BREAKING ADVANCES

6097 Highlights from Recent Cancer Literature

REVIEWS

6099 RSK Isoforms in Cancer Cell Invasion and Metastasis
Florian J. Sulzmaier and Joe W. Ramos

6106 The Evolution of Melanoma Resistance Reveals Therapeutic Opportunities
Meghna Das Thakur and Darrin D. Stuart

PERSPECTIVES

6111 Formalizing an Integrative, Multidisciplinary Cancer Therapy Discovery Workflow
Mary F. McGuire, Heiko Enderling, Dorothy I. Wallace, John C. Panetta, and Eddy Pasquier

6118 Redox Imbalance and Biochemical Changes in Cancer
Tonia C. Jorgenson, Weixiong Zhong, and Terry D. Oberley

MEETING REPORT

6124 Twenty-fifth Annual Pezcoller Symposium: Metabolism and Tumorigenesis
William Kaelin, David Livingston, Massimo Loda, Karen Vousden, and Enrico Mihich

PRIORITY REPORT

6128 A Comparative Genomic Approach for Identifying Synthetic Lethal Interactions in Human Cancer
Raamesh Deshpande, Michael K. Asiedu, Mitchell Klebig, Shari Sutor, Elena Kuzmin, Justin Nelson, Jeff Piotrowski, Seung Ho Shin, Minoru Yoshida, Michael Costanzo, Charles Boone, Dennis A. Wigle, and Chad L. Myers

Precis: Using the robust genetics of yeast, this study reveals new interactions between cancer-associated mutations in humans, leading to the identification of new candidate drug targets for suppressor functions widely deficient in cancers.

INTEGRATED SYSTEMS AND TECHNOLOGIES

6149 Novel Modeling of Cancer Cell Signaling Pathways Enables Systematic Drug Repositioning for Distinct Breast Cancer Metastases
Hong Zhao, Guangxiu Jin, Kemi Cui, Ding Ren, Timothy Liu, Peikai Chen, Solomon Wong, Fuhai Li, Yubo Fan, Angel Rodriguez, Jenny Chang, and Stephen TC Wong

Precis: A generally applicable modeling method based on integrative cancer biology is used to uncover tactics for repositioning existing drugs, with the potential to immediately improve treatments for advanced cancer.

6164 Optical Metabolic Imaging Identifies Glycolytic Levels, Subtypes, and Early-Treatment Response in Breast Cancer
Alex J. Walsh, Rebecca S. Cook, H. Charles Manning, Donna J. Hicks, Alec Lafontant, Carlos L. Arteaga, and Melissa C. Skala

Precis: Optical imaging can rapidly assess how cellular metabolism responds to molecular alterations and drug action, offering a tool to accelerate drug development.

MICROENVIRONMENT AND IMMUNOLOGY

6175 Integrin $\alpha v \beta 3$ and Fibronectin Upregulate Slug in Cancer Cells to Promote Clot Invasion and Metastasis
Lynn M. Knowles, Lisa A. Gurski, Charlotte Engel, James R. Gnarra, Jodi K. Maranich, and Jan Pilch

Precis: These findings establish a mechanism through which cancer cells can colonize blood clots in the lung vasculature, potentially explaining why certain tumors, such as renal carcinomas and soft tissue sarcomas, have a proclivity for lung metastasis.
## MOLECULAR AND CELLULAR PATHOBIOLOGY

### Targeting FSTL1 Prevents Tumor Bone Metastasis and Consequent Immune Dysfunction
Chie Kudo-Saito, Takafumi Fuwa, Kouichi Murakami, and Yutaka Kawakami

**Précis:** These important findings offer preclinical proof-of-concept for an attractive therapeutic target to prevent or treat bone metastasis, in part through a unique mechanism that can degrade an immune escape barrier erected by tumor cells.

### Carboxyl-Terminal Modulator Protein Positively Regulates Akt Phosphorylation and Acts as an Oncogenic Driver in Breast Cancer

**Précis:** These results address some controversy in the field by corroborating the concept that an Akt-binding molecule promotes Akt phosphorylation and functions as an oncogenic molecule in breast cancer.

### GPR116, an Adhesion G-Protein-Coupled Receptor, Promotes Breast Cancer Metastasis via the \( \text{Go}^q\)-p63RhoGEF-Rho GTPase Pathway
Xiaolong Tang, Rongrong Jin, Guojun Qu, Xiu Wang, Zhenxi Li, Zengjin Yuan, Chen Zhao, Stefan Siwko, Tieliu Shi, Ping Wang, Jianru Xiao, Mingyao Liu, and Jian Luo

**Précis:** Identification of a G-protein coupled receptor that is crucial for the metastasis of breast cancer cells has implications for prognosis and targeting of advanced forms of human breast cancer.

