

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. William 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 IIb Trial**
William B. Armstrong, Thomas H. Taylor, Ann R. Kennedy, Raymond J. Melrose, Diana V. Messadi, Mai Gu, Anh D. Le, Marjorie Perloff, Francisco Civantos, William Jarrard Goodwin, Lori J. Wirth, Alexander Ross Kerr, and Frank L. Meyskens Jr
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. Milne, 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 Methylnitrosourea-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 L. 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 Kim, Sung-Young Lee, Hua Xie, Si Jun Park, Jae Young Kim, Joydeb Kumar Kundu, Ann M. Bode, Young-Joon Surh, and Zigang 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, Behnoush Abedi-Ardekani, Masoud Khoshnia, Farhad Islami, Akram Pourshams, Michael Pawlita, Paolo Boffetta, Sanford M. Dawsey, Farin Kamangar, and Christian C. Abnet

483 | **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 Fleshner, Theodorus Van der Kwast, Reinhold Vieth, and Larisa Nonn

495 | **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

CORRECTION

506 | **Correction: A Feasibility Study of the Intraductal Administration of Chemotherapy**

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- κ B, 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.

