REVIEWS

1925 Advanced Glycation End-Products: A Biological Consequence of Lifestyle Contributing to Cancer Disparity
David P. Turner

1930 Genome Medicine in Cancer: What’s in a Name?
Anne F. Schott, Charles M. Perou, and Daniel F. Hayes

PRIORITY REPORTS

1936 Manic Fringe Promotes a Claudin-Low Breast Cancer Phenotype through Notch-Mediated PI3KCG Induction
Shubing Zhang, Wen-Cheng Chung, Guanning Wu, Sean E. Egan, Lucio Miele, and Keli Xu
Précis: These results define a glucosylpeptide transferase as an oncogene in an aggressive subtype of breast cancer, with mechanistic insights offering a preclinical justification to block PI3K-y as a treatment strategy in this setting.

1944 PLZF, a Tumor Suppressor Genetically Lost in Metastatic Castration-Resistant Prostate Cancer, Is a Mediator of Resistance to Androgen Deprivation Therapy
Précis: These findings identify a novel tumor-suppressive signaling event that controls cancer progression and metastasis by limiting the expansion of tumor-initiating cells.

INTEGRATED SYSTEMS AND TECHNOLOGIES

1949 A Chemical Genetics Approach for the Functional Assay of Novel Cancer Genes
Qianhe Zhou, Adnan Derti, Daniel Rakiec, Ira L. Kao, Michelle Lira, Veronica Gibaja, HoMan Chan, Yi Yang, J_train Min, Michael R. Schlabach, and Frank Stegmeier
Précis: The Degron-KI method represents a new approach to study the function of cancer genes that is more effective than current genetic approaches.

MICROENVIRONMENT AND IMMUNOLOGY

1959 TLR5 Ligand–Secreting T Cells Reshape the Tumor Microenvironment and Enhance Antitumor Activity
Degui Geng, Sabina Kaczanowska, Alexander Tsai, Kenisha Younger, Augusto Ochoa, Aaron P. Rapoport, Sue Ostrand-Rosenberg, and Eduardo Davila
Précis: These findings suggest that T cells engineered for use in adoptive T-cell immunotherapy can be further engineered to deliver TLR5 ligands that reshape the tumor environment to enhance antitumor efficacy.

1983 Identification of Rare High-Avidity, Tumor-Reactive CD8\(^+\) T Cells by Monomeric TCR–Ligand Off-Rates Measurements on Living Cells
Michael Hebeisen, Julien Schmidt, Philippe Guillaume, Petra Baumgarten, Daniel E. Speiser, Immanuel Luescher, and Nathalie Rufer
Précis: This study reports a novel peptide technology to readily isolate those rare high-avidity tumor-specific cytotoxic T cells from cancer patients that offer the greatest interest for use in adoptive cell therapies for treatment.

1992 The Endogenous Cell-Fate Factor Dachshund Restraints Prostate Epithelial Cell Migration via Repression of Cytokine Secretion via a CXCL Signaling Module
Ke Chen, Kongming Wu, Xuanmao Jiao, Liping Wang, Xiaoming Ju, Min Wang, Gabrielle Di Salvo, Shaoxue Xu, Qiong Wang, Kevin Li, Xin Sun, Congwen Xu, Zhiping Li, Mathew C. Castilho, Adam Ertel, Sankar Addya, Peter A. McCabe, Michael P. Lisanti, Chenguang Wang, Richard J. Davis, Graham Mardon, and Richard G. Pestell
Précis: These findings show how a cell fate determination factor that functions in normal development acts to inhibit the growth of androgen therapy-resistant prostate cancer.
## Table of Contents

### 2005

- **IDH2 and NPM1 Mutations Cooperate to Activate Hoxa9/Meis1 and Hypoxia Pathways in Acute Myeloid Leukemia**
  - Yoko Ogawara, Takuo Katsumoto, Yukiko Aikawa, Yutaka Shima, Yuki Kagiyama, Tomoyoshi Soga, Hironori Matsunaga, Takahiko Seki, Kazushi Araki, and Issay Kitabayashi

  **Précis:** These results show that IDH2 mutation is critical for the development and maintenance of stem-like cells in acute myeloid leukemia and offer a preclinical rationale to target mutant IDH enzymes as a strategy for therapy in this setting.

### 2017

- **Oncogenic HRAS Activates Epithelial-to-Mesenchymal Transition and Confers Stemness to p53-Deficient Urothelial Cells to Drive Muscle Invasion of Basal Subtype Carcinomas**
  - Feng He, Jonathan Melamed, Moon-shong Tang, Chuanshu Huang, and Xue-Ru Wu

  **Précis:** Multiple lines of experimental evidence establish a genetic synergism between receptor tyrosine kinase/RAS pathway activation and p53 inactivation as drivers in the malignant progression of bladder cancer.

### THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

### 2029

- **CDK2 Inhibition Causes Anaphase Catastrophe in Lung Cancer through the Centrosomal Protein CP110**

  **Précis:** This study describes how CDK2 inhibitors preferentially target KRAS mutant lung cancer cells that are genetically unstable, a disease type relatively resistant to other chemotherapeutic strategies.

