Highlights from Recent Cancer Literature

Janet Davison Rowley: In Memoriam (1925–2013)
Kathleen H. Goss and Michelle M. Le Beau

Cancer Cell Dormancy in Novel Mouse Models for Reversible Pancreatic Cancer: A Lingering Challenge in the Development of Targeted Therapies
Wan-Chi Lin, Nirakar Rajbhandari, and Kay-Uwe Wagner

A Specific STAT3-Binding Peptide Exerts Antiproliferative Effects and Antitumor Activity by Inhibiting STAT3 Phosphorylation and Signaling
Daejin Kim, In-Hyun Lee, Sunghyun Kim, Minsuk Choi, Hyungjun Kim, Sukyung Ahn, Phei Er Saw, Hyungsu Jeon, Yumi Lee, and Sangyong Jon

Detection of Brain Tumor Cells in the Peripheral Blood by a Telomerase Promoter-Based Assay
Kelly M. MacArthur, Gary D. Kao, Sanjay Chandrasekaran, Michelle Alonso-Basanta, Christina Chapman, Robert A. Lustig, E. Paul Wileyto, Stephen M. Hahn, and Jay F. Dorsey

Novel Methylated Biomarkers and a Robust Assay to Detect Circulating Tumor DNA in Metastatic Breast Cancer
Mary Jo Fackler, Zoila Lopez Bujanda, Christopher Umbricht, Wei Wen Teo, Soonweng Cho, Zhe Zhang, Kala Visvanathan, Stacie Jeter, Pedram Argani, Chenguang Wang, Jaclyn P. Lyman, Marina de Brot, James N. Ingle, Judy Boughey, Kandace McGuire, Tari A. King, Lisa A. Carey, Leslie Cope, Antonio C. Wolff, and Saraswati Sukumar

Immunosurveillance by Antiangiogenesis: Tumor Growth Arrest by T Cell–Derived Thrombospondin-1
Keri L. Schadler, Erika J. Crosby, Alice Yao Zhou, Dong Ha Bhang, Lior Braunstein, Kwan Hyuck Baek, Danielle Crawford, Alison Crawford, Jill Angelosanto, E. John Wherry, and Sandra Ryeeom

p53 and NF-κB Coregulate Proinflammatory Gene Responses in Human Macrophages
Julie M. Lowe, Daniel Menendez, Pierre R. Bushe1, Maria Shatz, Erin L. Kirk, Melissa A. Troester, Stavros Garantziotis, Michael B. Fessler, and Michael A. Resnick

RAE1 Ligands for the NKG2D Receptor Are Regulated by STING-Dependent DNA Sensor Pathways in Lymphoma
MOLECULAR AND CELLULAR PATHOBIOLOGY

2238 Vemurafenib Cooperates with HPV to Promote Initiation of Cutaneous Tumors
Matthew Holdenerfiel, Edward Lorenzana, Ben Weisburd, Lisa Lomovskaya, Lise Boussemart, Ludovic Lacroix, Gorana Tomasic, Michel Favre, Stephan Vagner, Caroline Robert, Majid Goldsdui, Dylan Daniel, Nancy Pryer, Frank McCormick, and Darrin Stuart
Précis: RAF inhibitors used to treat melanoma patients paradoxically activate MAPK signaling, which this report shows will cooperate with HPV infections in the skin to promote formation of squamous cancers and other skin lesions as a side effect of drug treatment.

2246 E3 Ubiquitin Ligase HOIP Attenuates Apoptotic Cell Death Induced by Cisplatin
Précis: These results identify a candidate therapeutic target for the development of combinatorial chemotherapies to potentiate the efficacy of platinum-based anticancer drugs, a mainstay of the medical oncology clinic.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

2295 IGF-I Regulates Redox Status in Breast Cancer Cells by Activating the Amino Acid Transport Molecule xC–
Yuzhe Yang and Douglas Yee
Précis: These findings suggest that targeting a cell surface amino acid transporter may heighten the therapeutic efficacy of anti-IGF1 receptor inhibitors, which may be broadly useful in treating various solid tumors.
A Systems Biology Approach Identifies Effective Tumor–Stroma Common Targets for Oral Squamous Cell Carcinoma

Wenxia Meng, Yun Wu, Xin He, Chuaxiu Liu, Qinghong Gao, Lin Ge, Lanyan Wu, Ying Liu, Yaqing Guo, Xiaoyu Li, Yurong Liu, Sixiu Chen, Xiangli Kong, Zhi Liang, and Hongmei Zhou

Précis: This study suggests a concept aimed at identifying drug targets that would be beneficial to attack in cancer cells and adjacent stromal cells simultaneously, offering a discovery framework for future drug combination strategies.

