

# Contents

# Cancer Research

November 15, 2011 • Volume 71 • Number 22

## BREAKING ADVANCES

- 6913 | **Highlights from Recent Cancer Literature**

## REVIEWS

- 6915 | **Targeting Regulatory T Cells in Cancer**  
William L. Byrne, Kingston H.G. Mills, James A. Lederer, and Gerald C. O'Sullivan
- 6921 | **Lactate: A Metabolic Key Player in Cancer**  
Franziska Hirschhaeuser, Ulrike G.A. Sattler, and Wolfgang Mueller-Klieser

## MEETING REPORT

- 6926 | **From Mice and Men to Earth and Space: Joint NASA–NCI Workshop on Lung Cancer Risk Resulting from Space and Terrestrial Radiation**  
Jerry W. Shay, Francis A. Cucinotta, Frank M. Sulzman, C. Norman Coleman, and John D. Minna

## PRIORITY REPORTS

- 6930 | **c-MYC Functions as a Molecular Switch to Alter the Response of Human Mammary Epithelial Cells to Oncostatin M**  
Charlene E. Kan, Rocky Cipriano, and Mark W. Jackson
- Précis:* Among its many roles in cancer, c-MYC may also serve as a molecular switch of the character of the tumor microenvironment, as illustrated by its ability to convert responses to a proinflammatory factor from suppressive to supportive for tumor growth.
- 6940 | **A Comprehensive View of Nuclear Receptor Cancer Cistromes**  
Qianzi Tang, Yiwen Chen, Clifford Meyer, Tim Geistlinger, Mathieu Lupien, Qian Wang, Tao Liu, Yong Zhang, Myles Brown, and Xiaole Shirley Liu
- Précis:* Nuclear receptors are widely important in cancer and this database offering comprehensive cistrome, epigenome, and transcriptome data sets and downstream analysis offers a unique and valuable resource to the cancer research community.

## INTEGRATED SYSTEMS AND TECHNOLOGIES

- 6948 | **Metabolic Signatures Imaged in Cancer-Induced Cachexia**  
Marie-France Penet, Mayur M. Gadiya, Balaji Krishnamachary, Sridhar Nimmagadda, Martin G. Pomper, Dmitri Artemov, and Zaver M. Bhujwala
- Précis:* The development of therapeutic strategies to manage cachexia, a wasting disease that occurs in patients with aggressive cancer, particularly certain types such as pancreatic cancer, could benefit enormously from noninvasive imaging strategies to better understand what remains a poorly managed condition.
- 6957 | **Volumetric and Angiogenic Evaluation of Antitumor Effects with Acoustic Liposome and High-Frequency Ultrasound**  
Tetsuya Kodama, Noriko Tomita, Yoko Yagishita, Sachiko Horie, Kenichi Funamoto, Toshiyuki Hayase, Maya Sakamoto, and Shiro Mori
- Précis:* This article describes a noninvasive ultrasound-based in vivo imaging method that may be especially useful for preclinical studies of experimental therapeutics designed to target tumor angiogenesis.

## MICROENVIRONMENT AND IMMUNOLOGY

- 6965 | **Combined Blockade of Integrin- $\alpha 4\beta 1$  Plus Cytokines SDF-1 $\alpha$  or IL-1 $\beta$  Potently Inhibits Tumor Inflammation and Growth**  
Michael C. Schmid, Christie J. Avraamides, Philippe Foubert, Yuval Shaked, Sang Won Kang, Robert S. Kerbel, and Judith A. Varner
- Précis:* This study defines nodal modifier molecules in recruitment of myeloid cells into the inflammatory tumor microenvironment, where they are vital for tumor growth.



6976 **Chemotherapy Enhances Metastasis Formation via VEGFR-1-Expressing Endothelial Cells**

Laura G.M. Daenen, Jeanine M.L. Roodhart, Miranda van Amersfoort, Mantre Dehnad, Wijnand Roessingh, Laurien H. Ulfman, Patrick W.B. Derksen, and Emile E. Voest

*Précis: VEGFR-1 upregulation promotes metastasis induced by chemotherapy, suggesting that in combination with traditional chemotherapy anti-VEGFR-1 treatment may augment antimetastatic responses.*

6986 **Host Response to Short-term, Single-Agent Chemotherapy Induces Matrix Metalloproteinase-9 Expression and Accelerates Metastasis in Mice**

Svetlana Gingis-Velitski, David Loven, Liat Benayoun, Michal Munster, Rotem Bril, Tali Voloshin, Dror Alishekevitz, Francesco Bertolini, and Yuval Shaked

*Précis: Cytotoxic chemotherapy may be beneficial to patients in the short term, but it carries inherent risks of worsening subsequent relapses due to the mobilization of bone marrow-derived cells that promote metastasis.*

