


CANCER IMMUNOPREVENTION SERIES

- 95** Immunoprevention of Human Papillomavirus–Associated Malignancies
Joshua W. Wang, Chein-fu Hung, Warner K. Huh, Cornelia L. Trimble, and Richard B.S. Roden

COMMENTARY

- 105** Physical Inactivity and Low Fitness Deserve More Attention to Alter Cancer Risk and Prognosis
Fabian Sanchis-Gomar, Alejandro Lucia, Thomas Yvert, Ana Ruiz-Casado, Helios Pareja-Galeano, Alejandro Santos-Lozano, Carmen Fiuza-Luces, Nuria Garatachea, Giuseppe Lippi, Claude Bouchard, and Nathan A. Berger

RESEARCH ARTICLES

- 111** Urinary Protein Biomarkers in the Early Detection of Lung Cancer
Brian M. Nolen, Aleksey Lomakin, Adele Marrangoni, Liudmila Velikokhatnaya, Denise Prosser, and Anna E. Lokshin
- 120** Chemoprevention Activity of 25-Hydroxyvitamin D in the MMTV-PyMT Mouse Model of Breast Cancer
Lionel Rossdeutsch, Jiarong Li, Aimée-Lee Luco, Ibtihal Fadhil, Benoit Ochiatti, Anne Camirand, Dao Chao Huang, Timothy A. Reinhardt, William Muller, and Richard Kremer
- 129** Enhanced Antitumor Effects of Novel Intracellular Delivery of an Active Form of Menaquinone-4, Menahydroquinone-4, into Hepatocellular Carcinoma
 Shuichi Setoguchi, Daisuke Watase, Kazuhisa Matsunaga, Misa Matsubara, Yohei Kubo, Mariko Kusuda, Nami Nagata-Akaho, Munechika Enjoji, Manabu Nakashima, Morishige Takeshita, Yoshiharu Karube, and Jiro Takata

- 139** Combined Use of Vitamin D3 and Metformin Exhibits Synergistic Chemopreventive Effects on Colorectal Neoplasia in Rats and Mice
Wan Li, Qi-Long Wang, Xia Liu, Shu-Hong Dong, Hong-Xia Li, Chun-Yang Li, Li-Shu Guo, Jing-Miao Gao, Nathan A. Berger, Li Li, Lan Ma, and Yong-Jie Wu
- 149** Genomic Profiling of Human Penile Carcinoma Predicts Worse Prognosis and Survival
Ariane F. Busso-Lopes, Fábio A. Marchi, Hellen Kuasne, Cristovam Scapulatempo-Neto, José Carlos S. Trindade-Filho, Carlos Márcio N. de Jesus, Ademar Lopes, Gustavo C. Guimarães, and Silvia R. Rogatto
- 157** Spectrin Repeat Containing Nuclear Envelope 1 and Forkhead Box Protein E1 Are Promising Markers for the Detection of Colorectal Cancer in Blood
Veerle Melotte, Joo Mi Yi, Marjolein H.F.M. Lentjes, Kim M. Smits, Leander Van Neste, Hanneke E.C. Niessen, Kim A.D. Wouters, Joost Louwagie, Kornel E. Schuebel, James G. Herman, Stephen B. Baylin, Wim van Criekinge, Gerrit A. Meijer, Nita Ahuja, and Manon van Engeland
- 165** Salivary microRNAs Show Potential as a Noninvasive Biomarker for Detecting Resectable Pancreatic Cancer
Zijun Xie, Xiaoyu Yin, Bo Gong, Wenjing Nie, Bin Wu, Xuchao Zhang, Jian Huang, Pingyou Zhang, Zhiwei Zhou, and Zijun Li
- 174** Metformin Use and Lung Cancer Risk in Patients with Diabetes
Lori C. Sakoda, Assiamira Ferrara, Ninah S. Achacoso, Tiffany Peng, Samantha F. Ehrlich, Charles P. Quesenberry Jr, and Laurel A. Habel

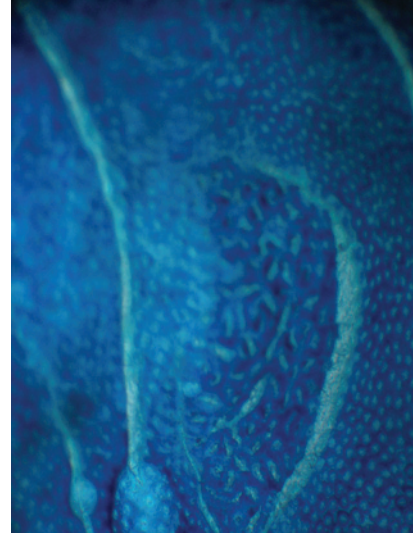
 AC icon indicates Author Choice

For more information please visit www.aacrjournals.org

Table of Contents

ABOUT THE COVER

Vitamin D3 and metformin are widely used in humans for regulating mineral metabolism and as an anti-diabetic drug respectively; and both of them have been shown to have chemopreventive effects against various tumors. Potential synergistic chemopreventive effects of vitamin D3 and metformin against the development of early colon neoplasia was investigated in two models: DMH-induced colon cancer rat model and DMH-DSS-induced colitis-associated colon neoplasia mouse model. The combination of vitamin D3 and metformin showed a more pronounced effect in reducing the numbers of aberrant crypt foci and tumor in the colon when compared to vitamin D3 or metformin alone (shown: macroscopic image of mucosal hyperplasia in rat colon). Results from this study showed that enhancement of metformin's chemopreventive effects by vitamin D3 was associated with down-regulation of S6P expression, via the AMPK (IGF-1)/mTOR pathway. Furthermore, enhancement of vitamin D3's chemopreventive effects by metformin was associated with inhibition of the protein expressions of c-Myc and Cyclin D1, via the vitamin D receptor/ β -catenin pathway. These findings suggest that combined use of vitamin D3 and metformin exhibits synergistic effects against the development of early colon neoplasia and that its use may represent a novel strategy for chemoprevention of colorectal cancer. See article by Li et al. (beginning on page 139) for more information.



Cancer Prevention Research

8 (2)

Cancer Prev Res 2015;8:95-179.

Updated version Access the most recent version of this article at:
<http://cancerpreventionresearch.aacrjournals.org/content/8/2>

E-mail alerts [Sign up to receive free email-alerts](#) related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, use this link <http://cancerpreventionresearch.aacrjournals.org/content/8/2>. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.