**Contents**

**BREAKING ADVANCES**

3191 Highlights from Recent Cancer Literature

**REVIEWS**

3193 The *MET* Oncogene in Glioblastoma Stem Cells: Implications as a Diagnostic Marker and a Therapeutic Target
Carla Boccaccio and Paolo M. Comoglio

3200 Vesicle Trafficking and RNA Transfer Add Complexity and Connectivity to Cell–Cell Communication
Charles T. Roberts Jr and Peter Kurre

**INTEGRATED SYSTEMS AND TECHNOLOGIES**

3206 Application of Raman Spectroscopy to Identify Microcalcifications and Underlying Breast Lesions at Stereotactic Core Needle Biopsy

3216 Manganese-Enhanced MRI Reveals Early-Phase Radiation-Induced Cell Alterations In Vivo
Shigeo Saito, Sumitaka Hasegawa, Aiko Sekita, Rumiyan Bakalova, Takako Furukawa, Kenya Murase, Tsumeo Saga, and Ichio Aoki

**MICROENVIRONMENT AND IMMUNOLOGY**

3225 The Endogenous Tryptophan Metabolite and NAD⁺ Precursor Quinolinic Acid Confers Resistance of Gliomas to Oxidative Stress
Felix Sahm, Iris Oezen, Christiane A. Opitz, Bernhard Radlwimmer, Andreas von Deimling, Tilman Ahrendt, Seray Adams, Helge Bode, Gilles J. Guillemin, Wolfgang Wick, and Michael Platten

**MOLECULAR AND CELLULAR PATHOBIOLOGY**

3235 Hypoxia Triggers Hedgehog-Mediated Tumor–Stromal Interactions in Pancreatic Cancer

3248 Single Copies of Mutant *KRAS* and Mutant *PIK3CA* Cooperate in Immortalized Human Epithelial Cells to Induce Tumor Formation

**Cancer Research**
June 1, 2013 • Volume 73 • Number 11
Prevention and Epidemiology

Colorectal Cancer Risk Associated with Hormone Use Varies by Expression of Estrogen Receptor-β
Anja Rudolph, Csaba Toth, Michael Hoffmeister, Wilfried Roth, Esther Herpel, Peter Schirmacher, Hermann Brenner, and Jenny Chang-Claude

Precis: Expression of estrogen receptor β, the predominant estrogen receptor in colon tissue, appears to be involved in the reduction of colorectal cancer risk that may arise with use of oral contraceptives or menopausal hormone therapy.

Therapeutics, Targets, and Chemical Biology

Inhibition of Tumor Cell Migration by LD22-4, an N-Terminal Fragment of 24-kDa FGFR2, Is Mediated by Neuropilin 1
Ling Zhang, Graham C. Parry, and Eugene G. Levin

Precis: Definition of a cell surface receptor for an inhibitor of cancer cell migration suggests a novel approach to tumor suppression.

DNA Methylation-Mediated Repression of miR-886-3p Predicts Poor Outcome of Human Small Cell Lung Cancer
Jianzhong Cao, Yongmei Song, Nan Bi, Jie Shen, Wenyang Liu, Jing Fan, Guogui Sun, Tong Tong, Jie He, Yuankai Shi, Xun Zhang, Ning Lu, Yinghua He, Hongyu Zhang, Kelong Ma, Xiaoying Luo, Lei Lu, Hui Deng, Jing Cheng, Jingde Zhu, Luhua Wang, and Qimin Zhan

Precis: These findings identify a little-studied microRNA the epigenetic downregulation of which strongly affects clinical outcomes and malignant cell behaviors in small-cell lung cancer.

PFI-1, a Highly Selective Protein Interaction Inhibitor, Targeting BET Bromodomains
Sarah Picard, David Da Costa, Angeliki Thanasopoulos, Panagis Filippakopoulos, Paul V. Fish, Martin Philpott, Oleg Fedorov, Paul Brennan, Mark E. Bunnage, Dafydd R. Owen, James E. Bradner, Philippe Taniere, Brendan O’Sullivan, Susanne Müller, Juerg Schwaller, Tatjana Stankovic, and Stefan Knapp

Precis: This study suggests that it may be possible to target an important transcriptional regulatory domain that has been implicated in a broad number of aggressive blood cancers, as a generalizable therapeutic approach.

