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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. McKinstrey, 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
   Evanthia Galanis, Pamela J. Atherton, Matthew J. Maurer, Keith L. Knutson, Sean C. Dowdy,
   William A. Cliby, Paul Halinka Jr, Harry J. Long, Ann Oberg, Beana Aderca, Matthew S. Block,
   Jamie Baldukian, Mark J. Federspiel, Stephen J. Russell, Kimberly R. Kalli, Gary Keeney,
   Kah Whye Peng, and Lynn C. Hartmann
   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
   Thuy L. Phung, Wu Du, Qi Xue, Sriram Ayyaswamy, Damien Gerald, Zeus Antonello, Sokha Nhek,
   Carole A. Perruzzi, Isabel Acevedo, Rajesh Ramanna-Valmiki, Paul Rodriguez-Waitkus,
   Ladan Enayati, Marcelo I. Hochman, Dina Lev, Sandaruwan Geeganage, and Laura E. Benjamin
   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

Tropomodulin 1 Expression Driven by NF-

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

MOLECULAR AND CELLULAR PATHOBIOLGY

62 Tropomodulin 1 Expression Driven by NF-κB Enhances Breast Cancer Growth

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

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

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Deepak K. Kadavakkara, Michael J. Korrer, Jeff W.M. Bulte, and Hyam I. Levitsky

Precis: An adjuvant molecule that enhances the therapeutic effects of a cancer vaccine was found paradoxically to reduce the efficiency of antigen delivery to lymph nodes, challenging what has been thought to be necessary in an effective adjuvant—at least as formed by expectations from studies of infectious disease vaccines.

Taku Ito-Kureha, Naohiko Koshikawa, Mizuki Yamamoto, Rentaro Sembba, Noritaka Yamaguchi, Tadashi Yamamoto, Motoharu Seki, and Jun-ichiro Inoue

Precis: These findings highlight a novel mechanistic linkage to help explain the NF-κB-dependent malignant phenotype of triple-negative breast cancer, with implications for defining useful theranostic targets in this aggressive disease.

Keun-Woo Lee, So-Young Yeo, Chang Ohk Sung, and Seok-Hyung Kiin

Precis: Already known as a central contributor to EMT, which drives metastatic progression in cancer cells, the transcription factor Twist1 is also found to function in cancer-associated fibroblasts, where it appears to offer a compelling target to depromog even the tumor-supporting features of the cancer microenvironment.

Xiaoyu Fan, Chunyan He, Wei Jing, Xuyu Zhou, Rui Chen, Lei Cao, Minhui Zhu, Rongjie Jia, Hao Wang, Yajun Guo, and Jian Zhao

Precis: Osteopontin is known to act in the tumor microenvironment to promote inflammatory processes that facilitate progression, but this study reveals that it also acts within macrophages that infiltrate budding liver tumors to achieve this end by altering Toll-like receptor signaling.

Verena Thalhammer, Laura A. Lopez-Garcia, David Herrera-Martín, Regina Hecker, Dominik Laubscher, Maria E. Giersch, Marco Wachtel, Peter Bode, Paolo Nanni, Bernd Blank, Ewa Koscielniak, and Beat W. Schafer

Precis: These findings offer a preclinical proof of concept to target the mitotic kinase PLK1 as a rational strategy to treat an aggressive pediatric tumor.

Tiansuo Zhao, He Ren, Jing Li, Jing Chen, Huan Zhong, Wen Xin, Yan Sun, Lei Sun, Yongwei Yang, Junwei Sun, Xiuchao Wang, Song Cao, Chonghiao Huang, Huafeng Zhang, Shengyu Yang, and Jihui Hao

Precis: This study identifies a key mediator of metastasis in pancreatic ductal carcinomas that are typically already disseminated at the time of diagnosis, a central challenge in the management of this disease.

Matteo Curtarello, Elisabetta Zulato, Giorgia Nardo, Silvia Vallotta, Giulia Guzzo, Elisabetta Rossi, Giovanni Esposito, Aichi Msaki, Anna Pasto, Andrea Rasola, Luca Persano, Francesco Ciccarese, Roberta Bertorelle, Sergio Todde, Mario Plebani, Henrike Schroer, Stefan Walenta, Wolfgang Mueller-Klieser, Alberto Amadori, Rosa Maria Morescos, and Stefano Indraccolo

Precis: These findings suggest that the application of antiangiogenic therapy in cancer selects for metabolic traits of tumors that not only confer treatment resistance but also potentially have a more aggressive character, challenging a central tenet of antiangiogenic therapy as inherently less susceptible to the evolution of resistance.

Claudia C. Faria, Brian J. Golbourn, Adrian M. Dubuc, Marc Remke, Roberto J. Dizaz, Sameer Agnihotri, Amanda Luck, Nesrin Sabha, Samantha Olsen, Xiaocong Wu, Livia Garzia, Vijay Ramaswamy, Stephen C. Rask, Xin Wang, Michael Leadley, 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

Precis: 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.

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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

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 Pousyssegur

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. Ecsedy, Jeffrey N. Johnston, and Ann Richmond

Contributions to Drug Resistance in Glioblastoma Derived from Malignant Cells in the Sub-Ependymal Zone

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 B. Ioffe, Kimberly C. Tuttle, Jana Slovic, Yiling Lu, Gordon B. Mills, and Stuart S. Martin

B-Raf Inhibitors Induce Epithelial Differentiation in BRAF-Mutant Colorectal Cancer Cells
Ricarda Herr, Martin Köhler, Hana Andrlůvá, Florian Weinberg, Yvonne Mölller, Sebastian Halbach, Lisa Lutz, Justin Mastroianni, Martin Klose, Nicola Bittermann, Silke Kowar, Robert Zeiset, Monilola A. Olayioye, Silke Lassmann, Hauke Busch, Melanie Boerries, and Tilman Brummer

SYK Is a Candidate Kinase Target for the Treatment of Advanced Prostate Cancer
Veerander P.S. Ghona, Shuning He, Geerje van der Horst, Steffen Nijhoff, Hans de Bont, Annemarie Dekker, Richard Janssen, Guido Jenster, Geert J.H. van Leenders, Melanie Boerries, and Tilman Brummer

TUMOR AND STEM CELL BIOLOGY

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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 Kadayakka and colleagues on page 51.