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1259 Regulation of the \( \text{Na}^+/\text{H}^+ \) Exchanger (NHE1) in Breast Cancer Metastasis
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**CLINICAL STUDIES**

1265 Oncolytic Vaccinia Virus Disrupts Tumor-Associated Vasculature in Humans
Caroline J. Breitbach, Rozanne Arulanandam, Naomi De Silva, Steve H. Thorne, Richard Patt, Manijeh Daneshmand, Anne Moon, Carolina Ilkow, James Burke, Tae-Ho Hwang, Jeong Heo, Mong Cho, Hannah Chen, Christina Addisson, J. Andrea McCart, John C. Bell, and David H. Kirn

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1276 Nitroreductase, a Near-Infrared Reporter Platform for In Vivo Time-Domain Optical Imaging of Metastatic Cancer
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**MICROENVIRONMENT AND IMMUNOLOGY**

1287 STC1 Expression By Cancer-Associated Fibroblasts Drives Metastasis of Colorectal Cancer
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**MOLECULAR AND CELLULAR PATHOBIOLOGY**

1298 Amplification of FRS2 and Activation of FGFR/FRS2 Signaling Pathway in High-Grade Liposarcoma
Keqiang Zhang, Kevin Chu, Xiwei Wu, Hanlin Gao, Jinhuil Wang, Yate-Ching Yuan, Sofia Loera, Kimberley Ho, Yafan Wang, Warren Chow, Frank Un, Peiguo Chu, and Yun Yen

1308 BRMS1 Suppresses Lung Cancer Metastases through an E3 Ligase Function on Histone Acetyltransferase p300
Yuan Liu, Marty W. Mayo, Alykhan S. Nagji, Emily H. Hall, Lisa S. Shock, Azizhen Xiao, Edward B. Stelow, and David R. Jones

1318 Midkine Promotes Neuroblastoma through Notch2 Signaling
Satoshi Kishida, Ping Mu, Shin Miyakawa, Masatoshi Fujiwara, Tomoyuki Abe, Kazuma Sakamoto, Akira Onishi, Yoshikazu Nakamura, and Kenji Kadomatsu

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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. Shifflett, 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.

Dual Inhibition of Bel-2 and Bel-xl Strikingly Enhances P38K Inhibition-Induced Apoptosis in Human Myeloid Leukemia Cells through a GSK3- 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.

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.

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.

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, Jiabin An, Huiren Liu, Clara E. Magyar, 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.

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.

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.

Autocrine Motility Factor Promotes HER2 Cleavage and Signaling in Breast Cancer Cells
Dhung 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.

Contrasting Hypoxic Effects on Breast Cancer Stem Cell Hierarchy Is Dependent on ERα 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.

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.
ABOUT THE COVER

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.