Bevacizumab-Induced Normalization of Blood Vessels in Tumors Hampers Antibody Uptake
Marlous Arjaans, Thijs H. Oude Munnink, Sjoukje F. Oosting, Anton G.T. Tervissecha van Scheltinga, Jourik A. Gietema, Erik T. Garbacik, Martin Philpott, Oleg Fedorov, Paul Brennan, Mark E. Bunnage, Dafydd R. Owen, and Elisabeth G.E. de Vries

Precis: Bevacizumab treatment decreases tumor uptake of antibodies by vessel normalization, and this should be taken into account in the design of clinical trials that combine bevacizumab with other antibodies.
Threshold Levels of ABL Tyrosine Kinase Inhibitors Retained in Chronic Myeloid Leukemia Cells Determine Their Commitment to Apoptosis

Thomas O'Hare, Christopher A. Eide, Anupriya Agarwal, Lauren T. Adrian, Matthew S. Zabriskie, Ryan J. Mackenzie, Dorian H. LaTocha, Kara J. Johnson, Huihong You, Jenny Luo, Steven M. Riddle, Bryan D. Marks, Kurt W. Vogel, Dennis R. Koop, John Appgar, Jeffrey W. Tyner, Michael W. Deininger, and Brian J. Druker

Precise: By providing deeper insights into the pharmacodynamic requirements for the cytotoxic effects of the paradigm kinase inhibitor imatinib, this study may more broadly assist the development of maximally effective kinase inhibitors for cancer treatment.

Simultaneous Targeting of Tumor Antigens and the Tumor Vasculature Using T Lymphocyte Transfer Synergize to Induce Regression of Established Tumors in Mice

Dhanalakshmi Chinnasamy, Eric Tran, Zhiya Yu, Richard A. Morgan, Nicholas P. Restifo, and Steven A. Rosenberg

Precise: This study offers proof of principle for using antiangiogenic drugs to enhance the efficacy of adoptive T-cell therapies for cancer treatment.

Hedgehog Signaling Alters Reliance on EGF Receptor Signaling and Mediates Anti-EGFR Therapeutic Resistance in Head and Neck Cancer


Precise: Preclinical results show that resistance to the widely used EGFR targeting drug cetuximab, which occurs widely in the clinic, could be prevented by administration of inhibitors of the hedgehog pathway, which appears to be emerging as a major factor in cancer drug resistance more broadly.

Regulation of FANC D2 by the mTOR Pathway Contributes to the Resistance of Cancer Cells to DNA Double-Strand Breaks

Changxian Shen, Duane Oswald, Doris Pheplos, Hakan Cam, Christopher E. Pellekosi, Qishen Pang, and Peter J. Houghton

Precise: This study provides the basis for the sensitization of cancer cells to DNA damaging agents by targeting the mTOR pathway and gives insight into potential strategies that may enhance therapeutic activity or reduce sequelae from high-dose therapies, particularly in children.
Dual Role of the Antioxidant Enzyme Peroxiredoxin 6 in Skin Carcinogenesis
Frank Rolfs, Marcel Huber, Florian Gruber, Friederike Böhm, Herbert J. Pfister, Valery N. Bochkov, Erwin Tschachler, Reinhard Dummer, Daniel Hohl, Matthias Schäfer, and Sabine Werner

Précis: Antioxidant functions do not contribute exclusively to tumor suppression, as widely believed, but can also promote tumor development depending on the stage of the disease.

Growth of Triple-Negative Breast Cancer Cells Relies upon Coordinate Autocrine Expression of the Proinflammatory Cytokines IL-6 and IL-8

Précis: Findings offer a preclinical proof of principle to improve therapy of triple-negative breast cancer, a particularly aggressive disease subtype lacking effective mechanism-based interventions.

ABOUT THE COVER
In gliomas, constitutive metabolism of the essential amino acid tryptophan leads to the accumulation of the tryptophan metabolite quinolinic acid. Quinolinic acid is used by tumor cells to generate NAD⁺, thus contributing to the resistance towards radiotherapy and chemotherapy by replenishing depleted intracellular NAD pools. Using Western blot analyses and immunohistochemistry, it was found that the key enzyme leading to accumulation of quinolinic acid, 3-hydroxyanthranilate oxygenate (3-HAO), is expressed by tumor-infiltrating monocytes. Thus, infiltrating monocytes contribute to resistance to cytotoxic therapies in malignant gliomas. For details, see article by Sahm and colleagues on page 3225.
Cancer Research


73 (11)


Updated version Access the most recent version of this article at: http://cancerres.aacrjournals.org/content/73/11

E-mail alerts Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.