BREAKING ADVANCES

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3 A Perspective on Cancer as an Abortive Autoimmune Response to Altered-Self
George C. Prendergast

REVIEWS

5 Cancer Immunotherapy and Breaking Immune Tolerance: New Approaches to an Old Challenge
Amani Makkouk and George J. Weiner

11 Regulation of Epithelial–Mesenchymal Transition through SUMOylation of Transcription Factors
Maria V. Bogachek, James P. De Andrade, and Ronald J. Weigel

PRIORITY REPORT

16 The Cyclic AMP Pathway Is a Sex-Specific Modifier of Glioma Risk in Type I Neurofibromatosis Patients
Nicole M. Warrington, Tao Sun, Jingqin Luo, Robert C. McKinstry, Patricia C. Parkin, Sara Ganzhorn, Debra Spoljaric, Anne C. Albers, Amanda Merkelson, Douglas R. Stewart, David A. Stevenson, David Viskochil, Todd E. Druley, Jason T. Forys, Karlyne M. Reilly, Michael J. Fisher, Uti Tabori, Jeffrey C. Allen, Joshua D. Schiffman, David H. Gutmann, and Joshua B. Rubin

PRécis: These results establishing a sex-specific role for cAMP regulation in affecting the risk of gliomas in NF1 patients may offer new rational strategies to reduce risk or treat brain tumors in this population.

CLINICAL STUDIES

22 Oncolytic Measles Virus Expressing the Sodium Iodide Symporter to Treat Drug-Resistant Ovarian Cancer

PRécis: Although clinical application of oncolytic viruses as experimental therapies has frequently been challenged on the grounds of efficacy, more recently engineered vectors based on measles virus may offer effective options to treat certain advanced cancers such as metastatic ovarian cancer.

INTEGRATED SYSTEMS AND TECHNOLOGIES

31 A Noninvasive Procedure for Early-Stage Discrimination of Malignant and Precancerous Vocal Fold Lesions Based on Laryngeal Dynamics Analysis
Jakob Unger, Jörg Lohscheller, Maximilian Reiter, Katharina Eder, Christian S. Betz, and Maria Schuster

PRécis: This study offers a proof of concept for a procedure to diagnose most types of laryngeal cancers, possibly helping avoid current invasive diagnostic procedures that are associated with greater time, morbidity, and cost.

MICROENVIRONMENT AND IMMUNOLOGY

40 Akt1 and Akt3 Exert Opposing Roles in the Regulation of Vascular Tumor Growth

PRécis: These findings offer a preclinical proof of concept for the therapeutic utility of treating poorly understood vascular tumors such as angiosarcoma with S6K inhibitors.
Intracellular Osteopontin Inhibits Toll-like

Twist1 Is a Key Regulator of Cancer-Associated Fibroblasts

Intracellular Osteopontin Inhibits Toll-like Receptor Signaling and Impedes Liver Carcinogenesis

PLK1 Phosphorylates PAX3-FOXO1, the Inhibition of Which Triggers Regression of Alveolar Rhabdomyosarcoma

LASP1 Is a HIF1α Target Gene Critical for Metastasis of Pancreatic Cancer

VEGF-Targeted Therapy Stably Modulates the Glycolytic Phenotype of Tumor Cells

Foretinib Is Effective Therapy for Metastatic Sonic Hedgehog Medulloblastoma
TUMOR AND STEM CELL BIOLOGY

147 Cables1 Complex Couples Survival Signaling to the Cell Death Machinery
Zhi Shi, Hae R. Park, Yuhong Du, Zijian Li, Kejun Cheng, Shi-Yong Sun, Zenggang Li, Haian Fu, and Fadil R. Khuri
Précis: The novel regulatory interface described in this report may offer a new strategy for the development of AKT inhibitors for cancer intervention.

159 Four-in-One Antibodies Have Superior Cancer Inhibitory Activity against EGFR, HER2, HER3, and VEGF through Disruption of HER/MET Crosstalk
Shi Hu, Wenyan Fu, Weihao Xu, Yang Yang, Hiroaki Takeda, and Wangdong Zhu
Précis: These results establish a new principle to achieve combined HER receptor inhibition and limit drug resistance using a single antibody.

