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446 Immune Chaperone gp96 Drives the Contributions of Macrophages to Inflammatory Colon Tumorigenesis
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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

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.
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497 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
Précis: These results reveal a 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.

508 Identification of a Cdc42 Network in Prostate Cancer That Antagonizes Epithelial–Mesenchymal Restraint
Xiaoming Ju, Mathew C. Casimiro, Michael Gormley, Hui Meng, Xuanmao Jiao, Sanjay Katiyar, Marco Crusario, Ke Chen, Min Wang, Andrew A. Quong, Michael P. Lisanti, Adam Ertel, and Richard G. Pestell
Précis: This study reveals a novel function for cdc42 in mediating the expansion of prostate stem cells that contribute to prostate cancer.

520 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, 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 oncogenic ubiquitin ligase CUL4A in regulating the metastatic behavior of breast cancer cells, with implications for therapeutic targeting of the pathway it regulates.

532 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, Thomas Kirchner, and Heiko Hermeking
Précis: 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.

552 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
Précis: 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.

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
Hirosi Sawayama, Takatsugu Ishimoto, Masayuki Watanabe, Naoya Yoshida, Hidetaka Sugihara, Junji Kurashige, Kotaro Hirashima, Masaaki lwatsuki, 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, Shu 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.

THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY

543 Circadian Regulation of mTOR by the Ubiquitin Pathway in Renal Cell Carcinoma
Hiroyuki Okazaki, Naoya Matsunaga, Takashi Fujioka, Fumiyasuo Okazaki, Yui Akagawa, Yunya 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.
TUMOR AND STEM CELL BIOLOGY

609 FGF1–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 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, Mahesh 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

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.