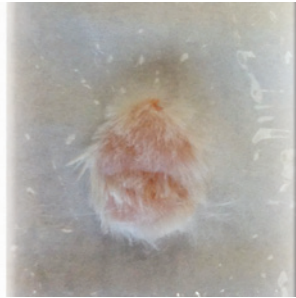


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- 3199 **Sialic Acids Sweeten a Tumor's Life**
Christian Büll, Marieke A. Stoel, Martijn H. den Brok,
and Gosse J. Adema

MICROENVIRONMENT AND IMMUNOLOGY

- 3205 **Immune-Based Antitumor Effects of BRAF Inhibitors Rely on Signaling by CD40L and IFN γ**
Ping-Chih Ho, Katrina M. Meeth, Yao-Chen Tsui,
Bhaskar Srivastava, Marcus W. Bosenberg, and
Susan M. Kaech

Précis: The robust antitumor properties of B-Raf kinase inhibitors appear to relate to an ability to correct immune escape, suggesting new uses for these drugs in cancer treatment through combination with active immunotherapies.

MOLECULAR AND CELLULAR PATHOBIOLOGY

- 3218 **p53 Is Positively Regulated by miR-542-3p**
Yemin Wang, Jen-Wei Huang, Maria Castella,
David George Huntsman, and Toshiyasu Taniguchi

Précis: These findings define a microRNA that potently activates p53 and suppresses ribosome biogenesis, defining a novel core regulatory pathway in cell proliferation and survival.

- 3228 **Global Transcriptome Analysis of Formalin-Fixed Prostate Cancer Specimens Identifies Biomarkers of Disease Recurrence**
Qi Long, Jianpeng Xu, Adeboye O. Osunkoya,
Soma Sannigrahi, Brent A. Johnson, Wei Zhou,
Theresa Gillespie, Jong Y. Park, Robert K. Nam,
Linda Sugar, Aleksandra Stanimirovic, Arun K. Seth,
John A. Petros, and Carlos S. Moreno

Précis: This study defines a novel biomarker panel that outperforms existing technology, with the potential to improve the clinical management of prostate cancer by predicting patients who are likely to progress to advanced metastatic disease.

- 3238 **Colorectal Cancer Cell Lines Are Representative Models of the Main Molecular Subtypes of Primary Cancer**

Dmitri Mouradov, Clare Sloggett, Robert N. Jorissen, Christopher G. Love, Shan Li, Antony W. Burgess, Diego Arango, Robert L. Strausberg, Daniel Buchanan, Samuel Wormald, Liam O'Connor, Jennifer L. Wilding, David Bicknell, Ian P.M. Tomlinson, Walter F. Bodmer, John M. Mariadason, and Oliver M. Sieber

Précis: This study positively addresses the question of how well in vitro-established colorectal cancer cell lines represent primary human tumors, in the absence of any stromal or organismal context, providing a genome-level validation that supports their continued use as tools to investigate colorectal cancer biology and drug responses.

PREVENTION AND EPIDEMIOLOGY

- 3248 **Insulin, Estrogen, Inflammatory Markers, and Risk of Benign Proliferative Breast Disease**

Chelsea Catsburg, Marc J. Gunter, Chu Chen, Michele L. Cote, Geoffrey C. Kabat, Rami Nassir, Lesley Tinker, Jean Wactawski-Wende, David L. Page, and Thomas E. Rohan

Précis: This study identifies independent risk factors for benign proliferative breast disease, suggesting that these factors directly influence the early stages of breast cancer development.

- 3259 **Noninvasive Urinary Metabolomic Profiling Identifies Diagnostic and Prognostic Markers in Lung Cancer**

Ewy A. Mathé, Andrew D. Patterson, Majda Haznadar, Soumen K. Manna, Kristopher W. Krausz, Elise D. Bowman, Peter G. Shields, Jeffrey R. Idle, Philip B. Smith, Katsuhiko Anami, Dickran G. Kazandjian, Emmanuel Hatzakis, Frank J. Gonzalez, and Curtis C. Harris

Précis: Global metabolomics can be used to uncover novel metabolites detected in urine and lung tumor tissue, which have diagnostic and prognostic utility.

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THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

- 3271** **Novel Polymeric Nanoparticles for Intracellular Delivery of Peptide Cargos: Antitumor Efficacy of the BCL-2 Conversion Peptide NuBCP-9**
Manoj Kumar, Dikshi Gupta, Gurpal Singh, Sapna Sharma, Madhusudan Bhat, C.K. Prashant, A.K. Dinda, Surender Kharbanda, Donald Kufe, and Harpal Singh

Précis: Striking demonstrations of in vivo efficacy are a highlight of this study, which reports an effective nanoparticle formulation for sustained delivery of anticancer peptides to target intracellular oncoproteins.

- 3282** **Notch3 Pathway Alterations in Ovarian Cancer**

Wei Hu, Tao Liu, Cristina Ivan, Yunjie Sun, Jie Huang, Lingegowda S. Mangala, Takahito Miyake, Heather J. Dalton, Sunila Pradeep, Rajesh Rupaimoole, Rebecca A. Previs, Hee Dong Han, Justin Bottsford-Miller, Behrouz Zand, Yu Kang, Chad V. Pecot, Alpa M. Nick, Sherry Y. Wu, Ju-Seog Lee, Vasudha Sehgal, Prahlad Ram, Jinsong Liu, Susan L. Tucker, Gabriel Lopez-Berestein, Keith A. Baggerly, Robert L. Coleman, and Anil K. Sood

Précis: These findings identify previously unknown mechanisms underlying an important signaling pathway in serous ovarian cancers, identifying new biomarker-driven approaches for therapy.