6997 **Chemotherapy Induces Intratumoral Expression of Chemokines in Cutaneous Melanoma, Favoring T-cell Infiltration and Tumor Control**

Michelle Hong, Anne-Laure Puaux, Caleb Huang, Laure Loumagne, Charlene Tow, Charles Mackay, Masashi Kato, Armelle Prévost-Blondel, Marie-Françoise Avril, Alessandra Nardin, and Jean-Pierre Abastado

*Précis: Accumulating evidence shows that many benefits of chemotherapy relate to its ability to weaken immune escape and restore active tumor immunity, as illustrated by these results concerning how chemotherapy improves T-cell infiltration in cutaneous melanomas.*

7010 **ANGPTL4 Induction by Prostaglandin E<sub>2</sub> under Hypoxic Conditions Promotes Colorectal Cancer Progression**

Sun-Hee Kim, Yun-Yong Park, Sang-Wook Kim, Ju-Seog Lee, Dingzhi Wang, and Raymond N. DuBois

*Précis: A central mediator of inflammation in the tumor microenvironment acts in the context of hypoxia to drive progression in colon cancer, with potential implications for understanding why COX2 inhibitors help prevent this disease.*

7021 **Tumor-Surrogate Blood Vessel Subtypes Exhibit Differential Susceptibility to Anti-VEGF Therapy**

Basel Sitohy, Janice A. Nagy, Shou-Ching Shih Jaminet, and Harold F. Dvorak

*Précis: Anti-VEGF therapies preferentially antagonize less mature blood vessels, with important implications for understanding the limited effectiveness of these therapies in human tumors where blood vessels that develop independently of tumor-secreted VEGF may predominate.*

## MOLECULAR AND CELLULAR PATHOBIOLOGY

7029 **MYB Is Essential for Mammary Tumorigenesis**

Rebecca Yu Miao, Yvette Drabsch, Ryan Stanley Cross, Dane Cheasley, Sandra Carpinteri, Lloyd Pereira, Jordane Malaterre, Thomas J. Gonda, Robin L. Anderson, and Robert G. Ramsay

*Précis: The MYB oncogene has been widely studied in blood cancers, but the importance of its function in solid tumors including breast cancers where MYB is often elevated has not been known.*

7038 **p53 Negatively Regulates the Hepatoma Growth Factor HDGF**

Yasushi Sasaki, Hideaki Negishi, Masashi Idogawa, Ikuko Yokota, Ryota Koyama, Masanobu Kusano, Hiromu Suzuki, Masahiro Fujita, Reo Maruyama, Minoru Toyota, Tsuyoshi Saito, and Takashi Tokino

*Précis: Tumor suppressor genes may exert a significant part of their activity by regulating autocrine and paracrine growth factor pathways, as illustrated in this study which reveals how the transcriptional repression function of p53 mediates cancer cell growth and migration.*

7048 **Increased Skin Papilloma Formation in Mice Lacking Glutathione Transferase GSTP**

Colin J. Henderson, Kenneth J. Ritchie, Aileen McLaren, Probir Chakravarty, and C. Roland Wolf

*Précis: Glutathione transferase GstP may play a major role in carcinogenesis distinct from its role in detoxification, apparently as a key determinant of the proinflammatory tumor environment.*

7061 | **Sonic Hedgehog Pathway Promotes Metastasis and Lymphangiogenesis via Activation of Akt, EMT, and MMP-9 Pathway in Gastric Cancer**

Young A. Yoo, Myoung Hee Kang, Hyun Joo Lee, Baek-hui Kim, Jong Kuk Park, Hyun Koo Kim, Jun Suk Kim, and Sang Cheul Oh

*Précis:* Findings define a role for a major developmental pathway that activates cell migration in invasive and metastatic forms of gastric cancer, highlighting this pathway as a potential therapeutic target in this setting.

7103 | **Decreased Lymphangiogenesis and Lymph Node Metastasis by mTOR Inhibition in Head and Neck Cancer**

Vyomesh Patel, Christina A. Marsh, Robert T. Dorsam, Constantinos M. Mikelis, Andrius Masedunskas, Panomwat Amornphimoltham, Cherie Ann Nathan, Bhuvanesh Singh, Roberto Weigert, Alfredo A. Molinolo, and J. Silvio Gutkind

*Précis:* Findings rationalize future clinical evaluation of mTOR inhibitors as a strategy to prevent metastasis in head and neck cancers, an aggressive form of cancer with a rapidly rising incidence.

## THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

7071 | **p53 Modulates Acquired Resistance to EGFR Inhibitors and Radiation**

Shyhmin Huang, Sergio Benavente, Eric A. Armstrong, Chunrong Li, Deric L. Wheeler, and Paul M. Harari

*Précis:* Findings identify a central role of p53 in the development of acquired resistance to EGFR inhibitors, stimulating interest in applying p53 restoration strategies in treatment regimens that incorporate EGFR inhibitors and radiation.

