Microenvironment and Immunology

NF-kB Hyperactivation in Tumor Tissues Allows Tumor-Selective Reprogramming of the Chemokine Microenvironment to Enhance the Recruitment of Cytolytic T Effector Cells
Précis: Using a whole-colon tissue culture system, this study defines an immediately translatable combination of pharmacologic and biologic factors to promote the infiltration of colon tumors with cytolytic T-effector cells, a feature tightly correlated with improved survival outcomes regardless of tumor staging.

Molecular Identification of GD3 as a Suppressor of the Innate Immune Response in Ovarian Cancer
Tonya J. Webb, Xiangming Li, Robert L. Giuntoli II, Pablo H.H. Lopez, Christoph Heuser, Ronald L. Schnaar, Moriya Tsuji, Christian Kunts, Mathias Oelke, and Jonathan P. Schneck
Précis: Findings identify an endogenous cell surface glycolipid as an immune inhibitory molecule, which, when secreted by ovarian cancers, can block natural killer T-cell activation, offering a novel immunomodulatory target in this setting.

Molecular and Cellular Pathobiology

Molecular Signature of Smoking in Human Lung Tissues
Yohan Bossé, Dirkje S. Postma, Don D. Sin, Maxime Lamontagne, Christian Couture, Nathalie Gaudreault, Philippe Joubert, Vivien Wong, Mark Elliott, Maarten van den Berge, Corry A. Brandsma, Catherine Tribouley, Vladislav Malkov, Jeffrey A. Tsou, Gregory J. Opiteck, James C. Hogg, Andrew J. Sandford, Wim Timens, Peter D. Paré, and Michel Laviolette
Précis: This study used whole-genome gene expression to show the long-term impact of smoking on gene expression in nontumor lung tissues from patients with lung cancer.
The Oncogenic Lung Cancer Fusion Kinase CD74-ROS Activates a Novel Invasiveness Pathway through E-Syt1 Phosphorylation

Hyun Jung Jun, Hannah Johnson, Roderick T. Bronson, Sebastien de Feraudy, Forest White, and Alain Charest

Précis: Findings establish the oncogenicity of a recently discovered ROS fusion kinase in lung adenocarcinoma and show its utility as a therapeutic target in this setting.

Extensive Promoter DNA Hypermethylation and Hypomethylation Is Associated with Aberrant MicroRNA Expression in Chronic Lymphocytic Leukemia

Constance Baer, Rainer Claus, Lukas P. Frenzel, Manuela Zucknick, Yoon Jung Park, Lei Gu, Dieter Weichenhan, Martina Fischer, Christian Philipp Pallasch, Esther Herpel, Michael Rehli, John C. Byrd, Clemens-Martin Wendtner, and Christoph Plass

Précis: Findings extend the concept that epigenetic mechanisms are involved in cancer, influencing not only transcriptional control of protein coding genes but also microRNAs in chronic lymphocytic leukemia.

Autoregulatory Mechanisms of Phosphorylation of Checkpoint Kinase 1

Jingna Wang, Xiangzi Han, and Youwei Zhang

Précis: This study reveals a novel mechanism underlying cell-cycle checkpoint activation with implications for a novel approach to cancer therapy that involves artificially activating checkpoints under normal growth conditions.

Identification of a Molecular Signature Underlying Inhibition of Mammary Carcinoma Growth by Dietary N-3 Fatty Acids

Weiqin Jiang, Zongjian Zhu, John N. McGinley, Karam El Bayoumy, Andrea Manni, and Henry J. Thompson

Précis: This study identifies the pathways modulated by dietary fatty acid ratios in a rat model of breast cancer, with implications for cancer prevention.
Embryonic Protein Nodal Promotes Breast Cancer Vascularization
Daniela F. Quail, Logan A. Walsh, Guihua Zhang, Scott D. Findlay, Juan Moreno, Laura Fung, Amber Ablack, John D. Lewis, Susan J. Done, David A. Hess, and Lynne-Marie Postovit

Précis: Findings suggest that inhibitors of the developmental regulator Nodal may be useful as targeted therapies to block vascularization of breast cancers.

Numb Regulates Stability and Localization of the Mitotic Kinase PLK1 and Is Required for Transit through Mitosis
Travis L. Schmit, Minakshi Nihal, Mary Ndiaye, Vijayasardadhi Setaluri, Vladimir S. Spiegelman, and Nihal Ahmad

Précis: A developmental protein, Numb, which functions in cell fate determination, is found to exert a tumor-suppressive function during symmetric cell division.

Fibulin-3 Promotes Glioma Growth and Resistance through a Novel Paracrine Regulation of Notch Signaling

Précis: This seminal work highlights the major regulatory role of the tumor extracellular matrix on Notch signaling to promote glioma invasion and survival, with immediate clinical implications for improvement of adjuvant treatment strategies in malignant brain tumors.

ABOUT THE COVER
Activation of chemokine receptors on breast cancer cells can control their invasiveness. Analyzing microarray data from human breast cancer samples, increased expression of CCR5 in the basal subtype was found. Using in vivo and ex vivo bioluminescence in xenograft models, it was found that the CCR5 antagonist Maraviroc reduced lung colonization and metastasis in basal breast cancer cells. These results may lead to a new use of CCR5 antagonists as antimetastatic drugs. For details, see article by Velasco-Velázquez and colleagues on page 3839 of this issue.