

CANCER PREVENTION RESEARCH

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Victor G. Vogel
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Lisa M. Fucito, Hannah Malinosky,
Stephen R. Baldassarri, and Roy S. Herbst

RESEARCH BRIEF

- 11 Hallmark Circulating Tumor-Associated Cell Clusters Signify 230 Times Higher One-Year Cancer Risk**
Anantbhushan Ranade, Amit Bhatt, Raymond Page, Sewanti Limaye, Timothy Crook, Dadasaheb Akolkar, and Darshana Patil
The study evaluated a blood test that can determine if healthy ('asymptomatic') individuals without a history of cancer have an increased risk of developing cancer within the next one year. This test can significantly minimize radiological or invasive screening in the majority individuals who do not have any increased risk.

RESEARCH ARTICLES

- 17 Targeting the Cholecystokinin Receptor: A Novel Approach for Treatment and Prevention of Hepatocellular Cancer**
Martha D. Gay, Anita Safronenka, Hong Cao, Felice H. Liu, Zoe X. Malchiodi, Robin D. Tucker, Alexander Kroemer, Narayan Shivapurkar, and Jill P. Smith
This investigation demonstrates the role of the gastrointestinal peptide cholecystokinin (CCK) in hepatocellular carcinoma (HCC) and how CCK-BR blockade reverses the premalignant state of the hepatic extracellular matrix hence, rendering it less susceptible to the development of HCC. Thereby, CCK-BR blockade is a novel approach for the prevention/treatment of HCC.

- 31 Reducing Fatty Acid Oxidation Improves Cancer-free Survival in a Mouse Model of Li-Fraumeni Syndrome**

Ping-Yuan Wang, Jin Ma, Jie Li, Matthew F. Starost, Michael J. Wolfgang, Komudi Singh, Mehdi Pirooznia, Ju-Gyeong Kang, and Paul M. Hwang

Mildly inhibiting the increased fatty acid oxidation observed in a mouse model of Li-Fraumeni syndrome, a cancer predisposition disorder caused by inherited mutations of *TP53*, dampens aberrant pro-tumorigenic cell signaling and improves the survival time of these mice, thereby revealing a potential strategy for cancer prevention in patients.

- 41 Genome-wide Association Analysis of Proinflammatory Cytokines and Gene-lifestyle Interaction for Invasive Breast Cancer Risk: The WHI dbGaP Study**

Su Yon Jung, Peter A. Scott, Jeanette C. Papp, Eric M. Sobel, Matteo Pellegrini, Herbert Yu, Sihao Han, and Zuo-Feng Zhang

The top GWA-SNPs associated with pro-inflammatory biomarkers have implications for breast carcinogenesis by interacting with obesity factors. Our findings may suggest interventions for women who carry the inflammatory-risk genotypes to reduce breast cancer risk.

- 55 Sleep Characteristics and Risk of Ovarian Cancer Among Postmenopausal Women**

Xiaoyun Liang, Holly R. Harris, Michael Hendryx, Aladdin H. Shadyab, Lauren Hale, Yueyao Li, Tracy E. Crane, Elizabeth M. Cespedes Feliciano, Marcia L. Stefanick, and Juhua Luo

This study shows no association between sleep duration, sleep quality, or insomnia with the risk of overall ovarian cancer among postmenopausal women. However, restful sleep quality was associated with a lower risk of invasive serous ovarian cancer, and insomnia was associated with a higher risk of invasive serous ovarian cancer.

