BREAKING ADVANCES

399 Highlights from Recent Cancer Literature

REVIEWS

401 Urinary Tobacco Smoke–Constituent Biomarkers for Assessing Risk of Lung Cancer
Jian-Min Yuan, Lesley M. Butler, Irina Stepanov, and Stephen S. Hecht

412 ERKs in Cancer: Friends or Foes?
Xavier Deschênes-Simard, Filippos Kottakis, Sylvain Meloche, and Gerardo Ferbeyre

420 Bookmarking Target Genes in Mitosis: A Shared Epigenetic Trait of Phenotypic Transcription Factors and Oncogenes?
Sayyed K. Zaidi, Rodrigo A. Grandy, Cesar Lopez-Camacho, Martin Montecino, Andre J. van Wijnen, Jane B. Lian, Janet L. Stein, and Gary S. Stein

INTEGRATED SYSTEMS AND TECHNOLOGIES

426 Bridging Population and Tissue Scale Tumor Dynamics: A New Paradigm for Understanding Differences in Tumor Growth and Metastatic Disease
Jill Gallaher, Aravind Babu, Sylvia Plevritis, and Alexander R.A. Anderson

460 MUC1 in Macrophage: Contributions to Cigarette Smoke–Induced Lung Cancer
Xiuling Xu, Mabel T. Padilla, Bilan Li, Alexandria Wells, Kosuke Kato, Carmen Tellez, Steven A. Belinsky, Kwang Chul Kim, and Yong Lin

471 Defective TGF-β Signaling in Bone Marrow–Derived Cells Prevents Hedgehog-Induced Skin Tumors
Qipeng Fan, Dongsheng Gu, Hailan Liu, Ling Yang, Xiaoli Zhang, Mervin C. Yoder, Mark H. Kaplan, and Jingwu Xie

MICROENVIRONMENT AND IMMUNOLOGY

436 CCL2/CCR2-Dependent Recruitment of Functional Antigen-Presenting Cells into Tumors upon Chemotherapy
Yuting Ma, Stephen R. Mattarollo, Sandy Adjemian, Heng Yang, Laetitia Aymeric, Dalil Hannani, Joao Paulo Portela Catani, Helene Duret, Michele W.L. Teng, Oliver Kepp, Yidan Wang, Antonella Sistigu, Joachim L. Schultze, Gautier Stoll, Lorenzo Galluzzi, Laurence Zitvogel, Mark J. Smyth, and Guido Kroemer

464 Immune Chaperone gp96 Drives the Contributions of Macrophages to Inflammatory Colon Tumorigenesis
Crystal Morales, Saleh Rachidi, Feng Hong, Shaoli Sun, Xinshou Ouyang, Caroline Wallace, Yongliang Zhang, Elizabeth Garret-Mayer, Jennifer Wu, Bei Liu, and Zhihai Li

484 Cyclophilin B Supports Myc and Mutant p53-Dependent Survival of Glioblastoma Multiforme Cells
Jae Won Choi, Mark A. Schroeder, Jann N. Sarkaria, and Richard J. Bram

MOLECULAR AND CELLULAR PATHOBIOLOGY

446 MUC1 in Macrophage: Contributions to Cigarette Smoke–Induced Lung Cancer
Xiuling Xu, Mabel T. Padilla, Bilan Li, Alexandria Wells, Kosuke Kato, Carmen Tellez, Steven A. Belinsky, Kwang Chul Kim, and Yong Lin

 précis: By using a macrophage-specific gene knockout mouse, this important study reveals how tumor-associated macrophages not only orchestrate local inflammation but also cell mutagenesis to drive the development of colon cancer.

471 Defective TGF-β Signaling in Bone Marrow–Derived Cells Prevents Hedgehog-Induced Skin Tumors
Qipeng Fan, Dongsheng Gu, Hailan Liu, Ling Yang, Xiaoli Zhang, Mervin C. Yoder, Mark H. Kaplan, and Jingwu Xie

 précis: These results shed light on the mechanisms of inflammation-associated lung carcinogenesis, showing how cigarette smoke promotes contributions from lung macrophages in the tissue microenvironment to promote lung cancer.

 précis: Dysregulation of the Hedgehog pathway in cancer cells drives the formation of a supportive microenvironment, by stimulating a core mechanism of support for the development of myeloid-derived suppressor cells.

 précis: These results define the protein chaperone cyclophilin B as a promising molecular target for treatment of glioblastoma multiforme, with immediate clinical implications for repositioning the approved drug cyclosporin as a potential therapeutic to treat this aggressive malignancy.
Identification of a Cyclin D1 Network in Prostate Cancer That Antagonizes Epithelial–Mesenchymal Restraint

Xiaoming Ju, Mathew C. Casimiro, Michael Gormley, Hui Meng, Xuanmao Jiao, Sanjay Katiyar, Marco Cressariol, Ke Chen, Min Wang, Andrew A. Quong, Michael P. Lisanti, Adam Ertel, and Richard G. Pestell

**Précis:** This study reveals a novel function for cyclin D1 in mediating the expansion of prostate stem cells that contribute to prostate cancer.

