

## EDITORIALS

- 607** Targeting "Retired Antigens" for Cancer Immunoprevention  
Robert H. Shoemaker and Thomas G. Forsthuber  
*See related article, p. 612*
- 609** What Factors Influence Decision-Making about Breast Cancer Chemoprevention among High-Risk Women?  
Katherine D. Crew  
*See related article, p. 625*

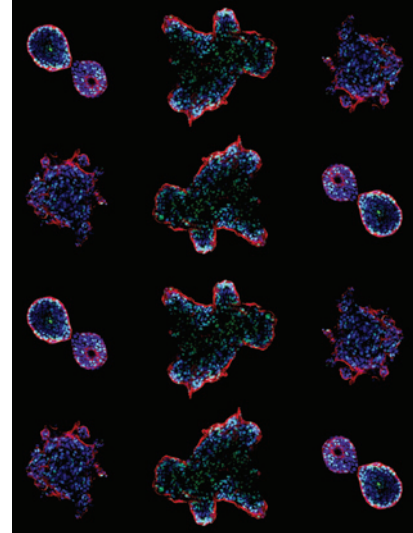
## RESEARCH ARTICLES

- 612** Primary Immunoprevention of Epithelial Ovarian Carcinoma by Vaccination against the Extracellular Domain of Anti-Müllerian Hormone Receptor II  
Suparna Mazumder, Justin M. Johnson, Valerie Swank, Nina Dvorina, Elizabeth Martelli, Jennifer Ko, and Vincent K. Tuohy  
*See related editorial, p. 607*
- 625** NRG Oncology/National Surgical Adjuvant Breast and Bowel Project Decision-Making Project-1 Results: Decision Making in Breast Cancer Risk Reduction  
Christine Holmberg, Hanna Bandos, Angela Fagerlin, Therese B. Bevers, Tracy A. Battaglia, D. Lawrence Wickerham, and Wortia J. McCaskill-Stevens  
*See related editorial, p. 609*
- 635** Gene Methylation Biomarkers in Sputum and Plasma as Predictors for Lung Cancer Recurrence  
Steven A. Belinsky, Shuguang Leng, Guodong Wu, Cynthia L. Thomas, Maria A. Picchi, Sandra J. Lee, Seena Aisner, Suresh Ramalingam, Fadlo R. Khuri, and Daniel D. Karp
- 641** Targeting Aberrant p70S6K Activation for Estrogen Receptor–Negative Breast Cancer Prevention  
Xiao Wang, Jun Yao, Jinyang Wang, Qingling Zhang, Samuel W. Brady, Banu Arun, Victoria L. Seewaldt, and Dihua Yu
- 651** Alterations in Bronchial Airway miRNA Expression for Lung Cancer Detection  
Ana B. Pavel, Joshua D. Campbell, Gang Liu, David Elashoff, Steven Dubinett, Kate Smith, Duncan Whitney, Marc E. Lenburg, and Avrum Spira for the AEGIS Study Team
- 660** Caloric Restriction Prevents Carcinogen-Initiated Liver Tumorigenesis in Mice  
Jonathan M. Ploeger, Juan C. Manivel, Lauren N. Boatner, and Douglas G. Mashek
- 671** The Second-Generation PGI<sub>2</sub> Analogue Treprostinil Fails to Chemoprevent Tumors in a Murine Lung Adenocarcinoma Model  
Lori Dwyer-Nield, Gregory A. Hickey, Micah Friedman, Kevin Choo, Debbie G. McArthur, Meredith A. Tennis, Melissa L. New, Mark Geraci, and Robert L. Keith

# Table of Contents

## ABOUT THE COVER

While estrogen receptor (ER) negative (ER<sup>-</sup>) breast cancer remains a major challenge in the cancer prevention field, ER modulators and aromatase inhibitors have shown adequate efficacy in the prevention of ER<sup>+</sup> breast cancer. The activation of Akt signaling pathway has been detected in atypical hyperplastic early stage lesions of patients. In the current study, Akt and the downstream aberrantly activated 70 kDa ribosomal protein S6 (p70S6K) and MAP kinase pathways were identified to confer targeting advantages of premalignant breast lesions in progression to ER<sup>-</sup> breast cancer using small molecule kinase inhibitors. The micrograph images show human mammary epithelial cells (hMECs) under 3D culture conditions stained for polarity (Laminin V, red) and proliferation (Ki-67, green) markers. The third row of cells: left, normal hMEC acini in a rounded shape with defined boundary and limited cell proliferation (growth arrested); middle, ErbB2-transformed hMEC acini showing increased cell proliferation, which resulted in a disorganized "grape-like" shape with intact boundary; and right, targeting aberrant Akt/p70S6K activation with Phase I–tested dual inhibitor LY2780301 in ErbB2-transformed hMEC acini drastically suppressed cell proliferation and partially reversed the disorganized acini shape, suggesting that p70S6K may potentially be an effective target for the prevention of ER<sup>-</sup> breast cancer. See the article by Wang et al. (beginning on page 641) for more information.



# Cancer Prevention Research

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