. METHODS: From 2003 to 2010, 201 patients were enrolled in this study. All patients received chemotherapy with concurrent thoracic three-dimensional radiotherapy. The study endpoints were the assessment of overall survival (OS) and acute toxicity. RESULTS: For all patients, the median survival time (MST) was 10.0 months, and the 1-, 2- and 3-year OS rates were 40.2%, 16.4%, and 9.6%, respectively. The MST was 14.0 months for patients who received a total radiation dose ≥ 63 Gy to the primary tumor, whereas it was 8.0 months for patients who received a total dose < 63 Gy ($P = 0.000$). On multivariate analysis, a total dose ≥ 63 Gy, a single site of metastatic disease, and undergoing ≥ 4 cycles of chemotherapy were independent prognostic factors for better OS ($P = 0.007$, $P = 0.014$, and $P = 0.038$, respectively); radiotherapy involving metastatic sites was a marginally significant prognostic factor ($P = 0.063$). When the whole group was subdivided into patients with metastasis at a single site and multiple sites, a higher radiation dose to the primary tumor remained a significant prognostic factor for improved OS. For patients who received ≥ 4 cycles of chemotherapy, high radiation dose remained of benefit for OS ($P = 0.001$). Moreover, for the subgroup that received < 4 chemotherapy cycles, the radiation dose was of marginal statistical significance regarding OS ($P = 0.063$). Treatment-related toxicity was found to be acceptable. CONCLUSIONS: Radiation dose to primary tumor, the number of metastatic sites, and the number of chemotherapy cycles were independent prognostic factors for OS in stage IV NSCLC patients treated with concurrent chemoradiotherapy. In addition to systemic chemotherapy, aggressive thoracic radiotherapy was shown to play an important role in improving OS. TRIAL REGISTRATION: Registered on (ChiCTR-TNC-10001026).

[664]

TÍTULO / TITLE: - Delphinidin reduces cell proliferation and induces apoptosis of non-small-cell lung cancer cells by targeting EGFR/VEGFR2 signaling pathways.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 4;8(10):e77270. doi: 10.1371/journal.pone.0077270.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077270](https://doi.org/10.1371/journal.pone.0077270)

AUTORES / AUTHORS: - Pal HC; Sharma S; Strickland LR; Agarwal J; Athar M; Elmets CA; Afaq F

INSTITUCIÓN / INSTITUTION: - Department of Dermatology, University of Alabama at Birmingham, Birmingham, Alabama, United States of America.

RESUMEN / SUMMARY: - Epidermal growth factor receptor (EGFR) and vascular endothelial growth factor receptor 2 (VEGFR2) have emerged as two effective clinical targets for non-small-cell lung cancer (NSCLC). In the present study, we found that delphinidin, an anthocyanidin, present in pigmented fruits and vegetables, is a potent

inhibitor of both EGFR and VEGFR2 in NSCLC cells that overexpress EGFR/VEGFR2. Using these cells, we next determined the effects of delphinidin on cell growth and apoptosis in vitro and on tumor growth and angiogenesis in vivo. Delphinidin (5-60 microM) treatment of NSCLC cells inhibited the activation of PI3K, and phosphorylation of AKT and MAPKs. Additionally, treatment of NSCLC cells with delphinidin resulted in inhibition of cell growth without having significant toxic effects on normal human bronchial epithelial cells. Specifically, treatment of NCI-H441 and SK-MES-1 cells with delphinidin (5-60 microM) resulted in (i) cleavage of PARP protein, (ii) activation of caspase-3 and -9, (iii) downregulation of anti-apoptotic proteins (Bcl2, Bcl-xL and Mcl-1), (iv) upregulation of pro-apoptotic proteins (Bax and Bak), and (v) decreased expression of PCNA and cyclin D1. Furthermore, in athymic nude mice subcutaneously implanted with human NSCLC cells, delphinidin treatment caused a (i) significant inhibition of tumor growth, (ii) decrease in the expression of markers for cell proliferation (Ki67 and PCNA) and angiogenesis (CD31 and VEGF), and (iii) induction of apoptosis, when compared with control mice. Based on these observations, we suggest that delphinidin, alone or as an adjuvant to current therapies, could be used for the management of NSCLC, especially those that overexpress EGFR and VEGFR2.

[665]

TÍTULO / TITLE: - Stereotactic Body Radiation Therapy in Octogenarians With Stage I Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Oct 21. pii: S1525-7304(13)00184-8. doi: 10.1016/j.clc.2013.08.007.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.clc.2013.08.007](#)

AUTORES / AUTHORS: - Sandhu AP; Lau SK; Rahn D; Nath SK; Kim D; Song WY; Gulaya S; Fuster MM; Bazhenova L; Mundt AJ

INSTITUCIÓN / INSTITUTION: - Department of Radiation Medicine and Applied Sciences, Moores University of California San Diego Cancer Center, La Jolla, CA. Electronic address: apsandhu@ucsd.edu.

RESUMEN / SUMMARY: - BACKGROUND: The purpose of this study was to describe our clinical experience using stereotactic body radiation therapy (SBRT) to treat medically inoperable stage I non-small-cell lung cancer (NSCLC) in very elderly patients. PATIENTS AND METHODS: Twenty-four consecutive octogenarians with stage I NSCLC were treated with SBRT between 2007 and 2011 at a single center. Median prescription dose was 48 Gy (range, 48-56). Follow-up clinical examination and computed tomography (CT) were performed every 2 to 3 months. RESULTS: Median age was 85 years (range, 80-89). Twenty-three (96%) patients had peripheral tumors, and median tumor size was 22 mm (range, 11-49). Tissue diagnosis was obtained in 16 (67%) patients. Median follow-up for all patients was 27.6 months (range, 4.3-61.2). The 24-month disease-free survival was 77% (95% confidence interval [CI], 61%-97%). The 24-month overall survival (OS) was 74% (95% CI, 57%-94%). No local failure (LF) was observed during the period of observation. Nodal failure (NF) and distant failure (DF) occurred in 2 and 4 patients, respectively. The cumulative incidence of competing mortality at 24 months was estimated at 13% (95% CI, 3%-30%). No difference in outcomes with or without tissue diagnosis was observed. No grade \geq 3 early or late treatment-related toxicities were observed. CONCLUSION: Octogenarians tolerate SBRT well, which makes it an attractive treatment option.

[666]

TÍTULO / TITLE: - Relationships of coagulation factor XIII activity with cell-type and stage of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Yonsei Med J. 2013 Nov;54(6):1394-9. doi: 10.3349/ymj.2013.54.6.1394.

●● Enlace al texto completo (gratis o de pago) [3349/ymj.2013.54.6.1394](#)

AUTORES / AUTHORS: - Lee SH; Suh IB; Lee EJ; Hur GY; Lee SY; Lee SY; Shin C; Shim JJ; In KH; Kang KH; Yoo SH; Kim JH

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary, Sleep and Critical Care Medicine, Department of Internal Medicine, Korea University Ansan Hospital, 123 Jeokgeum-ro, Danwon-gu, Ansan 425-707, Korea. chepraxis@korea.ac.kr.

RESUMEN / SUMMARY: - PURPOSE: Factor XIII (FXIII), a thrombin-activated plasma transglutaminase zymogen, is involved in cancer development and progression through a triggered coagulation pathway. The aim of this study was to examine whether FXIII activity levels differed in non-small cell lung cancer (NSCLC) patients according to histological types and TNM stage when compared with healthy subjects. MATERIALS AND METHODS: Twenty-eight NSCLC patients and 28 normal controls who had been individually age-, gender-, body mass index-, smoking status-, and smoking amount-matched were enrolled: 13 adenocarcinomas, 11 squamous cell carcinomas, and four undifferentiated NSCLCs; four stage I, two stage II, 12 stage III, and 10 stage IV NSCLCs. FXIII activity was measured using fluorescence-based protein arrays. RESULTS: The median FXIII activity level of the NSCLC group [24.2 Loewy U/mL, interquartile range (IQR) 14.9-40.4 Loewy U/mL] was significantly higher than that of the healthy group (17.5 Loewy U/mL, IQR 12.6-26.4 Loewy U/mL) ($p=0.01$). There were no differences in FXIII activity between adenocarcinoma (median 18.6 Loewy U/mL) and squamous cell carcinoma (median 28.7 Loewy U/mL). NSCLC stage significantly influenced FXIII activity ($p=0.02$). The FXIII activity of patients with stage III NSCLC (median 27.3 Loewy U/mL, IQR 19.3-40.5 Loewy U/mL) was significantly higher than those of patients with stage I or II (median 14.0 Loewy U/mL, IQR 13.1-23.1 Loewy U/mL, $p=0.04$). FXIII activity was negatively correlated with aPTT in NSCLC patients ($r=-0.38$, $p=0.04$). CONCLUSION: Patients with advanced-stage NSCLC exhibited higher coagulation FXIII activity than healthy controls and early-stage NSCLC patients.

[667]

TÍTULO / TITLE: - Association of cigarette smoking with the expression of nuclear survivin in pathological Stage IA lung adenocarcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Mol Morphol. 2013 Nov 9.

●● Enlace al texto completo (gratis o de pago) [1007/s00795-013-0061-9](#)

AUTORES / AUTHORS: - Hirano H; Maeda H; Takeuchi Y; Susaki Y; Kobayashi R; Hayashi A; Ose N; Nakazawa Y; Yamaguchi T; Yokota S; Mori M

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Toneyama National Hospital, Toyonaka, Osaka, Japan, hihirano@toneyama.go.jp.

RESUMEN / SUMMARY: - Survivin is expressed in the cytoplasm and/or nucleus of various types of malignant tumor cells. Cytoplasmic survivin functions as an apoptosis inhibitor, while nuclear survivin is indispensable for complete mitosis completion. To investigate the effect of cigarette smoking on the survivin expression in lung adenocarcinomas at the early developmental stage, we examined the expression of nuclear and cytoplasmic survivin in pathological Stage IA lung adenocarcinomas resected from 38 non-smokers and 44 smokers (current smokers and ex-smokers) using an immunohistochemical method. Labeling indices of nuclear survivin in tumors of smokers were significantly greater than those of non-smokers. The labeling index of nuclear survivin was above 3 % in only 1 (2.6 %) of the 38 tumors of the non-smokers, while the labeling indices in 19 (43.2 %) of 44 tumors of the smokers were above 3 % with a significantly greater frequency. There was no significant difference in the labeling index of nuclear survivin between current smokers and ex-smokers. There was no significant difference in the labeling index of cytoplasmic survivin between tumors of the non-smokers and the smokers. The present results show that cigarette smoking is associated with the higher nuclear surviving expression in lung adenocarcinomas at the early stage, suggesting that cigarette smoking affects the nuclear survivin expression in lung adenocarcinomas at the early developmental stage.

[668]

TÍTULO / TITLE: - Giant Solitary Fibrous Tumor of the Pleura Causing Respiratory Insufficiency: Report of 3 Cases.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Oct 3.

AUTORES / AUTHORS: - Abe M; Nomori H; Fukazawa M; Sugimura H; Narita M; Takeshi A

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Kameda Medical Center, Kamogawa, Chiba, Japan.

RESUMEN / SUMMARY: - We present 3 cases of solitary fibrous tumors (SFTs) occupying entire hemithorax and resulting in respiratory insufficiency. All patients were treated by complete resection, resulting in immediate re-expansion of the lungs and recovery from respiratory insufficiency. Although, two patients remain alive without recurrence, one patient had pleural recurrences three times over a 20-year period, all of which were treated by surgical resection. All of the primary tumors exhibited areas of hypercellularity, hemorrhage, or necrosis. All of the recurrent tumors in the recurrent case displayed large areas of hypercellularity, similar to the part of primary tumor. Although, the MIB-1 index in primary tumors was less than 5%, the index of the recurrent tumors increased up to 11% with repeated recurrence. Giant SFTs usually display hypercellularity, hemorrhage, or necrosis. Tumors with hypercellularity could recur. MIB-1 index could display malignant characteristics of recurrent tumors. Long-term follow-up for more than 10 years after surgery is necessary, particularly for tumors with areas of hypercellularity.

[669]

TÍTULO / TITLE: - Molecular characterization of scant lung tumor cells using iron-oxide nanoparticles and micro-nuclear magnetic resonance.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nanomedicine. 2013 Nov 4. pii: S1549-9634(13)00584-4. doi: 10.1016/j.nano.2013.10.008.

●● Enlace al texto completo (gratis o de pago) [1016/j.nano.2013.10.008](https://doi.org/10.1016/j.nano.2013.10.008)

AUTORES / AUTHORS: - Ghazani A; Pectasides M; Sharma A; Castro CM; Mino-Kenudson M; Lee H; Shepard JA; Weissleder R

INSTITUCIÓN / INSTITUTION: - Center for Systems Biology, Massachusetts General Hospital, Boston, MA.

RESUMEN / SUMMARY: - Advances in nanotechnology and microfluidics are enabling the analysis of small amounts of human cells. We tested whether recently developed micro-nuclear magnetic resonance (muNMR) technology could be leveraged for diagnosing pulmonary malignancy using fine needle aspirate (FNA) of primary lesions and/or peripheral blood samples. We enrolled a cohort of 35 patients referred for CT biopsy of primary pulmonary nodules, liver or adrenal masses and concurrently obtained FNA and peripheral blood samples. FNA sampling yielded sufficient material for muNMR analysis in 91% of cases and had a sensitivity and specificity of 91.6% and 100% respectively. Interestingly, among blood samples with positive circulating tumor cells (CTC), muNMR analysis of each patient's peripheral blood led to similar diagnosis (malignant vs benign) and differential diagnosis (lung malignancy subtype) in 100% and 90% (18/20) of samples, respectively. muNMR appears to be a valuable, non-invasive adjunct in the diagnosis of lung cancer.

[670]

TÍTULO / TITLE: - The Codon 399 Arg/Gln XRCC1 Polymorphism is Associated with Lung Cancer in Indians.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5275-9.

AUTORES / AUTHORS: - Natukula K; Jamil K; Pingali UR; Attili VS; Madireddy UR

INSTITUCIÓN / INSTITUTION: - Genetics Department, Bhagwan Mahavir Medical Research Centre, Masab tank, India E-mail : kaiser.jamil@gmail.com.

RESUMEN / SUMMARY: - Background: The XRCC1 (X-ray repair cross complementing group-I) gene in BER (base excision repair) pathway is essential for DNA repair process. Polymorphisms in this gene are associated with variations in the repair efficiency which might predispose individuals to development of various cancers. Two variants of XRCC1 gene (at codon 399), Gln/Gln and Arg/Gln, have been shown to be related to lowered DNA repair capacity and increased genomic instability in multiple studies. Hence our investigation focused on genotyping these variants to correlate with other multiple risk factors in lung cancer (NSCLC) patients since we hypothesized that these variants of the XRCC1 gene might influence disease susceptibility. Materials and Methods: We examined the frequency of the polymorphism in one hundred cases and an almost equal number of controls after recording their demographics with a structured questionnaire. Genomic DNA from blood samples was extracted for PCR studies, followed by RFLP to determine the variants. The significance of the data was statistically analyzed. Results: The three genotypes in cases and controls were Arg/Arg (40% and 54.45%); Gln/Gln (19% and 9.90%), and Arg/Gln (41.0% and 35.64%) respectively. Among these 3 genotypes, we found Gln/Gln and Arg/Gln to show association with lung cancer. Correlating these genotypes with several parameters, we also found that these two variants were associated with risk in males ($p < 0.05$) and with smoking habits ($p < 0.05$). In females Arg/Gln genotype showed association with stage

of the disease ($p=0.04$). This is the first report in South Indian scenario where Arg399Gln genotypes were found to be associated with stage of the disease in females. Conclusions: It is concluded that XRCC1 genotypes Gln/Gln and Arg/Gln may influence cancer susceptibility in patients with smoking habits and these functional SNPs in XRCC1 gene may act as attractive candidate biomarkers in lung cancer for diagnosis and prognosis.

[671]

TÍTULO / TITLE: - How Molecular Understanding Affects to Prescribing Patterns and Clinical Outcome of Gefitinib in Non-small Cell Lung Cancer? 10 Year Experience of Single Institution.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Res. Acceso gratuito al texto completo a partir de 1 año de la fecha de publicación.

- Enlace a la Editora de la Revista <http://cancerres.aacrjournals.org/>

- Cita: Cancer Research: <> Treat. 2013 Sep;45(3):178-85. doi: 10.4143/crt.2013.45.3.178. Epub 2013 Sep 30.

- Enlace al texto completo (gratis o de pago) 4143/crt.2013.45.3.178

AUTORES / AUTHORS: - Keam B; Kim DW; Park JH; Lee JO; Kim TM; Lee SH; Chung DH; Heo DS

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea. ; Cancer Research Institute, Seoul National University College of Medicine, Seoul, Korea.

RESUMEN / SUMMARY: - PURPOSE: Gefitinib was introduced in 2002 for treatment of non-small cell lung cancer (NSCLC); however, it is not clear whether its use in daily practice has changed the outcome of patients. The purpose of this study is to evaluate the question of how molecular understanding regarding gefitinib and epidermal growth factor receptor (EGFR) mutation affect the prescribing patterns and clinical outcomes of treatment with gefitinib in NSCLC, in a real practical field. MATERIALS AND METHODS: We conducted a retrospective analysis of the consecutive database of NSCLC patients who were treated with gefitinib at Seoul National University Hospital between January 2002 and December 2011. Prescribing patterns and clinical outcomes were analyzed by year. RESULTS: A total of 1,115 NSCLC patients, who received gefitinib at recurrent or metastatic setting, were included in this study. Proportion of patients receiving gefitinib, for the first line, showed a gradual increase, from 5.2% in 2002-2003 to 30.6% in 2010-2011. Proportion of patients who underwent EGFR mutation testing showed a rapid increase, from 0.6% in 2004-2005 to 73.5% in 2010-2011. The response rate also showed a gradual increase, from 17.2% in 2002-2003 to 57.1% in 2010-2011 ($p<0.001$). The median progression-free survival of gefitinib was increased with statistical significance from 2.8 months in 2002-2003 to 9.1 months in 2010-2011 ($p<0.001$). CONCLUSION: We demonstrated that molecular understanding and practical use of EGFR mutation testing have resulted in a change in the prescription patterns of gefitinib. Use of an enrichment strategy can lead to improvement in the efficacy of gefitinib in real practice.

[672]

TÍTULO / TITLE: - Evaluating proton stereotactic body radiotherapy to reduce chest wall dose in the treatment of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Dosim. 2013 Winter;38(4):442-7. doi: 10.1016/j.meddos.2013.08.001.

●● Enlace al texto completo (gratis o de pago) [1016/j.meddos.2013.08.001](#)

AUTORES / AUTHORS: - Welsh J; Amini A; Ciura K; Nguyen N; Palmer M; Soh H; Allen PK; Paolini M; Liao Z; Bluett J; Mohan R; Gomez D; Cox JD; Komaki R; Chang JY

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, The University of Texas, MD Anderson Cancer Center, Houston, TX. Electronic address: jwelsh@mdanderson.org.

RESUMEN / SUMMARY: - Stereotactic body radiotherapy (SBRT) can produce excellent local control of several types of solid tumor; however, toxicity to nearby critical structures is a concern. We found previously that in SBRT for lung cancer, the chest wall (CW) volume receiving 20, 30, or 40Gy (V20, V30, or V40) was linked with the development of neuropathy. Here we sought to determine whether the dosimetric advantages of protons could produce lower CW doses than traditional photon-based SBRT. We searched an institutional database to identify patients treated with photon SBRT for lung cancer with tumors within < 2.5cm of the CW. We found 260 cases; of these, chronic grade ≥ 2 CW pain was identified in 23 patients. We then selected 10 representative patients from this group and generated proton SBRT treatment plans, using the identical dose of 50Gy in 4 fractions, and assessed potential differences in CW dose between the 2 plans. The proton SBRT plans reduced the CW doses at all dose levels measured. The median CW V20 was 364.0cm³ and 160.0cm³ ($p < 0.0001$), V30 was 144.6cm³ vs 77.0cm³ ($p = 0.0012$), V35 was 93.9cm³ vs 57.9cm³ ($p = 0.005$), V40 was 66.5cm³ vs 45.4cm³ ($p = 0.0112$), and mean lung dose was 5.9Gy vs 3.8Gy ($p = 0.0001$) for photons and protons, respectively. Coverage of the planning target volume (PTV) was comparable between the 2 sets of plans (96.4% for photons and 97% for protons). From a dosimetric standpoint, proton SBRT can achieve the same coverage of the PTV while significantly reducing the dose to the CW and lung relative to photon SBRT and therefore may be beneficial for the treatment of lesions closer to critical structures.

[673]

TÍTULO / TITLE: - Improvement of orthotopic lung cancer mouse model via thoracotomy and orotracheal intubation enabling in vivo imaging studies.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Lab Anim. 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1177/0023677213512821](#)

AUTORES / AUTHORS: - Im GH; Jang MS; Chung JJ; Kim KN; Kim JH; Kim SI; Lee JH

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine and Center for Molecular and Cellular Imaging, Samsung Biomedical Research Institute, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - Investigation of molecular mechanisms and the efficiency of novel therapeutics for the treatment and prevention of a disease require accurate and accessible preclinical models. Recent developments in personalized medicine employing molecular medicine concepts have favored mice because their genetic make-up is well known and easy to manipulate. For lung cancer, however, orthotopic

models in mice are difficult to create due to their narrow glottis openings which act as obstacles to intubation. In the present study, we develop an orotracheal intubation device which gives a clearer view of the narrow mouse glottis and increases the success rate of intubation. We achieved anesthetization via orotracheal intubation using this novel device and then performed a thoracotomy by making an incision between the fourth and fifth intercostal ribs on the right side of the chest. Lung tumor cells were then inoculated at this site. Tumor formation was monitored through bioluminescence optical and magnetic resonance (MR) imagings, which was confirmed by histological analysis. Temperature drop (<35) and/or loss of body weight (>30% of the initial body weight) observed during any procedure were used as interruption criteria. This method exhibited high tumorigenicity (100%) and a low mortality rate (8%) at specific sites making it ideal for creating orthotopic lung tumor models and making it particularly useful for sequential follow-up studies using in vivo image analysis.

[674]

TÍTULO / TITLE: - Prognostic significance of basic laboratory methods in non- small-cell-lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(9):5473-6.

AUTORES / AUTHORS: - Kaya V; Yildirim M; Demirpence O; Yildiz M; Yalcin AY

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Suleyman Demirel University School of Medicine, Isparta, Turkey E-mail : vildansimsir@yahoo.com.

RESUMEN / SUMMARY: - Background: In our study, the LDH, albumin, hemoglobin, neutrophile, thrombocyte, lymphocyte counts and prognostic significance of neutrophile-lymphocyte and thrombocyte-lymphocyte ratios in NSCLC derived from these counts obtained during regular examinations of patients were examined. Materials and Methods: Histopathologically diagnosed non-small-cell-lung cancer patients between 2008 and 2010 were included in the study. Before the treatment, full blood count including routine lymphocyte count, blood biochemistry examinations including liver (AST, ALT, total protein, Albumin), LDH and kidney (BUN, Cre) function tests were performed. Results: A total of 156 patients, 76 of whom (48.7%) were female and 80 of whom (51.3%) were male were included. Mean hemoglobin level was determined as 12. Overall survival was found to be significantly dependent on whether patients were anemic or not (p: 0.005). Mean LDH level was determined as 233.4. There was no survival difference between patients with and without high LDH (p: 0.532). In patients where NLR showed systemic inflammatory response, overall survival was 10.8 months whereas this duration was 19.6 months in patients where the systemic inflammatory response was negative (p: 0.012). In patients where TLR showed systemic inflammatory response, overall survival was 13.6 months whereas this duration was 21.9 months in patients where the systemic inflammatory response was negative (p: 0.04). Conclusions: Molecular methods have been changing rapidly in today's world and they manage the treatment besides defining the prognosis of patients. However, easily accessible and cheap laboratory parameters should be considered in the prognosis of patients besides these new methods.

[675]

TÍTULO / TITLE: - Bevacizumab treatment for advanced non-small cell lung cancer: A case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Dec;6(6):1779-1783. Epub 2013 Oct 4.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1603](#)

AUTORES / AUTHORS: - Fan Y; Huang Z; Mao W

INSTITUCIÓN / INSTITUTION: - Department of Chemotherapy, Zhejiang Cancer Hospital, Hangzhou, Zhejiang 310022, P.R. China.

RESUMEN / SUMMARY: - The safety of Avastin in lung cancer (SAiL) study is a multi-center, open-source, stand-alone study. Patients with untreated, locally advanced, metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC) were administered up to six cycles of chemotherapy combined with bevacizumab-humanized monoclonal antibodies, followed by maintenance therapy with bevacizumab until further progression of the disease. From August, 2006 to July, 2008 there were a total of 2,172 patients enrolled in the study, with a median progression-free survival time of 7.8 months and an overall survival time of 14.6 months. The present study describes the case of a 54-year-old male with lung cancer and T3N0M1 subcutaneous metastasis, which was initially treated with bevacizumab-combined carboplatin/paclitaxel (C/P) therapy and then maintained solely with bevacizumab for five years. Following six cycles of C/P bevacizumab treatment, the therapeutic evaluation revealed a stable disease (SD). The patient was kept on bevacizumab maintenance therapy for 50 months without disease progression until a persistent 3+ proteinuria was diagnosed in a follow-up review, which led to bevacizumab withdrawal and concomitant tumor growth. The present study concluded that the long-term application of bevacizumab monoclonal antibodies (mABs) was safe in a late-stage non-small cell lung cancer patient. The major adverse reaction that was exhibited was proteinuria, which was associated with the cumulative dose of bevacizumab and was able to be reversed by withdrawal. Patients with a prolonged SD may benefit from bevacizumab maintenance therapy.

[676]

TÍTULO / TITLE: - Successful treatment of non-small cell lung tumor with 15 lesions by CyberKnife radiosurgery: A case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Ther Med. 2013 Sep;6(3):808-810. Epub 2013 Jun 28.

●● Enlace al texto completo (gratis o de pago) [3892/etm.2013.1188](#)

AUTORES / AUTHORS: - Yang G; Li M; Wang Y; Wang Y; Liu X

INSTITUCIÓN / INSTITUTION: - Center for Tumor Treatment, People's Liberation Army 107th Hospital, Yantai, Shandong 264002, P.R. China ; Binzhou Medical College, Lai Shan Qu, Yantai, Shandong 264003, P.R. China.

RESUMEN / SUMMARY: - Stereotactic body radiation therapy (SBRT) plays an important role in the treatment of early stage non-small cell lung cancer (NSCLC), particularly when patients are unable to tolerate surgical resection due to comorbid conditions or are unwilling to undergo surgery. High rates of local tumor control that may rival the results of surgery have been demonstrated in certain cases with the practical advantage of a short course of treatment and acceptable toxicity. However, there are few reports of a marked change in the complete response of high risk lung cancer with more than ten lesions. In the present study, we report a case of

adenocarcinoma of the lung with 15 lesions which had metastasized to the mediastinal lymph nodes. Due to advanced age, multiple lesions and metastasis to the mediastinal lymph nodes and the hilar region of the lung, the patient was treated using CyberKnife. A marked response was noted 42 days after CyberKnife radiosurgery with complete disappearance of the tumor and metastatic lesions.

[677]

TÍTULO / TITLE: - Is diabetes mellitus a negative prognostic factor for the treatment of advanced non-small-cell lung cancer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rev Port Pneumol. 2013 Nov 5. pii: S0873-2159(13)00123-2. doi: 10.1016/j.rppneu.2013.09.001.

●● Enlace al texto completo (gratis o de pago) [1016/j.rppneu.2013.09.001](#)

AUTORES / AUTHORS: - Inal A; Kaplan MA; Kucukoner M; Urakci Z; Kilinc F; Isikdogan A

INSTITUCIÓN / INSTITUTION: - Dicle University, Department of Medical Oncology, Diyarbakir, Turkey. Electronic address: dr.ainal@gmail.com.

RESUMEN / SUMMARY: - BACKGROUND: It has been demonstrated that there are a lot of different prognostic factors which are worthy of consideration whereas diabetes mellitus (DM) has not been clearly or consistently identified as a prognostic value in advanced non-small cell lung cancer (NSCLC). The aim of this study was to investigate the prognostic significance of the characteristics of patients in advanced NSCLC. Specifically, we investigated the impact of DM for progression-free survival (PFS) and overall survival (OS) in patients receiving first-line platinum-based doublets chemotherapy. METHODS: We retrospectively reviewed 442 patients with advanced NSCLC. DM and other potential prognostic variables were chosen for analysis in this study. Univariate and multivariate analyses were conducted to identify prognostic factors associated with survival. RESULT: The results of univariate analysis for OS were identified as having prognostic significance: performance status ($p < 0.001$), stage ($p < 0.001$), DM ($p < 0.001$), liver metastasis ($p = 0.02$) and brain metastasis ($p < 0.001$). Stage, diabetes mellitus, and liver metastasis were identified as having prognostic significance for PFS. Multivariate analysis showed that poor performance status, presence of DM and advanced stage were considered independent negative prognostic factors for OS ($p = 0.001$, $p < 0.001$ and $p < 0.001$ respectively). Furthermore, DM and stage were considered independent negative prognostic factors for PFS ($p = 0.005$ and $p = 0.001$ respectively). CONCLUSION: In conclusion, DM at the time of diagnosis was associated with the negative prognostic importance for PFS and OS in the advanced stage patients who were receiving first-line platinum-based doublets chemotherapy. In addition poor performance status and advanced stage were identified as negative prognostic factors.

[678]

TÍTULO / TITLE: - Suppression of low-dose hyper-radiosensitivity in human lung cancer cell line A549 by radiation-induced autophagy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Huazhong Univ Sci Technolog Med Sci. 2013 Oct;33(5):770-4. doi: 10.1007/s11596-013-1195-7. Epub 2013 Oct 20.

●● Enlace al texto completo (gratis o de pago) [1007/s11596-013-1195-7](#)

AUTORES / AUTHORS: - Zhao YX; Cheng C; Zhu F; Wu HG; Ren JH; Chen WH; Cheng J

INSTITUCIÓN / INSTITUTION: - Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430023, China, sophia7781@126.com.

RESUMEN / SUMMARY: - This study explored the role of radiation-induced autophagy in low-dose hyperradiosensitivity (HRS) in the human lung cancer cell line A549. A549 cells, either treated with an autophagic inhibitor 3-methyladenine (3-MA), or with a vehicle control, were irradiated at different low doses (≤ 0.5 Gy). The generation of autophagy was examined by laser scanning confocal microscopy. Western blotting was used to detect the expression of microtubule-associated protein I light chain 3B II (LC3B-II). Flow cytometry (FCM) and clonogenic assays were used to measure the fraction of surviving cells at the low irradiation doses. Our results showed that there was a greater inhibition of autophagic activity, but a higher degree of low-dose HRS in A549 cells treated with 3-MA than in control group. Our data demonstrated that radiation-induced autophagy is correlated with HRS in A549 cells, and is probably one of the mechanisms underlying HRS.

[679]

TÍTULO / TITLE: - Identification of TNM stage-specific genes in lung adenocarcinoma by genome-wide expression profiling.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Sep;6(3):763-768. Epub 2013 Jul 15.

●● [Enlace al texto completo \(gratis o de pago\) 3892/ol.2013.1469](#)

AUTORES / AUTHORS: - Liu M; Pan H; Zhang F; Zhang Y; Zhang Y; Xia H; Zhu J; Fu W; Zhang X

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, Affiliated Daping Hospital, Third Military Medical University, Chongqing 400042, P.R. China.

RESUMEN / SUMMARY: - The present study aimed to investigate the molecular basis of lung cancer development using a microarray to identify the differentially-expressed genes associated with the various tumor-node-metastasis (TNM) stages of lung adenocarcinoma. This subtype of lung cancer has increased in incidence within recent years in China. A 35K oligo gene array covering ~25,100 genes was used to screen the differentially-expressed genes among 90 lung adenocarcinoma samples of various TNM stages. To verify the data from the gene arrays, three genes [human zinc finger-containing, Miz1, PIAS-like protein on chromosome 7 (Zimp7), GINS complex subunit 2 (GINS2) and NSAID activated gene 1 (NAG-1)] were validated using quantitative (q)PCR in an alternative set of samples to the gene array. A total of 640 genes were identified that were differentially-expressed in lung adenocarcinoma compared with the surrounding normal lung tissues. From these 640 candidate genes, 10 were observed to be differentially-expressed among TNM stages I, II and IIIA, of which, the Zimp7, GINS2 and NAG-1 genes were reported for the first time to be expressed at high levels in lung adenocarcinoma. The results of the qPCR for the three genes were consistent with those from the gene array. In total, 10 candidate genes were identified to be associated with the various TNM stages of lung adenocarcinoma in the population studied, which may provide new insights into the molecular basis underlying

the development of lung adenocarcinoma and offer new targets for the diagnosis, therapy and prognosis.

[680]

TÍTULO / TITLE: - The SNP rs402710 in 5p15.33 Is Associated with Lung Cancer Risk: A Replication Study in Chinese Population and a Meta-Analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 23;8(10):e76252. doi: 10.1371/journal.pone.0076252.

●● Enlace al texto completo (gratis o de pago) 1371/journal.pone.0076252

AUTORES / AUTHORS: - Lu X; Ke J; Luo X; Zhu Y; Zou L; Li H; Zhu B; Xiong Z; Chen W; Deng L; Lou J; Wang X; Zhang Y; Wang Z; Miao X; Cheng L

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Environment Health (Incubation), MOE (Ministry of Education) Key Laboratory of Environment & Health, Ministry of Environmental Protection Key Laboratory of Environment and Health (Wuhan), and Department of Epidemiology and Biostatistics, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China ; Guangdong Maternal and Child Health Care Hospital, Guangzhou, China.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the most commonly diagnosed cancer and leading cause of cancer mortality in the world. A single nucleotide polymorphism (SNP), rs402710, located in 5p15.33, was firstly identified to be associated with the lung cancer risk in a genome-wide association study. However, some following replication studies yielded inconsistent results. METHODOLOGY AND FINDINGS: A case-control study of 611 cases and 1062 controls in a Chinese population was conducted, and then a meta-analysis integrating the current and previously published studies with a total 31811 cases and 36333 controls was performed to explore the real effect of rs402710 on lung cancer susceptibility. Significant associations between the SNP rs402710 and lung cancer risk were observed in both case-control study and meta-analysis, with ORs equal to 0.77 (95%CI = 0.63-0.95) and 0.83 (95%CI = 0.81-0.86) in dominant model, respectively. By stratified analysis of our case-control study, the associations were also observed in never smoker group and non-small cell lung cancer(NSCLC) group with ORs equal to 0.71 (95%CI = 0.53-0.95) and 0.69 (95%CI = 0.55-0.87), which was remarkable that larger effect of the minor allele T was seen in the two groups than that in overall lung cancer. Besides, the sensitive and cumulative analysis indicated the robust stability of the current results of meta-analysis. CONCLUSION: The results from our replication study and the meta-analysis provided firm evidence that rs402710 T allele significantly contributed to decreased lung cancer risk, and the case-control study implied that the variant may yield stronger effect on NSCLC and never smokers. However, the mechanism underlying the polymorphism conferring susceptibility to lung cancer is warranted to clarify in the follow-up studies.

[681]

TÍTULO / TITLE: - CyberKnife therapy of 24 multiple brain metastases from lung cancer: A case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):534-536. Epub 2013 Jun 7.

●● Enlace al texto completo (gratis o de pago) 3892/ol.2013.1383

AUTORES / AUTHORS: - Yang G; Wang Y; Wang Y; Lin S; Sun D

INSTITUCIÓN / INSTITUTION: - Center for Tumor Treatment, People's Liberation Army 107th Hospital, Lai Shan Qu, Yantai, Shandong 264003, P.R. China ; Binzhou Medical College, Lai Shan Qu, Yantai, Shandong 264003, P.R. China.

RESUMEN / SUMMARY: - Brain metastasis is a significant cause of morbidity and mortality and a critical complication of non-central nervous system primary carcinoma. The present study describes the clinical case of a 46-year-old male with lung cancer and life-threatening brain metastases. The patient was diagnosed with lung cancer with a clinical stage of T2N0M1 (stage IV). Six months after the initial diagnosis and administration of conformal radiotherapy combined with three cycles of chemotherapy, an enhanced computed tomography (CT) scan of the brain revealed abnormalities with double-dosing of intravenous contrast. The CT scan identified >24 lesions scattered in the whole brain. The patient was treated with three-fraction Cyberknife radiotherapy at 22 Gy, delivered to the brain metastases at the Center for Tumor Treatment of People's Liberation Army 107th Hospital. Following CyberKnife therapy, a CT scan of the brain revealed that most of the tumors had disappeared with almost no residual traces. The stereotactic radiosurgery (SRS) conducted using CyberKnife, an image-guided frameless robotic technology for whole-body radiosurgery, had produced a marked response. The present case report demonstrates that CyberKnife therapy plays a significant role in the management of multiple meta-static brain tumors.

[682]

TÍTULO / TITLE: - Clinical significance of the induction of macrophage differentiation by the costimulatory molecule B7-H3 in human non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Nov;6(5):1253-1260. Epub 2013 Sep 13.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1586](#)

AUTORES / AUTHORS: - Sun J; Mao Y; Zhang YQ; Guo YD; Mu CY; Fu FQ; Zhang XG

INSTITUCIÓN / INSTITUTION: - Institute of Medical Biotechnology, Suzhou Health College, Suzhou, Jiangsu 215009, P.R. China.

RESUMEN / SUMMARY: - B7-H3, a member of the B7 family of molecules, is expressed in certain types of human cancer and is important in tumor development and progression. Although several studies have reported that the expression of B7-H3 is correlated with poor outcomes in patients with cancer, its exact role in cancer remains unknown. In the present study, the expression levels of B7-H3 in the pathological specimens of 105 patients treated for non-small cell lung cancer (NSCLC) were examined by immunohistochemistry. A high expression level of B7-H3 was observed in 46.9% of the 105 NSCLC tissue specimens. These patients demonstrated a more advanced tumor grade and a shorter survival time. In addition, we also examined the levels of tumor-associated macrophages (TAMs) in NSCLC tissues and observed that the levels were positively correlated with the expression of B7-H3, and that higher levels of macrophages were associated with lower levels of infiltrating T cells and a shorter survival time. These results demonstrated that TAMs are important in the evasion of tumor immune surveillance in NSCLC. Furthermore, through knockdown of B7-H3 by RNA interference, we observed that soluble B7-H3 was capable of inducing macrophages to express higher levels of macrophage mannose receptor (MMR) and lower levels of human leukocyte antigen (HLA)-DR, as well as higher levels of interleukin-10 (IL-10) and lower levels of IL-1beta in vitro. These observations are

characteristic of an anti-inflammatory/reparatory (alternative/M2) phenotype. Therefore, our data suggests that B7-H3 proteins are involved in the progression of NSCLC by inducing the development of monocytes into anti-inflammatory cells.

[683]

TÍTULO / TITLE: - Stereotactic body radiation therapy (SBRT) for lung malignancies: preliminary toxicity results using a flattening filter-free linear accelerator operating at 2400 monitor units per minute.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiat Oncol. 2013 Nov 20;8(1):273.

●● Enlace al texto completo (gratis o de pago) [1186/1748-717X-8-273](#)

AUTORES / AUTHORS: - Prendergast BM; Dobelbower MC; Bonner JA; Popple RA; Baden CJ; Minnich DJ; Cerfolio RJ; Spencer SA; Fiveash JB

RESUMEN / SUMMARY: - BACKGROUND: Flattening filter-free (FFF) linear accelerators (linacs) are capable of delivering dose rates more than 4-times higher than conventional linacs during SBRT treatments, causing some to speculate whether the higher dose rate leads to increased toxicity owing to radiobiological dose rate effects. Despite wide clinical use of this emerging technology, clinical toxicity data for FFF SBRT are lacking. In this retrospective study, we report the acute and late toxicities observed in our lung radiosurgery experience using a FFF linac operating at 2400 MU/min. METHODS: We reviewed all flattening filter-free (FFF) lung SBRT cases treated at our institution from August 2010 through July 2012. Patients were eligible for inclusion if they had at least one clinical assessment at least 30 days following SBRT. Pulmonary, cardiac, dermatologic, neurologic, and gastrointestinal treatment related toxicities were scored according to CTCAE version 4.0. Toxicity observed within 90 days of SBRT was categorized as acute, whereas toxicity observed more than 90 days from SBRT was categorized as late. Factors thought to influence risk of toxicity were examined to assess relationship to grade ≥ 2 toxicity. RESULTS: Sixty-four patients with >30 day follow up were eligible for inclusion. All patients were treated using 10 MV unflattened photons beams with intensity modulated radiation therapy (IMRT) inverse planning. Median SBRT dose was 48 Gy in 4 fractions (range: 30--60 Gy in 3--5 fractions). Six patients (9%) experienced \geq grade 2 acute pulmonary toxicity; no non-pulmonary acute toxicities were observed. In a subset of 49 patients with greater than 90 day follow up (median 11.5 months), 11 pulmonary and three nerve related grade ≥ 2 late toxicities were recorded. Pulmonary toxicities comprised six grade 2, three grade 3, and one each grade 4 and 5 events. Nerve related events were rare and included two cases of grade 2 chest wall pain and one grade 3 brachial plexopathy which spontaneously resolved. No grade ≥ 2 late gastrointestinal, skin, or cardiac toxicities were observed. Tumor size, biologically effective dose (BED10, assuming alpha/beta of 10), and tumor location (central vs peripheral) were not significantly associated with grade ≥ 2 toxicity. CONCLUSIONS: In this early clinical experience, lung SBRT using a FFF linac operating at 2400 MU/min yields minimal acute toxicity. Preliminary results of late treatment related toxicity suggest reasonable rates of grade ≥ 2 toxicities. Further assessment of late effects and confirmation of the clinical efficacy of FFF SBRT is warranted.

[684]

TÍTULO / TITLE: - Expression of the Mismatch Repair Gene hMLH1 Is Enhanced in Non-Small Cell Lung Cancer with EGFR Mutations.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 24;8(10):e78500. doi: 10.1371/journal.pone.0078500.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078500](#)

AUTORES / AUTHORS: - Li M; Zhang Q; Liu L; Lu W; Wei H; Li RW; Lu S

INSTITUCIÓN / INSTITUTION: - Central Laboratory, The Second Hospital of Dalian Medical University, Dalian, PR China.

RESUMEN / SUMMARY: - Mismatch repair (MMR) plays a pivotal role in keeping the genome stable. MMR dysfunction can lead to carcinogenesis by gene mutation accumulation. HMSH2 and hMLH1 are two key components of MMR. High or low expression of them often mark the status of MMR function. Mutations (EGFR, KRAS, etc) are common in non-small cell lung cancer (NSCLC). However, it is not clear what role MMR plays in NSCLC gene mutations. The expression of MMR proteins hMSH2 and hMLH1, and the proliferation markers PCNA and Ki67 were measured by immunohistochemistry in 181 NSCLCs. EGFR and KRAS mutations were identified by high resolution melting analysis. Stronger hMLH1 expression correlated to a higher frequency of EGFR mutations in exon 19 and 21 ($p < 0.0005$). Overexpression of hMLH1 and the adenocarcinoma subtype were both independent factors that related to EGFR mutations in NSCLCs ($p = 0.013$ and $p < 0.0005$). The expression of hMLH1, hMSH2 and PCNA increased, while Ki67 expression significantly decreased ($p = 0.030$) in NSCLCs with EGFR mutations. Overexpression of hMLH1 could be a new molecular marker to predict the response to EGFR-TKIs in NSCLCs. Furthermore, EGFR mutations might be an early event of NSCLC that occur before MMR dysfunction.

[685]

TÍTULO / TITLE: - Comparative study of the anatomic segmentectomy versus lobectomy for clinical stage I A peripheral lung cancer by video assistant thoracoscopic surgery.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S106-9. doi: 10.4103/0973-1482.119121.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119121](#)

AUTORES / AUTHORS: - Zhang L; Ma W; Li Y; Jiang Y; Ma G; Wang G

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Shandong Provincial Hospital Affiliated to Shandong University, Jinan 250021, China.

RESUMEN / SUMMARY: - Objective: The objective of this study was to compare the completely thoracoscopic anatomic segmentectomy with lobectomy to treat stage I A peripheral lung cancer <2 cm. Materials and Methods: A retrospective study was performed that 54 cases stage I A peripheral lung cancer patients were selected, including 26 cases of segmentectomy and 28 cases of lobectomy. We observed the operative time, blood loss, number of lymphadenectomy, post-operative chest drainage, hospital days, post-operative complications and mortality, post-operative recurrence and 3-year survival rate. Results: There was no significant difference about complications such as post-operative atelectasis, severe pneumonia, arrhythmia and cardiovascular/cerebrovascular in two groups ($P > 0.05$). The local recurrence rate was not significant different in two groups ($P > 0.05$). Two groups of operative time, blood

loss and number of dissected lymph nodes was not statistically significant ($P > 0.05$), However, the difference was statistically significant in average chest drainage and less decreased pulmonary function, which led to patients received segmentectomy recovered faster and hospitalized less time ($P < 0.05$). We also found there was no significant difference on survival rate with 1 and 3 year follow-up of two groups (log-rank Chi-square = 0.028, $P > 0.05$). Conclusions: For stage I A peripheral lung cancer, the thoracoscopic anatomic segmentectomy was safe and effective just as thoracoscopic lobectomy, and furthermore with faster post-operative recovery.

[686]

TÍTULO / TITLE: - Combination of EGFR-TKIs and Chemotherapy as First-Line Therapy for Advanced NSCLC: A Meta-Analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 13;8(11):e79000. doi: 10.1371/journal.pone.0079000.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0079000](#)

AUTORES / AUTHORS: - Ouyang PY; Su Z; Mao YP; Deng W; Xie FY

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, China ; Department of Radiation Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China.

RESUMEN / SUMMARY: - The impact of combining epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs) and chemotherapy as first-line therapy for patients with advanced non-small-cell lung cancer (NSCLC) remains controversial. Therefore, randomized trials that compared this combined regimen with chemotherapy or EGFR-TKIs monotherapy were included for this meta-analysis. We used published hazard ratios (HRs), if available, or derived treatment estimates from other survival data. Pooled estimates of treatment efficacy of the combined regimen in the entire unselected population and selected patients by EGFR-mutation status and smoking history were calculated. Eight trials eventually entered into this meta-analysis, including 4585 patients. Overall, the combined regimen significantly delayed disease progression (HR = 0.81, 95% CI 0.69-0.95, $P = 0.01$); subgroup analysis showed significantly higher progression free survival advantages in Asian patients ($P < 0.001$), with sequential combination of TKIs and chemotherapy ($P = 0.02$). In selected patients by EGFR-mutation, both mutation positive (HR = 0.48, 95% CI 0.28-0.83, $P = 0.009$) and negative (HR = 0.84, 95% CI 0.72-0.98, $P = 0.02$) patients gained progression free survival benefit from the combined regimen, albeit the magnitude of benefit was marginally larger in mutation positive patients ($P = 0.05$). In selected patients by smoking history, never/light smokers achieved a great progression free survival benefit from the combined regimen (HR = 0.51, 95% CI 0.35-0.74, $P = 0.0004$). Unfortunately, the combined regimen had no significant impact on overall survival, irrespective of ethnicity, dose schedules or EGFR-mutation status. Severe anorexia (RR = 2.01, 95% CI 1.11-3.63; $P = 0.02$) and diarrhea (RR = 2.70, 95% CI 1.94-3.76; $P < 0.001$) were more frequent in the combined regimen arm. This strategy of combining EGFR-TKIs and chemotherapy deserved to be considered in the future, although it is not approved for advanced NSCLC at the moment.

[687]

TÍTULO / TITLE: - Phytochemical Linarin Enriched in the Flower of *Chrysanthemum indicum* Inhibits Proliferation of A549 Human Alveolar Basal Epithelial Cells Through Suppression of Akt-Dependent Signaling Pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Med Food. 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [1089/jmf.2012.2674](#)

AUTORES / AUTHORS: - Seo DW; Cho YR; Kim W; Eom SH

INSTITUCIÓN / INSTITUTION: - 1 Department of Pharmacy, College of Pharmacy, Dankook University, Cheonan, Republic of Korea.

RESUMEN / SUMMARY: - Abstract In this study, we report the anti-proliferative effect and molecular mechanism of *Chrysanthemum indicum* (C. indicum) on A549 human alveolar basal epithelial cells. We also analyzed the changes in C. indicum component profiles due to modifications of predrying process, flower size, and extraction method. Among the varieties of modifications tested, high-temperature heat dry (HTD) of small flower biotype followed by the methanolic extraction resulted in the strongest anti-proliferative activity of C. indicum extract in A549 cells. High-performance liquid chromatography of C. indicum revealed that the levels of acacetin 7-O-rutinoside (linarin) are markedly increased by heat treatment, especially HTD. Finally, we showed that linarin-mediated inhibition of cell proliferation is associated with suppression of Akt activation and induction of cyclin-dependent kinase inhibitor p27Kip1 as evidenced by cell cycle analysis and treatment with LY294002, an inhibitor of phosphatidylinositol 3-kinase/Akt pathway. Taken together, these findings suggest the need for further development and evaluation of linarin from C. indicum for the treatment and prevention of lung cancer.

[688]

TÍTULO / TITLE: - Interruption of Lung Cancer Cell Migration and Proliferation by Fungal Immunomodulatory Protein FIP-fve from *Flammulina velutipes*.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Agric Food Chem. 2013 Nov 22.

●● Enlace al texto completo (gratis o de pago) [1021/jf4030272](#)

AUTORES / AUTHORS: - Chang YC; Hsiao YM; Wu MF; Ou CC; Lin YW; Lue KH; Ko JL

INSTITUCIÓN / INSTITUTION: - Institute of Medicine, Chung Shan Medical University, No. 110, Sec. 1, Chien-Kuo N. Road, Taichung 40203, Taiwan.

RESUMEN / SUMMARY: - FIP-fve is an immunomodulatory protein isolated from *Flammulina velutipes* that possesses anti-inflammatory and immunomodulatory activities. However, little is known about its anticancer effects. It is suppressed cell proliferation of A549 lung cancer cells on MTT assay following 48 h treatment of FIP-fve. FIP-fve treatment also resulted in cell cycle arrest but not apoptosis on flow cytometry. This immunomodulatory protein was observed to increase p53 expression, as well as the expression of its downstream gene p21, on Western blot. FIP-fve inhibited migration of A549 cells on wound healing assay and decreased filopodia fiber formation on labeling with Texas Red-X phalloidin. To confirm the effect of FIP-fve on the role of Rac1 in filopodia formation, we investigated the activity of Rac1 in A549 cells following FIP-fve treatment. FIP-fve inhibited EGF-induced activation of Rac1. We demonstrated that FIP-fve decreases RACGAP1 mRNA and protein levels on RT-PCR and Western blot. In addition, the reporter activity of RACGAP1 was reduced by

FIP-fve on RacGAP1 promoter assay. Silencing of RacGAP1 decreased cell migration, and overexpression of RacGAP1 increased cell migration in A549 cells. In conclusion, FIP-fve inhibits lung cancer cell migration via RacGAP1 and suppresses the proliferation of A549 via p53 activation pathway.

[689]

TÍTULO / TITLE: - A Novel Herbal Formula Induces Cell Cycle Arrest and Apoptosis in Association With Suppressing the PI3K/AKT Pathway in Human Lung Cancer A549 Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Integr Cancer Ther. 2013 Oct 7.

●● [Enlace al texto completo \(gratis o de pago\) 1177/1534735413503544](#)

AUTORES / AUTHORS: - Xiong F; Jiang M; Huang Z; Chen M; Chen K; Zhou J; Yin L; Tang Y; Wang M; Ye L; Zhan Z; Duan J; Fu H; Zhang X

RESUMEN / SUMMARY: - AIM OF THE STUD: . In recent years, the incidence of lung cancer, as well as the mortality rate from this disease, has increased. Moreover, because of acquired drug resistance and adverse side effects, the effectiveness of current therapeutics used for the treatment of lung cancer has decreased significantly. Chinese medicine has been shown to have significant antitumor effects and is increasingly being used for the treatment of cancer. However, as the mechanisms of action for many Chinese medicines are undefined, the application of Chinese medicine for the treatment of cancer is limited. The formula tested has been used clinically by the China National Traditional Chinese Medicine Master, Professor Zhonging Zhou for treatment of cancer. In this article, we examine the efficacy of Ke formula in the treatment of non-small cell lung cancer and elucidate its mechanism of action. METHOD: . A Balb/c nude mouse xenograft model using A549 cells was previously established. The mice were randomly divided into normal, mock, Ke, cisplatin (DDP), and co-formulated (Ke + DDP) groups. After 15 days of drug administration, the animals were sacrificed, body weight and tumor volume were recorded, and the tumor-inhibiting rate was calculated. A cancer pathway finder polymerase chain reaction array was used to monitor the expression of 88 genes in tumor tissue samples. The potential antiproliferation mechanism was also investigated by Western blot analysis. RESULT: . Ke formula minimized chemotherapy-related weight loss in tumor-bearing mice without exhibiting distinct toxicity. Ke formula also inhibited tumor growth, which was associated with the downregulation of genes in the PI3K/AKT, MAPK, and WNT/beta-catenin pathways. The results from Western blot analyses further indicated that Ke blocked the cell cycle progression at the G1/S phase and induced apoptosis mainly via the PI3K/AKT pathway. CONCLUSIO: . Ke formula inhibits tumor growth in an A549 xenograft mouse model with no obvious side effects. Moreover, Ke exhibits synergistic antitumor effects when combined with DDP. The mechanism of action of Ke is to induce cell cycle arrest and apoptosis by suppressing the PI3K/AKT pathway. Further research will be required to determine the mechanism of action behind the synergistic effect of Ke and DDP.

[690]

TÍTULO / TITLE: - Destruxin B Isolated from Entomopathogenic Fungus *Metarhizium anisopliae* Induces Apoptosis via a Bcl-2 Family-Dependent Mitochondrial Pathway in Human Nonsmall Cell Lung Cancer Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Evid Based Complement Alternat Med. 2013;2013:548929. doi: 10.1155/2013/548929. Epub 2013 Sep 24.

●● Enlace al texto completo (gratis o de pago) [1155/2013/548929](#)

AUTORES / AUTHORS: - Wu CC; Chen TH; Liu BL; Wu LC; Chen YC; Tzeng YM; Hsu SL

INSTITUCIÓN / INSTITUTION: - Institute of Medicine, Chung Shan Medical University, Taichung, Taiwan ; Department of Medical Research, Chung Shan Medical University Hospital, Taichung, Taiwan.

RESUMEN / SUMMARY: - Destruxin B, isolated from entomopathogenic fungus *Metarhizium anisopliae*, is one of the cyclodepsipeptides with insecticidal and anticancer activities. In this study, destruxin B was extracted and purified by ion-exchange chromatography, silica gel chromatography, and semipreparative high-performance liquid chromatography. The potential anticancer effects and molecular mechanisms of destruxin B in human nonsmall cell lung cancer cell lines were characterized. Our results showed that destruxin B induced apoptotic cell death in A549 cells. This event was accompanied by the activation of caspase-2, -3, and -9. Moreover, destruxin B increased the expression level of proapoptotic molecule, PUMA, while decreased antiapoptotic molecule Mcl-1. Additionally, the translocation of Bax from cytosol to mitochondrial membrane was observed upon destruxin B treatment. Knockdown of Bax by shRNA effectively attenuated destruxin-B-triggered apoptosis in A549 cells. Interestingly, similar toxic effects and underlying mechanisms including caspase activation, upregulation of PUMA, and downregulation of Mcl-1 were also observed in a p53-null lung cancer H1299 cell line upon destruxin B treatment. Taken together, our findings suggest that destruxin-B-induced apoptosis in human nonsmall cell lung cancer cells is via a Bcl-2 family-dependent mitochondrial pathway.

[691]

TÍTULO / TITLE: - *Crocus sativus* L. (Saffron) Stigma Aqueous Extract Induces Apoptosis in Alveolar Human Lung Cancer Cells through Caspase-Dependent Pathways Activation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:417928. doi: 10.1155/2013/417928. Epub 2013 Oct 29.

●● Enlace al texto completo (gratis o de pago) [1155/2013/417928](#)

AUTORES / AUTHORS: - Samarghandian S; Borji A; Farahmand SK; Afshari R; Davoodi S

INSTITUCIÓN / INSTITUTION: - Department of Basic Medical Sciences, Neyshabur Faculty of Medicine, Neyshabur, Iran.

RESUMEN / SUMMARY: - Worldwide, lung cancer is the most common form of cancer. Saffron has been used in folk medicine for centuries. We investigated the potential of saffron to induce cytotoxic and apoptotic effects in lung cancer cells (A549). We also examined the caspase-dependent pathways activation of saffron-induced apoptosis against the A549 cells. A549 cells were incubated with different concentrations of saffron extract; then cell morphological changes, cell viability, and apoptosis were

determined by the normal invertmicroscope, MTT assay, Annexin V and propidium iodide, and flow cytometric analysis, respectively. Activated caspases were detected by treatment of saffron in lung cancer cells using fluorescein-labeled inhibitors of polycaspases. The proliferation of the A549 cells were decreased after treatment with saffron in a dose- and time-dependent manner. The percentage of apoptotic cells increased with saffron concentrations. Saffron induced morphological changes, decreased percentage of viable cells, and induced apoptosis. Saffron could induce apoptosis in the A549 cells and activate caspase pathways. The levels of caspases involved in saffron-induced apoptosis in the A549 cells indicating caspase-dependent pathway were induced by saffron. The anticancer activity of the aqueous extract of saffron could be attributed partly to its inhibition of the cell proliferation and induction of apoptosis in cancer cells through caspase-dependent pathways activation.

[692]

TÍTULO / TITLE: - The common anesthetic, sevoflurane, induces apoptosis in A549 lung alveolar epithelial cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2014 Jan;9(1):197-203. doi: 10.3892/mmr.2013.1806. Epub 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1806](#)

AUTORES / AUTHORS: - Wei GH; Zhang J; Liao DQ; Li Z; Yang J; Luo NF; Gu Y

INSTITUCIÓN / INSTITUTION: - Laboratory of Anesthesiology and Critical Care Medicine, West China Hospital, Sichuan University, Chengdu, Sichuan 610041, P.R. China.

RESUMEN / SUMMARY: - Lung alveolar epithelial cells are the first barrier exposed to volatile anesthetics, such as sevoflurane, prior to reaching the targeted neuronal cells. Previously, the effects of volatile anesthetics on lung surfactant were studied primarily with physicochemical models and there has been little experimental data from cell cultures. Therefore it was investigated whether sevoflurane induces apoptosis of A549 lung epithelial cells. A549 cells were exposed to sevoflurane via a calibrated vaporizer with a 2 l/min flow in a gastight chamber at 37 C. The concentration of sevoflurane in Dulbecco's modified Eagle's medium was detected with gas chromatography. Untreated cells and cells treated with 2 microM daunorubicin hydrochloride (DRB) were used as negative and positive controls, respectively. Apoptosis factors, including the level of ATP, apoptoticbodies by terminal deoxynucleotidyl transferasemediated dUTP nick end labeling (TUNEL) assay, DNA damage and the level of caspase 3/7 were analyzed. Cells treated with sevoflurane showed a significant reduction in ATP compared with untreated cells. Effects in the DRB group were greater than in the sevoflurane group. The difference of TUNEL staining between the sevoflurane and untreated groups was statistically significant. DNA degradation was observed in the sevoflurane and DRB groups, however this was not observed in the untreated group. The sevoflurane and DRB groups induced increased caspase 3/7 activation compared with untreated cells. These results suggest that sevoflurane induces apoptosis in A549 cells. In conclusion, 5% sevoflurane induced apoptosis of A549 lung alveolar epithelial cells, which resulted in decreased cell viability, increased apoptotic bodies, impaired DNA integrity and increased levels of caspase 3/7.

[693]

TÍTULO / TITLE: - Clinical evaluation and cost-effectiveness analysis of serum tumor markers in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:195692. doi: 10.1155/2013/195692. Epub 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) [1155/2013/195692](#)

AUTORES / AUTHORS: - Wang R; Wang G; Zhang N; Li X; Liu Y

INSTITUCIÓN / INSTITUTION: - School of Laboratory Medicine, Tianjin Medical University, No. 1 Guangdong Road, Hexi District, Tianjin 300203, China.

RESUMEN / SUMMARY: - The detection of serum tumor markers is valuable for the early diagnosis of lung cancer. Tumor markers are frequently used for the management of cancer patients. However, single markers are less efficient but marker combinations increase the cost, which is troublesome for clinics. To find an optimal serum marker combination panel that benefits the patients and the medical management system as well, four routine lung cancer serum markers (SCCA, NSE, CEA, and CYFRA21-1) were evaluated individually and in combination. Meanwhile, the costs and effects of these markers in clinical practice in China were assessed by cost-effectiveness analysis. As expected, combinations of these tumor markers improved their sensitivity for lung cancer and different combination panels had their own usefulness. NSE + CEA + CYFRA21-1 was the optimal combination panel with highest Youden's index (0.64), higher sensitivity (75.76%), and specificity (88.57%), which can aid the clinical diagnosis of lung cancer. Nevertheless, the most cost-effective combination was SCCA + CEA, which can be used to screen the high-risk group.

[694]

TÍTULO / TITLE: - Video-Assisted Thoracic Surgery Lobectomy for Lung Cancer with Displaced B

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Nov 8.

AUTORES / AUTHORS: - Asakura K; Imanishi N; Matsuoka T; Nagai S; Matsuoka K; Ueda M; Miyamoto Y

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, National Hospital Organization Himeji Medical Center, Hyogo, Japan.

