COMMENTARIES

371 Not Significant But Important
James L. Mulshine and Frank G. Ondrey
See article, p. 410

375 Optimizing Biomarkers and Endpoints in Oral Cancer Chemoprevention Trials
William N. Williams Jr and Vassiliki A. Papadimitrakopoulou
See article, p. 410

379 Early-Phase Development of Cancer Prevention Agents: Challenges and Opportunities
Marjorie Perloff and Vernon E. Steele

PERSPECTIVE

384 Is Lycopene an Effective Agent for Preventing Prostate Cancer?
Michael B. Sporn and Karen T. Liby
See article, p. 419

REVIEWS

387 New Perspectives of Curcumin in Cancer Prevention
Wungki Park, A.R.M. Ruhul Amin, Zhuo Georgia Chen, and Dong M. Shin

401 MicroRNA and Cancer Chemoprevention
Bin Yi, Gary A. Piazza, Xiulan Su, and Yaguang Xi

RESEARCH ARTICLES

410 Bowman Birk Inhibitor Concentrate and Oral Leukoplakia: A Randomized Phase Ib Trial
See commentaries, pp. 371 and 375

419 Effects of Lycopene on Protein Expression in Human Primary Prostatic Epithelial Cells
Xi Qiu, Yang Yuan, Avani Vaishnav, Michael A. Tessel, Larisa Nonn, and Richard B. van Breemen
See commentary, p. 384

428 Increased Levels of Urinary PGE-M, a Biomarker of Inflammation, Occur in Association with Obesity, Aging, and Lung Metastases in Patients with Breast Cancer
Patrick G. Morris, Xi Kathy Zhou, Ginger L. Mine, Daniel Goldstein, Laura C. Hawks, Chau T. Dang, Shanu Modi, Monica N. Fornier, Clifford A. Hudis, and Andrew J. Dannenberg

437 Chemoprevention Activity of Dipyridamole in the MMTV-PyMT Transgenic Mouse Model of Breast Cancer
Chunmei Wang, Luciana P. Schwab, Meiyun Fan, Tiffany N. Seagroves, and John K. Buolamwini

448 Effect of Intermittent Dosing Regimens of Erlotinib on Methylxinitrosourea-Induced Mammary Carcinogenesis
Ronald A. Lubet, Eva Szabo, Kenneth K. Iwata, Stanley C. Gill, Chris Tucker, Ann Bode, Vernon E. Steele, M. Margaret Juliana, Holly N. Nicastro, and Clinton J. Grubbs

455 Direct Targeting of MEK1/2 and RSK2 by Silybin Induces Cell-Cycle Arrest and Inhibits Melanoma Cell Growth
Mee-Hyun Lee, Zunnan Huang, Dong Joon Kim, Sung-Hyun Kim, Myoung Ok Km, Sung-Young Lee, Hua Xie, Si Jun Park, Jae Young Kim, Joydeb Kumar Kundu, Ann M. Bode, Young-Joon Surh, and Ziqiang Dong

466 Molecular Imaging of Cyclooxygenase-2 in Canine Transitional Cell Carcinomas In Vitro and In Vivo
Maria Cekanova, Md. Jashim Uddin, Joseph W. Bartges, Amanda Callens, Alfred M. Legendre, Kusum Rathore, Laura Wright, Amanda Carter, and Lawrence J. Marnett

477 Association of Tooth Loss and Oral Hygiene with Risk of Gastric Adenocarcinoma
Ramin Shakeri, Reza Malekzadeh, Arash Etemadi, Dariush Nasrollahzadeh, Behroush Abedi-Ardekani, Masoud Khoshnia, Farhad Rashed, Akram Poursamans, Michael Pawlita, Paolo Bottetta, Sanford M. Dawsey, Farin Kamangar, and Christian C. Abnet
Tumor Suppressor microRNAs, miR-100 and -125b, Are Regulated by 1,25-dihydroxyvitamin D in Primary Prostate Cells and in Patient Tissue
Angeline A. Giangreco, Avani Vaishnav, Dennis Wagner, Antonio Finelli, Neil Flesner, Theodorus Van der Kwast, Reinhold Vieth, and Larisa Nonn

Curcumin-Targeting Pericellular Serine Protease Matriptase Role in Suppression of Prostate Cancer Cell Invasion, Tumor Growth, and Metastasis
Tai-Shan Cheng, Wen-Chi Chen, Ya-Yun Lin, Chin-Hsien Tsai, Chia-I Liao, Hsin-Yi Shyu, Chun-Jung Ko, Sheue-Fen Tzeng, Chun-Yin Huang, Pan-Chyr Yang, Pei-Wen Hsiao, and Ming-Shyue Lee

ABOUT THE COVER

Melanoma, the most aggressive form of skin cancer, accounts for 75% of skin cancer mortality. The activation of the signaling cascade comprising BRAF-NRAS-MEK1/2-ERK1/2 is an important trigger for melanoma survival, growth and proliferation. Several studies have demonstrated the chemopreventive and/or chemotherapeutic effects of silybin, a major bioactive component of milk thistle (Silybum marianum), against various cancers. Virtual screening revealed that silybin is a potent inhibitor of the BRAF-MEK-ERK-RSK2 signaling pathway. The direct binding of silybin with RSK2 (ribbon structure shown) and MEK1/2 (not shown) was generated using the Schrödinger Induced Fit docking program. Silybin was shown to significantly inhibit melanoma cell growth in vitro and in vivo through its direct binding with MEK1/2 and RSK2, resulting in the inhibition of their catalytic kinase activities and subsequent reduction in the activation of NF-kB, AP-1 and STAT3—transcriptional regulators of a variety of proliferative genes in melanomas. See article by Lee and colleagues (beginning on page 455) for more information.