

COMMENTARY

- 969** Urinary PGE-M in Colorectal Cancer: Predicting More than Risk?
Karen Colbert Maresso, Eduardo Vilar, and Ernest T. Hawk

REVIEW

- 973** Convergence of Nanotechnology and Cancer Prevention: Are We There Yet?
David G. Menter, Sherri L. Patterson, Craig D. Logsdon, Scott Kopetz, Anil K. Sood, and Ernest T. Hawk

RESEARCH ARTICLES

- 993** Breast Cancer Risk in Young Women in the National Breast Screening Programme: Implications for Applying NICE Guidelines for Additional Screening and Chemoprevention
D. Gareth Evans, Adam R. Brentnall, Michelle Harvie, Sarah Dawe, Jamie C. Sergeant, Paula Stavrinou, Susan Astley, Mary Wilson, John Ainsworth, Jack Cuzick, Iain Buchan, Louise S. Donnelly, and Anthony Howell
- 1002** Analysis of DNA Methylation in Bowel Lavage Fluid for Detection of Colorectal Cancer
Taku Harada, Eiichiro Yamamoto, Hiro-o Yamano, Masanori Nojima, Reo Maruyama, Kohei Kumegawa, Masami Ashida, Kenjiro Yoshikawa, Tomoaki Kimura, Eiji Harada, Ryo Takagi, Yoshihito Tanaka, Hironori Aoki, Masayo Nishizono, Michiko Nakaoka, Akihiro Tsuyada, Takeshi Niinuma, Masahiro Kai, Kazuya Shimoda, Yasuhisa Shinomura, Tamotsu Sugai, Kohzoh Imai, and Hiromu Suzuki

- 1011** Biomarkers for Personalizing Omega-3 Fatty Acid Dosing
Yan Jiang, Zora Djuric, Ananda Sen, Jianwei Ren, Dmitry Kuklev, Ian Waters, Lili Zhao, Charis L. Uhlson, Yu H. Hong, Robert C. Murphy, Daniel P. Normolle, William L. Smith, and Dean E. Brenner
- 1023** Molecular Markers of Carcinogenesis for Risk Stratification of Individuals with Colorectal Polyps: A Case-Control Study
Samir Gupta, Han Sun, Sang Yi, Joy Storm, Guanghua Xiao, Bijal A. Balasubramanian, Song Zhang, Raheela Ashfaq, and Don C. Rockey
- 1035** Widefield Optical Imaging of Changes in Uptake of Glucose and Tissue Extracellular pH in Head and Neck Cancer
Zhen Luo, Melissa N. Loja, D. Greg Farwell, Quang C. Luu, Paul J. Donald, Deborah Amott, Anh Q. Truong, Regina Gandour-Edwards, and Nitin Nitin
- 1045** Progesterone Inhibits Endometrial Cancer Invasiveness by Inhibiting the TGF β Pathway
Amber A. Bokhari, Laura R. Lee, Dewayne Raboteau, Chad A. Hamilton, George L. Maxwell, Gustavo C. Rodriguez, and Viqar Syed
- 1056** Caffeic Acid Directly Targets ERK1/2 to Attenuate Solar UV-Induced Skin Carcinogenesis
Ge Yang, Yang Fu, Margarita Malakhova, Igor Kurinov, Feng Zhu, Ke Yao, Haitao Li, Hanyong Chen, Wei Li, Do Young Lim, Yuqiao Sheng, Ann M. Bode, Ziming Dong, and Zigang Dong

Table of Contents

ABOUT THE COVER

Functional and acquired characteristics of the early *pre-cancer* phenotype are intrinsically different from those of a more advanced anaplastic or invasive malignancy. The biologic conversion of pre-malignancy to invasive disease is complex and is likely to influence delivery of nanoparticles (grey circles) to tumors. Intraepithelial neoplasia (IEN) are early pre-cancerous lesions (pink cells) that proliferate until the normal basement membrane is breached by cancerous cells (brown cells). Switching on angiogenesis and chronic inflammation involving the accumulation of proinflammatory, stromal, and blood factors can dilate blood vessels and alter pericyte (green cells) behavior. Elevated hypoxia and apoptosis (condensed yellow cells) further increase vessel leakiness. Angiogenic sprouting and tip cell (elongated yellow cells) driven angiogenesis leads to further recruitment of additional cells during the angiogenic switch. See article by Menter and colleagues (beginning on page 973) for more information.



Cancer Prevention Research

7 (10)

Cancer Prev Res 2014;7:969-1066.

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