ABERRANT LIPID METABOLISM IN HEPATOCELLULAR CARCINOMA REVEALED BY PLASMA METABOLOMICS AND LIPID PROFILING
Andrew D. Patterson, Olivier Maurhofer, Diren Beyoglu, Christian Lanz, Kristopher W. Krausz, Thomas Pabst, Frank J. Gonzalez, Jean-François Dufour, and Jeffrey R. Idle

Précis: A sophisticated set of metabolomic discovery platforms were employed in this study to define plasma markers of intermediate-stage hepatocellular carcinoma, revealing a number of new molecular alterations and illustrating the potential of this technology for developing pathophysiological understanding and discovering informative diagnostics.

ANTIANGIOGENIC AND ANTIMETASTATIC ACTIVITY OF JAK INHIBITOR AZD1480
Hong Xin, Andreas Herrmann, Karen Reckamp, Wang Zhang, Sumanta Pal, Michael Hedvat, Chunyan Zhang, Wei Liang, Anna Scuto, Shaobu Weng, Deborah Morosini, Zhi A. Cao, Michael Zinda, Robert Figlin, Dennis Huszar, Richard Jove, and Hua Yu

Précis: JAK inhibitors in clinical development effectively inhibit tumor angiogenesis and metastasis mediated by STAT3 in tumor stromal cells as well as tumor cells themselves, encouraging their broader evaluation for cancer treatment than only in malignancies characterized by JAK/STAT mutations.

TARGETING THE IMMUNOREGULATOR SRA/CD204 POTENTIATES SPECIFIC DENDRITIC CELL VACCINE-INDUCED T-CELL RESPONSE AND ANTIMETASTATIC IMMUNITY
Huanfa Yi, Chunqing Guo, Xiaofei Yu, Ping Gao, Jie Qian, Daming Zuo, Masoud H. Manjili, Paul B. Fisher, John R. Subjeck, and Xiang-Yang Wang

Précis: Findings offer a straightforward strategy to enhance the potency of dendritic cell vaccines, for which Provenge is the first FDA-approved example, by targeting a pattern recognition scavenger receptor that limits the ability of dendritic cells to restore T-cell-mediated antitumor immunity.
Human Breast Tumor Cells Induce Self-Tolerance Mechanisms to Avoid NKG2D-Mediated and DXAM-Mediated NK Cell Recognition
Emilie Mamessier, Aude Sylvain, François Bertucci, Rémy Castellano, Pascal Finetti, Gilles Houvenaeghel, Emmanuelle Charaffe-Jauffret, Daniel Birnbaum, Alessandro Moretta, and Daniel Olive

MOLECULAR AND CELLULAR PATHOBIOLOGY

HB-EGF and PDGF Mediate Reciprocal Interactions of Carcinoma Cells with Cancer-Associated Fibroblasts to Support Progression of Uterine Cervical Cancers
Takuya Murata, Hiroto Mizushima, Ichino Chinen, Hiroki Moribe, Shigeo Yagi, Robert M. Hoffman, Tadashi Kimura, Kiyoshi Yoshino, Yutaka Ueda, Takayuki Enomoto, and Eisuke Mekada

Human Cytomegalovirus US28 Found in Glioblastoma Promotes an Invasive and Angiogenic Phenotype
Liliana Soroceanu, Lisa Matlaf, Vladimir Bezrookove, Loui Harkins, Roxanne Martinez, Mary Greene, Patricia Soteropoulos, and Charles S. Cobbs

SIRT1 Is Essential for Oncogenic Signaling by Estrogen/Estrogen Receptor α in Breast Cancer
Selvakumar Elangovan, Sabarish Ramachandran, Narayanan Venkatesan, Sudha Ananth, Jaya P. Gnanai Prakasam, Pamela M. Martin, Darren D. Browning, Patricia V. Schoenlein, Purtur D. Prasad, Vadivel Ganapathy, and Muthusamy Thangaraju