- 3294** **Inhibiting Tankyrases Sensitizes KRAS-Mutant Cancer Cells to MEK Inhibitors via FGFR2 Feedback Signaling**

Marie Schoumacher, Kristen E. Hurov, Joseph Lehár, Yan Yan-Neale, Yuji Mishina, Dmitriy Sonkin, Joshua M. Korn, Daisy Flemming, Michael D. Jones, Brandon Antonakos, Vesselina G. Cooke, Janine Steiger, Jebediah Ledell, Mark D. Stump, William R. Sellers, Nika N. Danial, and Wenlin Shao

Précis: This study addresses the long-standing challenge of developing highly effective therapeutics against KRAS-mutant cancers, also identifying a strategy to suppress a newly discovered resistance mechanism

- 3306** **Separating Tumorigenicity from Bile Acid Regulatory Activity for Endocrine Hormone FGF19**



Mei Zhou, Xueyan Wang, Van Phung, Darrin A. Lindhout, Kalyani Mondal, Jer-Yuan Hsu, Hong Yang, Mark Humphrey, Xunshan Ding, Taruna Arora, R. Marc Learned, Alex M. DePaoli, Hui Tian, and Lei Ling

Précis: These results conclusively link the cancerous properties of the FGF19–FGFR4 pathway in liver to STAT3 activation, with potential implications for how to improve the treatment of chronic liver disease and cancer.

- 3317** **IDH1 Mutations Alter Citric Acid Cycle Metabolism and Increase Dependence on Oxidative Mitochondrial Metabolism**

Alexandra R. Grassian, Seth J. Parker, Shawn M. Davidson, Ajit S. Divakaruni, Courtney R. Green, Xiamei Zhang, Kelly L. Slocum, Mingying Pu, Fallon Lin, Chad Vickers, Carol Joud-Caldwell, Franklin Chung, Hong Yin, Erika D. Handly, Christopher Straub, Joseph D. Gowney, Matthew G. Vander Heiden, Anne N. Murphy, Raymond Pagliarini, and Christian M. Metallo

Précis: These results suggest therapeutic opportunities to exploit a set of metabolic vulnerabilities specific to IDH1 mutation in cancer cells.

TUMOR AND STEM CELL BIOLOGY

- 3332** **Activation of SOX2 Expression by BRD4-NUT Oncogenic Fusion Drives Neoplastic Transformation in NUT Midline Carcinoma**

Ranran Wang, Wei Liu, Christine M. Helfer, James E. Bradner, Jason L. Hornick, Susan M. Janicki, Christopher A. French, and Jianxin You

Précis: The discovery of an aberrant stem-like cell proliferation associated with dysregulation of a factor that binds chromosomes during mitosis has general implications in cancers in which that factor is dysregulated.

- 3344** **Impaired JNK Signaling Cooperates with Kras^{G12D} Expression to Accelerate Pancreatic Ductal Adenocarcinoma**



Clare C. Davies, Emma Harvey, Raymond F.T. McMahon, Katherine G. Finegan, Frances Connor, Roger J. Davis, David A. Tuveson, and Cathy Tournier

Précis: Evidence gleaned from a preclinical model of pancreatic cancer suggests that JNK activation limits K-ras-induced tumor development, identifying a suppressor pathway in this system.

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3357 **Transient Induction of ING4 by Myc Drives Prostate Epithelial Cell Differentiation and Its Disruption Drives Prostate Tumorigenesis**

Penny L. Berger, Sander B. Frank, Veronique V. Schulz, Eric A. Nollet, Mathew J. Edick, Brittany Holly, Ting-Tung A. Chang, Galen Hostetter, Suwon Kim, and Cindy K. Miranti

Précis: *This study identifies a pivotal signaling node that may explain why MYC and PTEN inactivation cooperate in prostate tumorigenesis.*

3369 **E2F1 Responds to Ultraviolet Radiation by Directly Stimulating DNA Repair and Suppressing Carcinogenesis**



Anup Kumar Biswas, David L. Mitchell, and David G. Johnson

Précis: *This article defines a nontranscriptional function in DNA repair for the core cell-cycle regulatory transcription factor E2F1.*

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ABOUT THE COVER

B-Raf^{V600E} inhibitors are potent at halting melanoma progression in patients harboring oncogenic B-Raf^{V600E} mutation. Recent studies indicate that chemotherapies and other target treatments suppress tumor growth via a host immunity-dependent manner. Using a genetically modified mouse model of melanoma, it was found that diminished CD40L- and IFN γ -mediated signaling contributed to the formation of immunosuppressive tumor microenvironment and that treatment with a Braf^{V600E} inhibitor, PLX4720, could reinvigorate local immune function. Indeed, maximal effectiveness of PLX4720 was dependent on restoration of CD40L- and IFN γ -mediated immune signals. This study illustrates that certain chemotherapies directed at the tumor rely on immune signaling pathways and that this has relevance for the design of combined treatments with immunotherapies. For details, see the article by Ho and colleagues on page 3205.



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