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6583  Oxygen Is a Master Regulator of the Immunogenicity of Primary Human Glioma Cells

Précis: The efficacy of hundreds of dendritic cell vaccines currently in clinical development might be improved dramatically simply by reducing the oxygen level in tumor cell cultures that are used as source of antigens to prime the vaccine.

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6590  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.

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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.

6611  Targeting the Immunoregulator SRA/CD204 Potentiates Specific Dendritic Cell Vaccine-Induced T-cell Response and Antitumor Immunity
Huana 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.
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**HB-EGF and PDGF Mediate Reciprocal Interactions of Carcinoma Cells with Cancer-Associated Fibroblasts to Support Progression of Uterine Cervical Cancers**  
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**Précis:** Findings define two central drivers of the reciprocal master-slave relationship created between cancer cells and cancer-associated fibroblasts in the tumor microenvironment.

**6643**  
**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  
**Précis:** Human cytomegalovirus infections that occur commonly in deadly brain glioblastomas may be contributing strongly to the aggressive progression which characterizes this disease, through expression of a viral G protein-like coupled receptor that can be therapeutically targeted.

**6654**  
**SIRT1 Is Essential for Oncogenic Signaling by Estrogen/Estrogen Receptor α in Breast Cancer**  
Selvakumar Elangovan, Sabarish Ramachandran, Narayanan Venkatesan, Sudha Ananth, Jaya P. Gnanaprakasam, Pamela M. Martin, Darren D. Browning, Patricia V. Schoenlein, Purtur D. Prasad, Vadivel Ganapathy, and Muthusamy Thangaraju  
**Précis:** Small molecule inhibitors of the histone deacetylase SIRT1 presently in clinical development may find an important application in potentiating the beneficial effects of antiestrogen treatments in breast cancer.

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**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, Jinli Chen, May-Lin Wilgus, Richard A. Friedman, Steven M. Albelda, and Charles A. Powell  
**Précis:** The important new model of lung cancer progression reported in this study recapitulates the genomics and clinical progression of human lung adenocarcinoma, also highlighting its control by an important TGF-β receptor.

**6676**  
**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  
**Précis:** This important study reveals a pivotal signaling node in cancer progression by demonstrating that the receptor for plasminogen, a key regulator of blood coagulation and metastasis, is essential for migration of tumor-promoting macrophages into tumor sites.

**6684**  
**Manganese Superoxide Dismutase Is a p53-Regulated Gene That Switches Cancers between Early and Advanced Stages**  
Sanjit K. Dhar, Jithanjong Tangpong, Luksana Chaiswing, Terry D. Oberley, and Daret K. St. Clair  
**Précis:** This study reports a novel genetic model of skin carcinogenesis that reveals the importance of a linkage between ROS scavenging networks and cellular stress responses involving p53.
A Journal of the American Association for Cancer Research v www.aacrjournals.org

Definition of a FoxA1 Cistrome That Is Crucial for G1 to S-Phase Cell-Cycle Transit in Castration-Resistant Prostate Cancer

PREVENTION AND EPIDEMIOLOGY

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

ThERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

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

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, Shaoemei Han, Heather H. Nelson, Mimi C. Yu, and Stephen S. Hecht

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Hongmei Nan, Mengmeng Du, Immaculata De Vivo, JoAnn E. Manson, Simin Liu, Anne McTiernan, J. David Curb, Lawrence S. Lessin, Matthew B. Bonner, Qun Guo, Abrar A. Qureshi, David J. Hunter, and Jiali Han

Itraconazole Inhibits Angiogenesis and Tumor Growth in Non–Small Cell Lung Cancer
Blake T. Aftab, Irina Dobromilskaya, Jun Q. 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. Miller, Justin M. Balko, Maria G. Kuba, Violeta Sanchez, R. Adam Smith, Shuying Liu, Ana Maria Gonzalez-Angulo, Gordon B. Mills, Fei Ye, Yu Shyr, H. Charles Manning, Elizabeth Buck, and Carlos L. Arteaga

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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 Mijiyad, 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-Kyoun 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. Prechtl, 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.
TNF-α Promotes c-REL/ΔNp63α Interaction and TAp73 Dissociation from Key Genes That Mediate Growth Arrest and Apoptosis in Head and Neck Cancer
Hai Lu, Xinping Yang, Praveen Duggal, Clint T. Allen, Bin Yan, Jonah Cohen, Liesl Nottingham, Rose-Anne Romano, Satrajit Sinha, Kathryn E. King, Wendy C. Weinberg, Zhong Chen, and Carter Van Waes

Precis: 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 EIA-Induced Chemosensitization
Jen-Liang Su, Xiaoyun Cheng, Hirohito Yamaguchi, Yi-Wen Chang, Chao-Feng Hou, Dung-Fang Lee, How-Wen Ko, Kuo-Tai Hua, Ying-Nai Wang, Michael Hsiao, Po-Shen B. Chen, Jung-Mao Hsu, Robert C. Bast, Jr, Gabriel N. Hortobagyi, and Mien-Chie Hung

Precis: 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 antimitic 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. Vafaiz, Francesca Vazquez, Pere Puigserver, Laszlo Boros, and Geoffrey D. Gifun

Precis: 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, Jiamu Wang, Di Zhang, Xiao Han, Zhi Yao, and Yongfeng Shang

Precis: Findings define a novel pharmacetically 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.
Cancer Research

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