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February 15, 2012 • Volume 72 • Number 4

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Metastatic Cells Can Escape the Proapoptotic Effects of TNF-α through Increased Autocrine IL-6/STAT3 Signaling
Shun Li, Ni Wang, and Pnina Brodt

Précis: This study defines an IGF-1-driven mechanism of cancer cell survival that is critical for metastatic colonization of the liver, suggesting that IGF-1 receptor antagonists currently in clinical trials may have particular utility in treating colon cancers and other cancers that metastasize frequently to liver.

876
Monocytic CCR2+ Myeloid-Derived Suppressor Cells Promote Immune Escape by Limiting Activated CD8 T-cell Infiltration into the Tumor Microenvironment

Précis: The cytokine GM-CSF, which is used to enhance white cell counts in many cancer patients, also expands a population of immune-suppressive monocytic cells that can block the entry of activated antitumor T cells into the tumor microenvironment, perhaps unwittingly contributing to immune escape.

887
Monocytic CCR2+ Myeloid-Derived Suppressor Cells Promote Immune Escape by Limiting Activated CD8 T-cell Infiltration into the Tumor Microenvironment

Précis: This study defines an IGF-1-driven mechanism of cancer cell survival that is critical for metastatic colonization of the liver, suggesting that IGF-1 receptor antagonists currently in clinical trials may have particular utility in treating colon cancers and other cancers that metastasize frequently to liver.

897
Hedgehog Signaling Inhibition Blocks Growth of Resistant Tumors through Effects on Tumor Microenvironment

Précis: This study extends knowledge concerning how an important inhibitory class of co-receptor molecules on T cells acts to block their specific cytotoxic activity against tumor cells, thereby deepening insights into how to reverse this key mechanism of immune escape in tumors for therapeutic benefit.
Précis: This study identifies the lactate transporter MCT1 as a critical mediator of p53-driven metabolic controls on glycolysis and respiration, and thus also potentially critical for supporting malignant progression of p53-deficient cancers.

MHC Class II Signaling Mediates Inward and Outward Lactate Transporter MCT1 Expression by p53

Précis: This study provides insights into the means by which bone cancers gain access to the lung, by modulating expression of a microRNA program that permits cancer cell survival in the lung microenvironment.
990 Histone Deacetylase Inhibition Increases Levels of Choline Kinase α and Phosphocholine Facilitating Noninvasive Imaging in Human Cancers
Mounia Beloueche-Babari, Vaitha Arunan, Helen Troy, Robert H. te Poele, Anne-Christine Wong Te Fong, L. Elizabeth Jackson, Geoffrey S. Payne, John R. Griffiths, Ian R. Judson, Paul Workman, Martin O. Leach, and Yuen-Li Chung

Précis: Noninvasive biomarkers offer critical tools for clinical trials of targeted drugs, as illustrated in this study providing mechanistic support for the use of phosphocholine as a candidate noninvasive biomarker for imaging the pharmacodynamic response to HDAC inhibitors.

LETTERS TO THE EDITOR

TUMOR AND STEM CELL BIOLOGY

Dysregulation of Ezrin Phosphorylation Prevents Metastasis and Alters Cellular Metabolism in Osteosarcoma
Ling Ren, Sung-Hyeok Hong, Qing-Rong Chen, Joseph Briggs, Jessica Cassavaugh, Satish Srivivasan, Michael M. Lizardo, Arulfo Mendoza, Ashley Y. Xia, Narayan Avadhan, Javed Khan, and Chand Khanna

Précis: This study offers mechanistic insights into the role of a pivotal regulator of metastasis that links the plasma cell membrane to the actin cytoskeleton, and that may act in part by linking metabolic and respiratory capacity to metastatic capability.

Hedgehog and Notch Signaling Regulate Self-Renewal of Undifferentiated Pleomorphic Sarcomas
Chang Ye Yale Wang, Qingxia Wei, Ilkyo Han, Shingo Sato, Ronak Ghanbari-Azarnier, Heather Whetstone, Raymond Poon, Jiaoy Hu, Feifei Zheng, Phil Zhang, Weishi Wang, Jay S. Wunder, and Benjamin A. Alman

Corrections
Correction: Endoglin Regulates Cancer–Stromal Cell Interactions in Prostate Tumors
Correction: Sirtuin 1 Is Upregulated in a Subset of Hepatocellular Carcinomas where It Is Essential for Telomere Maintenance and Tumor Cell Growth
Correction: Long Noncoding RNA HOTAIR Regulates Polycomb-Dependent Chromatin Modification and Is Associated with Poor Prognosis in Colorectal Cancers

ABOUT THE COVER
Vemurafenib recently achieved FDA approval for treating patients with metastatic melanoma harboring the BRAF V600E mutation. The BRAFV600E-driven uncontrolled proliferation is effectively blocked by vemurafenib, reflected in the remarkable regressions observed in the clinic. However, most patients eventually relapse, and in many instances, progression is associated with reactivation of ERK signaling, as observed by high levels of ERK phosphorylation in tumor biopsies taken at progression. The cover shows an example of a tumor biopsy taken at progression. Su and colleagues identify a novel KRAS mutation that mediates the acquired resistance of melanoma cells to vemurafenib. Both MAPK and PI3K pathways are active despite the presence of drug. Combinations of vemurafenib with either MEK or AKT inhibitors are able to overcome this resistance, providing hope that these combinations could mitigate disease relapse in patients. For details, see the article by Su and colleagues on page 969 of this issue.