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Cancer Research

February 15, 2013 • Volume 73 • Number 4

BREAKING ADVANCES

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REVIEW

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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
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

- 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. Lorens, Bengt Erik Haug, Michael E. Cooper, and Bjørn 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

- 1287 | **STC1 Expression By Cancer-Associated Fibroblasts Drives Metastasis of Colorectal Cancer**
Cristina Peña, María Virtudes Céspedes, Maja Bradic Lindh, Sara Kiflemariam, Artur Mezheyeuski, Per-Henrik Edqvist, Christina Hägglöf, Helgi Birgisson, Linda Bojmar, Karin Jirström, Per Sandström, Eleonor Olsson, Srinivas Veerla, Alberto Gallardo, Tobias Sjöblom, Andy C.-M. Chang, Roger R. Reddel, Ramón Mangues, Martin Augsten, and Arne Östman
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, Jinhui Wang, Yate-Ching Yuan, Sofia Loera, Kimberley Ho, Yafan Wang, Warren Chow, Frank Un, Peiguo 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, Aizhen 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 Fujiwara, 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.

1328 **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
Précis: Findings prompt immediate clinical testing of approved drugs that may improve the efficacy of treatments for a certain subtype of lung cancer.

1386 **Tasquinimod Is an Allosteric Modulator of HDAC4 Survival Signaling within the Compromised Cancer Microenvironment**
John T. Isaacs, Lizamma Antony, Susan L. Dalrymple, W. Nathaniel Brennen, Stephanie Gerber, Hans Hammers, Michel Wissing, Sushant Kachhap, Jun Luo, Li Xing, Per Björk, Anders Olsson, Anders Björk, and Tomas Leanderson
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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

1340 **Dual Inhibition of Bcl-2 and Bcl-xL Strikingly Enhances PI3K Inhibition-Induced Apoptosis in Human Myeloid Leukemia Cells through a GSK3- and Bim-Dependent Mechanism**
Mohamed Rahmani, Mandy Mayo Aust, Elisa Attkisson, 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.

1352 **Application of a Proapoptotic Peptide to Intratumorally Spreading Cancer Therapy**
Renwei Chen, Gary B. Braun, Xiuquan Luo, Kazuki N. Sugahara, Tambat 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.

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
Précis: 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, Huiren Liu, Clara E. Magyar, Yanchuan Guo, Mysore S. Veena, Eri S. Srivatsan, Jiaoti Huang, and Matthew B. Rettig
Précis: This study provides insight into HIF α -independent mechanisms that drive renal cancer and offers new opportunities for therapeutic targeting of this disease.

TUMOR AND STEM CELL BIOLOGY

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
Précis: 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
Précis: 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
Précis: 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**
Hiroshi Okuda, Fei Xing, Puspa R. Pandey, Sambad Sharma, Misako Watabe, Sudha K. Pai, Yin-Yuan Mo, Megumi Iizumi-Gairani, Shigeru Hirota, Yin Liu, Kerui Wu, Radhika Pochampally, and Kounosuke Watabe
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.

LETTER TO THE EDITOR

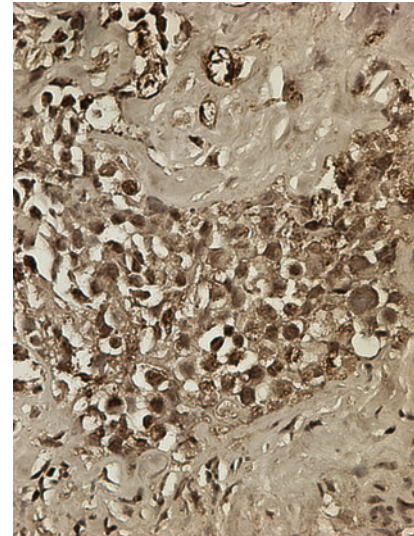
1445 | **Oxidation-Mediated DNA Crosslinking
Contributes to Toxicity of 6-
Thioguanine in Human Cells — Letter**
Nanne K.H. de Boer, Dirk P. van Asseldonk,
Margien L. Seinen, and
Adriaan A. van Bodegraven

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.



Cancer Research

The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

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Cancer Res 2013;73:1257-1446.

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