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426 Bridging Population and Tissue Scale Tumor Dynamics: A New Paradigm for Understanding Differences in Tumor Growth and Metastatic Disease
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#### 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
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#### 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 Zihai 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, 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.

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.
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543 Circadian Regulation of mTOR by the Ubiquitin Pathway in Renal Cell Carcinoma
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Precis: 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 Mémin, Mainul Hoque, Mohit R. Jain, Debra S. Heller,Hong Li, Berenadette Crucchiola, Hartmut M. Hanuske-Abel, Tsafi Pe'ery, and Michael B. Mathews
Precis: 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.

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

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
Precis: Synonymous "silent" polymorphisms in the multiple drug resistance gene can nonetheless alter the function of the gene product and drive chemotherapeutic resistance.
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*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.

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PPARα Activation Can Help Prevent and Treat Non–Small Cell Lung Cancer
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*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.

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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.