BREAKING ADVANCES

7337  Highlights from Recent Cancer Literature

REVIEWS

7339  The Evolution of Endothelial Regulatory Paradigms in Cancer Biology and Vascular Repair
Joseph W. Franses and Elazer R. Edelman

7345  The Pax-5 Gene: A Pluripotent Regulator of B-cell Differentiation and Cancer Disease
Pierre O'Brien, Pier Morin Jr, Rodney J. Ouellette, and Gilles A. Robichaud

MEETING REPORT

7351  Targeting PI3K/mTOR Signaling in Cancer
Brooke M. Emerling and Argun Akcakanat

PRIORITY REPORT

7360  5-Hydroxymethylcytosine Is Strongly Depleted in Human Cancers but Its Levels Do Not Correlate with IDH1 Mutations
Seung-Gi Jin, Yong Jiang, Runxiang Qiu, Tibor A. Rauch, Yinhong Wang, Gabriele Schackert, Dietmar Krex, Qiang Lu, and Gerd P. Pfeifer

INTEGRATED SYSTEMS AND TECHNOLOGIES

7366  Quantifying the Role of Angiogenesis in Malignant Progression of Gliomas: In Silico Modeling Integrates Imaging and Histology
Kristin R. Swanson, Russell C. Rockne, Jonathan Claridge, Mark A. Chaplain, Ellsworth C. Alvord Jr, and Alexander R.A. Anderson

Précis: This modeling study shows that malignant progression of a tumor does not necessarily rely on changes in either the rate of proliferation or invasion.

7376  Metabolomic Profiling Reveals Potential Markers and Bioprocesses Altered in Bladder Cancer Progression

Précis: Metabolic profiling in bladder cancer reveals candidate biomarkers that may be effective in urine sample analysis, with the potential to offer a simple, cost-effective means of diagnosis and prognosis in this disease.

7387  In Vivo Magnetic Resonance Imaging of the Estrogen Receptor in an Orthotopic Model of Human Breast Cancer
Adi Pais, Chidambaram Gunanathan, Baanan Margalit, Inbal Eti Biton, Ady Yosepovich, David Milstein, and Hadassa Degani

Précis: Findings offer preclinical proof-of-concept for a novel ER-targeting contrast agent that can detect ER-positive tumors in a noninvasive manner in vivo.
A Framework to Select Clinically Relevant Cancer Cell Lines for Investigation by Establishing Their Molecular Similarity with Primary Human Cancers
Garrett M. Dancik, Yuanbin Ru, Charles R. Owens, and Dan Theodorescu

Precise: Unfortunately, experimental findings from established human cancer cell lines often do not translate to clinical settings, but by selecting cell lines that better reflect human pathobiology it may be possible to improve this situation.

FUNCTIONAL CHARACTERIZATION OF AN scFv-Fc Antibody that Immunotherapeutically Targets the Common Cancer Cell Surface Proteoglycan CSPG4
Xinhui Wang, Akihiro Katayama, Yangyang Wang, Ling Yu, Elvira Favoino, Koichi Sakakura, Alessandra Favole, Takahiro Tsuchikawa, Susan Silver, Simon C. Watkins, Toshiro Kageshita, and Soldano Ferrone

Precise: Antibody targeting of cell surface proteoglycans that are widely overexpressed in human tumors offers an appealing general approach for passive immunotherapy in cancer patients.

SmaD7 Expression in T cells Prevents Colitis-Associated Cancer
Angelamaria Rizzo, Maximilian J. Waldner, Carmine Stolfi, Massimiliano Sarra, Daniele Fina, Christoph Becker, Markus F. Neurath, Thomas T. Macdonald, Francesco Pallone, Giovanni Monte Leone, and Massimo C. Fantini

Precise: This study illustrates that chronic inflammation in colitis does not necessarily heighten risks of colorectal tumorigenesis, based on epigenetic differences in the immune microenvironment that dictate whether colitis-associated inflammation promotes or retards tumor development.

