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.
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, GillesHouvenaeghel, EmmanuelleCharaffe-Jauffret, Daniel Birnbaum, Alessandro Moretta, and Daniel Olive
Précis: All breast cancer subtypes develop mechanisms to escape natural killer cell–mediated immune recognition, rationalizing the development of immunotherapies that can relieve escape and/or enhance natural killer cell function.

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, TakayukiEnomoto, and EisukeMekada
Précis: Findings define two central drivers of the reciprocal master-slave relationship created between cancer cells and cancer-associated fibroblasts in the tumor microenvironment.

Human Cytomegalovirus US28 Found in Glioblastoma Promotes an Invasive and Angiogenic Phenotype
LilianaSoroceanu, LisaMatlaf, VladimirBezrookove, LouiHarkins, RoxanneMartinez, MaryGreene, PatriciaSoteropoulos, 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.

SIRT1 Is Essential for Oncogenic Signaling by Estrogen/Estrogen Receptor α in Breast Cancer
Selvakumar Elangovan, SabarishRamachandran, NarayananVenkatesan, SudhaAnanth, Jaya P. Gnana-Prakasam, Pamela M. Martin, Darren D. Browning, Patricia V. Schoeienlein, Putter 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.

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, MarietaSole, PingLu, JinliChen, May-LinWilgus, Richard A. Friedman, Steven M. Albeda, 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.

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.

Manganese Superoxide Dismutase Is a p53-Regulated Gene That Switches Cancers between Early and Advanced Stages
Sanjit K. Dhar, JitbanjongTangpong, LuksanaChaiswing, 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 Novel MLL5 Isoform That Is Essential to Activate E6 and E7 Transcription in HPV16/18-Associated Cervical Cancers
Chow Wenn Yew, Pei Lee, Wai Keong Chan, Vania Kai Jun Lim, Sun Kuie Tay, Theresa M.C. Tan, and Lih-Wen Deng

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

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

Précis: 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.

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 Le-Ming Shih

Précis: A member of the SWI/SNF chromatin remodeling complex is shown to be a tumor suppressor in the development of several types of gynecological cancers, suggesting that aberrant chromatin remodeling activity has a central role in their pathogenesis.

An Iron Regulatory Gene Signature Predicts Outcome in Breast Cancer

Précis: 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.

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

Précis: A Forkhead transcription factor controlling global chromatin structure is a pivotal organizer of G1-S cell cycle transit in castration-resistant prostate cancer.
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

Precis: 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

Precis: 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.

Verticill 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

Precis: 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

Precis: 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

Precis: 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

Precis: 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

Precis: 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

Precis: 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

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

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

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, Lihue Ou, William Twaddel, Hong-bin Fang, Scott B. Vafai, Francesca Vazquez, Pere Puigserver, Laszlo Boros, and Geoffrey D. Giriun

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, Jianmu 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)

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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