**MICROENVIRONMENT AND IMMUNOLOGY**

**3735**

NF-κB 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.

**3744**

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 Kurts, 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**

**3753**

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, Vladimir Malkov, Jeffrey A. Tsou, Gregory J. Opitesek, 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

Precis: 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

Precis: 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

Precis: 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

Precis: This study identifies the pathways modulated by dietary fatty acid ratios in a rat model of breast cancer, with implications for cancer prevention.

Manganese Superoxide Dismutase Regulates a Metabolic Switch during the Mammalian Cell Cycle
Ehab H. Sarsour, Amanda L. Kalen, Zhen Xiao, Timothy D. Veenstra, Leena Chaudhuri, Sujatha Venkataraman, Philip Reigan, Garry R. Buettnner, and Prabhat C. Goswami

Precis: Studies of cells deficient in MnSOD, a mitochondrial enzyme that controls cellular redox flux, show that MnSOD regulates glucose consumption during transit through the cell cycle, implying a role in the Warburg Effect.

Loss of Rassfla Synergizes with Deregulated Runx2 Signaling in Tumorigenesis
Louise van der Weyden, Angelos Papaspyropoulos, George Poulogiannis, Alistair G. Rust, Mamunur Rashid, David J. Adams, Mark J. Arends, and Eric O’Neill

Precis: Findings reveal a new intersection between Ras signaling and the HIPPO signaling pathway for cell-cycle and survival control that is critical in leukemia development.

MET Signaling Regulates Glioblastoma Stem Cells
Kyeung Min Joo, Juyoun Jin, Eunhee Kim, Kang Ho Kim, Yonghyun Kim, Bong Gu Kang, Youn-Jung Kang, Justin D. Lathia, Kwang Ho Cheong, Paul H. Song, Hyungkee Kim, Ho Jun Seol, Do-Sik Kong, Jung Il Lee, Jeremy N. Rich, Jeongu Lee, and Do-Hyun Nam

Precis: The results of this study suggest that MET kinase may represent a promising therapeutic target in these aggressive brain tumors, a timely issue given the late-stage clinical development of MET kinase inhibitors.

CCR5 Antagonist Blocks Metastasis of Basal Breast Cancer Cells
Marco Velasco-Velázquez, Xuanmao Jiao, Marisol De La Fuente, Timothy G. Pestell, Adam Ertel, Michael P. Lisanti, and Richard G. Pestell

Precis: CCR5 antagonists, originally developed as HIV-entry inhibitors, reduce invasiveness and metastatic capability of breast cancer cells with basal phenotype and therefore may be used to prevent metastasis in patients with this currently nontargetable subtype of breast cancer.
Embryonic Protein Nodal Promotes Breast Cancer Vascularization
Daniela F. Quail, Logan A. Walsh, Guihuai Zhang, Scott D. Findlay, Juan Moreno, Laura Fung, Amber Ablack, John D. Lewis, Susan J. Done, David A. Hess, and Lynne-Marie Postovit

Precis: 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, Vijayasaradhi Setaluri, Vladimir S. Spiegelman, and Nihal Ahmad

Precis: 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

Precis: 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.

Correction: YM155, a Novel Small-Molecule Survivin Suppressant, Induces Regression of Established Human Hormone-Refractory Prostate Tumor Xenografts

Correction: Identification and Characterization of Nuclease-Stabilized RNA Molecules That Bind Human Prostate Cancer Cells via the Prostate-Specific Membrane Antigen

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.

Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/72/15

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.