### Novel Oncogenic PDGFRA Mutations in Pediatric High-Grade Gliomas
Barbara S. Paugh, Xiaoyan Zhu, Chunxu Qu, Raelene Endersby, Alexander K. Diaz, Junyuan Zhang, Dorine A. Bax, Diana Carvalho, Rui M. Reis, Arza Omar-Thomas, Alberto Broniscer, Cynthia Wetmore, Jinghui Zhang, Chris Jones, David W. Ellison, and Suzanne J. Baker

**Précis:** These results suggest that there is a distinct spectrum of PDGF receptor alpha mutations in adult and pediatric cancers, with implications for etiology and therapy.

### Carboxyl-Terminal Modulator Protein Positively Regulates Akt Phosphorylation and Acts as an Oncogenic Driver in Breast Cancer

**Précis:** These results address some controversy in the field by corroborating the concept that an Akt-binding molecule promotes Akt phosphorylation and functions as an oncogenic molecule in breast cancer.

### BRD4 Sustains Melanoma Proliferation and Represents a New Target for Epigenetic Therapy
Miguel F. Segura, Barbara Fontanals-Cirera, Avital Gaziel-Sorran, Maria V. Guijarro, Doug Hanniford, Guangtao Zhang, Pilar González-Gomez, Marta Morante, Luz Jubierre, WeiJia Zhang, Farbod Darvishian, Michael Ohlmeyer, Iman Osman, Ming-Ming Zhou, and Eva Hernando

**Précis:** These findings strengthen a rationale for epigenetic treatment of melanomas based on pharmacologic targeting of a core transcriptional program that sustains melanoma cell identity.
**NSD2 Is Recruited through Its PHD Domain to Oncogenic Gene Loci to Drive Multiple Myeloma**
Zheng Huang, Haiping Wu, Shannon Chuai, Fiona Xu, Feng Yan, Nathan Englund, Zhaofu Wang, Hailong Zhang, Ming Fang, Youzhen Wang, Justin Gu, Man Zhang, Teddy Yang, Kehao Zhao, Yanyan Yu, Jingquan Dai, Wei Yi, Shaolian Zhou, Qian Li, Jing Wu, Jun Liu, Xi Wu, Homan Chan, Chris Lu, Peter Atadja, En Li, Yan Wang, and Min Hu

**Precis:** These findings deepen insights into how to target a transcription factor activated in multiple myeloma by a genetic translocation, with more general implications on how to attack this molecular class of targets.

**Integrative Radiogenomic Profiling of Squamous Cell Lung Cancer**

**Precis:** Genomic and epigenomic predictors of cancer radiosensitivity have remained frustratingly elusive, a challenge addressed here by a more highly integrative marker study than has been advanced previously.

**Epithelial–Mesenchymal Transition and Tumor Suppression Are Controlled by a Reciprocal Feedback Loop between ZEB1 and Grainyhead-like-2**
Benjamin Cieply, Joshua Farris, James Denvir, Heide L. Ford, and Steven M. Frisch

**Precis:** A feedback loop between an activator of EMT and a repressor of EMT sets up a restriction point that must be breached by an overwhelming confluence of microenvironmental factors in order for a tumor cell to undergo EMT.

**Targeting Sonic Hedgehog-Associated Medulloblastoma through Inhibition of Aurora and Polo-like Kinases**
Shirley L. Markant, Lourdes Adriana Espanza, Jesse Sun, Kelly L. Barton, Lisa M. McCoig, Gerald A. Grant, John R. Crawford, Michael L. Levy, Paul A. Northcott, David Shih, Marc Remke, Michael D. Taylor, and Robert J. Wechsler-Reya

**Precis:** This study identifies a critical vulnerability in some pediatric medulloblastomas that is well suited to therapeutic attack by inhibiting pivotal G2–M phase cell-cycle kinases.

**CORRECTION**

**Correction: Rational Drug Redesign to Overcome Drug Resistance in Cancer Therapy: Imatinib Moving Target**

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ABOUT THE COVER

The prognosis and quality of life of patients with breast cancer brain metastases is generally poor and there is no effective treatment. A generally applicable computational model integrated with systems biology experiments was developed and applied to reposition existing drugs that would inhibit brain metastases. Ten repositioned drug candidates with potential brain permeability were identified. In xenograft models, sunitinib (approved for treating advanced renal cell carcinoma and gastrointestinal stromal tumors) and dasatinib (approved for treating chronic myelogenous leukemia) were repositioned to prevent metastatic outgrowth of breast cancer cells in the brain. For details, see article by Zhao and colleagues on page 6149.
Cancer Research


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