BREAKING INSIGHTS

421 Highlights from Recent Cancer Literature

REVIEW

423 A Blazing Landscape: Neuroinflammation Shapes Brain Metastasis
   Hila Doron, Tobias Pukrop, and Neta Erez

CANCER RESEARCH HIGHLIGHTS

437 Epigenetic Drift in Colorectal Cancer—It's Probably Later Than You Think
   Carmen Sapienza
   See related article, p. 495

439 A Dynamic Cis-Regulation Pattern Underlying Epithelial Ovarian Cancer Susceptibility
   Jiyeon Choi and Kevin M. Brown
   See related article, p. 467

CONTROVERSY AND CONSENSUS

441 Is Adjuvant Chemotherapy Efficient in Colon Cancer with High Microsatellite Instability? A Look Towards the Future
   Guido V. Schiappacasse Cocio and Enrico D. Schiappacasse

PRIORITY REPORTS

445 Activation of Peroxisome Proliferator-Activated Receptors α and δ Synergizes with Inflammatory Signals to Enhance Adoptive Cell Therapy
   Significance: Dual activation of peroxisome proliferator-activated receptors α and δ improves the efficacy of adoptive cell therapy by reprogramming T-cell metabolism and cytokine expression.

452 Radiosensitivity Is an Acquired Vulnerability of PARPi-Resistant BRCA1-Deficient Tumors
   Marco Barazas, Alessia Gasparini, Yike Huang, Aîli Küçüksmanoğlu, Stefano Annunziato, Peter Bouwman, Wendy Sol, Ariena Kersbergen, Natalie Proost, Renske de Korte-Grimmerink, Marieke van de Ven, Jos Jonkers, Gerben R. Borst, and Sven Rottenberg
   Significance: These findings uncover radiosensitivity as a novel, therapeutically viable vulnerability of BRCA1-deficient mouse mammary cells that have acquired drug resistance due to the loss of the 53BP1 pathway.

461 Mosaic Y Loss Is Moderately Associated with Solid Tumor Risk
   Erika Lojfield, Weiying Zhou, Meredith Yeager, Stephen J. Chanock, Neal D. Freedman, and Mitchell J. Machiela
   Significance: Evidence from the UK Biobank indicates mosaic chromosome Y loss in leukocytes is moderately associated with increased incidence of select solid tumors.

467 Functional Analysis and Fine Mapping of the 9p22.2 Ovarian Cancer Susceptibility Locus
   Significance: Mapping the 9p22.2 ovarian cancer risk locus identifies BNC2 as an ovarian cancer risk gene.
   See related commentary, p. 439

482 TET2-Dependent Hydroxymethylome Plasticity Reduces Melanoma Initiation and Progression
   Elise Bonvin, Enrico Radaelli, Martin Bizet, Flavie Luciani, Emilie Calonne, Pascale Putmans, David Nittner, Nitesh Kumar Singh, Sara Francesca Santagostino, Valérie Petit, Lionel Larue, Jean Christophe Marine, and François Fuks
   Significance: This work emphasizes the importance of epigenome plasticity in cancer development and highlights the involvement of druggable epigenetic factors in cancer.
505 Genetic Data from Nearly 63,000 Women of European Descent Predicts DNA Methylation Biomarkers and Epithelial Ovarian Cancer Risk

Significance: Identification of novel DNA methylation markers associated with EOC risk suggests that methylation at multiple CpG may affect EOC risk through regulation of gene expression.

See related commentary, p. 437

546 Differential Subcellular Localization Regulates Oncogenic Signaling by ROS1 Kinase Fusion Proteins

Significance: ROS1 fusion oncoproteins exhibit differential localization, with ROS1 fusions localized to endosomes the strongest activators of MAPK signaling according to subcellular localization, with ROS1 fusions localized to endosomes the strongest activators of MAPK signaling.
Hepatic Endothelial Notch Activation Protects against Liver Metastasis by Regulating Endothelial-Tumor Cell Adhesion Independent of Angiocrine Signaling

Sebastian A. Wohlfeil, Verena Hafele, Bianca Dietzsch, Kai Schledzewski, Manuel Winkler, Johanna Zierow, Thomas Leibing, Mona Malek Mohammad, Ilona Heinke, Carsten Sticht, Victor Olaszewsky, Philipp-Sebastian Koch, Cyrill Gafle, Bianca Dietsch, Etienne Daguindau, Francine Garnache-Ottou, Severine Valmary-Degano, Sabeha Biichle, Denis Caillot, Marius Moldovan, Rim Trad, Eric Deconinck, Ziad Fajloun, Cyril Faure, Walid Warda, Fabrice Larosa, Mathieu Neto Da Rocha, Receptor IL1RAP Can Be Targeted by Chimeric Antigen Receptor Directed against IL1RAP Expressed by Leukemic Cells

Significance: These findings present the first characterization and proof of concept of a chimeric antigen receptor directed against IL1RAP expressed by leukemic stem cells in the context of CML.
Smoking and Urinary Cotinine Levels Are Predictors of Increased Risk for Gastric Intestinal Metaplasia
Kyungun Kim, Yoosoo Chang, Jiin Ahn, Hyo-Joon Yang, Ju Young Jung, Seokkyun Kim, Chong Il Sohn, and Seungho Ryu
Significance: A large-scale cohort study of nearly 200,000 adults associates smoking with increased risk for gastric intestinal metaplasia, a precursor lesion of stomach cancer.

Correction: Celastrol Suppresses Angiogenesis-Mediated Tumor Growth through Inhibition of AKT/Mammalian Target of Rapamycin Pathway
Xiufeng Pang, Zhengfang Yi, Jing Zhang, Binbin Lu, Bokyung Sung, Weijing Qu, Bharat B. Aggarwal, and Mingyao Liu

ABOUT THE COVER
The incidence of brain metastasis is on the rise and despite advances in treatment strategies, prognosis remains poor. Integrated data from multiple resources show the epidemiology and survival of patients with brain metastasis from several cancer types. The brain microenvironment is crucial in facilitating metastatic growth, and neuroinflammation plays a central role in shaping the brain metastatic niche. For details on recent advances in our understanding of the brain metastatic microenvironment and neuroinflammation, see review by Doron and colleagues on page 423.