**Breaking Advances**

1257 Highlights from Recent Cancer Literature

**Review**

1259 Regulation of the Na⁺/H⁺ Exchanger (NHE1) in Breast Cancer Metastasis
Schammim R. Amith and Larry Fliegel

**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, Fernando A. Angarita, Christina Addison, J. Andrea McCart, John C. Bell, and David H. Kirn

**Integrated Systems and Technologies**

1276 Nitroreductase, a Near-Infrared Reporter Platform for In Vivo Time-Domain Optical Imaging of Metastatic Cancer
Emmet McCormack, Elisabeth Silden, Richard M. West, Tina Pavlin, David R. Micklem, James B. Lorenz, Bengt Erik Haug, Michael E. Cooper, and Bjorn Tore Gjertsen

**Microenvironment and Immunology**

1287 STC1 Expression By Cancer-Associated Fibroblasts Drives Metastasis of Colorectal Cancer
Cristina Peña, Maria Virtudes Céspedes, Maja Bradic Lindh, Sara Kiflenamiram, Artur Mezhuyevskii, Per-Henrik Edqvist, Christina Haggjöf, Helgi Birgisson, Linda Bojmar, Karin Jirström, Per Sandström, Eleanor Olsson, Srinivas Veerla, Alberto Gallardo, Tobias Sjöblom, Andy C.-M. Chang, Roger R. Reddel, Ramón Mangués, Martin Augsten, and Arne Ostman

**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, Jinhui Wang, Yate-Ching Yuan, Sofia Loera, Kimberley Ho, Yafan Wang, Warren Chow, Frank Un, Peigao 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, Azhien Xiao, Edward B. Stelow, and David R. Jones

1318 Midkine Promotes Neuroblastoma through Notch2 Signaling
Satoshi Kishida, Ping Mu, Shin Miyakawa, Masatoshi Fujiiwara, Tomoyuki Abe, Kazuma Sakamoto, 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.
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 Lao, Yi C. Chen, Brandon S. Shiflett, and Piyali Dasgupta

 précis: 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 Atttkisson, David C. Williams Jr, Andrea Ferreira-Gonzalez, and Steven Grant

 précis: 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, Xinquan Luo, Kazuki N. Sugahara, Tambet Teesalu, and Erkki Ruoslahti

 précis: 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

 précis: 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, and Matthew B. Rettig

 précis: 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

Tasquinimod Is an Allosteric Modulator of HDAC4 Survival Signaling within the Compromised Cancer Microenvironment


 précis: 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

 précis: 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

 précis: 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

 précis: 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


 précis: 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.
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

CORRECTION

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.