1 Highlights from Recent Cancer Literature

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

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

16 The Cyclic AMP Pathway Is a Sex-Specific Modifier of Glioma Risk in Type 1 Neurofibromatosis Patients
   Nicole M. Warrington, Tao Sun, Jingqin Luo, Robert C. McKimsey, 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.

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.

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.

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 86
Twist1 Is a Key Regulator of Cancer-Associated 73
Tropomodulin 1 Expression Driven by NF-κB Enhances Breast Cancer Growth 62

Paradoxical Decrease in the Capture and Lymph Node Delivery of Cancer Vaccine Antigen Induced by a TLR4 Agonist as Visualized by Dual-Mode Imaging 51

98 PLK1 Phosphorylates PAX3-FOXO1, the Inhibition of Which Triggers Regression of Alveolar Rhabdomyosarcoma
Verena Thalhammer, Laura A. Lopez-Garcia, David Herrero-Martin, Regina Hecker, Dominik Laubscher, Maria E. Gietsch, Marco Wachtel, Peter Bode, Paolo Nanni, Bernd Blank, Ewa Koscielniak, and Beat W. Schafer

MOLECULAR AND CELLULAR PATHOBIOLOGY

73 Twist1 Is a Key Regulator of Cancer-Associated Fibroblasts
Keun-Woo Lee, So-Young Yeo, Chang Ohk Sung, and Seok-Hyung Kim

86 Intracellular Osteopontin Inhibits Toll-like Receptor Signaling and Impedes Liver Carcinogenesis
Xiaoyu Fan, Chunyan He, Wei Jing, Xuyu Zhou, Rui Chen, Lei Gao, Minhui Zhu, Rongjie Jia, Hao Wang, Yajun Guo, and Jian Zhao

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

120 VEGF-Targeted Therapy Stably Modulates the Glycolytic Phenotype of Tumor Cells
Matteo Curtarello, Elisabetta Zulato, Giorgia Nardo, Silvia Vallotta, Giulia Guzzo, Elisabetta Rossi, Giovanni Esposito, Aichi Msaki, Anna Pastic, Andrea Rasola, Luca Persano, Francesco Ciccarese, Roberta Bertorelle, Sergio Todde, Mario Plebani, Henrike Schroer, Stefan Walenta, Wolfgang Mueller-Klieser, Alberto Amadori, Rosa Maria Moresco, and Stefano Indraccolo

134 Foretinib Is Effective Therapy for Metastatic Sonic Hedgehog Medulloblastoma
Claudia C. Faria, Brian J. Golbourn, Adrian M. Dubuc, Marc Remke, Roberto J. Diaz, Sameer Agnihotri, Amanda Luck, Nesrin Sabha, Samantha Olsen, Xiaochong Wu, Livia Garzia, Vijay Ramaswamy, Denis Reynaud, Leonardo Ermini, Martin Post, Paul A. Northcott, Stefan M. Pfister, Sidney E. Croul, Marcel Kool, Andrey Korshunov, Christian A. Smith, Michael D. Taylor, and James T. Rutka

These findings provide a strong rationale to clinically evaluate foretinib immediately as a therapy for a defined subset of patients with the most common form of malignant pediatric brain tumor.
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.

Genetic Disruption of Lactate/H⁺ Symporters (MCTs) and Their Subunit CD147/BASIGIN Sensitizes Glycolytic Tumor Cells to Phenformin
Ibtissam Marchiq, Renaud Le Floch, Danièle 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 antiobiatric biguanide drug.

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.

Contributions to Drug Resistance in Glioblastoma Derived 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.

B-Raf Inhibitors Induce Epithelial Differentiation in BRAF-Mutant Colorectal Cancer Cells
Précis: This article reveals a novel facet of BRAF and MEK inhibitors currently in early clinical trials for evaluation in patients with basal-like breast cancers.

SYK Is a Candidate Kinase Target for the Treatment of Advanced Prostate Cancer
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.