BREAKING ADVANCES

6107 Highlights from Recent Cancer Literature

REVIEW

6109 Monitoring of Natural Killer Cell Immunotherapy Using Noninvasive Imaging Modalities
Priyanka Jha, Daniel Golovko, Sukhmine Bains, Daniel Hostetter, Reinhard Meier, Michael F. Wendland, and Heike E. Daldrup-Link

6114 Cyclins, Cdk5, E2f, Skp2, and More at the First International RB Tumor Suppressor Meeting
Rod Bremner and Eldad Zacksenhaus

MEETING REPORT

6119 A Novel Imaging Approach for Early Detection of Prostate Cancer Based on Endogenous Zinc Sensing
Subrata K. Ghosh, Pilhan Kim, Xiao-an Zhang, Seok-Hyun Yun, Anna Moore, Stephen J. Lippard, and Zdravka Medarova

Précis: This paper illustrates how differences in zinc levels in normal and cancerous prostates can be exploited for purposes of non-invasive imaging, with the potential for rapid clinical translation.

MICROENVIRONMENT AND IMMUNOLOGY

6128 A Microfluidic Platform for Systems Pathology: Multiparameter Single-Cell Signaling Measurements of Clinical Brain Tumor Specimens

Précis: This study describes a microfluidic imaging technology that can enhance pathological analysis of tumor biopsies.

6139 Gr-1+CD11b+ Myeloid Cells Tip the Balance of Immune Protection to Tumor Promotion in the Premetastatic Lung
Hamnah H. Yan, Michael Pickup, Yanli Pang, Agnieszka E. Gorska, Zhaoyang Li, Anna Chytil, Yipeng Geng, Jerome W. Gray, Harold L. Moses, and Li Yang

Précis: Findings promote the concept that blocking the activity of myeloid derived suppressor cells could normalize the pre-metastatic lung environment, strengthening immune surveillance that prevents metastasis.

6150 Receptor Activator of NF-κB Ligand Enhances Breast Cancer--Induced Osteolytic Lesions through Upregulation of Extracellular Matrix Metalloproteinase Inducer/CD147
Nadia Rucci, Danilo Millimaggi, Marianna Mari, Andrea Del Fattore, Mauro Bologna, Anna Teti, Adriano Angelucci, and Vincenza Dolo

Précis: A cancer cell surface molecule plays a critical role in supporting breast cancer metastasis to bone, validating a target for therapeutic blockade of this process.
Antigen-Experienced CD4⁺ T Cells Limit Naive T-Cell Priming in Response to Therapeutic Vaccination In vivo
Chris Schiering, Jlenia Guarnerio, Veronica Basso, Luca Muzzio, and Anna Mondino
Précis: Results emphasize limitations imposed by tumor-primed CD4⁺ T lymphocytes that block the ability of cancer vaccines to generate immunogenicity.

Antiangiogenic Agents Can Increase Lymphocyte Infiltration into Tumor and Enhance the Effectiveness of Adoptive Immunotherapy of Cancer
Rajeev K. Shrimlal, Zhiya Yu, Marc R. Theoret, Dhanalakshmi Chinnasamy, Nicholas P. Restifo, and Steven A. Rosenberg
Précis: Findings rationalize testing of a combination of antiangiogenic agents with cell transfer immunotherapies in clinical oncology trials.

Single-Cell Analysis of T-Cell Receptor Repertoire of HTLV-1 Tax-Specific Cytotoxic T Cells in Allogeneic Transplant Recipients with Adult T-Cell Leukemia/Lymphoma
Yukie Tanaka, Hideki Nakasone, Rie Yamazaki, Ken Sato, Miki Sato, Kenji Kimura, Shinichi Kako, Kumi Oshima, Aki Tanihara, Junji Nishida, Yoshinobu Kanda
Précis: This study suggests a basis to understand the efficacy of allogeneic hematopoietic stem cell transplantation as a treatment for HTLV-1-associated T cell leukemia.

The ITK-SYK Fusion Oncogene Induces a T-Cell Lymphoproliferative Disease in Mice Mimicking Human Disease
Christine Dierks, Francisco Adrian, Paul Fisch, Hong Ma, Helga Maurer, Dieter Herchenbach, Christine Ulrike Forster, Clara Sprissler, Guoxun Liu, Sabine Rottmann, Gui-Rong Guo, Zirlik Katja, Hendrik Veelken, and Markus Warmuth
Précis: Findings argue that Syk kinase fusions present in peripheral T-cell lymphomas might be effective therapeutic targets.

FOXO3 Encodes a Carcinogen-Activated Transcription Factor Frequently Deleted in Early-Stage Lung Adenocarcinoma
Oliver R. Mikos, Daniel C. Blake, Jr., Nathan R. Jones, Yaan-Wan Sun, Shantu Amin, Carla J. Gallgher, Philip Lazarus, Judith Weisz, and Christopher R. Herzog
Précis: Findings identify deletions of a suspected tumor suppressor gene in the setting of lung adenocarcinoma.

