RESEARCH ARTICLES

1251 Chemopreventive Efficacy of Raloxifene, Bexarotene, and Their Combination on the Progression of Chemically Induced Colon Adenomas to Adenocarcinomas in Rats
Naveena B. Janakiram, Altaf Mohammed, Yuting Zhang, Misty Brewer, Taylor Bryant, Stan Lightfoot, Vernon E. Steele, and Chinthalapally V. Rao

1262 The Antidepressant Desipramine and α2-Adrenergic Receptor Activation Promote Breast Tumor Progression in Association with Altered Collagen Structure
Mercedes J. Szpunar, Kathleen A. Burke, Ryan P. Dawes, Edward B. Brown, and Kelley S. Madden

1273 A Multiantigen Vaccine Targeting Neu, IGFBP-2, and IGF-IR Prevents Tumor Progression in Mice with Preinvasive Breast Disease
Mary L. Disis, Ekram Gad, Daniel R. Herendeen, Vy Phan-Lai, Kyong Hwa Park, Denise L. Cecil, Megan M. O’Meara, Piper M. Treuting, and Ronald A. Lubet

1283 Evidence of a Chemopreventive Effect of Progestin Unrelated to Ovulation on Reproductive Tract Cancers in the Egg-laying Hen

1293Isoangustone A, A Novel Licorice Compound, Inhibits Cell Proliferation by Targeting PI3K, MKK4, and MKK7 in Human Melanoma
Nu Ry Song, Eunjung Lee, Sanguine Byun, Jong-Eun Kim, Madhusoodanan Mettamal, Jung Han Yoon Park, Soon Sung Lim, Ann M. Bode, Hyong Joo Lee, Ki Won Lee, and Zigang Dong

1304 Lycopene Metabolite, Apo-10'-Lycopenoic Acid, Inhibits Diethylnitrosamine-Initiated, High Fat Diet-Promoted Hepatic Inflammation and Tumorigenesis in Mice
Blanche C. Ip, Kang-Qian Hu, Chun Liu, Donald E. Smith, Martin S. Ohin, Lynne M. Ausman, and Xiang-Dong Wang

1317 Black Raspberries Protectively Regulate Methylation of Wnt Pathway Genes in Precancerous Colon Tissue
Li-Shu Wang, Chieh-Ti Kuo, Tim H.-M. Huang, Martha Yearsley, Kiyoko Oshima, Gary D. Stoner, Jianhua Yu, John F. Lehner, and Yi-Wen Huang

1328 Cost-effectiveness of a Genetic Test for Breast Cancer Risk
Henry J. Folse, Linda E. Green, Andrea Kress, Richard Allman, and Tuan A. Dinh

1337 The Involvement of Endoplasmic Reticulum Stress in the Suppression of Colorectal Tumorigenesis by Tolfenamic Acid
Xiaobo Zhang, Seong-Ho Lee, Kyung-Won Min, Michael F. McIntee, Jin Boo Jeong, Qingwang Li, and Seung Joon Baek

1348 Aberrant DNA Methylation at Genes Associated with a Stem Cell-like Phenotype in Cholangiocarcinoma Tumors

1356 Esculetin Suppresses Proliferation of Human Colon Cancer Cells by Directly Targeting β-Catenin

1365 KAVA Chalcone, Flavokawain A, Inhibits Urothelial Tumorigenesis in the UPII-SV40T Transgenic Mouse Model
Zhongbo Liu, Xia Xu, Xuesen Li, Shuman Liu, Anne R. Simoneau, Feng He, Xue-Ru Wu, and Xiaolin Zi
ABOUT THE COVER

Epidemiologic evidence suggests that progestins may be potent ovarian cancer preventives. Using the chicken ovarian cancer model, the primary objective of the present study was to prospectively evaluate progestins as reproductive tract cancer chemopreventives. A secondary objective assessed whether vitamin D would confer cancer protection either alone or in addition to progestin. Single Comb White Leghorns were randomized into six groups with hormonal and dietary manipulation for 2 years as follows: (i) no intervention, regular feed/caloric intake, (ii) control, (iii) vitamin D, (iv) the progestin levonorgestrel, (v) vitamin D plus levonorgestrel, and (vi) the progestin Provera (medroxyprogesterone acetate). Groups 2–6 were calorically restricted to inhibit ovulation. The results indicated caloric restriction decreased egg production by over 60% (cover image: cumulative production of eggs by treatment group; thick lines are the means for each treatment group) and was associated with a greater than 70% decrease in reproductive tract cancers. Ovulatory events did not differ among the calorically restricted groups (groups 2–6), except for the group receiving levonorgestrel, which had fewer ovulatory events compared to controls ($P = 0.046$). After correcting for egg production, birds receiving progestins had significantly fewer reproductive tract cancers (odds ratio 0.61; CI 0.39–0.95, $P = 0.03$), with similar proportionate reductions in tumors arising in either the ovary or oviduct. Vitamin D did not significantly affect cancer incidence overall, or add to the cancer-preventive effect of progestins. This study suggests a protective effect of progestins against ovarian and oviductal cancers and supports the concept that progestins provide a chemopreventive effect unrelated to ovulation. See article by Rodriguez and colleagues (beginning on page 1283) for more information.