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**Significance:** This study identifies a MYCN-dependent metabolic vulnerability and suggests a coupled relationship between metabolic reprogramming and increased sensitivity to metabolic stress, which could be exploited for cancer therapy.

See related commentary p. 3818

**Significance:** This study proposed targeted metabolic reprogramming as a valid combinatorial strategy to enhance the translational efficacy of oncolytic virus–based cancer therapies.

**Significance:** This study couples a novel experimental tool with state-of-the-art approaches to delineate molecular mechanisms underlying stem cell-related characteristics in leukemia cells.
**Genetic Ablation of the Cystine Transporter xCT in PDAC Cells Inhibits mTORC1, Growth, Survival, and Tumor Formation via Nutrient and Oxidative Stresses**

Boutaina Daher, Scott K. Parks, Jerome Durivault, Yann Cormerais, Hanane Baidarjad, Eric Tambutte, Jacques Pouyssegur, and Milica Vucetic

**Significance:** The cystine/glutamate exchanger xCT is essential for amino acid and redox homeostasis and its inhibition has potential for anticancer therapy by inducing ferroptosis.

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**Deletion of Calcineurin Promotes a Protumorigenic Fibroblast Phenotype**

Allyson Lieberman, Richard Barrett, Jaewon Kim, Kathy L. Zhang, Diana Avery, James Monslow, Hyunsoo Kim, Bang-Jin Kim, Ellen Puré, and Sandra Ryeom

**Significance:** Calcineurin signaling is a key pathway underlying fibroblast homeostasis that could be targeted to potentially prevent fibroblast activation in distant metastatic sites.

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**SUMO-Specific Protease 1 Is Critical for Myeloid-Derived Suppressor Cell Development and Function**

Xian Huang, Yong Zuo, Xiuzhi Wang, Xuefeng Wu, Hongsheng Tan, Qiju Fan, Baijun Dong, Wei Xue, Guo-Qiang Chen, and Jinke Cheng

**Significance:** These findings show that increased SUMOylation of CD45 via loss of SENP1 suppresses CD45-mediated dephosphorylation of STAT3, which promotes MDSC development and function, leading to tumorigenesis.

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**Retinoblastoma Inactivation Induces a Protumoral Microenvironment via Enhanced CCL2 Secretion**

Fengkai Li, Shunsuke Kitajima, Susumu Kohno, Akiyo Yoshida, Shoichiro Tange, Soichiro Sasaki, Nobuhiro Okada, Yuuki Nishimoto, Hayato Muranaka, Naoko Nagatan, Misa Suzuki, Sayuri Masuda, Tran C. Thai, Takumi Nishinomi, Tomoaki Tanaka, David A. Barber, Naofumi Mukaida, and Chiaki Takahashi

**Significance:** These findings demonstrate the cell-nonautonomous role of the tumor suppressor retinoblastoma in the tumor microenvironment, linking retinoblastoma loss to tumor suppression.

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**CBP/p300 Drives the Differentiation of Regulatory T Cells through Transcriptional and Non-Transcriptional Mechanisms**


**Significance:** This study provides insights into the dynamic role of CBP/p300 in the differentiation of Tregs, with potential clinical implications in the alteration of the immune landscape in follicular lymphoma.

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**Deletion of Calcineurin Promotes a Protumorigenic Fibroblast Phenotype**

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**Significance:** Calcineurin signaling is a key pathway underlying fibroblast homeostasis that could be targeted to potentially prevent fibroblast activation in distant metastatic sites.

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**Inhibition of ATM Increases Interferon Signaling and Sensitizes Pancreatic Cancer to Immune Checkpoint Blockade Therapy**

Qiang Zhang, Michael D. Green, Xueting Lang, Jenny Lazarus, Joshua D. Parsels, Shuang Wei, Leslie A. Parsels, Iaiqi Shi, Nithya Ramnath, Daniel R. Wahl, Martina Pasca di Magliano, Timothy L. Frankel, Ilona Kryczek, Yu L. Lei, Theodore S. Lawrence, Weiping Zou, and Meredith A. Morgan

**Significance:** This study demonstrates that ATM inhibition induces a T1IFN-mediated innate immune response in pancreatic cancer that is further enhanced by radiation and leads to increased sensitivity to anti–PD-L1 therapy.

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**Multiparametric MRI and Coregistered Histology Identify Tumor Habitats in Breast Cancer Mouse Models**

Bruna V. Jardim-Perassi, Suning Huang, William Dominguez-Viqueira, Jan Polesczuk, Mikalai M. Budzевич, Mahmoud A. Abdalah, Smitha R. Pillai, Epifanio Ruiz, Marilyn M. Bui, Debora A.P.C. Zuccari, Robert J. Gillies, and Gary V. Martinez

**Significance:** This study demonstrates that noninvasive imaging metrics can be used to distinguish subregions within heterogeneous tumors with histopathologic correlation.

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**Psychologic Distress Is Associated with Cancer-Specific Mortality among Patients with Cervical Cancer**

Donghao Lu, Bengt Andrae, Unnur Valdimarsdóttir, Karin Sundström, Katja Fall, Pat Sparén, and Fang Fang

**Significance:** These findings support the integration of psychological screening and intervention in the clinical management of patients with cervical cancer, particularly around the time of cancer diagnosis.
Anthropometric Risk Factors for Cancers of the Biliary Tract in the Biliary Tract Cancers Pooling Project

Significance: These findings identify a correlation between adiposity and biliary tract cancers, indicating that weight management programs may help minimize the risk of these diseases.

Modeling Gliomas Using Two Recombinases
Toshiro Hara and Inder M. Verma

Significance: This study presents a new glioma mouse model derived using lentiviral vectors and two recombination systems that will expand the ability to dissect developmental processes of gliomagenesis.

About the Cover
Mouse models for gliomas shed light on the importance of cell of origin, progression, heterogeneity, and the tumor stroma that cannot be easily studied in human cancers. GFAP-FLPo mouse strain expresses FLPo recombinase exclusively in GFAP-positive cells in the brain, which allows restriction of the initial sources of cell of origin of gliomas with the lentiviral delivery of cancer genes. Furthermore, this glioma model enables additional manipulation of mouse genome mediated by Cre recombinase in any cell type at any time in vivo and, therefore, accelerates the precise understanding of cellular and molecular mechanisms in the developmental processes of this deadly disease. For details, see article by Hara and Verma on page 3983.