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Satoshi Kishida, Ping Mu, Shin Miyakawa, Masatoshi Fujiwara, Tomoyuki Abe, Kazuma Sakanoto, Akira Onishi, Yoshikazu Nakamura, and Kenji Kadomatsu

Précis: 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.

Précis: 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.

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

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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

Dual Inhibition of Bel-2 and Bel-xL Strikingly Enhances P13K 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 Erikki 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, Huiren 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

FGF-2 Disrupts Mitotic Stability in Prostate Cancer through the Intracellular Trafficking Protein CEP57
Rolando Cuevas, Nina Korzeniewska, 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
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.

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.

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.

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.
LETTER TO THE EDITOR

1445

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

CORRECTION

1446

Correction: Chloroquine in Cancer Therapy: A Double-Edged Sword of Autophagy

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.