EDITORIAL

681 The Next Frontier: Head and Neck Cancer Immunoprevention
J. Silvio Gutkind and Jack D. Bui
See related article, p. 684

RESEARCH ARTICLES

684 PD-1 Blockade Prevents the Development and Progression of Carcinogen-Induced Oral Premalignant Lesions
Jin Wang, Tongxin Xie, Bingbing Wang, William N. William Jr, John V. Heymach, Adel K. El-Naggar, Jeffrey N. Myers, and Carlos Caulin
See related editorial, p. 681

694 Differential Gene Regulation and Tumor-Inhibitory Activities of Alpha-, Delta-, and Gamma-Tocopherols in Estrogen-Mediated Mammary Carcinogenesis
Soumyasri Das Gupta, Misaal Patel, Joseph Wahlner, Min H Bak, Brian Wall, Mao-Jung Lee, Yong Lin, Weichung Joe Shih, Li Cui, Chung S. Yang, and Nanjoo Suh

704 Association between Cigar or Pipe Smoking and Cancer Risk in Men: A Pooled Analysis of Five Cohort Studies
Jyoti Malhotra, Claire Borron, Neal D. Freedman, Christian C. Abnet, Piet A. van den Brandt, Emily White, Roger L. Milne, Graham G. Giles, and Paolo Boffetta

710 A Randomized Controlled Trial of Green Tea Extract Supplementation and Mammographic Density in Postmenopausal Women at Increased Risk of Breast Cancer
Hamed Samavat, Giske Ursin, Tim H. Emory, Eunjin Lee, Renwei Wang, Carolyn J. Torkelson, Allison M. Dostal, Karen Swenson, Chap T. Le, Chung S. Yang, Mimi C. Yu, Douglas Yee, Anna H. Wu, Jian-Min Yuan, and Mindy S. Kurzer

719 Voluntary Wheel Running Reduces the Acute Inflammatory Response to Liver Carcinogen in a Sex-specific Manner
M.L. Bay, Julie Gehl, Bente Klarlund Pedersen, and Pernille Hojman

729 The Anti-inflammatory Effect of Personalized Omega-3 Fatty Acid Dosing for Reducing Prostaglandin E2 in the Colonic Mucosa Is Attenuated in Obesity
Zora Djuric, D. Kim Turgon, Ananda Sen, Jianwei Ren, Kirk Herman, Devon Ramaswamy, Lili Zhao, Mack T. Ruffin IV, Daniel P. Normolle, William L. Smith, and Dean E. Brenner

738 IKZF1 Gene in Childhood B-cell Precursor Acute Lymphoblastic Leukemia: Interplay between Genetic Susceptibility and Somatic Abnormalities
Bruno A. Lopes, Thayana C. Barbosa, Bruna S. Souza, Caroline P. Poubel, Maria S. Pombo-de-Oliveira for the Brazilian Study Group for Childhood Leukemia, and Mariana Emerenciano

745 Risk Prediction of Cervical Cancer and Precancers by Type-Specific Human Papillomavirus: Evidence from a Population-Based Cohort Study in China
Li Dong, Shang-Ying Hu, Qian Zhang, Rui-Mei Feng, Li Zhan, Xue-Lian Zhao, Xun Zhang, You-Lin Qiao, and Fang-Hui Zhao

752 Acknowledgment to Reviewers
ABOUT THE COVER

Tocopherols (T), consisted of α-, β-, δ- and γ-T forms, have been tested for their anti-cancer activities in different models of cancer prevention, but the differences among individual forms of tocopherol remain unclear. For an unbiased understanding of the mechanisms underlying the anti-cancer activity of the different forms of tocopherol, high-throughput RNA-seq analysis was performed on mammary tumors from ACI rats treated with estrogen and α-, δ- or γ-T. The cover image shows a heatmap of the clustered genes regulated by the different tocopherols. α-T (the first set of columns), which did not significantly inhibit the growth of rat mammary tumors compared to the estrogen control (the second set of columns), had minimal effect on the transcriptome (47 differentially expressed genes). Moreover, the 5 genes upregulated by α-T were unique, sharing no common genes with δ- or γ-T. γ-T (the third set of columns), which was most effective in inhibiting mammary tumorigenesis, had the most profound influence on the rat transcriptome, leading to the differential expression of 192 genes. δ-T (the fourth set of columns), with moderate tumor inhibitory potential, modulated the expression of 51 genes. IPA analysis identified ‘Cancer’ as a top disease pathway and ‘Tumor growth’ and ‘Metastasis’ as the top signaling pathways modulated by γ-T. This study presents an unbiased attempt to understand the differences between biological activities of individual forms of tocopherol. The current study has identified the top genes and biological networks modulated by individual tocopherols at the whole transcriptome level, providing new insights into their differential chemopreventive activities. See the article by Das Gupta et al. (beginning on page 694) for more information.