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 Deschénes-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
Précis: Vascular response is a primary cause of the differences in rates of tumor growth and metastatic disease in two of the most common cancers.

MICROENVIRONMENT AND IMMUNOLOGY

436 CCL2/CCR2-Dependent Recruitment of Functional Antigen-Presenting Cells into Tumors upon Chemotherapy
Précis: These findings illustrate the importance of CCL2/CCR2 signaling pathways for immunogenic chemotherapeutics to elicit their antitumor effects, suggesting risks that CCL2/CCR2 targeting strategies being tested clinically may actually worsen clinical outcomes in cancer patients.

446 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 Zhai Li
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.

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

460 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: 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.

465 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
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.
543 Circadian Regulation of mTOR by the Ubiquitin Pathway in Renal Cell Carcinoma

Hiroyuki Okazaki, Naoya Matsunaga, Takashi Fujioka, Fumiyasu Okazaki, Yui Akagawa, Yunya Tsurudome, Mayumi Ono, Michihiko Kuwano, Satoru Koyanagi, and Shigeo Ohdo

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

552 Blocking eIF5A Modification in Cervical Cancer Cells Alters the Expression of Cancer-Related Genes and Suppresses Cell Proliferation

Elisabeth Mémé, Mainul Hoque, Mohit R. Jain, Debra S. Heller, Hong Li, Bernadette Cricchio, Hartmut M. Hanauske-Abel, Tsafi Pe'ery, and Michael B. Mathews

 précis: These findings suggest a mechanistic rationale to immediately repurpose two approved drugs for cancer treatment, offering a low-risk clinical opportunity to evaluate new therapeutic modalities for cancer treatment.

563 Novel Mechanism of MDA-7/IL-24 Cancer-Specific Apoptosis through SARI Induction


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

575 Small Molecule Agonists of PPAR-γ Exert Therapeutic Effects in Esophageal Cancer

Hiroshi Sawayama, Takatsugu Ishimoto, Masayuki Watanabe, Naoya Yoshida, Hidetaka Sugihara, Junji Kurashige, Kotaro Hirashima, Masaaki Iwatsuki, Yoshifumi Baba, Eiji Oki, Masaru Morita, Yoshinobu Shiose, and Hideo Baba

 précis: A new-generation small molecule agonist of PPAR-γ that is more selective than existing agents may offer a novel route to treat esophageal squamous cancers, with immediate implications for clinical translation.

586 Preclinical Therapeutic Efficacy of a Novel Pharmacologic Inducer of Apoptosis in Malignant Peripheral Nerve Sheath Tumors

Vincent Chau, S. Kyun Lim, Wei Mo, Chiachi Liu, Amish J. Patel, Renée M. McKay, Shuguang Wei, Bruce A. Posner, Jef K. De Brabander, Noelle S. Williams, Luis F. Parada, and Lu Q. Le

 précis: Using a robust new model of malignant peripheral nerve sheath tumors that recapitulates features of the human malignancy, this study identified a novel proapoptotic small molecule that inhibits tumor cell growth.

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

King Leung Fung, James Pan, Shinobu Ohnuma, 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, Yiqun Zhang, Amber Seamans, Mamatha Seshammagari, 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, Mahesha Gangadhariah, Shouzuo Wei, John R. Falck, Jawahar Lal Jat, Roy Zent, Jorge H. Capdevila, and Ambra Pozzi

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.