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

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, Laretitia Aymeric, Dalil Hannani, João 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

MOLECULAR AND CELLULAR PATHOBIOLOGY

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

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

460 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

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

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

Precis: 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.
547  IRP2 Regulates Breast Tumor Growth
Wei Wang, Zhiyong Deng, Heather Hatcher, Lance D. Miller, Xiaomin Di, Lia Tesfay, Guangchao Sui, Ralph B. D’Agostino Jr, Frank M. Torti, and Suzy V. Torti

_Precis_: These results reveal a new pathway of iron dysregulation in breast cancer and identify IRP2, a master regulator of intracellular iron homeostasis, as an important driver of breast cancer growth.

550  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 Katipally, Marco Crusariol, Ke Chen, Min Wang, Andrew A. Quong, Michael P. Lisanti, Adam Ertel, and Richard G. Pestell

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

553  CUL4A Induces Epithelial–Mesenchymal Transition and Promotes Cancer Metastasis by Regulating ZEB1 Expression
Yunshan Wang, Mingxin Wen, Yongwon Kwon, Yangyang Xu, Yueyoung Liu, Pengju Zhang, Xiuxuan 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

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

556  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, Mark A. LaBarge, Liang You, Scott C. Kogan, Joe W. Gray, Jian-Hua Mao, and Guangwei Wei

_Precis_: This mechanistic study sheds new light on opposing circuitries of control for mesenchymal and epithelial states in cancer cells, the balance of which may influence invasive migration and metastasis.

559  Blocking eIF5A Modification in Cervical Cancer Cells Alters the Expression of Cancer-Related Genes and Suppresses Cell Proliferation
Elisabeth Mémin, Mainul Hoque, Mohit R. Jain, Debra S. Heller, Hong Li, Bernadette Crucchiolo, Hartmut M. Hanauske-Abel, Tsafi Pe’ery, and Michael B. Mathews

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

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

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

565  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 Shiiose, and Hideo Baba

_Precis_: 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.

568  Preclinical Therapeutic Efficacy of a Novel Pharmacologic Inducer of Apoptosis in Malignant Peripheral Nerve Sheath Tumors
Vincent Chau, Chuan-Kei 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

_Precis_: 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.

571  MDRI 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

_Precis_: 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 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, 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 3α (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.