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477  Piper Betel Leaf: A Reservoir of Potential Xenohormetic Nutraceuticals with Cancer-Fighting Properties
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RESEARCH ARTICLES

487  Molecular Profiling of Premalignant Lesions in Lung Squamous Cell Carcinomas Identifies Mechanisms Involved in Stepwise Carcinogenesis
Aik T. Ooi, Adam C. Gower, Kelvin X. Zhang, Jessica L. Vick, Longsheng Hong, Brian Nagao, W. Dean Wallace, David A. Elashoff, Tonya C. Waiset, Steven M. Dubinett, Matteo Pellegrini, Marc E. Lenburg, Avrum Spira, and Brigitte N. Gomperts

496  A Randomized, Double-Blind, Placebo-Controlled Phase II Clinical Trial of Lovastatin for Various Endpoints of Melanoma Pathobiology

505  SERMs Attenuate Estrogen-Induced Malignant Transformation of Human Mammary Epithelial Cells by Upregulating Detoxification of Oxidative Metabolites

516  Association between Five Lifestyle Habits and Cancer Risk: Results from the E3N Cohort
Laureen Dartois, Guy Fagherazzi, Marie-Christine Boutron-Ruault, Sylvie Mesrine, and Françoise Clavel-Chapelon

526  Methylation of Twelve CpGs in Human Papillomavirus Type 16 (HPV16) as an Informative Biomarker for the Triage of Women Positive for HPV16 Infection
Janet L. Brandsma, Malini Harigopal, Nancy B. Kiviat, Ying Sun, Yanhong Deng, Daniel Zelterman, Paul M. Lizardi, Veronika S. Shabanova, Angelique Levi, Tian Yaping, Xinyuan Hu, and Qinghua Feng

534  Genistein Protects Hematopoietic Stem Cells against G-CSF–Induced DNA Damage
Liliana R. Souza, Erica Silva, Elissa Calloway, Omer Kucuk, Michael Rossi, and Morgan L. McLemore

545  Classifying Patients for Breast Cancer by Detection of Autoantibodies against a Panel of Conformation-Carrying Antigens
Rick L. Evans, James V. Pottala, and Kristi A. Egland
Lung squamous cell carcinoma (SCC) is thought to arise from premalignant lesions in the airway epithelium; therefore, studying these lesions is critical for understanding lung carcinogenesis. RNA sequencing was performed on laser-microdissected representative cell populations along the SCC pathological continuum of patient-matched normal basal cells, premalignant lesions, and tumor cells. Transcriptomic changes and genomic pathways altered with initiation and progression of SCC within individual patients were identified. Immunofluorescent staining confirmed gene expression changes in premalignant lesions and tumor cells, including increased expression of SLC2A1, CEACAM5, and PTBP3 at the protein level and increased activation of MYC via nuclear translocation. The cover micrograph shows merged immunofluorescently stained SCCs (PTBP3, green; KRT5, red; nuclei, blue) showing increased expression of PTBP3 in KRT5-expressing premalignant lesions and SCCs compared to basal cells in normal airway epithelium (not shown). The present study is the first gene expression profiling study of airway premalignant lesions with patient-matched normal airway epithelium and SCC samples, and provides much needed information about the biology of premalignant lesions and the molecular changes that occur during stepwise carcinogenesis of SCC. Importantly, it highlights a novel approach for identifying some of the earliest molecular changes associated with initiation and progression of lung carcinogenesis within individual patients. See the article by Ooi and colleagues (beginning on page 487) for more information.