RESUMEN / SUMMARY: - A 52-year-old man was diagnosed with lung adenocarcinoma in the left upper lobe (c-T1bN0M0). Preoperative bronchoscopy revealed a displaced anomalous B1+2 arising from the left main bronchus. Multiplanar reconstruction computed tomography showed that the displaced B1+2 was located behind the left main pulmonary artery, and the interlobar fissure was largely fused. Video-assisted thoracic surgery (VATS) left upper lobectomy was performed successfully. The "no-touch fissure" technique was efficient not only for avoiding accidental cutting of the displaced bronchus but also post-operative air leakage. This is the first reported case of VATS lobectomy for lung cancer associated with a displaced B1+2.

[695]

TÍTULO / TITLE: - Effect of adjuvant magnetic fields in radiotherapy on non-small-cell lung cancer cells in vitro.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:657259. doi: 10.1155/2013/657259. Epub 2013 Oct 10.

●● Enlace al texto completo (gratis o de pago) [1155/2013/657259](https://doi.org/10.1155/2013/657259)

AUTORES / AUTHORS: - Feng J; Sheng H; Zhu C; Jiang H; Ma S

INSTITUCIÓN / INSTITUTION: - Cancer Research Institute, Zhejiang Cancer Hospital, No. 38 Guangji Road, Hangzhou, Zhejiang 310022, China ; Key Laboratory Diagnosis and Treatment Technology on Thoracic Oncology, Hangzhou, Zhejiang 310022, China.

RESUMEN / SUMMARY: - Objectives. To explore sensitization and possible mechanisms of adjuvant magnetic fields (MFs) in radiotherapy (RT) of non-small-cell lung cancer. Methods. Human A549 lung adenocarcinoma cells were treated with MF, RT, and combined MF-RT. Colony-forming efficiency was calculated, cell cycle and apoptosis were measured, and changes in cell cycle- and apoptosis-related gene expression were measured by microarray. Results. A 0.5 T, 8 Hz stationary MF showed a duration-dependent inhibitory effect lasting for 1-4 hours. The MF-treated groups had significantly greater cell inhibition than did controls ($P < 0.05$). Surviving fractions and growth curves derived from colony-forming assay showed that the MF-only, RT-only, and MF-RT groups had inhibited cell growth; the MF-RT group showed a synergistic effect. Microarray of A549 cells exposed for 1 hour to MF showed that 19 cell cycle- and apoptosis-related genes had 2-fold upregulation and 40 genes had 2-fold downregulation. MF significantly arrested cells in G2 and M phases, apparently sensitizing the cells to RT. Conclusions. MF may inhibit A549 cells and can increase their sensitivity to RT, possibly by affecting cell cycle- and apoptosis-related signaling pathways.

[696]

TÍTULO / TITLE: - Application of proteomics to identify the target molecules involved in Lonicera japonica-induced photokilling in human lung cancer CH27 cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Complement Altern Med. 2013 Oct 1;13:244. doi: 10.1186/1472-6882-13-244.

●● Enlace al texto completo (gratis o de pago) [1186/1472-6882-13-244](https://doi.org/10.1186/1472-6882-13-244)

AUTORES / AUTHORS: - Liao JC; Chang WT; Lan YH; Hour MJ; Lee HZ

INSTITUCIÓN / INSTITUTION: - School of Pharmacy, China Medical University, Taichung, Taiwan. hong@mail.cmu.edu.tw.

RESUMEN / SUMMARY: - BACKGROUND: The Lonicera japonica has been used as natural and healthy drink for its anti-inflammatory effect and pleasant odor in China and Taiwan. METHODS: 2D electrophoresis was used to analyze the proteins involved in photoactivated Lonicera japonica-induced CH27 cell apoptosis. The fluorescent dyes MitoTracker Red CMXRos, calcein AM and JC-1 were used to elucidate mitochondrial function. The protein expression was performed by Western blotting. Fluorescent image of endoplasmic reticulum was accomplished by using ER-Tracker Green. This study used fluorescent dye CM-H2DCFDA to detect intracellular generation of reactive oxygen species. RESULTS: The identified proteins can be classified into three major groups, which include proteins involved in mitochondrial function, cytoskeleton-related proteins and proteins associated with endoplasmic reticulum (ER) stress. Photoactivated Lonicera japonica caused a significant effect on the mitochondrial function and ER stress in CH27 cells. The reactive oxygen species producing was found to be involved in photoactivated Lonicera japonica-induced CH27 cell apoptosis.

CONCLUSION: Mitochondria and endoplasmic reticulum are the integral targets in photoactivated *Lonicera japonica*-induced CH27 cell apoptosis. We also demonstrated that ethyl acetate fraction of *Lonicera japonica* extracts caused photocytotoxicity in a dose-dependent manner in CH27 cells. This could explain the fact that the ethyl acetate fraction of *Lonicera japonica* extracts may contain compounds which exhibit the photosensitizing activity in CH27 cells.

[697]

TÍTULO / TITLE: - Cigarette smoke induces distinct chromatin histone modifications in lung cells: implication in pathogenesis of COPD and lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Proteome Res. 2013 Nov 27.

- Enlace al texto completo (gratis o de pago) [1021/pr400998n](#)

AUTORES / AUTHORS: - Rahman I; Sundar IK; Nevid MZ; Friedman AE

RESUMEN / SUMMARY: - Cigarette smoke (CS)-mediated oxidative stress induces several signaling cascades, including kinases, which results in chromatin modifications (histone acetylation/deacetylation and histone methylation/demethylation). We have previously reported that CS induces chromatin remodeling in pro-inflammatory gene promoters; however, the underlying site-specific histone marks formed in histones H3 and H4 during CS exposure in lungs in vivo and in lung cells in vitro, which can either drive gene expression or repression are not known. We hypothesize that CS exposure in mouse and human bronchial epithelial cells (H292) can cause site-specific posttranslational histone modifications (PTMs) that may play an important role in the pathogenesis of CS-induced chronic lung diseases. We used a bottom-up mass spectrometry approach to identify some potentially novel histone marks, including acetylation, mono-methylation and di-methylation in specific lysine and arginine residues of histones H3 and H4 in mouse lungs and H292 cells. We found that CS-induced distinct posttranslational histone modification patterns in histone H3 and histone H4 in lung cells, which may be considered as usable biomarkers for CS-induced chronic lung diseases. These identified histone marks (histone H3 and histone H4) may play an important role in epigenetic state during the pathogenesis of smoking-induced chronic lung diseases, such as chronic obstructive pulmonary disease and lung cancer.

[698]

TÍTULO / TITLE: - Downregulation of IFNG in CD4(+) T Cells in Lung Cancer through Hypermethylation: A Possible Mechanism of Tumor-Induced Immunosuppression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 11;8(11):e79064. doi: 10.1371/journal.pone.0079064.

- Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079064](#)

AUTORES / AUTHORS: - Wang F; Xu J; Zhu Q; Qin X; Cao Y; Lou J; Xu Y; Ke X; Li Q; Xie E; Zhang L; Sun R; Chen L; Fang B; Pan S

INSTITUCIÓN / INSTITUTION: - Department of Laboratory Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China ; National Key Clinical Department of Laboratory Medicine, Nanjing, China.

RESUMEN / SUMMARY: - Tumor survival is significantly correlated with the immune response of patients. IFNG plays an important role in the tumor host response and

decreased IFNG expression is often observed in lung cancer. Studies have shown that CpG island hypermethylation plays a critical role in transcriptional silencing of IFNG gene expression. However, there is limited understanding regarding the molecular mechanisms of altered methylation, and whether the tumor microenvironment has any effect on DNA methylation and IFNG production. In the current study, we demonstrate that plasma and intra-cellular IFNG levels are significantly lower in lung cancer patients. Hypermethylation of the IFNG promoter in CD4(+) T cells and plasma IFNG was negatively correlated. CD4(+) T cells from healthy individuals co-cultured with SPC-A1 cells generated lower levels of IFNG after activation, elevated expression of DNA methyltransferases (DNMTs), and exhibited hypermethylation of the IFNG promoter. In conclusion, decreased IFNG expression of CD4(+) T cells co-cultured with lung cancer cell is associated with IFNG promoter hypermethylation. Our study suggests that interaction between lung cancer cells and CD4(+) T cells induces DNMT expression and IFNG promoter hypermethylation in CD4(+) T cell, which may serve as an important mechanism of tumor-induced immunosuppression.

[699]

TÍTULO / TITLE: - Preoperative 18F-Fluorodeoxyglucose Positron Emission Tomography can Predict the Tumor Malignancy of Small Peripheral Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Nov 27.

AUTORES / AUTHORS: - Kosaka T; Yamaki E; Tanaka S; Mogi A; Kuwano H

INSTITUCIÓN / INSTITUTION: - Department of General Surgical Science, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan.

RESUMEN / SUMMARY: - Purpose: Recent advances in image diagnostic technology have enhanced the discovery of peripheral small size lung cancers. Here, we examined the utility of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) for the evaluation of grade of tumor malignant potency. Methods: Seventy-nine patients with peripheral small lung cancers (≤ 2 cm) who underwent surgical resections and preoperative FDG-PET were enrolled. The correlations between the maximum standardized uptake value (SUVmax) and various clinicopathological features related to tumor invasiveness, nodal metastasis, and recurrence were analyzed. Results: The median SUVmax of all tumors was 2.4 (range, 0-16.1). The SUVmax was significantly higher in patients with vascular invasion (5.6 \pm 3.5 vs. 2.4 \pm 2.4; $P < 0.0001$), lymphatic invasion (4.9 \pm 3.7 vs. 2.7 \pm 2.6; $P = 0.0029$), lymph node metastasis (6.1 \pm 4.4 vs. 3.0 \pm 2.7; $P = 0.0022$), and recurrences (5.8 \pm 3.3 vs. 3.1 \pm 3.1; $P = 0.0219$). Patients with SUVmax ≥ 2.5 had a significantly higher incidence rate of vascular invasion (56% vs. 7%; $P < 0.0001$), lymphatic invasion (51% vs. 15%; $P = 0.0006$), lymph node metastasis (26% vs. 3%; $P = 0.0033$), and recurrence (18% vs. 3%; $P = 0.0289$). The patients with SUVmax ≥ 1.5 also had a significantly higher incidence of vascular invasion, lymphatic invasion, lymph node metastasis, and recurrence. It is particularly worth noting that patients with SUVmax < 1.5 had no vascular invasion, lymph node metastasis, or recurrence. Conclusion: Preoperative SUVmax of peripheral small lung cancers were significantly associated with tumor malignancy.

[700]

TÍTULO / TITLE: - Pro-Inflammatory Cytokine Induction of 11beta-hydroxysteroid Dehydrogenase Type 1 in A549 Cells Requires Phosphorylation of C/EBPbeta at Thr235.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Sep 26;8(9):e75874. doi: 10.1371/journal.pone.0075874.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0075874](#)

AUTORES / AUTHORS: - Esteves CL; Verma M; Rog-Zielinska E; Kelly V; Sai S; Breton A; Donadeu FX; Seckl JR; Chapman KE

INSTITUCIÓN / INSTITUTION: - Endocrinology Unit, University/BHF Centre for Cardiovascular Science, Queen's Medical Research Institute, The University of Edinburgh, Edinburgh, United Kingdom.

RESUMEN / SUMMARY: - 11beta-hydroxysteroid dehydrogenase type 1 (11beta-HSD1) converts inert glucocorticoids into active forms, thereby increasing intracellular glucocorticoid levels, important to restrain acute inflammation. 11beta-HSD1 is induced by pro-inflammatory cytokines in a variety of cells. Here, we show 11beta-HSD1 expression in human A549 epithelial cells is increased by pro-inflammatory cytokines (IL-1alpha/TNFalpha) via the P2 promoter of the HSD11B1 gene. Inhibition of p38 MAPK attenuated the pro-inflammatory cytokine induction of mRNA encoding 11beta-HSD1 as well as that encoding C/EBPbeta. IL-1alpha/TNFalpha-induced phosphorylation of C/EBPbeta at Thr235 was also attenuated by p38 MAPK inhibition suggesting involvement of a p38 MAPK-C/EBPbeta pathway. siRNA-mediated knock-down of C/EBPbeta and NF-kappaB/RelA implicated both transcription factors in the IL-1alpha/TNFalpha induction of HSD11B1 mRNA. Transient transfections of HSD11B1 promoter-reporter constructs identified the proximal region of the P2 promoter of HSD11B1 as essential for this induction. IL-1alpha increased binding of C/EBPbeta to the HSD11B1 P2 promoter, but this was not observed for NF-kappaB/RelA, suggesting indirect regulation by NF-kappaB/RelA. Ectopic expression of mutant chicken C/EBPbeta constructs unable to undergo phosphorylation at the threonine equivalent to Thr235 attenuated the IL-1alpha-induction of HSD11B1, whereas mimicking constitutive phosphorylation of Thr235 (by mutation to aspartate) increased basal expression of HSD11B1 mRNA without affecting IL-1alpha-induced levels. These data clearly demonstrate a role for both C/EBPbeta and NF-kappaB/RelA in the pro-inflammatory cytokine induction of HSD11B1 in human epithelial cells and show that p38 MAPK-induced phosphorylation of C/EBPbeta at Thr235 is critical in this.

[701]

TÍTULO / TITLE: - Involvement of TGFbeta-Induced Phosphorylation of the PTEN C-Terminus on TGFbeta-Induced Acquisition of Malignant Phenotypes in Lung Cancer Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 22;8(11):e81133. doi: 10.1371/journal.pone.0081133.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0081133](#)

AUTORES / AUTHORS: - Aoyama D; Hashimoto N; Sakamoto K; Kohnoh T; Kusunose M; Kimura M; Ogata R; Imaizumi K; Kawabe T; Hasegawa Y

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan.

RESUMEN / SUMMARY: - Transforming growth factor beta (TGFbeta) derived from the tumor microenvironment induces malignant phenotypes such as epithelial-mesenchymal transition (EMT) and aberrant cell motility in lung cancers. TGFbeta-induced translocation of beta-catenin from E-cadherin complexes into the cytoplasm is involved in the transcription of EMT target genes. PTEN (phosphatase and tensin homologue deleted from chromosome 10) is known to exert phosphatase activity by binding to E-cadherin complexes via beta-catenin, and recent studies suggest that phosphorylation of the PTEN C-terminus tail might cause loss of this PTEN phosphatase activity. However, whether TGFbeta can modulate both beta-catenin translocation and PTEN phosphatase activity via phosphorylation of the PTEN C-terminus remains elusive. Furthermore, the role of phosphorylation of the PTEN C-terminus in TGFbeta-induced malignant phenotypes has not been evaluated. To investigate whether modulation of phosphorylation of the PTEN C-terminus can regulate malignant phenotypes, here we established lung cancer cells expressing PTEN protein with mutation of phosphorylation sites in the PTEN C-terminus (PTEN4A). We found that TGFbeta stimulation yielded a two-fold increase in the phosphorylated -PTEN/PTEN ratio. Expression of PTEN4A repressed TGFbeta-induced EMT and cell motility even after snail expression. Our data showed that PTEN4A might repress EMT through complete blockade of beta-catenin translocation into the cytoplasm, besides the inhibitory effect of PTEN4A on TGFbeta-induced activation of smad-independent signaling pathways. In a xenograft model, the tumor growth ratio was repressed in cells expressing PTEN4A. Taken together, these data suggest that phosphorylation sites in the PTEN C-terminus might be a therapeutic target for TGFbeta-induced malignant phenotypes in lung cancer cells.

[702]

TÍTULO / TITLE: - Stimulatory effects of sorafenib on human nonsmall cell lung cancer cells in vitro by regulating MAPK/ERK activation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2014 Jan;9(1):365-9. doi: 10.3892/mmr.2013.1782. Epub 2013 Nov 7.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1782](#)

AUTORES / AUTHORS: - Zhang YN; Wu XY; Zhong N; Deng J; Zhang L; Chen W; Li X; Zhong CJ

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Kunshan First People's Hospital Affiliated to Jiangsu University, Kunshan, Jiangsu 215300, P.R. China.

RESUMEN / SUMMARY: - Sorafenib is an inhibitor of a number of intracellular signaling kinases with antiproliferative, antiangiogenic and proapoptotic effects in tumor cells. Sorafenib has been used in the therapy of advanced renal cell carcinoma. In the present study, using two human nonsmall cell lung cancer (NSCLC) cell lines, A549 and NCIH1975, the effects of sorafenib on proliferation, apoptosis and intracellular signaling were systematically characterized. The results revealed that at a low concentration (5 microM) and early time point (6 h), sorafenib is capable of significantly stimulating proliferation of A549 cells, but not NCIH1975 cells. In addition, the comparison of the two cell lines revealed different cell cycle redistribution and apoptotic susceptibility to sorafenib at this concentration and time point. Western blot analysis revealed that sorafenib upregulated the expression of cyclin D1 and cyclin dependent

kinase 2 and downregulated the expression of BAX at this specific point. Furthermore, sorafenib was confirmed to regulate the expression of cyclin D1 and apoptosis-associated proteins through the regulation of extracellular signal-regulated kinase 1/2 phosphorylation in A549 cells. These findings suggest that, although sorafenib has the potential for use in the treatment of renal cell carcinoma, this compound may also activate NSCLC cells at a specific time point.

[703]

TÍTULO / TITLE: - Curcumin inhibits human non-small cell lung cancer A549 cell proliferation through regulation of Bcl-2/Bax and cytochrome C.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4599-602.

AUTORES / AUTHORS: - Li Y; Zhang S; Geng JX; Hu XY

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, The Third Affiliated Hospital of Harbin Medical University, Harbin, China E-mail : pda1981@163.com.

RESUMEN / SUMMARY: - We intended to study the mechanism of the inhibitory action of curcumin on human non-small cell lung cancer A549 cell. The cell growth was determined by CCK-8 assay, and the results indicated that curcumin inhibited the cell proliferation in a concentration dependent manner. And to further confirm the relative anti-cancer mechanism of curcumin, RT-PCR was carried out to analysis the expression of relative apoptotic proteins Bax, Bcl-2. We found that curcumin could up-regulate the expression of Bax but down-regulate the expression of Bcl-2 in A549 cells. In addition, curcumin affect the mitochondrial apoptosis pathway. These results suggested that curcumin inhibited cancer cell growth through the regulation of Bcl-2/Bax and affect the mitochondrial apoptosis pathway.

[704]

TÍTULO / TITLE: - A Look at the Grouping Effect on Population-level Risk Assessment of Radon-Induced Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Glob J Health Sci. 2013 Jul 21;5(6):1-11. doi: 10.5539/gjhs.v5n6p1.

AUTORES / AUTHORS: - Chen J; Moir D

INSTITUCIÓN / INSTITUTION: - Radiation Protection Bureau, Health Canada.

jing.chen@hc-sc.gc.ca.

RESUMEN / SUMMARY: - On the basis of considerable knowledge gained by studying health effects in uranium and other underground miners who worked in radon-rich environments, radon exposure has been identified as a cause of lung cancer. Recent pooled analyses of residential studies have shown that radon poses a similar risk of causing lung cancer in the general public when exposure occurs at generally lower levels found in homes. With the increasing accessibility of statistical data via the internet, people are performing their own analyses and asking why, in some cases, the lung cancer occurrence at the community level does not correlate to the radon levels. This study uses statistical data available to the general public from official websites and performs simple analyses. The results clearly show the difficulty in linking observed lung cancer incidence rates at the provincial/territorial level, with possible cause, such as smoking or radon exposure. Even the effect of smoking, a well-documented cause

of lung cancer, can be overlooked or misinterpreted if the data being investigated is too general (i.e., summary data at population level) or is influenced by other factors. These difficulties with simple comparisons are one of the main reasons that epidemiological studies of lung cancer incidence and radon exposure requires the use of cohorts or case controls at the individual level as opposed to the more easily performed ecological studies at the population level.

[705]

TÍTULO / TITLE: - Comparison of lobe-specific mediastinal lymphadenectomy versus systematic mediastinal lymphadenectomy for clinical stage T1a N0 M0 non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S101-5. doi: 10.4103/0973-1482.119119.

●● [Enlace al texto completo \(gratis o de pago\) 4103/0973-1482.119119](#)

AUTORES / AUTHORS: - Ma W; Zhang ZJ; Li Y; Ma GY; Zhang L

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Shandong Provincial Hospital Affiliated to Shandong University, Shandong Province, 250021, China.

RESUMEN / SUMMARY: - Objective: This study was to explore the appropriate extent of mediastinal lymph node dissection for clinical stage T 1a N 0 M 0 non-small cell lung cancer (NSCLC) by comparison between two modes of mediastinal lymph node dissection. Materials and Methods: A total of 96 clinical stage T 1a N 0 M 0 NSCLC cases received radical surgery were randomly divided to lobe-specific mediastinal lymphadenectomy (LL) group and systematic mediastinal lymphadenectomy (SL) group from the year 2004 to 2008. The effects of SL and LL on morbidity, N staging, overall survival (OS) and disease-free survival (DFS) were investigated. Meanwhile, associations between clinicopathological parameters and metastasis of lymph nodes were analyzed. Results: The mean operating time and blood loss in LL group were significantly less than that in the SL group (135.48 +/- 25.44 min vs. 180.85 +/- 39.36 min, 155.11 +/- 25.17 ml vs. 161.32 +/- 28.20 ml, P < 0.05), the mean numbers of dissected lymph nodes of the SL group was significantly greater than that in the LL group (17.1 +/- 3.7 vs. 9.4 +/- 2.1, P < 0.05). The post-operative overall morbidity rate was higher in the SL group than that in the LL group (P < 0.05). There were no significant difference in migration of N staging, OS and DFS between two groups. The post-operative N staging, the tumor cells differentiation and the ratio of ground glass opacity (GGO) in tumor were the independent factors influencing long-term survival. Moreover, the significant correlation was seen between the metastasis of lymph nodes and clinicopathological parameters including tumor location and the GGO ratio. Conclusion: The LL group had similar efficacy as the SL group in the clinical stage T 1a N 0 M 0 NSCLC and there was unnecessary to perform systematic lymphadenectomy in such patients with a high ratio of GGO.

[706]

TÍTULO / TITLE: - Erythropoietin receptor expression is a potential prognostic factor in human lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 14;8(10):e77459. doi: 10.1371/journal.pone.0077459.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077459](https://doi.org/10.1371/journal.pone.0077459)

AUTORES / AUTHORS: - Rozsas A; Berta J; Rojko L; Horvath LZ; Keszthelyi M; Kenessey I; Laszlo V; Berger W; Grusch M; Hoda MA; Torok S; Klepetko W; Renyi-Vamos F; Hegedus B; Dome B; Tovari J

INSTITUCIÓN / INSTITUTION: - Department of Tumor Biology, National Koranyi Institute of Pulmonology, Budapest, Hungary ; Division of Thoracic Surgery, Medical University of Vienna, Vienna, Austria.

RESUMEN / SUMMARY: - Recombinant human erythropoietins (rHuEPOs) are used to treat cancer-related anemia. Recent preclinical studies and clinical trials, however, have raised concerns about the potential tumor-promoting effects of these drugs. Because the clinical significance of erythropoietin receptor (EPOR) signaling in human non-small cell lung cancer (NSCLC) also remains controversial, our aim was to study whether EPO treatment modifies tumor growth and if EPOR expression has an impact on the clinical behavior of this malignancy. A total of 43 patients with stage III-IV adenocarcinoma (ADC) and complete clinicopathological data were included. EPOR expression in human ADC samples and cell lines was measured by quantitative real-time polymerase chain reaction. Effects of exogenous rHuEPOalpha were studied on human lung ADC cell lines in vitro. In vivo growth of human ADC xenografts treated with rHuEPOalpha with or without chemotherapy was also assessed. In vivo tumor and endothelial cell (EC) proliferation was determined by 5-bromo-2'-deoxy-uridine (BrdU) incorporation and immunofluorescent labeling. Although EPOR mRNA was expressed in all of the three investigated ADC cell lines, rHuEPOalpha treatment (either alone or in combination with gemcitabine) did not alter ADC cell proliferation in vitro. However, rHuEPOalpha significantly decreased tumor cell proliferation and growth of human H1975 lung ADC xenografts. At the same time, rHuEPOalpha treatment of H1975 tumors resulted in accelerated tumor endothelial cell proliferation. Moreover, in patients with advanced stage lung ADC, high intratumoral EPOR mRNA levels were associated with significantly increased overall survival. This study reveals high EPOR level as a potential novel positive prognostic marker in human lung ADC.

[707]

TÍTULO / TITLE: - 1,25-Dihydroxyvitamin D3 (1,25(OH)2D3) Signaling Capacity and the Epithelial-Mesenchymal Transition in Non-Small Cell Lung Cancer (NSCLC): Implications for Use of 1,25(OH)2D3 in NSCLC Treatment.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancers (Basel). 2013 Nov 8;5(4):1504-21. doi: 10.3390/cancers5041504.

●● Enlace al texto completo (gratis o de pago) [3390/cancers5041504](https://doi.org/10.3390/cancers5041504)

AUTORES / AUTHORS: - Upadhyay SK; Verone A; Shoemaker S; Qin M; Liu S; Campbell M; Hershberger PA

INSTITUCIÓN / INSTITUTION: - Department of Pharmacology and Therapeutics, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263, USA. pamela.hershberger@roswellpark.org.

RESUMEN / SUMMARY: - 1,25-dihydroxyvitamin D3 (1,25(OH)2D3) exerts anti-proliferative activity by binding to the vitamin D receptor (VDR) and regulating gene expression. We previously reported that non-small cell lung cancer (NSCLC) cells

which harbor epidermal growth factor receptor (EGFR) mutations display elevated VDR expression (VDR^{high}) and are vitamin D-sensitive. Conversely, those with K-ras mutations are VDR^{low} and vitamin D-refractory. Because EGFR mutations are found predominately in NSCLC cells with an epithelial phenotype and K-ras mutations are more common in cells with a mesenchymal phenotype, we investigated the relationship between vitamin D signaling capacity and the epithelial mesenchymal transition (EMT). Using NSCLC cell lines and publically available lung cancer cell line microarray data, we identified a relationship between VDR expression, 1,25(OH)₂D₃ sensitivity, and EMT phenotype. Further, we discovered that 1,25(OH)₂D₃ induces E-cadherin and decreases EMT-related molecules SNAIL, ZEB1, and vimentin in NSCLC cells. 1,25(OH)₂D₃-mediated changes in gene expression are associated with a significant decrease in cell migration and maintenance of epithelial morphology. These data indicate that 1,25(OH)₂D₃ opposes EMT in NSCLC cells. Because EMT is associated with increased migration, invasion, and chemoresistance, our data imply that 1,25(OH)₂D₃ may prevent lung cancer progression in a molecularly defined subset of NSCLC patients.

[708]

TÍTULO / TITLE: - Research on the relationship between serum levels of inflammatory cytokines and non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(8):4765-8.

AUTORES / AUTHORS: - Song XY; Zhou SJ; Xiao N; Li YS; Zhen DZ; Su CY; Liu ZD

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Beijing Chest Hospital, Capital Medical University, Beijing, China E-mail : liuzhidongbj@163.com.

RESUMEN / SUMMARY: - AIMS: This study was conducted to evaluate the levels of TNF- α , IL-6, IL-8 and VEGF in serum of patients with non- small cell lung cancer, for assessing their possible diagnostic and prognostic roles. METHODS: We enrolled 48 patients newly diagnosed with non-small cell lung cancer and 40 healthy controls. TNF- α , IL-6 and IL-8 levels were measured in the serum of all the subjects with specific radioimmunoassay kits, while EGF was analyzed by sandwich enzyme immunoassay techniques. RESULTS: A statistically significant difference was observed between lung cancer patients and the control group regarding the values of TNF- α , IL-6, IL-8 and VEGF in serum. Moreover, TNF- α , IL-8 and VEGF levels were higher in patients with advanced stages compared to early stages. In addition, higher serum levels of TNF- α , IL-6, IL-8 and VEGF were found in smokers than in non-smokers, both in patients and controls. CONCLUSION: Serum levels of TNF- α , IL-6, IL-8 and VEGF were all elevated in lung cancer patients, suggesting that inflammatory cytokines could be jointly used as a screening tool. Though TNF- α , IL-8 and VEGF levels were related to advanced disease, long-term survival studies of NSCLC patients should be performed to confirm whether they can act as biomarkers of advanced disease. In addition, smoking would be an important contributor to the processes of inflammation and lung cancer.

[709]

TÍTULO / TITLE: - Alternative Signaling Pathways as Potential Therapeutic Targets for Overcoming EGFR and c-Met Inhibitor Resistance in Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 4;8(11):e78398. doi: 10.1371/journal.pone.0078398.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078398](#)

AUTORES / AUTHORS: - Fong JT; Jacobs RJ; Moravec DN; Uppada SB; Botting GM; Nlend M; Puri N

INSTITUCIÓN / INSTITUTION: - Department of Biomedical Sciences, University of Illinois College of Medicine, Rockford, Illinois, United States.

RESUMEN / SUMMARY: - The use of tyrosine kinase inhibitors (TKIs) against EGFR/c-Met in non-small cell lung cancer (NSCLC) has been shown to be effective in increasing patient progression free survival (PFS), but their efficacy is limited due to the development of resistance and tumor recurrence. Therefore, understanding the molecular mechanisms underlying development of drug resistance in NSCLC is necessary for developing novel and effective therapeutic approaches to improve patient outcome. This study aims to understand the mechanism of EGFR/c-Met tyrosine kinase inhibitor (TKI) resistance in NSCLC. H2170 and H358 cell lines were made resistant to SU11274, a c-Met inhibitor, and erlotinib, an EGFR inhibitor, through step-wise increases in TKI exposure. The IC50 concentrations of resistant lines exhibited a 4-5 and 11-22-fold increase for SU11274 and erlotinib, respectively, when compared to parental lines. Furthermore, mTOR and Wnt signaling was studied in both cell lines to determine their roles in mediating TKI resistance. We observed a 2-4-fold upregulation of mTOR signaling proteins and a 2- to 8-fold upregulation of Wnt signaling proteins in H2170 erlotinib and SU11274 resistant cells. H2170 and H358 cells were further treated with the mTOR inhibitor everolimus and the Wnt inhibitor XAV939. H358 resistant cells were inhibited by 95% by a triple combination of everolimus, erlotinib and SU11274 in comparison to 34% by a double combination of these drugs. Parental H2170 cells displayed no sensitivity to XAV939, while resistant cells were significantly inhibited (39%) by XAV939 as a single agent, as well as in combination with SU11274 and erlotinib. Similar results were obtained with H358 resistant cells. This study suggests a novel molecular mechanism of drug resistance in lung cancer.

[710]

TÍTULO / TITLE: - Modeling of Non-Small Cell Lung Cancer Volume Changes during CT-Based Image Guided Radiotherapy: Patterns Observed and Clinical Implications.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Comput Math Methods Med. 2013;2013:637181. doi: 10.1155/2013/637181. Epub 2013 Oct 24.

●● Enlace al texto completo (gratis o de pago) [1155/2013/637181](#)

AUTORES / AUTHORS: - Gay HA; Taylor QQ; Kiriya F; Dieck GT; Jenkins T; Walker P; Allison RR; Ubezio P

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Washington University School of Medicine, 4921 Parkview Place, Campus Box 8224, St. Louis, MO, 63110, USA.

RESUMEN / SUMMARY: - Background. To characterize the lung tumor volume response during conventional and hypofractionated radiotherapy (RT) based on diagnostic quality CT images prior to each treatment fraction. Methods. Out of 26 consecutive patients who had received CT-on-rails IGRT to the lung from 2004 to

2008, 18 were selected because they had lung lesions that could be easily distinguished. The time course of the tumor volume for each patient was individually analyzed using a computer program. Results. The model fits of group L (conventional fractionation) patients were very close to experimental data, with a median Delta% (average percent difference between data and fit) of 5.1% (range 3.5-10.2%). The fits obtained in group S (hypofractionation) patients were generally good, with a median Delta% of 7.2% (range 3.7-23.9%) for the best fitting model. Four types of tumor responses were observed-Type A: "high" kill and "slow" dying rate; Type B: "high" kill and "fast" dying rate; Type C: "low" kill and "slow" dying rate; and Type D: "low" kill and "fast" dying rate. Conclusions. The models used in this study performed well in fitting the available dataset. The models provided useful insights into the possible underlying mechanisms responsible for the RT tumor volume response.

[711]

TÍTULO / TITLE: - Polymorphism of ERCC2 Asp312Asn with Lung Cancer Risk: Evidence from 20,101 Subjects.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Genet Test Mol Biomarkers. 2013 Oct 1.

●● Enlace al texto completo (gratis o de pago) [1089/gtmb.2013.0296](#)

AUTORES / AUTHORS: - Tan X; Wang Y; Shi L; Xian L; Guo J; Liang G; Chen M

INSTITUCIÓN / INSTITUTION: - 1 Department of Cardiothoracic Surgery, First Affiliated Hospital, Guangxi Medical University, Nanning, China.

RESUMEN / SUMMARY: - The association between excision repair cross complementing group 2 (ERCC2) Asp312Asn polymorphism and lung cancer has been reported by many articles recently, but the results were controversial and inconclusive. Therefore, a meta-analysis was conducted to assess the relationship between them. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were used to assess the strength of association. A total of 22 full studies with 20,101 subjects (8719 cases and 11,382 controls) were included in our research. The meta-analysis result showed that no significant association was found between ERCC2 Asp312Asn polymorphism and lung cancer in overall analysis (AA vs. GG, OR=1.023, 95% CI=0.824-1.270, p=0.838; AG vs. GG, OR=1.003, 95% CI=0.936-1.074, p=0.942; AA+AG vs. GG, OR=1.013, 95% CI=0.949-1.082, p=0.697; AA vs. AG+GG, OR=1.033, 95% CI=0.841-1.270, p=0.755). In subset analyses of stratified ethnicity, significantly increased risk was found among Asians (AA vs. GG, OR=3.212, 95% CI=1.518-6.795, p=0.002; AA vs. AG+GG, OR=3.174, 95% CI=1.500-6.712, p=0.003), whereas the association was not found among Caucasians under any genetic models. When analyses were conducted based on the study design, it indicated that the risk of lung cancer might be significantly increased in a hospital-based study (AA vs. GG, OR=1.323, 95% CI=1.096-1.596, p=0.004; AA+AG vs. GG, OR=1.109, 95% CI=1.000-1.229, p=0.050; AA vs. AG+GG, OR=1.285, 95% CI=1.076-1.535, p=0.006). In addition, a significantly increased risk for nonsmokers was detected under the dominant model (AA+AG vs. GG, OR=1.460, 95% CI=1.095-1.948, p=0.010). In conclusion, this meta-analysis suggested ERCC2 Asp312Asn polymorphism may increase the risk of lung cancer among Asians, whereas not among Caucasians.

[712]

TÍTULO / TITLE: - Primary pulmonary leiomyosarcoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Chin Med Assoc. 2013 Nov 18. pii: S1726-4901(13)00277-3. doi: 10.1016/j.jcma.2013.10.009.

●● Enlace al texto completo (gratis o de pago) [1016/j.jcma.2013.10.009](#)

AUTORES / AUTHORS: - Shen W; Chen J; Wei S; Wang X; Li X; Zhou Q

INSTITUCIÓN / INSTITUTION: - Department of Lung Cancer Surgery, Tianjin Key Laboratory of Lung Cancer Metastasis and Tumor Microenvironment, Tianjin Medical University General Hospital, Tianjin, China.

RESUMEN / SUMMARY: - Primary pulmonary leiomyosarcoma (PPL) is an extremely rare malignant tumor. In the case presented here, a 52-year-old Chinese female with a lung mass underwent a right upper-middle lobectomy with pulmonary artery sleeve resection and reconstruction, and was thereafter diagnosed with PPL. After 28 months, the patient was well and without local recurrence or distant metastasis.

[713]

TÍTULO / TITLE: - Diffuse malignant peritoneal mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Kaohsiung J Med Sci. 2013 Nov;29(11):642-5. doi: 10.1016/j.kjms.2013.05.003. Epub 2013 Aug 12.

●● Enlace al texto completo (gratis o de pago) [1016/j.kjms.2013.05.003](#)

AUTORES / AUTHORS: - Shih CA; Ho SP; Tsay FW; Lai KH; Hsu PI

INSTITUCIÓN / INSTITUTION: - Division of Gastroenterology, Department of Internal Medicine, Kaohsiung Veterans General Hospital and National Yang-Ming University, Taiwan.

RESUMEN / SUMMARY: - Mesothelioma often originates in the pleura and less frequently in the peritoneum. This article describes a rare case of diffuse malignant peritoneal mesothelioma in a 54-year-old male construction worker who was admitted to our hospital with a 2-month history of progressive abdominal distention. Abdominal computed tomography revealed extensive peritoneal nodularity and omental cake along with massive ascites. Imaging findings initially suggested peritoneal carcinomatosis, primary peritoneal carcinoma, and tuberculous peritonitis. Laparoscopic biopsy of the omentum and peritoneum confirmed the diagnosis of malignant peritoneal mesothelioma of epitheloid type. Although systemic chemotherapy was administered, no tumor regression was found. The patient finally died of nosocomial infection.

[714]

TÍTULO / TITLE: - Solitary fibrous tumor of the pleura manifesting as an air-containing cystic mass: radiologic and histopathologic correlation.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Korean J Radiol. 2013 Nov;14(6):981-4. doi: 10.3348/kjr.2013.14.6.981. Epub 2013 Nov 5.

●● Enlace al texto completo (gratis o de pago) [3348/kjr.2013.14.6.981](#)

AUTORES / AUTHORS: - Baek JE; Ahn MI; Lee KY

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul 137-701, Korea.

RESUMEN / SUMMARY: - Solitary fibrous tumor (SFT) is a rare mesenchymal neoplasm that typically presents as a well-defined lobular soft tissue mass commonly arising from the pleura. We report an extremely rare case of an SFT containing air arising from the right major fissure in a 58-year-old woman. Chest CT showed an ovoid air-containing cystic mass with an internal, homogeneously enhancing solid nodule. To our knowledge, this is the first case in the literature. The histopathologic findings were correlated with the radiologic findings, and the mechanism of air retention within the tumor is discussed.

[715]

TÍTULO / TITLE: - Malignant Pleural Mesothelioma Presenting as Acute Empyema with Severe Leukocytosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Thorac Cardiovasc Surg. 2013 Oct 3.

AUTORES / AUTHORS: - Matsuoka K

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, National Hospital Organization Himeji Medical Center, Himeji, Hyogo, Japan.

RESUMEN / SUMMARY: - Five months after the treatment for acute empyema, a 75-year-old woman was referred to our hospital because of marked elevation of the white blood cell (WBC) count and C-reactive protein (CRP) level, and a right pleural mass detected by chest computed tomography. At this time, the WBC count and CRP level had increased to 60400/microl and 18.2 mg/dl, respectively. We performed biopsy and the tumor was diagnosed as sarcomatoid malignant pleural mesothelioma. Malignant pleural mesothelioma occasionally presents the symptoms and findings like an acute empyema. We demonstrated the case of malignant pleural mesothelioma which had presented the symptoms and laboratory findings very similar to acute empyema and had treated as acute empyema.

[716]

TÍTULO / TITLE: - Liquid Crystalline Perylene Diimide Outperforming Nonliquid Crystalline Counterpart: Higher Power Conversion Efficiencies (PCEs) in Bulk Heterojunction (BHJ) Cells and Higher Electron Mobility in Space Charge Limited Current (SCLC) Devices.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - ACS Appl Mater Interfaces. 2013 Nov 13;5(21):11093-100. doi: 10.1021/am4033185. Epub 2013 Oct 30.

●● [Enlace al texto completo \(gratis o de pago\)](#) [1021/am4033185](#)

AUTORES / AUTHORS: - Zhang Y; Wang H; Xiao Y; Wang L; Shi D; Cheng C

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Fine Chemicals, Dalian University of Technology, Dalian 116024, People's Republic of China.

RESUMEN / SUMMARY: - In this work, we propose the application of liquid crystalline acceptors as a potential means to improve the performances of bulk heterojunction (BHJ) organic solar cells. LC-1, a structurally-simple perylene diimide (PDI), has been adopted as a model for thorough investigation. It exhibits a broad temperature range of liquid crystalline (LC) phase from 41 degrees C to 158 degrees C, and its LC properties have been characterized by differential scanning calorimetry (DSC), polarization optical

microscopy (POM), and X-ray diffraction (XRD). The BHJ devices, using P3HT:LC-1 (1:2) as an organic photovoltaic active layer undergoing thermal annealing at 120 degrees C, shows an optimized efficiency of 0.94 %. By contrast, the devices based on PDI-1, a nonliquid crystalline PDI counterpart, only obtain a much lower efficiency of 0.22%. Atomic force microscopy (AFM) images confirm that the active layers composed of P3HT:LC-1 have smooth and ordered morphology. In space charge limited current (SCLC) devices fabricated via a spin-coating technique, LC-1 shows the intrinsic electron mobility of $2.85 \times 10^{-4} \text{ cm}^2/(\text{V s})$ (at 0.3 MV/cm) which is almost 5 times that of PDI-1 ($5.83 \times 10^{-5} \text{ cm}^2/(\text{V s})$) under the same conditions for thermal annealing at 120 degrees C.

[717]

TÍTULO / TITLE: - Fhit delocalizes annexin a4 from plasma membrane to cytosol and sensitizes lung cancer cells to Paclitaxel.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 6;8(11):e78610. doi: 10.1371/journal.pone.0078610.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078610](#)

AUTORES / AUTHORS: - Gaudio E; Paduano F; Spizzo R; Ngankeu A; Zanesi N; Gaspari M; Ortuso F; Lovat F; Rock J; Hill GA; Kaou M; Cuda G; Aqeilan RI; Alcaro S; Croce CM; Trapasso F

INSTITUCIÓN / INSTITUTION: - Department of Molecular Immunology, Virology and Medical Genetics, The Ohio State University, Columbus, Ohio, United States of America ; Lymphoma and Genomics Research Program, IOR Institute of Oncology Research, Bellinzona, Switzerland ; Dipartimento di Medicina Sperimentale e Clinica, University Magna Graecia, Campus "S. Venuta", Catanzaro, Italy.

RESUMEN / SUMMARY: - Fhit protein is lost or reduced in a large fraction of human tumors, and its restoration triggers apoptosis and suppresses tumor formation or progression in preclinical models. Here, we describe the identification of candidate Fhit-interacting proteins with cytosolic and plasma membrane localization. Among these, Annexin 4 (ANXA4) was validated by co-immunoprecipitation and confocal microscopy as a partner of this novel Fhit protein complex. Here we report that overexpression of Fhit prevents Annexin A4 translocation from cytosol to plasma membrane in A549 lung cancer cells treated with paclitaxel. Moreover, paclitaxel administration in combination with AdFHIT acts synergistically to increase the apoptotic rate of tumor cells both in vitro and in vivo experiments.

[718]

TÍTULO / TITLE: - GSK3 Alpha and Beta Are New Functionally Relevant Targets of Tivantinib in Lung Cancer Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - ACS Chem Biol. 2013 Nov 20.

●● Enlace al texto completo (gratis o de pago) [1021/cb400660a](#)

AUTORES / AUTHORS: - Remsing Rix LL; Kuenzi BM; Luo Y; Remily-Wood E; Kinose F; Wright G; Li J; Koomen JM; Haura EB; Lawrence HR; Rix U

INSTITUCIÓN / INSTITUTION: - Department of Drug Discovery, double daggerDepartment of Thoracic Oncology, and section signMolecular Oncology and

Proteomics, H. Lee Moffitt Cancer Center & Research Institute , Tampa, Florida 33612-9497, United States.

RESUMEN / SUMMARY: - Tivantinib has been described as a potent and highly selective inhibitor of the receptor tyrosine kinase c-MET and is currently in advanced clinical development for several cancers including non-small cell lung cancer (NSCLC). However, recent studies suggest that tivantinib's anticancer properties are unrelated to c-MET inhibition. Consistently, in determining tivantinib's activity profile in a broad panel of NSCLC cell lines, we found that, in contrast to several more potent c-MET inhibitors, tivantinib reduces cell viability across most of these cell lines. Applying an unbiased, mass-spectrometry-based, chemical proteomics approach, we identified glycogen synthase kinase 3 (GSK3) alpha and beta as novel tivantinib targets. Subsequent validation showed that tivantinib displayed higher potency for GSK3alpha than for GSK3beta and that pharmacological inhibition or simultaneous siRNA-mediated loss of GSK3alpha and GSK3beta caused apoptosis. In summary, GSK3alpha and GSK3beta are new kinase targets of tivantinib that play an important role in its cellular mechanism-of-action in NSCLC.

[719]

TÍTULO / TITLE: - Gefitinib Inhibits Invasive Phenotype and Epithelial-Mesenchymal Transition in Drug-Resistant NSCLC Cells with MET Amplification.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 22;8(10):e78656. doi: 10.1371/journal.pone.0078656.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0078656](#)

AUTORES / AUTHORS: - La Monica S; Caffarra C; Sacconi F; Galvani E; Galetti M; Fumarola C; Bonelli M; Cavazzoni A; Cretella D; Sirangelo R; Gatti R; Tiseo M; Ardizzoni A; Giovannetti E; Petronini PG; Alfieri RR

INSTITUCIÓN / INSTITUTION: - Department of Clinical and Experimental Medicine, University of Parma, Parma, Italy.

RESUMEN / SUMMARY: - Despite the initial response, all patients with epidermal growth factor receptor (EGFR)-mutant non-small cell lung cancer (NSCLC) eventually develop acquired resistance to EGFR tyrosine kinase inhibitors (TKIs). The EGFR-T790M secondary mutation is responsible for half of acquired resistance cases, while MET amplification has been associated with acquired resistance in about 5-15% of NSCLCs. Clinical findings indicate the retained addiction of resistant tumors on EGFR signaling. Therefore, we evaluated the molecular mechanisms supporting the therapeutic potential of gefitinib maintenance in the HCC827 GR5 NSCLC cell line harbouring MET amplification as acquired resistance mechanism. We demonstrated that resistant cells can proliferate and survive regardless of the presence of gefitinib, whereas the absence of the drug significantly enhanced cell migration and invasion. Moreover, the continuous exposure to gefitinib prevented the epithelial-mesenchymal transition (EMT) with increased E-cadherin expression and down-regulation of vimentin and N-cadherin. Importantly, the inhibition of cellular migration was correlated with the suppression of EGFR-dependent Src, STAT5 and p38 signaling as assessed by a specific kinase array, western blot analysis and silencing functional studies. On the contrary, the lack of effect of gefitinib on EGFR phosphorylation in the H1975 cells (EGFR-T790M) correlated with the absence of effects on cell migration and invasion. In conclusion, our findings suggest that certain EGFR-mutated patients may still benefit

from a second-line therapy including gefitinib based on the specific mechanism underlying tumor cell resistance.

[720]

TÍTULO / TITLE: - Adenovirus vector-mediated FAM176A overexpression induces cell death in human H1299 non-small cell lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMB Rep. 2013 Nov 21. pii: 2327.

AUTORES / AUTHORS: - Xie H; Hu J; Pan H; Lou Y; Lv P; Chen Y

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Medical Immunology, Ministry of Health, Peking University Health Science Center; Peking University Center for Human Disease Genomics, Peking University, 38 Xueyuan Road, Beijing 100191, China
yingyu_chen@bjmu.edu.cn.

RESUMEN / SUMMARY: - FAM176A (family with sequence similarity 176 member A) is a novel molecule related to programmed cell death. A decreased expression of FAM176A has been found in several types of human tumors including lung cancers. In the present study, we investigated the biological activities of FAM176A on the human non-small cell lung cancer cell line H1299 cells. We constructed a recombinant adenovirus 5-FAM176A vector (Ad5-FAM176A) and evaluated the expression and anti-tumor activities in vitro. Cell viability analysis revealed that the adenovirus-mediated increase of FAM176A inhibited the growth of the tumor cells in a dose- and time-dependent manner. This inhibitory effect was mediated by both autophagy and apoptosis that involved caspase activation. In addition, cell cycle analysis suggested that Ad5-FAM176A could induce cell cycle arrest at the G2/M phase, all of which suggested that adenovirus-mediated FAM176A gene transfer might present a new therapeutic approach for lung cancer treatment.

[721]

TÍTULO / TITLE: - Synergy of Taxol and rhein lysinate associated with the downregulation of ERK activation in lung carcinoma cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):525-528. Epub 2013 Jun 14.

●● [Enlace al texto completo \(gratis o de pago\) 3892/ol.2013.1398](#)

AUTORES / AUTHORS: - Zhen YZ; Hu G; Zhao YF; Yan F; Li R; Gao JL; Lin YJ

INSTITUCIÓN / INSTITUTION: - Basic Medical College of Hebei United University, Tangshan, Hebei 063000, P.R. China.

RESUMEN / SUMMARY: - In previous studies we observed that rhein lysinate (RHL), a salt of rhein and lysine that is easily dissolved in water, inhibited the growth of tumor cells in breast cancer, ovarian cancer, hepatocellular carcinoma and cervical cancer. The present study aimed to investigate the effects of RHL on H460 and A549 non-small cell lung cancer (NSCLC) cells using a combination of RHL and Taxol. A 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide (MTT) assay was used to determine the growth inhibition effect of the drugs in the H460 and A549 cells. Cell apoptosis was analyzed by flow cytometry combined with fluorescein-isothiocyanate-Annexin V/propidium iodide (PI) staining. The expression levels of proteins were detected by western blotting. There was a significant reduction in the proliferation of the NSCLC cell lines treated with a combination of Taxol and RHL. The overall growth inhibition was directly correlated with apoptotic cell death. RHL potentiated Taxol-

induced cell killing by reducing extracellular signal-regulated kinase (ERK) activity and increasing the levels of cleaved poly(ADP-ribose) polymerase (PARP) and caspase-3. Notably, the results for the Bcl-2 and NF-kappaB proteins also showed downregulation in the combined treatment group compared with the single-agent treatment and the untreated control groups. The present results showed that RHL potentiates the growth inhibition induced by Taxol in NSCLC cells and showed that this synergy may be associated with the downregulation of ERK activation.

[722]

TÍTULO / TITLE: - Eicosanoid profiling in an orthotopic model of lung cancer progression by mass spectrometry demonstrates selective production of leukotrienes by inflammatory cells of the microenvironment.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 11;8(11):e79633. doi: 10.1371/journal.pone.0079633.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079633](#)

AUTORES / AUTHORS: - Poczobutt JM; Gijon M; Amin J; Hanson D; Li H; Walker D; Weiser-Evans M; Lu X; Murphy RC; Nemenoff RA

INSTITUCIÓN / INSTITUTION: - Department of Medicine, University of Colorado Denver, Aurora, Colorado, United States of America.

RESUMEN / SUMMARY: - Eicosanoids are bioactive lipid mediators derived from arachidonic acid(1) (AA), which is released by cytosolic phospholipase A2 (cPLA2). AA is metabolized through three major pathways, cyclooxygenase (COX), lipoxygenase (LO) and cytochrome P450, to produce a family of eicosanoids, which individually have been shown to have pro- or anti-tumorigenic activities in cancer. However, cancer progression likely depends on complex changes in multiple eicosanoids produced by cancer cells and by tumor microenvironment and a systematic examination of the spectrum of eicosanoids in cancer has not been performed. We used liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS) to quantitate eicosanoids produced during lung tumor progression in an orthotopic immunocompetent mouse model of lung cancer, in which Lewis lung carcinoma (LLC) cells are injected into lungs of syngeneic mice. The presence of tumor increased products of both the cyclooxygenase and the lipoxygenase pathways in a time-dependent fashion. Comparing tumors grown in cPLA2 knockout vs wild-type mice, we demonstrated that prostaglandins (PGE2, PGD2 and PGF2a) were produced by both cancer cells and the tumor microenvironment (TME), but leukotriene (LTB4, LTC4, LTD4, LTE4) production required cPLA2 expression in the TME. Using flow cytometry, we recovered tumor-associated neutrophils and 2 types of tumor-associated macrophages from tumor-bearing lungs and we defined their distinct eicosanoid profiles by LC/MS/MS. The combination of flow cytometry and LC/MS/MS unravels the complexity of eicosanoid production in lung cancer and provides a rationale to develop therapeutic strategies that target select cell populations to inhibit specific classes of eicosanoids.

[723]

TÍTULO / TITLE: - Lung cancer tumorigenicity and drug resistance are maintained through ALDH(hi)CD44(hi) tumor initiating cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncotarget. 2013 Oct;4(10):1698-1711.

AUTORES / AUTHORS: - Liu J; Xiao Z; Wong SK; Tin VP; Ho KY; Wang J; Sham MH; Wong MP

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR China.

RESUMEN / SUMMARY: - Limited improvement in long term survival of lung cancer patients has been achieved by conventional chemotherapy or targeted therapy. To explore the potentials of tumor initiating cells (TIC)-directed therapy, it is essential to identify the cell targets and understand their maintenance mechanisms. We have analyzed the performance of ALDH/CD44 co-expression as TIC markers and treatment targets of lung cancer using well-validated in vitro and in vivo analyses in multiple established and patient-derived lung cancer cells. The ALDH(hi)CD44(hi) subset showed the highest enhancement of stem cell phenotypic properties compared to ALDH(hi)CD44(lo), ALDH(lo)CD44(hi), ALDH(lo)CD44(lo) cells and unsorted controls. They showed higher invasion capacities, pluripotency genes and epithelial-mesenchymal transition transcription factors expression, lower intercellular adhesion protein expression and higher G2/M phase cell cycle fraction. In immunosuppressed mice, the ALDH(hi)CD44(hi)xenografts showed the highest tumor induction frequency, serial transplantability, shortest latency, largest volume and highest growth rates. Inhibition of sonic Hedgehog and Notch developmental pathways reduced ALDH+CD44+ compartment. Chemotherapy and targeted therapy resulted in higher AALDH(hi)CD44(hi) subset viability and ALDH(lo)CD44(lo) subset apoptosis fraction. ALDH inhibition and CD44 knockdown led to reduced stemness gene expression and sensitization to drug treatment. In accordance, clinical lung cancers containing a higher abundance of ALDH and CD44-coexpressing cells was associated with lower recurrence-free survival. Together, results suggested theALDH(hi)CD44(hi)compartment was the cellular mediator of tumorigenicity and drug resistance. Further investigation of the regulatory mechanisms underlying ALDH(hi)CD44(hi)TIC maintenance would be beneficial for the development of long term lung cancer control.

[724]

TÍTULO / TITLE: - Inhibition of SENP1 induces radiosensitization in lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Ther Med. 2013 Oct;6(4):1054-1058. Epub 2013 Aug 8.

●● Enlace al texto completo (gratis o de pago) [3892/etm.2013.1259](#)

AUTORES / AUTHORS: - Wang RT; Zhi XY; Zhang Y; Zhang J

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Xuanwu Hospital of Capital Medical University (CMU), Beijing 100053, P.R. China.

RESUMEN / SUMMARY: - Lung cancer is one of the most common and lethal types of malignancy. To date, radiotherapy and chemotherapy have been used as the two major treatment methods. However, radioresistance of lung cancer remains a therapeutic hindrance. The aim of this study was to identify whether small ubiquitin-related modifier (SUMO)-specific protease 1 (SENP1) is a marker of radioresistance that may serve as a target for enhancing the efficacy of lung carcinoma radiotherapy. SENP1 was observed to be overexpressed in lung cancer tissues, and the modulation of SENP1 expression was demonstrated to significantly affect the proliferation of lung cancer cells. Moreover, silencing the expression of SENP1 using small interfering RNA

(siRNA) significantly sensitized lung cancer cells to radiation. Mechanically, it was demonstrated that SENP1 depletion significantly enhanced ionizing radiation (IR)-induced cell cycle arrest, gamma-H2AX expression and apoptosis. Thus, these data suggest that SENP1 may be a desirable drug target for lung carcinoma radiotherapy.

[725]

TÍTULO / TITLE: - Antiproliferative Activity of Cyanophora paradoxa Pigments in Melanoma, Breast and Lung Cancer Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mar Drugs. 2013 Nov 1;11(11):4390-406. doi: 10.3390/md11114390.

●● Enlace al texto completo (gratis o de pago) [3390/md11114390](#)

AUTORES / AUTHORS: - Baudalet PH; Gagez AL; Berard JB; Juin C; Bridiau N; Kaas R; Thierry V; Cadoret JP; Picot L

INSTITUCIÓN / INSTITUTION: - University of La Rochelle, UMRi CNRS 7266 LIENSs, F-17042, La Rochelle, France. lpicot@univ-lr.fr.

RESUMEN / SUMMARY: - The glaucophyte *Cyanophora paradoxa* (Cp) was chemically investigated to identify pigments efficiently inhibiting malignant melanoma, mammary carcinoma and lung adenocarcinoma cells growth. Cp water and ethanol extracts significantly inhibited the growth of the three cancer cell lines in vitro, at 100 microg.mL⁻¹. Flash chromatography of the Cp ethanol extract, devoid of c-phycoerythrin and allophycoerythrin, enabled the collection of eight fractions, four of which strongly inhibited cancer cells growth at 100 microg.mL⁻¹. Particularly, two fractions inhibited more than 90% of the melanoma cells growth, one inducing apoptosis in the three cancer cells lines. The detailed analysis of Cp pigment composition resulted in the discrimination of 17 molecules, ten of which were unequivocally identified by high resolution mass spectrometry. Pheophorbide a, beta-cryptoxanthin and zeaxanthin were the three main pigments or derivatives responsible for the strong cytotoxicity of Cp fractions in cancer cells. These data point to *Cyanophora paradoxa* as a new microalgal source to purify potent anticancer pigments, and demonstrate for the first time the strong antiproliferative activity of zeaxanthin and beta-cryptoxanthin in melanoma cells.

[726]

TÍTULO / TITLE: - Andrographolide inhibits the activation of NF-kappaB and MMP-9 activity in H3255 lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Exp Ther Med. 2013 Sep;6(3):743-746. Epub 2013 Jul 2.

●● Enlace al texto completo (gratis o de pago) [3892/etm.2013.1196](#)

AUTORES / AUTHORS: - Luo W; Liu Y; Zhang J; Luo X; Lin C; Guo J

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, Taihe Hospital Affiliated to Hubei University of Medicine, Shiyan, Hubei 442000, P.R. China.

RESUMEN / SUMMARY: - This study aimed to determine the effect of andrographolide (AD) on the growth of H3255 lung cancer cells and its possible impact on the expression and activity of the matrix metalloproteinase (MMP)-9 protein. H3255 cells were cultured in vitro, and treated with AD (1, 5 or 10 muM) for 24, 48 or 72 h. Cell proliferation was detected using an MTT assay and the expression of MMP-9 mRNA was measured using a reverse transcription-polymerase chain reaction (RT-PCR). The

activity of MMP-9 was assessed by gelatin zymography, while the nuclear translocation of the nuclear factor-kappaB (NF-kappaB) p65 subunit and the phosphorylation of I kappa B were determined by western blotting. AD inhibited the proliferation of the H3255 cells in a concentration- and time-dependent manner, in addition to downregulating the expression of MMP-9 mRNA and the activity of MMP-9. Moreover, AD significantly inhibited the nuclear translocation of the NF-kappaB p65 subunit and suppressed I kappa B phosphorylation. The significant inhibition of H3255 cell proliferation by AD may have been correlated with the reduction in MMP-9 expression and activity through the inhibition of the phosphorylation of I kappa B and the translocation of NF-kappaB. The results suggest that AD is a promising drug candidate for the treatment of the migration and invasion of malignant tumors.

[727]

TÍTULO / TITLE: - Targeting Eukaryotic Translation in Mesothelioma Cells with an eIF4E-Specific Antisense Oligonucleotide.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 18;8(11):e81669. doi: 10.1371/journal.pone.0081669.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0081669](#)

AUTORES / AUTHORS: - Jacobson BA; Thumma SC; Jay-Dixon J; Patel MR; Dubear Kroening K; Kratzke MG; Etchison RG; Konicek BW; Graff JR; Kratzke RA

INSTITUCIÓN / INSTITUTION: - Department of Medicine, University of Minnesota, Minneapolis, Minnesota, United States of America.

RESUMEN / SUMMARY: - BACKGROUND: Aberrant cap-dependent translation is implicated in tumorigenesis in multiple tumor types including mesothelioma. In this study, disabling the eIF4F complex by targeting eIF4E with eIF4E-specific antisense oligonucleotide (4EASO) is assessed as a therapy for mesothelioma. METHODS: Mesothelioma cells were transfected with 4EASO, designed to target eIF4E mRNA, or mismatch-ASO control. Cell survival was measured in mesothelioma treated with 4EASO alone or combined with either gemcitabine or pemetrexed. Levels of eIF4E, ODC, Bcl-2 and beta-actin were assessed following treatment. Binding to a synthetic cap-analogue was used to study the strength of eIF4F complex activation following treatment. RESULTS: eIF4E level and the formation of eIF4F cap-complex decreased in response to 4EASO, but not mismatch control ASO, resulting in cleavage of PARP indicating apoptosis. 4EASO treatment resulted in dose dependent decrease in eIF4E levels, which corresponded to cytotoxicity of mesothelioma cells. 4EASO resulted in decreased levels of eIF4E in non-malignant LP9 cells, but this did not correspond to increased cytotoxicity. Proteins thought to be regulated by cap-dependent translation, Bcl-2 and ODC, were decreased upon treatment with 4EASO. Combination therapy of 4EASO with pemetrexed or gemcitabine further reduced cell number. CONCLUSION: 4EASO is a novel drug that causes apoptosis and selectively reduces eIF4E levels, eIF4F complex formation, and proliferation of mesothelioma cells. eIF4E knockdown results in decreased expression of anti-apoptotic and pro-growth proteins and enhances chemosensitivity.

