BREACKING ADVANCES

Highlights from Recent Cancer Literature

REVIEWS

Resistance to BRAF Inhibitors: Unraveling Mechanisms and Future Treatment Options
Jessie Villanueva, Adina Vultur, and Meenhard Herlyn

Diversity of Human Leukemia Xenograft Mouse Models: Implications for Disease Biology
Lüder Hinrich Meyer and Klaus-Michael Debatin

MICROENVIRONMENT AND IMMUNOLOGY

The LMP7-K Allele of the Immunoproteasome Exhibits Reduced Transcript Stability and Predicts High Risk of Colon Cancer
Barbara Fellerhoff, Songhai Gu, Barbara Laumbacher, Andreas G. Nerlich, Elisabeth H. Weiss, Jürgen Glas, Reinhard Kopp, Judith P. Johnson, and Rudolf Wank

Blockade of TGF-ß Signaling by the TGFßR-I Kinase Inhibitor LY2109761 Enhances Radiation Response and Prolongs Survival in Glioblastoma
Mengxian Zhang, Susanne Kleber, Manuel Röhrich, Carmen Timke, Na Han, Jochen Tuettenberg, Ana Martin-Villalba, Juergen Debus, Peter Peschke, Ute Wirkner, Michael Lahn, and Peter E. Huber

MOLECULAR AND CELLULAR PATHOBIOLOGY

Multiple Stress Signals Activate Mutant p53 In Vivo
Young-Ah Suh, Sean M. Post, Ana C. Elizondo-Fraire, Daniela R. Maccio, James G. Jackson, Adel K. El-Naggar, Carolyn Van Pelt, Tamara Terzian, and Guillermina Lozano

Précis: Mutant p53, like wild-type p53, is regulated by a host of cellular stimuli in vivo, and this stabilization provides the tumor with a growth advantage, manifesting in a more aggressive phenotype and decreased survival.

Egfl7 Promotes Tumor Escape from Immunity by Repressing Endothelial Cell Activation
Suzanne Delfortrie, Sébastien Pinte, Virginie Mattot, Chantal Samson, Gaëlle Villain, Bertrand Caetano, Gérardine Lauridant-Philippin, Marie-Christine Baranetzelli, Jacques Bonneterre, François Trottein, Christelle Faveneau, and Fabrice Soncin

Précis: A secreted endothelial cell protein promotes immune escape by downregulating leukocyte adhesion molecules that mediate immune cell extravasation from blood vessels into tumors.

Classification of Epstein–Barr Virus–Positive Gastric Cancers by Definition of DNA Methylation Epigenotypes
Keisuke Matsusaka, Atsushi Kaneda, Genta Nagae, Tetsuo Ushiku, Yasuko Kikuchi, Rumi Hino, Hiroshi Uozaki, Yasuyuki Seto, Kenzo Takada, Hiroyuki Aburatani, and Masashi Fukayama

Précis: A high DNA methylation epigenotype induced by Epstein–Barr virus may play a causative role in the setting of gastric cancers.
Chronic Activation of Wild-Type Epidermal Growth Factor Receptor and Loss of Cdkn2a Cause Mouse Glioblastoma Formation
Jaime Acquaviva, Hyun Jung Jun, Julie Lessard, Rolando Ruiz, Haihao Zhu, Melissa Donovan, Steve Woolfenden, Abraham Boskovitz, Ami Raval, Roderick T. Bronson, Rolf Pfannl, Charles A. Whittaker, David E. Housman, and Al Charest

**Précis:** Findings show that EGFR requires chronic ligand activation for gliomagenesis to occur, and in the context of Cdkn2a loss the tumors are addicted to EGFR signaling.

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**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

Cooperative Phosphorylation of FADD by Aur-A and Plk1 in Response to Taxol Triggers Both Apoptotic and Necrotic Cell Death
Moon-Sun Jang, Su-Jin Lee, Nam Sook Kang, and Eunhee Kim

**Précis:** Mitotic kinases currently thought of as oncogenes may play a supportive role in Taxol chemotherapy, suggesting that therapeutic inhibition of these kinases, which has been suggested, might actually be counterproductive for cancer treatment.

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Cell-Permeable NM23 Blocks the Maintenance and Progression of Established Pulmonary Metastasis
Junghee Lim, Giyong Jang, Seeun Kang, Guwha Lee, Do Thi Thuy Nga, Do Thi Lan Phuong, Hyuncheol Kim, Wael El-Rifai, H. Earl Ruley, and Daewoong Jo

**Précis:** Findings provide a striking preclinical illustration of the efficiency of a targeted protein-based therapy to eradicate metastases in the lung, where many advanced human cancers spread.

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**TUMOR AND STEM CELL BIOLOGY**

STAT3 Is Necessary for Proliferation and Survival in Colon Cancer–Initiating Cells
Li Lin, Aiguo Liu, Zhengang Peng, Huey-Jen Lin, Pui-Kai Li, Chenglong Li, and Jayuh Lin

**Précis:** By demonstrating the importance of STAT3 function in cancer-initiating stem-like cells in colon cancer, this study establishes a powerful rationale to develop IL-6 and STAT3 inhibitory strategies to treat advanced colorectal cancers.

