INTEGRATED SYSTEMS AND TECHNOLOGIES

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-Francois 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.

6601 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, Zhu 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.

MICROENVIRONMENT AND IMMUNOLOGY

6611 Targeting the Immunoregulator SRA/CD204 Potentiates Specific Dendritic Cell Vaccine-Induced T-cell Response and Antitumor 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 DNAM-Mediated NK Cell Recognition
Emilie Mamessier, Aule Sylvain, François Bertucci, Rémy Castellano, Pascal Finetti, Gilles Houveraeghel, Emmanuelle CHARAFFE-JAUFRET, Daniel Birnbaum, Alessandro Moretta, and Daniel Olive

Precis: 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.

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

Precis: 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
Liliana Soroceanu, Lisa Matlaf, Vladimir Bezrookove, Loui Harkins, Roxanne Martinez, Mary Greene, Patricia Soteropoulos, and Charles S. Cobbs

Precis: 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, Sabarish Ramachandran, Narayanan Venkatesan, Sudha Ananth, Jaya P. Gnana-Prakasam, Pamela M. Martin, Darren D. Browning, Patricia V. Schoenlein, Purtur D. Prasad, Vadivel Ganapathy, and Muthusamy Thangaraju

Precis: 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, Marieta Sole, Ping Lu, Jinli Chen, May-Lin Wilgus, Richard A. Friedman, Steven M. Albelda, and Charles A. Powell

Precis: 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

Precis: 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, Jitbanjong Tangpong, Luksana Chaiswing, Terry D. Oberley, and Daret K. St. Clair

Precis: 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

DEFINITION OF A FOXA1 CIStROME THAT IS CRUCIAL FOR G1 TO S-PHASE CELL-CYCLE TRANSIT IN CASTRATION-RESISTANT PROSTATE CANCER


Definition of a FOXA1 Cistrome That Is Crucial for G1 to S-Phase Cell-Cycle Transit in Castration-Resistant Prostate Cancer

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

RNA Helicase DDX5 IS A p53-Independent Target of ARF That Participates in Ribosome Biogenesis


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

P R E V E N T I O N A N D E P I D E M I O L O G Y

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

Metabolites of polycyclic aromatic hydrocarbon from cigarette smoke that appear in urine are independently associated with lung cancer risk, perhaps yielding a simple yet valuable monitoring tool in efforts to prevent lung cancer.

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

Findings challenge the traditional view that short telomeres are associated with increased risks of cancer, suggesting that telomeres have a unique role in the setting of cutaneous melanoma.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

ITRACONAZOLE INHIBITS ANGIOGENESIS AND TUMOR GROWTH IN NON–SMALL CELL LUNG CANCER

Blake T. Atia, Irina Dobromilskaya, Jun O. Liu, and Charles M. Rudin

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.

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 Sánchez-Angulo, Adam Smith, Shuying Liu, Ana Maria González-Angulo, Gordon B. Mills, Fei Ye, Yu Shyr, H. Charles Manning, Elizabeth Buck, and Carlos L. Arteaga

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

Precise: 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 Alcazar-Limones, Laura Lagares-Tena, Nadia El Mjiyad, Alfredo Caro-Maldonado, Oscar M. Tirado, and Cristina Muñoz-Pinedo

Precise: 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

Precise: 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

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

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 oncprotein 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

Precis: By providing a leap forward in understanding how the adenovirus oncprotein 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 Tweddell, Hong-bin Fang, Scott B. Vafa, Francesca Vazquez, Pere Puigserver, Laszlo Boros, and Geoffrey D. Gimnun.

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, Jiawu Wang, Di Zhang, Xiaoh Han, Zhi Yao, and Yongfeng Shang.

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

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.
Cancer Research

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