[728]

TÍTULO / TITLE: - Global Decrease of Histone H3K27 Acetylation in ZEB1-Induced Epithelial to Mesenchymal Transition in Lung Cancer Cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancers (Basel). 2013 Apr 3;5(2):334-56. doi: 10.3390/cancers5020334.

●● Enlace al texto completo (gratis o de pago) [3390/cancers5020334](#)

AUTORES / AUTHORS: - Roche J; Nasarre P; Gemmill R; Baldys A; Pontis J; Korch C; Guilhot J; Ait-Si-Ali S; Drabkin H

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Hematology Oncology Division, MUSC, 96 Jonathan Lucas St., Charleston, SC 29425, USA.
joelle.roche@univ-poitiers.fr.

RESUMEN / SUMMARY: - The epithelial to mesenchymal transition (EMT) enables epithelial cells with a migratory mesenchymal phenotype. It is activated in cancer cells and is involved in invasion, metastasis and stem-like properties. ZEB1, an E-box binding transcription factor, is a major suppressor of epithelial genes in lung cancer. In the present study, we show that in H358 non-small cell lung cancer cells, ZEB1 downregulates EpCAM (coding for an epithelial cell adhesion molecule), ESRP1 (epithelial splicing regulatory protein), ST14 (a membrane associated serine protease involved in HGF processing) and RAB25 (a small G-protein) by direct binding to these genes. Following ZEB1 induction, acetylation of histone H4 and histone H3 on lysine 9 (H3K9) and 27 (H3K27) was decreased on ZEB1 binding sites on these genes as demonstrated by chromatin immunoprecipitation. Of note, decreased H3K27 acetylation could be also detected by western blot and immunocytochemistry in ZEB1 induced cells. In lung cancers, H3K27 acetylation level was higher in the tumor compartment than in the corresponding stroma where ZEB1 was more often expressed. Since HDAC and DNA methylation inhibitors increased expression of ZEB1 target genes, targeting these epigenetic modifications would be expected to reduce metastasis.

[729]

TÍTULO / TITLE: - Gefitinib resistance resulted from STAT3-mediated Akt activation in lung cancer cells.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncotarget. 2013 Nov 24.

AUTORES / AUTHORS: - Wu K; Chang Q; Lu Y; Qiu P; Chen B; Thakur C; Sun J; Li L; Kowluru A; Chen F

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutical Sciences, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, USA.

RESUMEN / SUMMARY: - Hyperactivation of Epidermal Growth Factor Receptor (EGFR) tyrosine kinase is prevalent in human lung cancer and its inhibition by the tyrosine kinase inhibitors (TKIs), including gefitinib and erlotinib, initially controls tumor growth. However, most patients ultimately relapse due to the development of drug resistance. In this study, we have discovered a STAT3-dependent Akt activation that impairs the efficacy of gefitinib. Mechanistically, gefitinib increased association of EGFR with STAT3, which de-repressed STAT3 from SOCS3, an upstream suppressor of STAT3. Such a de-repression of STAT3 in turn fostered Akt activation. Genetic or pharmacological inhibition of STAT3 abrogated Akt activation and combined gefitinib with STAT3 inhibition synergistically reduced the growth of the tumor cells. Taken together, this study suggests that activation of STAT3 is an intrinsic mechanism of drug

resistance in response to EGFR TKIs. Combinational targeting on both EGFR and STAT3 may enhance the efficacy of gefitinib or other EGFR TKIs in lung cancer.

[730]

TÍTULO / TITLE: - Impact of a breathing-control system on target margins and normal-tissue sparing in the treatment of lung cancer: experience at the radiotherapy unit of Florence University.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiol Med. 2013 Nov 15.

●● Enlace al texto completo (gratis o de pago) [1007/s11547-013-0307-6](#)

AUTORES / AUTHORS: - Scotti V; Marrazzo L; Saieva C; Agresti B; Meattini I; Desideri I; Cecchini S; Bertocci S; Franzese C; De Luca Cardillo C; Zei G; Loi M; Greto D; Mangoni M; Bonomo P; Livi L; Biti GP

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Florence, Viale Morgagni 85, 50134, Florence, Italy, v.scotti@dfc.unifi.it.

RESUMEN / SUMMARY: - PURPOSE: In lung cancer, a high radiation dose to the target area correlates with better local control but is frequently counterbalanced by a higher risk of lung toxicity. Several methods exist to coordinate respiratory motion in lung radiotherapy. We aimed to investigate the impact of a breathing-control system on irradiated volumes and dosimetric parameters in three-dimensional conformal radiotherapy (3D-CRT) and stereotactic radiotherapy (SRT) treatments. MATERIALS AND METHODS: Twelve patients were scheduled for radical radiotherapy: five for SRT and seven for 3D-CRT. For each patient, in addition to the free-breathing computed tomography (CT) scan, four additional sets of CT slices were acquired using the Active Breathing Coordinator device (ABC, Elekta Oncology Systems Ltd., UK). RESULTS: The volumes acquired with the ABC device were significantly smaller than the free-breathing volumes [23 % reduction of planning tumour volume (PTV), $p = 0.002$]. ABC allowed a reduction of all dosimetric parameters [2.28 % reduction of percentage volume of lung treated to a dose of ≥ 20 Gy (V20), $p = 0.004$; 10 % reduction of mean lung dose (MLD), $p = 0.009$]. Significant differences were found both in SRT and in 3D-CRT, in peripheral and apical lesions. CONCLUSION: In our experience, ABC has the potential to reduce lung toxicity in the treatment of lung cancer; alternatively, it can allow the prescribed dose to be increased while maintaining the same risk of lung toxicity.

[731]

TÍTULO / TITLE: - Recombinant human endostatin combined with radiotherapy in the treatment of brain metastases of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Transl Oncol. 2013 Nov 6.

●● Enlace al texto completo (gratis o de pago) [1007/s12094-013-1129-7](#)

AUTORES / AUTHORS: - Jiang X; Ding M; Qiao Y; Liu Y; Liu L

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Lianyungang First People's Hospital, No. 182, Tongguan Road, Lianyungang, 222002, Jiangsu, China, jxdysy@sohu.com.

RESUMEN / SUMMARY: - OBJECTIVE: Since brain metastases (BM) is often accompanied by edema, and endostatin (ES) can prevent tumor tissue edema, we investigated the therapeutic effects of ES combined with radiotherapy in the treatment

of BM of NSCLC. We also determined the patients who are suitable for this therapy. METHODS: Eighty patients with BM of NSCLC were randomly divided into combination group and radiotherapy alone group. The primary endpoint was overall response rate, and secondary endpoints were overall survival time, cerebral edema index and adverse reactions. These were observed and the expressions of vascular endothelial growth factor receptor 2 (VEGFR2) protein and KDR gene in primary lesions were detected with immunohistochemical method and fluorescence in situ hybridization. RESULTS: Compared with radiotherapy alone, brain edema was significantly reduced in the ES group ($P = 0.003$) without marked adverse reactions. For the overall response rate, there was no statistical significant difference between the two groups (control, 90 % vs. ES, 75 %, $P = 0.07$), but there was statistical significance in the patients with positive VEGFR2 (93 vs. 67.7 %, $P = 0.012$) or positive KDR gene (94.4 vs. 47.3 %, $P = 0.002$). In overall survival time, there was no statistical significance in the two groups ($P = 0.35$), in the tumors with positive VEGFR2 ($P = 0.109$) or with positive KDR gene ($P = 0.147$). CONCLUSION: Compared with radiotherapy alone, ES combined with radiotherapy can reduce brain edema in NSCLC patients with BM and obtain better short-term response rate in tumors with positive VEGFR2 or positive KDR gene, but does not improve the overall survival.

[732]

TÍTULO / TITLE: - Expression of hENTI and ERCC1 genes in tumor tissues non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Trop Med. 2013 Nov;6(11):908-11. doi: 10.1016/S1995-7645(13)60162-5.

●● Enlace al texto completo (gratis o de pago) [1016/S1995-7645\(13\)60162-5](#)

AUTORES / AUTHORS: - Wu JJ; Jiao SC

INSTITUCIÓN / INSTITUTION: - Department of Training, PLA General Hospital, Beijing, China.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate the expression of hENTI and ERCC1 genes in tumor tissues non-small cell lung cancer (NSCLC). METHODS: Fresh non-small lung cancer specimens were transplanted into nude mice. Twenty mice were randomized into two groups: experimental group receiving gemcitabine plus cisplatin and control group receiving 0.9% physiological saline. The expressions of hENTI and ERCC1 mRNA in tumor tissue were detected by real-time fluorescent quantitative PCR. The volume of tumor, the weight of nude mice and tumor volume were respectively measured and calculated 2-3 times per week. Tissue samples were collected from NSCLC mice treated with gemcitabine plus carboplatin. RESULTS: The histological examination showed that many tumor cells were well preserved in nude mice. The rate of transplanted tumor cells was 86.7%. The concomitant treatment study showed that the rate of TV, RTV, T/C in GEM + DDP group was the lowest. LBP + DOC, DDP + DOC obviously influenced the body weight. Compared with NS group, DDP group, GEM group, the survival period and the level of hENTI of DDP+GEM group increased obviously, the level of ERCC1 decreased significantly ($P < 0.05$). CONCLUSIONS: The expression of hENT1 and ERCC1 genes in tumor tissues were closely correlated with the response to chemotherapy and prognosis of patients with NSCLC treated with gemcitabine plus cisplatin.

[733]

TÍTULO / TITLE: - Analysis of MAT3 gene expression in NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Diagn Pathol. 2013 Oct 9;8:166. doi: 10.1186/1746-1596-8-166.

●● Enlace al texto completo (gratis o de pago) [1186/1746-1596-8-166](#)

AUTORES / AUTHORS: - Zheng S; Du Y; Chu H; Chen X; Li P; Wang Y; Ma Y; Wang H; Zang W; Zhang G; Zhao G

INSTITUCIÓN / INSTITUTION: - College of Basic Medical Sciences, Zhengzhou University, No,100 Kexue Road, Zhengzhou 450001, China. gjzhangzhu@126.com.

RESUMEN / SUMMARY: - BACKGROUND: Many studies have suggested different roles of Metastasis-associated protein 3 (MAT3) in different types of human cancers. However, expression of MAT3 in primary lung cancer and its relationship with clinicopathological factors have not been examined and the biological roles of MTA3 in lung cancer cells are still unclear. METHODS: The expression of MAT3 mRNA and protein were detected with quantitative real-time RT-PCR and immunohistochemical methods in 118 NSCLC samples and corresponding non-neoplastic samples. Survival curves were made with follow-up data. The relations of the prognosis with clinical and pathological characteristics were analyzed. RESULTS: The expression level of MAT3 mRNA and the positive rate of MAT3 protein were significantly higher in NSCLC samples than that in non-neoplastic samples, and in NSCLC samples with lymph node metastasis than that in NSCLC samples without lymph node metastasis ($P < 0.01$). MAT3 mRNA expression level was a risk factor of lymph node metastasis in patients with NSCLC ($P = 0.006$). There were significant differences in survival curves between lymph node metastatic group and non-metastatic group ($P = 0.000$), among groups of MAT3 positive and negative ($P = 0.000$), among groups of TNM stage I, II and III ($P = 0.000$) and among groups of tumor status T1, T2 and T3T4 ($P = 0.000$); but no statistical significance between male patients and female patients ($P = 0.516$), between ≥ 60 years old patients and < 60 years old patients ($P = 0.133$), between histology types adenocarcinoma and squamous cell carcinoma ($P = 0.865$) and between well differentiation and moderate-poor differentiation ($P = 0.134$). The level of MAT3 mRNA ($P = 0.000$) and protein ($P = 0.000$) were risk factors of survival. CONCLUSION: Our study showed that MAT3 over-expression in NSCLC tissue, and MAT3 mRNA level is a risk factor of lymph node metastasis. The level of MAT3 mRNA and protein were risk factors of survival in patients with NSCLC. It suggested that this antigen could be used as a simple and efficient parameter with which to identify high-risk patients. VIRTUAL SLIDES: The virtual slides for this article can be found here: <http://www.diagnosticpathology.diagnomx.eu/vs/5585901065503943>.

[734]

TÍTULO / TITLE: - HapMap-based study identifies risk sub-region on chromosome 19q13.3 in relation to lung cancer among Chinese.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Epidemiol. 2013 Dec;37(6):923-9. doi: 10.1016/j.canep.2013.09.016. Epub 2013 Oct 17.

●● Enlace al texto completo (gratis o de pago) [1016/j.canep.2013.09.016](#)

AUTORES / AUTHORS: - Yin J; Vogel U; Wang H; Ma Y; Wang C; Liang D; Liu J; Yue L; Zhao Y; Ma J

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Environment and Population Health of Liaoning Education Ministry (Shenyang Medical College), Shenyang 110034, Liaoning Province, People's Republic of China; Department of Cell Biology and Genetics, Shenyang Medical College, Shenyang 110034, Liaoning Province, People's Republic of China. Electronic address: yinjye@163.com.

RESUMEN / SUMMARY: - Background: Chromosome 19q13.3 has been identified as one of the regions that associate with cancer risk in previous studies. Methods: We systematically examined the 70.772kb region comprising four genes on chromosome 19q13.3 among Chinese using the haplotype-tagging SNP (htSNP) approach and the HapMap platform. The study involved 339 lung cancer cases and 358 non-cancer controls. Two htSNPs (rs1046282 and rs735482) captured most of the common haplotypes of CD3EA and the combined effects of sixteen htSNPs provided high coverage of common haplotypes of ERCC2, PPP1R13L, CD3EAP and ERCC1. Results: Both carriers of variant CC genotype [adjusted OR (95% CI)=1.28 (1.02-1.60), P=0.04] and variant C-allele among >20 years' smokers [OR (95% CI)=2.13 (1.24-3.67), P=0.006] for CD3EAP rs735482 were at increased risk of lung cancer. Four haplotype blocks of strong linkage disequilibrium were identified. The haplotype ERCC2 rs3916874(G) and rs238415© [OR (95% CI)=1.26 (1.02-1.57), P=0.03] in block 1 and the haplotype PPP1R13L rs4803817(A), CD3EAP rs1046282(T), rs735482(C), ERCC1 rs3212980(A), rs3212964(G) [OR (95% CI)=3.56 (1.55-8.18), P=0.005] in block 3 were associated with lung cancer risk. MDR (multifactor dimensionality reduction) analysis demonstrated the best significant model of two-attributes containing smoking duration and rs2298881 in ERCC1 (P=0.004-0.005) and suggested that the effects of high-order interactions among smoking duration and ERCC2, PPP1R13, ERCC1 htSNPs could modulate lung cancer risk. Conclusions: HapMap-based study of 19q13.3 identified that genetic variation of CD3EAP and two loci were associated with lung cancer risk and interaction of smoking duration and genetic variants was the strongest predictor of lung cancer risk in a Chinese population.

[735]

TÍTULO / TITLE: - A semi-parametric approach to estimate risk functions associated with multidimensional exposure profiles: application to smoking and lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Med Res Methodol. 2013 Oct 23;13(1):129.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2288-13-129](#)

AUTORES / AUTHORS: - Hastie DJ; Liverani S; Azizi L; Richardson S; Stucker I

RESUMEN / SUMMARY: - BACKGROUND: A common characteristic of environmental epidemiology is the multi-dimensional aspect of exposure patterns, frequently reduced to a cumulative exposure for simplicity of analysis. By adopting a flexible Bayesian clustering approach, we explore the risk function linking exposure history to disease. This approach is applied here to study the relationship between different smoking characteristics and lung cancer in the framework of a population based case control study. METHODS: Our study includes 4658 males (1995 cases, 2663 controls) with full smoking history (intensity, duration, time since cessation, pack-years) from the ICARE multi-centre study conducted from 2001-2007. We extend Bayesian clustering techniques to explore predictive risk surfaces for covariate profiles of interest. RESULTS: We were able to partition the population into 12 clusters with different

smoking profiles and lung cancer risk. Our results confirm that when compared to intensity, duration is the predominant driver of risk. On the other hand, using pack-years of cigarette smoking as a single summary leads to a considerable loss of information. CONCLUSIONS: Our method estimates a disease risk associated to a specific exposure profile by robustly accounting for the different dimensions of exposure and will be helpful in general to give further insight into the effect of exposures that are accumulated through different time patterns.

[736]

TÍTULO / TITLE: - Optimal postoperative treatment for composite laryngeal small cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Case Rep Otolaryngol. 2013;2013:806284. doi: 10.1155/2013/806284. Epub 2013 Sep 15.

●● Enlace al texto completo (gratis o de pago) [1155/2013/806284](#)

AUTORES / AUTHORS: - Ebisumoto K; Sakai A; Okami K; Sugimoto R; Saito K; Iida M
INSTITUCIÓN / INSTITUTION: - Department of Otolaryngology-Head and Neck Surgery, Tokai University, School of Medicine, Isehara 259-1193, Japan.

RESUMEN / SUMMARY: - Small cell carcinoma (SmCC) most commonly occurs in the lung and rarely arises from the head and neck region. Further, composite SmCC is extremely rare. Therefore, no postoperative treatment strategy has been established. We report a 59-year-old male patient referred to our outpatient clinic for further examination and treatment of a laryngeal tumor. Biopsy from the tumor revealed squamous cell carcinoma (SCC). The preoperative diagnosis was supraglottic SCC (T3N2bM0), and total laryngectomy and bilateral neck dissection were performed. Pathological examination revealed 2 individual cancer components: SmCC and SCC. Postoperative chemoradiotherapy (2 courses of cisplatin (CDDP) and etoposide (VP-16)) was indicated. Following the postoperative chemoradiotherapy, 2 courses of adjuvant chemotherapy were administered. The patient is currently alive with no evidence of disease at 36 months following the completion of therapy. Postoperative chemoradiotherapy and adjuvant chemotherapy are optimal treatment strategies for laryngeal composite SmCC.

[737]

TÍTULO / TITLE: - Fluorodeoxyglucose positron emission tomography and chemotherapy-related tumor marker expression in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Nov 15;13(1):546.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-546](#)

AUTORES / AUTHORS: - Duan XY; Wang W; Wang JS; Shang J; Gao JG; Guo YM

RESUMEN / SUMMARY: - BACKGROUND: The chemotherapy resistance of non-small cell lung cancer (NSCLC) remains a clinic challenge and is closely associated with several biomarkers including epidermal growth factor receptor (EGFR) (Drugs 72(Suppl 1):28--36, 012.), p53 (Med Sci Monit 11(6):HY11--HY20, 2005.) and excision repair cross complementing gene 1 (ERCC1) (J Thorac Oncol 8(5):582--586, 2013.). Fluorodeoxyglucose positron emission tomography (FDG—PET) is the best non-invasive surrogate for tumor biology with the maximal standardized uptake values (SUVmax) being the most important paradigm. However, there are limited data

correlating FDG-PET with the chemotherapy resistant tumor markers. The purpose of this study was to determine the correlation of chemotherapy related tumor marker expression with FDG—PET SUVmax in NSCLC. METHODS: FDG—PET SUVmax was calculated in chemotherapy naive patients with NSCLC (n = 62) and immunohistochemical analysis was performed for EGFR, p53 or ERCC1 on the intraoperative NSCLC tissues. Each tumor marker was assessed independently by two pathologists using common grading criteria. The SUVmax difference based on the histologic characteristics, gender, differentiation, grading and age as well as correlation analysis among these parameters were performed. Multiple stepwise regression analysis was further performed to determine the primary predictor for SUVmax and the receiver operating characteristics (ROC) curve analysis was performed to detect the optimized sensitivity and specificity for SUVmax in suggesting chemotherapy resistant tumor markers. RESULTS: The significant tumor type (P = 0.045), differentiation (P = 0.021), p53 (P = 0.000) or ERCC1 (P = 0.033) positivity dependent differences of SUVmax values were observed. The tumor differentiation is significantly correlated with SUVmax (R = -0.327), tumor size (R = -0.286), grading (R = -0.499), gender (R = 0.286) as well as the expression levels for p53 (R = -0.605) and ERCC1 (R = -0.644). The expression level of p53 is significantly correlated with SUVmax (R = 0.508) and grading (R = 0.321). Furthermore, multiple stepwise regression analysis revealed that p53 expression was the primary predictor for SUVmax. When the cut-off value of SUVmax was set at 5.15 in the ROC curve analysis, the sensitivity and specificity of SUVmax in suggesting p53 positive NSCLC were 79.5% and 47.8%, respectively. CONCLUSION: The current study suggests that SUVmax of primary tumor on FDG-PET might be a simple and good non-invasive method for predicting p53-related chemotherapy resistance in NSCLC when we set the cu-off value of SUVmax at 5.15.

[738]

TÍTULO / TITLE: - On the possible benefits of a hybrid VMAT technique in the treatment of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Med Dosim. 2013 Winter;38(4):460-6. doi: 10.1016/j.meddos.2013.08.004. Epub 2013 Oct 4.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.meddos.2013.08.004](#)

AUTORES / AUTHORS: - Agapito J

INSTITUCIÓN / INSTITUTION: - Cancer program, Windsor Regional Hospital, Windsor, Ontario. Electronic address: john_agapito@wrh.on.ca.

RESUMEN / SUMMARY: - To assess, using clinical cases, the potential of a hybrid technique for the treatment of non-small cell lung cancer (NSCLC)-blending volumetric-modulated arc therapy (VMAT) and conformal radiation therapy (CRT) fields, and to consider potential issues with implementation of such a technique. Eight clinical cases already treated with CRT were used for a planning study comparing target coverage and organs at risk (OAR) sparing between CRT and hybrid VMAT (VMATh). Quality assurance (QA) implications of the resultant hybrid plans are discussed. The hybrid technique resulted in superior target conformity or improved sparing of OAR or both. The hybrid technique shows promise, but the QA implications of motion at treatment need careful consideration.

[739]

TÍTULO / TITLE: - Major cancer regressions in mesothelioma after treatment with an anti-mesothelin immunotoxin and immune suppression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Transl Med. 2013 Oct 23;5(208):208ra147. doi: 10.1126/scitranslmed.3006941.

●● Enlace al texto completo (gratis o de pago) [1126/scitranslmed.3006941](#)

AUTORES / AUTHORS: - Hassan R; Miller AC; Sharon E; Thomas A; Reynolds JC; Ling A; Kreitman RJ; Miettinen MM; Steinberg SM; Fowler DH; Pastan I

INSTITUCIÓN / INSTITUTION: - Laboratory of Molecular Biology, Center for Cancer Research (CCR), National Cancer Institute (NCI), National Institutes of Health (NIH), Bethesda, MD 20892, USA.

RESUMEN / SUMMARY: - Immunotoxins are potent anticancer agents with an unusual mechanism of action: inhibition of protein synthesis resulting in apoptotic cell death. Immunotoxins have produced many durable complete responses in refractory hairy cell leukemia, where patients rarely form antibodies to the bacterial toxin component of the immunotoxin. Patients with mesothelioma, however, have normal immune systems and form antibodies after one cycle, and tumor responses to the immunotoxin have not been observed in this disease. We describe the results of a trial in which major antitumor responses were seen in patients with advanced mesothelioma who received the anti-mesothelin immunotoxin SS1P, together with pentostatin and cyclophosphamide, to deplete T and B cells. Of 10 patients with chemotherapy-refractory mesothelioma, 3 have had major tumor regressions with 2 ongoing at 15 months, and 2 others responded to chemotherapy after discontinuing immunotoxin therapy. Antibody formation was markedly delayed, allowing more SS1P cycles to be given, but this alone does not appear to account for the marked antitumor activity observed.

[740]

TÍTULO / TITLE: - The effects of beta-elemene on the expression of mTOR, HIF-1A, survivin in lung adenocarcinoma A549 cell.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Afr J Tradit Complement Altern Med. 2013 May 16;10(4):18-23.

AUTORES / AUTHORS: - Tong E; Xu Y; Li G; Zou K; Zou L

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Dalian Medical University.

RESUMEN / SUMMARY: - The purpose of this manuscript was to study the regulation effects of beta-elemene combined with radiotherapy on three different gene expressions in lung adenocarcinoma A549 cell. mTOR gene, HIF-1alpha gene, Survivin gene were included in the gene group. Cell culture and RT-PCR were applied to finish this research. Hypoxia Control group, Hypoxia beta-elemene group, Hypoxia beta-elemene combined with irradiation group were set to compare the differences of three different gene expressions. The most active effects were found in the group of Hypoxia irradiation combined with beta-elemene. In this group, the mTOR gene, HIF-1alpha gene, Survivin gene expressions were all down-regulated when compared with the single treatment groups, and there were significantly statistical differences.

[741]

TÍTULO / TITLE: - Clinical experience of bronchoscopy-guided radiofrequency ablation for peripheral-type lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Case Rep Oncol Med. 2013;2013:515160. doi: 10.1155/2013/515160. Epub 2013 Sep 11.

●● Enlace al texto completo (gratis o de pago) [1155/2013/515160](#)

AUTORES / AUTHORS: - Koizumi T; Kobayashi T; Tanabe T; Tsushima K; Yasuo M

INSTITUCIÓN / INSTITUTION: - Department of Comprehensive Cancer Therapy, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto 390-8621, Japan.

RESUMEN / SUMMARY: - We have developed a new internal cooled electrode for radiofrequency ablation (RFA) (Japan Application no. 2006-88228) suitable for forceps channel bronchoscopy. Here, we present our clinical experience with bronchoscopy-guided RFA under computed tomography (CT) monitoring for patients with peripheral-type non-small-cell lung cancer (NSCLC). Bronchoscopy-guided RFA was performed in two patients (80 and 70 years old) with NSCLC, who had no lymph node involvement and distant metastases (T1N0M0), but not indicated for surgery because of other complications, such as advanced age, poor pulmonary function, and refusal of thoracic surgery. The locations of the tumors were right S2 and left S3, respectively. Although the tumors showed ground-glass opacity (GGO) with solid components in both cases, radiographic findings changed to reduced mass-like shadow and remained stable for 4 and 3.5 years after bronchoscopy-guided RFA. As the former case developed progressive disease on chest CT, bronchoscopy-guided RFA was repeated in the same lesion, resulting in no change for the subsequent 1 year. There were no adverse reactions during the procedures. Thus, bronchoscopy-guided RFA is a safe and feasible procedure that represents a potentially useful therapeutic tool in local control in medically inoperable patients with stage I NSCLC.

[742]

TÍTULO / TITLE: - TERT Genetic Polymorphism rs2736100 Was Associated with Lung Cancer: A Meta-Analysis Based on 14,492 Subjects.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Genet Test Mol Biomarkers. 2013 Dec;17(12):937-41. doi: 10.1089/gtmb.2013.0322.

●● Enlace al texto completo (gratis o de pago) [1089/gtmb.2013.0322](#)

AUTORES / AUTHORS: - Wang HM; Zhang XY; Jin B

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, People's Republic of China.

RESUMEN / SUMMARY: - Background: Previous studies focused on the association of the telomerase reverse transcriptase (TERT) gene polymorphism rs2736100 with lung cancer did not reach the same conclusion. In the present study, we performed a meta-analysis to systematically summarize the possible association between TERT polymorphism rs2736100 and the risk for lung cancer. Method: We conducted a search of case-control studies on the association of TERT with susceptibility to lung cancer in PubMed, EMBASE, ISI Web of Science, Wanfang database in China, and Chinese National Knowledge Infrastructure (CNKI) databases. Data from eligible studies were extracted for meta-analysis. Lung cancer risk associated with rs2736100 was estimated by pooled odds ratios (ORs) and 95% confidence intervals (95% CIs). Results: Six independent case-control studies on rs2736100 were included in our

meta-analysis. Our results showed that rs2736100 was associated with the risk of lung cancer not only in an additive model (OR=1.19, 95% CI: 1.04-1.35; p=0.01), but also in a dominant model (OR=1.14, 95% CI: 1.01-1.28; p=0.03). Conclusions: This meta-analysis suggests that rs2736100 is associated with the risk of lung cancer.

[743]

TÍTULO / TITLE: - Advances towards the design and development of personalized non-small-cell lung cancer drug therapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Expert Opin Drug Discov. 2013 Nov;8(11):1381-97. doi: 10.1517/17460441.2013.843523. Epub 2013 Oct 3.

●● Enlace al texto completo (gratis o de pago) [1517/17460441.2013.843523](#)

AUTORES / AUTHORS: - Vari S; Pilotto S; Maugeri-Sacca M; Ciuffreda L; Cesta Incani U; Falcone I; Del Curatolo A; Ceribelli A; Gelibter A; De Maria R; Tortora G; Cognetti F; Bria E; Milella M

INSTITUCIÓN / INSTITUTION: - Regina Elena National Cancer Institute, Division of Medical Oncology A, Via Elio Chianesi 53, 00144, Rome, Italy +39 06 52666919; +39 06 52665637; michelemilella@hotmail.com; milella@ifo.it.

RESUMEN / SUMMARY: - INTRODUCTION: Non-small-cell lung cancer (NSCLC) subtypes are driven by specific genetic aberrations. For reasons such as this, there is a call for treatment personalization. The ability to instigate NSCLC fragmentation poses new methodological problems, and new 'driver' molecular aberrations are being discovered at an unprecedented pace. AREAS COVERED: This article describes the clinical development of epidermal growth factor-tyrosine kinase inhibitors (EGFR-TKIs) and crizotinib for EGFR-mutant and anaplastic lymphoma kinase (ALK)-rearranged NSCLC. Further, the authors briefly describe the emerging molecular targets in NSCLC, in terms of both rationale for therapeutic targeting and strategies, for clinical development. EXPERT OPINION: Target identification and validation in NSCLC still requires considerable effort, as not all of the molecular alterations are clear 'drivers' nor can they be efficiently targeted with available drugs. However, 50% of the NSCLC cases are without clear-defined molecular aberrations. Clinical trial methodology will need to develop novel paradigms for targeted drug development, aiming at the validation of an ideal 'biology-to-trial' approach. Despite significant challenges, a truly 'personalized' approach to NSCLC therapy appears to be within our reach.

[744]

TÍTULO / TITLE: - Photodynamic therapy for intractable bronchial lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Photodiagnosis Photodyn Ther. 2013 Dec;10(4):672-6. doi: 10.1016/j.pdpdt.2013.08.002. Epub 2013 Sep 10.

●● Enlace al texto completo (gratis o de pago) [1016/j.pdpdt.2013.08.002](#)

AUTORES / AUTHORS: - Cai XJ; Li WM; Zhang LY; Wang XW; Luo RC; Li LB

INSTITUCIÓN / INSTITUTION: - Oncology Department of Nanfang Hospital, Southern Medical University, Guangzhou 51015, China.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate the effectiveness and side effects of photofrin-photodynamic therapy (PDT) for intractable bronchial lung cancer. METHODS: Thirty patients were classified as stage II-IV intractable bronchial lung cancer with lumen obstruction after they failed previous treatment regimens such as

surgery, radiotherapy and chemotherapy. PDT was performed with 630nm laser light (Diomed) delivered through cylinder diffusing tip quartz fibers that was passed through the biopsy channel of a flexible endoscope 48h after intravenous injection of the photosensitizer photofrin (2mg/kg body weight). 72h after the first irradiation, the endoscopic procedure was repeated, necrotic tissues were mechanically removed and the deep original lesions and newly exposed cancer lesions were re-treated, and, if necessary, the areas were cleaned repeatedly. RESULTS: The total response rate CR+PR was 86.7%, and the mean percentage of obstruction due to tumors at different treated sites decreased from 90% to 16.7% at discharge after PDT. The KPS score was significantly improved after PDT. CONCLUSIONS: PDT of intractable bronchial lung cancer effectively reduces the amount of lumen obstruction, and improves the patient's quality of life. It may be an effective palliative treatment with minor side effects on patients with advanced bronchial lung cancer.

[745]

TÍTULO / TITLE: - Acneiform rash during lung cancer therapy with erlotinib (Tarceva).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Postepy Dermatol Alergol. 2013 Jun;30(3):195-198. Epub 2013 Jun 20.

●● Enlace al texto completo (gratis o de pago) [5114/pdia.2013.35624](#)

AUTORES / AUTHORS: - Owczarczyk-Saczonek A; Witmanowski H; Placek W

INSTITUCIÓN / INSTITUTION: - Department of Dermatology, Sexually Transmitted Diseases and Clinical Immunology, Municipal Hospital, Olsztyn, Poland. Head: Prof. Waldemar Placek MD, PhD.

RESUMEN / SUMMARY: - Tyrosine kinase inhibitors are currently applied in the treatment of non-small cell lung cancer with overexpressed epidermal growth factor receptor (EGFR). Acneiform rash is the earliest and most characteristic side effect of EGFR inhibition. The incidence may be as high as 50-100% of cases. We report a case of a 47-year-old patient who developed acneiform rash after 1.5 weeks of treatment with erlotinib.

[746]

TÍTULO / TITLE: - The Seventh China's Forum on Minimally Invasive Therapy for Lung Cancer & the Fourth Asia-Pacific Assembly on VATS (December 14-15, 2013).

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Dis. 2013 Oct;5(5):E210-E216.

●● Enlace al texto completo (gratis o de pago) [3978/j.issn.2072-1439.2013.10.18](#)

[747]

TÍTULO / TITLE: - Autophagic protein beclin 1 serves as an independent positive prognostic biomarker for non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 15;8(11):e80338. doi: 10.1371/journal.pone.0080338.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0080338](#)

AUTORES / AUTHORS: - Zhou W; Yue C; Deng J; Hu R; Xu J; Feng L; Lan Q; Zhang W; Ji D; Wu J; Liu Q; Liu A

INSTITUCIÓN / INSTITUTION: - Department of Oncology, The Second Affiliated Hospital, Nanchang University, Nanchang, China ; State Key Laboratory of Oncology in South China, Cancer Center, Sun Yat-Sen University, Guangzhou, China.

RESUMEN / SUMMARY: - Beclin 1, a key regulator of autophagy, has been found to be aberrantly expressed in a variety of human malignancies. Herein, we employed immunohistochemistry (IHC) to detect the protein expression of Beclin 1 in non-small cell lung cancer (NSCLC) and paired normal adjacent lung tissues, and analyzed its clinicopathological/prognostic significance in NSCLC. Receiver operating characteristic (ROC) curve analysis was utilized to determine a cutoff point (>2 VS. ≤ 2) for Beclin 1 expression in a training set ($n = 105$). For validation, the ROC-derived cutoff value was subjected to analysis of the association of Beclin 1 with patients' clinical characteristics and outcome in a testing set ($n = 111$) and the overall patient cohort ($n = 216$). Our data showed that Beclin 1 was significantly lower in NSCLC tissues compared with the adjacent normal tissues, negatively associating with tumor recurrence rate (65.8% VS 32.3%; $p < 0.001$). In the testing set and the overall patient cohort, low expression of Beclin 1 showed significantly inferior overall survival (OS) ($p < 0.001$) and progression-free survival (PFS) ($p < 0.001$) compared to high expression of Beclin 1. In the testing set and the overall patient cohort, the median duration of OS for patients with high and low expression of Beclin 1 was 108 VS. 24.5 months ($p < 0.001$) and 108 VS. 28 months ($p < 0.001$), respectively. Furthermore, low expression of Beclin 1 was also a poor prognostic factor within each stage of NSCLC patients. Multivariate analysis identified that Beclin 1 was an independent prognostic factor for NSCLC. Our findings in the present study provided evidence that Beclin 1 may thus emerge as an independent prognostic biomarker in this tumor entity in the future.

[748]

TÍTULO / TITLE: - Role of the pulmonologist in ordering post-procedure molecular markers in non-small-cell lung cancer: implications for personalized medicine.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Nov;14(6):609-26. doi: 10.1016/j.clcc.2013.04.002.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.04.002](#)

AUTORES / AUTHORS: - Murgu S; Colt H

INSTITUCIÓN / INSTITUTION: - Pulmonary and Critical Care Medicine Division, University of Chicago Pritzker School of Medicine, Chicago, IL.

RESUMEN / SUMMARY: - In the growing era of personalized medicine for the treatment of non-small-cell lung cancer (NSCLC), it is becoming increasingly important that sufficient quality and quantity of tumor tissue are available for morphologic diagnosis and molecular analysis. As new treatment options emerge that might require more frequent and possibly higher volume biopsies, the role of the pulmonologist will expand, and it will be important for pulmonologists to work within a multidisciplinary team to provide optimal therapeutic management for patients with NSCLC. In this review, we discuss the rationale for individualized treatment decisions for patients with NSCLC, molecular pathways and specific molecular predictors relevant to personalized NSCLC therapy, assay technologies for molecular marker analysis, and specifics regarding tumor specimen selection, acquisition, and handling. Moreover, we briefly address issues regarding racial and socioeconomic disparities as they relate to molecular testing and treatment decisions, and cost considerations for molecular

testing and targeted therapies in NSCLC. We also propose a model for an institution-based multidisciplinary team, including oncologists, pathologists, pulmonologists, interventional radiologists, and thoracic surgeons, to ensure adequate material is available for cytological and histological studies and to standardize methods of tumor specimen handling and processing in an effort to provide beneficial, individualized therapy for patients with NSCLC.

[749]

TÍTULO / TITLE: - XRCC3 Thr241Met Is Associated with Response to Platinum-Based Chemotherapy but Not Survival in Advanced Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 8;8(10):e77005. doi: 10.1371/journal.pone.0077005.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0077005](#)

AUTORES / AUTHORS: - Qiu M; Xu L; Yang X; Ding X; Hu J; Jiang F; Xu L; Yin R

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Nanjing Medical University Affiliated Cancer Institute of Jiangsu Province, Nanjing, China ; The Fourth Clinical College of Nanjing Medical University, Nanjing, China.

RESUMEN / SUMMARY: - BACKGROUND: A lot of studies have investigated the correlation between x-ray repair cross-complementing group 3 (XRCC3) Thr241Met polymorphism and clinical outcomes in non-small cell cancer (NSCLC), while the conclusion is still conflicting. MATERIALS AND METHODS: We conducted this meta-analysis to evaluate the predictive value of XRCC3 Thr241Met polymorphism on response and overall survival of patients with NSCLC. Pooled odds ratios (ORs) and hazard ratios (HRs) and corresponding 95% confidence intervals (95% CIs) were used to estimate the association strength. RESULTS: A total of 14 eligible studies with 2828 patients were identified according to our inclusion criteria. Meta-analysis results showed that carriers of the variant 241Met allele were significantly associated with good response, compared with those harboring the wild 241Thr allele (Met vs. Thr, OR = 1.453, 95% CI: 1.116-1.892, Pheterogeneity = 0.968 and ThrMet+MetMet vs. ThrThr, OR = 1.476, 95% CI: 1.087-2.004, Pheterogeneity = 0.696). This significant association was observed in Caucasian population but not in Asian population. On the other hand, there was no significant association of XRCC3 Thr241Met polymorphism with survival (ThrMet+MetMet vs. ThrThr, HR = 1.082, 95% CI: 0.929-1.261, Pheterogeneity = 0.564), and there was no difference between Asian and Caucasian population. CONCLUSIONS: These findings suggest a predictive role of XRCC3 Thr241Met polymorphism on response to platinum-based chemotherapy in patients with advanced NSCLC. Additionally, we first report that the XRCC3 Thr241Met polymorphism is associated with response to platinum-based chemotherapy and highlights the prognostic value of the XRCC3 Thr241Met polymorphism.

[750]

TÍTULO / TITLE: - Clinicopathological significance of PTEN and PI3K/AKT signal transduction pathway in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Sep 15;6(10):2112-20.

AUTORES / AUTHORS: - Yun F; Jia Y; Li X; Yuan L; Sun Q; Yu H; Shi L; Yuan H

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The First Affiliated Hospital of Inner Mongolia Medical University Huhhot, 010059, China.

RESUMEN / SUMMARY: - A high frequency of mutations at the PTEN locus has been noticed in carcinoma of lung. However, the role of PTEN alternations and its association with outcome variables in the genesis of lung carcinoma are not understood fully. The purpose of our study was to examine the impact of EGFR, TGF-alpha, P-AKT and PTEN in the genesis of non-small cell lung cancer (NSCLC). Total numbers of 66 histopathologically confirmed cases of NSCLC and 10 cases of benign control samples embedded with wax were studied. We assessed EGFR, TGF-alpha and P-AKT by the use of specific antibody through immunohistochemistry as directed by the manufacturer, and detected PTEN expression by in situ hybridization. There were progressive loss of PTEN expression and significant increasing in EGFR, TGF-alpha, P-AKT expression from benign samples to NSCLC ($p < 0.05$). The overexpression of EGFR, TGF-alpha, P-AKT and loss of PTEN expression were correlated to differentiation extent of cancer tissue, metastasis of lymph nodes and histological classification. Thus, alteration of EGFR, TGF-alpha, P-AKT and PTEN are likely important molecular events in pathogenesis and carcinogenesis of NSCLC.

[751]

TÍTULO / TITLE: - Inhibition of Raf-MEK-ERK and Hypoxia pathways by Phyllanthus prevents metastasis in human lung (A549) cancer cell line.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Complement Altern Med. 2013 Oct 20;13(1):271.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1472-6882-13-271](#)

AUTORES / AUTHORS: - Lee SH; Jaganath IB; Manikam R; Sekaran SD

RESUMEN / SUMMARY: - **BACKGROUND:** Lung cancer constitutes one of the malignancies with the greatest incidence and mortality rates with 1.6 million new cases and 1.4 million deaths each year. Prognosis remains poor due to deleterious development of multidrug resistance resulting in less than 15% lung cancer patients reaching five years survival. We have previously shown that Phyllanthus induced apoptosis in conjunction with its antimetastatic action. In the current study, we aimed to determine the signaling pathways utilized by Phyllanthus to exert its antimetastatic activities. **METHODS:** Cancer 10-pathway reporter array was performed to screen the pathways affected by Phyllanthus in lung carcinoma cell line (A549) to exert its antimetastatic effects. Results from this array were then confirmed with western blotting, cell cycle analysis, zymography technique, and cell based ELISA assay for human total iNOS. Two-dimensional gel electrophoresis was subsequently carried out to study the differential protein expressions in A549 after treatment with Phyllanthus. **RESULTS:** Phyllanthus was observed to cause antimetastatic activities by inhibiting ERK1/2 pathway via suppression of Raf protein. Inhibition of this pathway resulted in the suppression of MMP2, MMP7, and MMP9 expression to stop A549 metastasis. Phyllanthus also inhibits hypoxia pathway via inhibition of HIF-1alpha that led to reduced VEGF and iNOS expressions. Proteomic analysis revealed a number of proteins downregulated by Phyllanthus that were involved in metastatic processes, including invasion and mobility proteins (cytoskeletal proteins), transcriptional proteins (proliferating cell nuclear antigen; zinc finger protein), antiapoptotic protein (Bcl2) and various glycolytic enzymes. Among the four Phyllanthus species tested, P. urinaria showed the greatest antimetastatic activity. **CONCLUSIONS:** Phyllanthus inhibits A549

metastasis by suppressing ERK1/2 and hypoxia pathways that led to suppression of various critical proteins for A549 invasion and migration.

[752]

TÍTULO / TITLE: - Clinicopathological and Extensive Immunohistochemical Study of a Type II Pleuropulmonary Blastoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Fetal Pediatr Pathol. 2013 Sep 30.

●● Enlace al texto completo (gratis o de pago) [3109/15513815.2013.839011](#)

AUTORES / AUTHORS: - Yu L; Cheng H; Yang SJ

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Xijing Hospital, Fourth Military Medical University, Xi'an, China.

RESUMEN / SUMMARY: - Pleuropulmonary blastoma (PPB) is a rare malignant dysontogenetic neoplasm primarily affecting younger children, even in newborns with an unfavorable outcome. PPB is histologically composed of a primitive, variably mixed blastematosus and sarcomatous components, and exclusively subclassified as type I (purely cystic), type II (both cystic and solid elements) and type III (completely solid) by increasing histological evidence of malignancy. At present, well-documented cases or cases of truly precise presentation of either pathological or immunohistochemical findings in PPB are rare. The authors report one case of PPB in a 44-month-old child presenting as a solid and cystic mass with special emphasis on its radiological, histopathological and immunohistochemical aspects. The histological diagnosis was PPB, which would belong to the type II category.

[753]

TÍTULO / TITLE: - Clinical applications of The Cancer Genome Atlas project (TCGA) for squamous cell lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncology (Williston Park). 2013 Sep;27(9):899-906.

AUTORES / AUTHORS: - Devarakonda S; Morgensztern D; Govindan R

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, St. Luke's Hospital, Chesterfield, Missouri, USA.

RESUMEN / SUMMARY: - Very little progress has been made in the treatment of patients with metastatic squamous cell lung cancer over the past 2 decades. Identification of novel molecular alterations for targeted therapies is necessary to improve outcomes. Advances in genomic technology have now made it possible to analyze the genomic landscape of tumor tissues comprehensively. We summarize here key findings from the comprehensive analysis of squamous cell lung cancer by The Cancer Genome Atlas group and discuss the clinical implications of these findings.

[754]

TÍTULO / TITLE: - Identification of candidate genes for lung cancer somatic mutation test kits.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Genet Mol Biol. 2013 Sep;36(3):455-64. doi: 10.1590/S1415-47572013000300022. Epub 2013 Aug 30.

●● Enlace al texto completo (gratis o de pago) [1590/S1415-47572013000300022](#)

AUTORES / AUTHORS: - Chen Y; Shi JX; Pan XF; Feng J; Zhao H

INSTITUCIÓN / INSTITUTION: - Thoracic Department, Shanghai Chest Hospital, Shanghai, China .

RESUMEN / SUMMARY: - Over the past three decades, mortality from lung cancer has sharply and continuously increased in China, ascending to the first cause of death among all types of cancer. The ability to identify the actual sequence of gene mutations may help doctors determine which mutations lead to precancerous lesions and which produce invasive carcinomas, especially using next-generation sequencing (NGS) technology. In this study, we analyzed the latest lung cancer data in the COSMIC database, in order to find genomic “hotspots” that are frequently mutated in human lung cancer genomes. The results revealed that the most frequently mutated lung cancer genes are EGFR, KRAS and TP53. In recent years, EGFR and KRAS lung cancer test kits have been utilized for detecting lung cancer patients, but they presented many disadvantages, as they proved to be of low sensitivity, labor-intensive and time-consuming. In this study, we constructed a more complete catalogue of lung cancer mutation events including 145 mutated genes. With the genes of this list it may be feasible to develop a NGS kit for lung cancer mutation detection.

[755]

TÍTULO / TITLE: - Malignant pleural effusion in the palliative care setting.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Palliat Nurs. 2013 Jul;19(7):320, 322-5.

AUTORES / AUTHORS: - Arber A; Clackson C; Dargan S

INSTITUCIÓN / INSTITUTION: - University of Surrey, Guildford, Surrey GU2 7TE, England. a.arber@surrey.ac.uk

RESUMEN / SUMMARY: - Malignant pleural effusion (MPE) is a distressing condition for the patient, causing many symptoms such as shortness of breath, dry cough, an uncomfortable feeling of heaviness in the chest, and pleuritic pain. MPE reduces quality of life and functional status. It indicates that the disease is now advanced and life expectancy is generally short, with a median prognosis of 3-12 months depending on the stage of the disease and the underlying malignancy. This paper discusses the palliative treatment options for MPE, which include thoracentesis, medical pleurodesis, and indwelling pleural catheter. It is important that decisions about treatment are made within the multidisciplinary team and alongside the patient and family. Treatment goals are concerned with the relief or elimination of dyspnoea, restoration of near-normal activity and function, and avoidance of inpatient care.

[756]

TÍTULO / TITLE: - The work left undone. Understanding the challenge of providing holistic lung cancer nursing care in the UK.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Oncol Nurs. 2013 Nov 15. pii: S1462-3889(13)00129-4. doi: 10.1016/j.ejon.2013.10.002.

●● [Enlace al texto completo \(gratis o de pago\) 1016/j.ejon.2013.10.002](#)

AUTORES / AUTHORS: - Leary A; White J; Yarnell L

INSTITUCIÓN / INSTITUTION: - London Southbank University, Faculty of Health & Social Care, LSBU, 103 Borough Rd, London SE1 0AA, United Kingdom. Electronic address: alisonleary@yahoo.com.

RESUMEN / SUMMARY: - In England best practice guidance in cancer recommends that all patients have access to a specialist nurse such as the tumour specific clinical nurse specialist. The role has become pivotal providing aspects of care e.g. meeting information needs, holistic nurse led follow up including symptom control, managing care and providing psychological and social interventions including referral to others in the role of keyworker. There are approximately 295 lung cancer nurse specialists in England and recent study to model optimum caseload used an on line survey to look at workload of lung cancer specialist nurses. A survey of 100 lung cancer nurses from across the UK (RR78%) examined the perception of the work left undone against best practice guidance, caseload size, workload and other factors. 67 of 78 respondents perceived they left work such as proactive management (52) undertaking holistic needs assessments (46) providing appropriate psychological care (26) and meeting information needs (16). The majority (70) worked unpaid overtime (mean 3.8 h range 1-10 h) per week. Although proactive management is thought to result in better outcomes for lung cancer patients in terms of survival, quality of life and decisions of end of life a substantial number of the specialist nurses felt that factors such as caseload and organisational factors inhibited this.

[757]

TÍTULO / TITLE: - miR-223 functions as a potent tumor suppressor of the Lewis lung carcinoma cell line by targeting insulin-like growth factor-1 receptor and cyclin-dependent kinase 2.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):359-366. Epub 2013 Jun 4.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1375](#)

AUTORES / AUTHORS: - Nian W; Ao X; Wu Y; Huang Y; Shao J; Wang Y; Chen Z; Chen F; Wang D

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Chongqing Tumor Hospital, Chongqing 400030, P.R. China ; Institute of Cancer Research, Xinqiao Hospital, Third Military Medical University, Chongqing 400037, P.R. China.

RESUMEN / SUMMARY: - microRNAs (miRNAs) have been hypothesized to function as oncogenes or tumor suppressors by targeting specific cancer-related genes. Previous studies have reported that miR-223 may serve as a tumor suppressor in a number of cancer types, however, knowledge of its targets in non-small cell lung cancer (NSCLC) remains limited. In the current study, miR-223 was found to inhibit cell proliferation in vitro by CCK-8 assay, growth curves and an anchorage-independent growth assay in a Lewis lung carcinoma (LLC) cell line. miR-223 transfection in the LLC cells was observed to significantly inhibit migration and invasion, induce G2/M arrest and decrease the expression levels of Sca-1, a marker of murine stem cells. In addition, miR-223 transfection markedly suppressed AKT and ERK signaling, as well as insulin-like growth factor-1 receptor (IGF-1R)-mediated downstream signaling, pathways that are crucial for cell proliferation and invasion in NSCLC cells. Analyses in C57BL/6 mice demonstrated that miR-223 suppresses tumorigenicity in vivo. Using a luciferase activity assay and western blot analysis, IGF-1R and cyclin-dependent kinase 2

(CDK2) were identified as direct targets of miR-223. In the present study, novel cancer-related targets of miR-223 were identified and verified in a LLC cell line, indicating that miR-223 functions as a tumor suppressor, which may fine-tune the activity of the IGF-1R pathway in lung cancer. Therefore, increasing miR-223 expression may provide a novel approach for the treatment of NSCLC.

[758]

TÍTULO / TITLE: - Prior knowledge enhanced random walk for lung tumor segmentation from low-contrast CT images.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Conf Proc IEEE Eng Med Biol Soc. 2013 Jul;2013:6071-4. doi: 10.1109/EMBC.2013.6610937.

●● [Enlace al texto completo \(gratis o de pago\) 1109/EMBC.2013.6610937](#)

AUTORES / AUTHORS: - Cui H; Wang X; Fulham M; Feng DD

RESUMEN / SUMMARY: - The separation of a lung tumor from adjacent normal tissue, which has similar intensity values and indistinct boundaries on low-contrast CT images is a challenging task. In this paper, a prior knowledge enhanced random walk (RW) is proposed to account for the prior functional knowledge from PET and intensity information from CT. The prior knowledge acquired from PET is used for the automated selection of foreground seeds, defined as the tumor confidence region, the background seeds and the walking range to increase computational efficiency of the RW algorithm in CT. The tumor confidence region is also used for balancing transition, and thus limiting the information propagation range through a weight factor. The experimental evaluation on 18 low-contrast CT images with manual tumor segmentation demonstrated that our method outperformed RW and random walk from restart (RWR) as measured by the Dice similarity coefficient (DSC).

[759]

TÍTULO / TITLE: - Molecular typing of lung adenocarcinoma on cytological samples using a multigene next generation sequencing panel.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 13;8(11):e80478. doi: 10.1371/journal.pone.0080478.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0080478](#)

AUTORES / AUTHORS: - Scarpa A; Sikora K; Fassan M; Rachiglio AM; Cappellesso R; Antonello D; Amato E; Mafficini A; Lambiase M; Esposito C; Bria E; Simonato F; Scardoni M; Turri G; Chilosi M; Tortora G; Fassina A; Normanno N

INSTITUCIÓN / INSTITUTION: - ARC-NET Research Centre, University of Verona, Verona, Italy ; Department of Pathology and Diagnostics, University of Verona, Verona, Italy.

RESUMEN / SUMMARY: - Identification of driver mutations in lung adenocarcinoma has led to development of targeted agents that are already approved for clinical use or are in clinical trials. Therefore, the number of biomarkers that will be needed to assess is expected to rapidly increase. This calls for the implementation of methods probing the mutational status of multiple genes for inoperable cases, for which limited cytological or bioptic material is available. Cytology specimens from 38 lung adenocarcinomas were subjected to the simultaneous assessment of 504 mutational hotspots of 22 lung cancer-associated genes using 10 nanograms of DNA and Ion Torrent PGM next-

generation sequencing. Thirty-six cases were successfully sequenced (95%). In 24/36 cases (67%) at least one mutated gene was observed, including EGFR, KRAS, PIK3CA, BRAF, TP53, PTEN, MET, SMAD4, FGFR3, STK11, MAP2K1. EGFR and KRAS mutations, respectively found in 6/36 (16%) and 10/36 (28%) cases, were mutually exclusive. Nine samples (25%) showed concurrent alterations in different genes. The next-generation sequencing test used is superior to current standard methodologies, as it interrogates multiple genes and requires limited amounts of DNA. Its applicability to routine cytology samples might allow a significant increase in the fraction of lung cancer patients eligible for personalized therapy.

[760]

TÍTULO / TITLE: - A Comprehensive Comparative Analysis of the Histomorphological Features of ALK-Rearranged Lung Adenocarcinoma Based on Driver Oncogene Mutations: Frequent Expression of Epithelial-Mesenchymal Transition Markers than Other Genotype.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 23;8(10):e76999. doi: 10.1371/journal.pone.0076999.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0076999](#)

AUTORES / AUTHORS: - Kim H; Jang SJ; Chung DH; Yoo SB; Sun P; Jin Y; Nam KH; Paik JH; Chung JH

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Seoul National University Bundang Hospital, Seongnam, Republic of Korea ; Department of Pathology, Seoul National University College of Medicine, Seoul, Republic of Korea.

RESUMEN / SUMMARY: - Molecular classification of lung cancer correlates well with histomorphological features. However, specific histomorphological features that differentiate anaplastic lymphoma kinase (ALK)-rearranged tumors from ALK-negative tumors have not been fully evaluated. Eighty ALK-rearranged and 213 ALK-negative (91 epidermal growth factor receptor-mutated; 29 K-ras-mutated; 93 triple-negative) resected lung adenocarcinomas were analyzed for several histomorphological parameters and histological subtype. ALK-rearranged tumors were associated with younger age at presentation, frequent nodal metastasis, and higher stage of disease at diagnosis. ALK-rearranged tumors were more likely to show a solid predominant pattern than ALK-negative tumors (43.8%; 35/80; $p < 0.001$). Unlike ALK-negative tumors, a lepidic predominant pattern was not observed in ALK-rearranged tumors ($p < 0.001$). In multivariate analysis, the most significant morphological features that distinguished ALK-rearranged tumors from ALK-negative tumors were cribriform formation (odds ratio [OR], 3.253; $p = 0.028$), presence of mucin-containing cells (OR, 4.899; $p = 0.008$), close relationship to adjacent bronchioles (OR, 5.361; $p = 0.001$), presence of psammoma bodies (OR, 4.026; $p = 0.002$), and a solid predominant pattern (OR, 13.685; $p = 0.023$). ALK-rearranged tumors exhibited invasive histomorphological features, aggressive behavior and frequent expression of epithelial-mesenchymal transition markers (loss of E-cadherin and expression of vimentin) compared with other genotype ($p = 0.015$). Spatial proximity between bronchus and ALK-rearranged tumors and frequent solid histologic subtype with p63 expression may cause diagnostic difficulties to differentiate squamous cell carcinoma in the small biopsy, whereas p40 was rarely expressed in ALK-rearranged adenocarcinoma.

Knowledge of these features may improve the diagnostic accuracy and lead to a better understanding of the characteristic behavior of ALK-rearranged tumors.

[761]

TÍTULO / TITLE: - Proteogenomic Analysis of Human Chromosome 9-Encoded Genes from Human Samples and Lung Cancer Tissues.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Proteome Res. 2013 Nov 25.

●● Enlace al texto completo (gratis o de pago) [1021/pr400792p](#)

AUTORES / AUTHORS: - Ahn JM; Kim MS; Kim YI; Jeong SK; Lee HJ; Lee SH; Paik YK; Pandey A; Cho JY

RESUMEN / SUMMARY: - The Chromosome-centric Human Proteome Project (C-HPP) was recently initiated as an international collaborative effort. Our team adopted chromosome 9 (Chr 9) and performed a bioinformatics and proteogenomic analysis to catalog Chr 9-encoded proteins from normal tissues, lung cancer cell lines and lung cancer tissues. Approximately 74.7% of the Chr 9 genes of the human genome were identified, which included approximately 28% of missing proteins (46 of 162) on Chr 9 compared with the list of missing proteins from the neXtProt master table (2013-09). In addition, we performed a comparative proteomics analysis between normal lung and lung cancer tissues. Based on the data analysis, 15 proteins from Chr 9 were detected only in lung cancer tissues. Finally, we conducted a proteogenomic analysis to discover Chr 9-residing single nucleotide polymorphisms (SNP) and mutations described in the COSMIC cancer mutation database. We identified 21 SNPs and 4 mutations containing peptides on Chr 9 from normal human cells/tissues and lung cancer cell lines, respectively. In summary, this study provides valuable information of the human proteome for the scientific community as part of C-HPP. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium with the data set identifier PXD.

[762]

TÍTULO / TITLE: - Pretreatment maximum standardized uptake value on 18F-fluorodeoxyglucose positron emission tomography is a predictor of outcome for stage I non-small cell lung cancer after stereotactic body radiotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asia Pac J Clin Oncol. 2013 Oct 31. doi: 10.1111/ajco.12128.

●● Enlace al texto completo (gratis o de pago) [1111/ajco.12128](#)

AUTORES / AUTHORS: - Tanaka H; Hayashi S; Hoshi H

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Gifu University Hospital, Gifu, Japan.

RESUMEN / SUMMARY: - AIMS: Stereotactic body radiotherapy (SBRT) is commonly considered an important treatment option for patients with stage I non-small cell lung cancer (NSCLC) who have contraindications for surgery or refuse surgery. Many studies have reported that the maximum standardized uptake value (SUVmax) on 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) of the primary tumor has prognostic value for resected NSCLC. The purpose of this study was to determine whether SUVmax is a predictor of disease-free survival (DFS) in patients with stage I NSCLC after SBRT. METHODS: In all patients, the diagnosis was pathologically or cytologically confirmed. The prescription dose was 48 Gy in four

fractions at the isocenter. FDG-PET was performed before SBRT. RESULTS: Twenty-nine patients were enrolled in this study. The median follow-up period was 14 months (range, 2-56 months). Regional lymph node metastasis and distant metastasis were observed in 5 (17%) and 2 (7%), respectively. The median SUVmax was 5.6 (range, 2.2-22.0). DFS at 2 years was significantly different between the low SUVmax (<8.0) and high SUVmax (≥ 8.0) groups (85 versus 17%). In univariate analysis, SUVmax and gross tumor volume were significantly correlated with DFS. Multivariate analysis included variables with P-values <0.20 and showed that only SUVmax was significantly correlated with DFS. CONCLUSION: Pretreatment SUVmax on FDG-PET predicted the DFS in patients with stage I NSCLC after SBRT.

[763]

TÍTULO / TITLE: - Lung cancer correlates in Lebanese adults: A pilot case-control study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Epidemiol Glob Health. 2013 Dec;3(4):235-44. doi: 10.1016/j.jegh.2013.06.005. Epub 2013 Jul 23.

●● Enlace al texto completo (gratis o de pago) [1016/j.jegh.2013.06.005](#)

AUTORES / AUTHORS: - Aoun J; Saleh N; Waked M; Salame J; Salameh P

INSTITUCIÓN / INSTITUTION: - Faculty of Public Health, Section II, Lebanese University, Beirut, Lebanon.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is one of the most prevalent types of cancers. However, there are no epidemiological studies concerning lung cancer and its risk factors in Lebanon. This study was carried out to determine the association between lung cancer and its most common risk factors in a sample of the Lebanese population. METHODS: A hospital-based case-control study was conducted. Patients were recruited in a tertiary health care center. A questionnaire in Arabic was designed to assess the possible risk factors for lung cancer. RESULTS: For females, cigarette smoking (ORa=9.76) and using fuel for heating (ORa=9.12) were found to be the main risk factors for lung cancer; for males, cigarette smoking (ORa=156.98), living near an electricity generator (ORa=13.26), consuming low quantities of fruits and vegetables (ORa=10.54) and a family history of cancer (ORa=8.75) were associated with lung cancer. Waterpipe smoking was significantly correlated with lung cancer in the bivariate analysis. CONCLUSION: In this pilot study, it was found that in addition to smoking, outdoor and indoor pollution factors were potential risk factors of lung cancer. Additional studies would be necessary to confirm these findings.

