PERSPECTIVES

259  NOTCH Mutations: Multiple Faces in Human Malignancies
Li Mao
See related article, p. 277

262  A Novel Target for Oral Cancer Chemoprevention? Notch Quite, Yet. . .
William N. William Jr and Adel K. El-Naggar
See related article, p. 277

CANCER IMMUNOPREVENTION SERIES

266  The Antigenic Repertoire of Premalignant and High-Risk Lesions
Juan Pablo Marquez, Sasha E. Stanton, and Mary L. Disis

REVIEW

271  Gonadal Tumor in Frasier Syndrome: A Review and Classification
Jiro Ezaki, Kazunori Hashimoto, Tatsuo Asano, Shoichiro Kanda, Yuko Akioka, Motoshi Hattori, Tomoko Yamamoto, and Noriyuki Shibata

RESEARCH ARTICLES

277  Notch1 Mutations Are Drivers of Oral Tumorigenesis
Evgeny Izumchenko, Kai Sun, Sian Jones, Mariana Braitt, Nishant Agrawal, Wayne Koch, Christine L. McCord, David R. Riley, Samuel V. Angioli, Victor E. Velculescu, Wei-Wen Jiang, and David Sidransky
See related perspectives, p. 259 and p. 262

287  Cleaved NOTCH1 Expression Pattern in Head and Neck Squamous Cell Carcinoma Is Associated with NOTCH1 Mutation, HPV Status, and High-Risk Features
Eleni M. Rettig, Christine H. Chung, Justin A. Bishop, Jason D. Howard, Rajni Sharma, Ryan J. Li, Christopher Douville, Rachel Karchin, Evgeny Izumchenko, David Sidransky, Wayne Koch, Joseph Califano, Nishant Agrawal, and Carole Fakhry

LETTER TO THE EDITOR

338  Targeting Apoptosis Pathways in Cancer—Letter
Stephen Safe
ABOUT THE COVER

Colorectal cancer (CRC) is the second leading cause of deaths among all cancers. The colonic tumor microenvironment is strongly associated with chronic inflammation, in that immune cells’ innate and adaptive responses usually favor tumor cell growth and progression. Sea cucumber extract Frondanol® A5 is known for its anti-inflammatory and immunostimulatory properties. In this study, Frondanol® A5 was tested for its chemopreventive activity against CRC using ApcMin/+ mice. Frondanol® A5 had a significant inhibitory effect on small intestine and colon tumors. It increased innate immune responses against tumor formation; treated animals displayed an increase in phagocytosis and an increase in gamma-interferon-inducible lysosomal thiol reductase (GILT) expression. Frondanol® A5 markedly decreased inflammatory cytokines with decreased proliferation. Further, a significant decrease in the angiogenic marker VEGF was observed in treated tumors as illustrated by the cover micrograph (immunohistofluorescence staining of VEGF in Frondanol®-A5-treated small intestinal polyps). These results suggest that Frondanol® A5 is a safer agent, which exhibits significant chemopreventive potential against intestinal tumorigenesis. For more information, see the article by Janakiram et al. (beginning on page 327).