

CANCER PREVENTION RESEARCH

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RESEARCH ARTICLES

- 165 **Regulatory T Cells Play an Important Role in the Prevention of Murine Melanocytic Nevi and Melanomas**
Tahseen H. Nasti, Nabiha Yusuf, Mohammad Asif Sherwani, Mohammad Athar, Laura Timares, and Craig A. Elmetts
There has been little progress in developing novel strategies for preventing premalignant dysplastic nevi from becoming melanomas. In this study in mice, regulatory-T cells enhanced progression of benign nevi to malignant melanomas; and by inhibiting their activity, melanomas could be retarded. The findings identify new possibilities for melanoma prevention in high risk individuals.
- 175 **Impact of Personalized Genetic Breast Cancer Risk Estimation With Polygenic Risk Scores on Preventive Endocrine Therapy Intention and Uptake**
Julian O. Kim, Daniel J. Schaid, Celine M. Vachon, Andrew Cooke, Fergus J. Couch, Christina A. Kim, Jason P. Sinnwell, Linda Hasadsri, Daniela L. Stan, Benjamin Goldenberg, Lonzetta Neal, Debjani Grenier, Amy C. Degnim, Lori A. Thicke, and Sandhya Pruthi
Counseling women at increased breast cancer risk using polygenic risk score (PRS) risk estimates can significantly impact preventive endocrine therapy uptake. Further development of PRS testing to personalize breast cancer risk assessments and endocrine therapy counselling may serve to potentially reduce the incidence of breast cancer in the future.

- 185 ***BRIP1*, a Gene Potentially Implicated in Familial Colorectal Cancer Type X**

Lorena Martín-Morales, Pilar Garre, Victor Lorca, Marta Cazorla, Patricia Llovet, Inmaculada Bando, Vanesa García-Barberan, María Luisa González-Morales, Clara Esteban-Jurado, Miguel de la Hoya, Sergi Castellví-Bel, and Trinidad Caldés

We suggest that *BRIP1* pathogenic germline variants may have a causal role in CRC as moderate cancer susceptibility alleles and be associated with hereditary CRC predisposition. A better understanding of hereditary CRC may provide important clues to disease predisposition and could contribute to molecular diagnostics, improved risk stratification, and targeted therapeutic strategies.

- 195 **Association of Common Use Pharmaceuticals in Reducing Risk of Esophageal Adenocarcinoma: A SEER-Medicare Analysis**

Holli A. Loomans-Kropp, Matthew Chaloux, Ellen Richmond, and Asad Umar

The use of common drugs, such as proton pump inhibitors, statins, non-steroidal anti-inflammatory drugs, or metformin, may reduce one's risk of developing esophageal adenocarcinoma. These results suggest that repurposing agents often used for common chronic conditions may be a new strategy for cancer prevention efforts.

- 205 **Assessment of and Interventions for Women at High Risk for Breast or Ovarian Cancer: A Survey of Primary Care Physicians**

AC Goli Samimi, Brandy M. Heckman-Stoddard, Christine Holmberg, Bethany Tennant, Bonny Bloodgood Sheppard, Kisha I. Coa, Shelley S. Kay, Leslie G. Ford, Eva Szabo, and Lori M. Minasian

Primary care physicians are becoming more involved in cancer prevention management, so it is important that cancer risk assessment and medical society guideline recommendations for cancer prevention are better integrated into primary care to improve appropriate prescribing of cancer prevention interventions and help reduce cancer risk.