- **Decoy Receptor DcR1 Is Induced in a p50/Bcl3–Dependent Manner and Attenuates the Efficacy of Temozolomide**
  - Nassir M. Mansour, Giovanna M. Bernal, Longtao Wu, Clayton D. Crawley, Kirk E. Cahill, David J. Voce, Irina V. Balysnukiva, Wei Zhang, Ruben Spretz, Luis Nunez, Gustavo F. Larsen, Ralph R. Weichselbaum, and Bakhtiar Yamini

  **Précis:** Upregulation of a Fas/TNF/TRAIL–related decoy receptor by a cytotoxic drug used widely to treat deadly brain tumors was found to limit drug efficacy, providing a rationale to target this receptor as a drug sensitization strategy.

### 2049

- **Nitrostyrene Derivatives Act as RXR Ligands to Inhibit TNFα Activation of NF-κB**
  - Zhiping Zeng, Zhe Sun, Mingfeng Huang, Weidong Zhang, Jie Liu, Luqin Chen, Fan Chen, Yuqi Zhou, Jiasheng Lin, Fengyu Huang, Lin Xu, Zixing Zhuang, Shangjie Gao, Gullimizan Alitongbieke, Guobin Xie, Yang Xu, Bingzhen Lin, Xihua Cao, Ying Su, Xiaokun Zhang, and Hu Zhou

  **Précis:** These results communicate a new class of small molecule modulators of RXRα that induces apoptosis of cancer cells through a unique binding mode and novel mechanism of action.

### 2061

- **Pharmacological Inhibition of KIT Activates MET Signaling in Gastrointestinal Stromal Tumors**
  - Noah A. Cohen, Shan Zeng, Adrian M. Seifert, Teresa S. Kim, Eric C. Sorenson, Jonathan B. Greer, Michael J. Beckman, Juan A. Santamaria-Barría, Megan H. Crawley, Benjamin L. Green, Ferdinand Rossi, Peter Besmer, Cristina R. Antonescu, and Ronald P. DeMatteo

  **Précis:** These findings offer a preclinical rationale to immediately reposition the MET kinase inhibitor cabozantinib for clinical evaluation in treatment of gastrointestinal stromal tumors that are either sensitive or resistant to imatinib, the kinase inhibitor used to treat this type of sarcoma.

### 2071

- **Metabolic Signature Identifies Novel Targets for Drug Resistance in Multiple Myeloma**
  - Patricia Maito, Daisy Huynh, Michele Moschetta, Antonio Sacco, Yosra Aljawai, Yuji Mishima, John M. Asara, Aldo M. Roccaro, Alec C. Kimmelman, and Irene M. Ghobrial

  **Précis:** Inhibitors of lactate dehydrogenase may be beneficial to block the growth and intrinsic drug resistance of multiple myeloma, still one of the deadliest blood tumors.

### TUMOR AND STEM CELL BIOLOGY

### 2083

- **MMP16 Mediates a Proteolytic Switch to Promote Cell–Cell Adhesion, Collagen Alignment, and Lymphatic Invasion in Melanoma**

  **Précis:** This study delineates a novel mechanism behind melanoma progression and reveals MMP16 as a prognostic marker candidate that could also guide diagnostic and therapeutic decisions in melanoma.
Tenascin-C Protects Cancer Stem–like Cells from Immune Surveillance by Arresting T-cell Activation
Elena Jachetti, Sara Caputo, Stefania Mazzoleni, Chiara Svetlana Brambillasca, Sara Martina Parigi, Matteo Grioni, Ignazio Stefano Piras, Umberto Restuccia, Arianna Calcino, Massimo Freschi, Angela Bachì, Rossella Gallì, and Matteo Bellone

Précis: These results shed light on how early-disseminating cancer stem-like cells seed quiescent future sites of metastasis in tumor-draining lymph nodes by engaging a protumorigenic extracellular matrix protein that mediates local immune escape.

Development of Resistance to EGFR-Targeted Therapy in Malignant Glioma Can Occur through EGFR-Dependent and -Independent Mechanisms
Stefan Klingler, Baofeng Guo, Jun Yao, Haiyan Yan, Ling Zhang, Angelina V. Vaseva, Sida Chen, Peter Canoll, James W. Horner, Y. Alan Wang, Ji-Hye Paik, Haoqiang Ying, and Hongwu Zheng

Précis: These findings provide mechanistic insight into EGFR drug resistance in glioma and offer a platform to test therapies targeting aberrant EGFR signaling in this setting.

Chronic Inflammation Induces a Novel Epigenetic Program That Is Conserved in Intestinal Adenomas and in Colorectal Cancer
Monther Abu-Remaileh, Sebastian Bender, Günter Raddatz, Ihab Ansari, Daphne Cohen, Julian Gutekunst, Tanja Musch, Heinz Linhart, Achim Beiling, Eli Pikarsky, Yehudit Bergman, and Frank Lyko

Précis: These findings showing how an altered epigenetic program links inflammation to colon cancer strongly reinforce the concept that the microenvironment dictates the development and maintenance of malignant characters.

ABOUT THE COVER
Pelvic lymph nodes are the most frequent sites of prostate cancer dissemination, as depicted here by pan-cytokeratin immunohistochemistry on a human specimen. However, there is little knowledge about how precociously disseminated cancer cells seed lymph nodes and protect themselves from immune surveillance. Jachetti and colleagues report that early-disseminating cancer stem-like cells seed quiescent future sites of metastasis in tumor-draining lymph nodes by engaging Tenascin-C, a protumorigenic extracellular matrix protein, which mediates local immune escape by arresting T lymphocyte activation. For details, see article by Jachetti and colleagues on page 2095.