Hypoxia Induces Escape from Innate Immunity in Cancer Cells via Increased Expression of ADAM10: Role of Nitric Oxide
Ivraym B. Barsoum, Thomas K. Hamilton, Xin Li, Tiziana Cotechini, Ellen A. Miles, D. Robert Siemens, and Charles H. Graham

Precise: Nitric oxide can block hypoxia-mediated evasion from innate immunity, suggesting the immediate clinical exploration of nitric oxide mimetics like nitroglycerin for cancer treatment.
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<td>Lysosomal Transmembrane Protein LAPTM4B Promotes Autophagy and Tolerance to Metabolic Stress in Cancer Cells</td>
<td>Yang Li, Qing Zhang, Ruiyang Tian, Qi Wang, Jean J. Zhao, J. Dirk Iglehart, Zhigang Charles Wang, and Andrea L. Richardson</td>
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<td>p53-Responsive miR-194 Inhibits Thrombospondin-1 and Promotes Angiogenesis in Colon Cancers</td>
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<td>Qian Zhang, Kazuhito Sakamoto, Chengbao Liu, Aleata A. Triplett, Wan-chi Lin, Halliagar Rui, and Kay-Uwe Wagner</td>
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## PREVENTION AND EPIDEMIOLOGY

**7568**

**Genome-Wide High-Density SNP Linkage Search for Glioma Susceptibility Loci: Results from the Gliogene Consortium**


Précis: Linkage analysis of families with 2 or more cases of glioma identifies loci linked to glioma susceptibility, suggesting an inherited predisposition to development of this deadly cancer.

## THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

**7597**

**Dual IGF-1R/InsR Inhibitor BMS-754807 Synergizes with Hormonal Agents in Treatment of Estrogen-Dependent Breast Cancer**

Xiaoman Hou, Fei Huang, Luciana F. Macedo, Sean C. Harrington, Karen A. Reeves, Ann Greer, Friedrich Graf Finckenstein, Angela Brodie, Marco M. Gottardis, Joan M. Carboni, and Paul Halaska

Précis: Findings offer preclinical proof-of-concept for a powerful new combinatorial approach to improve the eradication of estrogen-dependent breast cancers.

**7608**

**miR-221 Silencing Blocks Hepatocellular Carcinoma and Promotes Survival**

Jong-Kook Park, Takayuki Kogure, Gerard J. Nueso, Jinmaijiang, Lei He, Ji Hye Kim, Mitch A. Phelps, Tracey L. Penningt, Carlo M. Croce, Tushar Patel, and Thomas D. Schmittgen

Précis: In hepatocellular carcinomas with typically poor prognosis, antisense miR-221 treatments may be highly effective in blocking tumor proliferation.

**Chemotherapeutic Properties of Phospho-Nonsteroidal Anti-Inflammatory Drugs, a New Class of Anticancer Compounds**

Liqun Huang, Gerardo G. Mackenzie, Yu Sun, Nengtai Ouyang, Gang Xie, Kvetoslava Vrankova, Despina Komninou, and Basil Rigas

Précis: This important study addresses the quandary posed by NSAIDs, which exert useful anti-inflammatory effects but present safety and efficacy concerns that raise questions about their use in cancer prevention and treatment.

**7628**

**Wnt Inhibitor Screen Reveals Iron Dependence of β-Catenin Signaling in Cancers**


Précis: In identifying a new class of compounds suitable for development as inhibitors of Wnt-driven cancers, this study led to the important discovery of a fundamental requirement for iron that might be immediately clinically exploitable.
SMAC Mimetic (JP1201) Sensitizes Non–Small Cell Lung Cancers to Multiple Chemotherapy Agents in an IAP-Dependent but TNF-α–Independent Manner

Rachel M. Greer, Michael Peyton, Jill E. Larsen, Luc Girard, Yang Xie, Adi F. Gazdar, Patrick Harran, Lai Wang, Rolf A. Brekken, Xiaodong Wang, and John D. Minna

Précis: Chemical mimetics of the proapoptotic molecule SMAC may be useful to broadly sensitize chemoresistant cancers to clinically relevant concentrations of various cytotoxic drugs, addressing an urgent need in oncology.