Tumor Cells Secrete Galectin-1 to Enhance Endothelial Cell Activity
Victor L. Thijsen, Batya Barkan, Hiroki Shoji, Ingrid M. Aries, Véronique Mathieu, Louise Deltour, Tilman M. Hackeng, Robert Kiss, Yoel Kloog, Françoise Poirier, and Arjan W. Griffioen
Précis: This study identifies a novel angiogenic growth factor function for galectin-1 opening a new window for angiostatic cancer therapy.

Joint Loss of PAX2 and PTEN Expression in Endometrial Precancers and Cancer
Nicolas M. Monte, Kaitlyn A. Webster, Donna Neuberg, Gregory R. Dressler, and George L. Mutter
Précis: Combined loss of a tumor suppressor and a differentiation factor may drive the majority of sporadic endometrial cancers.

Met Receptor Sequence Variants R970C and T992I Lack Transforming Capacity
Jeffrey W. Tyner, Luke B. Fletcher, Ellen Q. Wang, Wayne F. Yang, Michael L. Rutenberg-Schoenberg, Carol Beadling, Motomi Mori, Michael C. Heinrich, Michael W. Deininger, Brian J. Druker, and Marc M. Loriaux
Précis: Findings illustrate the importance of distinguishing oncogenic mutations from normal polymorphisms in tumor cells before an oncogene-targeted drug strategy is justified.

Circadian Rhythm of Transferrin Receptor 1 Gene Expression Controlled by c-Myc in Colon Cancer–Bearing Mice
Fumiyasu Okazaki, Naoya Matsunaga, Hiroyuki Okazaki, Naoki Utaguchi, Ryo Suzuki, Kazuo Maruyama, Satoru Koyanagi, and Shigehiro Ohdo
Précis: c-Myc controlled circadian rhythms that regulate colon cancer gene expression may promote new concepts in dosing regimens for cancer therapy.
6247  Phosphomimetic Mutants of Pigment Epithelium-Derived Factor with Enhanced Antiangiogenic Activity as Potent Anticancer Agents  
Alexander Konson, Sunila Pradeep, and Rony Seger  
Précis: Findings may encourage the development of a specific neovascularization-targeting anticancer agent.

6258  DNA Damage–Induced Cytotoxicity Is Dissociated from BRCA1’s DNA Repair Function but Is Dependent on Its Cytosolic Accumulation  
Hong Wang, Eddy S. Yang, Juhong Jiang, Somaira Nowsheen, and Fen Xia  
Précis: BRCA1 nucleocytoplasmic shuttling may serve as marker of tumor response and possibly a mechanistic focus to sensitize cancer cells to DNA damage-based therapy.

6268  6-Thioguanine Selectively Kills BRCA2-Defective Tumors and Overcomes PARP Inhibitor Resistance  
Natalia Issaeva, Huw D. Thomas, Tatjana Djerensovic, Janneke E. Jaspers, Ivaylo Stoimenov, Suzanne Kyle, Nicholas Pedley, Pommari Gottipati, Rafał Zur, Kate Sleeth, Vicky Chatzakos, Evan A. Mulligan, Cecilia Landin, Evgenia Galantova, Ariena Kersbergen, Adrian L. Harris, Ricky A. Sharma, Sven Rottenberg, Nicola J. Curtis, and Thomas Helleday  
Précis: Strategies to anticipate and address resistance to PARP inhibitors that target tumors defective in BRCA1 or BRCA2 will extend patient survival and may help rationalize more effective combinatorial treatments.

6277  Poly(ADP-Ribose) Polymerase Inhibitor Induces Accelerated Senescence in Irradiated Breast Cancer Cells and Tumors  
Elena V. Efimova, Elena J. Mauceri, Daniel W. Golden, Edwardine Labay, Vytautas P. Bindokas, Thomas E. Darga, Chaitali Chakraborty, Juan Camilo Barreto-Andrade, Clayton Crawley, Harold G. Sutton, Stephen J. Kron, and Ralph R. Weichselbaum  
Précis: These studies suggest a novel mechanism for radiosensitization by PARP inhibitors, mediated by persistent DNA damage response resulting in accelerated cellular senescence both in vitro and in vivo, with significant implications for cancer therapy.

6283  Transplanting Normal Vascular Proangiogenic Cells to Tumor-Bearing Mice Triggers Vascular Remodeling and Reduces Hypoxia in Tumors  
Précis: This study describes a microfluidic imaging technology that can enhance pathological analysis of tumor biopsies.

6293  Construction and Characterization of a Bispecific Anti-CD20 Antibody with Potent Antitumor Activity against B-Cell Lymphoma  
Bohua Li, Xuminming Zhang, Shu Shi, Lei Zhao, Dapeng Zhang, Wei zhuo Qian, Lei Zheng, Jie Gao, Hao Wang, and Yajun Guo  
Précis: A bispecific anti-CD20 antibody that engages both apoptosis and complement dependent cytotoxicity offers a promising agent to improve treatment of B cell neoplasms.