7080 | **Epithelial Junction Opener JO-1 Improves Monoclonal Antibody Therapy of Cancer**

Ines Beyer, Ruan van Rensburg, Robert Strauss, ZongYi Li, Hongjie Wang, Jonas Persson, Roma Yumul, Qinghua Feng, Hui Song, Jiri Bartek, Pascal Fender, and André Lieber

*Précis:* An adenoviral protein that loosens tumor epithelial cell junctions can dramatically increase tumor exposure and antitumor efficacy of therapeutic monoclonal antibodies, permitting tumor eradication in preclinical mouse models.

7113 | **Tyrosine Isomers Mediate the Classical Phenomenon of Concomitant Tumor Resistance**

Raúl A. Ruggiero, Juan Bruzzo, Paula Chiarella, Pedro di Gianni, Martín A. Isturiz, Susana Linskens, Norma Speziale, Roberto P. Meiss, Oscar D. Bustuoaabad, and Christiane D. Pasqualini

*Précis:* This seminal article addresses the long-standing question of why a tumor-bearing animal is often resistant to development of secondary tumors or metastases, a phenomenon known as concomitant tumor resistance, possibly offering a generalized nontoxic approach to block metastatic recurrences after resection and eradication of primary cancers, a pivotal problem for oncologists and their patients.

7125 | **EGFR-AKT-Smad Signaling Promotes Formation of Glioma Stem-like Cells and Tumor Angiogenesis by ID3-Driven Cytokine Induction**

Xun Jin, Jinlong Yin, Sung-Hak Kim, Young-Woo Sohn, Samuel Beck, Young Chang Lim, Do-Hyun Nam, Yun-Jaie Choi, and Hyunggee Kim

*Précis:* A member of the ID gene family implicated in tumor angiogenesis is also important to mediate EGFR signals that promote stem-like cell characteristics in glioma, linking these two important processes during tumor progression.

## TUMOR AND STEM CELL BIOLOGY

7091 | **AGR2 Is a Novel Surface Antigen That Promotes the Dissemination of Pancreatic Cancer Cells through Regulation of Cathepsins B and D**

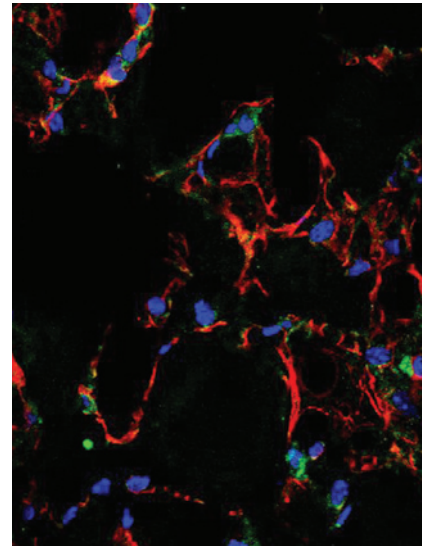
Laurent Dumartin, Hannah J. Whiteman, Mark E. Weeks, Deepak Hariharan, Branko Dmitrovic, Christine A. Iacobuzio-Donahue, Teresa A. Brentnall, Mary P. Bronner, Roger M. Feakins, John F. Timms, Caroline Brennan, Nicholas R. Lemoine, and Tatjana Crnogorac-Jurcevic

*Précis:* A prometastatic protein expressed on the cell surface of aggressive pancreatic cancers has features of an appealing theranostic target to improve management of this disease.

---

## ABOUT THE COVER

Pretreating mice with chemotherapy can enhance metastasis formation in the lungs of mice. Daenen and colleagues and Gingis-Velitski and colleagues report that chemotherapy has effects on the microenvironment that account for these protumorigenic effects. Expression of vascular endothelial growth factor receptor 1 (VEGFR-1) is enhanced on a subset of endothelial cells in the lungs of mice following chemotherapy exposure. On the cover, mouse lung endothelial cells after cisplatin pretreatment are shown, characterized by CD31 expression (red) and VEGFR-1 expression (green). Knowledge of the host effects induced by chemotherapy may facilitate strategies to improve therapy efficacy. For details, see the article by Daenen and colleagues on page 6976 and the article by Gingis-Velitski and colleagues on page 6986 of this issue.



# Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

## 71 (22)

*Cancer Res* 2011;71:6913-7134.

**Updated version** Access the most recent version of this article at:  
<http://cancerres.aacrjournals.org/content/71/22>

**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](mailto:pubs@aacr.org).

**Permissions** To request permission to re-use all or part of this article, use this link <http://cancerres.aacrjournals.org/content/71/22>.  
Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.