[764]

TÍTULO / TITLE: - Codelivery of curcumin and doxorubicin by MPEG-PCL results in improved efficacy of systemically administered chemotherapy in mice with lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Nanomedicine. 2013;8:3521-31. doi: 10.2147/IJN.S45250. Epub 2013 Sep 24.

●● Enlace al texto completo (gratis o de pago) [2147/IJN.S45250](#)

AUTORES / AUTHORS: - Wang BL; Shen YM; Zhang QW; Li YL; Luo M; Liu Z; Li Y; Qian ZY; Gao X; Shi HS

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, West China Medicine School, Sichuan University, Chengdu, Sichuan, People's Republic of China.

RESUMEN / SUMMARY: - Systemic administration of chemotherapy for cancer often has toxic side effects, limiting the doses that can be used in its treatment. In this study, we developed methoxy poly(ethylene glycol)-poly(caprolactone) (MPEG-PCL) micelles loaded with curcumin and doxorubicin (Cur-Dox/MPEG-PCL) that were tolerated by recipient mice and had enhanced antitumor effects and fewer side effects. It was shown that these Cur-Dox/MPEG-PCL micelles could release curcumin and doxorubicin slowly *in vitro*. The long circulation time of MPEG-PCL micelles and the slow rate of release of curcumin and doxorubicin *in vivo* may help to maintain plasma concentrations of active drug. We also demonstrated that Cur-Dox/MPEG-PCL had improved antitumor effects both *in vivo* and *in vitro*. The mechanism by which Cur-Dox/MPEG-PCL micelles inhibit lung cancer might involve increased apoptosis of tumor cells and inhibition of tumor angiogenesis. We found advantages using Cur-Dox/MPEG-PCL micelles in the treatment of cancer, with Cur-Dox/MPEG-PCL achieving better inhibition of LL/2 lung cancer growth *in vivo* and *in vitro*. Our study indicates that Cur-Dox/MPEG-PCL micelles may be an effective treatment strategy for cancer in the future.

[765]

TÍTULO / TITLE: - Stage II-IV lung cancer cases with lymphovascular invasion relapse within 2 years after surgery.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Gen Thorac Cardiovasc Surg. 2013 Nov 2.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s11748-013-0340-3](#)

AUTORES / AUTHORS: - Shiono S; Kanauchi N; Yanagawa N; Abiko M; Sato T

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Yamagata Prefectural Central Hospital, 1800, Oazaoyagi, Yamagata, 990-2292, Japan, sshiono@ypch.gr.jp.

RESUMEN / SUMMARY: - **OBJECTIVE:** For recurrent lung cancer, postoperative follow-up methods have not been adequately assessed, and no evidence-based postoperative surveillance methods currently exist. Herein, we evaluated postoperative lung cancer recurrence and the personalized postoperative surveillance periods and methods used. **METHODS:** Follow-up after surgery consisted of a regular outpatient clinic check-up, including physical examination, history, blood tests, and chest X-ray, which were conducted three or four times per year for 5 years. During the follow-up period, annual chest and brain computed tomography scanning was performed. Between May 2004 and December 2011, 547 lung cancer patients underwent complete resection in our institution. We retrospectively reviewed their prospectively collected data. **RESULTS:** We selected 106 patients (19.4 %) who had a postoperative recurrence. Multivariate analysis showed that advanced stage (stage II-IV; $p < 0.01$) and lymphovascular invasion positivity (LVI; $p = 0.01$) were independent risk factors for earlier recurrence. Overall, 90.8 % of patients with advanced-stage disease and LVI positivity experienced a relapse within 2 years after surgery, compared to 55.1 % of patients who did not have these factors ($p < 0.01$). Multivariate analysis showed that recurrence with symptoms ($p < 0.01$) and shorter time to recurrence (< 24 months; $p < 0.01$) were independent prognostic factors after recurrence. **CONCLUSIONS:** Although this study was retrospective and included some biases, patients with advanced-stage

lung cancer and LVI positivity should be intensively followed up. Personalized follow-up programs should be considered for lung cancer patients who have undergone resection.

[766]

TÍTULO / TITLE: - A novel platform to enable inhaled naked RNAi medicine for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Rep. 2013 Nov 25;3:3325. doi: 10.1038/srep03325.

●● Enlace al texto completo (gratis o de pago) [1038/srep03325](#)

AUTORES / AUTHORS: - Fujita Y; Takeshita F; Mizutani T; Ohgi T; Kuwano K; Ochiya T

INSTITUCIÓN / INSTITUTION: - 1] Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, 5-1-1, Tsukiji, Chuo-ku, Tokyo 104-0045, Japan [2] Division of Respiratory Diseases, Department of Internal Medicine, Jikei University School of Medicine, 3-19-18, Nishi-shinbashi, Minato-ku, Tokyo 105-8471, Japan.

RESUMEN / SUMMARY: - Small interfering RNA (siRNA)-based therapeutics have been used in humans and offer distinct advantages over traditional therapies. However, previous investigations have shown that there are several technical obstacles that need to be overcome before routine clinical applications are used. Currently, we are launching a novel class of RNAi therapeutic agents (PnkRNA, nkRNA) that show high resistance to degradation and are less immunogenic, less cytotoxic, and capable of efficient intracellular delivery. Here, we develop a novel platform to promote naked RNAi approaches administered through inhalation without sophisticated delivery technology in mice. Furthermore, a naked and unmodified novel RNAi agent, such as ribophorin II (RPN2-PnkRNA), which has been selected as a therapeutic target for lung cancer, resulted in efficient inhibition of tumor growth without any significant toxicity. Thus, this new technology using aerosol delivery could represent a safe, potentially RNAi-based strategy for clinical applications in lung cancer treatment without delivery vehicles.

[767]

TÍTULO / TITLE: - Analysis of GAGE, NY-ESO-1 and SP17 cancer/testis antigen expression in early stage non-small cell lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 8;13:466. doi: 10.1186/1471-2407-13-466.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-466](#)

AUTORES / AUTHORS: - Gjerstorff MF; Pohl M; Olsen KE; Ditzel HJ

INSTITUCIÓN / INSTITUTION: - Department of Cancer and Inflammation Research, Institute for Molecular Medicine (IMM), University of Southern Denmark, Winsloewparken 25, 3, Odense C, DK-5000, Denmark. mgjerstorff@health.sdu.dk.

RESUMEN / SUMMARY: - BACKGROUND: The unique expression pattern and immunogenic properties of cancer/testis antigens make them ideal targets for immunotherapy of cancer. The MAGE-A3 cancer/testis antigen is frequently expressed in non-small cell lung cancer (NSCLC) and vaccination with MAGE-A3 in patients with MAGE-A3-positive NSCLC has shown promising results. However, little is known about the expression of other cancer/testis antigens in NSCLC. In the present study the

expression of cancer/testis antigens GAGE, NY-ESO-1 and SP17 was investigated in patients with completely resected, early stage, primary NSCLC. METHODS: Tumor biopsies from normal lung tissue and from a large cohort (n = 169) of NSCLC patients were examined for GAGE, NY-ESO-1 and SP17 protein expression by immunohistochemical analysis. The expression of these antigens was further matched to clinical and pathological features using univariate cox regression analysis. RESULTS: GAGE and NY-ESO-1 cancer/testis antigens were not expressed in normal lung tissue, while SP17 was expressed in ciliated lung epithelia. The frequency of GAGE, NY-ESO-1 and SP17 expression in NSCLC tumors were 26.0% (44/169), 11.8% (20/169) and 4.7% (8/169), respectively, and 33.1% (56/169) of the tumors expressed at least one of these antigens. In general, the expression of GAGE, NY-ESO-1 and SP17 was not significantly associated with a specific histotype (adenocarcinoma vs. squamous cell carcinoma), but high-level GAGE expression (>50%) was more frequent in squamous cell carcinoma (p = 0.02). Furthermore, the frequency of GAGE expression was demonstrated to be significantly higher in stage II-IIIa than stage I NSCLC (17.0% vs. 35.8%; p = 0.02). Analysis of the relation between tumor expression of GAGE and NY-ESO-1 and survival endpoints revealed no significant associations. CONCLUSION: Our study demonstrates that GAGE, NY-ESO-1 and SP17 cancer/testis antigens are candidate targets for immunotherapy of NSCLC and further suggest that multi-antigen vaccines may be beneficial.

[768]

TÍTULO / TITLE: - Lung cancer: DNA methylation prognostic biomarker for stage I NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Dec;10(12):666. doi: 10.1038/nrclinonc.2013.187. Epub 2013 Oct 15.

- [Enlace al texto completo \(gratis o de pago\) 1038/nrclinonc.2013.187](#)

[769]

TÍTULO / TITLE: - A Case of Small Cell Cancer of the Breast in a Male with Synchronous Stage IV Non-Small Cell Lung Carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rare Tumors. 2013 Sep 24;5(3):e52. doi: 10.4081/rt.2013.e52.

- [Enlace al texto completo \(gratis o de pago\) 4081/rt.2013.e52](#)

AUTORES / AUTHORS: - Matt L; Limjoco T; Sehgal R

INSTITUCIÓN / INSTITUTION: - Department of Hematology/Oncology, Edwards Comprehensive Cancer Center, Cabell Huntington Hospital, Huntington, WV.

RESUMEN / SUMMARY: - Extrapulmonary small cell carcinomas (EPSCC) are extremely rare. Most reports indicate success with therapy directed at the tumor as if it was pulmonary small cell carcinoma. Primary small cell carcinoma of the breast is an uncommon form of EPSCC. Differentiating between a primary small cell carcinoma of the breast from metastatic disease to the breast is very important. According to the literature, there have been approximately 70 cases reported worldwide. Of these cases, only two cases are documented in men. Prognosis is varied and depends on stage of disease at presentation. A combination of surgery, chemotherapy and/or radiation is required to adequately treat patients with small cell carcinoma of the breast. We present a case of a male patient diagnosed with stage IV non-small cell

lung carcinoma first and then subsequently diagnosed with a concurrent small cell carcinoma of the breast responding to treatment with concurrent chemotherapy and radiation.

[770]

TÍTULO / TITLE: - Circulating MicroRNAs in Relation to EGFR Status and Survival of Lung Adenocarcinoma in Female Non-Smokers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 25;8(11):e81408. doi: 10.1371/journal.pone.0081408.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0081408](#)

AUTORES / AUTHORS: - Zhang H; Su Y; Xu F; Kong J; Yu H; Qian B

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology and Biostatistics, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center of Cancer, Tianjin, P.R. China ; Key Laboratory of Cancer Prevention and Therapy, Tianjin Medical University, Ministry of Education, Tianjin, P.R. China.

RESUMEN / SUMMARY: - OBJECTIVES: Lung adenocarcinoma is considered a unique disease for Asian female non-smokers. We investigated whether plasma microRNA (miRNA) expression profiles are different by the EGFR status and are associated with survival outcomes of the patients. METHODS: Using real-time RT-PCR, we analyzed the expression of 20 miRNAs in the plasma of 105 female patients with lung adenocarcinoma. Kaplan-Meier survival analysis and Cox proportional hazards regression were performed to determine the association between miRNA expression and overall survival. Time dependent receiver operating characteristic (ROC) analysis was also performed. RESULTS: In the 20 miRNAs, miR-122 were found differently expressed between wild and mutant EGFR carriers (P=0.018). Advanced disease stage and tumor metastasis were independently associated with poor prognosis of patients with lung adenocarcinoma (P=0.010 and 1.0x10⁻⁴). Plasma levels of miR-195 and miR-122 expression were also associated with overall survival in the patients, especially in those with advanced stage (HR=0.23, 95%CI:0.07-0.84; and HR=0.22, 95%CI:0.06-0.77) and EGFR mutation (HR=0.27, 95%CI:0.08-0.96; and HR=0.23, 95%CI=0.06-0.81). Moreover, a model including miR-195, miR-122 may predict survival outcomes of female patients with lung adenocarcinoma (AUC=0.707). CONCLUSIONS: Circulating miR-195 and miR-122 may have prognostic values in predicting the overall survival as well as predicting EGFR mutation status in non-smoking female patients with lung adenocarcinoma. Measuring plasma levels of miR-195 and miR-122 may especially be useful in EGFR mutant patients with lung adenocarcinoma.

[771]

TÍTULO / TITLE: - A Cross-Platform Comparison of Affymetrix and Agilent Microarrays Reveals Discordant miRNA Expression in Lung Tumors of c-Raf Transgenic Mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 12;8(11):e78870. doi: 10.1371/journal.pone.0078870.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078870](#)

AUTORES / AUTHORS: - Del Vescovo V; Meier T; Inga A; Denti MA; Borlak J

INSTITUCIÓN / INSTITUTION: - Centre of Integrative Biology (CIBIO), University of Trento, Trento, Italy ; Centre for Pharmacology and Toxicology, Hannover Medical School, Hannover, Germany.

RESUMEN / SUMMARY: - Non-coding RNAs play major roles in the translational control of gene expression. In order to identify disease-associated miRNAs in precursor lesions of lung cancer, RNA extracts from lungs of either c-Raf transgenic or wild-type (WT) mice were hybridized to the Agilent and Affymetrix miRNA microarray platforms, respectively. This resulted in the detection of a range of miRNAs varying between 111 and 267, depending on the presence or absence of the transgene, on the gender, and on the platform used. Importantly, when the two platforms were compared, only 11-16% of the 586 overlapping genes were commonly detected. With the Agilent microarray, seven miRNAs were identified as significantly regulated, of which three were selectively up-regulated in male transgenic mice. Much to our surprise, when the same samples were analyzed with the Affymetrix platform, only two miRNAs were identified as significantly regulated. Quantitative PCR performed with lung RNA extracts from WT and transgenic mice confirmed only partially the differential expression of significant regulated miRNAs and established that the Agilent platform failed to detect miR-433. Finally, bioinformatic analyses predicted a total of 152 mouse genes as targets of the regulated miRNAs of which 4 and 11 genes were significantly regulated at the mRNA level, respectively in laser micro-dissected lung dysplasia and lung adenocarcinomas of c-Raf transgenic mice. Furthermore, for many of the predicted mouse target genes expression of the coded protein was also repressed in human lung cancer when the publically available database of the Human Protein Atlas was analyzed, thus supporting the clinical significance of our findings. In conclusion, a significant difference in a cross-platform comparison was observed that will have important implications for research into miRNAs.

[772]

TÍTULO / TITLE: - Sensitive methods for the detection of an insertion in exon 20 of the gene in the metastasis of non-small cell lung cancer to the central nervous system.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Oct;6(4):1063-1067. Epub 2013 Jul 26.

●● [Enlace al texto completo \(gratis o de pago\) 3892/ol.2013.1495](#)

AUTORES / AUTHORS: - Krawczyk P; Nicooe M; Powrozek T; Mlak R; Sawicki M; Jarosz B; Pajak B; Kucharczyk K; Stencel D; Trojanowski T; Milanowski J

INSTITUCIÓN / INSTITUTION: - Department of Pneumology, Oncology and Allergology, Medical University of Lublin, Lubin 20-954, Poland.

RESUMEN / SUMMARY: - The HER2 (ErbB2/neu) protein is a member of the HER (ErbB) receptor family (EGFR, HER2, HER3 and HER4) that expresses tyrosine kinase activity in the intracellular domain. EGFR and HER2 overexpression is observed in numerous types of cancer, nevertheless, the susceptibility of patients with non-small cell lung cancer (NSCLC) to therapy with EGFR and HER2 tyrosine kinase inhibitors (TKIs) depends on mutations present in the respective coding genes (driver mutations). In the present study, PCR and amplified DNA fragment length analysis (FLA) were used along with the multi-temperature single-strand conformation polymorphism (MSSCP) technique in order to identify the 12 base pair insertion in exon 20 of the HER2 gene in 143 patients with NSCLC metastasis to the central nervous system. The prevalence of the HER2 gene mutation was correlated with mutations in the EGFR and

BRAF genes. The insertion in exon 20 of the HER2 gene was observed in a single 77-year-old, non-smoking male, with poorly-differentiated adenocarcinoma of the lung (1.5% of adenocarcinoma patients). No other genetic abnormalities were identified in this patient. In the therapy of NSCLC patients with HER2 gene mutations, drugs that inhibit the EGFR and HER2 receptors, for example afatinib, may be effective. The identification of other driving mutations in NSCLC cells appears to be key to the appropriate qualification of molecular targeted therapies.

[773]

TÍTULO / TITLE: - The Tumor Suppressor Gene TUSC2 (FUS1) Sensitizes NSCLC to the AKT Inhibitor MK2206 in LKB1-dependent Manner.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 17;8(10):e77067. doi: 10.1371/journal.pone.0077067.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077067](#)

AUTORES / AUTHORS: - Meng J; Majidi M; Fang B; Ji L; Bekele BN; Minna JD; Roth JA

INSTITUCIÓN / INSTITUTION: - Section of Thoracic Molecular Oncology, Department of Thoracic and Cardiovascular Surgery, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States of America.

RESUMEN / SUMMARY: - TUSC2-defective gene expression is detected in the majority of lung cancers and is associated with worse overall survival. We analyzed the effects of TUSC2 re-expression on tumor cell sensitivity to the AKT inhibitor, MK2206, and explored their mutual signaling connections, in vitro and in vivo. TUSC2 transient expression in three LKB1-defective non-small cell lung cancer (NSCLC) cell lines combined with MK2206 treatment resulted in increased repression of cell viability and colony formation, and increased apoptotic activity. In contrast, TUSC2 did not affect the response to MK2206 treatment for two LKB1-wild type NSCLC cell lines. In vivo, TUSC2 systemic delivery, by nanoparticle gene transfer, combined with MK2206 treatment markedly inhibited growth of tumors in a human LKB1-defective H322 lung cancer xenograft mouse model. Biochemical analysis showed that TUSC2 transient expression in LKB1-defective NSCLC cells significantly stimulated AMP-activated protein kinase (AMPK) phosphorylation and enzymatic activity. More importantly, AMPK gene knockdown abrogated TUSC2-MK2206 cooperation, as evidenced by reduced sensitivity to the combined treatment. Together, TUSC2 re-expression and MK2206 treatment was more effective in inhibiting the phosphorylation and kinase activities of AKT and mTOR proteins than either single agent alone. In conclusion, these findings support the hypothesis that TUSC2 expression status is a biological variable that potentiates MK2206 sensitivity in LKB1-defective NSCLC cells, and identifies the AMPK/AKT/mTOR signaling axis as an important regulator of this activity.

[774]

TÍTULO / TITLE: - Upregulation of Tissue Factor by Activated Stat3 Contributes to Malignant Pleural Effusion Generation via Enhancing Tumor Metastasis and Vascular Permeability in Lung Adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Sep 27;8(9):e75287. doi: 10.1371/journal.pone.0075287.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0075287](https://doi.org/10.1371/journal.pone.0075287)

AUTORES / AUTHORS: - Yeh HH; Chang WT; Lu KC; Lai WW; Liu HS; Su WC

INSTITUCIÓN / INSTITUTION: - Institute of Basic Medical Sciences, College of Medicine, National Cheng Kung University, Tainan, Taiwan ; Cancer Center, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan.

RESUMEN / SUMMARY: - Malignant pleural effusion (MPE) is a poor prognostic sign for patients with lung cancer. Tissue factor (TF) is a coagulation factor that participates in angiogenesis and vascular permeability and is abundant in MPE. We previously demonstrated that autocrine IL-6-activated Stat3 contributes to tumor metastasis and upregulation of VEGF, resulting in the generation of MPE in lung adenocarcinoma. In this study, we found IL-6-triggered Stat3 activation also induces TF expression. By using pharmacologic inhibitors, it was shown that JAK2 kinase, but not Src kinase, contributed to autocrine IL-6-induced TF expression. Inhibition of Stat3 activation by dominant negative Stat3 (S3D) in lung adenocarcinoma suppressed TF-induced coagulation, anchorage-independent growth in vitro, and tumor growth in vivo. Consistently, knockdown of TF expression by siRNA resulted in a reduction of anchorage-independent growth of lung adenocarcinoma cells. Inhibition of TF expression also decreased the adhesion ability of cancer cells in normal lung tissues. In the nude mouse model, both lung metastasis and MPE generation were decreased when PC14PE6/AS2-siTF cells (TF expression was silenced) were intravenously injected. PC14PE6/AS2-siTF cells also produced less malignant ascites through inhibition of vascular permeability. In summary, we showed that TF expression plays a pivotal role in the pathogenesis of MPE generation via regulating of tumor metastasis and vascular permeability in lung adenocarcinoma bearing activated Stat3.

[775]

TÍTULO / TITLE: - Wilms' tumour suppressor gene 1 (WT1) is involved in the carcinogenesis of Lung cancer through interaction with PI3K/Akt pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Cell Int. 2013 Nov 14;13(1):114.

●● Enlace al texto completo (gratis o de pago) [1186/1475-2867-13-114](https://doi.org/10.1186/1475-2867-13-114)

AUTORES / AUTHORS: - Wang X; Gao P; Lin F; Long M; Weng Y; Ouyang Y; Liu L; Wei J; Chen X; He T; Zhang H; Dong K

RESUMEN / SUMMARY: - Although studies have shown the oncogene WT1 is overexpressed in lung cancer, there is no data showing the implication of WT1 in lung cancer biology. In the present study, we first demonstrated that isotype C of WT1 was conservely overexpressed in 20 lung cancer patient specimens. Knockdown of WT1 by small interference RNA (siRNA) transfection resulted in a significant inhibition of cell proliferation, induction of cell cycle arrest at G1 phase, and the expression change of BCL-2 family genes in WT1+ A549 cells. Furthermore, we found that DDP treatment could decrease the WT1 mRNA expression level by 5% and 15% at a dose of 1 mug/ml, by 25% and 40% at a dose of 2 mug/ml for 24 and 48 h, respectively. In the mean time, DDP treatment also reduced the PI3K/AKT pathway activity. Further analysis by using siRNA targeting the AKT-1 and the PI3K pathway inhibitor Ly294002 revealed that the AKT-1 siRNA reduced the WT1 expression effectively in A549 cells, and the same result was observed in Ly294002 treated cells, indicating that DDP treatment could down regulate WT1 expression through the PI3K/AKT pathway. Of

particular interest, knockdown of WT1 also inhibited the AKT expression effectively, Chip assay further confirmed that WT1 is a transcription factor of AKT-1. We thus concluded that there is a positive feedback loop between WT1 and AKT-1. Taken together, DDP treatment downregulates the WT1 expression through the PI3K/AKT signaling pathway, and there is a feedback between WT1 and AKT-1; WT1 is involved in cellular proliferation in A549 cells, WT1 inhibition in combination with DDP will provide a new light for lung cancer therapy.

[776]

TÍTULO / TITLE: - Delisheng injection (), a Chinese medicinal compound, enhanced the effect of cis-platinum on lung carcinoma cell line PGCL3.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Chin J Integr Med. 2013 Oct 23.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s11655-013-1335-0](#)

AUTORES / AUTHORS: - Dong XL; Gong Y; Chen ZZ; Wang YJ

INSTITUCIÓN / INSTITUTION: - Department of Respiratory, the Second Affiliated Hospital, College of Medicine of Xi'an Jiaotong University, Xi'an, 710004, China, dxl1103@163.com.

RESUMEN / SUMMARY: - OBJECTIVE: To investigate the effect of Delisheng Injection (, DLS), a Chinese medicinal compound, DLS combined with cis-platinum (DDP), an active agent used in lung cancer chemotherapy, on a human highly metastatic giant lung carcinoma cell line PGCL3. METHODS: The suspended PGCL3 cells at 10 /mL cultured in 96-well tissue culture plates were divided into 4 groups: DLS treatment group (2 μL/mL, 5 μL/mL, 10 μL/mL, 25 μL/mL), DDP treatment group (1 μg/mL, 2 μg/mL, 5 μg/mL, 15 μg/mL), combined DLS with DDP treatment group (DLS:DDP 2 μL/mL:1 μg/mL, 5 μL/mL:2 μg/mL, 10 μL/mL:5 μg/mL, 25 μL/mL:15 μg/mL) and a control group. The cytotoxicity of DLS with different concentrations (2 μL/mL, 5 μL/mL, 10 μL/mL, 25 μL/mL) on PGCL3 cells was determined by 3-(4,5)-dimethylthiazoliazol(-z-y1)-3,5-di-phenyltetrazoliumromide (MTT) assay. Effect of DLS on adhesion of PGCL-3 cells was tested by cell-matrigel adhesion assay. Chemotactic movement model of transwell camerula was used to determine the effect of DLS on invasion and migration of PGCL-3 cells. RESULTS: Compared with the control group, DLS (2 μL/mL, 5 μL/mL, 10 μL/mL, 25 μL/mL) could significantly decrease cell proliferation, adhesion, invasion and migration abilities (P <0.05). Cell adhesion, invasion and migration abilities were significantly decreased after combination treatment of DLS:DDP (2 μL/mL:1 μg/mL, 5 μL/mL:2 μg/mL, 10 μL/mL:5 μg/mL, 25 μL/mL:15 μg/mL) compared with DDP single-agent treatment (1 μg/mL, 2 μg/mL, 5 μg/mL, 15 μg/mL, P<0.05), respectively. CONCLUSIONS: DLS single-agent has a satisfying inhibition effect in PGCL3 cell line and DLS might enhance the inhibition effect of DDP on cancer metastasis. Our research provided a experimental basis about the treatment on highly metastatic lung caner.

[777]

TÍTULO / TITLE: - Successful combination chemotherapy with irinotecan hydrochloride and cisplatin for primary gastric small cell carcinoma: report of a case.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Oct 7;11(1):263. doi: 10.1186/1477-7819-11-263.

●● Enlace al texto completo (gratis o de pago) [1186/1477-7819-11-263](https://doi.org/10.1186/1477-7819-11-263)

AUTORES / AUTHORS: - Funahashi H; Miyai H; Wakasugi T; Ishiguro H; Matsuo Y; Kimura M; Takeyama H

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterological Surgery, Nagoya City University Graduate School of Medical Sciences, 1 Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya 4678601, Japan. funa84@med.nagoya-cu.ac.jp.

RESUMEN / SUMMARY: - Primary gastric small cell carcinoma is a rare and aggressive malignant disease with a poor prognosis that was first reported in 1976 by Matsusaka et al. The incidence is very low and the clinicopathological features are similar to those of small cell lung carcinoma. We herein report a case of successful treatment by combination chemotherapy consisting of irinotecan hydrochloride and cisplatin for primary gastric small cell carcinoma. The patient was a 71-year-old male who was admitted to a local hospital with anemia. Gastrointestinal endoscopy revealed the presence of advanced gastric carcinoma at the upper region of the stomach. The patient underwent surgery, and the pathological diagnosis was small cell carcinoma due to the presence of the typical features of small round cells with scant cytoplasm that were positive for synaptophysin and chromogranin A in the resected specimen. The patient underwent subsequent combination chemotherapy, which provided him with over 1 year of survival and a good quality of life. We also present a review of the literature regarding chemotherapy for primary gastric small cell carcinoma.

[778]

TÍTULO / TITLE: - Expression and prognostic relevance of MET and phospho-BAD in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Sep 18;6:1315-23. doi: 10.2147/OTT.S50428.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S50428](https://doi.org/10.2147/OTT.S50428)

AUTORES / AUTHORS: - Sun W; Ai T; Gao Y; Zhang Y; Cui J; Song L

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, First Affiliated Hospital, Medical College of Xi'an Jiaotong University, Xi'an, People's Republic of China.

RESUMEN / SUMMARY: - BACKGROUND: MET is involved in the progression of several types of human cancers, while phospho-BAD(Ser-136) is a key molecule in apoptosis and might be regulated by MET. The aim of this study was to investigate the correlation between altered expression of MET and phospho-BAD in non-small cell lung cancer (NSCLC) and their association with clinicopathologic parameters and overall survival. METHODS: MET and phospho-BAD(Ser-136) proteins were evaluated by immunohistochemical analysis in 183 paraffin-embedded specimens and were also assessed by Western blotting analysis in 12 frozen tumor tissue samples, which were representative examples of immunohistochemical staining. RESULTS: Positive expression of MET and phospho-BAD(Ser-136) occurred in 67.2% and 49.2% of the 183 cases of NSCLC, respectively. However, neither MET expression nor phospho-BAD(Ser-136) expression was associated with any clinicopathologic parameter. A significant correlation was found between MET and phospho-BAD(Ser-136) expression levels evaluated by immunohistochemistry ($r = 0.268$, $P < 0.001$).

Overexpression of MET was significantly associated with shortened overall survival in univariate analysis ($P < 0.001$). Moreover, patients with a MET+/phospho-BAD(Ser-136)+ phenotype had a poorer prognosis than others ($P < 0.001$). Multivariate Cox proportional hazard analysis confirmed that MET expression is a prognostic factor for NSCLC. CONCLUSION: MET expression might be correlated with phospho-BAD(Ser-136) expression, and may be an adverse predictor for NSCLC. Activation of the MET/phospho-BAD(Ser-136) signaling pathway might play a role in the development and progression of NSCLC.

[779]

TÍTULO / TITLE: - Elevated expression of SHIP2 correlates with poor prognosis in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Sep 15;6(10):2185-91.

AUTORES / AUTHORS: - Fu M; Fan W; Pu X; Ni H; Zhang W; Chang F; Gong L; Xiong L; Wang J; Gu X

INSTITUCIÓN / INSTITUTION: - Department of Infectious Diseases, The First People's Hospital of Kunshan Affiliated with Jiangsu University Suzhou 215000, China.

RESUMEN / SUMMARY: - SH2-containing inositol 5'-phosphatase 2 (SHIP2) is a vital regulator of phosphoinositide pools in metabolic pathways and is considered to downregulate phosphatidylinositol 3'-kinase signaling, which underlies the development of several kinds of human cancers. However, SHIP2 expression in non-small cell lung cancer (NSCLC) and its relationship with the clinical characteristics of NSCLC remain poorly understood. In this study, one-step quantitative reverse transcription-polymerase chain reaction and immunohistochemistry analysis with tissue microarray was used to evaluate SHIP2 expression in NSCLC and to investigate the relationship of this expression to NSCLC prognosis. Results showed that the expression of SHIP2 messenger RNA and protein was significantly higher in NSCLC than in corresponding non-cancerous tissues (both $p < 0.05$). SHIP2 protein expression in NSCLC was related to lymph node metastasis ($p = 0.042$), TNM stage ($p = 0.036$), and 5-year survival rate ($p = 0.046$). The Kaplan-Meier method and log-rank test suggested that high SHIP2 expression, tobacco consumption, and advanced tumor stage were significantly associated with low survival of NSCLC patients. The results of this research suggested that SHIP2 expression was correlated with malignant phenotypes of NSCLC and may thus serve as a poor prognostic factor and valuable oncogene for NSCLC.

[780]

TÍTULO / TITLE: - Malignant transformation of well differentiated papillary mesothelioma thirteen years after the diagnosis: a case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Respir J. 2013 Oct 4. doi: 10.1111/crj.12057.

●● [Enlace al texto completo \(gratis o de pago\) 1111/crj.12057](#)

AUTORES / AUTHORS: - Costanzo L; Scarlata S; Perrone G; Rossi L; Papa A; Di Matteo FM; Tonini G; Onetti Muda A; Antonelli-Incalzi R; Tomao S

INSTITUCIÓN / INSTITUTION: - Chair of Geriatrics, Unit of Respiratory Pathophysiology, Campus Bio Medico University, Rome, Italy.

RESUMEN / SUMMARY: - Well-differentiated papillary mesothelioma is a rare mesothelial tumor affecting mostly the peritoneum of women in their reproductive age, but it may occur also at other sites, including the pleura. It is considered a specific pathological entity different from diffuse malignant mesothelioma as it displays a characteristic histological pattern and is associated with a slowly progressive clinical course. We report the case of a 79-year-old man with a history of right pleural well-differentiated papillary mesothelioma at age 64, which was successfully treated with chemotherapy, radiotherapy and talc pleurodesis. Thirteen years after the first diagnosis, he presented with mediastinal lymph nodes metastasis and with an extremely rare pattern of tracheal and bronchial infiltration, that was detected at bronchoscopy. Biopsy samples revealed loss of histological differentiation of the neoplastic cells. This case report highlights that well-differentiated papillary mesothelioma is a tumour of uncertain malignant potential, that may undergo transformation over many years. Finally, the role of immunohistochemistry in the diagnosis of well-differentiated papillary mesothelioma and the possible mechanisms leading to this unique way of metastatization are discussed.

[781]

TÍTULO / TITLE: - Mutation of TP53 and Alteration of p14 Expression in EGFR- and KRAS-Mutated Lung Adenocarcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Oct 26. pii: S1525-7304(13)00180-0. doi: 10.1016/j.clcc.2013.08.003.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.08.003](#)

AUTORES / AUTHORS: - Cortot AB; Younes M; Martel-Planche G; Guibert B; Isaac S; Souquet PJ; Commo F; Girard P; Fouret P; Brambilla E; Hainaut P; Soria JC

INSTITUCIÓN / INSTITUTION: - International Agency for Research on Cancer, Lyon, France; Department of Thoracic Oncology, Hospices Civils de Lyon, Centre Hospitalier Lyon Sud, Pierre-Benite, France; Thoracic Oncology Department, Lille University Hospital, Universite Lille Nord de France, Lille, France. Electronic address: alexis.cortot@chru-lille.fr.

RESUMEN / SUMMARY: - BACKGROUND: In lung adenocarcinoma, inactivation of the tumor suppressor p53 may abrogate a safeguard mechanism preventing the development of tumors with activating mutations in EGFR or KRAS. To assess this hypothesis, we analyzed TP53 mutations and downregulation of p14arf, a negative regulator of p53 activated by oncogenic signals, in a retrospective series of 96 patients with primary adenocarcinoma of the lung. PATIENTS AND METHODS: Mutations in TP53 (exons 4-9), KRAS (exon 1), and EGFR (exons 18-21) were identified by direct sequencing of DNA from formalin-fixed, paraffin-embedded resected tumors. Expression of p14arf was semiquantitatively evaluated by immunohistochemical analysis. RESULTS: TP53, KRAS, and EGFR mutations were detected in 42 of 93 (45.2%), 15 of 95 (15.8%), and 31 of 90 (34.4%) cases, respectively. Low p14arf expression was observed in 19 of 91 cases (20.9%). Disruption of the p53/p14arf pathway (defined as TP53 mutation or decreased p14arf expression, or both) was observed in 18 of 31 EGFR-mutated (58.1%) tumors and in 9 of 13 KRAS-mutated (69.2%) tumors. CONCLUSION: Inactivation of the p53/p14arf pathway is common but not systematic in EGFR- or KRAS-mutated lung adenocarcinomas. Our work highlights

the need to better investigate the association between EGFR and KRAS mutations and alterations in tumor suppressor pathways.

[782]

TÍTULO / TITLE: - iRGD Conjugated TPGS Mediates Codelivery of Paclitaxel and Survivin shRNA for the Reversal of Lung Cancer Resistance.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Pharm. 2013 Nov 18.

●● Enlace al texto completo (gratis o de pago) [1021/mp400576f](#)

AUTORES / AUTHORS: - Shen J; Meng Q; Sui H; Yin Q; Zhang Z; Yu H; Li Y

INSTITUCIÓN / INSTITUTION: - Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai 201203, China.

RESUMEN / SUMMARY: - Multidrug resistance (MDR) is one of the major obstacles in tumor treatment. Herein, we reported an active targeting strategy with peptide-mediated nanoparticles deep into tumor parenchyma, which iRGD conjugated d-alpha-tocopheryl polyethylene glycol 1000 succinate (TPGS) mediated codelivery of paclitaxel (PTX) and survivin shRNA (shSur) for the reversal of lung cancer resistance. Pluronic P85-polyethyleneimine/TPGS complex nanoparticles incorporated with iRGD-TPGS conjugate codelivering PTX and shSur systems (iTPNs) could induce effective cellular uptake, RNAi effects, and cytotoxicity on A549 and A549/T cells. In particular, iTPNs showed superiority in biodistribution, survivin expression, tumor apoptosis, and antitumor efficacy by simultaneously exerting an enhanced permeability and retention (EPR) effect and iRGD mediated active targeting effects. iTPNs significantly enhanced the accumulation of PTX and shSur, down-regulated survivin expression, and induced cell apoptosis in tumor tissue. The in vivo antitumor efficacy showed the tumor volume of iTPNs group (10 mg/kg) was only 12.7% of the Taxol group. Therefore, the iRGD mediated PTX and shSur codelivery system could be a very powerful approach for the reversal and therapy of lung cancer resistance.

[783]

TÍTULO / TITLE: - Loss of p53 Attenuates the Contribution of IL-6 Deletion on Suppressed Tumor Progression and Extended Survival in Kras-Driven Murine Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 15;8(11):e80885. doi: 10.1371/journal.pone.0080885.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0080885](#)

AUTORES / AUTHORS: - Tan X; Carretero J; Chen Z; Zhang J; Wang Y; Chen J; Li X; Ye H; Tang C; Cheng X; Hou N; Yang X; Wong KK

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Proteomics, Genetic Laboratory of Development and Diseases, Institute of Biotechnology, Beijing, China ; Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, United States of America ; Department of Medicine, Harvard Medical School, Boston, Massachusetts, United States of America.

RESUMEN / SUMMARY: - Interleukin-6 (IL-6) is involved in lung cancer tumorigenesis, tumor progression, metastasis, and drug resistance. Previous studies show that blockade of IL-6 signaling can inhibit tumor growth and increase drug sensitivity in mouse models. Clinical trials in non-small cell lung cancer (NSCLC) reveal that IL-6

targeted therapy relieves NSCLC-related anemia and cachexia, although other clinical effects require further study. We crossed IL-6 (-/-) mice with Kras (G12D) mutant mice, which develop lung tumors after activation of mutant Kras (G12D), to investigate whether IL-6 inhibition contributes to tumor progression and survival time in vivo. Kras (G12D); IL-6 (-/-) mice exhibited increased tumorigenesis, but slower tumor growth and longer survival, than Kras (G12D) mice. Further, in order to investigate whether IL-6 deletion contributes to suppression of lung cancer metastasis, we generated Kras (G12D); p53 (flox/flox); IL-6 (-/-) mice, which developed lung cancer with a trend for reduced metastases and longer survival than Kras (G12D); p53 (flox/flox) mice. Tumors from Kras (G12D); IL-6 (-/-) mice showed increased expression of TNF α and decreased expression of CCL-19, CCL-20 and phosphorylated STAT3 (pSTAT3) than Kras (G12D) mice; however, these changes were not present between tumors from Kras (G12D); p53 (flox/flox); IL-6 (-/-) and Kras (G12D); p53 (flox/flox) mice. Upregulation of pSTAT3 and phosphorylated AKT (pAKT) were observed in Kras (G12D) tumors with p53 deletion. Taken together, these results indicate that IL-6 deletion accelerates tumorigenesis but delays tumor progression and prolongs survival time in a Kras-driven mouse model of lung cancer. However, these effects can be attenuated by p53 deletion.

[784]

TÍTULO / TITLE: - The overexpression of glypican-5 promotes cancer cell migration and is associated with shorter overall survival in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Dec;6(6):1565-1572. Epub 2013 Oct 11.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1622](#)

AUTORES / AUTHORS: - Li Y; Miao L; Cai H; Ding J; Xiao Y; Yang J; Zhang D

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, The Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, Jiangsu 210008, P.R. China.

RESUMEN / SUMMARY: - Although the correlation between glypican-5 (GPC5) and lung cancer is well known, the effect of GPC5 expression on non-small cell lung cancer (NSCLC) survival remains to be determined. In the present study, GPC5 expression in A549, H3255, and SPC-A1 NSCLC cell lines was evaluated by reverse transcription-polymerase chain reaction (RT-PCR) and western blot analysis. GPC5 mRNA and protein expression levels were found to be higher in A549 and H3255 cells compared with SPC-A1 cells. The role of GPC5 in NSCLC cell migration was evaluated in vitro by shRNA-mediated knockdown or the overexpression of GPC5 through scratch and transwell assays. The mean migration rates of cancer cells transfected with pRNAT-shRNA-GPC5-1 were reduced compared with the controls in A549 ($P < 0.001$) and H3255 ($P = 0.001$), while the migration rate of SPC-A1 with GPC5 overexpression was higher than that of the control ($P = 0.001$). The downregulation of GPC5 impeded the transmigration of A549 and H3255 while the upregulation of GPC5 expression promoted the transmembrane invasion of SPC-A1. Furthermore, a panel of formalin-fixed paraffin-embedded NSCLC tissues from 127 patients undergoing curative resection (stages I, II and III) between January, 2003 and December, 2008 were obtained in order to investigate the correlation between GPC5 expression and clinicopathological factors using immunohistochemical methods. The results demonstrated that high GPC5 expression levels in NSCLC were associated with

respiratory symptoms in lung cancer diagnosis, poor differentiation, vascular invasion, regional lymph node metastasis and a higher TNM stage. Using the Kaplan-Meier method, NSCLC patients with high levels of GPC5 expression demonstrated a significantly shorter overall survival time compared with those with low GPC5 expression levels (median postsurgical survival time: 14.0 months vs. 59.0 months, $P=0.001$). GPC5 expression was also identified as an independent prognostic factor by Cox regression analysis [adjusted hazard ratio: 2.18; 95% confidence interval (CI): 1.35-3.52; $P=0.001$]. This study suggested that increased levels of GPC5 expression are a poor prognostic marker for NSCLC.

[785]

TÍTULO / TITLE: - A high-throughput screen identifies miRNA inhibitors regulating lung cancer cell survival and response to paclitaxel.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - RNA Biol. 2013 Sep 30;10(11).

AUTORES / AUTHORS: - Du L; Borkowski R; Zhao Z; Ma X; Yu X; Xie XJ; Pertsemidid A

INSTITUCIÓN / INSTITUTION: - Greehey Children's Cancer Research Institute; Department of Cellular and Structural Biology; UT Health Science Center at San Antonio; San Antonio, TX USA.

RESUMEN / SUMMARY: - microRNAs (miRNAs) are small RNAs endogenously expressed in multiple organisms that regulate gene expression largely by decreasing levels of target messenger RNAs (mRNAs). Over the past few years, numerous studies have demonstrated critical roles for miRNAs in the pathogenesis of many cancers, including lung cancer. Cellular miRNA levels can be easily manipulated, showing the promise of developing miRNA-targeted oligos as next-generation therapeutic agents. In a comprehensive effort to identify novel miRNA-based therapeutic agents for lung cancer treatment, we combined a high-throughput screening platform with a library of chemically synthesized miRNA inhibitors to systematically identify miRNA inhibitors that reduce lung cancer cell survival and those that sensitize cells to paclitaxel. By screening three lung cancer cell lines with different genetic backgrounds, we identified miRNA inhibitors that potentially have a universal cytotoxic effect on lung cancer cells and miRNA inhibitors that sensitize cells to paclitaxel treatment, suggesting the potential of developing these miRNA inhibitors as therapeutic agents for lung cancer. We then focused on characterizing the inhibitors of three miRNAs (miR-133a/b, miR-361-3p, and miR-346) that have the most potent effect on cell survival. We demonstrated that two of the miRNA inhibitors (miR-133a/b and miR-361-3p) decrease cell survival by activating caspase-3/7-dependent apoptotic pathways and inducing cell cycle arrest in S phase. Future studies are certainly needed to define the mechanisms by which the identified miRNA inhibitors regulate cell survival and drug response, and to explore the potential of translating the current findings into clinical applications.

[786]

TÍTULO / TITLE: - Lung cancer in women: an overview with special focus on Spanish women.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Transl Oncol. 2013 Nov 26.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s12094-013-1137-7](#)

AUTORES / AUTHORS: - Remon J; Molina-Montes E; Majem M; Lianes P; Isla D; Garrido P; Felip E; Vinolas N; de Castro J; Artal A; Sanchez MJ

INSTITUCIÓN / INSTITUTION: - Hospital de Mataro, Carretera de la cirera s/n, 08304, Mataro, España, jremon@cscdm.cat.

RESUMEN / SUMMARY: - Lung cancer incidence is decreasing worldwide among men but rising among women due to recent changes in smoking patterns in both sexes. In Europe, the smoking epidemic has evolved different rates and times, and policy responses to it, vary substantially between countries. Differences in smoking prevalence are much more evident among European women reflecting the heterogeneity in cancer incidence rates. Other factors rather than smoking and linked to sex may increase women's susceptibility to lung cancer, such as genetic predisposition, exposure to sex hormones and molecular features, all of them linked to epidemiologic and clinical characteristics of lung cancer in women. However, biological bases of sex-specific differences are controversial and need further evaluation. This review focuses on the epidemiology and outcome concerning non-small cell lung cancer in women, with emphasis given to the Spanish population.

[787]

TÍTULO / TITLE: - Cancer stem cell-related marker expression in lung adenocarcinoma and relevance of histologic subtypes based on IASLC/ATS/ERS classification.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Nov 8;6:1597-604. doi: 10.2147/OTT.S52353.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S52353](#)

AUTORES / AUTHORS: - Shimada Y; Saji H; Nomura M; Matsubayashi J; Yoshida K; Kakihana M; Kajiwara N; Ohira T; Ikeda N

INSTITUCIÓN / INSTITUTION: - Department of Surgery I, Tokyo Medical University Hospital, Tokyo, Japan.

RESUMEN / SUMMARY: - BACKGROUND: The cancer stem cell (CSC) theory has been proposed to explain tumor heterogeneity and the carcinogenesis of solid tumors. The aim of this study was to clarify the clinical role of CSC-related markers in patients with lung adenocarcinoma and to determine whether each CSC-related marker expression correlates with the histologic subtyping proposed by the International Association for the Study of Lung Cancer (IASLC), the American Thoracic Society (ATS), and the European Respiratory Society (ERS) classifications. METHODS: We reviewed data for all 103 patients in whom complete resection of adenocarcinoma had been performed. Expression of CSC-related markers, ie, aldehyde dehydrogenase 1A1 (ALDH1A1), aldo-keto reductase 1C family member 1 (AK1C1), and 1C family member 3 (AK1C3), was examined using immunostaining on whole-mount tissue slides, and the tumors were reclassified according to the IASLC/ATS/ERS classification. RESULTS: ALDH1A1 expression was observed in 66.0% of tumors, AK1C1 in 62.7%, and AK1C3 in 86.1%. Immunoreactivities with the frequency of mean expression of ALDH1A1 in papillary predominant adenocarcinoma were significantly higher than those of solid predominant adenocarcinoma ($P < 0.05$). Papillary predominant adenocarcinoma had significantly lower expression of AK1C1 when compared with noninvasive or solid predominant adenocarcinomas ($P < 0.05$). On multivariate analysis, larger tumor size (hazards ratio 1.899, $P = 0.044$), lymph node metastasis (hazards ratio 2.702, $P = 0.005$), and low expression of ALDH1A1 (hazards ratio 3.218, $P < 0.001$) were shown to be

independently associated with an unfavorable prognosis. CONCLUSION: Immunohistochemistry of ALDH1A1 expression is strongly associated with prognosis. Expression of each CSC-related marker varies according to subtype, suggesting that a comprehensive histologic subtyping approach in the IASLC/ATS/ERS classification provides new molecular biology insights into the genesis of lung adenocarcinoma according to CSC theory.

[788]

TÍTULO / TITLE: - Fibroblast growth factor receptor 1 amplification in non-small cell lung cancer by quantitative real-time PCR.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 8;8(11):e79820. doi: 10.1371/journal.pone.0079820.

●● Enlace al texto completo (gratis o de pago) 1371/journal.pone.0079820

AUTORES / AUTHORS: - Gadgeel SM; Chen W; Cote ML; Bollig-Fischer A; Land S; Schwartz AG; Bepler G

INSTITUCIÓN / INSTITUTION: - Karmanos Cancer Institute & Department of Oncology, Wayne State University, Detroit, Michigan, United States of America.

RESUMEN / SUMMARY: - INTRODUCTION: Amplification of the fibroblast growth factor receptor 1 (FGFR1) gene has been described in tumors of non-small-cell lung cancer (NSCLC) patients. Prior reports showed conflicting rates of amplification frequency and clinical relevance. MATERIALS AND METHODS: We developed a reliable real-time quantitative PCR assay to assess the frequency of FGFR1 amplification and assessed the optimal cutoff level of amplification for clinical application. RESULTS: In a training cohort of 203 NSCLCs, we established that a 3.5-fold amplification optimally divided patients into groups with different survival rates with a clear threshold level. Those with FGFR1 amplification levels above 3.5-fold had an inferior survival. These data were confirmed in a validation cohort of 142 NSCLC. After adjusting for age, sex, performance status, stage, and histology, patients with FGFR1 amplification levels above 3.5 fold had a hazard ratio of 2.91 (95% CI- 1.14, 7.41; pvalue-0.025) for death in the validation cohort. The rates of FGFR1 amplification using the cutoff level of 3.5 were 5.1% in squamous cell and 4.1% in adenocarcinomas. There was a non-significant trend towards higher amplifications rates in heavy smokers (> 15 pack-years of cigarette consumption) as compared to light smokers. DISCUSSION: Our data suggest that a 3.5-fold amplification of FGFR1 is of clinical importance in NSCLC. Our cutpoint analysis showed a clear threshold effect for the impact of FGFR1 amplification on patients' survival, which can be used as an initial guide for patient selection in trials assessing efficacy of novel FGFR inhibitors.

[789]

TÍTULO / TITLE: - FBXW7 Mediates Chemotherapeutic Sensitivity and Prognosis in NSCLC.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Cancer Res. 2013 Oct 28.

●● Enlace al texto completo (gratis o de pago) 1158/1541-7786.MCR-13-0341

AUTORES / AUTHORS: - Yokobori T; Yokoyama Y; Mogi A; Endoh H; Altan B; Kosaka T; Yamaki E; Yajima T; Tomizawa K; Azuma Y; Onozato R; Miyazaki T; Tanaka S; Kuwano H

INSTITUCIÓN / INSTITUTION: - Graduate School of Medicine, Gunma University.

RESUMEN / SUMMARY: - Non-small cell lung cancer (NSCLC) is a leading cause of cancer-related deaths worldwide. To improve the prognosis of patients with NSCLC, new and validated therapeutic targets are critically needed. In this study, we focused on F-box and WD repeat domain containing-7 (FBXW7), a E3 ubiquitin ligase, that regulates the degradation of MCL1, Myc, Cyclin E, and TOP2A. Importantly, loss of FBXW7 was associated with increased sensitivity of tumors to a class I-specific HDAC inhibitor, MS-275. Immunohistochemical analysis revealed increased expression of FBXW7 targets, MCL1 and TOP2A, in NSCLC tumors with low expression of FBXW7. Moreover, clinical specimens exhibiting low FBXW7 expression presented with more progressive cancer and significantly shorter cancer-specific survival than patients with high FBXW7 expression. Mechanistic study of NSCLC cell lines with silenced FBXW7 revealed enhanced MS-275 sensitivity and Taxol resistance. Interestingly, Taxol resistance was eliminated by MS-275 treatment suggesting the potential of HDAC inhibitors for the treatment of aggressive Taxol-resistant NSCLC that lack FBXW7. Implications: FBXW7 status impacts chemosensitivity and is a prognostic marker in NSCLC.

[790]

TÍTULO / TITLE: - Subunit-specific mass spectrometry method identifies haptoglobin subunit alpha as a diagnostic marker in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Proteomics. 2013 Oct 11;94C:302-310. doi: 10.1016/j.jprot.2013.09.019.

●● Enlace al texto completo (gratis o de pago) [1016/j.jprot.2013.09.019](#)

AUTORES / AUTHORS: - Park J; Yang JS; Jung G; Woo HI; Park HD; Kim JW; Huh W; Ko JW; Kim H; Cho JY; Lee SY

INSTITUCIÓN / INSTITUTION: - Samsung Biomedical Research Institute, Samsung Medical Center, Seoul, South Korea.

RESUMEN / SUMMARY: - Haptoglobin (Hp) subunits have been suggested as a potential serum marker for lung cancer. Research is intense on the application of Hp subunits to predict the cancer earlier. Nevertheless, it remains difficult to accurately measure the content of Hp subunits. We developed stable isotope dilution-multiple reaction monitoring mass spectrometry (SID-MRM-MS) capable of measuring Hp subunits (alpha and beta chains). Three isotopic analogs (NPANPVQ, TEGDGVYTLNDK and ILGGHLDK for alpha, alpha2 and beta chain, respectively) were used as internal standard (IS) for SID-MRM-MS. Serum levels of each Hp subunit were measured in 210 clinical samples using SID-MRM-MS. A concentration ratio of each Hp subunit to total Hp was investigated. Secretion levels of alpha and beta chains were significantly increased in non-small cell lung cancer (NSCLC) compared to controls ($P < 0.0001$). Alterations of the alpha chain ratio were more apparent than beta chain between controls and NSCLC ($P = 0.0001$ and 0.338 for alpha and beta chains, respectively). In conclusion, this study provides not only an efficient quantitative method to determine each Hp subunit in crude sera, but also evidence that Hp alpha chain is a more prospective biomarker to diagnose NSCLC than beta chain.

BIOLOGICAL SIGNIFICANCE: Recent several studies have reported Hp as a potential biomarker for diagnosis of lung cancer. However a successful evaluation of the value of Hp subunits was not achieved on clinical samples. To evaluate the diagnostic performance of each Hp subunit, the development of an accurate quantitative assay of Hp subunits is necessary. In this regard, we employed a new analytical method using stable isotope dilution-multiple reaction monitoring mass spectrometry (SID-MRM-MS), capable of measuring Hp subunits in 210 clinical specimens. In this article, we measured the Hp subunit concentrations and Hp subunits/total Hp ratios in patients with NSCLC using SID-MRM-MS. This is the first report on the evaluation of each Hp subunit as a lung cancer marker using SID-MRM-MS. Consequently, we evaluated specific three tryptic peptides (e.g. NPANPVQ, TEGDGVYTLNDK and ILGGHLDK for alpha, alpha2 and beta chain, respectively) with high specificity and sensitivity for determination of Hp subunits. Through future large prospective cohort studies, the clinical application of Hp subunits as complementary markers, especially Hp alpha, would be useful for the diagnosis of NSCLC.

[791]

TÍTULO / TITLE: - Diagnostic pitfalls in the preoperative F-FDG PET/CT evaluation of a case of giant malignant solitary fibrous tumor of the pleura.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rev Esp Med Nucl. Acceso gratuito al texto completo a partir de los 2 años de la fecha de publicación.

- Enlace a la Editora de la Revista <http://db.doyma.es/>

- Cita: Revista Española de Medicina Nuclear: <> Imagen Mol. 2013 Sep 27. pii: S2253-654X(13)00131-5. doi: 10.1016/j.remnm.2013.07.007.

- Enlace al texto completo (gratuito o de pago) 1016/j.remnm.2013.07.007

AUTORES / AUTHORS: - Lococo F; Rapicetta C; Ricchetti T; Cavazza A; Filice A; Treglia G; Tenconi S; Paci M; Sgarbi G

INSTITUCIÓN / INSTITUTION: - Unit of Thoracic Surgery, IRCCS-Arcispedale Santa Maria Nuova, Reggio Emilia, Italy. Electronic address: filippo_lococo@yahoo.it.

RESUMEN / SUMMARY: - Solitary fibrous tumor of the pleura (SFTP) is an uncommon entity, generally with an indolent behavior. Nevertheless, some malignant forms have been rarely reported. These, often have an aggressive biological behavior with pathological findings of invasiveness. The preoperative diagnosis and evaluation of the grade of malignancy are extremely challenging. Herein we report a case of a 64-year-old man who presented with a left giant intra-thoracic mass imaged with fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG/PET-CT) and sampled via fine-needle aspiration biopsy (FNAB). Imaging and FNAB findings showed suspicion of a benign form of SFTP. Surgical radical resection of the giant mass was performed. The definitive histological diagnosis showed a malignant SFTP. Based on this report, we take the opportunity to briefly discuss the insidious pitfalls concerning the radiological and 18F-FDG/PET-CT features as well as cyto/histological findings in the pre-operative diagnostic work-up examination of this rare entity.

[792]

TÍTULO / TITLE: - Primary pleural synovial sarcoma: A rare cause of hemorrhagic pleural effusion in a young adult.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Jul-Sep;9(3):517-9. doi: 10.4103/0973-1482.119367.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119367](#)

AUTORES / AUTHORS: - Sandeepa HS; Kate AH; Chaudhari P; Chavan V; Patole K; Lokeshwar N; Chhajed PN

INSTITUCIÓN / INSTITUTION: - Department of Pulmonology, Fortis Hiranandani Hospital, Vashi, Navi Mumbai, Maharashtra, India.

RESUMEN / SUMMARY: - This is a case report of a young adult presenting with hemorrhagic pleural effusion. Chest CT scan showed loculated pleural effusion with pleural nodule. Whole body PET scan showed thickening of pleura with multiple enhancing pleural nodules with different metabolic activity. Pleural nodule was biopsied which on histopathology showed pleural synovial sarcoma.

[793]

TÍTULO / TITLE: - Saddle pulmonary tumor embolus secondary to renal cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - JAAPA. 2013 Nov;26(11):37-9. doi: 10.1097/01.JAA.0000436685.90928.ac.

●● Enlace al texto completo (gratis o de pago)

[1097/01.JAA.0000436685.90928.ac](#)

AUTORES / AUTHORS: - Khouzam RN; Soufi MK; Farah V

INSTITUCIÓN / INSTITUTION: - Rami N. Khouzam is an associate professor in the Department of Medicine, Division of Cardiovascular Diseases, at the University of Tennessee Health Science Center in Memphis, Tennessee. Mohamad Khaled Soufi is a resident in internal medicine at St. Vincent's Hospital in Cleveland, Ohio. Victor Farah is a cardiology fellow in the Department of Medicine, Division of Cardiovascular Diseases at the University of Tennessee. The authors have indicated no relationships to disclose relating to the content of this article.

RESUMEN / SUMMARY: - Most pulmonary tumor emboli are microscopic and occlude small arteries and arterioles with subsequent insidious clinical presentation. These emboli usually need conservative treatment. Emboli that spread to large proximal pulmonary arteries, although rare, can be life-threatening. This article focuses on the importance of prompt recognition, diagnosis, and appropriate management of pulmonary tumor emboli.

[794]

TÍTULO / TITLE: - Concurrent chemoradiotherapy with tomotherapy in locally advanced non-small cell lung cancer: a phase I, docetaxel dose-escalation study, with hypofractionated radiation regimen.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 31;13(1):513.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-513](#)

AUTORES / AUTHORS: - Bearz A; Minatel E; Abu Rumeileh I; Borsatti E; Talamini R; Franchin G; Gobitti C; Del Conte A; Trovo M; Baresic T

RESUMEN / SUMMARY: - BACKGROUND: Concurrent chemo-radiotherapy is demonstrably superior to sequential chemo-radiotherapy in the treatment of advanced

Non-Small-Cell Lung Cancer not suitable for surgery. Docetaxel is considered to enhance the cytotoxic effect of radiotherapy on the tumour cells. Tomotherapy (HT) is a novel radiotherapeutic technique, which allows the delivery of Image Guided-IMRT (IG-IMRT), with a highly conformal radiation dose distribution. The goal of the study was to estimate tolerability of Docetaxel concurrent with IMRT and to find the maximum tolerated dose of weekly Docetaxel concurrent with IMRT delivered with HT Tomotherapy after induction chemotherapy with Cisplatin and Docetaxel in patients affected with stage III Non-Small Cell Lung Cancer. METHODS: We designed a phase I, dose-finding study to determine the dose of weekly Docetaxel concurrent with Tomotherapy after induction chemotherapy, in patients affected by Non-Small Cell Lung Cancer with Stage III disease, not suitable for surgery. RESULTS: Concurrent weekly Docetaxel and Tomotherapy are feasible; we did not reach a maximum tolerated dose, because no life-threatening toxicity was observed, stopping the accrual at a level of weekly docetaxel 38 mg/m², a greater dose than in previous assessments, from both phase-I studies with weekly docetaxel alone and with Docetaxel concomitant with standard radiotherapy. CONCLUSIONS: Concurrent weekly Docetaxel and Tomotherapy are feasible, and even with Docetaxel at 38 mg/m²/week we did not observe any limiting toxicity. For those patients who completed the combined chemo-radio treatment, median progression-free survival (PFS) was 20 months and median overall survival (OS) was 24 months.

[795]

TÍTULO / TITLE: - Bronchopleural fistula following infection 11 years after lobectomy for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Springerplus. 2013 Oct 26;2:568.

●● Enlace al texto completo (gratis o de pago) [1186/2193-1801-2-568](#)

AUTORES / AUTHORS: - Inayama M; Shinohara T; Yoshida M; Hino H; Hatakeyama N; Ogushi F

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary Medicine, National Hospital Organization National Kochi Hospital, 1-2-25 Asakuranishimachi, Kochi, 780-8077 Japan.

RESUMEN / SUMMARY: - Bronchopleural fistula (BPF) is a potentially fatal complication of lung cancer resection surgery that occurs during the healing process of the bronchial stump. However, the vulnerability of the healed surgical wound to overlapping acquired airway destruction has not yet been determined in detail. We herein present a case of fatal BPF following Mycobacterium abscessus (M. abscessus) infection, which occurred 11 years after right upper lobectomy for lung cancer. The findings of the present study suggest that patients with M. abscessus pulmonary disease in which airway destruction is progressing towards the bronchial stump of previous lobectomy should be considered for early completion pneumonectomy to prevent fatal BPF.

[796]

TÍTULO / TITLE: - Automated method for extraction of lung tumors using a machine learning classifier with knowledge of radiation oncologists on data sets of planning CT and FDG-PET/CT images.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Conf Proc IEEE Eng Med Biol Soc. 2013 Jul;2013:2988-91. doi: 10.1109/EMBC.2013.6610168.