6303  EGFRvIII Antibody–Conjugated Iron Oxide Nanoparticles for Magnetic Resonance Imaging–Guided Convection-Enhanced Delivery and Targeted Therapy of Glioblastoma  
Précis: Target directed magnetic nanoparticles are being developed for MRI contrast enhancement and treatment of brain tumors.

6313  Vorinostat and Sorafenib Increase CD95 Activation in Gastrointestinal Tumor Cells through a Ca2+-De novo Ceramide-PP2A-Reactive Oxygen Species–Dependent Signaling Pathway  
Margaret A. Park, Clint Mitchell, Guo Zhang, Adly Yacoub, Jeremy Allegood, Dieter Häussinger, Roland Reinehr, Andrew Larner, Sarah Spiegel, Paul B. Fisher, Christina Voelkel-Johnson, Besim Ogretmen, Steven Grant, and Paul Dent  
Précis: Mechanistic investigations reveal the critical steps through which a combination of targeted therapies now entering clinical trials activates a central cancer cell death pathway.
A Chemosensitization Screen Identifies TP53RK, a Kinase that Restrains Apoptosis after Mitotic Stress
David Peterson, James Lee, Xingye C. Lei, William F. Forrest, David P. Davis, Peter K. Jackson, and Lisa D. Belmont

Précis: A novel chemo-sensitization screen identifies a molecule that may confer taxane resistance and serve as a novel therapeutic target.

Reprogramming Human Cancer Cells in the Mouse Mammary Gland
Karen M. Bussard, Corinne A. Boulanger, Brian W. Booth, Robert D. Bruno, and Gilbert H. Smith

Précis: Findings argue that human cancer cells can be reprogrammed to a non-cancerous phenotype by the microenvironment of a regenerating mammary gland.

GlcNAcylation Plays an Essential Role in Breast Cancer Metastasis
Yuchao Gu, Wenyi Mi, Yuqing Ge, Haiyan Liu, Qiong Fan, Cuifang Han, Jing Yang, Feng Han, Xinzhi Lu, and Wengong Yu

Précis: This study elucidates how a nuclear and cytoplasmic carbohydrate modification in breast cancer cells influences their malignant properties.

CIIA Is a Novel Regulator of Detachment-Induced Cell Death
Kwang Je Kim, Je-Wook Yu, Hyan Sub Hwang, and Eui-Ju Choi

Précis: Findings define a novel mechanistic realm to trigger anoikis in cancer cells as a possible therapeutic strategy.

Suppression of Integrin α3β1 in Breast Cancer Cells Reduces Cyclooxygenase-2 Gene Expression and Inhibits Tumorigenesis, Invasion, and Cross-Talk to Endothelial Cells

Précis: Findings reveal a novel role for COX-2 as a downstream effector of integrin α3β1 in tumor cells, identifying this integrin as a potential therapeutic target in breast cancer treatment.

LETTER TO THE EDITOR

Spontaneous Malignant Transformation of Human Mesenchymal Stem Cells Reflects Cross-Contamination: Putting the Research Field on Track – Letter

CORRECTIONS

Correction: Oncogenic Ras Promotes Reovirus Spread by Suppressing IFN-β Production through Negative Regulation of RIG-I Signaling

Correction: Myc-Induced MicroRNAs Integrate Myc-Mediated Cell Proliferation and Cell Fate

Fructose Induces Transketolase Flux to Promote Pancreatic Cancer Growth
Haibo Liu, Danshan Huang, David L. McArthur, Laszlo G. Boros, Nicholas Nissen, and Anthony P. Heaney

Précis: Dietary fructose which is commonly added to processed foods may promote pancreatic cancer growth, given a distinct metabolism relative to glucose that more strongly favors DNA and RNA synthesis.

Transforming Growth Factor-β (TGF-β)–Inducible Gene TMEPAI Converts TGF-β from a Tumor Suppressor to a Tumor Promoter in Breast Cancer
Prajjal K. Singha, I-Tien Yeh, Manjeri A. Venkatachalam, and Pothana Saikumar

Précis: Findings suggest novel insights into how cancer cell responses to TGF-beta are converted from growth inhibitory to growth promoting in nature.

HERC2 Is an E3 Ligase That Targets BRCA1 for Degradation

Précis: This study identifies an E3 ligase that may balance regulation of BRCA1 stability and influence breast carcinogenesis.
Correction: Endothelial Cell Migration and Vascular Endothelial Growth Factor Expression Are the Result of Loss of Breast Tissue Polarity

Correction: Periostin, a Cell Adhesion Molecule, Facilitates Invasion in the Tumor Microenvironment and Annotates a Novel Tumor-Invasive Signature in Esophageal Cancer

ABOUT THE COVER

DNA damage induced by 6-thioguanine is repaired by homologous recombination. Cells treated with 6-thioguanine were fixed, and DNA (blue), RAD51 (red), and γH2AX (green) were visualized by immunofluorescence. RAD51 foci formed in V-C8+B2 cells and colocalized with γH2AX foci. For details, see the article by Helleday and colleagues on page 6268 of this issue.