# Table of Contents

## SPOTLIGHT

1. Implementation of Risk-reducing Strategies for Breast Cancer is Long Overdue  
   Victor G. Vogel  
   See related article, p. 131

## COMMENTARY

5. Clearing the Haze: What Do We Still Need to Learn about Electronic Nicotine Delivery Systems?  
   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 Safrenkena, 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.

   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.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>Inflammation Modulation by Vitamin D and Calcium in the Morphologically Normal Colorectal Mucosa of Patients with Colorectal Adenoma in a Clinical Trial</td>
<td>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</td>
</tr>
<tr>
<td>77</td>
<td>Risk of Skin Cancer Associated with Metformin Use: A Meta-Analysis of Randomized Controlled Trials and Observational Studies</td>
<td>Michael S. Chang, Rebecca I. Hartman, Junchao Xue, Edward L. Giovannucci, Hongmei Nan, and Kening Yang</td>
</tr>
<tr>
<td>85</td>
<td>Changes in Dietary Inflammatory Index Patterns with Weight Loss in Women: A Randomized Controlled Trial</td>
<td>Catherine Duggan, Jean de Dieu Tapsoba, Nitin Shivappa, Holly R. Harris, James R. Hébert, Ching-Yun Wang, and Anne McTiernan</td>
</tr>
<tr>
<td>95</td>
<td>Association of Aspirin, Metformin, and Statin Use with Gastric Cancer Incidence and Mortality: A Nationwide Cohort Study</td>
<td>Mi Hee Cho, Tae Gon Yoo, Su-Min Jeong, and Dong Wook Shin</td>
</tr>
<tr>
<td>105</td>
<td>The Acceptability and Preference of Vaginal Self-sampling for Human Papillomavirus (HPV) Testing among a Multi-ethnic Asian Female Population</td>
<td>Su Pei Khoo, Wen Tzien Lim, Reena Rajsauriar, Nazrila Hairizan Nasir, Patti Gravitt, and Yin Ling Woo</td>
</tr>
<tr>
<td>113</td>
<td>Utilization Pattern of Computed Tomographic Colonography in the United States: Analysis of the U.S. National Health Interview Survey</td>
<td>Young-Rock Hong, Zhigang Xie, Kea Turner, Santanu Datta, Rohit Bishnoi, and Chintan Shah</td>
</tr>
<tr>
<td>123</td>
<td>Health Insurance Coverage Mandates: Colorectal Cancer Screening in the Post-ACA Era</td>
<td>Michael A. Preston, Levi Ross, Askar Chukmaidov, Sharla A. Smith, Michelle L. Odlum, Bassam Dahman, and Vanessa B. Sheppard</td>
</tr>
<tr>
<td>145</td>
<td>Acknowledgment to Reviewers</td>
<td></td>
</tr>
</tbody>
</table>
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).