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- **Breaking Advances**
  - 1923: Highlights from Recent Cancer Literature

- **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 PIK3CG Induction
    Shubing Zhang, Wen-Cheng Chung, Guanming 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
    Chen-Lin Hsieh, Ginevra Botta, Shuai Gao, Tiantian Li, Eliezer M. Van Allen, Daniel J. Treacy, Changmeng Cai, Housheng Hansen He, Christopher I. Sweeney, Myles Brown, Steven P. Balk, Peter S. Nelson, Levi A. Garraway, and Philip W. Kantoff
    *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 Assessment of Novel Cancer Genes
    Qianhe Zhou, Adnan Derti, David Ruddy, Daniel Rakiec, Iris Kao, Michelle Lira, Petra Baumgaertner, Daniel E. Speiser, Immanuel Luescher, and Nathalie Rufer
    *Précis: The Degron-KI method represents a new approach to study the function of cancer genes that is able to better mimic the effects of small molecule inhibitors 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.*
  
  - 1972: Paracrine WNT5A Signaling Inhibits Expansion of Tumor-Initiating Cells
    Nicholas Borcherding, David Kusner, Ryan Kolb, Qing Xie, Wei Li, Fang Yuan, Gabriel Velez, Ryan Askeland, Ronald J. Weigel, and Weizhou Zhang
    *Précis: These results identify a novel tumor-suppressive signaling event that controls cancer progression and metastasis by limiting the expansion of tumor-initiating cells.*

- **Molecular and Cellular Pathobiology**
  - 1983: Identification of Rare High-Avidity, Tumor-Reactive CD8⁺ T Cells by Monomeric TCR–Ligand Off-Rates Measurements on Living Cells
    Michael Hebeisen, Julien Schmid, Philippe Guillaume, Petra Baumgartner, 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.*

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*American Association for Cancer Research*
Nitrostyrene Derivatives Act as RXRα Ligands to Inhibit TNFα Activation of NF-kB

Zhiping Zeng, Zhe Sun, Mingfeng Huang, Weidong Zhang, Jie Liu, Liqun Chen, Fan Chen, Yuqi Zhou, Jiasheng Lin, Pengru Huang, Lin Xu, Zixing Zhan, Shangjie Gao, Guimin Aliotongbier, Guobin Xie, Yang Xu, Bingzhen Lin, Xihua Cao, Ying Su, Xiao-kun 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.

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-Barria, 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 reposist 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.

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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
Shanhu Hu, Alexey V. Danilov, Kristina Godek, Bernardo Orr, Laura J. Tafe, Jaime Rodriguez-Canales, Carmen Behrens, Barbara Mino, Cesar A. Moran, Vincent A. Memoli, Lisa Maria Mustachio, Fabrizio Galimberti, Saranya Ravi, Andrew DeCastro, Yun Lu, David Sekula, Angeline S. Andrew, Ignacio J. Wistuba, Sarah Freemantle, Duane A. Compton, and Ethan Dmitrovsky

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.

2039 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. Balysnikova, 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 widely used 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 RXRα Ligands to Inhibit TNFα Activation of NF-kB
Zhiping Zeng, Zhe Sun, Mingfeng Huang, Weidong Zhang, Jie Liu, Liqun Chen, Fan Chen, Yuqi Zhou, Jiasheng Lin, Pengru Huang, Lin Xu, Zixing Zhan, Shangjie Gao, Guimin Aliotongbier, Guobin Xie, Yang Xu, Bingzhen Lin, Xihua Cao, Ying Su, Xiao-kun 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 Metabolic Signature Identifies Novel Targets for Drug Resistance in Multiple Myeloma
Patricia Maiso, Daisy Huynh, Michele Moschetta, Antonio Sacco, Yosra Aljawai, Yuji Mishima, John M. Asara, Aldo M. Roccaro, Alec C. Kimmelman, 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 Mazzeoli, Chiara Svetlana Brambillasca, Sara Martina Parigi, Matteo Gritoni, Ignazio Stefano Piras, Umberto Restuccia, Arianna Calcinto, Massimo Freschi, Angela Bachi, Rossella Galli, 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, Günther Raddatz, Ihab Ansari, Daphnée Cohen, Julian Gütekunst, 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.
**Cancer Research**


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