171 Genetic Disruption of Lactate/H+ Symporters (MCTs) and Their Subunit CD147/BASIGIN Sensitizes Glycolytic Tumor Cells to Phenformin
Ibtissam Marchiq, Renaud Le Floch, Daniele Roux, Marie-Pierre Simon, and Jacques Pouyssegur
Précis: This study offers preclinical proof of concept for targeting lactic acid export as a therapeutic approach, the effect of which can be magnified by coupling it with phenformin, an anti-diabetic biguanide drug.

181 Mdm2 and Aurora Kinase A Inhibitors Synergize to Block Melanoma Growth by Driving Apoptosis and Immune Clearance of Tumor Cells
Anna E. Vilgelm, Jeff S. Pawlikowski, Yan Liu, Oriana E. Hawkins, Tyler A. Davis, Jessica Smith, Kevin P. Weller, Linda W. Horton, Colt M. McClain, Gregory D. Ayers, David C. Turner, David C. Essaka, Clinton F. Stewart, Jeffrey A. Sosman, Mark C. Kelley, Jeffrey A. Ecsedy, Jeffrey N. Johnston, and Ann Richmond
Précis: These findings offer preclinical proof of concept for a combination drug treatment that leverages both senescence and immune surveillance to improve therapeutic outcomes.

194 Contributions to Drug Resistance in GlioblastomaDerived from Malignant Cells in the Sub-Ependymal Zone
Précis: A particular region of the adult brain analogous to the embryonic forebrain germinal zone, which harbors various neural stem cell populations, is discovered in glioblastoma patients to harbor tumor-initiating cells, identifying this region as a target for immediate therapeutic attention by neuro-oncologists.

203 α-Tubulin Acetylation Elevated in Metastatic and Basal-like Breast Cancer Cells Promotes Microtentacle Formation, Adhesion, and Invasive Migration
Amanda E. Boggs, Michele I. Vitolo, Rebecca A. Whipple, Monica S. Charpentier, Olga G. Goloubeva, Olga B. Ioffe, Kimberly C. Tuttle, Jana Slovic, Yiling Lu, Gordon B. Mills, and Stuart S. Martin
Précis: These results identify a tight correlation between acetylated α-tubulin levels and aggressive metastatic behavior in breast cancer, with potential implications for the definition of a simple prognostic biomarker in patients with basal-like breast cancers.

216 B-Raf Inhibitors Induce Epithelial Differentiation in BRAF-Mutant Colorectal Cancer Cells
Ricarda Herr, Martin Köhler, Hana Andrllová, Florian Weinberg, Yvonne Möller, Sebastian Halbach, Lisa Lutz, Justin Mastrogianatis, Martin Kloos, Nicola Bittermann, Silke Kowar, Robert Zeieter, Monilola A. Olayioye, Silke Lasmann, Hauck Busch, Melanie Boerries, and Tilman Brummer
Précis: This article reveals a novel facet of BRAF and MEK inhibitors in triggering differentiation of colorectal tumors, providing a mechanistic rationale to immediately evaluate them clinically as antimetastatic agents in this setting.

230 SYK Is a Candidate Kinase Target for the Treatment of Advanced Prostate Cancer
Veerander P.S. Ghona, Shuning He, Geertje van der Horst, Steffen Nijhoff, Hans de Bent, Annemarie Lekkerkerker, Richard Janssen, Guido Jenster, Geert J.L.H. van Leenders, Melanie Boerries, and Tilman Brummer
Précis: These striking preclinical findings offer a mechanistic rationale to immediately reposition SYK kinase inhibitors currently in early clinical trials for evaluation in patients with metastatic prostate cancer.
ABOUT THE COVER

Timing of GLA in relation to vaccination impacts the pattern of OT1 cell accumulation. Representative bioluminescent images show site-specific accumulation of OT1 cells in different groups of mice 4 days post hind footpad vaccination. Vaccine-primed T cells accumulated in the draining lymph nodes in mice that received GVAX only or when GLA 24 was given 24 hrs post GVAX. However, when GLA is coadministered with GVAX, a systemic pattern of T-cell accumulation was observed. For details, see article by Kadayakkaza and colleagues on page 51.