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February 15, 2012 • Volume 72 • Number 4

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865 Precis: This study defines an IGF-I–driven mechanism of cancer cell survival that is critical for metastatic colonization of the liver, suggesting that IGF-I 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

887 Precis: 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 CD8+ T Cells Specific for Tumor Antigens Can Be Rendered Dysfunctional by the Tumor Microenvironment through Upregulation of the Inhibitory Receptors BTLA and PD-1
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897 Precis: 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.

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

Précis: This study describes an MRI imaging method that can be used to noninvasively monitor vascular disruption and normalization following VEGF blockade, addressing a clinical need to rapidly evaluate the likely impact of antangiogenic therapy in patients.

Précis: Expression of the glutathione detoxification system may be particularly important in mediating chemoresistance of tumors that harbor Myc family gene amplifications, as suggested here in studies of neuroblastoma, a common pediatric tumor.

Précis: Expression of the IGF-I receptor antagonists currently in clinical trials may have particular utility in treating colon cancers and other cancers that metastasize frequently to liver.

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.

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### MOLECULAR AND CELLULAR PATHOBIOLOGY

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Histone Deacetylase Inhibition Increases Levels of Choline Kinase α and Phosphocholine Facilitating Noninvasive Imaging in Human Cancers
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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

Impact of Epithelial Organization on Myc Expression and Activity—Letter
Johanna I. Partanen and Juha Klefstrom

Impact of Epithelial Organization on Myc Expression and Activity—Response
David Simpson Senthil Muthuswamy, and William P. Tansey

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 BRAF†V600E-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.