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Precis: 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.
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**Précis:** This important study shows how a pivotal 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, Bernadette Cracchiolo, Hartmut M. Hanuske-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.

558  **MDR1 Synonymous Polymorphisms Alter Transporter Specificity and Protein Stability in a Stable Epithelial Monolayer**
King Leung Fung, James Pan, Shinobu Ohtuma, Paul E. Lund, Jessica N. Pixley, Chava 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.

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

586  **Small Molecule Agonists of PPARγ 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 Shiose, and Hideo Baba

**Précis:** A new-generation small molecule agonist of PPARγ that is more selective than existing agents may offer a novel route to treat esophageal squamous cancers, with immediate implications for clinical translation.

592  **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 Cracchiolo, Hartmut M. Hanuske-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.

598  **Identification of a Cyclic D1 Network in Prostate Cancer That Antagonizes Epithelial–Mesenchymal Restraint**
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**Précis:** This study reveals a novel function for cyclin D1 in mediating the expansion of prostate stem cells that contribute to prostate cancer.

598  **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, Xinquan He, Qin Wang, Yurong Huang, Kuang-Yu Jen, Mark A. Laharge, 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.

606  **p53-Induced miR-15a/16-1 and AP4 Form a Double-Negative Feedback Loop to Regulate Epithelial–Mesenchymal Transition and Metastasis in Colorectal Cancer**
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**Précis:** These findings define a signaling axis in cancer-specific killing that suggests a strategy to treat both local and metastatic disease.

611  **MDR1 Synonymous Polymorphisms Alter Transporter Specificity and Protein Stability in a Stable Epithelial Monolayer**
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**Précis:** 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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609  FGFR1–WNT–TGF-β Signaling in Prostate Cancer Mouse Models Recapitulates Human Reactive Stroma
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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.

621  PPARγ 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 PPARγ 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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635  Editors’ Viewpoint—Response
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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

Anthraclyline-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.