●● Enlace al texto completo (gratis o de pago) [1109/EMBC.2013.6610168](https://doi.org/10.1109/EMBC.2013.6610168)

AUTORES / AUTHORS: - Arimura H; Jin Z; Shioyama Y; Nakamura K; Magome T; Sasaki M

RESUMEN / SUMMARY: - We have developed an automated method for extraction of lung tumors using a machine learning classifier with knowledge of radiation oncologists on data sets of treatment planning computed tomography (CT) and 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT images. First, the PET images were registered with the treatment planning CT images through the diagnostic CT images of PET/CT. Second, six voxel-based features including voxel values and magnitudes of image gradient vectors were derived from each voxel in the planning CT and PET /CT image data sets. Finally, lung tumors were extracted by using a support vector machine (SVM), which learned 6 voxel-based features inside and outside each true tumor region determined by radiation oncologists. The results showed that the average DSCs for 3 and 6 features for three cases were 0.744 and 0.899, and thus the SVM may need 6 features to learn the distinguishable characteristics. The proposed method may be useful for assisting treatment planners in delineation of the tumor region.

[797]

TÍTULO / TITLE: - “One-stop shop” spectral imaging for rapid on-site diagnosis of lung cancer: a future concept in nano-oncology.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Nanomedicine. 2013;8:4533-42. doi: 10.2147/IJN.S54418. Epub 2013 Nov 22.

●● Enlace al texto completo (gratis o de pago) [2147/IJN.S54418](https://doi.org/10.2147/IJN.S54418)

AUTORES / AUTHORS: - Darwiche K; Zarogoulidis P; Krauss L; Oezkan F; Walter RF; Werner R; Theegarten D; Sakkas L; Sakkas A; Hohenforst-Schmidt W; Zarogoulidis K; Freitag L

INSTITUCIÓN / INSTITUTION: - Department of Interventional Pneumology, Ruhrlandklinik, West German Lung Center, University Hospital, University Duisburg-Essen, Essen, Germany.

RESUMEN / SUMMARY: - BACKGROUND: There are currently many techniques and devices available for the diagnosis of lung cancer. However, rapid on-site diagnosis is essential for early-stage lung cancer, and in the current work we investigated a new diagnostic illumination nanotechnology. METHODS: Tissue samples were obtained from lymph nodes, cancerous tissue, and abnormal intrapulmonary lesions at our interventional pulmonary suites. The following diagnostic techniques were used to obtain the samples: endobronchial ultrasound bronchoscopy; flexible bronchoscopy; and rigid bronchoscopy. Flexible and rigid forceps were used because several of the patients were intubated using a rigid bronchoscope. In total, 30 tissue specimens from 30 patients were prepared. CytoViva® illumination nanotechnology was subsequently applied to each of the biopsy tissue slides. RESULTS: A spectral library was created for adenocarcinoma, epidermal growth factor receptor mutation-positive adenocarcinoma, squamous cell carcinoma, usual interstitial pneumonitis, non-specific interstitial pneumonitis, typical carcinoid tumor, sarcoidosis, idiopathic pulmonary fibrosis, small cell neuroendocrine carcinoma, thymoma, epithelioid and sarcomatoid

mesothelioma, cryptogenic organizing pneumonia, malt cell lymphoma, and Wegener's granulomatosis. CONCLUSION: The CytoViva software, once it had created a specific spectral library for each entity, was able to identify the same disease again in subsequent paired sets of slides of the same disease. Further evaluation of this technique could make this illumination nanotechnology an efficient rapid on-site diagnostic tool.

[798]

TÍTULO / TITLE: - Pulmonary alveolar microlithiasis with concurrent pleural mesothelioma in a dog.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Vet Diagn Invest. 2013 Nov;25(6):798-802. doi: 10.1177/1040638713504571. Epub 2013 Sep 30.

●● Enlace al texto completo (gratis o de pago) 1177/1040638713504571

AUTORES / AUTHORS: - de Brot S; Hilbe M

INSTITUCIÓN / INSTITUTION: - Simone de Brot, Institute of Veterinary Pathology, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 268, CH-8057 Zurich, Switzerland. simone.debrot@uzh.ch.

RESUMEN / SUMMARY: - Pulmonary alveolar microlithiasis (PAM) is a rare pulmonary disorder characterized by the accumulation of calcium phosphate microliths within the alveoli, with only a few cases described in animals. A 10-year-old female Bulldog was euthanized due to history of dyspnea and recurrent pleural and pericardial effusions. At necropsy, numerous multifocal to coalescent protruding nodules of 1-5 mm in diameter were scattered throughout the thoracic serosal surfaces. Moreover, lungs showed a diffuse pale gray color and had a generalized fine grainy consistency. Histological investigations revealed abundant intra-alveolar laminated microliths that stained positive with periodic acid-Schiff and von Kossa stains. The pulmonary interstitium showed multifocal, mild to moderate thickening, due to collagen deposition and mild hyperplasia of type 2 pneumocytes. The pulmonary lesion was not associated with any inflammatory response, and mineral deposition was not observed in any other organ or tissue. In addition, pulmonary, pericardial, and pleural surfaces were extensively infiltrated by an epithelioid mesothelioma. Immunohistochemical staining revealed neoplastic cells that strongly coexpressed vimentin and cytokeratin, supporting the diagnosis of mesothelioma. An overview of PAM, including pathogenesis and histological characteristics, are discussed in relation to the concurrent pleural mesothelioma. The potential cause and effect relationship between the 2 conditions could neither be established nor ruled out.

[799]

TÍTULO / TITLE: - Spontaneous pneumothorax as the initial manifestation of stage I B primary pulmonary carcinoma: Really early stage cancer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S118-20. doi: 10.4103/0973-1482.119125.

●● Enlace al texto completo (gratis o de pago) 4103/0973-1482.119125

AUTORES / AUTHORS: - Jiang H; Ma W; Zhang JP; Zhang L

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Shandong Provincial Hospital Affiliated to Shandong University, Jinan, 250021, China.

RESUMEN / SUMMARY: - Spontaneous pneumothorax (SP) is a rare manifestation of lung cancers, especially as the first sign. The mechanism producing pneumothorax from pulmonary cancer has three main reasons, One is that the cancer necrosis directly ruptured into the pleural space. Another is that endobronchial neoplasm acts as a check valve, leading to dilation and eventual rupture of distal alveolar spaces. The third is that the rupture of small subpleural blebs accidentally causes SP. However, the prognosis of lung cancer patients with initial manifestation of SP is very poor, SP seems to be an ominous sign for the primary cavity lung cancer patients, even in an early stage.

[800]

TÍTULO / TITLE: - Differential Effects of Drugs Targeting Cancer Stem Cell (CSC) and Non-CSC Populations on Lung Primary Tumors and Metastasis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 20;8(11):e79798. doi: 10.1371/journal.pone.0079798.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0079798](#)

AUTORES / AUTHORS: - Larzabal L; El-Nikhely N; Redrado M; Seeger W; Savai R; Calvo A

INSTITUCIÓN / INSTITUTION: - Laboratory of Novel Therapeutic Targets, Division of Oncology, CIMA of the University of Navarra, Pamplona, España.

RESUMEN / SUMMARY: - Cancer stem cells (CSCs) are thought to be responsible for tumor initiation and recurrence after chemotherapy. Targeting CSCs and non-CSCs with specific compounds may be an effective approach to reduce lung cancer growth and metastasis. The aim of this study was to investigate the effect of salinomycin, a selective inhibitor of CSCs, with or without combination with paclitaxel, in a metastatic model. To evaluate the effect of these drugs in metastasis and tumor microenvironment we took advantage of the immunocompetent and highly metastatic LLC mouse model. Aldefluor assays were used to analyze the ALDH+/- populations in murine LLC and human H460 and H1299 lung cancer cells. Salinomycin reduced the proportion of ALDH+ CSCs in LLC cells, whereas paclitaxel increased such population. The same effect was observed for the H460 and H1299 cell lines. Salinomycin reduced the tumorsphere formation capacity of LLC by more than 7-fold, but paclitaxel showed no effect. In in vivo experiments, paclitaxel reduced primary tumor volume but increased the number of metastatic nodules ($p < 0.05$), whereas salinomycin had no effect on primary tumors but reduced lung metastasis ($p < 0.05$). Combination of both drugs did not improve the effect of single therapies. ALDH1A1, SOX2, CXCR4 and SDF-1 mRNA levels were higher in metastatic lesions than in primary tumors, and were significantly elevated in both locations by paclitaxel treatment. On the contrary, such levels were reduced (or in some cases did not change) when mice were administered with salinomycin. The number of F4/80+ and CD11b+ cells was also reduced upon administration of both drugs, but particularly in metastasis. These results show that salinomycin targets ALDH+ lung CSCs, which has important therapeutic effects in vivo by reducing metastatic lesions. In contrast, paclitaxel (although reducing primary tumor growth) promotes the selection of ALDH+ cells that likely modify the lung microenvironment to foster metastasis.

[801]

TÍTULO / TITLE: - CD24+/CD38- as new prognostic marker for non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Multidiscip Respir Med. 2013 Oct 5;8(1):65. doi: 10.1186/2049-6958-8-65.

●● Enlace al texto completo (gratis o de pago) [1186/2049-6958-8-65](#)

AUTORES / AUTHORS: - Karimi-Busheri F; Rasouli-Nia A; Zadorozhny V; Fakhrai H

INSTITUCIÓN / INSTITUTION: - Stem Cell Department, NovaRx Corporation, 6828 Nancy Ridge Drive, San Diego, USA. fkarimi@ualberta.ca.

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the leading cause of death among cancers in the world. The annual death toll due to this disease exceeds the combined deaths caused by colon, breast, prostate, and pancreatic cancers. As a result, there has been a tremendous effort to identify new biomarkers for early detection and diagnosis of lung cancer. METHODS: In this study we report the results of screening a panel of eight non-small cell lung cancer (NSCLC) cell lines originating from different subtypes of lung cancer in an attempt to identify potential biomarkers unique to this disease. We used real-time polymerase chain reaction and flow cytometry techniques to analyze the expression of ALDH1, EpCAM, CD133, CD24, and CD38 in this panel. RESULTS: We demonstrate for the first time that the majority of NSCLC cells do not express levels of CD38 that would qualify it as a new biomarker for the disease. In contrast, we found that CD24 is over-expressed in 6 out of 8 of the cell lines. The combined CD24+/CD38-/low phenotype was detected in 50% of the cell lines that are also positive for CD133 and EpCAM. CONCLUSIONS: We report that CD24+/CD38-/low signature could potentially be used as a new biomarker for the early detection of NSCLC.

[802]

TÍTULO / TITLE: - Sequential Targeted Delivery of Paclitaxel and Camptothecin Using a Cross-Linked “Nanosponge” Network for Lung Cancer Chemotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Pharm. 2013 Nov 22.

●● Enlace al texto completo (gratis o de pago) [1021/mp400432b](#)

AUTORES / AUTHORS: - Hariri G; Edwards AD; Merrill TB; Greenbaum JM; van der Ende AE; Harth E

INSTITUCIÓN / INSTITUTION: - Department of Chemistry, Vanderbilt University, 7618 Stevenson Center, Nashville, Tennessee 37235-1822, United States.

RESUMEN / SUMMARY: - The applicability of a HVGGSV peptide targeted “nanosponge” drug delivery system for sequential administration of a microtubule inhibitor (paclitaxel) and topoisomerase I inhibitor (camptothecin) was investigated in a lung cancer model. Schedule-dependent combination treatment with nanoparticle paclitaxel (NP PTX) and camptothecin (NP CPT) was studied in vitro using flow cytometry and confocal imaging to analyze changes in cell cycle, microtubule morphology, apoptosis, and cell proliferation. Results showed significant G2/M phase cell cycle arrest, changes in microtubule dynamics that produced increased apoptotic cell death and decreased proliferation with initial exposure to NP PTX, followed by NP CPT in lung cancer cells. In vivo molecular imaging and TEM studies validated

HVGGSSV-NP tumor binding at 24 h and confirmed the presence of Nanogold labeled HVGGSSV-NPs in tumor microvascular endothelial cells. Therapeutic efficacy studies conducted with sequential HVGGSSV targeted NP PTX and NP CPT showed 2-fold greater tumor growth delay in combination versus monotherapy treated groups, and 4-fold greater delay compared to untargeted and systemic drug controls. Analytical HPLC/MS methods were used to quantify drug content in tumor tissues at various time points, with significant paclitaxel and camptothecin levels in tumors 2 days postinjection and continued presence of both drugs up to 23 days postinjection. The efficacy of the NP delivery system in sequential treatments was corroborated in both in vitro and in vivo lung cancer models showing increased G2/M phase arrest and microtubule disruption, resulting in enhanced apoptotic cell death, decreased cell proliferation and vascular density.

[803]

TÍTULO / TITLE: - Genomic and Transcriptional Alterations in Lung Adenocarcinoma in Relation to EGFR and KRAS Mutation Status.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 24;8(10):e78614. doi: 10.1371/journal.pone.0078614.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078614](#)

AUTORES / AUTHORS: - Planck M; Edlund K; Botling J; Micke P; Isaksson S; Staaf J
INSTITUCIÓN / INSTITUTION: - Department of Oncology, Clinical Sciences, Lund University and Skane University Hospital, Medicon Village, Lund, Sweden.

RESUMEN / SUMMARY: - INTRODUCTION: In lung adenocarcinoma, the mutational spectrum is dominated by EGFR and KRAS mutations. Improved knowledge about genomic and transcriptional alterations in and between mutation-defined subgroups may identify genes involved in disease development or progression. METHODS: Genomic profiles from 457 adenocarcinomas, including 113 EGFR-mutated, 134 KRAS-mutated and 210 EGFR and KRAS-wild type tumors (EGFRwt/KRASwt), and gene expression profiles from 914 adenocarcinomas, including 309 EGFR-mutated, 192 KRAS-mutated, and 413 EGFRwt/KRASwt tumors, were assembled from different repositories. Genomic and transcriptional differences between the three mutational groups were analyzed by both supervised and unsupervised methods. RESULTS: EGFR-mutated adenocarcinomas displayed a larger number of copy number alterations and recurrent amplifications, a higher fraction of total loss-of-heterozygosity, higher genomic complexity, and a more distinct expression pattern than EGFR-wild type adenocarcinomas. Several of these differences were also consistent when the three mutational groups were stratified by stage, gender and smoking status. Specific copy number alterations were associated with mutation status, predominantly including regions of gain with the highest frequency in EGFR-mutated tumors. Differential regions included both large and small regions of gain on 1p, 5q34-q35.3, 7p, 7q11.21, 12p12.1, 16p, and 21q, and losses on 6q16.3-q21, 8p, and 9p, with 20-40% frequency differences between the mutational groups. Supervised gene expression analyses identified 96 consistently differentially expressed genes between the mutational groups, and together with unsupervised analyses these analyses highlighted the difficulty in broadly resolving the three mutational groups into distinct transcriptional entities. CONCLUSIONS: We provide a comprehensive overview of the genomic and transcriptional landscape in lung adenocarcinoma stratified by EGFR and KRAS

mutations. Our analyses suggest that the overall genomic and transcriptional landscape of lung adenocarcinoma is affected, but only to a minor extent, by EGFR and KRAS mutation status.

[804]

TÍTULO / TITLE: - The anti-lung cancer activities of steroidal saponins of *P. polyphylla* Smith var. *chinensis* (Franch.) Hara through enhanced immunostimulation in experimental Lewis tumor-bearing C57BL/6 mice and induction of apoptosis in the A549 cell line.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - *Molecules*. 2013 Oct 17;18(10):12916-36. doi: 10.3390/molecules181012916.

●● [Enlace al texto completo \(gratis o de pago\) 3390/molecules181012916](#)

AUTORES / AUTHORS: - Li Y; Gu JF; Zou X; Wu J; Zhang MH; Jiang J; Qin D; Zhou JY; Liu BX; Zhu YT; Jia XB; Feng L; Wang RP

INSTITUCIÓN / INSTITUTION: - Department of Oncology, the Affiliated Hospital of Nanjing University of Chinese Medicine, No.155, Hanzhong Road, Nanjing 210029, Jiangsu, China. wenmoxiushi@163.com.

RESUMEN / SUMMARY: - *P. polyphylla* Smith var. *chinensis* (Franch.) Hara (PPSCFH) has been used as medicinal plant for the prevention and treatment of cancers in China for thousands of years. Its main components, steroidal saponins (PRS), have been confirmed to inhibit tumor growth. In the present study, the immunostimulation of PRS was investigated in Lewis bearing-C57BL/6 mice while the induction of apoptosis in A549 cells was also studied. The treatment with PRS (2.5, 5.0 and 7.5 mg/kg) significantly inhibited tumor, volume, and weight in the C57BL/6 mice. The rates of inhibition of PRS (at 2.5, 5.0 and 7.5 mg/kg) were 26.49 +/- 17.30%, 40.32 +/- 18.91% and 54.94 +/- 16.48%, respectively. The spleen and thymus indexes were increased remarkably, while the levels of inflammatory cytokines including TNF-alpha, IL-8 and IL-10 in serum were decreased according to ELISA assays. For A549 cells, Hoechst 33342 staining and annexin V/PI by flow cytometry showed that PRS (0.25, 0.50 and 0.75 mg/mL) induced nuclear changes of A549 cells with DNA condensation and fragmentations of chromatin, as well as inducing apoptosis. Furthermore, PRS could also attenuate the over-generation of intracellular ROS. Western blotting analysis showed a significant decrease on the expressions of proinflammatory cytokines MCP-1, IL-6 and TGF-beta1, as well as cell adhesion molecule ICAM-1, by treatment with PRS. Our results demonstrated that the inhibition of PRS on tumor growth might be associated with the amelioration of inflammation responses, induction of apoptosis, as well as the decrease of ROS. These results suggested that PRS implied a potential therapeutic effect in the lung cancer treatment.

[805]

TÍTULO / TITLE: - A Combination of Alkaloids and Triterpenes of *Alstonia scholaris* (Linn.) R. Br. Leaves Enhances Immunomodulatory Activity in C57BL/6 Mice and Induces Apoptosis in the A549 Cell Line.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - *Molecules*. 2013 Nov 12;18(11):13920-39. doi: 10.3390/molecules181113920.

●● [Enlace al texto completo \(gratis o de pago\) 3390/molecules181113920](#)

AUTORES / AUTHORS: - Feng L; Chen Y; Yuan L; Liu X; Gu JF; Zhang MH; Wang Y

INSTITUCIÓN / INSTITUTION: - Key Laboratory of New Drug Delivery Systems of Chinese Meteria Medica, Jiangsu Provincial Academy of Chinese Medicine, Nanjing 210028, Jiangsu, China. ychen202@hotmail.com.

RESUMEN / SUMMARY: - Experiments were conducted to evaluate the induction of apoptosis and the immunomodulatory activities of alkaloids and triterpenes of *Alstonia scholaris* (Linn.) R. Br. leaves (ASL). Importantly, their possible synergistic properties were also explored in this study. Human lung adenocarcinoma cell line A549 and Lewis tumor-bearing C57BL/6 mice were used for the evaluation of their activities. A MTT assay was used to determine the proliferation inhibition in A549 cells. Annexin-V/PI double staining as well as flow cytometry was performed to detect apoptosis and cell cycle status. Enzyme-linked immunosorbent assay (ELISA) was conducted to determine the levels of inflammatory mediators interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha) in serum. Furthermore, western blot analysis was applied to evaluate the expressions of proteins associated with cell death. Alkaloids or triterpenes showed a high anti-proliferative activity in A549 cells, with IC50 values of 14.4 microg/mL and 9.3 microg/mL, respectively. The alkaloids and triterpenes combination could significantly inhibit tumor growth in tumor-bearing C57BL/6 mice, compared with alkaloids or triterpenes alone (7.5, 15, 30 g raw material/kg). The immune organs indexes including spleen index and thymus index were increased remarkably by the combination of alkaloids and triterpenes, whereas the levels of IL-6 and TNF-alpha were up-regulated significantly. Moreover, Annexin-V/PI double staining and flow cytometry showed that the combination of alkaloids and triterpenes (1, 2 and 3 mg raw material/kg) could induce apoptosis and cause S cell cycle arrest in A549 cells. Western blot analysis also showed that their combination (2 mg raw material/kg) significantly down-regulated Bcl-2 expression and pro-casp8 level, whereas it remarkably increased the level of cleaved caspase-8 leading to apoptosis in A549 cells. These observations provide preliminary evidence that both alkaloids and triterpenes possess immune regulation and induction apoptosis activities. Their combination has a stronger activity than that of either class alone. Our findings suggested that these components might be beneficial for the prevention and treatment of NSCLC through a significant synergy effect.

[806]

TÍTULO / TITLE: - Aberrant Mucin5B expression in lung adenocarcinomas detected by iTRAQ labeling quantitative proteomics and immunohistochemistry.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Proteomics. 2013 Nov 1;10(1):15.

●● Enlace al texto completo (gratis o de pago) [1186/1559-0275-10-15](#)

AUTORES / AUTHORS: - Li Y; Wang X; Ao M; Gabrielson E; Askin F; Zhang H; Li QK

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer is the number one cause of cancer-related deaths in the United States and worldwide. The complex protein changes and/or signature of protein expression in lung cancer, particularly in non-small cell lung cancer (NSCLC) has not been well defined. Although several studies have investigated the protein profile in lung cancers, the knowledge is far from complete. Among early studies, mucin5B (MUC5B) has been suggested to play an important role in the tumor progression. MUC5B is the major gel-forming mucin in the airway. In this study, we investigated the overall protein profile and MUC5B expression in lung

adenocarcinomas, the most common type of NSCLCs. METHODS: Lung adenocarcinoma tissue in formalin-fixed paraffin-embedded (FFPE) blocks was collected and microdissected. Peptides from 8 tumors and 8 tumor-matched normal lung tissue were extracted and labeled with 8-channel iTRAQ reagents. The labeled peptides were identified and quantified by LC-MS/MS using an LTQ Orbitrap Velos mass spectrometer. MUC5B expression identified by iTRAQ labeling was further validated using immunohistochemistry (IHC) on tumor tissue microarray (TMA). RESULTS: A total of 1288 peptides from 210 proteins were identified and quantified in tumor tissues. Twenty-two proteins showed a greater than 1.5-fold differences between tumor and tumor-matched normal lung tissues. Fifteen proteins, including MUC5B, showed significant changes in tumor tissues. The aberrant expression of MUC5B was further identified in 71.1% of lung adenocarcinomas in the TMA. Discussions: A subset of tumor-associated proteins was differentially expressed in lung adenocarcinomas. The differential expression of MUC5B in lung adenocarcinomas suggests its role as a potential biomarker in the detection of adenocarcinomas.

[807]

TÍTULO / TITLE: - SIRT1 is highly expressed in brain metastasis tissues of non-small cell lung cancer (NSCLC) and in positive regulation of NSCLC cell migration.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Oct 15;6(11):2357-65.

AUTORES / AUTHORS: - Han L; Liang XH; Chen LX; Bao SM; Yan ZQ

INSTITUCIÓN / INSTITUTION: - The Experimental Animal Center, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences Shanghai, China.

RESUMEN / SUMMARY: - Brain metastases are a frequent and ongoing major complication of non-small cell lung cancer (NSCLC). To deepen our understanding to the underlying mechanisms by which NSCLC cells metastasize to brain and hence to improve the therapy, a high throughput RNAi screening with shRNA library of 153 epigenetic genes was subjected to A549, a NSCLC cell line with high migration ability, to examine the effects of these genes on cell migration by wound-healing assay. The screening results showed that knockdown of 2 genes (KDM5B and SIRT1) dramatically and specifically inhibits A549 migration but not affects the proliferation, which was subsequently confirmed through transwell migration assay. Furthermore, SIRT1 is found to be highly expressed in brain metastasis tissues of NSCLC, compared to the NSCLC tissues, suggesting that SIRT1 may play roles in brain metastasis of NSCLC. The relationship between SIRT1 expression and cell migration ability was further investigated in three NSCLC cell lines and the result indicated that SIRT1 expression is tightly correlated with cell migration ability. Collectively, our work provides potential biomarker and therapeutic target for brain metastasis of NSCLC.

[808]

TÍTULO / TITLE: - Stat3 Inhibits PTPN13 Expression in Squamous Cell Lung Carcinoma through Recruitment of HDAC5.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:468963. doi: 10.1155/2013/468963. Epub 2013 Sep 26.

●● [Enlace al texto completo \(gratis o de pago\) 1155/2013/468963](#)

AUTORES / AUTHORS: - Han XJ; Xue L; Gong L; Zhu SJ; Yao L; Wang SM; Lan M; Zhang W; Li YH

INSTITUCIÓN / INSTITUTION: - The Helmholtz Sino-German Research Laboratory for Cancer, Department of Pathology, Tangdu Hospital, The Fourth Military Medical University, Xi'an 710038, China.

RESUMEN / SUMMARY: - Proteins of the protein tyrosine phosphatase (PTP) family are known to be signaling molecules that regulate a variety of cellular processes including cell growth, differentiation, and apoptosis. PTPN13 (also known as FAP1, PTPL1, PTPLE, PTPBAS, and PTP1E), a putative tumor suppressor, is frequently inactivated in lung carcinoma through the loss of either mRNA or protein expression. However, the molecular mechanisms underlying its dysregulation have not been fully explored. Interleukin-6 (IL-6) mediated Stat3 activation is viewed as crucial for multiple tumor growth and progression. Here, we demonstrate that PTPN13 is a direct transcriptional target of Stat3 in the squamous cell lung carcinoma. Our data show that IL-6 administration or transfection of a constitutively activated Stat3 in HCC-1588 and SK-MES-1 cells inhibits PTPN13 mRNA transcription. Using luciferase reporter and ChIP assays, we show that Stat3 binds to the promoter region of PTPN13 and promotes its activity through recruiting HDAC5. Thus, our results suggest a previously unknown Stat3-PTPN13 molecular network controlling squamous cell lung carcinoma development.

[809]

TÍTULO / TITLE: - Expression of Id-1 and VEGF in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Sep 15;6(10):2102-11.

AUTORES / AUTHORS: - Kim MS; Park TI; Lee YM; Jo YM; Kim S

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Kyungpook National University Hospital 130 Dongdeok-ro, Jung-gu, Deagu, South Korea.

RESUMEN / SUMMARY: - Angiogenesis is essential for invasive tumor growth and metastasis. Bevacizumab has been widely used for the treatment of non-small cell lung cancer (NSCLC). Various studies clearly demonstrate the relevance of Id-1 and VEGF in angiogenesis. The aim of this study was to establish the role of Id-1 expression in tumor progression and angiogenesis in relation to VEGF in NSCLC. Seventy five patients underwent surgery for lung cancers. The expressions of Id-1 and VEGF in NSCLC samples were determined by immunohistochemistry. Expression of Id-1 and VEGF showed a close correlation in NSCLC ($p < 0.001$). In addition, Id-1 strong expression group showed high incidence of metastasis in multivariate analysis ($p = 0.028$). Id-1 strong expression group had short metastasis-free survival ($p = 0.008$) and short recurrence-free survival ($p = 0.027$). Strong Id-1 expression in NSCLC had a poor prognosis in association with VEGF expression. Id-1 may function in tumor growth and progression via angiogenesis. Therefore, Id-1 is considered to be a candidate for new therapeutic target and a prognostic factor in NSCLC.

[810]

TÍTULO / TITLE: - Differential expression and subcellular localization of Prohibitin 1 are related to tumorigenesis and progression of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Int J Clin Exp Pathol. 2013 Sep 15;6(10):2092-101.

AUTORES / AUTHORS: - Jiang P; Xiang Y; Wang YJ; Li SM; Wang Y; Hua HR; Yu GY; Zhang Y; Lee WH; Zhang Y

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Animal Models and Human Disease Mechanisms of The Chinese Academy of Sciences & Yunnan Province, Kunming Institute of Zoology, Chinese Academy of Sciences Kunming, Yunnan 650223, China ; University of Chinese Academy of Sciences Beijing 100049, China ; Department of Pathology and Pathophysiology, Kunming Medical University Kunming, Yunnan 650500, China.

RESUMEN / SUMMARY: - Lung cancer remains the leading cause of cancer-related deaths worldwide and non-small cell lung cancer (NSCLC) accounts for approximately 85% of all lung cancer. With a variety of biological functions, Prohibitin1 (PHB1) has been proved tumor-associated. But there are conflicting data regarding the involvement of PHB1 in tumorigenesis and few studies regarding the role of PHB1 in lung cancer. The studies reported herein used a combination of clinical observations and molecular methods to investigate the possible role of PHB1 in NSCLC tissues and cell lines. PHB1 expression was evaluated by RT-PCR, RT-qPCR, Western blotting and immunohistochemistry analysis. Flow cytometric analysis was used to determine the surface expression profiles of PHB1 in lung cell lines. The results showed that PHB1 expression were generally increased in lung cancer tissues when compared with matched noncancerous tissues and closely related with tumor differentiation and lymph node invasion. PHB1 expression levels was also increased in three lung cancer cell lines (SK-MES-1, NCI-H157 and NCI-H292) as compared with BEAS-2B cells. Moreover, there were various subcellular localization of PHB1 in different lung cancer cells and the presence of PHB1 on the surface of lung cancer cells was significantly reduced. In conclusion, PHB1 expression is increased in NSCLC and the up-regulation of PHB1 is associated with clinically aggressive phenotype. The different subcellular localization of PHB1 in NSCLC cells and the loss of the membrane-associated PHB1 probably related to the tumorigenesis and progression of NSCLC and suggests that PHB1 may play different roles in various types of NSCLC.

[811]

TÍTULO / TITLE: - Characterization of Lung Cancer by Amide Proton Transfer (APT) Imaging: An In-Vivo Study in an Orthotopic Mouse Model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 15;8(10):e77019. doi: 10.1371/journal.pone.0077019.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077019](#)

AUTORES / AUTHORS: - Togao O; Kessinger CW; Huang G; Soesbe TC; Sagiya K; Dimitrov I; Sherry AD; Gao J; Takahashi M

INSTITUCIÓN / INSTITUTION: - Advanced Imaging Research Center, Harold C. Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, Texas, United States of America.

RESUMEN / SUMMARY: - Amide proton transfer (APT) imaging is one of the chemical exchange saturation transfer (CEST) imaging methods which images the exchange between protons of free tissue water and the amide groups (-NH) of endogenous mobile proteins and peptides. Previous work suggested the ability of APT imaging for characterization of the tumoral grade in the brain tumor. In this study, we tested the feasibility of in-vivo APT imaging of lung tumor and investigated whether the method

could differentiate the tumoral types on orthotopic tumor xenografts from two malignant lung cancer cell lines. The results revealed that APT imaging is feasible to quantify lung tumors in the moving lung. The measured APT effect was higher in the tumor which exhibited more active proliferation than the other. The present study demonstrates that APT imaging has the potential to provide a characterization test to differentiate types or grade of lung cancer noninvasively, which may eventually reduce the need invasive needle biopsy or resection for lung cancer.

[812]

TÍTULO / TITLE: - eComment. Positron emission tomography reduces the incidence of surgery for non-malignant conditions in lung cancer screening programmes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Interact Cardiovasc Thorac Surg. 2013 Dec;17(6):973. doi: 10.1093/icvts/ivt458.

●● Enlace al texto completo (gratis o de pago) [1093/icvts/ivt458](#)

AUTORES / AUTHORS: - Scanagatta P; Sestini S

INSTITUCIÓN / INSTITUTION: - Division of Thoracic Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy.

[813]

TÍTULO / TITLE: - The long non-coding RNA HOTAIR indicates a poor prognosis and promotes metastasis in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 8;13:464. doi: 10.1186/1471-2407-13-464.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-464](#)

AUTORES / AUTHORS: - Liu XH; Liu ZL; Sun M; Liu J; Wang ZX; De W

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry and Molecular Biology, Nanjing Medical University, Nanjing, Jiangsu 210029, People's Republic of China. zhaoxiawang88@hotmail.com.

RESUMEN / SUMMARY: - BACKGROUND: The identification of cancer-associated long non-coding RNAs and the investigation of their molecular and biological functions are important for understanding the molecular biology and progression of cancer. HOTAIR (HOX transcript antisense intergenic RNA) has been implicated in several cancers; however, its role in non-small cell lung cancer (NSCLC) is unknown. The aim of the present study was to examine the expression pattern of HOTAIR in NSCLC and to evaluate its biological role and clinical significance in tumor progression. METHODS: Expression of HOTAIR was analyzed in 42 NSCLC tissues and four NSCLC cell lines by quantitative reverse-transcription polymerase chain reaction (qRT-PCR). Over-expression and RNA interference (RNAi) approaches were used to investigate the biological functions of HOTAIR. The effect of HOTAIR on proliferation was evaluated by MTT and colony formation assays, and cell migration and invasion were evaluated by transwell assays. Tail vein injection of cells was used to study metastasis in nude mice. Protein levels of HOTAIR targets were determined by western blot analysis. Differences between groups were tested for significance using Student's t-test (two-tailed). RESULTS: HOTAIR was highly expressed both in NSCLC samples and cell lines compared with corresponding normal counterparts. HOTAIR upregulation was correlated with NSCLC advanced pathological stage and lymph-node metastasis.

Moreover, patients with high levels of HOTAIR expression had a relatively poor prognosis. Inhibition of HOTAIR by RNAi decreased the migration and invasion of NSCLC cells in vitro and impeded cell metastasis in vivo. HOXA5 levels were affected by HOTAIR knockdown or over-expression in vitro. CONCLUSIONS: Our findings indicate that HOTAIR is significantly up-regulated in NSCLC tissues, and regulates NSCLC cell invasion and metastasis, partially via the down-regulation of HOXA5. Thus, HOTAIR may represent a new marker of poor prognosis and is a potential therapeutic target for NSCLC intervention.

[814]

TÍTULO / TITLE: - Microfluidic purification and concentration of malignant pleural effusions for improved molecular and cytomorphological diagnostics.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 28;8(10):e78194. doi: 10.1371/journal.pone.0078194.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078194](#)

AUTORES / AUTHORS: - Che J; Mach AJ; Go DE; Talati I; Ying Y; Rao J; Kulkarni RP; Di Carlo D

INSTITUCIÓN / INSTITUTION: - Department of Bioengineering, University of California Los Angeles, Los Angeles, California, United States of America.

RESUMEN / SUMMARY: - Evaluation of pleural fluids for metastatic cells is a key component of diagnostic cytopathology. However, a large background of smaller leukocytes and/or erythrocytes can make accurate diagnosis difficult and reduce specificity in identification of mutations of interest for targeted anti-cancer therapies. Here, we describe an automated microfluidic system (Centrifuge Chip) which employs microscale vortices for the size-based isolation and concentration of cancer cells and mesothelial cells from a background of blood cells. We are able to process non-diluted pleural fluids at 6 mL/min and enrich target cells significantly over the background; we achieved improved purity in all patient samples analyzed. The resulting isolated and viable cells are readily available for immunostaining, cytological analysis, and detection of gene mutations. To demonstrate the utility towards aiding companion diagnostics, we also show improved detection accuracy of KRAS gene mutations in lung cancer cells processed using the Centrifuge Chip, leading to an increase in the area under the curve (AUC) of the receiver operating characteristic from 0.90 to 0.99. The Centrifuge Chip allows for rapid concentration and processing of large volumes of bodily fluid samples for improved cytological diagnosis and purification of cells of interest for genetic testing, which will be helpful for enhancing diagnostic accuracy.

[815]

TÍTULO / TITLE: - PET/CT vs. non-contrast CT alone for surveillance 1-year post lobectomy for stage I non-small-cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Nucl Med Mol Imaging. 2013 Sep 19;3(5):408-16.

AUTORES / AUTHORS: - Dane B; Grechushkin V; Plank A; Moore W; Bilfinger T

INSTITUCIÓN / INSTITUTION: - New York University Langone Medical Center 550 First Avenue, New York, NY, USA.

RESUMEN / SUMMARY: - (18)F-FDG PET/CT was compared with non-contrast chest CT in monitoring for recurrence 1-year after lobectomy of stage 1 non-small-cell lung

cancer (NSCLC). For surveillance after treatment with curative intent, current (April 2012) National Comprehensive Cancer network guidelines recommend chest CT with or without contrast every 6-12 months for 2 years, then non-contrast chest CT annually. PET/CT is not currently indicated for routine follow-up. One hundred patients receiving surveillance PET/CT 1-year after lobectomy for the treatment of stage 1a or 1b NSCLC were included in the study. Exclusion criteria included the presence or interval diagnosis of a second malignancy, or surgical treatment more radical than single lobectomy. The non-contrast CT obtained from the 1-year PET/CT was interpreted by an experienced chest radiologist blinded to the PET/CT for evidence of recurrence using the following findings: pulmonary nodule, pleural effusion, pleural mass, adenopathy, and extrathoracic mass. The decision about recurrence was made solely from the non-contrast CT without PET/CT findings. This was compared with the determination made with PET/CT. The reference standard for determination of recurrence was the multi-disciplinary tumor board who had access to all imaging and clinical data. Recurrence at 1 year was documented in 16 of 90 patients. All 16 recurrences were documented with PET/CT and 9 were found with non-contrast CT. Five of the 7 recurrences missed with non-contrast CT were extrathoracic metastases. Sensitivity of CT and PET/CT for recurrence was 56.3% and 100%, respectively ($p = 0.015$). Specificity of CT and PET/CT for recurrence was 95.9% and 93.2%, respectively ($p = 0.62$).

[816]

TÍTULO / TITLE: - Higher Incidence of Lung Adenocarcinomas Induced by DMBA in Connexin 43 Heterozygous Knockout Mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:618475. doi: 10.1155/2013/618475. Epub 2013 Oct 3.

●● [Enlace al texto completo \(gratis o de pago\) 1155/2013/618475](#)

AUTORES / AUTHORS: - Duro de Oliveira K; Vannucci Tedardi M; Cogliati B; Zaidan Dagli ML

INSTITUCIÓN / INSTITUTION: - Department of Pathology, School of Veterinary Medicine and Animal Science, University of Sao Paulo, Avenue Professor Dr. Orlando Marques de Paiva 87, 05508-900 Sao Paulo, SP, Brazil.

RESUMEN / SUMMARY: - Gap junctions are communicating junctions which are important for tissue homeostasis, and their disruption is involved in carcinogenic processes. This study aimed to verify the influence of deletion of one allele of the Connexin 43 gene on cancer incidence in different organs. The 7, 12-dimethylbenzanthracene (DMBA) carcinogenic model, using hebdomadary doses by gavage of 9 mg per animal, was used to induce tumors in Connexin 43 heterozygous or wild-type mice. The experiment began in the eighth week of the mice life, and all of them were euthanized when reaching inadequate physical condition, or at the end of 53 weeks. No statistical differences occurred for weight gain and cancer survival time ($P = 0.9853$) between heterozygous and wild-type mice. Cx43(+/-) mice presented significantly higher susceptibility to lung cancer ($P = 0.0200$) which was not evidenced for benign neoplasms ($P = 0.3449$). In addition, incidence of ovarian neoplasms was 2.5-fold higher in Cx43(+/-) mice, although not statistically significant. Other organs showed a very similar cancer occurrence between Cx43 groups. The experiment

strengthens the evidence of the relationship between Connexin 43 deficiency and carcinogenesis.

[817]

TÍTULO / TITLE: - Pleuropulmonary Blastoma: A Case Report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Turk Patoloji Derg. 2013 Sep 24. doi: 10.5146/tjpath.2013.01191.

●● Enlace al texto completo (gratis o de pago) [5146/tjpath.2013.01191](#)

AUTORES / AUTHORS: - Ekmekci S; Aysal A; Olgun N; Olguner M; Cakmakci H; Ozer E

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Dokuz Eylul University, Faculty of Medicine, IZMIR, TURKEY.

RESUMEN / SUMMARY: - Pleuropulmonary blastoma is rare embryonal tumor of infancy and early childhood and it often arises from lung and more rarely from the parietal pleura. We present this entity which has no systematic data associated with its incidence in order to discuss clinical, histopathological, immunohistochemical features and the differential diagnosis. A three-year-old boy presented with fever showed signs of upper respiratory tract infection. Radiological examination revealed a solid mass filling the right hemithorax. The patient underwent core needle biopsy, wedge biopsy and lobectomy. Biopsy and surgical material were examined histopathologically. The tumor was composed of predominantly solid areas consisting blastemal cells with spindle, polygonal and round nuclei in the myxoid stroma. Immunohistochemical staining of the tumor cells were positive with vimentin and desmin. MIB-1 labeling index was above 90%. Histological diagnosis was pleuropulmonary blastoma type 3. The surgically sampled adjacent diaphragm was also infiltrated with the tumor. The patient was treated with chemotherapy and showed no signs of recurrence in the follow-up of 9 months. Pleuropulmonary blastoma is a very rare childhood cancer that needs to be kept in mind in the pathological differential diagnosis of thoracic tumors in the children.

[818]

TÍTULO / TITLE: - Pulmonary Lymphangiomyomatosis: A Rare Case.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Turk Patoloji Derg. 2013 Sep 24. doi: 10.5146/tjpath.2013.01190.

●● Enlace al texto completo (gratis o de pago) [5146/tjpath.2013.01190](#)

AUTORES / AUTHORS: - Agackiran Y; Erturk A; Yesiller FI; Hoca NT; Ustun LN; Capan N

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Ataturk Chest Diseases and Chest Surgery Training and Research Hospital, ANKARA, TURKEY.

RESUMEN / SUMMARY: - Lymphangiomyomatosis is an uncommon lung disease primarily affecting women of childbearing age. It is characterized by the progressive proliferation and infiltration of smooth muscle-like cells, which lead to cystic destruction of the lung parenchyma; obstruction of airways, blood vessels, and lymphatics; and loss of pulmonary function. We present the case of a 46-year-old female patient with chest pain, cough, sputum, and dyspnea on exertion for three weeks. Minimal pneumothorax was noted, and the patient was referred to our center for further investigation and treatment. High-resolution computed tomography revealed numerous

bilateral thin-walled air cysts and interstitial thickening affecting the central and peripheral part of the upper zone of the lung. We performed an open-lung biopsy to confirm lymphangiomyomatosis. Our aim is to discuss the pathogenesis and other lesions noted in the differential diagnosis of this rare disease.

[819]

TÍTULO / TITLE: - A case of pulmonary hamartoma showing rapid growth.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Case Rep Med. 2013;2013:231652. doi: 10.1155/2013/231652. Epub 2013 Sep 19.

●● Enlace al texto completo (gratis o de pago) [1155/2013/231652](#)

AUTORES / AUTHORS: - Itoga M; Kobayashi Y; Takeda M; Moritoki Y; Tamaki M; Nakazawa K; Sasaki T; Konno H; Matsuzaki I; Ueki S

INSTITUCIÓN / INSTITUTION: - Department of Infection, Allergy, Clinical Immunology and Laboratory Medicine, Akita University Graduate School of Medicine, 1-1-1 Hondo, Akita 010-8543, Japan.

RESUMEN / SUMMARY: - A 65-year-old man was admitted for detailed examination of a growing nodular shadow in the left lung. The nodular shadow was initially detected in a routine chest X-ray check-up in March 2012 that warranted regular chest X-ray follow-up. The nodular shadow increased in size from 12 x 15 mm to 15 x 20 mm within five months. The calculated tumor doubling time (TDT) in our case was approximately 132.2 days. A malignant tumor was strongly suspected based on the rapid growth, and tumorectomy was thus performed. Cartilaginous tissue accounted for most of the pathological specimen, but a small amount of an epithelial component was observed histologically, and we diagnosed a hamartoma. Hamartoma generally shows slow annual growth, but it is important to recognize that rapid enlargement occurs in some cases.

[820]

TÍTULO / TITLE: - Small cell lung cancer with endobronchial growth: A case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):553-555. Epub 2013 Jun 25.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1423](#)

AUTORES / AUTHORS: - Kurishima K; Kagohashi K; Miyazaki K; Tamura T; Ohara G; Kawaguchi M; Satoh H

INSTITUCIÓN / INSTITUTION: - Division of Respiratory Medicine, Mito Medical Center, University of Tsukuba, Mito, Ibaraki 310-0015, Japan.

RESUMEN / SUMMARY: - The current study presents a rare case of small cell lung cancer (SCLC) with endobronchial growth in a 68-year-old male. Chest CT scans revealed an ill-defined mass in the upper lobe of the right lung, with ipsilateral mediastinal lymph node swelling. An endobronchial polypoid tumor in the right B3 bronchus was located by bronchoscopic examination. The analysis of a biopsy specimen obtained from the tumor resulted in a diagnosis of SCLC. Although extremely rare, this case highlights the importance of considering a diagnosis of SCLC in patients presenting with a pulmonary tumor adjacent to the bronchus, with an endobronchial polypoid lesion.

[821]

TÍTULO / TITLE: - Inflammatory pseudotumor mimicking primary hepatic malignant tumor with hepatitis B virus-related cirrhosis: A case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):550-552. Epub 2013 Jun 10.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1386](#)

AUTORES / AUTHORS: - Ke Q; Fan L; Duan X; He Z; Zheng S

INSTITUCIÓN / INSTITUTION: - Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, College of Medicine, Key Laboratory of Combined Multiorgan Transplantation, Ministry of Health, Zhejiang University, Hangzhou, Zhejiang 310003, P.R. China.

RESUMEN / SUMMARY: - Inflammatory pseudotumors (IPT) of the liver are fairly uncommon lesions. IPTs are difficult to diagnose due to the absence of specific symptoms. The correct diagnosis is easily missed, particularly in livers with hepatitis B virus (HBV)-related cirrhosis. The current study presents the case of a 58-year-old male with a ten-year history of HBV infection, who was diagnosed with a primary liver tumor by computed tomography (CT) and magnetic resonance imaging (MRI). The alpha-fetoprotein levels ranged within normal limits. A local resection was performed and the histopathological analysis identified IPT of the liver. The patient recovered well following surgery.

[822]

TÍTULO / TITLE: - A rare collision tumor of squamous carcinoma and small cell carcinoma in esophagus involved with separate lymph nodes: a case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Dis. 2013 Oct;5(5):E203-E206.

●● Enlace al texto completo (gratis o de pago) [3978/j.issn.2072-1439.2013.09.13](#)

AUTORES / AUTHORS: - Li J; Chen X; Shen Y; Hou Y; Zhang S; Wang H; Feng M; Tan L; Wang Q; Zeng Z

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Zhongshan Hospital of Fudan University, Shanghai 200032, China.

RESUMEN / SUMMARY: - We report a case of an esophageal collision tumor composed of squamous cell carcinoma and small cell carcinoma (SmCC). A 66-year-old man complained of chest pain after oral intake for nearly one month. The patient received two cycles of neoadjuvant platinum-based combination chemotherapy and enhanced computed tomography showed a partial response of the tumor. He then underwent a thoracoscopic esophagectomy with extensive mediastinal lymphadenectomy. Two cycles of chemotherapy and prophylactic irradiation of the lymphatic drainage region were sequentially achieved after surgery. The patient has survived for more than 18 months with no evidence of recurrent disease since surgical resection.

[823]

TÍTULO / TITLE: - Concurrent occurrence of adenoid cystic carcinoma of the salivary glands with small cell carcinoma of the liver: A rare case report.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Oral Maxillofac Pathol. 2013 May;17(2):288-91. doi: 10.4103/0973-029X.119774.

●● Enlace al texto completo (gratis o de pago) [4103/0973-029X.119774](#)

AUTORES / AUTHORS: - Premkumar J; Karthik S; Sathyakumar M; Martin Y

INSTITUCIÓN / INSTITUTION: - Department of Oral and Maxillofacial Pathology, College of Dental Sciences and Hospital, Indore, Madhya Pradesh, India.

RESUMEN / SUMMARY: - Adenoid cystic carcinoma (ACC) is a clinically deceptive and histologically specific malignancy of salivary gland origin. It is the most common minor salivary gland malignancy. Small cell carcinoma (SCC) is a type of undifferentiated malignant neuroendocrine tumor reported rarely in the liver. Though there are many reported cases of SCC involving liver and ACC of minor salivary glands, the review of literature does not show any reports of concomitant occurrence of these two tumors. We describe a rare case of ACC of the oral cavity and its coexistence with a SCC involving liver, identified and confirmed by histological, and immunohistochemical observations. To our knowledge, this is the first reported case of an ACC of the oral cavity and SCC of liver occurring concomitantly in the same patient.

[824]

TÍTULO / TITLE: - Metastasis of lung adenocarcinoma to the mandible: Report of a case.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Oral Maxillofac Pathol. 2013 May;17(2):253-6. doi: 10.4103/0973-029X.119745.

●● Enlace al texto completo (gratis o de pago) [4103/0973-029X.119745](#)

AUTORES / AUTHORS: - Misir AF; Mercan U; Gunhan O

INSTITUCIÓN / INSTITUTION: - Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Bulent Ecevit University, Zonguldak, Turkey.

RESUMEN / SUMMARY: - Adenocarcinoma of the lung that metastasizes to the mandible is uncommon. There are only a few cases described in the English-language literature regarding metastasis to mandible from adenocarcinoma of the lung. This article shows a metastasis from adenocarcinoma of the lung affecting the mandible of a 55-year-old male patient where the metastatic lesion was detected before primary tumor. This article emphasizes the importance of detailed dentoalveolar examination and early diagnosis for finding the primary focus of metastatic lesions.

[825]

TÍTULO / TITLE: - Differences in and mutation spectra in lung adenocarcinoma of never and heavy smokers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Nov;6(5):1207-1212. Epub 2013 Aug 29.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1551](#)

AUTORES / AUTHORS: - Takamochi K; Oh S; Suzuki K

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, Juntendo University School of Medicine, Bunkyo-ku, Tokyo 113-8431, Japan.

RESUMEN / SUMMARY: - Epidermal growth factor receptor (EGFR) mutations are common in lung adenocarcinomas of never smokers, while KRAS mutations are more frequent among heavy smokers. Different clinicopathological and biological characteristics may, therefore, exist in lung adenocarcinoma according to smoking status. In the present study, a retrospective review was performed using 521 patients with surgically resected lung adenocarcinomas. The clinicopathological factors of age, gender, pathological tumor size, nodal status, lymphatic permeation and blood vessel

invasion and the EGFR and KRAS mutation spectra were compared between never and heavy smokers. EGFR mutations were detected in 233 (45%) patients, while KRAS mutations were detected in 56 (11%) patients. EGFR-mutated adenocarcinomas had a higher prevalence of females in the never smokers compared with the heavy smokers ($P < 0.001$). KRAS-mutated adenocarcinomas had a higher prevalence of females ($P < 0.001$) and showed less frequent vascular invasion ($P = 0.018$) in the never smokers compared with the heavy smokers. Minor EGFR mutations, excluding exon 21 L858R and exon 19 deletions, were more common in heavy smokers than never smokers ($P = 0.055$). KRAS G to A transition was more common in never smokers, while KRAS G to T and G to C transversions were more common in heavy smokers ($P = 0.036$). The clinicopathological characteristics and the spectra of the EGFR and KRAS mutations in lung adenocarcinoma were different between the never and heavy smokers. Further large-scale studies are required to evaluate the efficacy of molecular targeting agents with consideration to specific EGFR and KRAS mutations.

[826]

TÍTULO / TITLE: - Epigenomic analysis of lung adenocarcinoma reveals novel DNA methylation patterns associated with smoking.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Oct 21;6:1471-9. doi: 10.2147/OTT.S51041.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S51041](#)

AUTORES / AUTHORS: - Tan Q; Wang G; Huang J; Ding Z; Luo Q; Mok T; Tao Q; Lu S
INSTITUCIÓN / INSTITUTION: - Department of Shanghai Lung Cancer Center, Shanghai Chest Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, People's Republic of China.

RESUMEN / SUMMARY: - The importance of epigenetic regulation has been increasingly recognized in the development of cancer. In this study, we investigated the impact of smoking, a major risk factor of lung cancer, on DNA methylation by comparing the genome-wide DNA methylation patterns between lung adenocarcinoma samples from six smokers and six nonsmokers. We identified that smoking-induced DNA methylations were enriched in the calcium signaling and neuroactive ligand receptor signaling pathways, which are closely related to smoking-induced lung cancers. Interestingly, we discovered that two genes in the mitogen-activated protein kinase signaling pathway (RPS6KA3 and ARAF) were hypomethylated in smokers but not in nonsmokers. In addition, we found that the smoking-induced lung cancer-specific DNA methylations were mostly enriched in nuclear activities, including regulation of gene expression and chromatin remodeling. Moreover, the smoking-induced hypermethylation could only be seen in lung adenocarcinoma tissue but not in adjacent normal lung tissue. We also used differentially methylated DNA loci to construct a diagnostic model to distinguish smoking-associated lung cancer from nonsmoking lung cancer with a sensitivity of 88.9% and specificity of 83.2%. Our results provided novel evidence to support that smoking can cause dramatic changes in the DNA methylation landscape of lung cancer, suggesting that epigenetic regulation of specific oncogenic signaling pathways plays an important role in the development of lung cancer.

[827]

TÍTULO / TITLE: - The role of second-line chemotherapy in small cell lung cancer: a retrospective analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Oct 22;6:1493-500. doi: 10.2147/OTT.S52330.

●● Enlace al texto completo (gratis o de pago) [2147/OTT.S52330](#)

AUTORES / AUTHORS: - Zarogoulidis K; Boutsikou E; Zarogoulidis P; Darwiche K; Freitag L; Porpodis K; Latsios D; Kontakiotis T; Huang H; Li Q; Hohenforst-Schmidt W; Kipourou M; Turner JF; Spyrtos D

INSTITUCIÓN / INSTITUTION: - Pulmonary Department, "G Papanikolaou" General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece.

RESUMEN / SUMMARY: - BACKGROUND: To evaluate the benefit of second-line chemotherapy with platinum-based treatment in patients with recurrent small cell lung cancer (SCLC). PATIENTS AND METHODS: A total of 535 patients continued with follow-up or best supportive care if needed, and 229 patients who progressed after the completion of first-line chemotherapy were treated with second-line chemotherapy at the time of progression. In total, 103/229 patients received paclitaxel 190 mg/m² and carboplatin 5.5 area under the curve while 126/229 patients received etoposide 200 mg/m² and carboplatin 5.5 area under the curve every 28 days. RESULTS: Patients administered second-line chemotherapy lived significantly longer, with a median survival of 422 days compared to 228 days in patients with best supportive care alone (P<0.001). Patients who received paclitaxel as second-line chemotherapy lived for an average of 462 days (95% confidence interval: 409-514), versus 405 days in the etoposide group (95% confidence interval: 371-438), which was not statistically significant (P=0.086). The overall response rate was 8% for the paclitaxel group and 6% for the etoposide group. Patients with progression of the disease in more than 3 months had significantly better survival compared with those that progressed in less than 3 months (P<0.001). CONCLUSION: Continuation with carboplatin/paclitaxel or carboplatin/etoposide as second-line chemotherapy has no significant survival impact, and it did not improve response rates.

[828]

TÍTULO / TITLE: - Pleural cancer mortality in España: time-trends and updating of predictions up to 2020.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Nov 6;13(1):528.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-528](#)

AUTORES / AUTHORS: - Lopez-Abente G; Garcia-Gomez M; Menendez-Navarro A; Fernandez-Navarro P; Ramis R; Garcia-Perez J; Cervantes M; Ferreras E; Jimenez-Munoz M; Pastor-Barriuso R

RESUMEN / SUMMARY: - BACKGROUND: A total of 2,514,346 metric tons (Mt) of asbestos were imported into España from 1906 until the ban on asbestos in 2002. Our objective was to study pleural cancer mortality trends as an indicator of mesothelioma mortality and update mortality predictions for the periods 2011--2015 and 2016--2020 in España. METHODS: Log-linear Poisson models were fitted to study the effect of age, period of death and birth cohort (APC) on mortality trends. Change points in cohort- and period-effect curvatures were assessed using segmented regression. Fractional power-link APC models were used to predict mortality until 2020. In addition,

an alternative model based on national asbestos consumption figures was also used to perform long-term predictions. RESULTS: Pleural cancer deaths increased across the study period, rising from 491 in 1976--1980 to 1,249 in 2006--2010. Predictions for the five-year period 2016--2020 indicated a total of 1,319 pleural cancer deaths (264 deaths/year). Forecasts up to 2020 indicated that this increase would continue, though the age-adjusted rates showed a levelling-off in male mortality from 2001 to 2005, corresponding to the lower risk in post-1960 generations. Among women, rates were lower and the mortality trend was also different, indicating that occupational exposure was possibly the single factor having most influence on pleural cancer mortality. CONCLUSION: The cancer mortality-related consequences of human exposure to asbestos are set to persist and remain in evidence until the last surviving members of the exposed cohorts have disappeared. It can thus be assumed that occupationally-related deaths due to pleural mesothelioma will continue to occur in España until at least 2040.

[829]

TÍTULO / TITLE: - Four Common Vascular Endothelial Growth Factor Polymorphisms (-2578C>A, -460C>T, +936C>T, and +405G>C) in Susceptibility to Lung Cancer: A Meta-Analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 1;8(10):e75123. doi: 10.1371/journal.pone.0075123.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0075123](#)

AUTORES / AUTHORS: - Lin L; Cao K; Chen W; Pan X; Zhao H

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Shanghai Chest Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND AND OBJECTIVE: Vascular endothelial growth factor (VEGF) is one of the key initiators and regulators of angiogenesis and it plays a vital role in the onset and development of malignancy. The association between VEGF gene polymorphisms and lung cancer risk has been extensively studied in recent years, but currently available results remain controversial or ambiguous. The aim of this meta-analysis is to investigate the associations between four common VEGF polymorphisms (i.e., -2578C>A, -460C>T, +936C>T and +405C>G) and lung cancer risk. METHODS: A comprehensive search was conducted to identify all eligible studies to estimate the association between VEGF polymorphisms and lung cancer risk. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were used to evaluate the strength of this association. RESULTS: A total of 14 published case-control studies with 4,664 cases and 4,571 control subjects were identified. Our meta-analysis provides strong evidence that VEGF -2578C>A polymorphism is capable of increasing lung cancer susceptibility, especially among smokers and lung squamous cell carcinoma (SCC) patients. Additionally, for +936C>T polymorphism, increased lung cancer susceptibility was only observed among lung adenocarcinoma patients. In contrast, VEGF -460C>T polymorphism may be a protective factor among nonsmokers and SCC patients. Nevertheless, we did not find any association between +405C>G polymorphism and lung cancer risk, even when the groups were stratified by ethnicity, smoking status or histological type. CONCLUSION: This meta-analysis recommends more investigations into the relationship between -2578C>A and -460C>T lung cancer

risks. More detailed and well-designed studies should be conducted to identify the causal variants and the underlying mechanisms of the possible associations.

[830]

TÍTULO / TITLE: - Oxygen for end-of-life lung cancer care: managing dyspnea and hypoxemia.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Expert Rev Respir Med. 2013 Oct;7(5):479-90. doi: 10.1586/17476348.2013.816565.

●● Enlace al texto completo (gratis o de pago) [1586/17476348.2013.816565](#)

AUTORES / AUTHORS: - Tiep B; Carter R; Zachariah F; Williams AC; Horak D; Barnett M; Dunham R

INSTITUCIÓN / INSTITUTION: - City of Hope National Medical Center, Duarte, California, USA.

RESUMEN / SUMMARY: - Oxygen is commonly prescribed for lung cancer patients with advancing disease. Indications include hypoxemia and dyspnea. Reversal of hypoxemia in some cases will alleviate dyspnea. Oxygen is sometimes prescribed for non-hypoxemic patients to relieve dyspnea. While some patients may derive symptomatic benefit, recent studies demonstrate that compressed room air is just as effective. This raises the question as to whether to continue their oxygen. The most efficacious treatment for dyspnea is pharmacotherapy-particularly opioids. Adjunctive therapies include pursed lips breathing and a fan blowing toward the patient. Some patients may come to require high-flow oxygen. High-flow delivery devices include masks, high-flow nasal oxygen and reservoir cannulas. Each device has advantages and drawbacks. Eventually, it may be impossible or impractical to maintain a SpO₂ > 90%. The overall goal in these patients is comfort rather than a target SpO₂. It may eventually be advisable to remove continuous oximetry and transition focus to pharmacological management to achieve patient comfort.

[831]

TÍTULO / TITLE: - Personalized prediction of EGFR mutation-induced drug resistance in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Rep. 2013 Oct 4;3:2855. doi: 10.1038/srep02855.

●● Enlace al texto completo (gratis o de pago) [1038/srep02855](#)

AUTORES / AUTHORS: - Wang DD; Zhou W; Yan H; Wong M; Lee V

INSTITUCIÓN / INSTITUTION: - Department of Electronic Engineering, City University of Hong Kong, Kowloon, Hong Kong.

RESUMEN / SUMMARY: - EGFR mutation-induced drug resistance has significantly impaired the potency of small molecule tyrosine kinase inhibitors in lung cancer treatment. Computational approaches can provide powerful and efficient techniques in the investigation of drug resistance. In our work, the EGFR mutation feature is characterized by the energy components of binding free energy (concerning the mutant-inhibitor complex), and we combine it with specific personal features for 168 clinical subjects to construct a personalized drug resistance prediction model. The 3D structure of an EGFR mutant is computationally predicted from its protein sequence, after which the dynamics of the bound mutant-inhibitor complex is simulated via AMBER and the binding free energy of the complex is calculated based on the

dynamics. The utilization of extreme learning machines and leave-one-out cross-validation promises a successful identification of resistant subjects with high accuracy. Overall, our study demonstrates advantages in the development of personalized medicine/therapy design and innovative drug discovery.

