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6114 | **Cyclins, Cdk5, E2f, Skp2, and More at the First International RB Tumor Suppressor Meeting**

Rod Bremner and Eldad Zacksenhaus

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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

**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, Zhao Yang 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 Naïve T-Cell Priming in Response to Therapeutic Vaccination

In vivo

Chris Schiering, Jlenia Guarnerio, Veronica Basso, Luca Muzio, 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. Shrimali, 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, Kiriko Terasako, Shun-ichi Kimura, Shinya Okuda, Shinichi Kako, Kumi Oshima, and 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.

FOXO3 Encodes a Carcinogen-Activated Transcription Factor Frequently Deleted in Early-Stage Lung Adenocarcinoma

Oliver R. Mikse, Daniel C. Blake, Jr., Nathan R. Jones, Yaan-Wan Sun, Shantu Amin, Carla J. Gallagher, Philip Lazarus, Judith Weisz, and Christopher R. Herzenz

Précis: Findings identify deletions of a suspected tumor suppressor gene in the setting of lung adenocarcinoma.

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.

MOLECULAR AND CELLULAR PATHOBIOLOGY

The ITK-SYK Fusion Oncogene Induces a T-Cell Lymphoproliferative Disease in Mice Mimicking Human Disease

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Précis: Findings argue that Syk kinase fusions present in peripheral T-cell lymphomas might be effective therapeutic targets.
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.

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.

6-Thioguanine Selectively Kills BRCA2-Defective Tumors and Overcomes PARP Inhibitor Resistance

Natalia Issaeva, Huw D. Thomas, Tatjana Djurenovic, Janneke E. Jaspers, Iaylo Stoimenov, Suzanne Kyle, Nicholas Pedley, Pomnari Gottiati, Rafal Zur, Kate Sleeth, Vicky Chatzakos, Evan A. Mulligan, Cecilia Landin, Evgenia Gubanova, Ariena Kersbergen, Adrian L. Harris, Ricky A. Sharma, Sven Rottenberg, Nicola J. Curtin, and Thomas Hellday

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.

Poly(ADP-Ribose) Polymerase Inhibitor Induces Accelerated Senescence in Irradiated Breast Cancer Cells and Tumors


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.

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.

Construction and Characterization of a Bispecific Anti-CD20 Antibody with Potent Antitumor Activity against B-Cell Lymphoma

Bohua Li, Xuming Zhang, Shu Shi, Lei Zhao, Dapeng Zhang, Weizhu 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.

EGFvIII 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.

Vorinostat and Sorafenib Increase CD95 Activation in Gastrointestinal Tumor Cells through a Ca2+-Ceramide-PP2A-Reactive Oxygen Species–Dependent Signaling Pathway

Margaret A. Park, Clint Mitchell, Guo Zhang, Adly Yacoub, Jeremy Allegood, Dieter Häussinger, Roland Reinhe, Andrew Larner, Sarah Spiegel, Paul B. Fisher, Christina Voelkel-Johnson, Besim Ogtmnen, 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 chemosensitization 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.

Fructose Induces Transketolase Flux to Promote Pancreatic Cancer Growth
Haibo Liu, Dianshan 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.

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
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.