

## BREAKING INSIGHTS

- 5899** Highlights from Recent Cancer Literature

## REVIEWS

- 5901** **Wnt Signaling in Cancer: Not a Binary ON:OFF Switch**  
Dustin J. Flanagan, Elizabeth Vincan, and Toby J. Pesse
- 5907** **A Tumor Agnostic Therapeutic Strategy for Hexokinase 1–Null/Hexokinase 2–Positive Cancers**  
Shili Xu and Harvey R. Herschman

## CANCER RESEARCH HIGHLIGHTS

- 5915** **Clonal Selection Drives NF- $\kappa$ B Activation in Recurrent Nasopharyngeal Carcinoma**  
Kartik Sehgal and David A. Barbie  
*See related article, p. 5930*
- 5917** **It Takes Two (Genomes) to Cancer: Paired Viral and Host Transcriptome Analysis Provides New Insights about EBV Carcinogenicity**  
Sam M. Mbulaiteye and Ludmila Prokunina-Olsson  
*See related article, p. 6010*


## PRIORITY REPORT

- 5920** **BRCA1 Deficiency Upregulates NNMT, Which Reprograms Metabolism and Sensitizes Ovarian Cancer Cells to Mitochondrial Metabolic Targeting Agents**  
Arun Kanakkanthara, Kiran Kurmi, Thomas L. Ekstrom, Xiaonan Hou, Emma R. Purfeerst, Ethan P. Heinzen, Cristina Correia, Catherine J. Huntoon, Daniel O'Brien, Andrea E. Wahner Hendrickson, Sean C. Dowdy, Hu Li, Ann L. Oberg, Taro Hitosugi, Scott H. Kaufmann, S. John Weroha, and Larry M. Karnitz  
*Significance: Loss of BRCA1 reprograms metabolism, creating a therapeutically targetable vulnerability in ovarian cancer.*

## GENOME AND EPIGENOME

- 5930** **Clonal Mutations Activate the NF- $\kappa$ B Pathway to Promote Recurrence of Nasopharyngeal Carcinoma**  
Rui You, You-Ping Liu, De-Chen Lin, Qing Li, Tao Yu, Xiong Zou, Mei Lin, Xiao-Long Zhang, Gui-Ping He, Qi Yang, Yi-Nuan Zhang, Yu-Long Xie, Rou Jiang, Chen-Yan Wu, Chao Zhang, Cheng Cui, Jing-Qi Wang, Yue Wang, Ai-Hua Zhuang, Gui-Fang Guo, Yi-Jun Hua, Rui Sun, Jing-Ping Yun, Zhi-Xiang Zuo, Ze-Xian Liu, Xiao-Feng Zhu, Tie-Bang Kang, Chao-Nan Qian, Hai-Qiang Mai, Ying Sun, Mu-Sheng Zeng, Lin Feng, Yi-Xin Zeng, and Ming-Yuan Chen  
*Significance: This study uncovers genetic events that promote the progression and recurrence of nasopharyngeal carcinoma and has potential prognostic and therapeutic implications. See related commentary, p. 5915*

## MOLECULAR CELL BIOLOGY

- 5944** **Syndecan-Mediated Ligation of ECM Proteins Triggers Proliferative Arrest of Disseminated Tumor Cells**  
Tsukasa Shibue, Ferenc Reinhardt, and Robert A. Weinberg  
*Significance: This study identifies a novel signaling pathway that regulates the proliferative dormancy of individual disseminated tumor cells.*
- 5958** **Cleaved Caspase-3 Transcriptionally Regulates Angiogenesis-Promoting Chemotherapy Resistance**  
Antoine Bernard, Sandy Chevrier, Françoise Beltjens, Magalie Dosset, Etienne Viltard, Anaïs Lagrange, Valentin Derangère, Alexandra Oudot, François Ghiringhelli, Bertrand Collin, Lionel Apetoh, Olivier Feron, Suzie Chen, Laurent Arnould, Frédérique Végran, and Romain Boidot  
*Significance: These findings report a noncanonical function of caspase-3 by demonstrating its ability to transcriptionally regulate the VEGFR pathway.*
- 5971** **Upregulation of Myt1 Promotes Acquired Resistance of Cancer Cells to Wee1 Inhibition**  
Cody W. Lewis, Amirali B. Bukhari, Edric J. Xiao, Won-Shik Choi, Joanne D. Smith, Ellen Homola, John R. Mackey, Shelagh D. Campbell, Armin M. Gamper, and Gordon K. Chan  
*Significance: Myt1 is a candidate predictive biomarker of acquired resistance to the Wee1 kinase inhibitor adavosertib.*

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## TUMOR BIOLOGY AND IMMUNOLOGY

**5986** Vitamin D–VDR Signaling Inhibits Wnt/ $\beta$ -Catenin–Mediated Melanoma Progression and Promotes Antitumor Immunity

Sathya Muralidhar, Anastasia Filia, Jérémie Nsengimana, Joanna Poźniak, Sally J. O'Shea, Joey M. Diaz, Mark Harland, Juliette A. Randerson-Moor, Jörg Reichrath, Jonathan P. Laye, Louise van der Weyden, David J. Adams, D.T. Bishop, and Julia Newton-Bishop

*Significance:* VDR expression could potentially be used as a biomarker to stratify patients with melanoma that may respond better to immunotherapy.