Progression of Human Bronchioloalveolar Carcinoma to Invasive Adenocarcinoma Is Modeled in a Transgenic Mouse Model of K-ras–Induced Lung Cancer by Loss of the TGF-β Type II Receptor
Alain C. Borczuk, Marieta Sole, Ping Lu, Jini Li, May-Lin Wilgus, Richard A. Friedman, Steven M. Albelda, and Charles A. Powell

Plasminogen Receptor S100A10 Is Essential for the Migration of Tumor-Promoting Macrophages into Tumor Sites
Kyle D. Phipps, Alexi P. Surette, Paul A. O’Connell, and David M. Waisman

Manganese Superoxide Dismutase Is a p53-Regulated Gene That Switches Cancers between Early and Advanced Stages
Sanjit K. Dhar, Jitbanjong Tangpong, Luksana Chaiswing, Terry D. Oberley, and Daret K. St. Clair
A Novel MLL5 Isoform That Is Essential to Activate E6 and E7 Transcription in HPV16/18-Associated Cervical Cancers
Chow Weny Yew, Pei Lee, Wai Keong Chan, Vania Kai Jun Lim, Sun Kuie Tay, Theresa M.C. Tan, and Lih-Wen Deng

RNA Helicase DDX5 Is a p53-Independent Target of ARF That Participates in Ribosome Biogenesis

ARID1A, a Factor That Promotes Formation of SWI/SNF-Mediated Chromatin Remodeling, Is a Tumor Suppressor in Gynecologic Cancers
Bin Guan, Tian-Li Wang, and Ie-Ming Shih

An Iron Regulatory Gene Signature Predicts Outcome in Breast Cancer
Lance D. Miller, Lan G. Coffman, Jeff W. Chou, Michael A. Black, Jonas Bergh, Ralph D'Agostino Jr, Suzy V. Torti, and Frank M. Torti

Definition of a FoxA1 Cistrome That Is Crucial for Gj to S-Phase Cell-Cycle Transit in Castration-Resistant Prostate Cancer

Prevention and Epidemiology

Urinary Levels of Cigarette Smoke Constituent Metabolites Are Prospectively Associated with Lung Cancer Development in Smokers
Jian-Min Yuan, Yu-Tang Gao, Sharon E. Murphy, Steven G. Carmella, Renwei Wang, Yan Zhong, Kristin A. Moy, Andrew B. Davis, Li Tao, Menglan Chen, Shaomei Han, Heather H. Nelson, Mimi C. Yu, and Stephen S. Hecht

Shorter Telomeres Associate with a Reduced Risk of Melanoma
Hongmei Nan, Mengmeng Du, Immaculata De Vivo, JoAnn E. Manson, Simin Liu, Anne McTiernan, J. David Curb, Lawrence S. Lessin, Matthew R. Bonner, Qun Guo, Abrar A. Qureshi, David J. Hunter, and Jiali Han

Therapeutics, Targets, and Chemical Biology

Itraconazole Inhibits Angiogenesis and Tumor Growth in Non–Small Cell Lung Cancer
Blake T. Aftab, Irina Dobromilskaya, Jun O. Liu, and Charles M. Rudin

A Kinome-Wide Screen Identifies the Insulin/IGF-1 Receptor Pathway as a Mechanism of Escape from Hormone Dependence in Breast Cancer
Emily M. Fox, Todd W. Müller, Justin M. Balko, Maria G. Kuba, Violeta Sánchez, R. Adam Smith, Shuying Liu, Ana Maria González-Angulo, Gordon B. Mills, Fei Ye, Yu Shyr, H. Charles Manning, Elizabeth Buck, and Carlos L. Arteaga

Preąę: This study reports the discovery of a molecule exclusively expressed in HPV-associated cervical cancers, where it may offer a novel and disease-selective therapeutic target and biomarker.

