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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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134 Foretinib Is Effective Therapy for Metastatic Sonic Hedgehog Medulloblastoma

**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.

**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.

**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 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.

**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.

**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.
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 Fadilo R. Khuri

Precis: The novel regulatory interface described in this report may offer a new strategy for the development of AKT inhibitors for cancer intervention.

Four-in-One Antibodies Have Superior Cancer Inhibitory Activity against EGFR, HER2, HER3, and VEGF through Disruption of HER/MET Crosstalk
Shi Hu, Wennan Fu, Weihao Xu, Yang Yang, Hiroaki Takeda, and Wangdong Zhu

Precis: 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

Precis: 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.

Mdm2 and Aurora Kinase A Inhibitors Synergize to Block Melanoma Growth by Driving Apoptosis and Immune Clearance of Tumor Cells

Precis: 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

Precis: 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.

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

Precis: 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.

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

Precis: This article reveals a novel facet of BRAF and MEK inhibitors currently in early clinical trials for evaluation in patients with metastatic prostate cancer.

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

Precis: 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.
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