Interferon-α Suppresses cAMP to Disarm Human Regulatory T Cells
Précis: These findings suggest a new application for IFN-α in cancer treatment by using it to inactivate T-regulatory cells in combination with vaccines as a means to degrade immune escape barriers that limit therapeutic responses.

Adipocyte-Derived Fibroblasts Promote Tumor Progression and Contribute to the Desmoplastic Reaction in Breast Cancer
Ludivine Bochet, Camille Lehuédé, Stéphanie Dauvillier, Yuan Yuan Wang, Bréatrice Dirat, Victor Laurent, Cédric Dray, Romain Guiet, Isabelle Marikonneau-Parini, Sophie Le Gonidec, Bettina Coudere, Ghislaine Escourrou, Philippe Valet, and Catherine Muller
Précis: This article reports the discovery of a new stromal cell population in the breast tumor microenvironment that may offer unique new opportunities for targeted therapy in breast cancer.

Tumor Microenvironmental Conversion of Natural Killer Cells into Myeloid-Derived Suppressor Cells
Young-Jun Park, Boyeong Song, Yun-Sun Kim, Eun-Kyung Kim, Jung-Mi Lee, Ga-Eun Lee, Jae-Ouk Kim, Yeon-Jeong Kim, Woo-Sung Chang, and Chang-Yuil Kang
Précis: Striking findings in this study reveal new insights into how tumor cells hijack their local immune microenvironment to escape immune surveillance.

Reg3β Deficiency Impairs Pancreatic Tumor Growth by Skewing Macrophage Polarization
Meritxell Gironella, Carlos Calvo, Anna Fernández, Daniel Closa, Juan L. Iovanna, Joan Rosello-Catalafau, and Emma Folch-Puy
Précis: The findings reported in this article may guide further clinical research based on the inhibition of the Reg3β in the treatment pancreatic cancer.
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**THERAPEUTICS, TARGETS, AND CHEMICAL BIOLOGY**

- **Akt SUMOylation Regulates Cell Proliferation and Tumorigenesis**: Bong Li, Jie Wei, Cong Jiang, Dongmei Liu, Lu Deng, Kai Zhang, and Ping Wang
  - *Précis*: This important study reveals a fundamental feature for controlling the function of Akt, which is broadly activated in many human cancers where it contributes to survival, invasion, and therapeutic resistance.

  - *Précis*: Definition of a core determining factor for cell-cycle control in melanoma suggests a rational new direction for targeted treatment or prevention of this disease.

- **Epimorphin Is a Novel Regulator of the Progesterone Receptor Isoform-α**: Jamie L. Bascom, Derek C. Radisky, Eileen Koh, Jimmie E. Fata, Alvin Lo, Hidetoshi Mori, Neda Roosta, Yohei Hirai, and Mina J. Bissell
  - *Précis*: This study offers new insights into control of the expression of the progesterone receptor, a key driver and prognostic determinant in hormone-dependent breast cancers.

- **Rapid Induction of Lung Adenocarcinoma by Fibroblast Growth Factor 3 Signaling through FGF Receptor 3**: Yongjun Yin, Tomoko Betsuyaku, Joel R. Garbow, Jinbai Miao, Ramaswamy Govindan, and David M. Ornitz
  - *Précis*: These findings highlight a mouse model of lung adenocarcinomas that form near the bronchioalveolar duct junction that may be useful to evaluate a growing number of experimental anticancer drugs that interfere with FGF signaling.

- **Src Family Kinases as Novel Therapeutic Targets to Treat Breast Cancer Brain Metastases**: Siyuan Zhang, Wen-Chien Huang, Lin Zhang, Chenyu Zhang, Frank J. Lowery, Zhaoxi Ding, Hua Guo, Hai Wang, Suyun Huang, Aysegul A. Sahin, Kenneth D. Aldape, Patricia S. Steeg, and Dihua Yu
  - *Précis*: Inhibitors of Src family tyrosine kinases that have been examined clinically might have excellent prospects for treatment of brain metastases of breast cancer, a deadly and untreatable step in disease progression occurring in many patients with advanced disease.

- **Targeting ERBB Receptors Shifts Their Partners and Triggers Persistent ERK Signaling through a Novel ERBB/EFNB1 Complex**: Paola D. Vermeer, Paul L. Colbert, Bryant G. Wiekling, Daniel W. Vermeer, and John H. Lee
  - *Précis*: This study provides a mechanistic explanation for why EGFR targeting drugs work poorly in head and neck carcinoma despite common involvement of EGFR in this cancer.
Stem Cell Differentiation and Lumen Formation in Colorectal Cancer Cell Lines and Primary Tumors
Neil Ashley, Trevor M. Yeung, and Walter F. Bodmer

Précis: An in vitro model for functional characterization of colorectal stem-like cells and their differentiation also offers applications to enable high-throughput screening for novel anticancer compounds.

Breast Tumor Kinase (Brk/PTK6) Is a Mediator of Hypoxia-Associated Breast Cancer Progression
Tarah M. Regan Anderson, Danielle L. Peacock, Andrea R. Daniel, Gregory K. Hubbard, Kristopher A. Lofgren, Brian J. Girard, Alexandra Schörg, David Hoogewijs, Roland H. Wenger, Tiffany N. Seagroes, and Carol A. Lange

Précis: These findings define a kinase-based mechanism that drives the aggressive behavior of triple-negative breast cancers, which may offer a tractable target for therapy in this challenging disease.

ANTXR1, a Stem Cell-Enriched Functional Biomarker, Connects Collagen Signaling to Cancer Stem-like Cells and Metastasis in Breast Cancer
Daohong Chen, Poornima Bhat-Nakshatri, Chirayu Goswami, Sunil Badve, and Harikrishna Nakshatri

Précis: These findings illuminate functional links between the tumor microenvironment and stemness functions that contribute to metastatic progression, with potential implications for understanding breast cancer pathophysiology and therapy.

Comparative Expression Analysis Reveals Lineage Relationships between Human and Murine Gliomas and a Dominance of Glial Signatures during Tumor Propagation In Vitro

Précis: The brain tumor microenvironment strongly modifies tumor genetics that initiate disease, ultimately directing the pathway for growth dynamics, histology, and therapeutic responsiveness of brain tumors, with implications for understanding how to properly model and treat disease more effectively.

Correction: Quantitative In Vivo Characterization of Intracellular and Extracellular pH Profiles in Heterogeneous Tumors: A Novel Method Enabling Multiparametric pH Analysis

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ABOUT THE COVER

The importance of natural killer (NK) cells for eradicating cancer cannot be overemphasized. It was found that the tumor environment impairs the development and function of NK cells and even diminishes the number of NK cells in patients with chronic myelogenous leukemia. Here, Park and colleagues show that a part of CD11b<sup>high</sup>CD27<sup>high</sup> NK cells obtained from tumor-bearing mice were converted into CD11b<sup>+</sup>Gr1<sup>+</sup> MDSC phenotype by GM-CSF, while the phenotype of NK cells was retained in the presence of IL-2. For details, see article by Park and colleagues on page 5669.