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This study shows how HSF1 regulates a stromal transcriptional program associated with aggressive gastric cancer and identifies multiple proteins within this program as candidates for therapeutic intervention.

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Targeting TUG1 coupled with a cancer-specific drug delivery system effectively modulates 5-FU catabolism in TUG1-overexpressing PDAC cells, thus contributing to a new combinatorial strategy for cancer treatment.
A Large-Scale Association Study Detects Novel Rare Multiomics Characterization of Low-Grade Serous Germline and Somatic Genetic Variants in the p53 Pathway Interact to Affect Cancer Risk, Progression, and Drug Response
These results offer evidence of how cancer susceptibility SNPs can interact with cancer driver genes to affect cancer progression and present novel therapeutic targets.

Multimomics Characterization of Low-Grade Serous Ovarian Carcinoma Identifies Potential Biomarkers of MEK Inhibitor Sensitivity and Therapeutic Vulnerability
These findings highlight the utility of global multimomics to characterize LGSOC cell lines as research models, to determine biomarkers of MEKi resistance, and to identify potential novel therapeutic targets.

A Large-Scale Association Study Detects Novel Rare Variants, Risk Genes, Functional Elements, and Polygenic Architecture of Prostate Cancer Susceptibility
This study maps the biological relationships between diverse risk factors for prostate cancer, integrating different functional datasets to interpret and model genome-wide data from over 200,000 men with and without prostate cancer.

See related commentary, p. 1637

METABOLISM AND CHEMICAL BIOLOGY

ELOVL5 Is a Critical and Targetable Fatty Acid Elongase in Prostate Cancer
This study identifies phospholipid elongation as a new metabolic target of androgen action that is critical for prostate tumor metastasis.

MOLECULAR CELL BIOLOGY

CKAP2L Promotes Non-Small Cell Lung Cancer Progression through Regulation of Transcription Elongation
Tiziana Monteverde, Sudhakar Sahoo, Manuela La Montagna, Peter Magee, Lei Shi, Dave Lee, Robert Sellers, Alexander R. Baker, Hui Sun Leong, Matteo Fassan, and Michela Garofalo
These findings demonstrate the oncogenic function of CKAP2L through regulation of transcription elongation and suggest that targeting CKAP2L could enhance therapeutic response in patients with NSCLC.

Glia-Selective Deletion of Complement C1q Prevents Radiation-Induced Cognitive Deficits and Neuroinflammation
Clinically-relevant radiotherapy induces aberrant complement activation, leading to brain injury. Microglia-selective genetic deletion of CNS complement C1q ameliorates radiation-induced cognitive impairments, synaptic loss, and neuroinflammation, highlighting the potential for C1q as a novel therapeutic target.

See related commentary, p. 1635

PINK1-Mediated Inhibition of EGFR Dimerization and Activation Impedes EGFR-Driven Lung Tumorigenesis
Emily Pei-Ying Lin, Bo-Tsang Huang, Wei-Yun Lai, Yi-Ting Tseng, Shuenn-Chen Yang, Hao-Cheng Kuo, and Robert Sellers
This study identifies PINK1 as a critical tumor suppressor that impedes EGFR dimerization and highlights PINK1-CTD as a potential therapeutic agent in EGFR-driven lung cancer.
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*These findings show that RBM38 exerts opposing effects on survivin expression via two miRNAs, and disruption of the RBM38-AGO2 complex by an eight-amino acid peptide sensitizes tumor spheroids to survivin inhibitor YM155.*

*These findings demonstrate that the single-cell regulatory heterogeneity of small-cell lung cancer becomes increasingly elaborate in the liver, a common metastatic site for the disease.*
The Hydroxyquinoline Analogue YUM70 Inhibits GRP78 to Induce ER Stress–Mediated Apoptosis in Pancreatic Cancer

This study identifies a novel ER stress inducer that binds GRP78 and inhibits pancreatic cancer cell growth in vitro and in vivo, demonstrating its potential as a therapeutic agent for pancreatic cancer.

MYCN-Amplified Neuroblastoma Is Addicted to Iron and Vulnerable to Inhibition of the System Xc-/Glutathione Axis

The study shows how MYCN increases intracellular iron levels and subsequent GSH pathway activity and demonstrates the antitumor activity of FDA-approved SAS and auranofin in patient-derived xenograft models of MYCN-amplified neuroblastoma.

Local Targeting of NAD⁺ Salvage Pathway Alters the Immune Tumor Microenvironment and Enhances Checkpoint Immunotherapy in Glioblastoma

This study investigates cervical cancer cell-of-origin populations and describes a DLL-Notch1 phenotype that is associated with disease prognosis and that might help identify cells that are susceptible to HPV-induced carcinogenesis.
Immunofluorescent staining of DLL4 in a keratinocyte cell line, NIKS, highlights the high expression of this Notch1 ligand in migratory and proliferative cells of the leading edge of large monolayer gaps. This DLL4 phenotype is inherent to reserve cells in the normal, HPV-uninfected cervix, and HPV16 E6 expression sustains Notch1 ligand expression, likely facilitating a more durable skewing of squamous cell fate. Cervical tumors that show high DLL4 expression are associated with worse disease prognosis. For details, see Khelil and colleagues on page 1909.
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