[832]

TÍTULO / TITLE: - Myristoylated alanine-rich C-kinase substrate as a prognostic biomarker in human primary lung squamous cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Biomark. 2013 Jan 1;13(4):289-98. doi: 10.3233/CBM-130354.

●● Enlace al texto completo (gratis o de pago) [3233/CBM-130354](#)

AUTORES / AUTHORS: - Hanada S; Kakehashi A; Nishiyama N; Wei M; Yamano S; Chung K; Komatsu H; Inoue H; Suehiro S; Wanibuchi H

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Osaka City University Graduate School of Medicine, Osaka, Japan Department of Pathology, Osaka City University Graduate School of Medicine, Osaka, Japan.

RESUMEN / SUMMARY: - To identify novel biomarkers for the diagnosis and prognosis of human primary lung squamous cell carcinoma (SCC), we compared the spectrum of proteins expressed in SCC and in the adjacent non-cancer tissue, using QSTAR Elite liquid chromatography with tandem mass spectrometry (LC-MS/MS), coupled with iTRAQ technology. We identified 410 proteins differentially expressed in more than 75% of patients, and validated the expression of candidate target proteins by immunohistochemistry. Based on the results of LC-MS/MS, Ingenuity Pathway Analysis and immunohistochemical analyses, myristoylated alanine-rich C-kinase substrate (MARCKS) (upregulated 2.28-fold, $p < 0.005$) was selected as a potential biomarker of human lung SCC. In order to evaluate the association between patient prognosis and the expression of candidate biomarkers, univariate survival analysis was performed with disease-specific survival curves according to the Kaplan-Meier method, and differences in survival were assessed with the log-rank test. Immunohistochemical evaluation of MARCKS in 99 patients with lung SCC revealed a significant association between positive expression and poor prognosis compared with patients with negative expression (log-rank test; $p = 0.024$). These results indicate that MARCKS may represent a potential biomarker for the prognosis of primary lung SCC.

[833]

TÍTULO / TITLE: - Quantitative Identification of Mutant Alleles Derived from Lung Cancer in Plasma Cell-Free DNA via Anomaly Detection Using Deep Sequencing Data.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 21;8(11):e81468. doi: 10.1371/journal.pone.0081468.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0081468](#)

AUTORES / AUTHORS: - Kukita Y; Uchida J; Oba S; Nishino K; Kumagai T; Taniguchi K; Okuyama T; Imamura F; Kato K

INSTITUCIÓN / INSTITUTION: - Research Institute, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Osaka, Japan.

RESUMEN / SUMMARY: - The detection of rare mutants using next generation sequencing has considerable potential for diagnostic applications. Detecting circulating tumor DNA is the foremost application of this approach. The major obstacle to its use is the high read error rate of next-generation sequencers. Rather than increasing the accuracy of final sequences, we detected rare mutations using a semiconductor sequencer and a set of anomaly detection criteria based on a statistical model of the read error rate at each error position. Statistical models were deduced from sequence data from normal samples. We detected epidermal growth factor receptor (EGFR) mutations in the plasma DNA of lung cancer patients. Single-pass deep sequencing (>100,000 reads) was able to detect one activating mutant allele in 10,000 normal alleles. We confirmed the method using 22 prospective and 155 retrospective samples, mostly consisting of DNA purified from plasma. A temporal analysis suggested potential applications for disease management and for therapeutic decision making to select epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKI).

[834]

TÍTULO / TITLE: - Computed tomography surveillance scanning after lung cancer surgery: mathematical optimization of scanning interval based on tumour biology.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Interact Cardiovasc Thorac Surg. 2013 Nov 13.

●● [Enlace al texto completo \(gratis o de pago\) 1093/icvts/ivt449](#)

AUTORES / AUTHORS: - Poullis M

INSTITUCIÓN / INSTITUTION: - Department of Cardiothoracic Surgery, Liverpool Heart and Chest Hospital, Liverpool, UK.

RESUMEN / SUMMARY: - **OBJECTIVES:** To determine the optimal computed tomography (CT) scanning interval for the detection of a new primary lung cancer and recurrent disease, utilizing the known mathematical formula for tumour doubling. **METHODS:** where: T_i interval time, D_i initial diameter and D_f final diameter. Three doubling times were utilized for demonstration of the principle, 30, 80 and 100 days. **RESULTS:** A worst-case scenario for a doubling time of 30 days indicates that a 2-mm tumour will need 210 days (7 months) to reach 10 mm in diameter and 300 days (10 months) to reach 20 mm in diameter. Over a 5-year (60 months) follow-up period, this indicates that eight CT scans will be required if a threshold of 10 mm is desired or six if a threshold of 20 mm is desired. For an 80-day doubling time over a 5-year (60 months) follow-up period, three CT scans will be required if a threshold of 10 mm is desired or two if a threshold of 20 mm is desired and for a 100-day doubling time. Assuming complete histological clearance of the primary lung cancer and that recurrence occurs from a microscopic focus, a time period of 1700 days (56 months) is required to reach 10 mm in diameter. **CONCLUSIONS:** The exact timing of interval CT scanning to detect recurrence and new primary tumour depends on philosophy; however, three monthly CT scanning is probably inappropriate, and scanning every 7 months is probably the shortest interval that is clinically useful, particularly for small-cell lung cancer in the first year after treatment. We recommend, based on mathematical modelling, a scanning interval post-potentially curative resection surgery for primary lung cancer of 18 months, which is different from the current guidelines on surveillance, for non-small-cell lung cancer.

[835]

TÍTULO / TITLE: - Lung cancer screening: from imaging to biomarker.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomark Res. 2013 Jan 16;1(1):4.

●● Enlace al texto completo (gratis o de pago) [1186/2050-7771-1-4](#)

AUTORES / AUTHORS: - Xiang D; Zhang B; Doll D; Shen K; Kloecker G; Freter C

INSTITUCIÓN / INSTITUTION: - Division of Hematology and Medical Oncology, Ellis Fischel Cancer Center, University of Missouri, Columbia, MO, USA.

ghkloe01@gwise.louisville.edu.

RESUMEN / SUMMARY: - Despite several decades of intensive effort to improve the imaging techniques for lung cancer diagnosis and treatment, primary lung cancer is still the number one cause of cancer death in the United States and worldwide. The major causes of this high mortality rate are distant metastasis evident at diagnosis and ineffective treatment for locally advanced disease. Indeed, approximately forty percent of newly diagnosed lung cancer patients have distant metastasis. Currently, the only potential curative therapy is surgical resection of early stage lung cancer. Therefore, early detection of lung cancer could potentially increase the chance of cure by surgery and underlines the importance of screening and detection of lung cancer. In the past fifty years, screening of lung cancer by chest X-Ray (CXR), sputum cytology, computed tomography (CT), fluorescence endoscopy and low-dose spiral CT (LDCT) has not improved survival except for the recent report in 2010 by the National Lung Screening Trial (NLST), which showed a 20 percent mortality reduction in high risk participants screened with LDCT compared to those screened with CXRs. Furthermore, serum biomarkers for detection of lung cancer using free circulating DNA and RNA, exosomal microRNA, circulating tumor cells and various lung cancer specific antigens have been studied extensively and novel screening methods are being developed with encouraging results. The history of lung cancer screening trials using CXR, sputum cytology and LDCT, as well as results of trials involving various serum biomarkers, are reviewed herein.

[836]

TÍTULO / TITLE: - Overexpression of periostin predicts poor prognosis in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Dec;6(6):1595-1603. Epub 2013 Sep 18.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1590](#)

AUTORES / AUTHORS: - Hong LZ; Wei XW; Chen JF; Shi Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Nanjing First Hospital, Nanjing Medical University, Nanjing, Jiangsu 210006, P.R. China ; Department of Respiratory and Critical Care Medicine, Jinling Hospital, Nanjing University School of Medicine, Nanjing, Jiangsu 210002, P.R. China.

RESUMEN / SUMMARY: - The periostin protein, encoded by the POSTN gene, is a component of the extracellular matrix, which is expressed by fibroblasts and has been observed in a variety of human malignancies. The present study aimed to detect the expression of periostin in the tissues of non-small cell lung cancer (NSCLC) patients and benign lung tumors, and to correlate the results with the clinicopathological data of the subjects, in order to evaluate periostin as a potential prognostic marker. In total, 49 NSCLC patients and 6 benign lung tumors were included in this study. The protein level of periostin was detected in paired normal/paratumor/cancer tissues by a western

blot analysis and the mRNA level in paired normal/cancer tissues was detected by quantitative polymerase chain reaction (qPCR). The results were then correlated with established biological and prognostic factors. Immunohistochemistry was used to confirm the location of periostin in the NSCLC tissues. Uni- and multivariate analyses were performed using Cox's proportional hazards regression model. The protein level of periostin was elevated in the cancer tissue of the NSCLC patients compared with the normal (P=0.017) and paratumor (P=0.000) tissues. The expression level in the male patients was much higher than in the female patients at the protein (P=0.001) and mRNA (P=0.010) levels. The mRNA level in the non-adenocarcinoma (non-ADC) patients was much higher than in the adenocarcinoma (ADC) patients (P=0.029). Periostin was demonstrated higher expression at the protein level in the pseudotumors and tuberculosis patients than in the adjacent (P=0.016) and surrounding tissues (P=0.001). Immunostaining indicated that high levels of periostin were present in the mesenchymal areas, but not in the cancer cells themselves. The patients with tumors exhibiting high-level periostin expression showed a significantly shorter survival time (P=0.036, log-rank test). The 3-year survival rate was 81.5% for patients with low-level periostin expression (periostin-L; n=27) and 45.4% for patients with high-level periostin expression (periostin-H; n=22). Similarly, pathological node (pN) status was a significant prognostic marker in the univariate Cox survival analysis. Notably, periostin-H expression was also identified as an independent prognostic factor by the multivariate analysis (P=0.011). These results showed that the overexpression of periostin predicts a poor prognosis, therefore it may be regarded as a novel molecule in the progression and development of NSCLC. The results provide an additional target for the adjuvant treatment of NSCLC.

[837]

TÍTULO / TITLE: - Osteopontin is a prognostic biomarker in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Nov 11;13(1):540.

●● [Enlace al texto completo \(gratis o de pago\) 1186/1471-2407-13-540](#)

AUTORES / AUTHORS: - Rud AK; Boye K; Oijordsbakken M; Lund-Iversen M; Halvorsen AR; Solberg SK; Berge G; Helland A; Brustugun OT; Maelandsmo GM

RESUMEN / SUMMARY: - INTRODUCTION: In a previously published report we characterized the expression of the metastasis-associated proteins S100A4, osteopontin (OPN) and ephrin-A1 in a prospectively collected panel of non-small cell lung cancer (NSCLC) tumors. The aim of the present follow-up study was to investigate the prognostic impact of these potential biomarkers in the same patient cohort. In addition, circulating serum levels of OPN were measured and single nucleotide polymorphisms (SNP) in the -443 position of the OPN promoter were analyzed. METHODS: Associations between immunohistochemical expression of S100A4, OPN and ephrin-A1 and relapse free and overall survival were examined using univariate and multivariate analyses. Serum OPN was measured by ELISA, polymorphisms in the -443 position of the tumor OPN promoter were analyzed by PCR, and associations between OPN levels and promoter polymorphisms and clinicopathological parameters and patient outcome were investigated. RESULTS: High expression of OPN in NSCLC tumors was associated with poor patient outcome, and OPN was a strong, independent prognostic factor for both relapse free and overall survival. Serum OPN levels increased according to tumor pT classification and tumor size, and patients with OPN-

expressing tumors had higher serum levels than patients with OPN-negative tumors. S100A4 was a negative prognostic factor in several subgroups of adenocarcinoma patients, but not in the overall patient cohort. There was no association between ephrin-A1 expression and patient outcome. CONCLUSIONS: OPN is a promising prognostic biomarker in NSCLC, and should be further explored in the selection of patients for adjuvant treatment following surgical resection.

[838]

TÍTULO / TITLE: - Are the (18)F-FDG positron emission tomography/computed tomography findings in bronchopulmonary carcinoid tumors different than expected?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Hell J Nucl Med. 2013 Sep-Dec;16(3):213-7.

AUTORES / AUTHORS: - Alpay L; Lacin T; Kanbur S; Kiral H; Ersoz E; Bayram S; Dogruyol T; Baysungur V; Yalcinkaya I

INSTITUCIÓN / INSTITUTION: - Sureyyapasa Training and Research Hospital, Department of Thoracic Surgery Basibuyuk Mah, Maltepe, 34844, Istanbul, Turkey. leventalpay@yahoo.com.

RESUMEN / SUMMARY: - Bronchopulmonary carcinoid tumors (BPCT) are known as low malignancy tumors. Different surgical methods are therapeutically used, ranging from simple excision of the mass to large regional resections. Also, the role of positron emission tomography in the diagnosis and staging of BPCT is controversial as false negative results has been reported in literature. Our aim was to study the diagnostic value of fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography ((18)F-FDG PET/CT) and the therapeutic effect of specific surgical treatment on BPCT. We studied retrospectively from 2005 to 2011 75 cases of BPCT. Preoperative investigations included computerized tomography (CT), bronchoscopy and (18)F-FDG PET. Statistical comparisons were performed based on tumor type, extent of the resection and the standardized uptake value (SUV). Fifty six cases were typical, 15 atypical and 4 oncocyctic (a subtype of typical carcinoid). Of these patients, 27 (17 with typical, 8 with atypical and 2 with oncocyctic carcinoid) had undergone a (18)F-FDG PET scan. Operatory mortality was 0%, while the 7 years survival rate amounted to 97.5%. No recurrences were seen. Mean SUV was 5.28 for typical and 5.08 for atypical BPCT. The oncocyctic type exhibited a particularly high SUV. In conclusion, our study, contrary to the findings of others, showed that the (18)F-FDG uptake of BPCT was similar to that of malignant diseases. Aggressive surgical treatment resulted in a very good prognosis for these carcinoid tumors.

[839]

TÍTULO / TITLE: - Timing of thoracic irradiation in limited stage small-cell lung cancer: is it still a star on the rise?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiat Oncol J. 2013 Sep;31(3):175-6. doi: 10.3857/roj.2013.31.3.175. Epub 2013 Sep 30.

●● [Enlace al texto completo \(gratis o de pago\) 3857/roj.2013.31.3.175](#)

AUTORES / AUTHORS: - Manapov F; Niyazi M; Li M

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Munich, Germany.

[840]

TÍTULO / TITLE: - Pulmonary adenocarcinoma with osseous metaplasia: a rare occurrence possibly associated with early stage?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Onco Targets Ther. 2013 Nov 11;6:1631-4. doi: 10.2147/OTT.S48195.

●● [Enlace al texto completo \(gratis o de pago\) 2147/OTT.S48195](#)

AUTORES / AUTHORS: - Zhang Q; Yin L; Li B; Meng R; Dao R; Hu S; Qiu X

INSTITUCIÓN / INSTITUTION: - Department of Pathology, The First Affiliated Hospital and College of Basic Medical Sciences, China Medical University, Shenyang, People's Republic of China.

RESUMEN / SUMMARY: - Adenocarcinoma is the most common type of malignant pulmonary tumor, but osseous metaplasia of this tumor is extremely rare. To date, only 21 cases have been reported in the literature worldwide. Here, we report a case of primary pulmonary adenocarcinoma with benign osseous stromal metaplasia in a 60-year-old woman and discuss the pathogenesis of intratumoral ossification and review the relevant literature. We found that pulmonary adenocarcinoma with osseous metaplasia may be more likely to occur in early tumor stages.

[841]

TÍTULO / TITLE: - Inhibitory effect of a mixture containing vitamin C, lysine, proline, epigallocatechin gallate, zinc and alpha-1-antitrypsin on lung carcinogenesis induced by benzo(a) pyrene in mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Res Med Sci. 2013 May;18(5):427-34.

AUTORES / AUTHORS: - Ibrahim AM; Borai IH; Ali MM; Ghanem HM; Hegazi Ael-S; Mousa AM

INSTITUCIÓN / INSTITUTION: - Department of Biochemistry, National Research Centre, Cairo, Egypt.

RESUMEN / SUMMARY: - BACKGROUND: This study was aimed to evaluate protective and therapeutic effects of a specific mixture, containing vitamin C, lysine, proline, epigallocatechin gallate and zinc, as well as alpha-1-antitrypsin protein on lung tumorigenesis induced by benzo(a) pyrene [B(a)P] in mice. MATERIALS AND METHODS: Swiss albino mice were divided into two main experiments, experiment (1) the mice were injected with 100 mg/kg B(a)P and lasted for 28 weeks, while experiment (2) the mice were injected with 8 doses each of 50 mg/kg B(a)P and lasted for 16 weeks. Each experiment (1 and 2) divided into five groups, group (I) received vehicle, group (II) received the protector mixture, group (III) received the carcinogen B(a)P, group (IV) received the protector together with the carcinogen (simultaneously) and group (V) received the carcinogen then the protector (consecutively). RESULTS: Total sialic acid, thiobarbituric acid reactive substances, vascular epithelial growth factor, hydroxyproline levels, as well as elastase and gelatinase activities showed significant elevation in group (III) in the two experiments comparing to control group ($P < 0.001$). These biochemical alterations were associated with histopathological changes. Administration of the protector in group IV and group V causes significant decrease in such parameters with improvement in histopathological alterations with improvement in histopathological alterations when compared with group III in the two experiments ($P < 0.001$). CONCLUSION: The present protector mixture has the ability

to suppress neoplastic alteration and restore the biochemical and histopathological parameters towards normal on lung carcinogenesis induced by benzo(a) pyrene in mice. Furthermore, the present mixture have more protective rather than therapeutic action.

[842]

TÍTULO / TITLE: - Novel Immunocytokine IL12-SS1 (Fv) Inhibits Mesothelioma Tumor Growth in Nude Mice.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 15;8(11):e81919. doi: 10.1371/journal.pone.0081919.

●● Enlace al texto completo (gratis o de pago) 1371/journal.pone.0081919

AUTORES / AUTHORS: - Kim H; Gao W; Ho M

INSTITUCIÓN / INSTITUTION: - Antibody Therapy Section, Laboratory of Molecular Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland, United States of America.

RESUMEN / SUMMARY: - Mesothelin is a glycosylphosphatidylinositol-anchored glycoprotein that is highly expressed on the cell surface of malignant mesothelioma. Monoclonal antibodies against mesothelin are being evaluated for the treatment of mesothelioma. Immunocytokines represent a novel class of armed antibodies. To provide an alternative approach to current mesothelin-targeted antibody therapies, we have developed a novel immunocytokine based on interleukin-12 (IL12) and the SS1 Fv specific for mesothelin. IL12 possesses potent anti-tumor activity in a wide variety of solid tumors. The newly-developed recombinant immunocytokine, IL12-SS1 (Fv), was produced in insect cells using a baculovirus-insect cell expression system. The SS1 single-chain Fv was fused to the C terminus of the p35 subunit of IL12 through a short linker (GSADGG). The single-chain IL12-SS1 (Fv) immunocytokine bound native mesothelin proteins on malignant mesothelioma (NCI-H226) and ovarian (OVCAR-3) cells as well as recombinant mesothelin on A431/H9 cells. The immunocytokine retained sufficient bioactivity of IL12 and significantly inhibited human malignant mesothelioma (NCI-H226) grown in the peritoneal cavity of nude mice and showed comparable anti-tumor activity to that of the SS1P immunotoxin. IL12-SS1 (Fv) is the first reported immunocytokine to mesothelin-positive tumors and may be an attractive addition to mesothelin-targeted cancer therapies.

[843]

TÍTULO / TITLE: - Pleuroscopic punch biopsy using insulated-tip diathermic knife-2 for the diagnosis of desmoplastic malignant mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Bronchology Interv Pulmonol. 2013 Oct;20(4):345-8. doi: 10.1097/LBR.000000000000010.

●● Enlace al texto completo (gratis o de pago)

1097/LBR.000000000000010

AUTORES / AUTHORS: - Masai K; Sasada S; Izumo T; Taniyama T; Nakamura Y; Chavez C; Sakurai H; Tsuta K; Tsuchida T

INSTITUCIÓN / INSTITUTION: - *Department of Endoscopy, Respiratory Endoscopy Division Departments of Thoracic Surgery double daggerPathology and Clinical Laboratory, National Cancer Center Hospital, Tokyo, Japan.

RESUMEN / SUMMARY: - Desmoplastic malignant mesothelioma (DMM) is a rare subtype of malignant pleural mesothelioma (MPM) and is often difficult to distinguish from pleural fibrosis and reactive mesothelial hyperplasia, especially if the biopsy samples are small. We performed full-thickness pleural biopsy on a lesion suspected to be DMM using an insulated-tip diathermic knife-2 (IT knife-2) during flex-rigid pleuroscopy. IT knife-2 is a novel electrosurgical device for endoscopic submucosal dissection in the early gastrointestinal cancer. It consists of a needle knife with 3 short blades at the distal end attached to an insulated ceramic tip. A 54-year-old man presenting with chest wall mass and thickened pleura, in whom a computed tomography-guided percutaneous needle aspiration had remained negative, underwent flex-rigid pleuroscopy for definitive diagnosis. While applying electric current, we used the IT knife-2 to incise the pleura in a circular shape just above the endothoracic fascia. The incised pleura was removed by forceps and examined pathologically. The microscopic examination was compatible with DMM. We discovered that pleuroscopic punch biopsy using IT knife-2 can diagnose DMM. Use of IT knife-2 during flex-rigid pleuroscopy can obtain sufficient samples from densely thickened pleura, which is difficult to diagnose with small biopsies.

[844]

TÍTULO / TITLE: - The combination of antitumor drugs, exemestane and erlotinib, induced resistance mechanism in H358 and A549 non-small cell lung cancer (NSCLC) cell lines.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pharm Biol. 2013 Nov 5.

●● [Enlace al texto completo \(gratis o de pago\) 3109/13880209.2013.841718](#)

AUTORES / AUTHORS: - Kritikou I; Giannopoulou E; Koutras AK; Labropoulou VT; Kalofonos HP

INSTITUCIÓN / INSTITUTION: - Clinical Oncology Laboratory, University Hospital of Patras, Patras Medical School, Rion, Greece and.

RESUMEN / SUMMARY: - Abstract Context: Estrogens in non-small-cell lung cancer (NSCLC) are important, and their interaction with epidermal growth factor receptor (EGFR) might be crucial. Objective: This study investigates the effect of exemestane, an aromatase inhibitor, and erlotinib, an EGFR inhibitor, on human NSCLC cell lines; H23, H358 and A549. Materials and methods: A cell proliferation assay was used for measuring cell number, apoptosis assay for detecting apoptosis and necrosis and immunoblotting for beclin-1 and Bcl-2 proteins detection. An immunofluorescence assay was used for EGFR localization. A migration assay and zymography were used for cell motility and metalloproteinases (MMPs) expression, respectively. Results: Exemestane, erlotinib or their combination decreased cell proliferation and increased apoptosis. Exemestane's half maximal inhibitory concentration (IC50) was 50 μM for H23 and H358 cells and 20 μM for A549. The IC50 of erlotinib was 25 μM for all cell lines. Apoptosis increase induced by exemestane was 58.0 (H23), 186.3 (H358) and 34.7% (A549) and by erlotinib was 16.7 (H23), 65.3 (H358) and 66.3% (A549). A synergy effect was observed only in H23 cells. Noteworthy, the combination of exemestane and erlotinib decreased beclin-1 protein levels (32.3 +/- 19.2%), an indicator of autophagy, in H23 cells. The combination of exemestane and erlotinib partially reversed the EGFR translocation to mitochondria and decreased MMP levels and migration. Discussion and conclusions: The benefit from a dual targeting of

aromatase and EGFR seems to be regulated by NSCLC cell content. The diverse responses of cells to agents might be influenced by the dominance of certain molecular pathways.

[845]

TÍTULO / TITLE: - Functional analysis of microRNA and transcription factor synergistic regulatory network based on identifying regulatory motifs in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Syst Biol. 2013 Nov 7;7(1):122.

●● Enlace al texto completo (gratis o de pago) [1186/1752-0509-7-122](#)

AUTORES / AUTHORS: - Li K; Li Z; Zhao N; Xu Y; Liu Y; Zhou Y; Shang D; Qiu F; Zhang R; Chang Z; Xu Y

RESUMEN / SUMMARY: - BACKGROUND: Lung cancer, especially non-small cell lung cancer, is a leading cause of malignant tumor death worldwide. Understanding the mechanisms employed by the main regulators, such as microRNAs (miRNAs) and transcription factors (TFs), still remains elusive. The patterns of their cooperation and biological functions in the synergistic regulatory network have rarely been studied. RESULTS: Here, we describe the first miRNA-TF synergistic regulation network in human lung cancer. We identified important regulators (MYC, NFKB1, miR-590, and miR-570) and significant miRNA-TF synergistic regulatory motifs by random simulations. The two most significant motifs were the co-regulation of miRNAs and TFs, and TF-mediated cascade regulation. We also developed an algorithm to uncover the biological functions of the human lung cancer miRNA-TF synergistic regulatory network (regulation of apoptosis, cellular protein metabolic process, and cell cycle), and the specific functions of each miRNA-TF synergistic subnetwork. We found that the miR-17 family exerted important effects in the regulation of non-small cell lung cancer, such as in proliferation and cell cycle regulation by targeting the retinoblastoma protein (RB1) and forming a feed forward loop with the E2F1 TF. We proposed a model for the miR-17 family, E2F1, and RB1 to demonstrate their potential roles in the occurrence and development of non-small cell lung cancer. CONCLUSIONS: This work will provide a framework for constructing miRNA-TF synergistic regulatory networks, function analysis in diseases, and identification of the main regulators and regulatory motifs, which will be useful for understanding the putative regulatory motifs involving miRNAs and TFs, and for predicting new targets for cancer studies.

[846]

TÍTULO / TITLE: - Tumour-derived exosomes as antigen delivery carriers in dendritic cell-based immunotherapy for malignant mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Extracell Vesicles. 2013 Oct 24;2. doi: 10.3402/jev.v2i0.22492.

●● Enlace al texto completo (gratis o de pago) [3402/jev.v2i0.22492](#)

AUTORES / AUTHORS: - Mahaweni NM; Kaijen-Lambers ME; Dekkers J; Aerts JG; Hegmans JP

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, Erasmus MC Cancer Institute, Rotterdam, The Netherlands.

RESUMEN / SUMMARY: - BACKGROUND: In 2001, it was postulated that tumour-derived exosomes could be a potent source of tumour-associated antigens (TAA).

Since then, much knowledge is gained on their role in tumorigenesis but only very recently tumour-derived exosomes were used in dendritic cell (DC)-based immunotherapy. For this, DCs were cultured ex-vivo and loaded with exosomes derived from immunogenic tumours such as melanoma or glioma and re-administrated to induce anti-tumour responses in primary and metastatic tumour mouse models. In contrast, malignant mesothelioma (MM) is a non-immunogenic tumour and because only a few mesothelioma-specific TAA are known to date, we investigated whether mesothelioma-derived exosomes could be used as antigen source in DC-based immunotherapy. METHODS: Mouse MM AB1 cells were used to generate tumour lysate and tumour-derived exosomes. Tumour lysate was generated by 5 cycles of freeze-thawing followed by sonication of AB1 cells. Tumour exosomes were collected from the AB1 cell culture supernatant and followed a stepwise ultracentrifugation. Protein quantification and electron microscopy were performed to determine the protein amount and to characterise their morphology. To test whether MM derived exosomes are immunogenic and able to stimulate an anti-tumoral response, BALB/c mice were injected with a lethal dose of AB1 tumour cells at day 0, followed by intraperitoneal injection of a single dose of DCs loaded with tumour exosomes, DCs loaded with tumour lysate, or phosphate buffered saline (PBS), at day 7. RESULTS: Mice which received tumour exosome-loaded DC immunotherapy had an increased median and overall survival compared to mice which received tumour lysate-loaded DC or PBS. CONCLUSION: In this study, we showed that DC immunotherapy loaded with tumour exosomes derived from non-immunogenic tumours improved survival of tumour bearing mice.

[847]

TÍTULO / TITLE: - Role of pseudolaric acid B in A549 lung cancer cell proliferation and apoptosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2014 Jan;9(1):144-8. doi: 10.3892/mmr.2013.1800. Epub 2013 Nov 14.

●● [Enlace al texto completo \(gratis o de pago\) 3892/mmr.2013.1800](#)

AUTORES / AUTHORS: - Guan T; Yang Y

INSTITUCIÓN / INSTITUTION: - Department of Geriatrics, Shengjing Hospital of China Medical University, Shenyang, Liaoning 110004, P.R. China.

RESUMEN / SUMMARY: - Recently, traditional Chinese medicine has gained attention for its potential use as a chemotherapeutic agent. Pseudolaric acid B (PAB) is a diterpene acid isolated from *Pseudolarix kaempferi* and possesses antifungal, antimicrobial, antifertility and antiangiogenic properties. It was also reported that PAB may inhibit proliferation and induce apoptosis in various types of cancer. However, its effects on A549 lung cancer cells remain to be determined. The present study aimed to determine the potential roles of PAB in the proliferation and apoptosis of A549 cells. The results showed that PAB inhibited A549 cell proliferation in a time and dose-dependent manner. Fluorescence microscopy results showed that cells treated with 20 micromol/l PAB for 24 h exhibited karyorrhexis and apoptotic body formation. In addition, A549 cells were treated with 5, 10, 20, 40 or 80 micromol/l PAB for 24 h and apoptosis was analyzed using AnnexinV/propidium iodide kit. The apoptosis rates were 8.95, 18.71, 24.66, 35.02 and 43.64%, respectively, in PAB-treated cells and 0.80% in the control group. Furthermore, western blot analysis showed that PAB treatment

upregulated the protein levels of Bax, Bad and downregulated Bcl2 and Bclxl expression. In conclusion, PAB may serve as a potent chemotherapeutic agent against human lung cancer.

[848]

TÍTULO / TITLE: - Immune response after systematic lymph node dissection in lung cancer surgery: changes of interleukin-6 level in serum, pleural lavage fluid, and lung supernatant in a dog model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Oct 10;11(1):270. doi: 10.1186/1477-7819-11-270.

●● Enlace al texto completo (gratis o de pago) [1186/1477-7819-11-270](#)

AUTORES / AUTHORS: - Park SY; Kim DJ; Aldohayan A; Ahmed I; Husain S; Al Rikabi A; Aldawlatly A; Al Obied O; Hajjar W; Al Nassar S

INSTITUCIÓN / INSTITUTION: - Department of Thoracic and Cardiovascular Surgery, Yonsei University, College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Republic of Korea. kdjcool@yuhs.ac.

RESUMEN / SUMMARY: - BACKGROUND: Systematic nodal dissection (SND) is regarded as a core component of lung cancer surgery. However, there has been a concern on the increased morbidity associated with SND. This study was performed to investigate whether or not SND induces significant immune response. METHODS: Sixteen dogs were divided into two groups; group 1 (n = 8) underwent thoracotomy only, and group 2 (n = 8) underwent SND after thoracotomy. We compared interleukin-6 (IL-6) levels in serum, pleural lavage fluid and lung supernatant at the time of thoracotomy (T0) and at 2 h (T1) after thoracotomy (group 1) or SND (group 2). Severity of inflammation and IL-6 expression in lung tissue were evaluated in a semi-quantitative manner. RESULTS: The operative results were comparable. IL-6 was not detected in serum in either group. IL-6 in pleural lavage fluid marginally increased from 4.75 +/- 3.74 pg/mL at T0 to 19.75 +/- 8.67 pg/mL at T1 in group 1 (P = 0.112), and from 7.75 +/- 5.35 pg/mL to 17.72 +/- 8.58 pg/mL in group 2 (P = 0.068). IL-6 in lung supernatant increased from 0.36 +/- 0.14 pg/mL/mg to 1.15 +/- 0.17 pg/mL/mg in group 1 (P = 0.003), and from 0.25 +/- 0.08 pg/mL/mg to 0.82 +/- 0.17 pg/mL/mg in group 2 (P = 0.001). However, the degree of increase in IL-6 in pleural lavage fluid and lung supernatant were not different between two groups (P = 0.421 and P = 0.448). There was no difference in severity of inflammation and IL-6 expression between groups. CONCLUSIONS: SND did not increase IL-6 in pleural lavage fluid and lung supernatant. This result suggests that SND could be routinely performed in lung cancer surgery without increasing the significant inflammatory response.

[849]

TÍTULO / TITLE: - Synchronous bilateral bronchial carcinoid diagnosed with combined dual tracer (F-FDG and Ga-DOTATOC) PET/CT scans.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rev Esp Med Nucl. Acceso gratuito al texto completo a partir de los 2 años de la fecha de publicación.

●● Enlace a la Editora de la Revista <http://db.doyma.es/>

●● Cita: Revista Española de Medicina Nuclear: <> Imagen Mol. 2013 Oct 16. pii: S2253-654X(13)00160-1. doi: 10.1016/j.remnm.2013.08.007.

●● Enlace al texto completo (gratuito o de pago) 1016/j.remn.2013.08.007

AUTORES / AUTHORS: - Paci M; Lococo F; Rapicetta C; Roncali M; Cavazza A; Treglia G; Sgarbi G

INSTITUCIÓN / INSTITUTION: - Unit of Thoracic Surgery, IRCCS Arcispedale Santa Maria Nuova, Reggio Emilia, Italy.

[850]

TÍTULO / TITLE: - Audit of referral pathways in the diagnosis of lung cancer: a pilot study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Aust J Prim Health. 2013 Oct 18. doi: 10.1071/PY13043.

●● Enlace al texto completo (gratuito o de pago) 1071/PY13043

AUTORES / AUTHORS: - Largey G; Chakraborty S; Tobias T; Briggs P; Mazza D

[851]

TÍTULO / TITLE: - Plasma osteopontin is a useful diagnostic biomarker for advanced non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Tuberc Respir Dis (Seoul). 2013 Sep;75(3):104-10. doi: 10.4046/trd.2013.75.3.104. Epub 2013 Sep 30.

●● Enlace al texto completo (gratuito o de pago) 4046/trd.2013.75.3.104

AUTORES / AUTHORS: - Han SS; Lee SJ; Kim WJ; Ryu DR; Won JY; Park S; Cheon MJ

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Kangwon National University School of Medicine, Chuncheon, Korea.

RESUMEN / SUMMARY: - BACKGROUND: Osteopontin (OPN) and carbonic anhydrase IX (CAIX), which are expressed on the surface of tumor cells, are associated with hypoxia during tumor development and progression. However, the roles of these proteins in the plasma of patients with non-small cell lung cancer (NSCLC) are poorly understood. Herein, we hypothesized that plasma OPN and CAIX levels could be used as diagnostic and prognostic tumor markers in patients with NSCLC. METHODS: Fifty-three patients with NSCLC and 50 healthy control subjects were enrolled. We selected controls without malignancy and matched them with NSCLC patient cases according to age and gender. Blood samples were collected at the time of diagnosis; the plasma levels of OPN and CAIX were measured by enzyme-linked immunosorbent assays. RESULTS: The plasma levels of OPN in the patients with NSCLC were significantly elevated as compared to those in the controls ($p=0.016$). However, there was no difference in the plasma level of CAIX between the NSCLC patients and controls. NSCLC patients with a distant metastasis had a remarkable increase in plasma OPN compared with patients without metastasis ($p=0.026$), but no such correlation was found for CAIX. There was no difference in overall survival rates according to the plasma level of OPN between the two groups (by Kaplan-Meier survival analysis). CONCLUSION: Plasma OPN levels were elevated in patients with NSCLC as compared with the controls, with greater elevation of OPN levels in the advanced stages of disease. Therefore, plasma OPN may have utility as a diagnostic, but not prognostic, biomarker of advanced NSCLC.

[852]

TÍTULO / TITLE: - Quantitative diagnosis of malignant pleural effusions by single-cell mechanophenotyping.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Transl Med. 2013 Nov 20;5(212):212ra163. doi: 10.1126/scitranslmed.3006559.

●● Enlace al texto completo (gratis o de pago) [1126/scitranslmed.3006559](#)

AUTORES / AUTHORS: - Tse HT; Gossett DR; Moon YS; Masaeli M; Sohsman M; Ying Y; Mislick K; Adams RP; Rao J; Di Carlo D

INSTITUCIÓN / INSTITUTION: - Department of Bioengineering, University of California, Los Angeles, Los Angeles, CA 90095, USA.

RESUMEN / SUMMARY: - Biophysical characteristics of cells are attractive as potential diagnostic markers for cancer. Transformation of cell state or phenotype and the accompanying epigenetic, nuclear, and cytoplasmic modifications lead to measurable changes in cellular architecture. We recently introduced a technique called deformability cytometry (DC) that enables rapid mechanophenotyping of single cells in suspension at rates of 1000 cells/s—a throughput that is comparable to traditional flow cytometry. We applied this technique to diagnose malignant pleural effusions, in which disseminated tumor cells can be difficult to accurately identify by traditional cytology. An algorithmic diagnostic scoring system was developed on the basis of quantitative features of two-dimensional distributions of single-cell mechanophenotypes from 119 samples. The DC scoring system classified 63% of the samples into two high-confidence regimes with 100% positive predictive value or 100% negative predictive value, and achieved an area under the curve of 0.86. This performance is suitable for a prescreening role to focus cytopathologist analysis time on a smaller fraction of difficult samples. Diagnosis of samples that present a challenge to cytology was also improved. Samples labeled as “atypical cells,” which require additional time and follow-up, were classified in high-confidence regimes in 8 of 15 cases. Further, 10 of 17 cytology-negative samples corresponding to patients with concurrent cancer were correctly classified as malignant or negative, in agreement with 6-month outcomes. This study lays the groundwork for broader validation of label-free quantitative biophysical markers for clinical diagnoses of cancer and inflammation, which could help to reduce laboratory workload and improve clinical decision-making.

[853]

TÍTULO / TITLE: - Implications of False Negative and False Positive Diagnosis in Lymph Node Staging of NSCLC by Means of (18)F-FDG PET/CT.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 25;8(10):e78552. doi: 10.1371/journal.pone.0078552.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078552](#)

AUTORES / AUTHORS: - Li S; Zheng Q; Ma Y; Wang Y; Feng Y; Zhao B; Yang Y

INSTITUCIÓN / INSTITUTION: - Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Thoracic Surgery II, Peking University Cancer Hospital & Institute, Beijing, China.

RESUMEN / SUMMARY: - BACKGROUND: Integrated (18)F-fluorodeoxyglucose positron emission tomography/computed tomography ((18)F-FDG PET/CT) is widely performed in hilar and mediastinal lymph node (HMLN) staging of non-small cell lung cancer (NSCLC). However, the diagnostic efficiency of PET/CT remains controversial.

This retrospective study is to evaluate the accuracy of PET/CT and the characteristics of false negatives and false positives to improve specificity and sensitivity. METHODS: 219 NSCLC patients with systematic lymph node dissection or sampling underwent preoperative PET/CT scan. Nodal uptake with a maximum standardized uptake value (SUVmax) >2.5 was interpreted as PET/CT positive. The results of PET/CT were compared with the histopathological findings. The receiver operating characteristic (ROC) curve was generated to determine the diagnostic efficiency of PET/CT. Univariate and multivariate analysis were conducted to detect risk factors of false negatives and false positives. RESULTS: The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of PET/CT in detecting HMLN metastases were 74.2% (49/66), 73.2% (112/153), 54.4% (49/90), 86.8% (112/129), and 73.5% (161/219). The ROC curve had an area under curve (AUC) of 0.791 (95% CI 0.723-0.860). The incidence of false negative HMLN metastases was 13.2% (17 of 129 patients). Factors that are significantly associated with false negatives are: concurrent lung disease or diabetes ($p < 0.001$), non-adenocarcinoma ($p < 0.001$), and SUVmax of primary tumor > 4.0 ($p = 0.009$). Postoperatively, 45.5% (41/90) patients were confirmed as false positive cases. The univariate analysis indicated age > 65 years old ($p = 0.009$), well differentiation ($p = 0.002$), and SUVmax of primary tumor ≤ 4.0 ($p = 0.007$) as risk factors for false positive uptake. CONCLUSION: The SUVmax of HMLN is a predictor of malignancy. Lymph node staging using PET/CT is far from equal to pathological staging account of some risk factors. This study may provide some aids to pre-therapy evaluation and decision-making.

[854]

TÍTULO / TITLE: - Use of Circulating Tumor Cell Technology (CELLSEARCH®) for the Diagnosis of Malignant Pleural Effusions.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Ann Am Thorac Soc. 2013 Nov 15.

- [Enlace al texto completo \(gratis o de pago\) 1513/AnnalsATS.201303-068OC](#)

AUTORES / AUTHORS: - Schwed Lustgarten DE; Thompson J; Yu G; Vachani A; Vaidya B; Rao C; Connelly M; Udine M; Tan KS; Heitjan DF; Albelda S

INSTITUCIÓN / INSTITUTION: - University of Pennsylvania, Perelman School of Medicine, Division of Pulmonary, Allergy and Critical Care Medicine, Thoracic Oncology Group, Philadelphia, Pennsylvania, United States ; schwed@me.com.

RESUMEN / SUMMARY: - Rationale: Cytological analysis of pleural effusions (PEs) has a sensitivity of ~60%. We hypothesized that the CELLSEARCH® technology (Janssen Diagnostics, LLC) currently used to detect circulating tumor cells could be adapted for the identification of tumor cells in PEs. Methods: This was a single center, prospective, observational study. Pleural fluid from subjects with undiagnosed PEs were analyzed by CELLSEARCH® technology which uses an EpCAM antibody-based capture system/cytokeratin antibodies to identify tumor cells. Subjects were prospectively followed by periodic chart review to determine the etiology of the PE. Results: A total of 132 subjects were analyzed. A malignant etiology was established in 81 subjects. The median number of "positive" pleural epithelial cells (PECs) detected per ml of PF was 6 in the benign group. The number of PEC's was 52 in the malignant non-epithelial group (NS) and 526 in the malignant epithelial group ($p < 0.001$). Unlike blood, there

was a baseline number of “positive” cells in benign pleural fluids; however, any cutoff greater than 852 positive cells /ml had 100% specificity. The area under the ROC was 0.86. Nine percent of our cancer cases had high numbers of PECs (>280/ml) but a negative or non-definitive cancer diagnosis by cytology. Conclusion: Pleural CELLSEARCH® assay may serve as a valuable addition to traditional cytology and provide useful information with regard to the diagnosis of malignant effusions. Major advantages include that it is well standardized, relatively inexpensive, has a rapid turnaround, and is easily available. Our data support the conduct of additional studies of this approach to assist in the diagnosis of malignant PEs.

[855]

TÍTULO / TITLE: - An integrated inspection of the somatic mutations in a lung squamous cell carcinoma using next-generation sequencing.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 11;8(11):e78823. doi: 10.1371/journal.pone.0078823.

●● [Enlace al texto completo \(gratis o de pago\) 1371/journal.pone.0078823](#)

AUTORES / AUTHORS: - Stead LF; Egan P; Devery A; Conway C; Daly C; Berri S; Wood H; Belvedere O; Papagiannopoulos K; Ryan A; Rabbitts P

INSTITUCIÓN / INSTITUTION: - Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, West Yorkshire, United Kingdom.

RESUMEN / SUMMARY: - Squamous cell carcinoma (SCC) of the lung kills over 350,000 people annually worldwide, and is the main lung cancer histotype with no targeted treatments. High-coverage whole-genome sequencing of the other main subtypes, small-cell and adenocarcinoma, gave insights into carcinogenic mechanisms and disease etiology. The genomic complexity within the lung SCC subtype, as revealed by The Cancer Genome Atlas, means this subtype is likely to benefit from a more integrated approach in which the transcriptional consequences of somatic mutations are simultaneously inspected. Here we present such an approach: the integrated analysis of deep sequencing data from both the whole genome and whole transcriptome (coding and non-coding) of LUDLU-1, a SCC lung cell line. Our results show that LUDLU-1 lacks the mutational signature that has been previously associated with tobacco exposure in other lung cancer subtypes, and suggests that DNA-repair efficiency is adversely affected; LUDLU-1 contains somatic mutations in TP53 and BRCA2, allelic imbalance in the expression of two cancer-associated BRCA1 germline polymorphisms and reduced transcription of a potentially endogenous PARP2 inhibitor. Functional assays were performed and compared with a control lung cancer cell line. LUDLU-1 did not exhibit radiosensitisation or an increase in sensitivity to PARP inhibitors. However, LUDLU-1 did exhibit small but significant differences with respect to cisplatin sensitivity. Our research shows how integrated analyses of high-throughput data can generate hypotheses to be tested in the lab.

[856]

TÍTULO / TITLE: - Signal transducers and activators of transcription 3 function in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S67-73.

AUTORES / AUTHORS: - Li CJ; Li YC; Zhang DR; Pan JH

INSTITUCIÓN / INSTITUTION: - Department of Respiratory, Tianjin Chest Hospital, Tianjin 300051, China.

RESUMEN / SUMMARY: - Constitutively activation of signal transducers and activators of transcription 3 (STAT3) proteins are involved in multiple aberrant signaling pathway-oncogenic pathways, including pathways regulating tumor cell survival. STAT3 is one of the second messengers in the Janus activated family kinases/STAT signaling pathway and is regulated by many different factors involving tumorigenesis. Given that the activation of STAT3 is observed in nearly 50% of Lung cancers and more and more researches regarding STAT3 in tumors, here in, we reviewed the contribution of STAT3 to lung cancer growth and progression and then the context in which positive and negative regulation of STAT activation leading to cell competition provides a mechanism for therapeutic intervention for specific cancers is discussed.

[857]

TÍTULO / TITLE: - Role of thyroid transcription factor-1 and P63 immunocytochemistry in cytologic typing of non-small cell lung carcinomas.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Egypt Natl Canc Inst. 2013 Dec;25(4):209-18. doi: 10.1016/j.jnci.2013.05.005. Epub 2013 Aug 19.

●● Enlace al texto completo (gratis o de pago) [1016/j.jnci.2013.05.005](#)

AUTORES / AUTHORS: - Sinna EA; Ezzat N; Sherif GM

INSTITUCIÓN / INSTITUTION: - The Department of Pathology, Cytopathology Unit, NCI, Cairo University, Egypt.

RESUMEN / SUMMARY: - **PURPOSE:** Evaluation of the value of thyroid transcription factor (TTF-1) and P63 in subtyping of non-small cell lung cancer in cytologic material. **PATIENTS AND METHODS:** This is a retrospective study including 40 cases of primary lung lesions who underwent image guided FNAC from pulmonary nodules. The final histopathologic diagnosis was the gold standard. Cell blocks were stained with anti-TTF-1, and P63. Nuclear immunoreactivity for both markers was considered specific. Sensitivity, specificity, positive and negative predictive values, of the cytologic diagnosis and of the two markers, as well as the accuracy of the combined markers were calculated. **RESULTS:** Cytomorphology achieved a sensitivity of 83.3%, specificity of 91%, PPV of 91%, and NPV of 83.3%, for the diagnosis of AC, and 91% sensitivity, 83.3% specificity, 83.3% PPV, and 91% NPV, for the diagnosis of SCC. The concordance between cytologic and histopathologic diagnoses of AC and SCC was 87%. TTF-1 achieved 87.5% sensitivity, 94.7% specificity, 95.5% PPV, and 85.7% NPV for AC, while P63 achieved 94.7% sensitivity, 95.8% specificity, 94.7% PPV, and 95.8% NPV for SCC. TTF-1 enhanced the sensitivity of cytomorphology for AC from 83.3% to 87.5%, and specificity from 91% to 94.7%. Similarly P63 enhanced the sensitivity for SCC from 91% to 94.7%, and specificity from 83.3% to 95.8%. **CONCLUSION:** TTF-1 achieved moderate sensitivity, and high specificity in the diagnosis of AC, while P63 was highly sensitive and specific for the diagnosis of SCC. Immunocytochemistry raised the sensitivity and specificity of FNAC in diagnosing AC and SCC using TTF-1 and P63, respectively.

[858]

TÍTULO / TITLE: - Human blood plasma proteome mapping for search of potential markers of the lung squamous cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Eur J Mass Spectrom (Chichester, Eng). 2013;19(2):123-33.

AUTORES / AUTHORS: - Shevchenko VE; Kovalev SV; Arnotskaya NE; Zborovskaya IB; Akhmedov BB; Polotskii BE; Kostin AU; Moukeria AF; Zaridze DG; Davidov MI

INSTITUCIÓN / INSTITUTION: - Federal State Budgetary Institution N. N. Btokhin Russian Cancer Research Center Under the Russian Academy of Medical Science, Moscow, Russia. vshev@nm.ru

RESUMEN / SUMMARY: - Blood plasma proteomes obtained from 77 lung squamous cell carcinoma (LSCC) patients (Stages I-III) and 67 healthy controls (all males) were analyzed by using the label-free liquid chromatography tandem mass spectrometry (LC-MS/MS) method for the search of potential cancer biomarkers. All plasma samples were depleted of 14 highly-abundant plasma proteins by immune-affinity column chromatography before LC-MS/MS. We identified and quantified 809 differential proteins with molecular weights from 6.4 kDa to 3900 kDa using a label-free method. Three hundred and sixty four proteins were identified in all three groups. Changes in levels of an expression of blood plasma proteins associated with LSCC were discovered. Among them, 43 proteins were overexpressed and 39 proteins were down-regulated by more than two-fold between the plasmas of lung cancer patients and healthy men. We focused our attention on proteins whose expression levels increased from control to early stage and then to advanced stage tumor. Each of the 43 unique overexpressed proteins was classified according to its cellular localization, biological processes, molecular function and classes. Many of these proteins are involved in biological pathways pertinent to tumor progression and metastasis and some of these deregulated proteins may be useful clinical markers.

[859]

TÍTULO / TITLE: - ABCC3 as a marker for multidrug resistance in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Rep. 2013 Nov 1;3:3120. doi: 10.1038/srep03120.

●● [Enlace al texto completo \(gratis o de pago\) 1038/srep03120](#)

AUTORES / AUTHORS: - Zhao Y; Lu H; Yan A; Yang Y; Meng Q; Sun L; Pang H; Li C; Dong X; Cai L

INSTITUCIÓN / INSTITUTION: - 1] Department of Internal Medical Oncology, the Affiliated Tumor Hospital of Harbin Medical University, Harbin, Heilongjiang Province, China [2].

RESUMEN / SUMMARY: - Multidrug resistance (MDR) contributes to the failure of chemotherapy and high mortality in non-small cell lung cancer (NSCLC). We aim to identify MDR genes that predict tumor response to chemotherapy. 199 NSCLC fresh tissue samples were tested for chemosensitivity by MTT assay. cDNA microarray was done with 5 samples with highest resistance and 6 samples with highest sensitivity. Expression of ABCC3 mRNA and protein was detected by real-time PCR and immunohistochemistry, respectively. The association between gene expression and overall survival (OS) was examined using Cox proportional hazard regression. 44 genes were upregulated and 168 downregulated in the chemotherapy-resistant group. ABCC3 was one of the most up-regulated genes in the resistant group. ABCC3-positive expression correlated with lymph node involvement, advanced TNM stage, more malignant histological type, multiple-resistance to anti-cancer drugs, and reduced

OS. ABCC3 expression may serve as a marker for MDR and predictor for poor clinical outcome of NSCLC.

[860]

TÍTULO / TITLE: - CEA, SCC and NSE levels in exhaled breath condensate-possible markers for early detection of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Breath Res. 2013 Dec;7(4):047101. doi: 10.1088/1752-7155/7/4/047101. Epub 2013 Nov 1.

●● Enlace al texto completo (gratis o de pago) [1088/1752-7155/7/4/047101](#)

AUTORES / AUTHORS: - Zou Y; Wang L; Zhao C; Hu Y; Xu S; Ying K; Wang P; Chen X

INSTITUCIÓN / INSTITUTION: - Biosensor National Special Lab, Key Lab for Biomedical Engineering of Ministry of Education, Department of Biomedical Engineering, Zhejiang University, 310027 Hangzhou, People's Republic of China.

RESUMEN / SUMMARY: - Lung cancer (LC) is the leading cause of cancer-related death. The sensitive and non-invasive diagnostic tools in the early stage are still poor. We present a pilot study on the early diagnosis of LC by detecting markers in exhaled breath condensate (EBC). EBC samples were collected from 105 patients with LC and 56 healthy controls. We applied chemiluminescence immunoassay to detect CEA (carcinoembryonic antigen), SCC (squamous cell carcinoma) antigen and NSE (neuron specific enolase) in EBC and serum. Concentrations of markers were compared between independent groups and subgroups. A significantly higher concentration level of each marker was found in patients with LC than healthy controls. The areas under curve of receiver operating characteristic (ROC) curves were 0.800, 0.771, 0.659, 0.679, 0.636 and 0.626 for EBC-CEA, serum-CEA, EBC-SCC, serum-SCC, EBC-NSE and serum-NSE, respectively. Markers in EBC had a higher positive rate (PR) and were more specific to histologic types than markers in serum. In addition, multivariate analysis was performed to evaluate the association of presenting markers with the stages of non-small cell lung cancer (NSCLC). EBC-CEA showed the best predictive characteristic ($p < 0.006$) of early-NSCLC. Our study suggested that tumor markers in EBC may have a better diagnostic performance for LC than those in serum. With further investigation on the combination of markers in EBC, detection of EBC could probably be a novel and non-invasive method to detect NSCLC earlier.

[861]

TÍTULO / TITLE: - Classifications of n2 non-small-cell lung cancer based on the number and rate of metastatic mediastinal lymph nodes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Lung Cancer. 2013 Nov;14(6):651-7. doi: 10.1016/j.clcc.2013.04.012.

●● Enlace al texto completo (gratis o de pago) [1016/j.clcc.2013.04.012](#)

AUTORES / AUTHORS: - Ito M; Yamashita Y; Tsutani Y; Misumi K; Harada H; Miyata Y; Okada M

INSTITUCIÓN / INSTITUTION: - Department of General Thoracic Surgery, National Hospital Organization Kure Medical Center and Chugoku Cancer Center, Kure; Department of Surgical Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan.

RESUMEN / SUMMARY: - BACKGROUND: Subdivisions of N2 non-small-cell lung cancer (NSCLC) cases based on metastatic status of mediastinal and non-mediastinal lymph nodes have been proposed. This study aimed to evaluate N2 disease classification by mediastinal lymph nodes alone. PATIENTS AND METHODS: We reviewed 187 patients with NSCLC pN1-N2 who were surgically treated to evaluate the proposed classifications: number, rate, nodal zone of metastatic lymph nodes. We evaluated N2 disease classification based on mediastinal lymph nodes alone in 136 pN2 cases. RESULTS: The number (1-2, 3-5, and 6<=/) or rate (15%>=, 15%< to 40%>, and 40%<=/) classification based on all metastatic lymph nodes was validated by the log-rank test and Cox proportional hazards model. After reclassification by number or rate of metastatic mediastinal lymph nodes alone, a significant difference was maintained among all groups except between the 3-5 and 6<=/ groups. The 5-year survival rates of the 1-2, 3-5, and 6<=/ groups were 63.4%, 32.4%, and 18.2%, respectively (1-2 vs. 3-5, P = .015; 3-5 vs. 6<=/, P = .134). With rate classification, the 5-year survival rates of the 15%>=, 15%-40% (15%< to 40%>), and 40%<=/ groups were 56.0%, 27.3%, and 5.04%, respectively (15%>= vs. 15%-40%, P = .011; 15-40% vs. 40%<=/, P = .011). The Spearman's rank correlation coefficient showed a highly significant correlation of metastatic status between mediastinal lymph nodes and all lymph nodes (both P < .001). CONCLUSION: Classification by number and rate of mediastinal lymph nodes alone enabled subdivision of N2 NSCLC cases. Metastatic status of mediastinal lymph nodes reflects that of all lymph nodes and is prognostic indicators.

[862]

TÍTULO / TITLE: - Control of respiratory motion by hypnosis intervention during radiotherapy of lung cancer I.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Biomed Res Int. 2013;2013:574934. doi: 10.1155/2013/574934. Epub 2013 Sep 4.

●● [Enlace al texto completo \(gratis o de pago\) 1155/2013/574934](#)

AUTORES / AUTHORS: - Li R; Deng J; Xie Y

INSTITUCIÓN / INSTITUTION: - Institute of Biomedical and Health Engineering, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, 1068 Xueyuan Avenue, Shenzhen University Town, Shenzhen 518055, China.

RESUMEN / SUMMARY: - The uncertain position of lung tumor during radiotherapy compromises the treatment effect. To effectively control respiratory motion during radiotherapy of lung cancer without any side effects, a novel control scheme, hypnosis, has been introduced in lung cancer treatment. In order to verify the suggested method, six volunteers were selected with a wide range of distribution of age, weight, and chest circumference. A set of experiments have been conducted for each volunteer, under the guidance of the professional hypnotist. All the experiments were repeated in the same environmental condition. The amplitude of respiration has been recorded under the normal state and hypnosis, respectively. Experimental results show that the respiration motion of volunteers in hypnosis has smaller and more stable amplitudes than in normal state. That implies that the hypnosis intervention can be an alternative way for respiratory control, which can effectively reduce the respiratory amplitude and increase the stability of respiratory cycle. The proposed method will find useful application in image-guided radiotherapy.

[863]

TÍTULO / TITLE: - First-pass perfusion of non-small-cell lung cancer (NSCLC) with 64-detector-row CT: a study of technique repeatability and intra- and interobserver variability.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiol Med. 2013 Nov 22.

●● Enlace al texto completo (gratis o de pago) [1007/s11547-013-0300-0](#)

AUTORES / AUTHORS: - Larici AR; Calandriello L; Amato M; Silvestri R; Del Ciello A; Molinari F; de Waure C; Vita ML; Carnassale G; Bonomo L

INSTITUCIÓN / INSTITUTION: - Department of Bioimaging and Radiological Sciences, Catholic University, "A. Gemelli" Hospital, Largo A. Gemelli 8, 00168, Rome, Italy, anna.larici@rm.unicatt.it.

RESUMEN / SUMMARY: - PURPOSE: This study was done to prospectively assess the repeatability and intra- and interobserver variability of first-pass perfusion with 64-detector-row computed tomography (CT) in non-small-cell lung cancer (NSCLC) with a maximum diameter of up to 8 cm. MATERIALS AND METHODS: Twelve patients with NSCLC underwent 64-detector-row first-pass CT perfusion (CTP) of the whole tumour. Two different techniques were used according to lesion size (cine mode; sequential mode). After 24 h, each study was repeated to assess repeatability. Lesion blood volume (BV), blood flow (BF), mean transit time (MTT) and peak enhancement intensity (PEI) were automatically calculated by two chest radiologists in two different reading sessions. Intra- and interobserver variability was also assessed. RESULTS: The first-pass CTP technique was repeatable and precise with within-subject coefficient of variation (WCV) of 9.3, 16.4, 11.2 and 14.9 %, respectively, for BV, BF, MTT and PEI. High intra- and interobserver agreement was demonstrated for each perfusion parameter, with Cronbach's alpha coefficients and intraclass correlation coefficients ranging from 0.99 to 1. Precision of measurements was slightly better for intraobserver analysis with WCV ranging between 1.05 and 3.03 %. CONCLUSIONS: Non-small-cell lung cancer first-pass perfusion performed with 64-detector-row CT showed good repeatability and high intra- and interobserver agreement for all perfusion parameters and may be considered a reliable and robust tool for assessing tumour vascularisation.

[864]

TÍTULO / TITLE: - UNC5H4-induced apoptosis in non-small cell lung cancer is not dependent on p53 status only.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Nov;6(5):1363-1369. Epub 2013 Sep 9.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1571](#)

AUTORES / AUTHORS: - Zhao ZH; Lin L; Liang A; Li HQ; Zhu Y

INSTITUCIÓN / INSTITUTION: - Department of Orthopedics, The First Affiliated Hospital of China Medical University, Shenyang, Liaoning 110004, P.R. China.

RESUMEN / SUMMARY: - The aim of the present study was to investigate the expression profile and prognostic significance of uncoordinated 5 homolog 4 (UNC5H4) in patients with lung cancer and to evaluate whether UNC5H4 expression may serve as an index for radiosensitivity. UNC5H4 and p53 expression levels were detected by immunohistochemistry, apoptosis was determined by a terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling assay and caspase 3 activation was

determined by western blotting. The results showed that UNC5H4 expression was largely located in the membrane of the normal bronchial epithelium, but absent in the membranous regions or ectopic cytoplasm of 80/130 (61.5%) non-small cell lung cancer (NSCLC) tissue samples. Abnormal UNC5H4 expression was demonstrated to correlate with the degree of differentiation ($P=0.015$), TNM staging ($P=0.037$). Cytoplasmic UNC5H4 expression was shown to correlate negatively with p53 mutant type (mt) expression ($r=-0.270$; $P=0.002$) and positively with the apoptotic index ($r=0.254$; $P=0.004$). The statistical analyses indicated that the prognosis of patients with normal UNC5H4 expression was improved compared with that of patients with abnormal UNC5H4 expression, however, no significant difference was identified ($P=0.125$). Exposure of NSCLC tissue samples to X-radiation increased UNC5H4 expression and caspase 3 activity significantly, irrespective of p53 mutation status. In conclusion, these results indicate that X-rays induce apoptosis via the p53 pathway, and when this pathway is compromised, an additional pathway is utilized.

[865]

TÍTULO / TITLE: - Wogonin Has Multiple Anti-Cancer Effects by Regulating c-Myc/SKP2/Fbw7alpha and HDAC1/HDAC2 Pathways and Inducing Apoptosis in Human Lung Adenocarcinoma Cell Line A549.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 12;8(11):e79201. doi: 10.1371/journal.pone.0079201.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079201](#)

AUTORES / AUTHORS: - Chen XM; Bai Y; Zhong YJ; Xie XL; Long HW; Yang YY; Wu SG; Jia Q; Wang XH

INSTITUCIÓN / INSTITUTION: - Guangzhou Medical University, Guangzhou, Guangdong, PR China.

