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

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 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, Alexandria 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.

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: 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.

MOLECULAR AND CELLULAR PATHOBIOLOGY

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
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.
Circadian Regulation of mTOR by the Ubiquitin p53-Induced miR-15a/16-1 and AP4 Form a 532 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, Mei Qu, 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.

Identification of a Cyclin D1 Network in Prostate Cancer That Antagonizes Epithelial–Mesenchymal Restraining Xiaoming Ju, Mathew C. Casimiro, Michael Gormley, Hui Meng, Xuannao Jiao, Sanjay Katiyar, Marco Crussariol, 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.

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 Siemern, Huihui Li, Thomas Kirchner, and Heiko Hermeking

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

Cul4a Regulates Breast Tumor Growth Wei Wang, Zhiyong Deng, Heather Hatcher, Lance D. Miller, Xiumin 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.

Identification of a Cul4a Inducer of Epithelial–Mesenchymal Transition and Promotes Cancer Metastasis by Regulating Zeb1 Expression Yunshan Wang, Mingxin Wen, Yongwon Kwon, Yangyang Xu, Yueyong Liu, Pengju Zhang, Mei Qu, Andrew A. Quong, Michael P. Lisanti, Adam Ertel, and Richard G. Pestell

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.

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, Eji Oki, Masaru Morita, Yoshinobu Shiose, 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.

Preclinical Therapeutic Efficacy of a Novel Pharmacologic Inducer of Apoptosis in Malignant Peripheral Nerve Sheath Tumors Vincent Chau, S. Kyun Lim, Wei Wu, 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.

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, Chava 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.
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, Yiquan 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.

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.