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, 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-γ 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: This study interrogates an androgen responsive tumor suppressor gene whose loss of expression is associated with a new molecular subset of prostate cancer that participates in resistance to androgen deprivation therapy.

INTEGRATED SYSTEMS AND TECHNOLOGIES

1949 A Chemical Genetics Approach for the Functional Assessment of Novel Cancer Genes
Qianhe Zhou, Adnan Derti, David Ruddy, Daniel Rakic, Iris Kao, Michelle Lira, Veronica Gibaja, HoMan Chan, Yi Yang, Junxia 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 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 Borcherdinger, David Kusner, Ryan Kolb, Qing Xie, Wei Li, Fang Yuan, Gabriel Velez, Ryan Askland, Ronald J. Weigel, and Weizhao 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.

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 Baumgaertner, 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.

MOLECULAR AND CELLULAR PATHOBIOLOGY

1992 The Endogenous Cell-Fate Factor Dachshund Restrains Prostate Epithelial Cell Migration via Repression of Cytokine Secretion via a CXCL Signaling Module
Ke Chen, Kongming Wu, Xuanmao Jiao, Leping Wang, Xiaoming Ju, Min Wang, Gabrielle Di Sanza, Shaohua Xu, Qiong Wang, Kevin Li, Xin Sun, Congwen Xu, Zhijing Li, Mathew C. Castimiro, Adam Ertel, Sankar Addya, Peter A. McCue, Michael P. Lisanti, Chenguang Wang, Richard J. Davis, Graeme 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.
Nitostyrene Derivatives Act as RXRα Ligands to Inhibit TNFα Activation of NF-κB
Zhiping Zeng, Zhe Sun, Mingfeng Huang, Weidong Zhang, Jie Liu, Luqin Chen, Fan Chen, Yuqi Zhou, Jiazheng Lin, Fenghu Huang, Lin Xu, Zixing Zhuang, Shangjie Gao, Gulumiran Alitongbieke, 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-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 repurpose 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.

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.
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 Calcinotto, 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, Günter Raddatz, Ihab Ansari, Daphne Cohen, Julian Gutekunst, Tanja Mutsch, Heinz Linhart, Achim Beeling, 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.

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.