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Novel Histone Demethylase LSD1 Inhibitors Selectively Target Cancer Cells with Pluripotent Stem Cell Properties
Jing Wang, Fei Lu, Qi Ren, Hong Sun, Zhengshuang Xu, Rongfeng Lan, Yuqing Liu, David Ward, Junmin Quan, Tao Ye, and Hui Zhang

**Précis:** Whereas epigenetic regulators constitute some appealing targets for therapeutic inhibition, this study reveals a target for which cancer stem cell selectivity may be achievable.

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Identification of Tumorigenic Cells in KrasG12D–Induced Lung Adenocarcinoma
Huan-Chieh Cho, Chao-Yang Lai, Li-En Shao, and John Yu

**Précis:** Bronchiolar Clara cells are identified to be the cell of origin in KrasG12D–driven lung adenocarcinomas, a finding with implications for the detection and development of therapeutics against this group of lung cancers.

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Lactoferrin–Endothelin-1 Axis Contributes to the Development and Invasiveness of Triple-Negative Breast Cancer Phenotypes
Ngoc-Han Ha, Vasudha S. Nair, Divijendra Natha Sirigiri Reddy, Prakriti Mudvari, Kazufumi Ohshiro, Krishna Sumanth Ghanta, Suresh B. Pakala, Da-Qiang Li, Luis Costa, Allan Lipton, Rajendra A. Badwe, Suzanne Fuqua, Margarethe Wallon, George C. Prendergast, and Rakesh Kumar

**Précis:** Findings suggest that approved or experimental antagonists of the endothelin pathway, which is involved in the control of blood pressure, might be repositioned to render triple-negative breast cancers susceptible to existing receptor-targeted therapeutic options.

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Mucin Glycosylating Enzyme GALNT2 Regulates the Malignant Character of Hepatocellular Carcinoma by Modifying the EGF Receptor
Yao-Ming Wu, Chiung-Hui Liu, Rey-Heng Hu, Miao-Juei Huang, Jian-Jr Lee, Chi-Hau Chen, John Huang, Hong-Shiee Lai, Po-Huang Lee, Wen-Ming Hsu, Hsiu-Chin Huang, and Min-Chuan Huang

**Précis:** A tumor-suppressive enzyme that is often attenuated in liver cancer limits malignant character by modifying the O-glycosylation status of the EGF receptor, a novel type of modification that was not previously known.
Dishevelled 2 Signaling Promotes Self-Renewal and Tumorigenicity in Human Gliomas
Teodoro Pulvirenti, Maartje Van Der Heijden, Leif A. Droms, Jason T. Huse, Viviane Tabar, and Alan Hall

Précis: This study explored the role of Wnt signaling in glioblastoma and revealed that both canonical and noncanonical pathways are required for proliferation, offering new therapeutic targets for these brain tumors.

IKKβ and Nf-κB Transcription Govern Lymphoma Cell Survival through AKT-Induced Plasma Membrane Trafficking of GLUT1
Thomas G. Sommermann, Kathleen O'Neill, David R. Plas, and Ellen Cahir-McFarland

Précis: Findings suggest that induction of glucose import is an important prosurvival function of the NF-κB pathway.

LPA Receptor Heterodimerizes with CD97 to Amplify LPA-Initiated RHO-Dependent Signaling and Invasion in Prostate Cancer Cells
Yvona Ward, Ross Lake, Juan Juan Yin, Christopher D. Heger, Mark Raffeld, Paul K. Goldsmith, Maria Merino, and Kathleen Kelly

Précis: This study provides the initial preclinical validation of an adhesion-linked G protein-coupled receptor as a drug development target for prostate cancer therapy.

Src Activation Plays an Important Key Role in Lymphomagenesis Induced by FGFR1 Fusion Kinases
Mingqiang Ren, Haiyan Qin, Ruizhe Ren, Josephine Tidwell, and John K. Cowell

Précis: Findings suggest that Src kinase inhibitory drugs such as dasatinib should be positioned to treat lethal leukemia/lymphoma syndrome driven by dysfunctional hematopoietic stem cells.

Correction: ΔNp63 Versatilely Regulates a Broad NF-κB Gene Program and Promotes Squamous Epithelial Proliferation, Migration, and Inflammation

Correction:

ABOUT THE COVER
Mice carrying a germline p53 missense mutation equivalent to one commonly found in human cancers do not stabilize mutant p53 in healthy tissues, suggesting similarities to wild type p53 regulation. In this study, many of the same signals that contribute to the stabilization of wild type p53 (IR, ROS, p16INK4a loss, and activation of the Myc and K-Ras oncogenes) do in fact also stabilize mutant p53, often resulting in worse outcomes. This tumor sample has stable expression of mutant p53. For details, see the article by Suh and colleagues on page 7168 of this issue.