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CANCER PREVENTION RESEARCH

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403 **Diet-Dependent Metabolic Regulation of DNA Double-Strand Break Repair in Cancer: More Choices on the Menu**
Anna de Polo and David P. Labbé

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415 **Catch-up HPV Vaccination and Subsequent Uptake of Papanicolaou Testing in A State-mandated Health System**
Gabriel Chodick, Amy E. Leader, and Sharon Larson

We found that catch-up HPV vaccination was associated with increased attention to long-term cervical screening attendance. Whereas, those who are not vaccinated and unprotected from HPV, are more likely to abstain from secondary prevention screening tests too and further increase their cervical cancer risk.

RESEARCH ARTICLES

421 **The Role of Forkhead Box Q1 Transcription Factor in Anticancer Effects of Withaferin A in Breast Cancer**
Su-Hyeong Kim, Krishna B. Singh, Eun-Ryeong Hahm, and Shivendra V. Singh

Withaferin A (WA) is highly effective in reducing burden and/or incidence of breast cancer in various preclinical models. However, the mechanism underlying breast cancer prevention by WA is not fully understood. This study shows a role for FoxQ1 in antitumor response to WA.

433 **Germline Pathogenic Variants in the Ataxia Telangiectasia Mutated (*ATM*) Gene are Associated with High and Moderate Risks for Multiple Cancers**
AC Michael J. Hall, Ryan Bernhisel, Elisha Hughes, Katie Larson, Eric T. Rosenthal, Nanda A. Singh, Johnathan M. Lancaster, and Allison W. Kurian

This study estimated risks for multiple cancers associated with *ATM* pathogenic variants independent of family history. These results indicate that some common variants may be associated with higher breast cancer risks than previously appreciated and increased screening for prostate and gastric cancer may be warranted for carriers of *ATM* pathogenic variants.

441 **Functional Common and Rare *ERBB2* Germline Variants Cooperate in Familial and Sporadic Cancer Susceptibility**
Riyue Bao, Anita Ng, Mark Sasaki, Myvizhi Esai Selvan, Alyna Katti, Hyesan Lee, Lei Huang, Andrew D. Skol, Cinzia Lavarino, Hector Salvador, Robert J. Klein, Zeynep H. Gümüş, Jaume Mora, and Kenan Onel

By performing whole-exome sequencing on germline DNA from multiple cancer-affected individuals belonging to a family in which multiple cancer types track across three generations, we identified and then characterized functional common and rare variation in *ERBB2* associated with both sporadic and familial cancer. Our results suggest that heritable variation activating ERBB2 signaling is associated with risk for multiple cancer types, with increases in signaling correlated with increases in risk, and modified by ancestry or family history.

455 **Cost Effectiveness of Whole Population BRCA Genetic Screening for Cancer Prevention in Israel**
Nadav Michaan, Moshe Leshno, Tamar Safra, Amir Sonnenblick, Ido Laskov, and Dan Grisaru

Whole population *BRCA* mutation screening in Israel is cost effective across a wide prevalence rate and should be offered as part of general health screening strategies by national medical insurance providers for cancer prevention.

463 **Obesity is Associated with Shorter Telomere Length in Prostate Stromal Cells in Men with Aggressive Prostate Cancer**
Corinne E. Joshu, Christopher M. Heaphy, John R. Barber, Jiayun Lu, Reza Zarinshenas, Christine Davis, Misop Han, Tamara L. Lotan, Karen S. Sfanos, Angelo M. De Marzo, Alan K. Meeker, and Elizabeth A. Platz

This study investigates a potential mechanism underlying the association between obesity and prostate cancer death. Among men with aggressive prostate cancer, obesity was associated with shorter telomeres prostate cancer associated stromal cells, and shorter CAS telomeres have been associated with an increased risk of prostate cancer death.

