

CANCER PREVENTION RESEARCH

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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 María López, Sandra A. Russo, Pamela Maxwell, Leslie G. Ford, and Wortia 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**

Kevin J. Lee, Wen-Chi L. Chang, Xi Chen, Jacob Valiyaveetil, Veronica Ramirez-Alcantara, Elaine Gavin, Alla Musiyenko, Luciana Madeira da Silva, Naga S. Annamdevula, Silas J. Leavesley, Antonio Ward, Tyler Mattox, Ashley S. Lindsey, Joel Andrews, Bing Zhu, Charles Wood, Ashleigh Neese, Ashley Nguyen, Kristy Berry, Yulia Maxuitenko, Mary Pat Moyer, Elmar Nurmammedov, Greg Gorman, Lori Coward, Gang Zhou, Adam B. Keeton, Harry S. Cooper, Margie L. Clapper, and Gary A. Piazza

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**

C. Sloane Furniss, Matthew B. Yurgelun, Chinedu Ukaegbu, Pamela E. Constantinou, Catherine C. Lafferty, Eliana R. Talcove-Berko, Alison N. Schwartz, Jill E. Stopfer, Meghan Underhill-Blazey, Barbara Kenner, Scott H. Nelson, Sydney Okumura, Sherman Law, Alicia Y. Zhou, Tara B. Coffin, Nicolette J. Rodriguez, Hajime Uno, Allyson J. Ocean, Florencia McAllister, Andrew M. Lowy, Scott M. Lippman, Alison P. Klein, Lisa Madlensky, Gloria M. Petersen, Judy E. Garber, Michael G. Goggins, Anirban Maitra, and Sapna Syngal

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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1033 EUS-based Pancreatic Cancer Surveillance in *BRCA1/BRCA2/PALB2/ATM* Carriers Without a Family History of Pancreatic Cancer

Bryson W. Katona, Jessica M. Long, Nuzhat A. Ahmad, Sara Attalla, Angela R. Bradbury, Erica L. Carpenter, Dana F. Clark, Gillain Constantino, Koushik K. Das, Susan M. Domchek, Christina Dudzik, Jessica Ebrahimzadeh, Gregory G. Ginsberg, Jordan Heiman, Michael L. Kochman, Kara N. Maxwell, Danielle B. McKenna, Jacquelyn Powers, Payal D. Shah, Kirk J. Wangenstein, and Anil K. Rustgi

BRCA1/BRCA2/ATM/PALB2 carriers have increased pancreatic ductal adenocarcinoma (PDAC) risk, yet are typically not eligible for PDAC surveillance in the absence of PDAC family history. Herein we describe outcomes of PDAC surveillance in *BRCA1/BRCA2/ATM/PALB2* carriers without a family history of PDAC, showing that PDAC surveillance can be considered in this high-risk group.

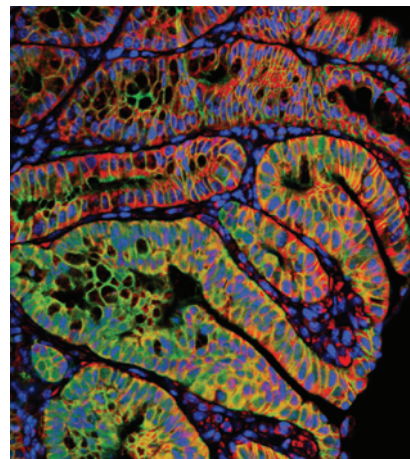
1041 Weight Loss During Intrauterine Progesterin Treatment for Obesity-associated Atypical Hyperplasia and Early-Stage Cancer of The Endometrium

Chloe E. Barr, Neil A.J. Ryan, A.E. Derbyshire, Y. Louise Wan, Michelle L. MacKintosh, Rhona J. McVey, James Bolton, Cheryl Fitzgerald, Dina Awad, Richard J. Slade, Akheel A. Syed, Basil J. Ammori, and Emma J. Crosbie

This study found that weight loss improves response rates in women with obesity and atypical hyperplasia or low-risk endometrial cancer undergoing conservative management with intrauterine progesterin. Given the additional benefits of weight loss for fertility, cardiovascular health and quality of life, future research should focus on how best to accomplish it.

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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