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**Précis:** While effective clinical applications of many oncolytic viruses have been frustrated, the use of oncolytic vaccinia to destroy established tumor vasculatures may offer a powerful outlet for this technology.

#### Integrated Systems and Technologies

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**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. Lorens, Bengt Erik Haug, Michael E. Cooper, and Bjorn Tore Gjertsen

**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.

#### Microenvironment and Immunology

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

**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.

#### 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, Jinlui Wang, Yate-Ching Yuan, Sofia Loera, Kimberly Ho, Yafan Wang, Warren Chow, Frank Un, Peigao Chu, and Yun Yen

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

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, Aiichen Xiao, Edward B. Stelow, and David R. Jones

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

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:** Preclinical investigations establish a critical cell survival signaling in MYCN-driven neuroblastoma, suggesting new therapeutic directions to improve 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, Yueqing Gu, Wei R. Chen, and Guangji Wang

Precis: This study provides insight into HIFα-independent mechanisms that drive renal cancer and offers new opportunities for therapeutic targeting of this disease.

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

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.
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.