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- 215 Phenotypic Differences in Juvenile Polyposis Syndrome With or Without a Disease-causing SMAD4/BMPRIA Variant**
Suzanne P. MacFarland, Jessica E. Ebrahimzadeh, Kristin Zelle, Lubna Begum, Lee M. Bass, Randall E. Brand, Beth Dudley, Douglas S. Fishman, Amanda Ganzak, Eve Karloski, Alicia Latham, Xavier Llor, Sharon Plon, Mary K. Riordan, Sarah R. Scollon, Zsofia K. Stadler, Sapna Syngal, Chinedu Ukaegbu, Jennifer M. Weiss, Matthew B. Yurgelun, Garrett M. Brodeur, Petar Mamula, and Bryson W. Katona
Juvenile Polyposis Syndrome (JPS) is a gastrointestinal cancer predisposition syndrome requiring lifelong surveillance, however there is limited data comparing individuals with and without a germline disease-causing variant in *SMAD4* or *BMPRIA*. Herein we show that individuals with JPS without an underlying disease-causing variant have distinct phenotypic differences including lack of upper gastrointestinal polyps and lower rates of a family history of JPS, suggesting that a different approach to management may be appropriate in this population.
- 223 THBS2/CA19-9 Detecting Pancreatic Ductal Adenocarcinoma at Diagnosis Underperforms in Prediagnostic Detection: Implications for Biomarker Advancement**
Shirsa Udgata, Naomi Takenaka, William R. Bamlet, Ann L. Oberg, Stephanie S. Yee, Erica L. Carpenter, Daniel Herman, Jungsun Kim, Gloria M. Petersen, and Kenneth S. Zaret
A blood biomarker panel of THBS2 and CA19-9 detects early stages of pancreatic ductal adenocarcinoma at diagnosis, but not when tested across a population up to 1 year earlier. Our findings suggest serial sampling over time, using prospectively collected samples for biomarker discovery, and more frequent screening of highrisk individuals.
- 233 DNA Methylation in Peripheral Blood and Risk of Gastric Cancer: A Prospective Nested Case-control Study**
James A Chamberlain, Pierre-Antoine Dugué, Julie K. Bassett, Roger L. Milne, Jihoon E. Joo, Ee Ming Wong, Maree T. Brinkman, Geoffrey W. Stuart, Alex Boussioutas, Melissa C. Southey, Graham G. Giles, Hazel Mitchell, Dallas R. English, and Allison M. Hodge
We studied DNA methylation in blood to try and predict who was at risk of gastric cancer before symptoms developed, by which stage survival is poor. We did not find any such markers, but the importance of early diagnosis in gastric cancer remains, and the search for markers continues.
- 241 The Performance of Colorectal Cancer Screening in Brazil: The First Two Years of the Implementation Program in Barretos Cancer Hospital**
Denise Peixoto Guimarães, Larissa Andreoli Mantuan, Marco Antonio de Oliveira, Raphael Luiz Junior, Allini Mafra da Costa, Silvana Rossi, Gilberto Fava, Leonardo Nogueira Taveira, Kelly Menezio Giardina, Thais Talarico, Maraisa Costa, Cristovam Scapulatempo-Neto, Marcus Medeiros Matsushita, Carlos Augusto Véio, Jose Humberto Tavares Fregnani, Rui Manuel Reis, Ernest T. Hawk, and Edmundo Carvalho Mauad
- 253 Proof of Concept of a Personalized Genetic Risk Tool to Promote Smoking Cessation: High Acceptability and Reduced Cigarette Smoking**
Alex T. Ramsey, Jessica L. Bourdon, Michael Bray, Amelia Dorsey, Maia Zalik, Amanda Pietka, Patricia Salyer, Li-Shiun Chen, Timothy B. Baker, Marcus R. Munafò, and Laura J. Bierut
This study demonstrates that personal genetic information can be incorporated into a risk feedback tool that was highly acceptable to current smokers and associated with reductions in smoking. These findings may pave the way for effectiveness and implementation research on genetically-informed behavior change interventions to enhance cancer prevention efforts.
- 263 PROgesterone Therapy for Endometrial Cancer Prevention in Obese Women (PROTEC) Trial: A Feasibility Study**
AC Abigail E. Derbyshire, Jennifer L. Allen, Matthew Gittins, Bhavna Lakhiani, James Bolton, Joseph Shaw, Philip W. Pemberton, Michelle Needham, Michelle L. MacKintosh, Richard J. Edmondson, Henry C. Kitchener, and Emma J. Crosbie
Novel strategies are urgently needed to prevent the rise in endometrial cancer diagnoses predicted by escalating obesity rates. Here, we show that women with class III obesity are willing to engage in risk reduction with a levonorgestrel intrauterine system, which could provide a strategy for an endometrial cancer prevention trial.
- 275 A Randomized Controlled Trial on Efficacy of Surgical Excision of Nondysplastic Leukoplakia to Prevent Oral Cancer**
Paolo G. Arduino, Giovanni Lodi, Marco Cabras, Alessandra Macciotta, Alessio Gambino, Davide Conrotto, Dora Karimi, Giorgia El Haddad, Mario Carbone, and Roberto Brocchetto
Oral white patches can transform into cancer and none has provided clinical guidelines to prevent it. For the first time ever, we have showed that the clinical follow up of non dysplastic lesions was able to provide benefits if compared with surgical excision.

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ABOUT THE COVER

In Brazil, colorectal cancer is the second most common cancer among men and women and exhibits high mortality rates, partially due to late-stage presentation. To date, Brazil has not implemented a nationally organized colorectal screening program. Barretos Cancer Hospital is one of the largest cancer hospitals in Brazil, which cares for underserved healthcare patients from all over the country. Barretos Cancer Hospital developed a FIT-based organized colorectal screening program as part of the efforts to improve CRC outcomes. In the study starting on page 241, Guimarães and colleagues demonstrated that this colorectal cancer screening program achieved desirable quality metrics aligned with the EU Guidelines' recommendations. Further, a shift towards earlier stages seen in screening-detected CRCs suggests an exciting opportunity to improve CRC outcomes. The cover image shows the distribution of screening participants across the Brazilian geographical regions, where the darkest green corresponds to the highest number of participants. The red dot is Barretos Cancer Hospital's location, in Barretos' city at the State of São Paulo.



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