RESEARCH ARTICLES

879 Randomized, Placebo-Controlled Trial of Green Tea Catechins for Prostate Cancer Prevention
Nagi B. Kumar, Julio Pow-Sang, Kathleen M. Egan, Philippe E. Spiess, Shohreh Dickinson, Raoul Salup, Mohamed Helal, Jerry McLarty, Christopher R. Williams, Fred Schreiber, Howard L. Parnes, Said Sebti, Aslam Kazi, Michael J. Schell

888 Effect of Metformin on Breast Ductal Carcinoma In Situ Proliferation in a Randomized Presurgical Trial
Andrea DeCensi, Matteo Puntoni, Aliana Guerrieri-Gonzaga, Massimiliano Cazzaniga, Davide Serrano, Matteo Lazzeroni, Andrea Vingiani, Oreste Gentilini, Marilena Petrera, Giuseppe Viale, Jack Cuzick, Bernardo Bonanni, and Giancarlo Pruneri

895 Vitamin D Repletion Reduces the Progression of Premalignant Squamous Lesions in the NTCU Lung Squamous Cell Carcinoma Mouse Model
Sarah A. Mazzilli, Pamela A. Hershberger, Mary E. Reid, Paul N. Bogner, Kristopher Atwood, Donald L. Trump, and Candace S. Johnson

905 Physical Activity from Early Adulthood and Risk of Prostate Cancer: A 24-Year Follow-Up Study among Icelandic Men
Sofía M. Heftfeldsdóttir, Jóhanna E. Torfadóttir, Thor Aspelund, Kristjan T. Magnusson, Laufey Tryggvadóttir, Vilmundur Gudnason, Lorelei A. Mucci, Meir Stampfer, and Candice S. Johnson

912 Modulation of Breast Cancer Risk Biomarkers by High-Dose Omega-3 Fatty Acids: Phase II Pilot Study in Postmenopausal Women
See related article, p. 922

922 Modulation of Breast Cancer Risk Biomarkers by High-Dose Omega-3 Fatty Acids: Phase II Pilot Study in Postmenopausal Women
See related article, p. 912

932 Robust In Vitro and In Vivo Neutralization against Multiple High-Risk HPV Types Induced by a Thermostable Thioredoxin-L2 Vaccine
Hanna Seitz, Lis Ribeiro-Müller, Elena Canali, Angelo Bolchi, Massimo Tommasino, Simone Ottonello, and Martin Müller

942 Double-Blind Randomized 12-Month Soy Intervention Had No Effects on Breast MRI Fibroglandular Tissue Density or Mammographic Density
Anna H. Wu, Darcy Spicer, Agustin Garcia, Chiu-Chen Tseng, Linda Hovanessian-Larsen, Pulin Sheth, Sue Ellen Martin, Debra Hawes, Christy Russell, Heather MacDonald, Debu Tripathy, Min-Ying Su, Giske Ursin, and Malcolm C. Pike

952 Colon Tumors with the Simultaneous Induction of Driver Mutations in APC, KRAS, and PIK3CA Still Progress through the Adenoma-to-Carcinoma Sequence

962 Physical Activity and Prostate Tumor Vessel Morphology: Data from the Health Professionals Follow-up Study

968 Low SFRP1 Expression Correlates with Poor Prognosis and Promotes Cell Invasion by Activating the Wnt/β-Catenin Signaling Pathway in NPC
Xian-Yue Ren, Guan-Qun Zhou, Wei Jiang, Ying Sun, Ya-Fei Xu, Ying-Qin Li, Xin-Ran Tang, Xin Wen, Qing-Mei He, Xiao-Jing Yang, Na Liu, and Jun Ma
Table of Contents

978  Hepatitis B Virus Combo Mutations Improve the Prediction and Active Prophylaxis of Hepatocellular Carcinoma: A Clinic-Based Cohort Study
  Jianhua Yin, Junxue Wang, Rui Pu, Haiguang Xin, Zixiong Li, Xue Han, Yibo Ding, Yan Du, Wenbin Liu, Yang Deng, Xiaowei Ji, Ming Wu, Min Yu, Hongwei Zhang, Hongyang Wang, Timothy C. Thompson, Wu Ni, and Guangwen Cao

989  Chemopreventive Effects of Dietary Eicosapentaenoic Acid Supplementation in Experimental Myeloid Leukemia
  Emily R. Finch, Avinash K. Kudva, Michael D. Quickel, Laura L. Goodfield, Mary J. Kennett, Jay Whelan, Robert F. Paulson, and K. Sandeep Prabhu

1000 Targeted DNA Methylation Screen in the Mouse Mammary Genome Reveals a Parity-Induced Hypermethylation of Igf1r That Persists Long after Parturition

ABOUT THE COVER

Breast ductal in situ carcinoma (DCIS) accounts for approximately 20% of all breast neoplasms, but its treatment is still controversial. Large randomized phase III trials are difficult to conduct, and new efficient clinical trial models are needed to accelerate drug discovery, particularly for HER2-positive DCIS. The oral antidiabetic drug metformin has been associated with lower breast cancer risk in epidemiological studies and has shown antitumor activity in HER2-positive preclinical models. In this randomized trial, proliferation of intraepithelial lesions surrounding breast cancer was assessed in 200 patients who received metformin or placebo for 28 days prior to surgery. Upon surgery, specimens of cancer-adjacent, unaffected tissue were screened for intraepithelial lesions and characterized by immunohistochemistry. Overall, metformin did not affect proliferation in premalignant disorders. However, proliferation of HER2-positive DCIS lesions was significantly lower in women allocated to metformin relative to placebo, especially when ER was coexpressed, providing the background for an adjuvant trial incorporating metformin in HER2-positive DCIS. The micrograph shown on the cover (40 × magnification) is stained for HER2 (membranous, brown) and Ki-67 (nuclear, violet) in a representative case of a grade 2 DCIS (upper left hand side) adjacent to a grade 3 ductal invasive carcinoma (lower right hand side). The DCIS component shows intense, circumferential membranous staining for HER2 in most cells, 14% of which coexpress Ki-67. The invasive tumor shows incomplete, faint HER2 and high Ki-67 staining. See the article by DeCensi et al. (beginning on page 888) for more information.