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471 **A Retrospective Chart Review of Children in Neurocutaneous Clinic Who May Benefit from Further Evaluation Beyond Neurofibromatosis Type I**
Stephanie R. Hicks, Amanda K. Cozart, Gary A. Bellus, and Kami W. Schneider
This study suggests that at-risk population with a suspected NF1 diagnosis may benefit from further evaluation. Correct diagnosis of constitutional mismatch repair deficiency is crucial to diagnose cancer at an early stage or prevent cancer from occurring.

479 **Circulating 27-hydroxycholesterol and Risk of Colorectal Adenomas and Serrated Polyps**
Michael N. Passarelli, Bonne M. Thompson, Jeffrey G. McDonald, Dale C. Snover, Thomas J. Palys, Judy R. Rees, Elizabeth L. Barry, and John A. Baron
This study found that plasma concentration of 27-hydroxycholesterol, a metabolite of cholesterol that regulates lipid metabolism and acts as a selective estrogen receptor modulator, is associated with the risk of developing precursor lesions for colorectal cancer.

489 **Specificity of the Multi-Target Stool DNA Test for Colorectal Cancer Screening in Average-Risk 45–49 Year-Olds: A Cross-Sectional Study**
AC Thomas F. Imperiale, John B. Kisiel, Steven H. Itzkowitz, Bradley Scheu, Emma Kate Duimstra, Sandra Statz, Barry M. Berger, and Paul J. Limburg
This study shows that mt-sDNA has high specificity among average-risk 45–49 year olds, supporting its use as a non-invasive option for colorectal cancer screening.

497 **Plasma and Urine Metabolite Profiles Impacted by Increased Dietary Navy Bean Intake in Colorectal Cancer Survivors: A Randomized-Controlled Trial**
AC Iman Zarei, Bridget A. Baxter, Renee C. Oppel, Erica C. Borresen, Regina J. Brown, and Elizabeth P. Ryan
This clinical study suggests that increased consumption of navy beans would deliver bioactive metabolites to individuals at high risk for colorectal cancer recurrence and produce metabolic shifts in plasma and urine profiles.

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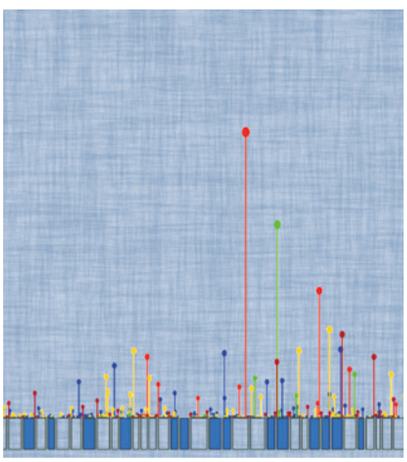
ABOUT THE COVER

Of the more than 270,000 breast cancers and 57,000 pancreatic cancers diagnosed annually, approximately 10-15% are hereditary and are associated with a germline pathogenic variant or likely pathogenic variant (PV) in a hereditary cancer risk gene. The *ATM* (ataxia telangiectasia mutated) gene is located on chromosome 11q22.3 and is comprised of 66 exons that code a 350.6 kDa protein involved in various cellular activities, including DNA double-strand break repair through its activity as a phosphorylase of key proteins involved in response to DNA damage. While the recessively inherited childhood disease Ataxia Telangiectasia requires two (homozygous) *ATM* PVs to manifest disease and is rare in the population, approximately 1 in 300 individuals carry one (heterozygous) *ATM* PV. In the study starting on page 433, Hall and colleagues examine the cancer risks in heterozygous *ATM* PV carriers using a large database of over 600,000 individuals tested with a multi-gene panel for hereditary cancer risk. Elevated risks for several cancers including breast, pancreatic, prostate, and gastric among others were identified in *ATM* PV carriers. The cover image shows the exons of the human *ATM*, as well as the PV location on the gene, frequency as represented by the height of the line at each location on the gene, and variant type represented by the color of the line, for the 4,607 *ATM* PVs identified in the study population.



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