CUL4A Induces Epithelial–Mesenchymal Transition and Promotes Cancer Metastasis by Regulating ZEB1 Expression

Yunshan Wang, Mingxin Wen, Yongwon Kwon, Yangyang Xu, Yueyong Liu, Pengju Zhang, Xiaquan He, Qin Wang, Yurong Huang, Kuang-Yu Jen, Mark A. LaBarge, Liang You, Scott C. Kogan, Joe W. Gray, Jian- Hua Mao, and Guangwei Wei

**Précis:** These findings suggest a pivotal role for the oncopgenic ubiquitin ligase CUL4A in regulating the metastatic behavior of breast cancer cells, with implications for therapeutic targeting of the pathway it regulates.

p53-Induced miR-15a/16-1 and AP4 Form a Double-Negative Feedback Loop to Regulate Epithelial–Mesenchymal Transition and Metastasis in Colorectal Cancer

Lei Shi, Rene Jackstadt, Helge Siemens, Huihui Li, Jian-Hua Mao, and Guangwei Wei

**Précis:** These findings define a signaling axis in cancer-specific killing that suggests a strategy to treat both local and metastatic disease.

Circadian Regulation of mTOR by the Ubiquitin Pathway in Renal Cell Carcinoma

Hiroyuki Okazaki, Naoya Matsunaga, Takashi Fujikawa, Fumiyasu Okazaki, Yui Akagawa, Yunyu Tsurudome, Mayumi Ono, Michihiko Kuwano, Satoru Koyanagi, and Shigehiro Ohdo

**Précis:** This important study shows how a pivot cell growth regulator is controlled by circadian clock systems, with significant therapeutic implications.

MDR1 Synonymous Polymorphisms Alter Transporter Specificity and Protein Stability in a Stable Epithelial Monolayer

King Leung Fung, James Pan, Shinobu Ohtsuka, Paul E. Lund, Jessica N. Pixley, Chaya Kimchi-Sarfaty, Suresh V. Ambudkar, and Michael M. Gottesman

**Précis:** Synonymous "silent" polymorphisms in the multiple drug resistance gene can nonetheless alter the function of the gene product and drive chemotherapeutic resistance.
TUMOR AND STEM CELL BIOLOGY

609 FGFR1–WNT–TGF-β Signaling in Prostate Cancer Mouse Models Recapitulates Human Reactive Stroma
Julienne L. Carstens, Payam Shahi, Susan Van Tsang, Billie Smith, Chad J. Creighton, Yuqin Zhang, Amber Seamans, Mamatha Seethammagari, Indira Vedula, Jonathan M. Levitt, Michael M. Ittmann, David R. Rowley, and David M. Spencer

Précis: Targeting the reactive stroma in aggressive prostate adenocarcinoma may generate a two-pronged attack that is more efficacious, by attacking cancer cells as well as the critical stromal tissue driving their outgrowth.

621 PPARα Activation Can Help Prevent and Treat Non-Small Cell Lung Cancer
Nataliya Skrypnyk, Xiwu Chen, Wen Hu, Yan Su, Stacey Mont, Shilin Yang, Maheshia Gangadhariah, Shouzuo Wei, Gordon J. Freeman, and John R. Falck

Précis: This important study provides a preclinical proof-of-concept for administering clinically approved PPARα agonists to treat lung cancer, with immediate implications to reposition an existing drug treatment that is well tolerated and may be highly efficacious in this setting.

LETTERS TO THE EDITOR

632 Dual Blockade of PD-1 and CTLA-4 Combined with Tumor Vaccine Effectively Restores T-Cell Rejection Function in Tumors—Letter
David C. Binder and Hans Schreiber

633 Dual Blockade of PD-1 and CTLA-4 Combined with Tumor Vaccine Effectively Restores T-Cell Rejection Function in Tumors—Response
Jaikumar Duraiswamy, Gordon J. Freeman, and George Coukos

635 Editors’ Viewpoint—Response
Mario P. Colombo and George C. Prendergast

CORRECTIONS

636 Correction: A Single-Nucleotide Substitution Mutator Phenotype Revealed by Exome Sequencing of Human Colon Adenomas

637 Correction: Neuropilin-2 Is Upregulated in Lung Cancer Cells during TGF-β1-Induced Epithelial–Mesenchymal Transition

ABOUT THE COVER

Anthracycline-based chemotherapy promotes the recruitment of CD11c⁺ (green) CD86⁺ (red) dendritic cells in close proximity to Caspase 3a⁺ (magenta) dying tumor cells. This process relies on "eat me" signal ATP and CCL2/CCR2 chemotactic axis. For details, see the article by Ma and colleagues on page 436 of this issue.