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**Précis:**

- Highlights from Recent Cancer Literature
- Hedgehog Fights Back: Mechanisms of Acquired Resistance against Smoothened Antagonists
- Chemotherapeutic Resistance: Surviving Stressful Situations
- Combinatorial Treatments That Overcome PDGFRb-Driven Resistance of Melanoma Cells to V600E-RAF Inhibition
- Mechanical Stiffness Grades Metastatic Potential in Patient Tumor Cells and in Cancer Cell Lines
- Tumor Microenvironment–Derived Proteins Dominate the Plasma Proteome Response during Breast Cancer Induction and Progression
- Myeloid-Derived Suppressor Cell Inhibition of the IFN Response in Tumor-Bearing Mice

**Contents**

Cancer Research
August 1, 2011 • Volume 71 • Number 15

A Journal of the American Association for Cancer Research www.aacrjournals.org
PD-1/PD-L1 Interactions Contribute to Functional T-Cell Impairment in Patients Who Relapse with Cancer After Allogeneic Stem Cell Transplantation


Précis: Findings show how leukemia cells can escape from graft-versus-tumor immune responses, and how interfering with this escape mechanism can restore antitumor immunity and possibly prevent relapses.

Systemic Cancer Therapy with a Small Molecule Agonist of Toll-like Receptor 7 Can Be Improved by Circumventing TLR Tolerance

Carole Bourquin, Christian Hotz, Daniel Noerenberg, Andreas Voelkl, Simon Heidegger, Bettina Storch, Nadja Sandholzer, Cornelia Wurzenberger, David Anz, and Stefan Endres

Précis: Findings offer insight into a cellular mechanism of immune tolerance that occurs during cancer immunotherapy with a Toll-like receptor agonist and provide a strategy to bypass this tolerance.

Antibody-Dependent Cell Cytotoxicity Synapses Form in Mice during Tumor-Specific Antibody Immunotherapy

Pascale Hubert, Adèle Heitzmann, Sophie Viel, André Nicolas, Xavier Sastre-Garau, Pablo Oppezzo, Otto Pritsch, Eduardo Osinaga, and Sebastien Amigorena

Précis: Findings demonstrate that a therapeutic monoclonal antibody specific for a ubiquitous tumor-associated antigen inhibits tumor growth via antibody-dependent cell toxicity.

Inhibition of miR-193a Expression by Max and RXRa Activates K-Ras and PLAU to Mediate Distinct Aspects of Cellular Transformation

Dimitrios Iliopoulos, Asaf Rotem, and Kevin Struhl

Précis: Findings describe a molecular pathway involved in cellular transformation that focuses on miR-193a as a regulator of both tumorigenicity and invasiveness.

IGFBP-3 Is a Metastasis Suppression Gene in Prostate Cancer


Précis: This study reports the first transgenic mouse model of spontaneous metastatic prostate cancer, a milestone that may help advance studies of progression and treatment at this deadly late stage of disease.

18F-Fluorodeoxy-glucose Positron Emission Tomography Marks MYC-Overexpressing Human Basal-Like Breast Cancers

Nicolaos Palaskas, Steven M. Larson, Nikolaus Schultz, Evangelia Komisopoulou, Justin Wong, Dan Rohle, Carl Campos, Nicolas Yannuzzi, Joseph R. Osborne, Irina Linkov, Edward R. Kastenhuber, Richard Taschereau, Seema B. Plaisier, Chris Tran, Adriana Heguy, Hong Wu, Chris Sander, Michael E. Phelps, Cameron Brennan, Elisa Port, Jason T. Huse, Thomas G. Graeber, and Ingo K. Mellinghoff

Précis: FDG-PET may be useful as a noninvasive biomarker for therapies that target either the basal-like breast cancer subtype or MYC-overexpressing tumors that rely heavily upon glycolysis and the glutamine pathway.

Genetic Variation in an miRNA-1827 Binding Site in MYCL1 Alters Susceptibility to Small-Cell Lung Cancer

Fang Xiong, Chen Wu, Jiang Chang, Dianke Yu, Binghe Xu, Peng Yuan, Kan Zhai, Jian Xu, Wen Tan, and Dongxin Lin

Précis: Findings suggest a broader significance than appreciated previously for the L-MYC gene in development of small cell lung cancer.

Combining Betulinic Acid and Mithramycin A Effectively Suppresses Pancreatic Cancer by Inhibiting Proliferation, Invasion, and Angiogenesis

Yong Gao, Zhiliang Jia, Xiangyu Kong, Qiang Li, David Z. Chang, Daoyan Wei, Xiangdong Le, Shengdong Huang, Liwei Wang, Suyun Huang, and Keping Xie

Précis: Findings demonstrate that targeting the transcription factor Sp1 can inhibit pancreatic tumor growth with greater efficacy and fewer side effects than traditional treatment.
**BMP4 Promotes Prostate Tumor Growth in Bone through Osteogenesis**
Yu-Chen Lee, Chien-Jui Cheng, Mehmet A. Bilen, Jing-Fang Lu, Robert L. Satcher, Li-Yuan Yu-Lee, Gary E. Gallick, Sankar N. Maity, and Sue-Hwa Lin

*Précis:* Osteogenesis is shown to be necessary for prostate cancer progression in bone and inhibition of this process may offer a treatment strategy for bone metastases.