Preąę: This study offers an answer to the longstanding question of how the tumor suppressor ARF inhibits ribosome biogenesis, which does not involve p53 but is essential to prevent Ras-induced cell transformation.

Preąę: This study identifies a link between genes that govern iron metabolism and breast cancer prognosis, and suggests new tools that may ultimately help guide breast cancer prognosis.

Preąę: The oral antifungal drug itraconazole demonstrates antiangiogenic efficacy in relevant tumor models of non-small cell lung cancer and is currently being tested in a phase II clinical trial of lung cancer patients.

Preąę: Clinical strategies to prevent ER+ breast cancers from escaping estrogen deprivation therapies are important to identify, because they could limit risks of progression to ER- cancers that are far more difficult to manage.
### Expression and Immunotherapeutic Targeting of the SSX Family of Cancer–Testis Antigens in Prostate Cancer
Heath A. Smith, Robert J. Cronk, Joshua M. Lang, and Douglas G. McNeel

**Précis:** Exclusive expression of a set of antigens expressed only in testis and metastatic prostate cancer may offer attractive targets for immunotherapy.

### 2-Deoxyglucose Induces Noxa-Dependent Apoptosis in Alveolar Rhabdomyosarcoma
Silvia Ramírez-Peinado, Fermín Alcázar-Limones, Laura Lagares-Tena, Nadia El Mijiad, Alfredo Caro-Maldonado, Oscar M. Tirado, and Cristina Muñoz-Pinedo

**Précis:** An aggressive pediatric muscle tumor was discovered to be highly sensitive to a glycolytic inhibitor similar to one used widely in the oncology clinic for PET imaging, suggesting it might be immediately repositioned as a therapeutic to treat what is often a fatal childhood cancer.

### Verticillin A Overcomes Apoptosis Resistance in Human Colon Carcinoma through DNA Methylation-Dependent Upregulation of BNIP3
Feiyan Liu, Qianqian Liu, Dafeng Yang, Wendy B. Bollag, Keith Robertson, Ping Wu, and Kebin Liu

**Précis:** To combat drug resistance, the primary cause of deaths from cancer, one top goal of laboratory research is to identify adjuvants that can safely and effectively cooperate with existing treatments to widen their therapeutic window of action.

### Inhibition of Neurotensin Receptor 1 Selectively Sensitizes Prostate Cancer to Ionizing Radiation
Nicholas C.K. Valerie, Eli V. Casarez, John O. DaSilva, Marya E. Dunlap-Brown, Sarah J. Parsons, George P. Amorino, and Jaroslaw Dziegielewski

**Précis:** A receptor that is absent from normal prostate cells, but switched on in prostate cancers, offers a therapeutic target for radiosensitizing this malignancy.

### Cell-Cycle Regulator Cks1 Promotes Hepatocellular Carcinoma by Supporting NF-κB-Dependent Expression of Interleukin-8
Eun-Kyung Lee, Dae-Ghon Kim, Jang-Seong Kim, and Yeup Yoon

**Précis:** Findings link an important cell cycle regulator to NF-κB control of a central regulator of the inflammatory tumor microenvironment, illustrating how the cell division processes of cancer cells are perhaps invariably linked to their coordination of local immune support.

### A NOTCH3-Mediated Squamous Cell Differentiation Program Limits Expansion of EMT-Competent Cells That Express the ZEB Transcription Factors

**Précis:** Novel insights into the progression of a class of esophageal cancers rising rapidly in incidence are provided by this mechanistic study of how Notch3 receptor signaling acts to prevent expansion of aggressive clones that can emerge during tumorigenesis.

### Generation of a Mouse Model of Von Hippel–Lindau Kidney Disease Leading to Renal Cancers by Expression of a Constitutively Active Mutant of HIF1α
Leiping Fu, Gang Wang, Maria M. Shevchuk, David M. Nanus, and Lorraine J. Gudas

**Précis:** This study describes a new transgenic mouse model for von Hippel-Lindau (VHL) kidney disease that mimics the genetic and molecular events leading to human renal cell carcinoma.

