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**RESEARCH
BRIEF** Case Fatality Rate of Cancer
Patients with COVID-19 in a
New York Hospital System 935

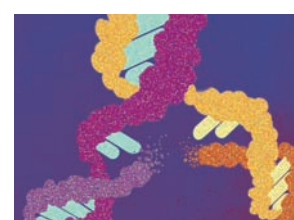
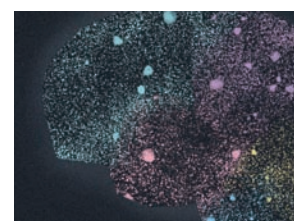
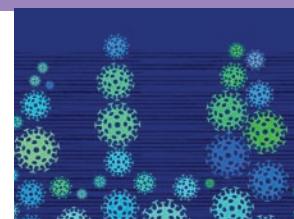
V. Mehta, S. Goel, R. Kabarriti, D. Cole,
M. Goldfinger, A. Acuna-Villaorduna,
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J.A. Sparano, B.A. Gartrell, R.V. Smith,
N. Ohri, M. Garg, A.D. Racine, S. Kalnicki,
R. Perez-Soler, B. Halmos, and A. Verma

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



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T. Bloom, C. Mitchell, E. Miele, G.S. Colafati,





F. Diomed-Camassei, S. Bailey, A.S. Moore, T.E.G. Hassall, S.P. Lewis, M. Tsoli, M.J. Cowley, D.S. Ziegler, M.A. Karajannis, K. Aquilina, D.R. Hargrave, F. Carceller, L.V. Marshall, A. von Deimling, C.M. Kramm, S.M. Pfister, F. Sahm, S.J. Baker, A. Mastronuzzi, A. Carai, M. Vinci, D. Capper, S. Popov, D.W. Ellison, T.S. Jacques, D.T.W. Jones, and C. Jones

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

A.R. Pine, S.M. Cirigliano, J.G. Nicholson, Y. Hu, A. Linkous, K. Miyaguchi, L. Edwards, R. Singhanian, T.H. Schwartz, R. Ramakrishna, D.J. Pisapia, M. Snuderl, O. Elemento, and H.A. Fine

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

S. Kato, Q.Y. Weng, M.L. Insko, K.Y. Chen, S. Muralidhar, J. Poznaniak, J.M.S. Diaz, Y. Drier, N. Nguyen, J.A. Lo, E. van Rooijen, L.V. Kemeny, Y. Zhan, Y. Feng, W. Silkworth, C.T. Powell, B.B. Liao, Y. Xiong, J. Jin, J. Newton-Bishop, L.I. Zon, B.E. Bernstein, and D.E. Fisher

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

T.E. León, T. Rapoz-D'Silva, C. Bertoli, S. Rahman, M. Magnussen, B. Philip, N. Farah, S.E. Richardson, S. Ahrabi, J.A. Guerra-Assunção, R. Gupta, E.P. Nacheva, S. Henderson, J. Herrero, D.C. Linch, R.A.M. de Bruin, and M.R. Mansour

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.

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Selective Alanine Transporter Utilization Creates a Targetable Metabolic Niche in Pancreatic Cancer 1018



S.J. Parker, C.R. Amendola, K.E.R. Hollinshead, Q. Yu, K. Yamamoto, J. Encarnación-Rosado, R.E. Rose, M.M. LaRue, A.S.W. Sohn, D.E. Biancur, J.A. Paulo, S.P. Gygi, D.R. Jones, H. Wang, M.R. Philips, D. Bar-Sagi, J.D. Mancias, and A.C. Kimmelman

Précis: Pancreatic ductal adenocarcinoma (PDAC) cells used the neutral amino acid transporter SLC38A2 to import necessary alanine, and lack of SLC38A2 caused a metabolic crisis in PDAC cells and tumor regression *in vivo*.

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



J. Leibold, M. Ruscetti, Z. Cao, Y.-J. Ho, T. Baslan, M. Zou, W. Abida, J. Feucht, T. Han, F.M. Barriga, K.M. Tsanov, L. Zamechek, A. Kulick, C. Amor, S. Tian, K. Rybczyk, N.R. Salgado, F.J. Sánchez-Rivera, P.A. Watson, E. de Stanchina, J.E. Wilkinson, L.E. Dow, C. Abate-Shen, C.L. Sawyers, and S.W. Lowe

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

P. Hou, A. Kapoor, Q. Zhang, J. Li, C.-J. Wu, J. Li, Z. Lan, M. Tang, X. Ma, J.J. Ackroyd, R. Kalluri, J. Zhang, S. Jiang, D.J. Spring, Y.A. Wang, and R.A. DePinho

Précis: Pancreatic ductal adenocarcinoma 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

ON THE COVER

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.