**Akt-Dependent Glucose Metabolism Promotes Mcl-1 Synthesis to Maintain Cell Survival and Resistance to Bcl-2 Inhibition**
Jonathan L. Coloff, Andrew N. Macintyre, Amanda G. Nichols, Tingyu Liu, Catherine A. Gallo, David R. Plas, and Jeffrey C. Rathmell

*Précis:* Inhibition of glucose metabolism alters expression of a key Bcl-2 family member, sensitizing cancer cells to apoptosis and illustrating how strategies to disrupt glycolysis disruptions may disable tumors.

**MicroRNA Replacement Therapy for miR-145 and miR-33a Is Efficacious in a Model of Colon Carcinoma**
Ahmed Fawzy Ibrahim, Ulrike Weirauch, Maren Thomas, Arnold Grünweller, Roland K. Hartmann, and Achim Aigner

*Précis:* This study establishes nonviral miRNA replacement therapy for cancer treatment.

**Combined Gene Expression Profiling and RNAi Screening in Clear Cell Renal Cell Carcinoma Identify PLK1 and Other Therapeutic Kinase Targets**
Yan Ding, Dan Huang, Zhongfa Zhang, Josh Smith, David Petillo, Brendan D. Looyenga, Kristin Feenstra, Jeffrey P. MacKeigan, Kyle A. Furge, andBin T. Teh

*Précis:* RNAi screening and gene expression profiling reveal new potential therapeutic targets to treat highly aggressive kidney cancers.

**Exosome Targeting of Tumor Antigens Expressed by Cancer Vaccines Can Improve Antigen Immunogenicity and Therapeutic Efficacy**
Ryan B. Bountree, Stefanie J. Mandl, James M. Nachtwey, Katie Dalpozzo, Lisa Do, John R. Lombardo, Peter L. Schoonmaker, Kay Brinkmann, Ulrike Dirmeier, Reiner Lau, and Alain Delcayre

*Précis:* This study shows how engineering the MVA-BN-PRO vaccine to express its antigens in secreted exosomes could greatly improve its immunotherapeutic activity.

**Retinoic Acid Enhances TRAIL-Induced Apoptosis in Cancer Cells by Upregulating TRAIL Receptor 1 Expression**
Latha Dhandapani, Ping Yue, Suresh S. Ramalingam, Fadlo R. Khuri, and Shi-Yong Sun

*Précis:* By establishing that retinoic acid can stimulate the proapoptotic activity of TRAIL by upregulating the TRAIL receptor DR4, this study suggests a strategy to augment the anticancer activity of TRAIL being studied in clinical trials.

**A Drug Resistance Screen Using a Selective MET Inhibitor Reveals a Spectrum of Mutations That Partially Overlap with Activating Mutations Found in Cancer Patients**
Ralph Tiedt, Elisa Degenkolbe, Pascal Furet, Brent A. Appleton, Sabrina Wagner, Joseph Schoepfer, Emily Buck, David A. Buddy, John E. Monahan, Michael D. Jones, Jutta Blank, Dorothea Haasen, Peter Drueckes, Markus Wartmann, Clive McCarthy, William R. Sellers, and Francesco Hofmann

*Précis:* Drug resistance mutation profiles reported in this manuscript are likely to predict clinical responses to MET kinase inhibitors, a number of which are currently in development.

**Overcoming Hypoxia-Induced Apoptotic Resistance through Combinatorial Inhibition of GSK-3β and CDK1**

*Précis:* Findings elucidate a novel therapeutic strategy to overcome the inherent resistance of hypoxic cancer cells to cell death, by targeting two kinases not previously linked to cell death protection in hypoxic tumor microenvironments.
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<td>\textbf{Précis:} Supporting applications of vitamin D as a chemopreventative agent for prostate cancer, this study shows that the metabolically active form of vitamin D can induce differentiation and senescence of prostate progenitor/stem cells and that its antiproliferative effects rely upon interleukin-1 alpha.</td>
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5357 MicroRNA Expression and Outcome in Resected NSCLC—Letter
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5358 MicroRNA Expression and Outcome in Resected NSCLC—Response
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CORRECTIONS

5360 Correction: Effects of Carbon Ion Beam on Putative Colon Cancer Stem Cells and Its Comparison with X-rays

5361 Correction: A Requirement of STAT3 DNA Binding Precludes Th-1 Immunostimulatory Gene Expression by NF-κB in Tumors

ABOUT THE COVER

The search for biomarkers of cancer has focused on the tumor cells themselves. Pitteri and colleagues, using an unbiased and in depth proteomic analysis of plasma from a model of Her2/neu driven breast cancer, have identified the signaling between the tumor cells and microenvironment as a primary source of biomarkers. Shown are tumor cells embedded within extensive extracellular collagen matrix stained with trichrome blue. For details, see the article by Pitteri and colleagues on page 5090 of this issue.

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