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MICROENVIRONMENT AND IMMUNOLOGY

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

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.
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51 Paradoxical Decrease in the Capture and Lymph Node Delivery of Cancer Vaccine Antigen Induced by a TLR4 Agonist as Visualized by Dual-Mode Imaging
Deepak K. Kadayakkara, Michael J. Korrer, Jeff W.M. Bulte, and Hyam I. Levitsky

Précis: 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.

MOLECULAR AND CELLULAR PATHOBIOLOGY

62 Tropomodulin 1 Expression Driven by NF-κB Enhances Breast Cancer Growth
Taku Ito-Kureha, Naohiko Roshikawa, Mizuki Yamamoto, Rentaro Sembha, Noritaka Yamaguchi, Tadasu Yamamoto, Motoharu Seki, and Jun-ichiro Inoue

Précis: 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.

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

Précis: 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 deprogram the tumor-supporting features of the cancer microenvironment.

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

Précis: 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.

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. Schäfer

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

111 LASP1 Is a HIF1α Target Gene Critical for Metastasis of Pancreatic Cancer
Tiansuo Zhao, He Ren, Jing Li, Jing Chen, Huan Zhang, Wen Xin, Yan Sun, Lei Sun, Yongwei Yang, Junwei Sun, Xiuchao Wang, Song Gao, Chonghiao Huang, Huafeng Zhang, Shengyu Yang, and Jiuhu Hao

Précis: 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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

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

Précis: 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.

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 Sahba, Samantha Olsen, Xiaochong Wu, Livia Garzia, Vijay Ramaswamy, Martijn Post, Paul A. Northcott, Stefan M. Pfister, Sidney E. Croul, Marcel Kool, Andrey Korshunov, Christian A. Smith, Michael D. Taylor, and James T. Rutka

Précis: 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.
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 Kadayakkara and colleagues on page 51.