RESUMEN / SUMMARY: - Wogonin is a plant monoflavonoid which has been reported to inhibit cell growth and/or induce apoptosis in various tumors. The present study examined the apoptosis-inducing activity and underlying mechanism of action of wogonin in A549 cells. The results showed that wogonin was a potent inhibitor of the viability of A549 cells. Apoptotic protein changes detected after exposure to wogonin included decreased XIAP and Mcl-1 expression, increased cleaved-PARP expression and increased release of AIF and cytochrome C. Western blot analysis showed that the activity of c-Myc/Skp2 and HDAC1/HDAC2 pathways, which play important roles in tumor progress, was decreased. Quantitative PCR identified increased levels of c-Myc mRNA and decreased levels of its protein. Protein levels of Fbw7alpha, GSK3beta and Thr58-Myc, which are involved in c-Myc ubiquitin-dependent degradation, were also analyzed. After exposure to wogonin, Fbw7alpha and GSK3beta expression decreased and Thr58-Myc expression increased. However, MG132 was unable to prevent c-Myc degradation. The present results suggest that wogonin has multiple anti-cancer effects associated with degradation of c-Myc, SKP2, HDAC1 and HDAC2. Its ability to induce apoptosis independently of Fbw7alpha suggests a possible use in drug-resistance cancer related to Fbw7 deficiency. Further studies are needed to determine which pathways are related to c-Myc and Fbw7alpha reversal and whether Thr58 phosphorylation of c-Myc is dependent on GSK3beta.

[866]

TÍTULO / TITLE: - CRK SH3N Domain Diminishes Cell Invasiveness of Non-Small Cell Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Genes Cancer. 2013 Jul;4(7-8):315-24. doi: 10.1177/1947601913497573.

- Enlace al texto completo (gratis o de pago) [1177_1947601913497573](#) [pii]
- Enlace al texto completo (gratis o de pago) [1177/1947601913497573](#)

AUTORES / AUTHORS: - Pezeshkpour GH; Moatamed F; Lewis M; Hoang B; Rettig M; Mortazavi F

INSTITUCIÓN / INSTITUTION: - Department of Pathology, West Los Angeles VA, Los Angeles, CA, USA.

RESUMEN / SUMMARY: - CRK (c-Crk) as an adaptor protein is involved in several oncogenic signal transduction pathways, conveying oncogenic signals to its downstream effectors and thereby affecting multiple cellular processes including proliferation, differentiation, and migration. For example, we have observed that CRK expression and phosphorylation influence the invasiveness of non-small cell lung cancer (NSCLC) cells. To intervene in CRK signaling pathway, we examined whether CRK protein domains can be used as therapeutic tools to interrupt CRK signaling, thus influencing the biological behavior of NSCLC cells. For this purpose, Src Homology domains of CRK-I (i.e., SH2 and SH3N domains) were overexpressed in H157, Rh2, and A549 cells. CRK-SH3N domain expression induced epithelial morphology in H157 cells and enhanced epithelial morphology of A549 and Rh2 cells as compared to cells transfected with CRK-SH2 domain or empty vector. In addition, CRK-SH3N domain expression significantly decreased the motility and invasiveness of A549 and H157 cells. Furthermore, CRK-SH3N domain expression disrupted the interaction of CRK-II with DOCK180. In summary, these data provide evidence that the CRK-SH3N domain can be used to influence the malignant phenotype of NSCLC cells and also reduce the metastatic potential of these cells.

[867]

TÍTULO / TITLE: - A novel molecular pathway for Snail-dependent, SPARC-mediated invasion in non-small cell lung cancer pathogenesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Prev Res (Phila). 2013 Nov 19.

●● Enlace al texto completo (gratis o de pago) [1158/1940-6207.CAPR-13-0263](#)

AUTORES / AUTHORS: - Grant JL; Fishbein MC; Hong LS; Krysan K; Minna JD; Shay JW; Walser TC; Dubinett SM

INSTITUCIÓN / INSTITUTION: - 1Pathology and Laboratory Medicine, University of California, Los Angeles; Jonsson Comprehensive Cancer Center.

RESUMEN / SUMMARY: - Definition of the molecular pathogenesis of lung cancer allows investigators an enhanced understanding of the natural history of the disease, thus fostering development of new prevention strategies. In addition to regulating epithelial-to-mesenchymal transition (EMT), the transcription factor Snail exerts global effects on gene expression. Our recent studies reveal that Snail is upregulated in non-small cell lung cancer (NSCLC), is associated with poor prognosis, and promotes tumor progression in vivo. Herein, we demonstrate that overexpression of Snail leads to upregulation of Secreted Protein, Acidic and Rich in Cysteine (SPARC) in models of

pre-malignancy and established disease, as well as in lung carcinoma tissues in situ. Snail overexpression leads to increased SPARC-dependent invasion in vitro, indicating that SPARC may play a role in lung cancer progression. Bioinformatic analysis implicates TGF-beta, ERK1/2, and miR-29b as potential intermediaries in Snail-mediated upregulation of SPARC. Both the TGF-beta1 ligand and TGF-betaR2 are upregulated following Snail overexpression. Treatment of human bronchial epithelial cell (HBE) lines with TGF-beta1 and inhibition of TGF-beta1 mRNA expression modulated SPARC expression. Inhibition of MEK phosphorylation downregulated SPARC. MiR-29b is downregulated in Snail overexpressing cell lines, while overexpression of miR-29b inhibited SPARC expression. In addition, miR-29b was upregulated following ERK inhibition, suggesting a Snail-dependent pathway by which Snail activation of TGF-beta and ERK signaling results in downregulation of miR-29b and subsequent upregulation of SPARC. Our discovery of pathways responsible for Snail-induced SPARC expression contributes to the definition of NSCLC pathogenesis.

[868]

TÍTULO / TITLE: - CT-guided core biopsy of malignant lung lesions: How many needle passes are needed?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Med Imaging Radiat Oncol. 2013 Dec;57(6):652-6. doi: 10.1111/1754-9485.12054. Epub 2013 Apr 1.

●● Enlace al texto completo (gratis o de pago) 1111/1754-9485.12054

AUTORES / AUTHORS: - Lim C; Lee KY; Kim YK; Ko JM; Han DH

INSTITUCIÓN / INSTITUTION: - Department of Radiology, Seoul St Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea.

RESUMEN / SUMMARY: - AIM: The study aims to determine the number of needle passes in the CT-guided core needle biopsy (CNB) in making a diagnosis of pulmonary malignancy. MATERIALS AND METHODS: A total of 434 CNB records were retrospectively reviewed. The specimen obtained from each needle pass was put in a formalin container and then labelled for separate histopathological reporting. The patients were divided into five groups according to the total number of needle passes (n = 1, n = 2, n = 3, n = 4 and n >= 5). In each of the groups 2-4, it was analysed how many needle passes are required before a plateau in diagnostic yield is achieved. RESULTS: CNB produced 283 true-positive and 23 false-negative diagnosis of malignancy. Cumulative sensitivity significantly (P < 0.05) increased between the first and second as well as the second and the third (if done) needle passes, but not between the third and fourth ones. CONCLUSION: Three coaxial needle passes might be optimal in the diagnosis of lung malignancy.

[869]

TÍTULO / TITLE: - Heterotrimeric G-protein, G16, is a critical downstream effector of non-canonical Wnt signaling and a potent inhibitor of transformed cell growth in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 18;8(10):e76895. doi: 10.1371/journal.pone.0076895.

●● Enlace al texto completo (gratis o de pago) 1371/journal.pone.0076895

AUTORES / AUTHORS: - Avasarala S; Bikkavilli RK; Van Scoyk M; Zhang W; Lapite A; Hostetter L; Byers JT; Heasley LE; Sohn JW; Winn RA

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary, Critical Care, Sleep and Allergy, College of Medicine, University of Illinois at Chicago, Chicago, Illinois, United States of America.

RESUMEN / SUMMARY: - G-protein-coupled receptors (GPCR) are the largest family of cell surface molecules that play important role/s in a number of biological and pathological processes including cancers. Earlier studies have highlighted the importance of Wnt7a signaling via its cognate receptor Frizzled9, a GPCR, in inhibition of cell proliferation, anchorage-independent growth, and reversal of transformed phenotype in non small cell lung cancer primarily through activation of the tumor suppressor, PPARgamma. However, the G-protein effectors that couple to this important tumor suppressor pathway have not been identified, and are of potential therapeutic interest. In this study, by using two independent Wnt7a/Frizzled9-specific read-outs, we identify Galpha16 as a novel downstream effector of Wnt7a/Frizzled9 signaling. Interestingly, Galpha16 expression is severely down-regulated, both at the messenger RNA levels and protein levels, in many non small cell lung cancer cell lines. Additionally, through gene-specific knock-downs and expression of GTPase-deficient forms (Q212L) of Galpha16, we also establish Galpha16 as a novel regulator of non small cell lung cancer cell proliferation and anchorage-independent cell growth. Taken together, our data not only establish the importance of Galpha16 as a critical downstream effector of the non-canonical Wnt signaling pathway but also as a potential therapeutic target for the treatment of non small cell lung cancer.

[870]

TÍTULO / TITLE: - Malignant mesothelioma after household exposure to asbestos.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Case Rep Oncol Med. 2013;2013:570487. doi: 10.1155/2013/570487. Epub 2013 Oct 10.

●● Enlace al texto completo (gratis o de pago) [1155/2013/570487](#)

AUTORES / AUTHORS: - Saba R; Aronu GN; Bhatti RP; Mirrakhimov AE; Anusim N; Barbaryan A; Kwatra SG; Iroegbu N

INSTITUCIÓN / INSTITUTION: - Saint Joseph Hospital, Department of Internal Medicine, 2900 North Lake Shore Drive, Chicago, IL 60657, USA.

RESUMEN / SUMMARY: - Malignant mesothelioma (MM) is an aggressive cancer that has been closely linked to asbestos exposure. Initially recognized as an occupational cancer in male workers, MM was later found to occur in their family members as well. We report the case of an 89-year-old female who presented with abdominal distention, pain, and findings consistent with malignant ascites. Family history was significant for fatal mesothelioma in her husband of 40 years, who was a worker at a tile factory. The diagnosis of MM was confirmed on pathologic examination of the omental core biopsy.

[871]

TÍTULO / TITLE: - Congenital Cystic Adenomatoid Malformation with Associated Mucinous Bronchioloalveolar Carcinoma in a Neonate.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Fetal Pediatr Pathol. 2013 Oct 7.

●● Enlace al texto completo (gratis o de pago) [3109/15513815.2013.842272](#)

AUTORES / AUTHORS: - Li J; Chen GS; Zhang X; Moore L; Cheng H

INSTITUCIÓN / INSTITUTION: - Department of Pathology, Xi'An Children's Hospital, Xi'An , Shaanxi Province , People's Republic of China.

RESUMEN / SUMMARY: - Congenital cystic adenomatoid malformation (CCAM) of lung is a rare hamartomatous disorder characterized by abnormal branching morphogenesis of the lung. We report an unusual case of a 2-day-old male newborn with a pulmonary cystic lesion and lobectomy revealed a CCAM of the lung that has overlapping features of type 1 and type 2, complicating with multifocal mucinous bronchioloalveolar carcinoma (BAC). The case indicates that malignant transformation can occur in very early stage of the infancy in the patients with CCAM of lung.

[872]

TÍTULO / TITLE: - Effect of 5- AZn-2 '-deoxycytidine on proliferation of human lung adenocarcinoma cell line A549 in vitro.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Asian Pac J Trop Med. 2013 Dec;6(12):982-5. doi: 10.1016/S1995-7645(13)60176-5.

●● Enlace al texto completo (gratis o de pago) [1016/S1995-7645\(13\)60176-5](#)

AUTORES / AUTHORS: - Li N; Huang HQ; Zhang GS; Cui W

INSTITUCIÓN / INSTITUTION: - Department of Intensive Care Unit, Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou 310009, China.

RESUMEN / SUMMARY: - OBJECTIVE: To explore effect of 5-AZn-2 '-deoxycytidine on proliferation of human lung adenocarcinoma cell line A549 in vitro. METHODS: Superoxide dismutase (SOD) activity was measured by hydroxylamine colorimetric method. Inhibition effect of 5-AZn-2' deoxycytidylic acid at different concentration and different time on growth of A549 cell was determined by MTT assay. Methylene dioxyamphetamine (MDA) was measured by thiobarbituric acid colorimetric method. Effect of 5-AZn-2' deoxycytidylic acid on apoptosis of A549 cell was determined by Hoechst 33258 dyeing detection. RESULTS: 5-AZn-2' deoxycytidylic acid had significant inhibition effect on proliferation of A549 cells in vitro, and the inhibition was notably dependent on time and dosage during 48-72 h; SOD level was significantly lower than those of control group (P<0.05, P<0.01), MDA level was significantly higher than those in the control group (P<0.05, P<0.01). A549 cells began to be in apoptosis after using 5-AZn-2' deoxycytidylic acid. CONCLUSIONS: 5- AZn-2' deoxycytidylic acid has significant inhibition effect on growth of A549 cell, and can lead the change of lipid peroxidation. It indicates that the mechanism has relationship with A549 cell cycle tissue and induction factor of apoptosis.

[873]

TÍTULO / TITLE: - omega-3 polyunsaturated fatty acids inhibit the proliferation of the lung adenocarcinoma cell line A549 in vitro.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Med Rep. 2013 Nov 26. doi: 10.3892/mmr.2013.1829.

●● Enlace al texto completo (gratis o de pago) [3892/mmr.2013.1829](#)

AUTORES / AUTHORS: - Yao QH; Zhang XC; Fu T; Gu JZ; Wang L; Wang Y; Lai YB; Wang YQ; Guo Y

INSTITUCIÓN / INSTITUTION: - Department of Oncology, The First Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou, Zhejiang 310006, P.R. China.

RESUMEN / SUMMARY: - omega-3 polyunsaturated fatty acids (n-3 PUFA), in particular the marine-derived forms eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have been demonstrated to affect cancer cell replication, the cell cycle and cell death. Epidemiological studies have also suggested diets rich in n-3 PUFA were inversely correlated with the development of cancer. In the present study, we explored the effects of DHA and EPA on the proliferation activity and apoptosis of the human lung adenocarcinoma cell line A549. A methyl thiazolyl tetrazolium (MTT) assay was used to detect cell proliferation, apoptosis was detected by flow cytometry and morphological analysis was determined by fluorescence microscopy and transmission electron microscopy. A549 cells were treated with different doses of DHA (40, 45, 50 and 55 microg/ml) or EPA (45, 50, 55 and 60 microg/ml) for 24, 48 and 72 h. The results demonstrated that DHA and EPA significantly suppressed the proliferation of A549 cells and induced apoptosis of A549 cells in a dose- and time-dependent manner. The apoptotic phenomenon was also confirmed by fluorescence microscopy and transmission electron microscopy. Furthermore, compared with the control, the formation of autophagosomes was clearly enhanced in DHA or EPAtreated cells. In conclusion, DHA and EPA inhibited the proliferation of A549 cells and induced cell apoptosis and autophagy, which may provide new safe and effective options for the treatment of lung cancer in the future.

[874]

TÍTULO / TITLE: - Low-dose computed tomography screening for lung cancer: results of the first screening round.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Comp Eff Res. 2013 Sep;2(5):433-6. doi: 10.2217/cer.13.57.

●● Enlace al texto completo (gratis o de pago) [2217/cer.13.57](#)

AUTORES / AUTHORS: - Horeweg N; Nackaerts K; Oudkerk M; de Koning HJ

INSTITUCIÓN / INSTITUTION: - Department of Public Health, Erasmus University Medical Center, PO Box 2040, 3000 CA Rotterdam, The Netherlands.

RESUMEN / SUMMARY: - Evaluation of: National Lung Screening Trial Research Team, Church TR, Black WC, Aberle DR et al. Results of initial low-dose computed tomographic screening for lung cancer. N. Engl. J. Med. 368, 1980-1991 (2013). In 2011, the US NLST trial demonstrated that mortality from lung cancer can be reduced by using low-dose computed tomography (LDCT) screening rather than chest x-ray (CXR) screening. This paper from the US NLST research team focuses on the results of the initial round of LDCT for lung cancer. A total of 53,439 participants were included and randomly assigned to LDCT screening (n = 26,715) or CXR screening (n = 26,724). In total, 27.3% of the participants in the LDCT group and 9.2% in the CXR group had a positive screening result. As a result, 3.8% (LDCT group) and 5.7% (CXR group) of these subjects were diagnosed with lung cancer. The sensitivity (93.8%) and specificity (73.4%) for lung cancer were higher for LDCT compared with CXR screening; 73.5 and 91.3%, respectively.

[875]

TÍTULO / TITLE: - Lung cancer: CT screening for lung cancer-do we have an answer?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Dec;10(12):672-3. doi: 10.1038/nrclinonc.2013.198. Epub 2013 Nov 5.

- Enlace al texto completo (gratis o de pago) [1038/nrclinonc.2013.198](#)

AUTORES / AUTHORS: - Pastorino U; Sverzellati N

INSTITUCIÓN / INSTITUTION: - Director of Thoracic Surgery, Fondazione IRCCS Istituto Nazionale Tumori, Via Venezian 1, 20133 Milan, Italy.

[876]

TÍTULO / TITLE: - Bacterial pleuritis with thickened mesothelial hyperplasia in a young beagle dog.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Toxicol Pathol. 2013 Sep;26(3):313-7. doi: 10.1293/tox.26.313. Epub 2013 Oct 15.

- Enlace al texto completo (gratis o de pago) [1293/tox.26.313](#)

AUTORES / AUTHORS: - Yamada N; Hashimoto S; Tomonari Y; Kokoshima H; Doi T; Sato J; Wako Y; Tsuchitani M

INSTITUCIÓN / INSTITUTION: - Pathology Department, Kashima Laboratory, Nonclinical Research Center, Mitsubishi Chemical Medience Corporation, 14-1 Sunayama, Kamisu, Ibaraki 314-0255, Japan.

RESUMEN / SUMMARY: - A five-month-old male beagle dog suddenly became moribund. Bloody fluid accumulated in the thoracic and abdominal cavities, and soft yellow flecks were floating in the thoracic fluid. The mediastinum and pericardium became dark reddish with villous thickening. Other parietal and pulmonary pleurae were rough, and the organs adhered to each other. Histologically, most mediastinal pleura formed papillary projections covered by a single layer of mesothelial cells. Many macrophages and neutrophils infiltrated the submesothelial connective tissue. At the mediastinum adjacent to the pericardium, cuboidal mesothelial cells proliferated solidly and formed a thick surface stratum. The flecks consisted of gram-negative filamentous or small bacillary (cocoid) bacteria. In the right posterior lobe of the lung, neutrophilic infiltration and a large encapsulated abscess including a bacterial colony were present. We diagnosed this case as "bacterial pleuritis with thickened mesothelial hyperplasia". The cause of the pleuritis might be a chronic pleural infection spread via the lung abscess.

[877]

TÍTULO / TITLE: - Lung tumor promotion by chromium-containing welding particulate matter in a mouse model.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Part Fibre Toxicol. 2013 Sep 5;10(1):45. doi: 10.1186/1743-8977-10-45.

- Enlace al texto completo (gratis o de pago) [1186/1743-8977-10-45](#)

AUTORES / AUTHORS: - Zeidler-Erdely PC; Meighan TG; Erdely A; Battelli LA; Kashon ML; Keane M; Antonini JM

INSTITUCIÓN / INSTITUTION: - Health Effects Laboratory Division, National Institute for Occupational Safety and Health, 1095 Willowdale Road MS L2015, Morgantown, WV 26505, USA. paz9@cdc.gov.

RESUMEN / SUMMARY: - BACKGROUND: Epidemiology suggests that occupational exposure to welding particulate matter (PM) may increase lung cancer risk. However, animal studies are lacking to conclusively link welding with an increased risk. PM derived from stainless steel (SS) welding contains carcinogenic metals such as

hexavalent chromium and nickel. We hypothesized that welding PM may act as a tumor promoter and increase lung tumor multiplicity in vivo. Therefore, the capacity of chromium-containing gas metal arc (GMA)-SS welding PM to promote lung tumors was evaluated using a two-stage (initiation-promotion) model in lung tumor susceptible A/J mice. METHODS: Male mice (n = 28-30/group) were treated either with the initiator 3-methylcholanthrene (MCA; 10 µg/g; IP) or vehicle (corn oil) followed by 5 weekly pharyngeal aspirations of GMA-SS (340 or 680 µg/exposure) or PBS. Lung tumors were enumerated at 30 weeks post-initiation. RESULTS: MCA initiation followed by GMA-SS welding PM exposure promoted tumor multiplicity in both the low (12.1 +/- 1.5 tumors/mouse) and high (14.0 +/- 1.8 tumors/mouse) exposure groups significantly above MCA/sham (4.77 +/- 0.7 tumors/mouse; p = 0.0001). Multiplicity was also highly significant (p < 0.004) across all individual lung regions of GMA-SS-exposed mice. No exposure effects were found in the corn oil groups at 30 weeks. Histopathology confirmed the gross findings and revealed increased inflammation and a greater number of malignant lesions in the MCA/welding PM-exposed groups. CONCLUSIONS: GMA-SS welding PM acts as a lung tumor promoter in vivo. Thus, this study provides animal evidence to support the epidemiological data that show welders have an increased lung cancer risk.

[878]

TÍTULO / TITLE: - Tumor-Promoting and -Suppressive Roles of Autophagy in the Same Mouse Model of BrafV600E-Driven Lung Cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Discov. 2013 Nov;3(11):1225-7. doi: 10.1158/2159-8290.CD-13-0664.

●● Enlace al texto completo (gratis o de pago) [1158/2159-8290.CD-13-0664](#)

AUTORES / AUTHORS: - Chen S; Guan JL

INSTITUCIÓN / INSTITUTION: - 1Divisions of Molecular Medicine and Genetics, Department of Internal Medicine, and 2Department of Cell and Developmental Biology, University of Michigan Medical School, Ann Arbor, Michigan.

RESUMEN / SUMMARY: - Summary: Although a role of autophagy in cancer development and progression has received increasing appreciation in recent years, there are still significantly uncertain and conflicting results about its tumor-suppressive and -promoting functions, and, more importantly, a lack of understanding of mechanisms underlying these opposing activities. The work presented by Strohecker and colleagues uses an innovative approach to address these challenges by examining the effects of inactivating the key autophagy gene Atg7 at different stages of oncogenic development in a Braf(V600E)-driven mouse lung cancer model. The authors show that autophagy blockage initially accelerated tumor development, but suppressed tumor progression in later stages, converting adenomas to oncocytomas and increasing mouse survival. Importantly, they identify a critical role of glutamine dependency in the suppression of Braf(V600E)-induced cancer, thus revealing an important mechanism by which autophagy may promote tumor progression in different cellular contexts. Cancer Discov; 3(11); 1225-7. ©2013 AACR.

[879]

TÍTULO / TITLE: - Surgically resected gastric metastasis of pulmonary squamous cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - World J Gastrointest Surg. 2013 Oct 27;5(10):278-81. doi: 10.4240/wjgs.v5.i10.278.

●● Enlace al texto completo (gratis o de pago) [4240/wjgs.v5.i10.278](#)

AUTORES / AUTHORS: - Kim YI; Kang BC; Sung SH

INSTITUCIÓN / INSTITUTION: - Yong Il Kim, Department of Surgery, Ewha Womans University College of Medicine, Seoul 158-710, South Korea.

RESUMEN / SUMMARY: - Gastric metastasis of pulmonary carcinoma has been reported to range from 0.19%-5.1%. An autopsy review of cancer disclosed 1.7%-29.6% of gastric metastases, primarily from breast cancer, lung cancer and melanoma. A 71-year-old man was referred to our department because of persistent cough, sputum and sweating for 20 d. Chest posteroanterior view and chest computed tomography scan demonstrated an irregular tumor mass measuring 5.8 cm with central necrosis at the right lower lung. Bronchoscopic biopsy revealed pulmonary squamous carcinoma. Esophagogastroduodenoscopy revealed a huge bleeding ulcer at the body of the stomach and a biopsy diagnosed a metastatic lesion. We performed a palliative total gastrectomy, splenectomy and distal pancreatectomy. The patient did not receive any adjuvant chemotherapy due to his refusal. He was controlled conservatively and survived for 11 mo after surgery. Surgical resection may provide an option for safe palliative treatment. Although gastric metastasis from lung cancer is associated with dismal outcomes, a longer survival or more favorable outcome has been demonstrated in patients undergoing palliative surgical resection of the metastatic site. Considerable improvements in the understanding of metastatic diseases and therapeutic strategies are needed to improve the clinical outcome.

[880]

TÍTULO / TITLE: - Microwave ablation of lung tumours: single-centre preliminary experience.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiol Med. 2013 Nov 15.

●● Enlace al texto completo (gratis o de pago) [1007/s11547-013-0301-z](#)

AUTORES / AUTHORS: - Carrafiello G; Mangini M; Fontana F; Ierardi AM; De Marchi G; Rotolo N; Chini C; Cuffari S; Fugazzola C

INSTITUCIÓN / INSTITUTION: - Unit of Radiology, Uninsubria, Viale Borri 57, 21100, Varese, Italy, gcarraf@gmail.com.

RESUMEN / SUMMARY: - **PURPOSE:** This study was done to evaluate the feasibility, effectiveness and safety of microwave (MW) ablation of lung tumours. **MATERIALS AND METHODS:** Twenty-four patients underwent percutaneous MW ablation of 26 intraparenchymal pulmonary masses. All patients were judged to be inoperable on the basis of tumour stage, comorbidities, advanced age and/or refusal to undergo surgery. Ablation was performed using a microwave generator (Evident Microwave Ablation System, Covidien Ltd., Dublin). Lesions with a diameter ≤ 3 cm were treated with a single antenna, lesions with a diameter > 3 cm were treated by positioning two or more antennae, simultaneously. All patients underwent computed tomography (CT) follow-up with and without contrast administration at 1, 3 and 6 months and then yearly in combination with complete blood and metabolic tests. **RESULTS:** Technical success was 100 %. No major complications were recorded. Asymptomatic grade-1 pneumothorax was recorded in 9 patients (37.5 %). One case of asymptomatic pleural

effusion and one of haemoptysis, not requiring transfusion, were observed. No patients were diagnosed with a post-ablation syndrome. Complete necrosis was observed in 16 of 26 lesions (61.6 %). Partial necrosis was obtained in 30.8 % (8/26 lesions); in one case (3.8 %) a progression of the disease was recorded and in another case (3.8 %) a stability was observed. CONCLUSIONS: Our preliminary experience may be considered in accordance with literature dates, in terms of efficacy and safety.

[881]

TÍTULO / TITLE: - Accuracy of deformable image registration for contour propagation in adaptive lung radiotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Radiat Oncol. 2013 Oct 18;8(1):243.

●● Enlace al texto completo (gratis o de pago) [1186/1748-717X-8-243](#)

AUTORES / AUTHORS: - Hardcastle N; van Elmp W; De Ruyscher D; Bzdusek K; Tome WA

RESUMEN / SUMMARY: - BACKGROUND: Deformable image registration (DIR) is an attractive method for automatic propagation of regions of interest (ROIs) in adaptive lung radiotherapy. This study investigates DIR for automatic contour propagation in adaptive Non Small Cell Lung Carcinoma patients. METHODS: Pre and mid-treatment fan beam 4D-kVCT scans were taken for 17 NSCLC patients. Gross tumour volumes (GTV), nodal-GTVs, lungs, esophagus and spinal cord were delineated on all kVCT scans. ROIs were propagated from pre- to mid-treatment images using three DIR algorithms. DIR-propagated ROIs were compared with physician-drawn ROIs on the mid-treatment scan using the Dice score and the mean slice-wise Hausdorff distance to agreement (MSHD). A physician scored the DIR-propagated ROIs based on clinical utility. RESULTS: Good agreement between the DIR-propagated and physician drawn ROIs was observed for the lungs and spinal cord. Agreement was not as good for the nodal-GTVs and esophagus, due to poor soft-tissue contrast surrounding these structures. 96% of OARs and 85% of target volumes were scored as requiring no or minor adjustments. CONCLUSIONS: DIR has been shown to be a clinically useful method for automatic contour propagation in adaptive radiotherapy however thorough assessment of propagated ROIs by the treating physician is recommended.

[882]

TÍTULO / TITLE: - Automatic contouring of brachial plexus using a multi-atlas approach for lung cancer radiotherapy.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Pract Radiat Oncol. 2013 Oct 1;3(4). pii: 3139-e147.

●● Enlace al texto completo (gratis o de pago) [1016/j.pro.2013.01.002](#)

AUTORES / AUTHORS: - Yang J; Amini A; Williamson R; Zhang L; Zhang Y; Komaki R; Liao Z; Cox J; Welsh J; Court L; Dong L

INSTITUCIÓN / INSTITUTION: - Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX.

RESUMEN / SUMMARY: - PURPOSE: To demonstrate a multi-atlas segmentation approach to facilitating accurate and consistent delineation of low-contrast brachial plexuses on CT images for lung cancer radiotherapy. MATERIALS AND METHODS: We retrospectively identified 90 lung cancer patients with treatment volumes near the brachial plexus. Ten representative patients were selected to form an atlas group, and

their brachial plexuses were delineated manually. We used deformable image registration to map each atlas brachial plexus to the remaining 80 patients. In each patient, a composite contour was created from 10 individual segmentations using the Simultaneous Truth and Performance Level Estimation (STAPLE) algorithm. This auto-delineated contour was reviewed and modified appropriately for each patient. We also performed 10 leave-one-out tests using the 10 atlases to validate the segmentation accuracy and demonstrate the contouring consistency using multi-atlas segmentation. RESULTS: The multi-atlas segmentation took less than 2 minutes to complete. Contour modification took 5 minutes compared with 20 minutes for manual contouring from scratch. The multi-atlas segmentation from the 10 leave-one-out tests had a mean 3D volume overlap of 59.2% +/- 8.2% and a mean 3D surface distance of 2.4 mm +/- 0.5 mm. The distances between the individual and average contours in the 10 leave-one-out tests demonstrated much better contouring consistency for modified contours than for manual contours. The auto-segmented contours did not require substantial modification, demonstrated by the good agreement between the modified and auto-segmented contours in the 80 patients. Dose volume histograms of auto-segmented and modified contours were also in good agreement, showing that editing auto-segmented contours is clinically acceptable in view of the dosimetric impact. CONCLUSIONS: Multi-atlas segmentation greatly reduced contouring time and improved contouring consistency. Editing auto-segmented contours to delineate the brachial plexus proved to be a better clinical practice than manually contouring from scratch.

[883]

TÍTULO / TITLE: - An Anti-CTLA4 Antibody May Be Effective in Malignant Mesothelioma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Discov. 2013 Nov;3(11):OF14. doi: 10.1158/2159-8290.CD-RW2013-209. Epub 2013 Sep 19.

- Enlace al texto completo (gratis o de pago) [1158/2159-8290.CD-RW2013-209](#)

RESUMEN / SUMMARY: - Tremelimumab shows activity and is well tolerated in previously treated malignant mesothelioma.

[884]

TÍTULO / TITLE: - -216G/T (rs712829), a functional variant of the promoter, is associated with the pleural metastasis of lung adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Sep;6(3):693-698. Epub 2013 Jul 3.

- Enlace al texto completo (gratis o de pago) [3892/ol.2013.1442](#)

AUTORES / AUTHORS: - Guo H; Xing Y; Liu R; Chen S; Bian X; Wang F; Yang C; Wang X

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Dongying People's Hospital, Dongying, Shandong 257091, P.R. China.

RESUMEN / SUMMARY: - Numerous mutations and variants in the epidermal growth factor receptor (EGFR) gene have been demonstrated to be associated with the occurrence, metastasis and prognosis of various types of tumors, including lung cancer. Thus, the present study aimed to investigate whether -216G/T (rs712829), a

functional polymorphism of the EGFR promoter that is able to induce EGFR activation and overexpression, is associated with the pleural metastasis of lung adenocarcinoma. The study subjects were comprised of 326 patients with primary lung adenocarcinoma and 312 matched cases with pleural metastasis. The -216G/T genotypes were determined in all subjects by PCR amplification and direct DNA sequencing, and EGFR expression was also evaluated by immunohistochemical staining in the primary tumor tissues with various -216G/T genotype backgrounds. The results showed that the frequencies of allele T and genotypes G/T and T/T in the pleural metastasis group were significantly higher compared with those in the non-metastasis group, with adjusted ORs of 1.46 (95% CI, 1.015-1.963) for G/T and 1.97 (95% CI, 1.051-3.152) for T/T. Furthermore, the expression of the EGFR protein was higher in the primary lung adenocarcinoma tissues with -216T/T and -216G/T compared with those with -216G/G ($P < 0.05$). These results collectively indicate that the -216G/T polymorphism in the EGFR promoter is associated with the risk of the pleural metastasis of lung adenocarcinoma and that this effect may be associated with -216G/T-induced overexpression of the EGFR protein.

[885]

TÍTULO / TITLE: - Identification of the methylation of p14ARF promoter as a novel non-invasive biomarker for early detection of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Transl Oncol. 2013 Oct 24.

●● [Enlace al texto completo \(gratis o de pago\) 1007/s12094-013-1122-1](#)

AUTORES / AUTHORS: - Li L; Shen Y; Wang M; Tang D; Luo Y; Jiao W; Wang Z; Yang R; Tian K

INSTITUCIÓN / INSTITUTION: - Thoracic Surgery of the Affiliated Hospital of Medical College, Qingdao University, 16 Jiangsu Road, Qingdao, 266003, China.

RESUMEN / SUMMARY: - **BACKGROUND:** Recent diagnostic procedure advances have greatly improved early lung cancer detection. However, the invasive, unpleasant and inconvenient nature of current diagnostic procedures limits their application. There is a great need of novel non-invasive biomarkers for early lung cancer diagnosis. In the present study, we intend to determine whether the blood signatures of p14ARF promoter methylation are suitable for early detection of lung cancer. **METHODS:** The study aimed to assess the probability of p14ARF promoter methylation in plasma samples to detect early lung cancer using nested methylation-specific PCR in the training set consisted of tumor tissues and paired blood. Besides, we were further to discuss the difference in time to progression between methylation and unmethylation of p14ARF promoter using univariate and multivariate analysis. **RESULTS:** The methylation of p14ARF promoter was detected in 33.6 % of tumor tissues, and 12.1 and 25.2 % in distant-cancer mucosa and matched plasma, respectively, and our study has also demonstrated the positive correlation between them by Pearson's test ($r = 0.300$). The tumor-free survival time of the unmethylation of p14ARF promoter is significantly longer than that of the methylation of p14ARF promoter in tumor tissues ($\chi^2 = 7.149$, $P = 0.008$). **CONCLUSION:** The methylation of p14ARF promoter in plasma samples has strong potential as a novel non-invasive biomarker for early detection of lung cancer, and the methylation of p14ARF promoter was considered as prognostic factor in our study.

[886]

TÍTULO / TITLE: - Association between MGMT Promoter Methylation and Non-Small Cell Lung Cancer: A Meta-Analysis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Sep 26;8(9):e72633. doi: 10.1371/journal.pone.0072633.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0072633](#)

AUTORES / AUTHORS: - Gu C; Lu J; Cui T; Lu C; Shi H; Xu W; Yuan X; Yang X; Huang Y; Lu M

INSTITUCIÓN / INSTITUTION: - Department of Epidemiology and Biostatistics and the Ministry of Education Key Laboratory of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, China.

RESUMEN / SUMMARY: - BACKGROUND: O(6)-methylguanine-DNA methyltransferase (MGMT) is one of most important DNA repair enzyme against common carcinogens such as alkylate and tobacco. Aberrant promoter methylation of the gene is frequently observed in non-small cell lung cancer (NSCLC). However, the importance of epigenetic inactivation of the gene in NSCLC published in the literature showed inconsistency. We quantified the association between MGMT promoter methylation and NSCLC using a meta-analysis method. METHODS: We systematically reviewed studies of MGMT promoter methylation and NSCLC in PubMed, EMBASE, Ovid, ISI Web of Science, Elsevier and CNKI databases and quantified the association between MGMT promoter methylation and NSCLC using meta-analysis method. Odds ratio (OR) and corresponding 95% confidence interval (CI) were calculated to evaluate the strength of association. Potential sources of heterogeneity were assessed by subgroup analysis and meta-regression. RESULTS: A total of 18 studies from 2001 to 2011, with 1,160 tumor tissues and 970 controls, were involved in the meta-analysis. The frequencies of MGMT promoter methylation ranged from 1.5% to 70.0% (median, 26.1%) in NSCLC tissue and 0.0% to 55.0% (median, 2.4%) in non-cancerous control, respectively. The summary of OR was 4.43 (95% CI: 2.85, 6.89) in the random-effects model. With stratification by potential source of heterogeneity, the OR was 20.45 (95% CI: 5.83, 71.73) in heterogeneous control subgroup, while it was 4.16 (95% CI: 3.02, 5.72) in the autologous control subgroup. The OR was 5.31 (95% CI: 3.00, 9.41) in MSP subgroup and 3.06 (95% CI: 1.75, 5.33) in Q-MSP subgroup. CONCLUSION: This meta-analysis identified a strong association between methylation of MGMT gene and NSCLC. Prospective studies should be required to confirm the results in the future.

[887]

TÍTULO / TITLE: - Identification of a seven glycopeptide signature for malignant pleural mesothelioma in human serum by selected reaction monitoring.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Clin Proteomics. 2013 Nov 8;10(1):16.

●● Enlace al texto completo (gratis o de pago) [1186/1559-0275-10-16](#)

AUTORES / AUTHORS: - Cerciello F; Choi M; Nicastri A; Bausch-Fluck D; Ziegler A; Vitek O; Felley-Bosco E; Stahel R; Aebbersold R; Wollscheid B

RESUMEN / SUMMARY: - BACKGROUND: Serum biomarkers can improve diagnosis and treatment of malignant pleural mesothelioma (MPM). However, the evaluation of potential new serum biomarker candidates is hampered by a lack of assay

technologies for their clinical evaluation. Here we followed a hypothesis-driven targeted proteomics strategy for the identification and clinical evaluation of MPM candidate biomarkers in serum of patient cohorts. RESULTS: Based on the hypothesis that cell surface exposed glycoproteins are prone to be released from tumor-cells to the circulatory system, we screened the surfaceome of model cell lines for potential MPM candidate biomarkers. Selected Reaction Monitoring (SRM) assay technology allowed for the direct evaluation of the newly identified candidates in serum. Our evaluation of 51 candidate biomarkers in the context of a training and an independent validation set revealed a reproducible glycopeptide signature of MPM in serum which complemented the MPM biomarker mesothelin. CONCLUSIONS: Our study shows that SRM assay technology enables the direct clinical evaluation of protein-derived candidate biomarker panels for which clinically reliable ELISA's currently do not exist.

[888]

TÍTULO / TITLE: - Reconstructing targetable pathways in lung cancer by integrating diverse omics data.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Commun. 2013 Oct 18;4:2617. doi: 10.1038/ncomms3617.

●● [Enlace al texto completo \(gratis o de pago\) 1038/ncomms3617](#)

AUTORES / AUTHORS: - Balbin OA; Prensner JR; Sahu A; Yocum A; Shankar S; Malik R; Fermin D; Dhanasekaran SM; Chandler B; Thomas D; Beer DG; Cao X; Nesvizhskii AI; Chinnaiyan AM

INSTITUCIÓN / INSTITUTION: - [1] Michigan Center for Translational Pathology, University of Michigan, Ann Arbor, Michigan 8109, USA [2] Department of Pathology, University of Michigan, Ann Arbor, Michigan 48109, USA [3] Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, Michigan 48109, USA.

RESUMEN / SUMMARY: - Global 'multi-omics' profiling of cancer cells harbours the potential for characterizing the signalling networks associated with specific oncogenes. Here we profile the transcriptome, proteome and phosphoproteome in a panel of non-small cell lung cancer (NSCLC) cell lines in order to reconstruct targetable networks associated with KRAS dependency. We develop a two-step bioinformatics strategy addressing the challenge of integrating these disparate data sets. We first define an 'abundance-score' combining transcript, protein and phospho-protein abundances to nominate differentially abundant proteins and then use the Prize Collecting Steiner Tree algorithm to identify functional sub-networks. We identify three modules centred on KRAS and MET, LCK and PAK1 and beta-Catenin. We validate activation of these proteins in KRAS-dependent (KRAS-Dep) cells and perform functional studies defining LCK as a critical gene for cell proliferation in KRAS-Dep but not KRAS-independent NSCLCs. These results suggest that LCK is a potential druggable target protein in KRAS-Dep lung cancers.

[889]

TÍTULO / TITLE: - Manic fringe inhibits tumor growth by suppressing Notch3 degradation in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Am J Cancer Res. 2013 Nov 1;3(5):490-9.

AUTORES / AUTHORS: - Yi F; Amarasinghe B; Dang TP

INSTITUCIÓN / INSTITUTION: - Division of Hematology and Medical Oncology, University of Virginia Charlottesville, VA, USA.

RESUMEN / SUMMARY: - Notch signaling plays an essential role in development as well as cancer. We have previously shown that Notch3 is important for lung cancer growth and survival. Notch receptors are activated through the interaction with their ligands, resulting in proteolytic cleavage of the receptors. This interaction is modulated by Fringe, a family of fucose-specific beta1,3 N-acetylglucosaminyltransferases that modify the extracellular subunit of Notch receptors. Studies in developmental models showed that Fringe enhances Notch's response to Delta ligands at the expense of Jagged ligands. We observed that Manic Fringe expression is down-regulated in lung cancer. Since Jagged1, a known ligand for Notch3, is often over-expressed in lung cancer, we hypothesized that Fringe negatively regulates Notch3 activation. In this study, we show that re-expression of Manic Fringe down-regulates Notch3 target genes HES1 and HeyL and reduces tumor phenotype in vitro and in vivo. The mechanism for this phenomenon appears to be related to modulation of Notch3 protein stability. Proteasome inhibition reverses Manic Fringe-induced protein turnover. Taken together, our data provide the first evidence that Manic Fringe functions as a tumor suppressor in the lung and that the mechanism of its anti-tumor activity is mediated by inhibition of Notch3 activation.

[890]

TÍTULO / TITLE: - A rare large tracheal glomus tumor with postoperative haematemesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Dis. 2013 Oct;5(5):E185-E188.

●● Enlace al texto completo (gratis o de pago) [3978/j.issn.2072-1439.2013.09.02](#)

AUTORES / AUTHORS: - Fan M; Liu C; Mei J; Pan L; Chen H; Liu L

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, West China Hospital, Sichuan University, Chengdu 610041, China.

RESUMEN / SUMMARY: - Glomus tumors are uncommon benign tumors which usually arise from the distal portion of the digits. A tracheal glomus tumor with large size is extremely rare. We present a case of a large tracheal glomus tumor that was resected using posterolateral thoracotomy and successful primary reconstruction of the trachea was achieved. Severe haematemesis happened after the patient was discharged. An emergency exploratory thoracotomy was performed but no signs of anastomotic bleeding were observed, while intraoperative gastroscopy revealed plenty of blood and blood clots in the patient's stomach. Medical treatments targeting hemorrhage of upper digestive tract were given and the patient finally recovered.

[891]

TÍTULO / TITLE: - Alterations of immune response of non-small cell lung cancer with Azacytidine.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncotarget. 2013 Nov;4(11):2067-79.

AUTORES / AUTHORS: - Wrangle J; Wang W; Koch A; Easwaran H; Mohammad HP; Vendetti F; Vancricking W; Demeyer T; Du Z; Parsana P; Rodgers K; Yen RW; Zahnow CA; Taube JM; Brahmer JR; Tykodi SS; Easton K; Carvajal RD; Jones PA;

Laird PW; Weisenberger DJ; Tsai S; Juergens RA; Topalian SL; Rudin CM; Brock MV; Pardoll D; Baylin SB

INSTITUCIÓN / INSTITUTION: - The Johns Hopkins University, School of Medicine, Oncology Center-Hematology/Medical Oncology, Baltimore, Maryland.

RESUMEN / SUMMARY: - Innovative therapies are needed for advanced Non-Small Cell Lung Cancer (NSCLC). We have undertaken a genomics based, hypothesis driving, approach to query an emerging potential that epigenetic therapy may sensitize to immune checkpoint therapy targeting PD-L1/PD-1 interaction. NSCLC cell lines were treated with the DNA hypomethylating agent azacytidine (AZA - Vidaza) and genes and pathways altered were mapped by genome-wide expression and DNA methylation analyses. AZA-induced pathways were analyzed in The Cancer Genome Atlas (TCGA) project by mapping the derived gene signatures in hundreds of lung adeno (LUAD) and squamous cell carcinoma (LUSC) samples. AZA up-regulates genes and pathways related to both innate and adaptive immunity and genes related to immune evasion in a several NSCLC lines. DNA hypermethylation and low expression of IRF7, an interferon transcription factor, tracks with this signature particularly in LUSC. In concert with these events, AZA up-regulates PD-L1 transcripts and protein, a key ligand-mediator of immune tolerance. Analysis of TCGA samples demonstrates that a significant proportion of primary NSCLC have low expression of AZA-induced immune genes, including PD-L1. We hypothesize that epigenetic therapy combined with blockade of immune checkpoints - in particular the PD-1/PD-L1 pathway - may augment response of NSCLC by shifting the balance between immune activation and immune inhibition, particularly in a subset of NSCLC with low expression of these pathways. Our studies define a biomarker strategy for response in a recently initiated trial to examine the potential of epigenetic therapy to sensitize patients with NSCLC to PD-1 immune checkpoint blockade.

[892]

TÍTULO / TITLE: - Bronchial carcinoid in college freshman with persistent focal wheeze.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Am Assoc Nurse Pract. 2013 Dec;25(12):641-3. doi: 10.1002/2327-6924.12059. Epub 2013 Aug 22.

●● Enlace al texto completo (gratis o de pago) [1002/2327-6924.12059](#)

AUTORES / AUTHORS: - Holzer R; Rosen D

INSTITUCIÓN / INSTITUTION: - Division of Respiratory Diseases, Children's Hospital Boston, Boston, Massachusetts.

RESUMEN / SUMMARY: - **PURPOSE:** To bring attention to a rare diagnosis in the pediatric population that is in the differential diagnosis for not well-controlled asthma. **DATA SOURCES:** Case presentation. **CONCLUSIONS:** Pulmonary carcinoid tumors are rare and usually present late in adolescence. Most of these tumors are located in the proximal airways and symptoms may be similar to those of asthma including cough, wheeze, chest pain, or recurrent pneumonia. **IMPLICATIONS FOR PRACTICE:** Bronchial carcinoid should be in the differential diagnosis for adolescents with difficult to control asthma, who have symptoms including chronic cough and focal wheeze. Referral to a pulmonary specialist should be considered to help work up the differential diagnoses.

[893]

TÍTULO / TITLE: - Knockdown of the Sodium-Dependent Phosphate Co-Transporter 2b (NPT2b) Suppresses Lung Tumorigenesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 23;8(10):e77121. doi: 10.1371/journal.pone.0077121.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0077121](#)

AUTORES / AUTHORS: - Hong SH; Minai-Tehrani A; Chang SH; Jiang HL; Lee S; Lee AY; Seo HW; Chae C; Beck GR Jr; Cho MH

INSTITUCIÓN / INSTITUTION: - Laboratory of Toxicology, College of Veterinary Medicine, Seoul National University, Seoul, Korea.

RESUMEN / SUMMARY: - The sodium-dependent phosphate co-transporter 2b (NPT2b) plays an important role in maintaining phosphate homeostasis. In previous studies, we have shown that high dietary inorganic phosphate (Pi) consumption in mice stimulated lung tumorigenesis and increased NPT2b expression. NPT2b has also been found to be highly expressed in human lung cancer tissues. The association of high expression of NPT2b in the lung with poor prognosis in oncogenic lung diseases prompted us to test whether knockdown of NPT2b may regulate lung cancer growth. To address this issue, aerosols that contained small interfering RNA (siRNA) directed against NPT2b (siNPT2b) were delivered into the lungs of K-ras (LA1) mice, which constitute a murine model reflecting human lung cancer. Our results clearly showed that repeated aerosol delivery of siNPT2b successfully suppressed lung cancer growth and decreased cancer cell proliferation and angiogenesis, while facilitating apoptosis. These results strongly suggest that NPT2b plays a role lung tumorigenesis and represents a novel target for lung cancer therapy.

[894]

TÍTULO / TITLE: - A systematic approach identifies FOXA1 as a key factor in the loss of epithelial traits during the epithelial-to-mesenchymal transition in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Genomics. 2013 Oct 4;14:680. doi: 10.1186/1471-2164-14-680.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2164-14-680](#)

AUTORES / AUTHORS: - Wang H; Meyer CA; Fei T; Wang G; Zhang F; Liu XS

INSTITUCIÓN / INSTITUTION: - School of Life Science and Technology, Tongji University, Shanghai 200092, China. wanghaiyun@tongji.edu.cn.

RESUMEN / SUMMARY: - BACKGROUND: The epithelial-to-mesenchymal transition is an important mechanism in cancer metastasis. Although transcription factors including SNAIL, SLUG, and TWIST1 regulate the epithelial-to-mesenchymal transition, other unknown transcription factors could also be involved. Identification of the full complement of transcription factors is essential for a more complete understanding of gene regulation in this process. Chromatin immunoprecipitation-sequencing (ChIP-Seq) technologies have been used to detect genome-wide binding of transcription factors; here, we developed a systematic approach to integrate existing ChIP-Seq and transcriptome data. We scanned multiple transcription factors to investigate their functional impact on the epithelial-to-mesenchymal transition in the human A549 lung adenocarcinoma cell line. RESULTS: Among the transcription factors tested, impact scores identified the forkhead box protein A1 (FOXA1) as the most significant transcription factor in the epithelial-to-mesenchymal transition. FOXA1 physically

associates with the promoters of its predicted target genes. Several critical epithelial-to-mesenchymal transition effectors involved in cellular adhesion and cellular communication were identified in the regulatory network of FOXA1, including FOXA2, FGA, FGB, FGG, and FGL1. The implication of FOXA1 in the epithelial-to-mesenchymal transition via its regulatory network indicates that FOXA1 may play an important role in the initiation of lung cancer metastasis. CONCLUSIONS: We identified FOXA1 as a potentially important transcription factor and negative regulator in the initial stages of lung cancer metastasis. FOXA1 may modulate the epithelial-to-mesenchymal transition via its transcriptional regulatory network. Further, this study demonstrates how ChIP-Seq and expression data could be integrated to delineate the impact of transcription factors on a specific biological process.

[895]

TÍTULO / TITLE: - Lung cancer: Drug-sensitivity-time for a rearrangement?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Dec;10(12):670. doi: 10.1038/nrclinonc.2013.216. Epub 2013 Nov 12.

●● Enlace al texto completo (gratis o de pago) [1038/nrclinonc.2013.216](#)

AUTORES / AUTHORS: - Hutchinson L

[896]

TÍTULO / TITLE: - Unusual region for pericardial malignant mesothelioma: cutaneous manifestation in a Turkish woman.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rare Tumors. 2013 Sep 4;5(3):e41. doi: 10.4081/rt.2013.e41.

●● Enlace al texto completo (gratis o de pago) [4081/rt.2013.e41](#)

AUTORES / AUTHORS: - Gunday M; Erinanc H; Geredeli C

INSTITUCIÓN / INSTITUTION: - Department of Cardiovascular Surgery, Faculty of Medicine, Baskent University , Ankara ;

RESUMEN / SUMMARY: - Malignant mesothelioma is a disease that originates from mesenchymal cells. It is related to the occupational or environmental exposure to asbestos. The treatment remains controversial because it is commonly diagnosed at a very late stage, and the prognosis is very poor. In this report, we present a 37-year-old female patient who was admitted with shortness of breath, palpitation and inability to sleep on her back for the previous 10 days. A large pericardial effusion was detected on echocardiography. Pericardiocentesis was performed and the patient's symptoms were alleviated. However, approximately 7 months later, she was readmitted to the clinic with complaints of a mass at the incision site. Pathological examination of the mass yielded a diagnosis of pericardial malignant mesothelioma. Malignant mesothelioma is a rare occurrence, and to our knowledge, there are no reports in the English literature of pericardial malignant mesothelioma local invasion to an incision site.

[897]

TÍTULO / TITLE: - DOK2 Inhibits EGFR-Mutated Lung Adenocarcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 8;8(11):e79526. doi: 10.1371/journal.pone.0079526.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079526](https://doi.org/10.1371/journal.pone.0079526)

AUTORES / AUTHORS: - Berger AH; Chen M; Morotti A; Janas JA; Niki M; Bronson RT; Taylor BS; Ladanyi M; Van Aelst L; Politi K; Varmus HE; Pandolfi PP

INSTITUCIÓN / INSTITUTION: - Cancer Genetics Program, Beth Israel Deaconess Cancer Center, Departments of Medicine and Pathology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, United States of America.

RESUMEN / SUMMARY: - Somatic mutations in the EGFR proto-oncogene occur in ~15% of human lung adenocarcinomas and the importance of EGFR mutations for the initiation and maintenance of lung cancer is well established from mouse models and cancer therapy trials in human lung cancer patients. Recently, we identified DOK2 as a lung adenocarcinoma tumor suppressor gene. Here we show that genomic loss of DOK2 is associated with EGFR mutations in human lung adenocarcinoma, and we hypothesized that loss of DOK2 might therefore cooperate with EGFR mutations to promote lung tumorigenesis. We tested this hypothesis using genetically engineered mouse models and find that loss of Dok2 in the mouse accelerates lung tumorigenesis initiated by oncogenic EGFR, but not that initiated by mutated Kras. Moreover, we find that DOK2 participates in a negative feedback loop that opposes mutated EGFR; EGFR mutation leads to recruitment of DOK2 to EGFR and DOK2-mediated inhibition of downstream activation of RAS. These data identify DOK2 as a tumor suppressor in EGFR-mutant lung adenocarcinoma.

[898]

TÍTULO / TITLE: - FDA approves afatinib for advanced lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncology (Williston Park). 2013 Aug;27(8):813-4.

[899]

TÍTULO / TITLE: - Epigenetic inactivation of heparan sulfate (glucosamine) 3-O-sulfotransferase 2 in lung cancer and its role in tumorigenesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 12;8(11):e79634. doi: 10.1371/journal.pone.0079634.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079634](https://doi.org/10.1371/journal.pone.0079634)

AUTORES / AUTHORS: - Hwang JA; Kim Y; Hong SH; Lee J; Cho YG; Han JY; Kim YH; Han J; Shim YM; Lee YS; Kim DH

INSTITUCIÓN / INSTITUTION: - Cancer Genomics Branch, Research Institute, National Cancer Center, Goyang-si, Korea.

RESUMEN / SUMMARY: - BACKGROUND: This study was aimed at investigating the functional significance of heparan sulfate (glucosamine) 3-O-sulfotransferase 2 (HS3ST2) hypermethylation in non-small cell lung cancer (NSCLC). METHODOLOGY/ PRINCIPAL FINDINGS: HS3ST2 hypermethylation was characterized in six lung cancer cell lines, and its clinical significance was analyzed using 298 formalin-fixed paraffin-embedded tissues and 26 fresh-frozen tissues from 324 NSCLC patients. MS-HRM (methylation-specific high-resolution melting) and EpiTYPER™ assays showed substantial hypermethylation of CpG island at the promoter region of HS3ST2 in six lung cancer cell lines. The silenced gene was demethylated and re-expressed by treatment with 5-aza-2'-deoxycytidine (5-Aza-dC). A promoter assay also showed the

core promoter activity of HS3ST2 was regulated by methylation. Exogenous expression of HS3ST2 in lung cancer cells H460 and H23 inhibited cell migration, invasion, cell proliferation and whereas knockdown of HS3ST2 in NHBE cells induced cell migration, invasion, and cell proliferation in vitro. A negative correlation was observed between mRNA and methylation levels of HS3ST2 in 26 fresh-frozen tumors tissues ($\rho = -0.51$, $P = 0.009$; Spearman's rank correlation). HS3ST2 hypermethylation was found in 95 (32%) of 298 primary NSCLCs. Patients with HS3ST2 hypermethylation in 193 node-negative stage I-II NSCLCs with a median follow-up period of 5.8 years had poor overall survival (hazard ratio = 2.12, 95% confidence interval = 1.25-3.58, $P = 0.005$) compared to those without HS3ST2 hypermethylation, after adjusting for age, sex, tumor size, adjuvant therapy, recurrence, and differentiation. CONCLUSIONS/SIGNIFICANCE: The present study suggests that HS3ST2 hypermethylation may be an independent prognostic indicator for overall survival in node-negative stage I-II NSCLC.

[900]

TÍTULO / TITLE: - Pleuropneumectomy for diffuse pleural metastasis in primary lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S92-7. doi: 10.4103/0973-1482.119115.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119115](#)

AUTORES / AUTHORS: - Jin WB; Liang CY; Peng YH; Zhou NK

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Surgery, Chinese People's Liberation Army Medical School, Beijing 100853, China.

RESUMEN / SUMMARY: - Objective: The purpose of this study is to analyze a single institution experience with pleuropneumectomy for pleural metastasis and malignant pleural effusion in primary lung cancer. Materials and Methods: From August 1978 to August 2011, 66 consecutive patients with lung cancer underwent pleuropneumectomy. Patients were followed-up after the operation. The quality-of-life and the survival time were recorded. Results: All the 66 patients were successfully operated on, including 38 patients in early years (1978-1993) and 28 patients in recent years (1994-2011). Two patients in early years died after the operation. Post-operative complications occurred including heart arrhythmia, respiratory insufficiency and bacterial infection of residual lung, chylothorax and mental disorder. A total of 61 patients have been successfully followed-up and three patients in early years were lost in 1 year after the operation. Local recurrence was found in seven cases (4 in early years, 3 in recent years) and distant metastasis was found in 48 cases (29 in early years, 19 in recent years). A total of 54 patients died from tumors, seven patients survived. The actuarial 1, 2 and 3-year survival rates are 72.7%, 27.2% and 6.1% of 36 in patients of early years and 85.7%, 46.4% and 21.4% in 28 patients of recent years. The mean survival and the median survival of the total 64 patients were 20.0 +/- 10.9 months and 17 months respectively. Further analysis showed that the mean survival and the median survival of the 36 patients in early years were 17.2 +/- 9.7 months and 15 months, in contrast to 23.4 +/- 11.3 months and 18 months of the 28 patients in recent years. Conclusion: Pleuropneumectomy is an option of patients with advanced-stage lung cancer associated with uncontrolled malignant pleural fluid by conservative therapies. Strict selection of patient to be operated, careful procedures

to eradicate obvious tumors and metastasis and enhanced post-operative combined therapy are beneficial to patients' long-term survival.

[901]

TÍTULO / TITLE: - The landscape of histone acetylation involved in epithelial-mesenchymal transition in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S86-91. doi: 10.4103/0973-1482.119113.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119113](#)

AUTORES / AUTHORS: - Zhang L; Liu Z; Ma W; Wang B

INSTITUCIÓN / INSTITUTION: - Shandong Health Education and Training Center, Jinan, 250014, China.

RESUMEN / SUMMARY: - Epithelial-mesenchymal transition (EMT) has been widely accepted as the early stage of tumor metastasis, which is accomplished by a group of transcription factors based on cancer genome. However, with the progress of epigenome profiling technique, it has been demonstrated that aberrant histone modifications especially acetylation play an important role in EMT and cancer metastasis. Besides this, numerous studies have elucidated the mechanisms of histone acetyltransferases and deacetylases involved in EMT. Moreover, the network of these histone-related proteins and those transcription factors that play key roles in EMT is under increasing investigation. In addition, the crosstalk among deoxyribonucleic acid methylation, histone acetylation and micro Ribonucleic acid, three major epigenetic modifications, is also an important part in tumor progression. Here, we explore the mechanisms of histone acetylation in EMT and discuss the potential clinical strategies using the epigenetic drugs.

[902]

TÍTULO / TITLE: - The regulation of cell polarity in the progression of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S80-5. doi: 10.4103/0973-1482.119110.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119110](#)

AUTORES / AUTHORS: - Liu Y; Chen LP

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Medicine, Shenzhou Hospital Affiliated to Shenyang Medical College, Shenyang 110002, China.

RESUMEN / SUMMARY: - Lung cancer is the most frequent malignant disease, since it has often metastasized to distant organs by the time of diagnosis. Epithelial-mesenchymal transition (EMT) is an important process during the progression of lung cancer. Epithelial cells lose the polarity, which contributes to uncontrolled invasion and metastasis of cancer cells. Cell polarity establishment and maintenance depends upon the three complex proteins which are par, crumbs and scribble complexes, of which are reported as tumor suppressors. The cell polarity proteins could interact with cell-cell contact and cell-extracellular matrix contact and cell-intrinsic signaling. These interactions are proved to be involved in lung cancer metastasis. However, our understanding of the mechanisms by which this occurs is poor. In this review, we will discuss the regulatory network of cell polarity in the lung cancer, especially on EMT.

[903]

TÍTULO / TITLE: - Preparation and in-vitro Evaluation of an Antisense-containing Cationic Liposome against Non-small Cell Lung Cancer: a Comparative Preparation Study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Iran J Pharm Res. 2013 Winter;12(Suppl):3-10.

