

## CANCER PREVENTION RESEARCH

## TABLE OF CONTENTS

## REVIEW

- 509** **Cancer Risk in Normal Weight Individuals with Metabolic Obesity: A Narrative Review**  
Bethina Liu, Hugh E. Giffney, Rhonda S. Arthur, Thomas E. Rohan, and Andrew J. Dannenberg

## RESEARCH BRIEF

- 521** **COVID-19 Disruptions to Endoscopic Surveillance in Lynch Syndrome**  
Danielle B. McKenna, Christina M. Dudzik, Shria Kumar, Nadim Mahmud, and Bryson W. Katona  
The COVID-19 pandemic has led to unprecedented disruptions in cancer screening, which may have disproportionate effects on individuals at increased cancer risk, including those with Lynch syndrome. Herein, we show that the COVID-19 pandemic led to significant disruptions in Lynch syndrome surveillance with potentially impactful delays, thus highlighting the importance of ensuring timely surveillance among this high-risk cohort.

## RESEARCH ARTICLES

- 527** **Prevention of Skin Carcinogenesis by the Non- $\beta$ -blocking R-carvedilol Enantiomer**  
Sherry Liang, Md Abdullah Shamim, Ayaz Shahid, Mengbing Chen, Kristan H. Cleveland, Cyrus Parsa, Robert Orlando, Bradley T. Andresen, and Ying Huang  
In this study, we demonstrated the skin cancer preventive activity of R-carvedilol, the non- $\beta$ -blocking enantiomer present in the racemic  $\beta$ -blocker, carvedilol. As R-carvedilol does not have  $\beta$ -blocking activity, such a preventive treatment would not lead to common cardiovascular side effects of  $\beta$ -blockers.

- 541** **Effects of Adiposity and Exercise on Breast Tissue and Systemic Metabo-Inflammatory Factors in Women at High Risk or Diagnosed with Breast Cancer**  
Neil M. Iyengar, Xi Kathy Zhou, Hillary Mendieta, Dilip D. Giri, Omar El-Hely, Lisle Winston, Domenick J. Falcone, Hanhan Wang, Lingsong Meng, Jonathan Landa, Michael Pollak, Laurie Kirstein, Monica Morrow, and Andrew J. Dannenberg

We report that individuals with high body fat and low exercise levels have breast inflammation, higher breast aromatase expression, and levels of circulating metabo-inflammatory factors that have been associated with increased breast cancer risk. These findings support interventions to lower adiposity, even among normal weight individuals, to prevent tumor growth.

- 551** **Phase I Trial of Encapsulated Rapamycin in Patients with Prostate Cancer Under Active Surveillance to Prevent Progression**  
Phillip M. Kemp Bohan, Robert C. Chick, Anne E. O'Shea, Timothy J. Vreeland, Annelies T. Hickerson, Jessica L. Cindass, Daniel C. Ensley, Diane Hale, Guy T. Clifton, Vance Y. Sohn, Ian M. Thompson Jr, George E. Peoples, and Michael A. Liss

There is an unmet medical need for a well-tolerated treatment capable of delaying progression of newly diagnosed low-grade prostate cancer. This treatment would potentially obviate the need for future surgical intervention and improve the perception of active surveillance as a more acceptable option among this patient population.

- 563** **The Effect of Metformin in Treatment of Adenomas in Patients with Familial Adenomatous Polyposis**  
Jae Jun Park, Byung Chang Kim, Sung Pil Hong, Yoojeong Seo, Hye Sun Lee, Young Sook Park, Soo-Young Na, Sung Chul Park, Jongha Park, Jae Hak Kim, Chang Mo Moon, Kyu Chan Huh, Soo Jung Park, Jae Hee Cheon, Won Ho Kim, and Tae Il Kim

A 7-month metformin treatment (500 mg or 1,500 mg) did not reduce the number or size of polyps in the colorectum or duodenum of FAP patients as compared to placebo. These results do not support the use of metformin to promote regression of intestinal adenomas in FAP patients.

