REVIEWS

3709 ATP-Citrate Lyase: A Key Player in Cancer Metabolism
Nousheen Zaidi, Johannes V. Swinnen, and Karine Smans

Awaiting a New Era of Cancer Immunotherapy
Cheng William Hong and Qi Zeng

 awaiting a new era of cancer immunotherapy

MEETING REPORT

3720 The Global Cancer Genomics Consortium: Interfacing Genomics and Cancer Medicine
The Global Cancer Genomics Consortium

 STAGING AND CLINICAL OUTCOMES

3725 Prognostic PET 18F-FDG Uptake Imaging Features Are Associated with Major Oncogenic Alterations in Patients with Resected Non–Small Cell Lung Cancer
Viswam S. Nair, Olivier Gevaert, Guido Davidzon, Sandy Napel, Edward E. Graves, Chuong D. Hoang, Joseph B. Shrager, Andrew Quon, Daniel L. Rubin, and Sylvia K. Plevritis

 Precis: The molecular association of 18F-FDG uptake and positron emission tomography image features with gene expression can enhance our understanding of lung cancer progression and may facilitate new management strategies for patients.

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

 Precis: 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, Xiangning Li, Robert L. Giuntoli II, Pablo H.H. Lopez, Christoph Heuser, Ronald L. Schnaar, Moriya Tsuji, Christian Kurts, Mathias Oelke, and Jonathan P. Schneck

 Precis: 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, Vladislav Malkov, Jeffrey A. Tsou, Gregory J. Opiteck, James C. Hogg, Andrew J. Sandford, Wim Timens, Peter D. Paré, and Michel Laviolette

 Precis: 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.

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

Précis: 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 Deregluated Runx2 Signaling in Tumorigenesis
Louise van der Weyden, Angelos Papaspyropoulos, George Poulougiannis, Alistair G. Rust, Mamunur Rashid, David J. Adams, Mark J. Arens, and Eric O’Neill

Précis: 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, Yoon-Jung Kang, Justin D. Lathia, Kwang Ho Cheong, Paul H. Song, Hyunghee Kim, Ho Jun Seol, Do-Sik Kong, Jung Il Lee, Jeremy N. Rich, Jeongou Lee, and Do-Hyun Nam

Précis: 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

Précis: 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, 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, Vijayasaradhi 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.
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