### Breast Cancer Subtype-Specific Interactions with the Microenvironment Dictate Mechanisms of Invasion
Tuyen T. Dang, Amanda M. Precht1, and Gray W. Pearson

**Précis:** Real-time imaging of tumor-fibroblast interactions in breast cancer suggests how interactions with the microenvironment control malignant progression, and also how basal and luminal subtypes of breast cancer do not progress in the same way.
Tumor growth is a complex process involving the interaction of various signaling pathways. In this study, the TNF-α receptor promotes c-REL/ΔNp63α interaction and TAp73 dissociation from key genes that mediate growth arrest and apoptosis in head and neck cancer. This indicates a mechanism by which inflammatory signals can affect tumor suppressor functions in cancer cells, as illustrated by the study of how TNF-β and the NF-κB oncoprotein c-REL repress the antiproliferative and proapoptotic activities of ΔNp63-bound p73 in cancer cells harboring mutant p53.

**Précis**: Inflammatory signals in the tumor microenvironment can attenuate tumor suppressor functions in cancer cells, as illustrated by this study of how TNF-β and the NF-κB oncoprotein c-REL repress the antiproliferative and proapoptotic activities of ΔNp63-bound p73 in cancer cells harboring mutant p53.

**FOXO3a-Dependent Mechanism of E1A-Induced Chemosensitization**

By providing a leap forward in understanding how the adenovirus oncoprotein E1A sensitizes cancer cells to paclitaxel, this study provides a strong mechanistic rationale to use E1A gene therapy which has been tested clinically as an adjuvant to chemosensitize cancers to this widely used antimitotic drug.

**Précis**: By providing a leap forward in understanding how the adenovirus oncoprotein E1A sensitizes cancer cells to paclitaxel, this study provides a strong mechanistic rationale to use E1A gene therapy which has been tested clinically as an adjuvant to chemosensitize cancers to this widely used antimitotic drug.

**PGC1α Promotes Tumor Growth by Inducing Gene Expression Programs Supporting Lipogenesis**

Kavita Bhalla, Bor Jang Hwang, Ruby E. Dewi, Lihui Ou, William Twaddel, Hong-bin Fang, Scott B. Vafai, Francesca Vazquez, Pere Puigserver, Laszlo Boros, and Geoffrey D. Gimnun

**Précis**: Results show how a central regulator of energy metabolism controls multiple metabolic pathways to drive carcinogenesis and cancer growth.

**Binding of the JmjC Demethylase JARID1B to LSD1/NuRD Suppresses Angiogenesis and Metastasis in Breast Cancer Cells by Repressing Chemokine CCL14**

Qian Li, Lei Shi, Bin Gui, Wenhua Yu, Jianlu Wang, Di Zhang, Xiao Han, Zhi Yao, and Yongfeng Shang

**Précis**: Findings define a novel pharmaceutically tractable target that is part of an important transcriptional repression complex broadly implicated in malignant progression.

**OBITUARY**

**On the Passing of Gerald C. Mueller, MD, PhD (1920–2010)**

**CORRECTIONS**

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

**Correction**: Online Publication Date for *Cancer Research* September 1, 2011, Article

**ABOUT THE COVER**

Macrophages play a key role in tumor growth, invasion, and metastasis. Phipps and colleagues identified the mechanism that controls the migration of macrophages to the tumor site. They showed that the generation of plasmin at the cell surface of the macrophage is regulated by the plasminogen receptor S100A10, and that S100A10-regulated plasmin generation is necessary for both the movement of the macrophages to the tumor site and tumor growth and vascularization. The photomicrograph shows that the vascular density, monitored by CD31 immunofluorescence (green), of Lewis lung carcinoma tumors grown in S100A10-null mice can be restored by the adoptive transfer of wild-type macrophages. For details, see the article by Phipps and colleagues on page 6676 of this issue.
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