Thrombospondin-1 Triggers Cell Migration and Development of Advanced Prostate Tumors

Virginie Firlej, Jacques R.R. Mathieu, Christele Gilbert, Loïc Lemonnier, Jessica Naklele, Catherine Gallou-Kabani, Basma Guarmit, Aurélie Morin, Natalia Prevarskaya, Nicolas Barry Delongchamps, and Florence Cabon

Précis: An extracellular protein known to be anti-angiogenic was found to stimulate invasion in prostate cancers, suggesting that disruption of this protein might actually confer therapeutic benefits.

Sorcin Induces a Drug-Resistant Phenotype in Human Colorectal Cancer by Modulating Ca2⁺ Homeostasis

Francesca Maddalena, Gabriella Laudiero, Annamaria Piscazzi, Agnese Secondo, Antonella Scorziello, Valentina Lombardi, Danilo Swann Matassa, Alberto Fersini, Vincenzo Neri, Franca Esposito, and Matteo Landriscina

Précis: Findings elucidate what appears to be a broadly active mechanism of multidrug resistance in human colorectal cancers, potentially responsible for much of the mortality in this common cancer in developed countries.

TUMOR AND STEM CELL BIOLOGY

Targets of the Tumor Suppressor miR-200 in Regulation of the Epithelial–Mesenchymal Transition in Cancer

Mark J. Schliekelman, Don L. Gibbons, Vitor M. Faca, Chad J. Creighton, Zain H. Rizvi, Qing Zhang, Chee-Hong Wong, Hong Wang, Christin Ungewiss, Young-Ho Ahn, Dong-Hoon Shin, Jonathan M. Kurie, and Samir M. Hanash

Précis: Findings offer insights into how a family of tumor suppressive microRNAs restricts metastatic progression, identifying key roles for a TGF-β protein network and extracellular cell adhesion molecules and proteases in the tumor microenvironment.

Selectin Ligand Sialyl-Lewis x Antigen Drives Metastasis of Hormone-Dependent Breast Cancers

Sylvain Julien, Aleksandar Ivetic, Anita Grigoriadis, Ding QiZe, Brian Burford, Daisy Sproviero, Gianfranco Picco, Cheryl Gillett, Suzanne L. Papp, Lana Schaffer, Andrew Tutt, Joyce Taylor-Papadimitriou, Sarah E. Pinder, and Joy M. Burchell

Précis: Findings identify a cell surface glycosylation marker on breast cancer cells that is associated with metastasis to the bone, offering insights into the context of its activity.

GLIPR1 Suppresses Prostate Cancer Development through Targeted Oncoprotein Destruction

Likun Li, Chengzheng Ren, Guang Yang, Elmoataz Abdel Fattah, Alexei A. Goltsov, Soo Mi Kim, Ju-Seog Lee, Sanghee Park, Francesco J. Demayo, Michael M. Ittmann, Patricia Troncoso, and Timothy C. Thompson

Précis: This study offers important new insights into how the c-myc gene becomes deregulated in human cancers, addressing long-standing questions of general interest to the field and suggesting new ideas on how to attack this pivotal molecule.

Apoptosis Inhibitor ARC Promotes Breast Tumorigenesis, Metastasis, and Chemoresistance

Christina M. Medina-Ramirez, Sumanta Goswami, Tatiana Smirnova, Danilo Swann, Benjamin Benson, Neal Ferrick, Jeffrey Segall, Jeffrey W. Pollard, and Richard N. Kititis

Précis: This study reveals multiple pathobiologic roles for the apoptosis suppressor ARC in driving carcinogenesis and chemoresistance.
ABOUT THE COVER

Chronic inflammation plays important roles at different stages of cancer development, including carcinogenesis, tumor invasion, and metastasis. In this study, expression of angiopoietin-like protein 2 (Angptl2), recently identified as a chronic inflammation mediator in skin tissues, is highly correlated with the frequency of carcinogenesis in a chemically induced skin squamous cell carcinoma (SCC) mouse model. Furthermore, expression of Angptl2 in tumor cells promotes not only tumor angiogenesis and lymphangiogenesis, but also the acquisition of mesenchymal invasive characteristics in tumor cells through activation of TGF-β/Smad signaling, resulting in worse outcomes. This image represents a significantly increased tumor angiogenesis in SCC of Angptl2 transgenic (K14-Angptl2) mice. For details, see the article by Aoi and colleagues on page 7502 of this issue.
Cancer Research

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