PERSPECTIVES

573 Statins and the Colorectum: Hope for Chemoprevention?  
John A. Baron  
See articles pp. 588 and 597

576 Is Prostate Cancer Prevention with Selenium All in the Genes?  
Elizabeth A. Platz  
See article p. 604

COMMENTARY

579 Premalignant Breast Neoplasia: A Paradigm of Interlesional and Intraleisional Molecular Heterogeneity and Its Biological and Clinical Ramifications  
Hal K. Berman, Mona L. Gauthier, and Thea D. Tlsty

RESEARCH ARTICLES

588 Statin Use and Colorectal Adenoma Risk: Results from the Adenoma Prevention with Celecoxib Trial  
Monica M. Bertagnolli, Meier Hsu, Ernest T. Hawk, Craig J. Eagle, and Ann G. Zauber, for the Adenoma Prevention with Celecoxib (APC) Study Investigators  
See perspective p. 573

597 Genetic Variation in 3-Hydroxy-3-Methylglutaryl CoA Reductase Modifies the Chemopreventive Activity of Statins for Colorectal Cancer  
Steven M. Lipkin, Elizabeth C. Chao, Victor Moreno, Laura S. Rozek, Hedy Rennert, Mila Pinchev, Diana Dizon, Gad Rennert, Levy Kopelovich, and Stephen R. Gruber  
See perspective p. 573

604 A Large Prospective Study of SEP15 Genetic Variation, Interaction with Plasma Selenium Levels, and Prostate Cancer Risk and Survival  
Kathryn L. Penney, Fredrick R. Schumacher, Haojie Li, Peter Kraft, J. Steven Morris, Tobias Kurth, Lorelei A. Mucci, David J. Hunter, Philip W. Kantoff, Meir J. Stampfer, and Jing Ma  
See perspective p. 576

Blood Biomarker Levels to Aid Discovery of Cancer-Related Single-Nucleotide Polymorphisms: Kallikreins and Prostate Cancer  
Robert J. Klein, Christer Hallén, Angel M. Cronin, Alexander Ploner, Fredrik Wiklund, Anders S. Bjartell, Pär Stattin, Jianfeng Xu, Peter T. Scardino, Kenneth Offit, Andrew J. Vickers, Henrik Grönnberg, and Hans Lilja  

Social Isolation Reduces Mammary Development, Tumor Incidence, and Expression of Epigenetic Regulators in Wild-type and p53-Heterozygotic Mice  
Nina S. Hasen, Kathleen A. O’Leary, Anthony P. Auger, and Linda A. Schuler  

Deficiency in the 15-kDa Selenoprotein Inhibits Tumorigenicity and Metastasis of Colon Cancer Cells  
Robert Irons, Petra A. Tsuji, Bradley A. Carlson, Ping Ouyang, Min-Hyuk Yoo, Xue-Ming Xu, Dolph L. Hatfield, Vadim N. Gladyshev, and Cindy D. Davis  

Methylselenocysteine Resets the Rhythmic Expression of Circadian and Growth-Regulatory Genes Disrupted by Nitrosomethylurea In vivo  
Ming Zhu Fang, Xun Zhang, and Helmut Zarbl  

Extract of Oregano, Coffee, Thyme, Clove, and Walnuts Inhibits NF-κB in Monocytes and in Transgenic Reporter Mice  
Ingvild Paur, Trude R. Balstad, Marit Kolberg, Marit K. Pedersen, Liv M. Austenaa, David R. Jacobs, Jr., and Rune Blomhoff
ABOUT THE COVER

The cover illustration shows two breast ducts containing ductal carcinoma in situ (DCIS; courtesy of Drs. Hal Berman and Mona Gauthier) and representing opposite ends of the theoretical spectrum of molecular heterogeneity in DCIS. The two heterogeneous ducts theoretically could occur in different individuals (i.e., interlesional heterogeneity) or between two regions within a patient’s single DCIS lesion (i.e., intralesional heterogeneity). DCIS can range from homogeneity (left) to a surprising degree of heterogeneity (right) within a single lesion. The continuum of DCIS heterogeneity includes differences in nucleus and cell size, presence and number of coexisting molecular subtypes, and genetic and epigenetic alterations. Well established in invasive breast disease, molecular heterogeneity increasingly clearly is becoming a prevalent, distinct phenotype of DCIS. Key pathways of tumorigenesis modulate critical features of premalignant lesions such as proliferation, differentiation, stress response, and even the generation of diversity. Current studies demonstrate that evaluation of these lesions may provide clinically useful information on future tumor formation as well as biological insights into the origin and functional significance of this distinct phenotype. It is hypothesized that increased heterogeneity marks an increased risk of transformation of DCIS. See article by Berman et al. (beginning on page 579) for more information.