# TABLE OF CONTENTS

**573**     **Randomized Phase II Trial of Polyphenon E versus Placebo in Patients at High Risk of Recurrent Colonic Neoplasia**

**AC**

Frank A. Sinicrope, Thomas R. Viggiano, Navtej S. Buttar, Louis M. Wong Kee Song, Kenneth W. Schroeder, Robert E. Kraichely, Mark V. Larson, Robert E. Sedlack, John B. Kisiel, Christopher J. Gostout, Abdul M. Kalaiger, Árpád V. Patai, Gary Della’Zanna, Asad Umar, Paul J. Limburg, Jeffrey P. Meyers, Nathan R. Foster, Chung S. Yang, and Stephen Sontag

We report a chemoprevention trial of polyphenon E in subjects at high risk of colorectal cancer. The results show that polyphenon E was well tolerated, but did not significantly reduce the number of rectal aberrant crypt foci, a surrogate endpoint biomarker of colorectal cancer.

**581**     **HCV Eradication in Primary or Secondary Prevention Optimizes Hepatocellular Carcinoma Curative Management**

Pierre Nahon, Richard Layese, Carole Cagnot, Tarik Asselah, Dominique Guyader, Stanislas Pol, Georges-Philippe Pageaux, Victor De Lédighen, Denis Ouzan, Fabien Zoulim, and Etienne Audureau; for the ANRS CO12 CirVir group

Liver failure is a competing risk of death in patients with HCC eligible for curative procedures. HCV eradication does not decrease risk of HCC recurrence in the first two years, but enables sequential curative HCC treatments through preservation of liver function. Direct-acting antiviral agent intake is not associated with HCC recurrence and improves survival.

**593**     **Cancer-related Beliefs and Preventive Health Practices among Residents of Rural versus Urban Counties in Alabama**

Salma Aly, Casey L. Daniel, Sejong Bae, Isabel C. Scarinci, Claudia M. Hardy, Mona N. Fouad, Monica L. Baskin, Teri Hoenebeyer, Aras Acemgil, and Wendy Demark-Wahnefried

Cancer incidence and mortality are higher in the U.S. Deep South, likely due to increased tobacco-use, obesity, poor diet, and physical inactivity. This study explores whether cancer-related beliefs and lifestyle practices differ by rural-urban status or other sociodemographic factors in a random sample of 855 residents across Alabama.

**603**     **National Survey of Patient Factors Associated with Colorectal Cancer Screening Preferences**

Xuan Zhu, Philip D. Parks, Emily Weiser, Kristin Fischer, Joan M. Griffin, Paul J. Limburg, and Lila J. Finney Rutten

Our national survey demonstrated broad patient preference for stool-based tests over colonoscopy, contrasting the heavy reliance on colonoscopy for colorectal cancer screening in clinical practice and highlighting the importance of considering patient preference in colorectal screening recommendations.

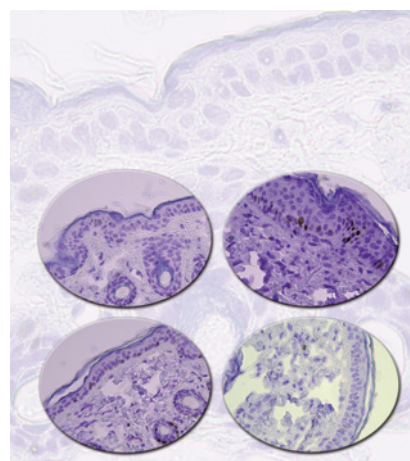
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# TABLE OF CONTENTS

## ABOUT THE COVER

Skin cancer is the most common malignancy worldwide, representing a significant challenge in public health. The  $\beta$ -blocker carvedilol, commonly used to manage cardiovascular conditions, has shown promising activity in preventing skin cancer. However, as a potent  $\beta$ -blocker, repurposing carvedilol into a cancer preventive agent is limited because systemic administration will reduce heart rate and cardiac output, resulting in depressed cardiac function. The chiral compound carvedilol is marketed as a racemic mixture consisting of an equal amount of S- and R-carvedilol. Although S-carvedilol is a  $\beta$ -blocker, R-carvedilol does not possess  $\beta$ -blocking activity. In the study starting on page 527, Liang and colleagues examined the non- $\beta$ -blocking enantiomer R-carvedilol as a skin cancer preventive agent. R-carvedilol is equally effective in preventing neoplastic transformation of mouse epidermal cells, and R-carvedilol is also effective in preventing UV-induced development of squamous cell carcinoma in mice. Therefore, R-carvedilol, lacking  $\beta$ -blocking activity and related depressed cardiac function while retaining anticancer efficacy, is an excellent candidate to prevent skin cancer. The cover image shows that R-carvedilol and racemic carvedilol reduce expression of Ki-67, a cell proliferation marker, in mouse skin acutely irradiated with UV.



# Cancer Prevention Research

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