PERSPECTIVE
119 The Case for a Pre-Cancer Genome Atlas (PCGA) Joshua D. Campbell, Sarah A. Mazzilli, Mary E. Reid, Samjot S. Dhillon, Suso Platero, Jennifer Beane, and Avrum E. Spira

EDITORIAL
125 When "Effective" Prevention Agents Fail to Elicit Anticipated Effects: Challenges in Trial Design Kenneth Y. Tsai and Ernest T. Hawk See related article, p. 128

RESEARCH ARTICLES
128 Phase IIB Randomized Study of Topical Difluoromethylornithine and Topical Diclofenac on Sun-Damaged Skin of the Forearm Joanne M. Jeter, Clara Curiel-Lewandrowski, Steven P. Stratton, Paul B. Myrdal, James A. Warneke, Janine G. Einspahr, Chengcheng Hu, Peter Bartels, and David S. Alberts See related article, p. 125

135 Serum Antibodies to HPV16 Early Proteins Warrant Investigation as Potential Biomarkers for Risk Stratification and Recurrence of HPV-Associated Oropharyngeal Cancer Carole Fakhry, Jesse R. Qualliotine, Zhe Zhang, Nishant Agrawal, Daria A. Gaykalova, Justin A. Bishop, Yira Bermudez, Chengcheng Hu, Peter Bartels, and David S. Alberts

142 Double-Blind, Randomized Trial of Alternative Letrozole Dosing Regimens in Postmenopausal Women with Increased Breast Cancer Risk Ana Maria López, Sandhya Pruthi, Judy C. Boughey, Marjorie Perloff, Chiu-Hsieh Hsu, Julie E. Lang, Michele Ley, Denise Frank, Josephine A. Taverna, and H-H. Sherry Chow

149 Relationship of Terminal Duct Lobular Unit Involution of the Breast with Area and Volume Mammographic Densities Gretchen L. Gierach, Deesha A. Patel, Ruth M. Pfeiffer, Jonine D. Figueroa, Laura Linville, Daphne Paphathomas, Jason M. Johnson, Rachael E. Chicoine, Sally D. Herschorn, John A. Shepherd, Jeff Wang, Serghei Mălăkov, Pamela M. Vacek, Donald L. Weaver, Bo Fan, Amit Pasha Mahmoudzadeh, Maya Palakal, Jackie Xiang, Hannah Oh, Hisani N. Home, Brian L. Sprague, Stephen M. Hewitt, Louise A. Brinton, and Mark E. Sherman


172 The Doylestown Algorithm: A Test to Improve the Performance of AFP in the Detection of Hepatocellular Carcinoma Mengqian Wang, Karthik Devarajan, Amit G. Singal, Jorge A. Marrero, Jianliang Dai, Ziding Feng, Jo Ann S. Rinaudo, Sudhir Srivastava, Alison Evans, Hie-Won Hann, Yinzihi Lai, Hushan Yang, Timothy M. Block, and Anand Mehta

180 Unconjugated Bilirubin Is a Novel Prognostic Biomarker for Nasopharyngeal Carcinoma and Inhibits Its Metastasis via Antioxidation Activity Cheng-Cheng Deng, Miaoxu Xu, Jing Li, Xiao-Lin Luo, Yu-Jia Zhu, Rou Jiang, Meng-Xia Zhang, Jin-Ju Lei, Yi-Fan Lian, Xiong Zou, Rui You, Li-Zhen Chen, Qi-Sheng Feng, Jin-Xin Bei, Ming-Yuan Chen, and Yi-Xin Zeng
Louis Lacombe, Vincent Fradet, Éric Lévesque, Frédéric Pouliot, Hélène Lane, Alain Bergeron, Hélène Hovington, André Caron, Molière Nguile-Makao, Mario Harvey, Yves Fradet, and Chantal Guillemette

Inflammatory Marker Changes in Postmenopausal Women after a Year-long Exercise Intervention Comparing High Versus Moderate Volumes
Christine M. Friedenreich, Rachel O’Reilly, Eileen Shaw, Frank Z. Stanczyk, Yutaka Yasui, Darren R. Brenner, and Kerry S. Courneya

ABOUT THE COVER
A digitized image of a hematoxylin and eosin-stained breast tissue section represents a benign diagnostic breast biopsy specimen largely comprised of adipose tissue and with marked terminal duct lobular unit (TDLU) involution. TDLUs are the structures responsible for lactation and are also the histologic source of most breast cancers. TDLU involution, a normal process of aging, is characterized by a reduction in the number and size of TDLUs and their secretory substructures called acini. In this image, rare ducts and equivocal acini are present, but well-developed TDLUs are not identified. Involution of TDLUs has been associated with lower mammographic density and reduced breast cancer risk. See the article by Gierach and colleagues (beginning on page 149) for more information.