AUTORES / AUTHORS: - Saffari M; H Shirazi F; Oghabian MA; Moghimi HR

INSTITUCIÓN / INSTITUTION: - Department of Pharmaceutics, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

RESUMEN / SUMMARY: - The current methods for treatment of cancers are inadequate and more specific methods such as gene therapy are in progress. Among different vehicles, cationic liposomes are frequently used for delivery of genetic material. This investigation aims to prepare and optimize DOTAP cationic liposomes containing an antisense oligonucleotide (AsODN) against protein kinase C alpha in non-small cells lung cancer (NSCLC). To perform this investigation, two different methods of ethanol injection and thin film hydration were used to prepare AsODN-loaded DOTAP liposomes. The formulated liposomes were then evaluated for their morphology, particle size, zeta potential and encapsulation efficiency, and the best formulation was chosen. In-vitro growth inhibitory effect of encapsulated ODN on A549 cells were evaluated by MTT and colonogenic assay. The physical and serum stability of liposomal ODN were also evaluated. Thin film hydration method resulted in large liposomes that required downsizing by extrusion with an encapsulation efficiency of 13%. Ethanol injection, in a single step gave liposomes with a small size of 115 nm and an encapsulation efficiency of around 90% which were physically stable for 6 months. The optimized liposome could protect oligonucleotides from degradation by nuclease. Cell studies showed a 20% sequence-specific inhibition of cell growth in MTT assay and revealed an LC50 of 103 nM in colonogenic studies. In conclusion, ethanol injection was able to provide suitable liposomes from the permanently charged DOTAP. Also the resulted liposomes were able to inhibit the growth of lung cancer cells.

[904]

TÍTULO / TITLE: - Primary small cell carcinoma of the liver, a rare entity.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - British Medical J (BMJ). Acceso gratuito al texto completo.

●● Enlace a la Editora de la Revista <http://bmj.com/search.dtl>

●● Cita: British Medical J. (BMJ): <> Case Rep. 2013 Nov 5;2013. pii: bcr2013201990. doi: 10.1136/bcr-2013-201990.

●● Enlace al texto completo (gratis o de pago) 1136/bcr-2013-201990

AUTORES / AUTHORS: - Otten M; Sepehrkhoy S; van Everdingen K; Haas L

INSTITUCIÓN / INSTITUTION: - Department of Intensive Care, Diaconessenhuis Utrecht, Utrecht, The Netherlands.

[905]

TÍTULO / TITLE: - Targeting angiogenesis in advanced non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Natl Compr Canc Netw. 2013 Oct 1;11(10):1235-47.

AUTORES / AUTHORS: - Lammers PE; Horn L

INSTITUCIÓN / INSTITUTION: - From Vanderbilt-Ingram Cancer Center, Vanderbilt University, Nashville, Tennessee.

RESUMEN / SUMMARY: - Lung cancer is the leading cause of cancer-related mortality in the United States. Over the past 40 years, treatments with standard chemotherapy agents have not resulted in substantial improvements in long-term survival for patients with advanced lung cancer. Therefore, new targets have been sought, and angiogenesis is a promising target for non-small cell lung cancer (NSCLC). Bevacizumab, a monoclonal antibody targeted against the vascular endothelial growth factor, is the only antiangiogenic agent currently recommended by NCCN for the treatment of advanced NSCLC. However, several antibody-based therapies and multitargeted tyrosine kinase inhibitors are currently under investigation for the treatment of patients with NSCLC. This article summarizes the available clinical trial data on the efficacy and safety of these agents in patients with advanced lung cancer.

[906]

TÍTULO / TITLE: - The challenges of lung cancer in China.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Cancer Res Ther. 2013 Sep;9 Suppl:S65-6. doi: 10.4103/0973-1482.119098.

●● Enlace al texto completo (gratis o de pago) [4103/0973-1482.119098](#)

AUTORES / AUTHORS: - Liu Q; Zhou Q

INSTITUCIÓN / INSTITUTION: - Tianjin Key Laboratory of Lung Cancer Metastasis and Tumor Microenvironment, Tianjin Lung Cancer Institute, Tianjin Medical University General Hospital, Tianjin 300052, China.

[907]

TÍTULO / TITLE: - Squamous cell lung cancer: where do we stand and where are we going?

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncology (Williston Park). 2013 Sep;27(9):914-5.

AUTORES / AUTHORS: - Hirsch FR

INSTITUCIÓN / INSTITUTION: - University of Colorado Cancer Center, Aurora, Colorado, USA.

[908]

TÍTULO / TITLE: - The deubiquitinating enzyme USP17 is associated with non-small cell lung cancer (NSCLC) recurrence and metastasis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncotarget. 2013 Oct;4(10):1836-43.

AUTORES / AUTHORS: - McFarlane C; McFarlane S; Paul I; Arthur K; Scheaff M; Kerr K; Stevenson M; Fennell DA; Johnston JA

INSTITUCIÓN / INSTITUTION: - Centre for Infection and Immunity, Queen's University Belfast, Belfast, Northern Ireland, UK.

RESUMEN / SUMMARY: - USP17 is a cell cycle regulated deubiquitinating enzyme that is highly expressed in tumor-derived cell lines and has an established role in cell proliferation and chemotaxis. This is the first study to examine the clinical significance of USP17 expression in non-small cell lung cancer (NSCLC). USP17 was overexpressed in both squamous and adenocarcinoma NSCLC tissue. Patients with

USP17 positive tumors had significantly reduced recurrence-free survival than patients with USP17 negative tumors. Moreover, USP17 was more highly expressed in patients with recurrence of disease at distant sites, suggesting that USP17 levels may correlate with NSCLC distant metastases. Overall, these findings establish USP17 as a potentially valuable novel biomarker for metastatic lung cancer.

[909]

TÍTULO / TITLE: - Influence of Stromal Components on Lung Cancer Carcinogenesis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Carcinog Mutagen. 2013 Jun 25;13(8). doi: 10.4172/2157-2518.S13-008.

●● Enlace al texto completo (gratis o de pago) [4172/2157-2518.S13-008](#)

AUTORES / AUTHORS: - Shuman Moss LA; Stetler-Stevenson WG

INSTITUCIÓN / INSTITUTION: - Radiation Oncology Branch, National Cancer Institute, NIH, Bethesda, MD 20892-1500, USA.

RESUMEN / SUMMARY: - The association between tumor growth and angiogenesis was first observed over 100 years ago. Since then, research has shown the dependence of tumor growth on angiogenesis and the ability of cancer cells to alter the stromal microenvironment. Technological advancements have enabled researchers to identify cell types within a tumor, identify chemokines, cytokines, and growth factors secreted by tumor cells, show the interaction between tumor cells and stroma, and investigate the function of distinct genes using knockout and transgenic mouse technology. This review provides an overview of tumor growth, emphasizing research using in vivo mouse models on vascular endothelial growth factor (VEGF), fibrinogen, fibronectin, plasminogen, and MMPs in primary tumor growth and metastasis of lung cancer in particular.

[910]

TÍTULO / TITLE: - On the combination of wavelet and curvelet for feature extraction to classify lung cancer on chest radiographs.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Conf Proc IEEE Eng Med Biol Soc. 2013 Jul;2013:3674-7. doi: 10.1109/EMBC.2013.6610340.

●● Enlace al texto completo (gratis o de pago) [1109/EMBC.2013.6610340](#)

AUTORES / AUTHORS: - Al-Absi HR; Samir BB; Alhersh T; Sulaiman S

RESUMEN / SUMMARY: - This paper investigates the combination of multiresolution methods for feature extraction for lung cancer. The focus is on the impact of combining wavelet and curvelet on the accuracy of the disease diagnosis. The paper investigates feature extraction with two different levels of wavelet, two different wavelet functions and the combination of wavelet and curvelet to obtain a high classification rate. The findings suggest the potential of combining different multiresolution methods in achieving high accuracy rates.

[911]

TÍTULO / TITLE: - Lung-sparing approach for an intrapulmonary bronchogenic cyst involving the right upper and middle lobes.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - British Medical J (BMJ). Acceso gratuito al texto completo.

●● Enlace a la Editora de la Revista <http://bmi.com/search.dtl>
●● Cita: British Medical J. (BMJ): <> Case Rep. 2013 Oct 16;2013. pii: bcr2013201227. doi: 10.1136/bcr-2013-201227.

●● Enlace al texto completo (gratis o de pago) [1136/bcr-2013-201227](http://bmi.com/search.dtl/1136/bcr-2013-201227)

AUTORES / AUTHORS: - Criscione A; Scamporlino A; Calvo D; Migliore M

INSTITUCIÓN / INSTITUTION: - Section of Thoracic Surgery, Department of Surgery, University of Catania, Catania, Italy.

RESUMEN / SUMMARY: - Intrapulmonary bronchogenic cysts (IBC) represent 20% of abnormal budding of the respiratory tract. Lobectomy is the recommended treatment for IBC in symptomatic adults. We presented a case of a patient with an IBC involving the right upper and middle lobes (RUL-RML). A 27-year-old woman presented with a 2-month history of thoracic pain, cough and haemoptysis. An opacity was found on the chest X-ray. High-resolution CT/MRI showed a 7x4.5 cm marginated mass with an air bubble inside. A video-assisted thoracoscopic surgery was performed. The cyst was neither palpable nor visible. An intraoperative ultrasonography localised the cyst involving the RUL-RML. The lung above the cyst was incised, and a greenish-mucoid content was aspirated. A branch of the superior pulmonary vein was visible. The remaining cystic wall was cauterised. The patient was discharged on day 4. Histology confirmed the IBC. The patient is asymptomatic at a 16-month follow-up. The lung-sparing operation in a young woman with IBC involving the RUL-RML has been beneficial. A long-term follow-up is mandatory.

[912]

TÍTULO / TITLE: - Choroidal metastasis of non-small cell lung cancer that responded to gefitinib.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Case Rep Ophthalmol Med. 2013;2013:213124. doi: 10.1155/2013/213124. Epub 2013 Sep 12.

●● Enlace al texto completo (gratis o de pago) [1155/2013/213124](http://bmi.com/search.dtl/1155/2013/213124)

AUTORES / AUTHORS: - Shimomura I; Tada Y; Miura G; Suzuki T; Matsumura T; Tsushima K; Terada J; Kurimoto R; Sakaida E; Sekine I; Takiguchi Y; Yamamoto S; Tatsumi K

INSTITUCIÓN / INSTITUTION: - Department of Respiriology, Graduate School of Medicine, Chiba University, 1-8-1 Inohana Chuo-ku, Chiba 260-8677, Japan.

RESUMEN / SUMMARY: - A 52-year-old Japanese woman presented with optical symptoms, including left-sided myodesopsia, blurred vision, narrowed visual field, and diminished visual acuity. Ocular evaluation revealed a metastatic tumor in the choroid. Further examinations identified pulmonary adenocarcinoma as the primary tumor. Because an epidermal growth factor receptor gene (EGFR) mutation was detected in a biopsy specimen, gefitinib treatment was initiated. Dramatic responses were obtained in the primary tumor and metastatic foci. Optical symptoms improved and remained stable for 5 months during the treatment, until relapse. This report demonstrates that gefitinib is effective for choroidal metastasis of pulmonary adenocarcinoma harboring an EGFR mutation.

[913]

TÍTULO / TITLE: - Isolated solitary brain metastasis as a relapse of small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Oct;6(4):1108-1110. Epub 2013 Jul 24.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1489](#)

AUTORES / AUTHORS: - Sakurai H; Kurishima K; Homma S; Kagohashi K; Miyazaki K; Kawaguchi M; Satoh H; Hizawa N

INSTITUCIÓN / INSTITUTION: - Division of Respiratory Medicine, Faculty of Medicine, University of Tsukuba, Tsukuba 305-8575, Japan.

RESUMEN / SUMMARY: - The brain is one of the most common sites for the metastasis of small cell lung cancer (SCLC). The present study describes two cases of an isolated solitary brain metastasis as a relapse of SCLC, which occurred more than one year after the completion of the initial successful treatment for SCLC. The tumors were identified during a regular check-up computed tomography (CT) scan and were successfully treated. To the best of our knowledge, this is the first study to report the cases of two patients with an isolated solitary brain metastasis as a relapse of SCLC. Although extremely rare, the possibility of such recurrences should be considered, particularly in patients who have refused prophylactic cranial irradiation.

[914]

TÍTULO / TITLE: - Targeting and retargeting in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Discov. 2013 Nov;3(11):1210-1. doi: 10.1158/2159-8290.CD-NB2013-139. Epub 2013 Sep 26.

●● Enlace al texto completo (gratis o de pago) [1158/2159-8290.CD-NB2013-139](#)

RESUMEN / SUMMARY: - Oncologists say they may need to trade off efficacy and toxicity in today's targeted drugs for EGFR-mutated non-small cell lung cancer.

[915]

TÍTULO / TITLE: - Merkel cell polyomavirus and extrapulmonary small cell carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Oct;6(4):1049-1052. Epub 2013 Jul 23.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1483](#)

AUTORES / AUTHORS: - Hourdequin KC; Lefferts JA; Brennick JB; Ernstoff MS; Tsongalis GJ; Pipas JM

INSTITUCIÓN / INSTITUTION: - Department of Medicine, Section of Hematology/Oncology, Geisel School of Medicine at Dartmouth, Hanover, NH, USA ; Dartmouth Hitchcock Medical Center and Norris Cotton Cancer Center, Lebanon, NH, USA.

RESUMEN / SUMMARY: - The Merkel cell polyomavirus (MCV) is involved in the development of up to 100% of Merkel cell cancer (MCC) cases. Early studies have reported that the virus was infrequently detected in other small cell or neuroendocrine lung carcinomas, which share histological features with MCC. The present study investigated the presence of MCV in cases of extrapulmonary small cell carcinoma (ESCC), which also shares histological features with MCC. A total of 25 cases of ESCC that were diagnosed between 2004 and 2009 were identified at The Dartmouth Hitchcock Medical Center. Archived tissue was available for testing in 16 of these cases. A total of 11 tissue specimens of MCC were used as positive controls. DNA that was extracted from the archived tissue was subjected to five separate quantitative

(q)PCR assays for the detection of four MCV genomic targets. MCV DNA was detected in 3/16 (19%) of the ESCCs and in all 11 MCCs. In the three MCV-positive ESCCs, the viral target was only detected by either one or two of the PCR assays. In 8/11 MCV-positive MCCs, the DNA tested positive by either three or all four assays and the remaining three MCCs tested positive by either one or two assays. The beta-globin endogenous control was detected in all the samples that were tested. Although MCC and ESCC share numerous histological features, MCV is detected at a lower frequency in ESCC. The possible role for MCV in the etiology of ESCC remains uncertain and may account for the rare cases of ESCC with no other identifiable etiology. The failure of other assays to detect MCV may be due to sequence variability in the MCV genome.

[916]

TÍTULO / TITLE: - Overexpression of JAM-A in Non-Small Cell Lung Cancer Correlates with Tumor Progression.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Nov 12;8(11):e79173. doi: 10.1371/journal.pone.0079173.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0079173](#)

AUTORES / AUTHORS: - Zhang M; Luo W; Huang B; Liu Z; Sun L; Zhang Q; Qiu X; Xu K; Wang E

INSTITUCIÓN / INSTITUTION: - Department of Pathology, First Affiliated Hospital and College of Basic Medical Sciences, China Medical University, Shenyang, People's Republic of China ; Department of Pathology, College of Basic Medical Sciences, Shenyang Medical College, Shenyang, People's Republic of China.

RESUMEN / SUMMARY: - The objective of the current study was to determine the clinical significance of junctional adhesion molecule A (JAM-A) in patients with non-small cell lung cancer (NSCLC) and the biological function of JAM-A in NSCLC cell lines. We showed that JAM-A is predominantly expressed in cell membranes and high expression of JAM-A occurred in 37% of lung tumor specimens compared to corresponding normal tissues. High expression of JAM-A was significantly correlated with TNM stage ($P = 0.021$), lymph node metastasis ($P = 0.007$), and decreased overall survival ($P = 0.02$). In addition, we observed that silencing JAM-A by small interfering RNA inhibited tumor cell proliferation and induced cell cycle arrest at the G1/S boundary. Western blotting analysis revealed that knockdown of JAM-A decreased the protein levels of cyclin D1, CDK4, 6, and P-Rb. Thus, JAM-A plays an important role in NSCLC progression.

[917]

TÍTULO / TITLE: - Comparisons of microRNA Patterns in Plasma before and after Tumor Removal Reveal New Biomarkers of Lung Squamous Cell Carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 9;8(10):e78649. doi: 10.1371/journal.pone.0078649.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078649](#)

AUTORES / AUTHORS: - Aushev VN; Zborovskaya IB; Laktionov KK; Girard N; Cros MP; Herceg Z; Krutovskikh V

INSTITUCIÓN / INSTITUTION: - Epigenetics Unit, International Agency for Research on Cancer (IARC), Lyon, France ; Carcinogenesis Institute of N.N Blokhin Russian Cancer Research Center, Russian Academy of Medical Sciences, Moscow, Russia.

RESUMEN / SUMMARY: - Lung cancer is the major human malignancy, accounting for 30% of all cancer-related deaths worldwide. Poor survival of lung cancer patients, together with late diagnosis and resistance to classic chemotherapy, highlights the need for identification of new biomarkers for early detection. Among different cancer biomarkers, small non-coding RNAs called microRNAs (miRNAs) are considered the most promising, owing to their remarkable stability, their cancer-type specificity, and their presence in body fluids. However, results of multiple previous attempts to identify circulating miRNAs specific for lung cancer are inconsistent, likely due to two main reasons: prominent variability in blood miRNA content among individuals and difficulties in distinguishing tumor-relevant miRNAs in the blood from their non-tumor counterparts. To overcome these impediments, we compared circulating miRNA profiles in patients with lung squamous cell carcinoma (SCC) before and after tumor removal, assuming that the levels of all tumor-relevant miRNAs would drop after the surgery. Our results revealed a specific panel of the miRNAs (miR-205, -19a, -19b, -30b, and -20a) whose levels decreased strikingly in the blood of patients after lung SCC surgery. Interestingly, miRNA profiling of plasma fractions of lung SCC patients revealed high levels of these miRNA species in tumor-specific exosomes; additionally, some of these miRNAs were also found to be selectively secreted to the medium by cultivated lung cancer cells. These results strengthen the notion that tumor cells secrete miRNA-containing exosomes into circulation, and that miRNA profiling of the exosomal plasma fraction may reveal powerful cancer biomarkers.

[918]

TÍTULO / TITLE: - Probable initial pulmonary lymphangiomyomatosis and mediastinal lymphangiomyoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rev Port Pneumol. 2013 Nov 20. pii: S0873-2159(13)00104-9. doi: 10.1016/j.rppneu.2013.06.007.

●● Enlace al texto completo (gratis o de pago) [1016/j.rppneu.2013.06.007](#)

AUTORES / AUTHORS: - Pontes M; Barbosa C; Coelho ML; Carvalho L

INSTITUCIÓN / INSTITUTION: - Serviço de Anatomia Patológica, Centro Hospitalar Universitário de Coimbra, Hospitais da Universidade de Coimbra, Coimbra, Portugal. Electronic address: manuelpontes1@sapo.pt.

RESUMEN / SUMMARY: - A 68 year old woman was submitted to a mediastinal lymphangiomyoma resection found in a follow-up study of lower left lung resection due to bronchiectasis complicated by chylothorax. This led to a reevaluation of the pulmonary specimen that revealed, in addition to inflammatory bronchiectasis, small spindle cell nodules in the lung parenchyma, similar to minute pulmonary meningothelial-like nodules, but with smooth muscle actin immunohistochemical positivity. The possibility of initial pulmonary development of lymphangiomyomatosis is discussed.

[919]

TÍTULO / TITLE: - Signal stratification of autoantibody levels in serum samples and its application to the early detection of lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Dis. 2013 Oct;5(5):618-625.

●● Enlace al texto completo (gratis o de pago) [3978/j.issn.2072-1439.2013.08.65](#)

AUTORES / AUTHORS: - Healey GF; Lam S; Boyle P; Hamilton-Fairley G; Peek LJ; Robertson JF

INSTITUCIÓN / INSTITUTION: - Oncimmune Ltd, Nottingham City Hospital, Nottingham, UK;

RESUMEN / SUMMARY: - BACKGROUND: Further signal stratification for the EarlyCDT®-Lung test should facilitate interpretation of the test, leading to more precise interventions for particular patients. METHODS: Samples were measured for the presence of autoantibodies to seven tumor-associated antigens (TAAs) (p53, NY-ESO-1, CAGE, GBU4-5, SOX2, MAGE A4, and HuD). In addition to the current test cut-offs (determined using a previously reported Validation case-control sample set, set A; n=501), new high and low cut-offs were set in order to maximize the test's positive and negative predictive values (PPV and NPV, respectively). All three sets of cut-offs were applied to two confirmatory datasets: (I) the case-control set B (n=751), and (II) Population-derived set C (n=883), and all three datasets combined (n=2,135). RESULTS: For the Validation dataset, cancer/non-cancer positivity for current cut-offs was 41%/9% (PPV =0.109, 1 in 9). The high positive stratum improved this to 25%/2% (PPV =0.274, 1 in 4). The low negative stratum improved this to 8%/23% (NPV =0.990, 1 in 105). This provides a 25-fold difference in lung cancer probability between the highest and lowest groups. The test performs equally well in subjects who fulfilled the entry risk criteria for the National Lung Screening Trial (NLST) and subjects who did not meet the NLST criteria. CONCLUSIONS: The EarlyCDT®-Lung test has been converted to a four-stratum test by the addition of high and low sets of cut-offs: patients are thus stratified into four risk categories. This stratification will enable personalization of subsequent screening and treatment programs for high risk individuals or patients with lung nodules.

[920]

TÍTULO / TITLE: - Lung cancer and peritoneal carcinomatosis.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Sep;6(3):705-708. Epub 2013 Jul 15.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1468](#)

AUTORES / AUTHORS: - Sereno M; Rodriguez-Esteban I; Gomez-Raposo C; Merino M; Lopez-Gomez M; Zambrana F; Casado E

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Infanta Sofia University Hospital, San Sebastian de los Reyes, Madrid 28708, España.

RESUMEN / SUMMARY: - Lung cancer is currently one of the most common malignancies in the world and peritoneal involvement is rare in these types of tumors. Clinical manifestations of these metastases are also uncommon and include intestinal perforation and obstruction. The present study reviewed certain aspects of the complication of peritoneal involvement and illustrated it with four cases of patients that were diagnosed with primary lung carcinoma and secondary peritoneal carcinomatosis (PC). The outcome of these patients is poor and they rarely respond to chemotherapy. Surgery is successful in the majority of cases.

[921]

TÍTULO / TITLE: - “Unique trend” and “contradictory trend” in discrimination of primary synchronous lung cancer and metastatic lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - BMC Cancer. 2013 Oct 9;13:467. doi: 10.1186/1471-2407-13-467.

●● Enlace al texto completo (gratis o de pago) [1186/1471-2407-13-467](#)

AUTORES / AUTHORS: - Shen C; Xu H; Liu L; Zhou Y; Chen D; Du H; Han Z; Che G

INSTITUCIÓN / INSTITUTION: - Department of Cardiovascular and Thoracic Surgery, West-China Hospital, Sichuan University, Chengdu 610041, China.

chequowei_hx@aliyun.com.

RESUMEN / SUMMARY: - BACKGROUND: Distinguishing between multiple primary lung cancers and metastatic tumors is often difficult when the tumor histology is same. Since genomic instability is a common feature of cancer, we hypothesized that independently arising neoplasms in an individual patient would exhibit measurable genomic variation, enabling discrimination of tumor lineage and relatedness. The feasibility of analyzing genomic instability expression profiles to distinguish multiple primary lung cancers from metastatic tumors was evaluated. METHODS: This study enrolled 13 patients, with multiple primary lung cancers demonstrating with the histology, who underwent surgery between April 2003 and December 2012 at the Department of the Thoracic Surgery at West China Hospital in Sichuan province of China and 10 patients who were diagnosed as metastasis disease during the same period for comparison purposes. Genomic DNA from lung cancers from individual patients was analyzed by six microsatellites (D2S1363, D6S1056, D7S1824, D10S1239, D15S822, and D22S689) with PCR to identify discordant allelic variation. The experiments were approved by the West China Hospital Ethics committee (No.2013 (33)) and all patients agreed to participate in the study and signed an informed consent form. RESULTS: All of the 10 patients with distant metastasis showed a consistent consequence that we called “unique trend” between primary tumor and distant metastasis. The “trend” is representative in this study, which means that all alleles corresponding to six microsatellite markers were detected in DNA from primary tumors but were reduced or not observed in DNA from metastatic tumors. In the group of synchronous lung tumor with different histological types, the result showed a “contradictory trend”. Some alleles were detected in DNA from primary tumors but were reduced or not observed in DNA from metastatic tumors and other alleles corresponding to six microsatellite markers were detected in DNA from metastatic tumors but were reduced or not observed in DNA from primary tumors. In the third group (synchronous lung tumor with same histological types), 2 of 8 patients showed “unique trend” and the others showed “contradictory trend”. CONCLUSIONS: With polymorphic microsatellite markers, the “unique trend” that represents metastasis cancers and the “contradictory trend” that represents primary multiple tumors are useful in the diagnosis between tumors found at the same time in the pulmonary even diagnosed with the histopathological evaluation from a single patient.

[922]

TÍTULO / TITLE: - Small cell lung carcinoma metastasis to palatine tonsils.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Braz J Otorhinolaryngol. 2013 Sep-Oct;79(5):645. doi: 10.5935/1808-8694.20130117.

●● Enlace al texto completo (gratis o de pago) [5935/1808-8694.20130117](https://doi.org/10.5935/1808-8694.20130117)

AUTORES / AUTHORS: - Arroyo HH; Takehara J; Ogawa AI; Frizzarini R; Imamura R; de Paula HM

INSTITUCIÓN / INSTITUTION: - departamento de Otorrinolaringología, Faculdade de Medicina, Universidade de Sao Paulo.

[923]

TÍTULO / TITLE: - Activation of the PD-1 Pathway Contributes to Immune Escape in EGFR-Driven Lung Tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Discov. 2013 Nov 22.

●● Enlace al texto completo (gratis o de pago) [1158/2159-8290.CD-13-0310](https://doi.org/10.1158/2159-8290.CD-13-0310)

AUTORES / AUTHORS: - Akbay EA; Koyama S; Carretero J; Altabef A; Tchaicha JH; Christensen CL; Mikse OR; Cherniack AD; Beauchamp EM; Pugh TJ; Wilkerson MD; Fecci PE; Butaney M; Reibel JB; Soucheray M; Cohoon TJ; Janne PA; Meyerson M; Hayes DN; Shapiro GI; Shimamura T; Sholl LM; Rodig SJ; Freeman GJ; Hammerman PS; Dranoff G; Wong KK

INSTITUCIÓN / INSTITUTION: - Departments of 1Medicine and 2Medical Oncology and Cancer Vaccine Center, Dana-Farber Cancer Institute; 3Harvard Medical School; 4Ludwig Institute for Cancer Research; 5Department of Neurosurgery, Massachusetts General Hospital; 6Belfer Institute for Applied Cancer Science; 7Department of Pathology, Brigham and Women's Hospital, Boston; 8Broad Institute, Cambridge, Massachusetts; 9UNC Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; and 10Department of Molecular Pharmacology and Therapeutics, Oncology Institute, Loyola University, Chicago, Illinois; 11Department of Physiology, University of Valencia, Valencia, España.

RESUMEN / SUMMARY: - The success in lung cancer therapy with programmed death (PD)-1 blockade suggests that immune escape mechanisms contribute to lung tumor pathogenesis. We identified a correlation between EGF receptor (EGFR) pathway activation and a signature of immunosuppression manifested by upregulation of PD-1, PD-L1, CTL antigen-4 (CTLA-4), and multiple tumor-promoting inflammatory cytokines. We observed decreased CTLs and increased markers of T-cell exhaustion in mouse models of EGFR-driven lung cancer. PD-1 antibody blockade improved the survival of mice with EGFR-driven adenocarcinomas by enhancing effector T-cell function and lowering the levels of tumor-promoting cytokines. Expression of mutant EGFR in bronchial epithelial cells induced PD-L1, and PD-L1 expression was reduced by EGFR inhibitors in non-small cell lung cancer cell lines with activated EGFR. These data suggest that oncogenic EGFR signaling remodels the tumor microenvironment to trigger immune escape and mechanistically link treatment response to PD-1 inhibition.

[924]

TÍTULO / TITLE: - A Drug Repositioning Approach Identifies Tricyclic Antidepressants as Inhibitors of Small Cell Lung Cancer and Other Neuroendocrine Tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cancer Discov. 2013 Sep 26.

●● Enlace al texto completo (gratis o de pago) [1158/2159-8290.CD-13-0183](https://doi.org/10.1158/2159-8290.CD-13-0183)

AUTORES / AUTHORS: - Jahchan NS; Dudley JT; Mazur PK; Flores N; Yang D; Palmerton A; Zmoos AF; Vaka D; Tran KQ; Zhou M; Krasinska K; Riess JW; Neal JW; Khatri P; Park KS; Butte AJ; Sage J

INSTITUCIÓN / INSTITUTION: - Departments of 1Pediatrics, 2Genetics, and 5Medicine-Oncology, 3Vincent Coates Mass Spectrometry Laboratory, Stanford University, Stanford; and 4Division of Hematology/Oncology, Department of Internal Medicine, University of California Davis Cancer Center, University of California Davis School of Medicine, Sacramento, California.

RESUMEN / SUMMARY: - Small cell lung cancer (SCLC) is an aggressive neuroendocrine subtype of lung cancer with high mortality. We used a systematic drug repositioning bioinformatics approach querying a large compendium of gene expression profiles to identify candidate U.S. Food and Drug Administration (FDA)-approved drugs to treat SCLC. We found that tricyclic antidepressants and related molecules potentially induce apoptosis in both chemonaive and chemoresistant SCLC cells in culture, in mouse and human SCLC tumors transplanted into immunocompromised mice, and in endogenous tumors from a mouse model for human SCLC. The candidate drugs activate stress pathways and induce cell death in SCLC cells, at least in part by disrupting autocrine survival signals involving neurotransmitters and their G protein-coupled receptors. The candidate drugs inhibit the growth of other neuroendocrine tumors, including pancreatic neuroendocrine tumors and Merkel cell carcinoma. These experiments identify novel targeted strategies that can be rapidly evaluated in patients with neuroendocrine tumors through the repurposing of approved drugs.

[925]

TÍTULO / TITLE: - A genomics-based classification of human lung tumors.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Transl Med. 2013 Oct 30;5(209):209ra153. doi: 10.1126/scitranslmed.3006802.

●● Enlace al texto completo (gratis o de pago) [1126/scitranslmed.3006802](#)

RESUMEN / SUMMARY: - We characterized genome alterations in 1255 clinically annotated lung tumors of all histological subgroups to identify genetically defined and clinically relevant subtypes. More than 55% of all cases had at least one oncogenic genome alteration potentially amenable to specific therapeutic intervention, including several personalized treatment approaches that are already in clinical evaluation. Marked differences in the pattern of genomic alterations existed between and within histological subtypes, thus challenging the original histomorphological diagnosis. Immunohistochemical studies confirmed many of these reassigned subtypes. The reassignment eliminated almost all cases of large cell carcinomas, some of which had therapeutically relevant alterations. Prospective testing of our genomics-based diagnostic algorithm in 5145 lung cancer patients enabled a genome-based diagnosis in 3863 (75%) patients, confirmed the feasibility of rational reassignments of large cell lung cancer, and led to improvement in overall survival in patients with EGFR-mutant or ALK-rearranged cancers. Thus, our findings provide support for broad implementation of genome-based diagnosis of lung cancer.

[926]

TÍTULO / TITLE: - Advanced malignant mesothelioma mimicking acute contained thoracic aortic rupture.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Interact Cardiovasc Thorac Surg. 2013 Oct 30.

●● Enlace al texto completo (gratis o de pago) [1093/icvts/ivt465](#)

AUTORES / AUTHORS: - Mouawad NJ; Daniel VC; Starr JE

INSTITUCIÓN / INSTITUTION: - Division of Vascular Diseases and Surgery, The Ohio State University Wexner Medical Center, Columbus, OH, USA.

RESUMEN / SUMMARY: - In the emergent setting, patients presenting with acute interscapular pain along with haemodynamic instability require immediate evaluation. We describe the case of a patient in which computed tomographic scanning demonstrated a large hyper-dense, periaortic collection on post-contrast imaging. Urgent endovascular repair was performed for descending thoracic aortic rupture. Her postoperative course, however, was atypical with a readmission 1 week after discharge with symptoms similar to her primary presentation. Alternative pathologies were then considered in a more elective setting in which the correct diagnosis of diffuse malignant mesothelioma was ultimately discovered in a patient with no previous exposure to occupational toxins. The tumour burden was advanced and the patient opted for palliative care. Herein, we suggest a consideration for oncological thoracic pathology in patients presenting with signs and symptoms mimicking acute thoracic aortic rupture or dissection, who may demonstrate atypical symptoms.

[927]

TÍTULO / TITLE: - MiR-200c Increases the Radiosensitivity of Non-Small-Cell Lung Cancer Cell Line A549 by Targeting VEGF-VEGFR2 Pathway.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - PLoS One. 2013 Oct 30;8(10):e78344. doi: 10.1371/journal.pone.0078344.

●● Enlace al texto completo (gratis o de pago) [1371/journal.pone.0078344](#)

AUTORES / AUTHORS: - Shi L; Zhang S; Wu H; Zhang L; Dai X; Hu J; Xue J; Liu T; Liang Y; Wu G

INSTITUCIÓN / INSTITUTION: - Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

RESUMEN / SUMMARY: - MicroRNAs (miRNAs) have been demonstrated to participate in many important cellular processes including radiosensitization. VEGF family, an important regulator of angiogenesis, also plays a crucial role in the regulation of cancer cell radiosensitivity. VEGFR2 mediates the major growth and permeability actions of VEGF in a paracrine/autocrine manner. MiR-200c, at the nexus of epithelial-mesenchymal transition (EMT), is predicted to target VEGFR2. The purpose of this study is to test the hypothesis that regulation of VEGFR2 pathway by miR-200c could modulate the radiosensitivity of cancer cells. Bioinformatic analysis, luciferase reporter assays and biochemical assays were carried out to validate VEGFR2 as a direct target of miR-200c. The radiosensitizing effects of miR-200c on A549 cells were determined by clonogenic assays. The downstream regulating mechanism of miR-200c was explored with western blotting assays, FCM, tube formation assays and migration assays. We identified VEGFR2 as a novel target of miR-200c. The ectopic miR-200c increased the radiosensitivity of A549 while miR-200c down-regulation decreased it. Besides, we proved that miR-200c radiosensitized A549 cells by targeting VEGF-

VEGFR2 pathway specifically, thus leading to inhibition of its downstream pro-survival signaling transduction and angiogenesis, and serves as a potential target for radiosensitization research.

[928]

TÍTULO / TITLE: - LHX6 acts as a novel potential tumour suppressor with epigenetic inactivation in lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cell Death Dis. 2013 Oct 24;4:e882. doi: 10.1038/cddis.2013.366.

●● [Enlace al texto completo \(gratis o de pago\)](#) [1038/cddis.2013.366](#)

AUTORES / AUTHORS: - Liu WB; Jiang X; Han F; Li YH; Chen HQ; Liu Y; Cao J; Liu JY

INSTITUCIÓN / INSTITUTION: - Institute of Toxicology, College of Preventive Medicine, Third Military Medical University, Chongqing 400038, China.

RESUMEN / SUMMARY: - LIM homeobox domain 6 (LHX6) is a putative transcriptional regulator that controls the differentiation and development of neural and lymphoid cells. However, the function of LHX6 in cancer development remains largely unclear. Recently, we found that LHX6 is hypermethylated in lung cancer. In this study, we analysed its epigenetic regulation, biological functions, and related molecular mechanisms in lung cancer. Methylation status was evaluated by methylation-specific PCR and bisulfite genomic sequencing. LHX6 mRNA levels were measured in relation to the methylation status. The effects of LHX6 expression on tumorigenesis were studied in vitro and in vivo. LHX6 was readily expressed in normal lung tissues without methylation, but was downregulated or silenced in lung cancer cell lines and tissues with hypermethylation status. Treatment of lung cancer cells with the demethylating agent 5-aza-2'-deoxycytidine restored LHX6 expression. Moreover, LHX6 hypermethylation was detected in 56% (52/93) of primary lung cancers compared with none (0/20) of the tested normal lung tissues. In lung cancer cell lines 95D and H358, forced expression of LHX6 suppressed cell viability, colony formation, and migration, induced apoptosis and G1/S arrest, and inhibited their tumorigenicity in nude mice. On the other hand, knockdown of LHX6 expression by RNA interference increased cell proliferation and inhibited apoptosis and cell cycle arrest. These effects were associated with upregulation of p21 and p53, and downregulation of Bcl-2, cyclinD1, c-myc, CD44, and MMP7. In conclusion, our results suggest that LHX6 is a putative tumour suppressor gene with epigenetic silencing in lung cancer.

[929]

TÍTULO / TITLE: - Malignant mesothelioma presenting as a gradually enlarging pneumothorax.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Case Rep Pulmonol. 2013;2013:374960. doi: 10.1155/2013/374960. Epub 2013 Oct 2.

●● [Enlace al texto completo \(gratis o de pago\)](#) [1155/2013/374960](#)

AUTORES / AUTHORS: - Prasad A; Olsen D; Sriram PS

INSTITUCIÓN / INSTITUTION: - Division of Pulmonary, Critical Care and Sleep Medicine, University of Florida, Gainesville, FL 32610-0225, USA.

RESUMEN / SUMMARY: - Malignant mesothelioma is an extremely aggressive tumor arising from the pleura with median survival of approximately 9-12 months. It can rarely

present as a spontaneous pneumothorax. Less than 35 cases of malignant mesothelioma presenting as spontaneous pneumothorax have been reported in the literature. Pathology may show florid mesothelial hyperplasia. We herein report a case of mesothelioma presenting as a pneumothorax that gradually enlarged over a one-year period and also review the relevant literature.

[930]

TÍTULO / TITLE: - HOXA11 hypermethylation is associated with progression of non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncotarget. 2013 Oct 28.

AUTORES / AUTHORS: - Hwang JA; Lee BB; Kim Y; Park SE; Heo K; Hong SH; Kim YH; Han J; Shim YM; Lee YS; Kim DH

INSTITUCIÓN / INSTITUTION: - Cancer Genomics Branch, Research Institute, National Cancer Center, Goyang-si, Korea.

RESUMEN / SUMMARY: - This study was aimed at understanding the functional significance of HOXA11 hypermethylation in non-small cell lung cancer (NSCLC). HOXA11 hypermethylation was characterized in six lung cancer cell lines, and its clinical significance was analyzed using formalin-fixed paraffin-embedded tissues from 317 NSCLC patients, and Ki-67 expression was analyzed using immunohistochemistry. The promoter region of HOXA11 was highly methylated in six lung cancer cell lines, but not in normal bronchial epithelial cells. The loss of expression was restored by treatment of the cells with a demethylating agent, 5-aza-2'-deoxycytidine (5-Aza-dC). Transient transfection of HOXA11 into H23 lung cancer cells resulted in the inhibition of cell migration and proliferation. HOXA11 hypermethylation was found in 218 (69%) of 317 primary NSCLCs. HOXA11 hypermethylation was found at a higher prevalence in squamous cell carcinoma than in adenocarcinoma (74% vs. 63%, respectively). HOXA11 hypermethylation was associated with Ki-67 proliferation index ($P = 0.03$) and pT stage ($P = 0.002$), but not with patient survival. Patients with pT2 and pT3 stages were 1.85 times (95% confidence interval [CI] = 1.04-3.29; $P = 0.04$) and 5.47 times (95% CI = 1.18-25.50; $P = 0.01$), respectively, more likely to show HOXA11 hypermethylation than those with pT1 stage, after adjusting for age, sex, and histology. In conclusion, the present study suggests that HOXA11 hypermethylation may contribute to the progression of NSCLC by promoting cell proliferation or migration.

[931]

TÍTULO / TITLE: - Solitary pulmonary plasmacytoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Blood Res. 2013 Sep;48(3):170. doi: 10.5045/br.2013.48.3.170.

●● [Enlace al texto completo \(gratis o de pago\) 5045/br.2013.48.3.170](#)

AUTORES / AUTHORS: - Ryu H; Lee C; Jo DY

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, School of Medicine, Chungnam National University, Daejeon, Korea.

[932]

TÍTULO / TITLE: - Inhibition of cell migration by ouabain in the A549 human lung cancer cell line.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncol Lett. 2013 Aug;6(2):475-479. Epub 2013 Jun 17.

●● Enlace al texto completo (gratis o de pago) [3892/ol.2013.1406](#)

AUTORES / AUTHORS: - Liu N; Li Y; Su S; Wang N; Wang H; Li J

INSTITUCIÓN / INSTITUTION: - The Key Laboratory of Pharmacology and Toxicology for New Drugs, Department of Pharmacology, Hebei Medical University; ; The Key Laboratory of Neural and Vascular Biology, Ministry of Education, Hebei Medical University, Shijiazhuang, Hebei 050017;

RESUMEN / SUMMARY: - The Na⁺/K⁺-ATPase alpha subunit is highly expressed in malignant cells. Ouabain, a cardioactive glycoside, binds to the Na⁺/K⁺-ATPase alpha subunit and inhibits the activity of Na⁺/K⁺-ATPase. In the present study, the effect of ouabain on the migration of A549 cells was analyzed using the wound healing and transwell chamber migration assays. The impact of ouabain on the expression of E-cadherin, N-cadherin, vimentin, matrix metalloprotease (MMP)-2 and MMP-9 was also evaluated. Ouabain treatment not only inhibited the epidermal growth factor (EGF)-enhanced migration of A549 cells, but also inhibited the basal migration of A549 cells in the absence of EGF. Ouabain decreased the overexpression of N-cadherin and vimentin induced by EGF, and decreased the expression of MMP-2 and -9 in the presence or absence of EGF. Na⁺/K⁺-ATPase is a potent therapeutic target in lung cancer and these observations indicated that the Na⁺/K⁺-ATPase inhibitor, ouabain, retards the invasion of lung cancer cells.

[933]

TÍTULO / TITLE: - Small cell lung cancer presenting with a left iliac fossa mass.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - British Medical J (BMJ). Acceso gratuito al texto completo.

●● Enlace a la Editora de la Revista <http://bmj.com/search.dtl>

●● Cita: British Medical J. (BMJ): <> Case Rep. 2013 Nov 14;2013. pii: bcr2013200857. doi: 10.1136/bcr-2013-200857.

●● Enlace al texto completo (gratis o de pago) [1136/bcr-2013-200857](#)

AUTORES / AUTHORS: - Jethwa H; Savage L

INSTITUCIÓN / INSTITUTION: - NHS, London, UK.

RESUMEN / SUMMARY: - We report a 59-year-old lifelong smoker with severe chronic obstructive pulmonary disease who presented with an acute onset 3-day history of left iliac fossa pain and abdominal distension. Clinical examination revealed a palpable mass in the left iliac fossa. The differential diagnosis was that of a diverticular abscess or colonic tumour. She subsequently underwent a CT scan which showed extensive metastatic liver disease from a primary lung tumour, with hepatomegaly abutting the anterior abdominal wall in the left iliac fossa.

[934]

TÍTULO / TITLE: - MiRNA-218, a new regulator of HMGB1, suppresses cell migration and invasion in non-small cell lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Acta Biochim Biophys Sin (Shanghai). 2013 Dec;45(12):1055-61. doi: 10.1093/abbs/gmt109. Epub 2013 Nov 17.

- Enlace al texto completo (gratis o de pago) 1093/abbs/gmt109

AUTORES / AUTHORS: - Zhang C; Ge S; Hu C; Yang N; Zhang J

INSTITUCIÓN / INSTITUTION: - Department of Geriatrics, The Affiliated Hospital of Yan'an University, Yan'an 716000, China.

RESUMEN / SUMMARY: - MicroRNAs (miRNAs) function as negative regulators of gene expression involved in cancer metastasis. The aim of this study is to investigate the potential roles of miR-218 in non-small cell lung cancer and validate its regulation mechanism. Functional studies showed that miR-218 overexpression inhibited cell migration and invasion, but had no effect on cell viability. Enhanced green fluorescent protein reporter assay, real-time polymerase chain reaction and western blot analysis confirmed that miR-218 suppressed the expression of high mobility group box-1 (HMGB1) by directly targeting its 3'-untranslated region. Accordingly, silencing of HMGB1 accorded with the effects of miR-218 on cell migration and invasion, and overexpression of HMGB1 can restore cell migration and invasion which were reduced by miR-218. In conclusion, these findings demonstrate that miR-218 functions as a tumor suppressor in lung cancer. Furthermore, miR-218 may act as a potential therapeutic biomarker for metastatic lung cancer patients.

[935]

TÍTULO / TITLE: - Functional and pathway enrichment analysis for integrated regulatory network of high- and low-metastatic lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Mol Biosyst. 2013 Dec 29;9(12):3080-90. doi: 10.1039/c3mb70288j. Epub 2013 Sep 30.

- Enlace al texto completo (gratis o de pago) 1039/c3mb70288j

AUTORES / AUTHORS: - Chen QY; Jiao DM; Wu YQ; Wang L; Hu HZ; Song J; Yan J; Wu LJ

INSTITUCIÓN / INSTITUTION: - Department of Respiratory Disease, The 117th Hospital of PLA, Hangzhou, Zhejiang 310013, P.R. China. cqyong117@163.com.

RESUMEN / SUMMARY: - Metastasis is a common feature of lung cancer, involving relationships between genes, proteins and miRNAs. However, lack of early detection and limited options for targeted therapies are weaknesses that contribute to the dismal statistics observed in lung cancer metastasis. In this paper, gene expression profiling analysis for genes differentially expressed between high- (95D) and low-metastatic lung cancer cell lines (95C) was performed using gene annotation, pathway analysis, literature mining, and the integrated regulatory network as well as motif analysis of miRNA-DEG and TF-DEG. In addition, the expression of EGR-1 (early growth response-1) in surgically resected lung squamous carcinomas, adenocarcinomas and normal lung tissue was detected by immunohistochemistry to reveal the relationships between EGR-1 and lung cancer metastasis. A total of 570 different expressed genes (DEGs) were screened, the vast majority of up-regulated DEGs were connected to cell adhesion and focal adhesion. EGR-1 was observed in the center node of the regulatory network, which seems to play a role in the process of cancer metastasis, and further immunohistochemistry detection confirmed this reasoning. Besides EGR-1, several significant module-related DEGs were enriched in the pathway within cancer and focal adhesion according to KEGG pathway enrichment analysis of network modules. The construction of an integrated regulatory network and the functional prediction of EGR-1 provided us with the cytological basis of lung cancer metastasis research and an

understanding of the mechanism of metastasis in lung cancer. EGR-1 should be considered as a potential target gene in therapeutic agent for lung cancer metastasis.

[936]

TÍTULO / TITLE: - Mitral valve and coronary artery bypass surgeries 13 years after pneumonectomy for lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Cardiovasc J Afr. 2013 Sep 23;24(8):e1-4. doi: 10.5830/CVJA-2013-031.

●● Enlace al texto completo (gratis o de pago) [5830/CVJA-2013-031](#)

AUTORES / AUTHORS: - Dag O; Kaygin MA; Arslan U; Kiyamaz A; Kahraman N; Erkut B
INSTITUCIÓN / INSTITUTION: - Department of Cardiovascular Surgery, Erzurum Regional Training and Research Hospital, Erzurum, Turkey.

RESUMEN / SUMMARY: - We successfully performed coronary artery bypass grafting and mitral valve replacement in a 72-year-old man who had undergone a left pneumonectomy 13 years previously due to a malignant mass. The patient was admitted to our clinic with symptoms of dyspnoea, palpitations, chest pain and fatigue. He was diagnosed with mitral valve disease and two-vessel coronary artery disease, as seen from echocardiography and catheterisation studies. Conventional cardiopulmonary bypass grafting was performed following sternotomy. The patient's heart was completely displaced to the left hemithorax. Saphenous vein grafts were harvested. Distal anastomoses were performed with the use of the on-pump beating heart technique without cross clamping. Afterwards a cross clamping was placed and a left atriotomy was performed. The mitral valve was severely calcific. A mitral valve replacement was performed using number 27 mechanical valve after the valve had been excised. The patient's postoperative course was uneventful. Cardiac contractility was seen to be normal and the mitral valve was functioning on echocardiography done in the second postoperative month.

[937]

TÍTULO / TITLE: - The role of interleukin-10 in the progression of human papillomavirus-associated lung carcinoma.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Oncoimmunology. 2013 Sep 1;2(9):e25854. Epub 2013 Jul 29.

●● Enlace al texto completo (gratis o de pago) [4161/onci.25854](#)

AUTORES / AUTHORS: - Sung WW; Lee H

INSTITUCIÓN / INSTITUTION: - School of Medicine; Chung Shan Medical University; Taichung, Taiwan ; Institute of Medicine; Chung Shan Medical University; Taichung, Taiwan.

RESUMEN / SUMMARY: - The secretion of interleukin-10 by both malignant and immune cells promotes the progression of lung tumors, hence negatively impacting on patient prognosis. As interleukin-10 mediates oncogenic effects through the PI3K/AKT signaling pathway, PI3K/AKT inhibitors might sensitize cancer cells to chemotherapy, thus favoring tumor regression and improving disease outcome.

[938]

TÍTULO / TITLE: - Lung cancer in Northern Portugal: A hospital-based study.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Rev Port Pneumol. 2013 November - December;19(6):245-251. doi: 10.1016/j.rppneu.2013.05.005. Epub 2013 Oct 9.

●● Enlace al texto completo (gratis o de pago) 1016/j.rppneu.2013.05.005

AUTORES / AUTHORS: - Hespanhol V; Parente B; Araujo A; Cunha J; Fernandes A; Figueiredo MM; Neveda R; Soares M; Joao F; Queiroga H

INSTITUCIÓN / INSTITUTION: - Servico Pneumologia, Faculdade de Medicina do Porto, Centro Hospitalar de Sao Joao, Porto, Portugal. Electronic address: hespanholv@gmail.com.

RESUMEN / SUMMARY: - INTRODUCTION: Lung cancer is the deadliest cancer worldwide. In Portugal, the disease remains the main cause of cancer death in males. AIM: This study aims to evaluate the demographic and clinical characteristics of lung cancer patients diagnosed and treated in northern Portugal hospitals from 2000 to 2010. PATIENTS AND METHODS: Twelve hospitals in the north of Portugal contributed to this study. The demographic and clinic characteristics of the patients registered in each hospital from 2000 to 2010 and the patterns of their occurrence were analyzed. RESULTS: During an 11-year period (2000-2010), 9767 lung cancer patients were registered in the participating hospitals. Comparing the number of the patients registered in the year 2000 to those registered during 2010, there was a significant increase in lung cancer cases. Females represent only 20% of the total registered lung cancer cases; however, during the study period, the number of female patients increased by 30%. A significant number of the patients, 3117 (48.6%), had poor performance status at presentation. The adenocarcinoma histology became more preponderant over the study period. Most of the patients were diagnosed as stages IIIB or IV: 7206 of 9267 (77.8%). Chemotherapy was the treatment of choice for 3529 (40.4%) patients, whereas surgical treatment was achieved in 1301 (14.9%) cases. CONCLUSION: A significant number of lung cancer patients have been diagnosed and treated in hospitals in northern Portugal, and the incidence of the disease among females has been increasing. The overwhelming majority of the tumors were diagnosed in advanced stage; nevertheless, surgical treatment was possible in 14.9% of the patients.

[939]

TÍTULO / TITLE: - In-flight arterial gas emboli from a ruptured bronchogenic cyst.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - CJEM. 2013 Nov 1;15(6):385-8.

AUTORES / AUTHORS: - Mak E; Cheung KW; Mondor F

[940]

TÍTULO / TITLE: - Lung cancer.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - J Thorac Dis. 2013 Oct;5(Suppl 5):S452-3. doi: 10.3978/j.issn.2072-1439.2013.10.04.

●● Enlace al texto completo (gratis o de pago) [3978/j.issn.2072-](http://3978/j.issn.2072-1439.2013.10.04)

1439.2013.10.04

AUTORES / AUTHORS: - Fong KM

INSTITUCIÓN / INSTITUTION: - Department of Thoracic Medicine, The Prince Charles Hospital; Professor, School of Medicine, The University of Queensland; Director UQ Thoracic Research Ctr at TPCH; Rode Road, Chermside, Brisbane 4032, Australia.

[941]

TÍTULO / TITLE: - Anti-Tumor Effects of Atractylenolide I Isolated from *Atractylodes macrocephala* in Human Lung Carcinoma Cell Lines.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - *Molecules*. 2013 Oct 29;18(11):13357-68. doi: 10.3390/molecules181113357.

●● Enlace al texto completo (gratis o de pago) [3390/molecules181113357](#)

AUTORES / AUTHORS: - Liu H; Zhu Y; Zhang T; Zhao Z; Zhao Y; Cheng P; Li H; Gao H; Su X

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Chengdu Military General Hospital, Chengdu 610083, Si Chuan Province, China. xmsucdmh@126.com.

RESUMEN / SUMMARY: - Atractylenolide I (ATL-1) is the major sesquiterpenoid of *Atractylodes macrocephala*. This study was designed to investigate whether ATL-1 induced apoptosis in A549 and HCC827 cells in vitro and in vivo. In our results, ATL-1 significantly decreased the percentage of in vitro viability, in a dose-dependent manner. In addition, DAPI staining and flow cytometry tests demonstrated the induction of apoptosis by ATL-I. Western blot analysis indicated that the protein levels of caspase-3, caspase-9 and Bax were increased in A549 and HCC827 cells after ATL-I exposure; to the contrary, the expressions of Bcl-2, Bcl-XL were decreased after treatment with ATL-1. In the in vivo study, ATL-I effectively suppressed tumor growth (A549) in transplanted tumor nude mice with up-regulation of caspase-3, caspase-9, and Bax and down-regulation of Bcl-2 and Bcl-XL. In conclusion, our results demonstrated that ATL-I has significant antitumor activity in lung carcinoma cells, and the possible mechanism of action may be related to apoptosis induced by ATL-I via a mitochondria-mediated apoptosis pathway.

[942]

TÍTULO / TITLE: - ZFX knockdown inhibits growth and migration of non-small cell lung carcinoma cell line H1299.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - *Int J Clin Exp Pathol*. 2013 Sep 15;6(11):2460-7.

AUTORES / AUTHORS: - Li K; Zhu ZC; Liu YJ; Liu JW; Wang HT; Xiong ZQ; Shen X; Hu ZL; Zheng J

INSTITUCIÓN / INSTITUTION: - Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology 130 Meilong Road, Shanghai, China ; Shanghai Institute of Materia Medica, Chinese Academy of Sciences Shanghai, China.

RESUMEN / SUMMARY: - ZFX (zinc finger transcription factor, X chromosome-linked) contributes to the maintenance of different types of stem cells and the progression of various cancers. We have previously reported that ZFX knockdown inhibits proliferation of glioma in vitro and in vivo. Since overexpression of ZFX in lung cancer tissue correlates with lymph node metastasis, we hypothesized that ZFX may play a role in lung cancer. In this study, we identified ZFX as a promoter of lung cancer growth and migration in a NSCLC (non-small cell lung carcinoma) cell line H1299. ZFX knockdown caused proliferation inhibition determined by MTT assay and colony formation assay, G0/G1 arrest of cell cycle and slightly increased proportion of apoptotic cells assessed by flow cytometry assay, decreased population of migrating cells showed by wound-

healing assay, increased cell senescence evidenced by senescence-associated beta-galactosidase staining. ZFX knockdown also led to decreased proportion of tumor bearing mice and reduced mean tumor volume in a subcutaneous tumor model. In addition, western blot showed that ZFX knockdown down regulated a set of proteins involved in proliferation, survival and motility. Altogether, these results suggest that ZFX may be a potential therapeutic target for NSCLC.

[943]

TÍTULO / TITLE: - SGOL1 variant B induces abnormal mitosis and resistance to taxane in non-small cell lung cancers.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Sci Rep. 2013 Oct 22;3:3012. doi: 10.1038/srep03012.

●● Enlace al texto completo (gratis o de pago) [1038/srep03012](#)

AUTORES / AUTHORS: - Matsuura S; Kahyo T; Shinmura K; Iwaizumi M; Yamada H; Funai K; Kobayashi J; Tanahashi M; Niwa H; Ogawa H; Takahashi T; Inui N; Suda T; Chida K; Watanabe Y; Sugimura H

INSTITUCIÓN / INSTITUTION: - 1] Department of Tumor Pathology, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka, 431-3192, Japan [2] Second Division, Department of Internal Medicine, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka, 431-3192, Japan.

RESUMEN / SUMMARY: - Mitosis is the most conspicuous cell cycle phase and Shugoshin-like 1 (SGOL1) is a key protein in protecting sister chromatids from precocious separation during mitosis. We studied the role of SGOL1 and its splice variants in non-small cell lung cancer (NSCLC) using 82 frozen NSCLC tissue samples. SGOL1-B expression was prevalent in smokers, in cases with a wild-type (WT) EGFR status, and in cases with the focal copy number amplification of genes that are known to be important for defining the biological behaviors of NSCLC. The overexpression of SGOL1-B1 in an NSCLC cell line induced aberrant chromosome missegregation, precociously separated chromatids, and delayed mitotic progression. A higher level of SGOL1-B mRNA was related to taxane resistance, while the forced downregulation of SGOL1-B increased the sensitivity to taxane. These results suggest that the expression of SGOL1-B causes abnormal mitosis and taxane resistance in NSCLC cells.

[944]

TÍTULO / TITLE: - Genitourinary small-cell carcinoma: a single-institution experience.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Curr Oncol. 2013 Oct;20(5):258-64. doi: 10.3747/co.20.1338.

●● Enlace al texto completo (gratis o de pago) [3747/co.20.1338](#)

AUTORES / AUTHORS: - Pervez N; El-Gehani F; Joseph K; Dechaphunkul A; Kamal M; Pertschy D; Venner P; Ghosh S; North S

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, University of Alberta and Cross Cancer Institute, Edmonton, AB.

RESUMEN / SUMMARY: - BACKGROUND: Small-cell carcinomas (sccs) of the genitourinary (gu) tract are rare systemic diseases, and there is no standard treatment strategy for patients with this malignancy. The objectives of the present study were to report the management and outcome of patients with scc of the gu tract treated at a

tertiary-care institution from 1982 to 2009. METHODS: In a chart review of all patients diagnosed with scc of the gu tract between 1982 and 2009, data on demographics, clinical and pathologic characteristics, treatment, and patient outcomes were collected. RESULTS: The 58 patients identified had scc in the following primary sites: urinary bladder (n = 35), prostate (n = 17), and upper urinary tract (n = 6). In 38 patients (66%), the scc was of pure histology; in the remainder, histology was mixed. Overall, 28 patients had limited-stage disease; 24 had extensive-stage disease; and staging was unknown in 6 patients. Median survival for the entire cohort was 7.5 months, with extensive-stage disease being identified as a poor prognostic factor (survival was 22.0 months for limited-stage patients and 4.1 months for extensive-stage patients, $p < 0.001$). Based on site, prostate patients fared worst, with a median survival of only 5.1 months. Compared with best supportive care, treatment was associated with better outcomes (median survival: 12.3 months vs. 2.3 months, $p < 0.0001$). CONCLUSIONS: Small-cell cancer of the gu tract is an aggressive cancer, with a poor prognosis overall. Although there is no standard of care, patients should be treated using a multimodality approach analogous to that used in the treatment of small-cell lung cancer.

[945]

TÍTULO / TITLE: - Status of Anti-Lung Cancer Drug Patents Applications in China from 2003 to 2012.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Recent Pat Anticancer Drug Discov. 2013 Oct 28.

AUTORES / AUTHORS: - Chen DM; Mao KY; Yang L; Jiang HB

INSTITUCIÓN / INSTITUTION: - Shanghai Information Center for Life Sciences, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 200031, Shanghai, China. hbjiang@sibs.ac.cn.

RESUMEN / SUMMARY: - Background: During the past 10 years, dramatic progress has been made in the development of effective lung cancer drugs in China. However, little is known about their patents. Objective: To summarize and analyze lung cancer patents or potential drug candidates issued in China over the last 10 years, and thus help researchers and developers to understand the current situation and potential candidates of lung cancer drug patents in China. Methods: Data were obtained from China Intellectual Property Right Net (CNIPR), a website maintained by the Intellectual Property Publishing House (IPPH) subordinate to the State Intellectual Property Office (SIPO), and analyzed by bibliometric methods. Results: A total of 707 lung cancer drug patents have been granted in China over the past 10 years. These patents include synthetic compounds, traditional Chinese medicines (TCM), combinations of synthetic compounds and TCM, biological products and medical apparatus. Current TCM approaches focus primarily on alteration of natural product rather than whole herb treatments, and there is an effort to modify TCM components and natural products to achieve optimal cancer targeting effects. The patents on synthetic lung cancer drug compounds in China mainly focus on well-known targets, such as EGFR, which comprises 93% of patents for validated targets. Conclusion: There has been a surge in lung cancer patents filed in China in recent years due to advancements in the Chinese pharmaceutical industries, improved practices that protect intellectual property rights, and a growing demand for lung cancer drugs. Therefore, there are great opportunities for obtaining lung cancer drug patents, particularly patents on active ingredients from TCM in China.

[946]

TÍTULO / TITLE: - Lung cancer: Cetuximab, you're fired.

RESUMEN / SUMMARY: - [Enlace al Resumen / Link to its Summary](#)

REVISTA / JOURNAL: - Nat Rev Clin Oncol. 2013 Nov 26. doi:
10.1038/nrclinonc.2013.227.

●● Enlace al texto completo (gratis o de pago) [1038/nrclinonc.2013.227](#)

AUTORES / AUTHORS: - Villanueva MT