**5999** Gastrointestinal Tract Dysbiosis Enhances Distal Tumor Progression through Suppression of Leukocyte Trafficking

Samir V. Jenkins, Michael S. Robeson II, Robert J. Griffin, Charles M. Quick, Eric R. Siegel, Martin J. Cannon, Kieng B. Vang, and Ruud P.M. Dings

*Significance:* Antibiotic-induced dysbiosis enhances distal tumor progression by altering host cytokine levels, resulting in suppression of tumor endothelial adhesion molecules and activated and effector CD8<sup>+</sup> T cells in the tumor.

**6010** Integrated Pan-Cancer Map of EBV-Associated Neoplasms Reveals Functional Host–Virus Interactions



Srishti Chakravorty, Bingyu Yan, Chong Wang, Luopin Wang, Joseph Taylor Quaid, Chin Fang Lin, Scott D. Briggs, Joydeb Majumder, D. Alejandro Canaria, Daniel Chauss, Gaurav Chopra, Matthew R. Olson, Bo Zhao, Behdad Afzali, and Majid Kazemian

*Significance:* This study provides a comprehensive map of the host cell-pathogen interactome in EBV<sup>+</sup> malignancies.

See related commentary, p. 5917

## TRANSLATIONAL SCIENCE

**6024** Cys34 Adductomics Links Colorectal Cancer with the Gut Microbiota and Redox Biology

Hasmik Grigoryan, Courtney Schiffman, Marc J. Gunter, Alessio Naccarati, Silvia Polidoro, Sonia Dagnino, Sandrine Dudoit, Paolo Vineis, and Stephen M. Rappaport

*Significance:* Infiltration of gut microbes into the intestinal mucosa and the resulting inflammation are causal factors for colorectal cancer.

**6032** Radiation Drives the Evolution of Orthotopic Xenografts Initiated from Glioblastoma Stem–like Cells

Joseph H. McAbee, Barbara H. Rath, Kristin Valdez, Dejauwne L. Young, Xiaolin Wu, Uma T. Shankavaram, Kevin Camphausen, and Philip J. Tofilon

*Significance:* Radiation drives the evolution of glioblastoma orthotopic xenografts; when translated to the clinic, this may have therapeutic implications for recurrent tumors.

## CONVERGENCE AND TECHNOLOGIES

**6044** A Model of Indirect Cell Death Caused by Tumor Vascular Damage after High-Dose Radiotherapy

Pedro Rodríguez-Barbeito, Pablo Díaz-Botana, Araceli Gago-Arias, Manuel Feijoo, Sara Neira, Jacobo Guiu-Souto, Óscar López-Pouso, Antonio Gómez-Caamaño, and Juan Pardo-Montero

*Significance:* A novel biomathematical model of indirect tumor cell death caused by vascular radiation damage could potentially help clinicians interpret experimental data and design better radiotherapy schedules.

## EDITOR'S NOTE

**6054** Editor's Note: PrLZ Protects Prostate Cancer Cells from Apoptosis Induced by Androgen Deprivation via the Activation of Stat3/Bcl-2 Pathway

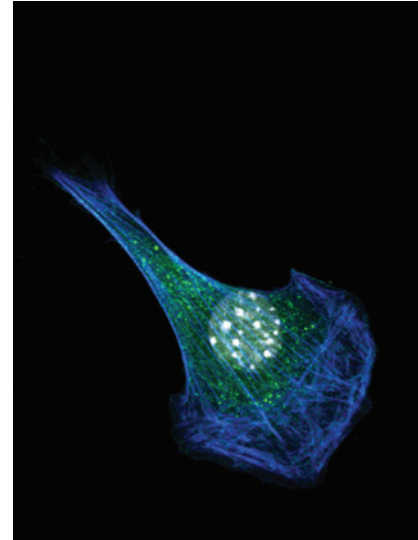
Dong Zhang, Dalin He, Yan Xue, Ruoxiang Wang, Kaijie Wu, Hongjun Xie, Jin Zeng, Xinyang Wang, Haiyen E. Zhou, Leland W.K. Chung, Luke S. Chang, and Lei Li

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## ABOUT THE COVER

The molecular machinery governing cell polarity controls various aspects of cell behaviors including directional migration of cells under monolayer culture conditions. Immunofluorescence revealed that the Par-1 kinase, a critical component of the polarity-regulating machinery, is enriched on the lateral side of such migrating cells. However, in cells that were surrounded by extracellular matrix proteins, including tumor cells that have recently extravasated into the parenchyma of foreign tissues during metastasis, the Par-1 kinase was diffusely distributed throughout the cytosol. In these cells, cytosolically distributed Par-1 interfered with the critical signaling pathway driving cell proliferation, accounting for the difficulty of the recently extravasated tumor cells to initiate rapid proliferation. For details, see the article by Shibue and colleagues on page 5944.



# Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

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