COMMENTARY

977 Establishing a Primary Care Alliance for Conducting Cancer Prevention Clinical Research at Community Sites
Bernard W. Parker, Barbara L. McAneny, Edith P. Mitchell, Ana Maria López, Sandra A. Russo, Pamela Maxwell, Leslie G. Ford, and Worta McCaskill-Stevens; for the National Cancer Institute PARTNRS Planning Committee

REVIEW

983 Bilateral Salpingo-oophorectomy and Breast Cancer Risk for BRCA1 and BRCA2 Mutation Carriers: Assessing the Evidence
Ciara Conduit, Roger L. Milne, Michael L. Friedlander, and Kelly-Anne Phillips

RESEARCH ARTICLES

995 Suppression of Colon Tumorigenesis in Mutant Apc Mice by a Novel PDE10 Inhibitor that Reduces Oncogenic β-Catenin

PDE10 is overexpressed in colon tumors whereby inhibition activates cGMP/PKG signaling and suppresses Wnt/β-catenin transcription to selectively induce apoptosis of colon cancer cells. ADT 061 is a novel PDE10 inhibitor that shows promising cancer chemopreventive activity and tolerance in a mouse model of colon cancer.

1009 Proton Pump Inhibitor Omeprazole Suppresses Carcinogen-induced Colonic Adenoma Progression to Adenocarcinoma in F344 Rat
Venkateshwar Madka, Gaurav Kumar, Gopal Pathuri, Janani Panneerselvam, Yuting Zhang, Vishal Ganta, Stanley Lightfoot, Ronald Lubet, Chen S. Suen, Vernon E. Steele, Naveena B. Janakiram, Altaf Mohammed, and Chinthalapally V. Rao

Preventing colon cancer is urgently needed because of its high incidence and mortality rates worldwide. Toward this end, preventive efficacy of omeprazole, a common medication, was evaluated in animal model of colorectal cancer and was found to suppress colonic adenoma progression to carcinoma. These findings warrant its further evaluation in humans.

1021 Novel Models of Genetic Education and Testing for Pancreatic Cancer Interception: Preliminary Results from the GENERATE Study

Preliminary data from the GENERATE study indicate success of remote alternatives for pancreatic cancer genetic testing and education, with genetic testing uptake rates over 90% and a high rate of identification of germline pathogenic variant carriers who would be ideal candidates for pancreatic cancer interception.
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### ABOUT THE COVER

Mutations in the adenomatous polyposis coli (APC) gene that activates Wnt/β-catenin signaling and drives the transcription of oncoproteins (e.g., MYC) essential for malignant progression, occur in over 80% of patients with colorectal cancer. Mutations in APC or other members of the Wnt/β-catenin signaling cascade impair β-catenin degradation and promote translocation of β-catenin to the nucleus, where it mediates a proliferative/survival transcriptional program. Novel compounds that inhibit Wnt/β-catenin signaling can block the effect of such mutations and are attractive drug candidates for cancer chemoprevention or therapy. In a publication starting on page 995 of this issue, Lee and colleagues report that a novel phosphodiesterase 10A (PDE10) inhibitor (ADT 061) suppresses the formation of colorectal adenomas in the Apc\(^{+/-}\)/Min-FCCC mouse model, where tumorigenesis is driven by an APC mutation and nuclear accumulation of β-catenin. PDE10 inhibition activates cGMP/PKG signaling and phosphorylates the oncogenic pool of β-catenin, resulting in its degradation and mitigation of proliferative/survival transcription. The cover shows the colocalization of PDE10 (red) and β-catenin (green) in colon adenomas from Apc\(^{+/-}\)/Min-FCCC mice.

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