HO-3867, a Safe STAT3 Inhibitor, Is Selectively Cytotoxic to Ovarian Cancer


Précis: The orally active compound described may offer a long awaited translational opportunity to target STAT3 in the large number of cancer patients in whom STAT3 upregulation not only drives tumor cell growth but also immune escape, as an appealing tool for immunochemotherapy.

Context-Selective Death of Acute Myeloid Leukemia Cells Triggered by the Novel Hybrid Retinoid-HDAC Inhibitor MC2392

Floriana De Bellis, Vincenzo Carafa, Mariarosaria Conte, Dante Rotili, Francesca Petraglia, Filomena Matarese, Kees-Jan François, Julien Ablain, Sergio Valente, Remy Castellano, Armelle Goubard, Yves Collette, Amit Mandoli, Joost H.A. Martens, Hendrik G. Stunnenberg, and Lucia Altucci

Précis: These findings offer preclinical evidence that targeting multiple signaling pathways with a single hybrid drug is a feasible and attractive paradigm for new cancer therapies.

Loss of NF1 in Cutaneous Melanoma Is Associated with RAS Activation and MEK Dependence

Moriah H. Nissan, Christine A. Pratilas, Alexis M. Jones, Ricardo Ramirez, Helen Won, Callian Liu, Shakuntala Tiwari, Li Kong, Aphrophiti J. Hanrahan, Zhan Yao, Taha Merghoub, Antoni Ribas, Paul B. Chapman, Rona Yaeger, Barry S. Taylor, Nikolaus Schultz, Michael F. Berger, Neal Rosen, and David B. Solit

Précis: The mechanistic consequences of NF1 loss in melanoma have clinical impact not only for treatment of melanoma, but also for neurofibromatosis type 1 and other cancers in which NF1 is altered.

Identification of FoxR2 as an Oncogene in Medulloblastoma

Hideto Koso, Asano Tsuhako, Eli Lyons, Jerrold M. Ward, Alistair G. Rust, David J. Adams, Nancy A. Jenkins, Neel G. Copeland, and Sumiko Watanabe

Précis: A transposon screen for medulloblastoma cancer genes identifies new genes that regulate SHH signaling and proliferation of granule neuron precursors.

Cofilin Drives Cell-Invasive and Metastatic Responses to TGF-β in Prostate Cancer

Joanne Collazo, Beibei Zhu, Spencer Larkin, Sarah K. Martin, Hong Pu, Craig Horbinski, Shahriar Koochekpour, and Natasha Kyripanou

Précis: An F-actin severing protein that is required for cytoskeletal reorganization, filopodia formation, and cell migration is found to be critical for metastasis, with potential implications on how to disrupt this central feature of cancer progression.

Correction: A Transgenic Mouse Model for Early Prostate Metastasis to Lymph Nodes

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Androgen receptor (AR) nuclear accumulation and transcriptional activity is critical for prostate cancer growth in hormone-naive and castration resistant disease (CRPC). The taxanes, microtubule-stabilizing drugs, are widely used in the treatment of CRPC. The dynein motor protein to efficiently traffic AR to the nucleus utilizes microtubule dynamics. Taxane treatment interferes with this process and sequesters AR in the cytoplasm. AR splice variants are often expressed in CRPC and confer resistance to androgen deprivation therapies. Using confocal microscopy of prostate cancer cells expressing ARv567 (green) and the dynein accessory protein dynamin (red) whose expression inhibits dynein-cargo binding, we show that ARv567 variant, similar to the AR wt, utilizes dynein motor protein and microtubules to efficiently translocate to the nucleus. For details, see article by Thadani-Mulero and colleagues on page 2270.