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1318 BRMS1 Suppresses Lung Cancer Metastases through an E3 Ligase Function on Histone Acetyltransferase p300
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Precis:Findings reveal a mechanistic basis for understanding how cancer-associated fibroblasts activated in the tumor microenvironment act to promote cancer metastasis, with implications for arresting this deadly process.

Precis: FGFR/FRS2 signaling may play an important role in the development of high-grade liposarcoma and, therefore, represents a potential therapeutic target.

Precis: Improvements to noninvasive imaging methods are important to assist the preclinical development of drugs that are active in clinically relevant orthotopic models of advanced metastatic cancer, where the core challenge for treatment remains.

Precis: Findings offer a mechanistic explanation for how the metastasis suppressor gene BRMS1 acts to suppress metastases in a lung cancer model.

### THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

**1340**  
**Inhibition of Cholinergic Signaling Causes Apoptosis in Human Bronchioalveolar Carcinoma**  
Jamie K. Lau, Kathleen C. Brown, Brent A. Thornhill, Clayton M. Crabtree, Aaron M. Dom, Theodore R. Witte, W. Elaine Hardman, Christopher A. McNees, Cody A. Stover, A. Betts Carpenter, Haitao Luo, Yi C. Chen, Brandon S. Shiflett, and Piyali Dasgupta  
*Precis:* Findings prompt immediate clinical testing of approved drugs that may improve the efficacy of treatments for a certain subtype of lung cancer.

**1348**  
**Dual Inhibition of Bcl-2 and Bcl-xL Strikingly Enhances PI3K Inhibition-Induced Apoptosis in Human Myeloid Leukemia Cells through a GS3- and Bim-Dependent Mechanism**  
Mohamed Rahmani, Mandy Mayo Aust, Elisa Attiksson, David C. Williams Jr, Andrea Ferreira-Gonzalez, and Steven Grant  
*Precis:* This study defines a combinatorial strategy to block key nodes in cell survival signaling to greatly enhance the killing of acute myeloid leukemia cells exhibiting AKT activation.

**1352**  
**Application of a Proapoptotic Peptide to Intratumorally Spreading Cancer Therapy**  
Renwei Chen, Gary B. Braun, Xiuquan Luo, Kazuki N. Sugahara, Tambet Teesalu, and Erkki Ruoslahti  
*Precis:* Results offer preclinical proof of concept for an injectable peptide modality that may be useful to treat tumors that are either surgically inoperable or otherwise difficult to treat systemically.

**1362**  
**Targeted Cancer Therapy with a 2-Deoxyglucose–Based Adriamycin Complex**  
Jie Cao, Sisi Cui, Siwen Li, Changli Du, Junmei Tian, Shunan Wan, Zhiyu Qian, Yueqing Gu, Wei R. Chen, and Guangji Wang  
*Precis:* A simple conjugate of adriamycin that improves cancer cell targeting limits the cardiotoxic liabilities of this drug, offering broad applications in cancer treatment.

**1374**  
**Hyperactivated JNK Is a Therapeutic Target in pVHL-Deficient Renal Cell Carcinoma**  
Jiabin An, Huiyen Liu, Clara E. Magyar, Yanchuan Guo, Mysore S. Veena, Eri S. Srivatsan, Jiaoti Huang, and Matthew B. Rettig  
*Precis:* This study provides insight into HIFα-independent mechanisms that drive renal cancer and offers new opportunities for therapeutic targeting of this disease.

### TUMOR AND STEM CELL BIOLOGY

**1386**  
**Tasquinimod Is an Allosteric Modulator of HDAC4 Survival Signaling within the Compromised Cancer Microenvironment**  
*Precis:* Findings define the mechanism of action of an antiangiogenic drug currently in phase III trials and suggest how to leverage its efficacy in combination with other drugs that target the tumor microenvironment.

**1400**  
**FGF-2 Disrupts Mitotic Stability in Prostate Cancer through the Intracellular Trafficking Protein CEP57**  
Rolando Cuevas, Nina Korzeniewski, Yanis Tolstov, Markus Hohenfellner, and Stefan Duensing  
*Precis:* This provocative study reveals an unexpected link between the tumor microenvironment and chromosomal instability.

**1411**  
**Autocrine Motility Factor Promotes HER2 Cleavage and Signaling in Breast Cancer Cells**  
Dhong Hyo Kho, Pratima Nangia-Makker, Vitaly Balan, Victor Hogan, Larry Tait, Yi Wang, and Avraham Raz  
*Precis:* Insights into how resistance arises to HER2 targeting therapies in breast cancer could improve paradigms for its management.

**1420**  
**Contrasting Hypoxic Effects on Breast Cancer Stem Cell Hierarchy Is Dependent on ER-α Status**  
Hannah Harrison, Lynsey Rogerson, Hannah J. Gregson, Keith R. Brennan, Robert B. Clarke, and Göran Landberg  
*Precis:* This study describes the response of a breast cancer subtype to hypoxia, with implications for more effective anti-hypoxic and antiangiogenic therapies.

**1434**  
**miR-7 Suppresses Brain Metastasis of Breast Cancer Stem-Like Cells By Modulating KLF4**  
*Precis:* This important study identifies a functional biomarker or therapeutic target for brain metastasis in breast cancer, which remains a mainly untreatable and deadly aspect of progression in this disease.
LETTER TO THE EDITOR

Oxidation-Mediated DNA Crosslinking Contributes to Toxicity of 6-Thioguanine in Human Cells — Letter
Nanne K.H. de Boer, Dirk P. van Asseldonk, Margien L. Seinen, and Adriaan A. van Bodegraven

ABSTRACT

The microRNA network is considered to play critical roles in tumor progression; however, little information is available for microRNA in cancer stem-like cells (CSC). The results of microRNA profile analysis revealed that miR-7 is significantly downregulated in CSCs that are highly metastatic to the brain, and the expression of this microRNA significantly suppressed the ability of CSCs to metastasize to the brain in vivo. miR-7 was also found to be capable of modulating KLF4. Consistently, the expression of miR-7 and KLF4 in brain-metastatic lesions of breast cancer patients was found to be significantly downregulated and upregulated, respectively. High expression of KLF4 was also inversely correlated to brain-metastasis free survival of breast cancer patients. For details, see the article by Okuda and colleagues on page 1434.