## COMMENTARY

**715** A Proposal to Improve the Early Diagnosis of Symptomatic Cancers in the United States
Elizabeth A. Sarma, Sarah C. Kobrin, and Matthew J. Thompson

## REVIEW

**721** A Comprehensive Review and Perspective on Anticancer Mechanisms of Withaferin A in Breast Cancer
Eun-Ryeong Hahm, Su-Hyeong Kim, Krishna B. Singh, Kamayani Singh, and Shivendra V. Singh

## RESEARCH ARTICLES

**735** Prevention of Tobacco Carcinogen-Induced Lung Tumor Development by a Novel STAT3 Decoy Inhibitor
Christian Njatcha, Mariya Farooqui, Abdulaziz A. Almotlak, and Jill M. Siegfried

**747** Stress-induced Norepinephrine Downregulates CCL2 in Macrophages to Suppress Tumor Growth in a Model of Malignant Melanoma
Kayla J. Steinberger, Michael T. Bailey, Amy C. Gross, Laura A. Sumner, Jeffrey L. Voorhees, Nisha Crouser, Jennifer M. Curry, Yijie Wang, A. Courtney DeVries, Clay B. Marsh, Ronald Glaser, Eric V. Yang, and Timothy D. Eubank

**761** HER2-Overexpressing Ductal Carcinoma In Situ Associated with Increased Risk of Ipsilateral Invasive Recurrence, Receptor Discordance with Recurrence
Thomas J. O’Keefe, Sarah L. Blair, Ava Hosseini, Olivier Harismendy, and Anne M. Wallace

**773** Endoscopic History and Provider Characteristics Influence Gastric Cancer Survival in Asian Americans

**783** HIST1H2BB and MAGI2 Methylation and Somatic Mutations as Precision Medicine Biomarkers for Diagnosis and Prognosis of High-grade Serous Ovarian Cancer
Blanca L. Valle, Sebastian Rodriguez-Torres, Elisabetta Kuhn, Teresa Díaz-Montes, Edgardo Parrilla-Castellar, Fahcina P. Lawson, Oluwasina Folawiyo, Carmen Ill-Gangas, Priscilla Brebi-Mievile, James R. Eshleman, James Herman, Ie-Ming Shih, David Sidransky, and Rafael Guerrero-Preston

**795** Biomarker Modulation Study of Celecoxib for Chemoprevention in Women at Increased Risk for Breast Cancer: A Phase II Pilot Study
Soley Bayraktar, Sema Baghaki, Jimin Wu, Diane D. Liu, Angelica M. Gutierrez-Barrera, Therese B. Bevers, Vicente Valero, Nour Sneige, and Banu K. Arun
Former smokers continue to be at elevated lung cancer risk, making up a large proportion of newly diagnosed lung cancer. Former smokers with airway dysplasia received some benefit in randomized trials of chemoprevention, but preventive effects to date have been modest. There is a great need for more effective chemoprevention agents for former smokers at high risk for lung cancer. Njatcha and colleagues (in a study beginning on page 735) determined the efficacy of a novel STAT3 inhibitor, CS3D, for chemoprevention using a tobacco carcinogen-induced mouse model of lung cancer that mimics an ex-smoker. CS3D is a cyclic double-stranded decoy oligonucleotide corresponding to the DNA response element for STAT3. CS3D interacts with p-STAT3 dimers to compete for their binding to the promoters of STAT3 target genes, and also triggers p-STAT3 degradation. CS3D given as a short-term intermittent therapy blocked formation and progression of airway preneoplasia and adenomas in tobacco carcinogen-exposed mice, and reduced both incidence and size of lung tumors that arose over time. The cover depicts immunohistochemical detection of p-STAT3 in lung adenomas from these mice. After treatment with CS3D (lower left image) p-STAT3 staining is reduced compared to that seen in an adenoma from a mouse treated with the inactive mutant version of the cyclic oligonucleotide, CS3M (upper right image). Detection of p-STAT3 over time showed that phosphorylated STAT3 remained suppressed eight weeks after the end of the treatment course. Results show that a short course of CS3D therapy has persistent effects to reduce STAT3 signaling in the airways and prevent lung cancer development.