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436 CCL2/CCR2-Dependent Recruitment of Functional Antigen-Presenting Cells into Tumors upon Chemotherapy
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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

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.

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 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.

471 Defective TGF-β Signaling in Bone Marrow–Derived Cells Prevents Hedgehog-Induced Skin Tumors
Qipeng Fan, Dongsheng Gu, Haiian 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.
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543  Circadian Regulation of mTOR by the Ubiquitin Pathway in Renal Cell Carcinoma
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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.

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

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.

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.

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

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.

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

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.

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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.
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, 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.

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
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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.