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, 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-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 Rakiec, Iris Kao, Philippe Guillaume, Petra Baumgaertner, Daniel E. Speiser, Immanuel Luescher, and Nathalie Rufer

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.

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 R. 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 Borcharding, David Kusner, Ryan Kolb, Qing Xie, Wei Li, Fang Yuan, Gabriel Velez, Ryan Askeland, Ronald J. Weigel, and Weizhong Zhan

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 Restains Prostate Epithelial Cell Migration via Repression of Cytokine Secretion via a CXCL1 Signaling Module
Ke Chen, Kongming Wu, Xuanmao Jiao, Liping Wang, Xiaoming Ju, Min Wang, Gabrielle Di Sanle, Shaoxu Hu, Qiong Wang, Kevin Li, Xin Sun, Congwen Xu, Zhiping Li, Mathew C. Castimiro, Adam Ertel, Sankar Addhya, Peter A. McGuire, Michael P. Lisanti, Chengguang 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.
Decoy Receptor DcR1 Is Induced in a p50/2039 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.

Nitrostyrene Derivatives Act as RXRα Ligands to Inhibit TNFα Activation of NF-κB
Zhiping Zeng, Zhe Sun, Mingleng Huang, Weidong Zhang, Jie Liu, Laiqin Chen, Fan Chen, Yuqi Zhou, Jiaosheng Lin, Fengru Huang, Lin Xu, Zixing Zhuang, Shangjie Cao, Guilimanz Alitongbiek, Guoqin Xie, Yang Xu, Bingqian Lin, Xihua Cao, Ying Su, Xiao-kun Zhang, and Hu Zhou
Précis: These results communicate a new class of small molecule modulators of RXRαs that induces apoptosis of cancer cells through a unique binding mode and novel mechanism of action.

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, Feng He, Jonathan Melamed, Moon-shong Tang, Yun Lu, David Sekula, Angelina S. Andrew, Ignacio I. Wistuba, Sarah Freemantle, Duane A. Compton, and Ethan Dmitrovsky
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.

Human centrosomal protein CP110 is required for focal adhesion assembly and organization and for anchorage-dependent cell survival.

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Decoy Receptor DcR1 Is Induced in a p50/2039 Bcl3–Dependent Manner and Attenuates the Efficacy of Temozolomide
Nassir M. Mansour, Giovanna M. Bernal, Longtiao Wu, Clayton D. Crawley, Kirk E. Cahill, David J. Vorce, Irina V. Babayanikova, 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.

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, Jonthan 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. Matteo
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.

Metabolic Signature Identifies Novel Targets for Drug Resistance in Multiple Myeloma
Patricia Maiso, Daisy Huynh, Michele Moschetta, Antonio Sacco, Yostra Ajajwai, 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.

MMP16 Mediates a Proteolytic Switch to Tumor and Stem Cell Biology

Ronald P. Matteo, Peter Besmer, Cristina R. Antonescu, and Megan H. Crawley, Benjamin L. Green, Ferdinand Rossi, Peter Besmer, Cristina R. Antonescu, and Ronald P. Matteo
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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.
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, Günther 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.

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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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