In Focus

The Landscape of Human Cancer Proteins Targeted by SARS-CoV-2 ..........916
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MINI REVIEW

Targeting MET Dysregulation in Cancer .................922
G. Recondo, J. Che, P.A. Jänne, and M.M. Awad

RESEARCH BRIEF

Case Fatality Rate of Cancer Patients with COVID-19 in a New York Hospital System ....935
Précis: Patients with cancer in a New York hospital system were much more vulnerable to COVID-19 death than the general population, with a case fatality rate that varied by cancer type and was 28% overall.

RESEARCH ARTICLES

Infant High-Grade Gliomas Comprise Multiple Subgroups Characterized by Novel Targetable Gene Fusions and Favorable Outcomes .....942
Précis: A subset of infant high-grade gliomas with shared molecular and clinical characteristics were associated with better prognosis and often harbored targetable fusions involving genes encoding receptor tyrosine kinases.

See commentary, p. 904

Tumor Microenvironment Is Critical for the Maintenance of Cellular States Found in Primary Glioblastomas ............ 964

Précis: Of four glioma stem cell–derived glioblastoma models, glioblastoma cerebral organoids most closely recapitulated the transcriptome and cell composition of primary tumors, a microenvironment-dependent effect.

See commentary, p. 907

Gain-of-Function Genetic Alterations of G9a Drive Oncogenesis ............. 980

Précis: Amplification of or activating mutations in the histone methyltransferase–encoding gene EHMT2 reduced DKK1-mediated inhibition of the WNT pathway to promote melanoma development.

EZH2-Deficient T-cell Acute Lymphoblastic Leukemia Is Sensitized to CHK1 Inhibition through Enhanced Replication Stress ... 998

Précis: In T-cell acute lymphoblastic leukemia (T-ALL), loss-of-function mutations affecting EZH2 confer poor prognosis, but elevated replication stress may render EZH2-mutant T-ALL sensitive to CHK1 inhibition.

Somatic Tissue Engineering in Mouse Models Reveals an Actionable Role for WNT Pathway Alterations in Prostate Cancer Metastasis ................. 1038

Précis: A rapid, targeted method to generate genetically engineered mouse models of prostate cancer was developed and used to show that tankyrase inhibition may be useful in WNT pathway–activated disease.

Tumor Microenvironment Remodeling Enables Bypass of Oncogenic KRAS Dependency in Pancreatic Cancer ... 1058

Précis: Pancreatic ductal adenocarcinoma (PDAC) escaped dependence on oncogenic KRAS via an HDAC5-mediated mechanism that resulted in macrophage recruitment to the tumor microenvironment via a druggable pathway.

See commentary, p. 910

Correction

Correction: Targeting HER2 with Trastuzumab Deruxtecan: A Dose-Expansion, Phase I Study in Multiple Advanced Solid Tumors ............... 1078

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Because no model is perfect, Pine, Cirigliano, and colleagues sought to characterize four commonly used glioblastoma models: two-dimensional glioma sphere cultures, three-dimensional tumor organoids, glioblastoma cerebral organoids (GLICO), and patient-derived xenografts. GLICOs stood out as most closely resembling primary glioblastomas in several important ways, with closely overlapping transcriptomes and similarities in cell-type composition. GLICOs’ ability to recapitulate many aspects of glioblastoma biology depended on the microenvironment: When cultured in two-dimensional conditions, GLICO-derived cells lost many similarities with primary glioblastomas. This work showcases the strengths of GLICOs and provides detailed characterizations of the three other models, providing researchers with data to make informed decisions about which model best suits their purposes. For more information, see the article by Pine, Cirigliano, and colleagues on page 964.