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65	Inflammation Modulation by Vitamin D and Calcium in the Morphologically Normal Colorectal Mucosa of Patients with Colorectal Adenoma in a Clinical Trial David Corley Gibbs, Veronika Fedirko, John A. Baron, Elizabeth L. Barry, W. Dana Flanders, Marjorie L. McCullough, Rami Yacoub, Tapasya Raavi, Robin E. Rutherford, March E. Seabrook, and Roberd M. Bostick Supplemental calcium and vitamin D reduce indicators of cancer-promoting inflammation in normal colorectal tissue in humans, thus furthering our understanding of how they may help prevent colorectal cancer.	113	Utilization Pattern of Computed Tomographic Colonography in the United States: Analysis of the U.S. National Health Interview Survey Young-Rock Hong, Zhigang Xie, Kea Turner, Santanu Datta, Rohit Bishnoi, and Chintan Shah Although computed tomographic (CT) colonography has been proved to be cost-effective and have better patient acceptance, its overall utilization for colorectal cancer (CRC) screening is low (<1.4%) among US adults aged 45+ in 2018. More efforts are needed to implement strategies to increase CT colonography for effective CRC prevention.
77	Risk of Skin Cancer Associated with Metformin Use: A Meta-Analysis of Randomized Controlled Trials and Observational Studies Michael S. Chang, Rebecca I. Hartman, Junchao Xue, Edward L. Giovannucci, Hongmei Nan, and Keming Yang Meta-analyses of RCT and cohort studies showed no significant association between metformin and skin cancer, although suggestive evidence of modestly reduced skin cancer risks among metformin users was observed. These findings suggest metformin use should not influence current medical decision making for diabetes patients at risk of developing skin cancer.	123	Health Insurance Coverage Mandates: Colorectal Cancer Screening in the Post-ACA Era Michael A. Preston, Levi Ross, Askar Chukmaitov, Sharla A. Smith, Michelle L. Odlum, Bassam Dahman, and Vanessa B. Sheppard The value added includes future health care reforms that increase access to preventive services, such as CRC screening, are likely with lower out-of-pocket costs and will increase the number of people who are considered "up-to-date". Such policies have been used historically to improve health outcomes, and they are currently being used as public health strategies to increase access to preventive health services in an effort to improve the nation's health.
85	Changes in Dietary Inflammatory Index Patterns with Weight Loss in Women: A Randomized Controlled Trial Catherine Duggan, Jean de Dieu Tapsoba, Nitin Shivappa, Holly R. Harris, James R. Hébert, Ching-Yun Wang, and Anne McTiernan Diets high in saturated fats and low in fruit and vegetable intake are associated with increased inflammation, which increases cancer risk. This study showed that changes in diet quality had effects on factors associated with cancer; however, the majority of beneficial effects were associated with weight loss rather than diet quality.	131	Breast Cancer Chemoprevention: Use and Views of Australian Women and Their Clinicians Courtney Macdonald, Christobel M. Saunders, Louise A. Keogh, Morgan Hunter, Danielle Mazza, Sue-Anne McLachlan, Sandra C. Jones, Stephanie Nesci, Michael L. Friedlander, John L. Hopper, Jon D. Emery, Martha Hickey, Roger L. Milne, and Kelly-Anne Phillips, for the Kathleen Cuninghame Consortium for Research Into Familial Breast Cancer Despite its efficacy in reducing breast cancer incidence, chemoprevention is underutilised. This survey study of Australian women and their clinicians used behavioural change theory to identify modifiable barriers to chemoprevention uptake, and to suggest interventions such as policy change, educational resources and public campaigns, that may increase awareness and use.
95	Association of Aspirin, Metformin, and Statin Use with Gastric Cancer Incidence and Mortality: A Nationwide Cohort Study Mi Hee Cho, Tae Gon Yoo, Su-Min Jeong, and Dong Wook Shin Long-term use of aspirin was independently associated with reduced incidence and mortality of gastric cancer in the general population. Metformin or statin use, however, was only associated with a reduction of gastric cancer mortality in diabetic patients and in the general population in a dose-response manner, respectively.		See related Spotlight, p. 1
105	The Acceptability and Preference of Vaginal Self-sampling for Human Papillomavirus (HPV) Testing among a Multi-ethnic Asian Female Population Su Pei Khoo, Wen Tzian Lim, Reena Rajasuriar, Nazrila Hairizan Nasir, Patti Gravitt, and Yin Ling Woo Organized cervical cancer screening remains unachievable in many countries. Self-sampling HPV testing is an evidence-based method that can remove barriers to cervical screening. This is particularly important for developing countries in order to achieve the WHO global strategy to accelerate cervical cancer elimination.	145	Acknowledgment to Reviewers

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ABOUT THE COVER

Nonalcoholic steatohepatitis (NASH) is a severe form of fatty liver disease characterized by inflammation, steatosis, and fibrosis and balloon degeneration from hepatocyte injury. NASH increases the risk for development of cirrhosis and hepatocellular carcinoma (HCC). Currently, there are no FDA-approved agents to reverse hepatic fibrosis and NASH. In this issue, an investigation by Gay and colleagues (starting on page 17) demonstrates a novel approach to preventing HCC by treatment with a cholecystokinin receptor antagonist, proglumide. Treatment of mice with proglumide reversed NASH; lowered hepatic inflammatory cytokines and chemokines; reduced oxidative stress; and prevented HCC. The anti-fibrotic, anti-inflammatory, and anti-proliferative effects of proglumide may provide hope for future studies to reverse hepatic fibrosis and prevent HCC. Proglumide has a broad safety profile in human subjects and could therefore easily be repurposed for prevention of HCC. The cover histological images show periportal fibrosis altering the microenvironment in the liver of a mouse with NASH (left panel) and prevention of these histologic changes with proglumide therapy (right panel).

