EDITORIAL

251 Targeting Toll-like Receptors in Cancer Prevention
Karen S. Sfanos
See related article, p. 265

COMMENTARY

255 Towards Prevention of Breast Cancer: What Are the Clinical Challenges?
Signe Borgquist, Per Hall, Isaac Lippus, and Judy E. Garber

RESEARCH ARTICLES

265 Pharmacological TLR4 Antagonism Using Topical Resatorvid Blocks Solar UV-Induced Skin Tumorigenesis in SKH-1 Mice
See related editorial, p. 251

279 Distinct Chemopreventive Effects of Aspirin in Diffuse and Intestinal-Type Gastric Cancer
Ryota Niikura, Yoku Hayakawa, Yoshihiro Hirata, Mitsunori Konishi, Nobumi Suzuki, Sozaburo Ihara, Atsuo Yamada, Tetsuo Ushiku, Mitsuhiro Fujishiro, Masashi Fukayama, and Kazuhiko Koike

287 Adiposity at Age 10 and Mammographic Density among Premenopausal Women
Aliya Alimujiang, Kellie R. Imm, Catherine M. Appleton, Graham A. Colditz, Catherine S. Berkey, and Adetunji T. Toriola

295 A System-Level Approach to Improve the Uptake of Antiestrogen Preventive Therapy among Women with Atypical Hyperplasia and Lobular Cancer In Situ
Abenaa M. Brewster, Priya Thomas, Powel Brown, Robin Coyne, Yuanqing Yan, Cristina Checca, Lavinia Middleton, Kim-anh Do, and Therese Bevers

303 Metabolomics Profiles of Hepatocellular Carcinoma in a Korean Prospective Cohort: The Korean Cancer Prevention Study-II
Sun Ha Jee, Minjoo Kim, Minkyung Kim, Hye Jin Yoo, Hyungyo Kim, Jeung Ji Jung, Seri Hong, and Jong Ho Lee

ABOUT THE COVER

An urgent need exists for the development of more efficacious molecular strategies targeting non-melanoma skin cancer (NMSC), the most common malignancy worldwide. Inflammatory signaling downstream of Toll-like receptor 4 (TLR4) has been implicated in several forms of tumorigenesis, yet its role in solar UV-induced skin carcinogenesis remains undefined. Recently, we have shown TLR4 contributes to UV-induced stress and inflammatory signaling in keratinocytes, and that the specific TLR4 antagonist resatorvid (TAK-242) blocks acute UV-induced AP-1 and NF-κB activity. In the current study, topical resatorvid has been employed for skin photochemoprevention, suppressing tumor area and multiplicity in SKH-1 mice exposed to solar simulated light (SSL). In the cover figure, we highlight the inhibition of UV-induced epidermal immune cell infiltration in chronically exposed mouse epidermis (background), and the potentiation of apoptosis mediated by resatorvid treatment in skin tumors (inset). SKH-1 mice were exposed to SSL three times weekly for 15 weeks, during which time they were topically treated with either vehicle (acetone) or resatorvid 1 hour prior to SSL. Some mice were then sacrificed and chronically exposed skin was examined for epidermal immune cell infiltration using H&E stained tissue (400x). Skin treated with SSL + vehicle displayed significant infiltration of lymphocytic cells (not shown), while skin treated with SSL + resatorvid lack infiltrates, as displayed in the background image. See the article by Blohm-Mangone et al. beginning on page 265 for more information.