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IEWS In The Spotlight

Fusing the Genetic Landscape of Infantile High-Grade Gliomas 904

F. Szulzewsky and P.J. Cimino

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Utility of Human-Derived Models for Glioblastoma 907

X. Luo and W.A. Weiss

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It Takes a Village to Overcome KRAS Dependence in Pancreatic Cancer 910

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The Era of COVID-19 and the Rise of Science Collectivism in Cancer Research 913

T. Janowitz and D.A. Tuveson

In Focus

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

B. Tutuncuoglu, M. Cakir, J. Batra, M. Bouhaddou, M. Eckhardt, D.E. Gordon, and N.J. Krogan

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

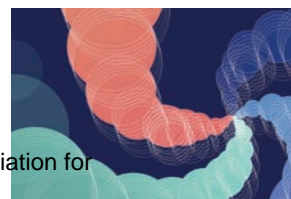
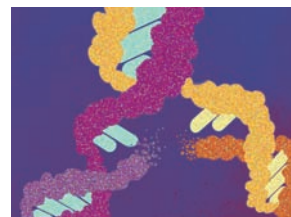
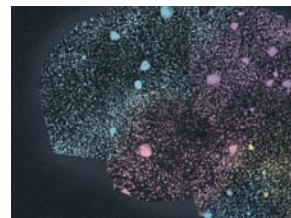
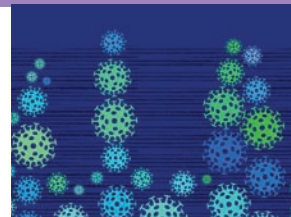
V. Mehta, S. Goel, R. Kabarriti, D. Cole, M. Goldfinger, A. Acuna-Villaorduna, K. Pradhan, R. Thota, S. Reissman, J.A. Sparano, B.A. Gartrell, R.V. Smith, N. Ohri, M. Garg, A.D. Racine, S. Kalnicki, R. Perez-Soler, B. Halmos, and A. Verma

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



M. Clarke, A. Mackay, B. Ismer, J.C. Pickles, R.G. Tatevossian, S. Newman, T.A. Bale, I. Stoler, E. Izquierdo, S. Temelso, D.M. Carvalho, V. Molinari, A. Burford, L. Howell, A. Virasami, A.R. Fairchild, A. Avery, J. Chalker, M. Kristiansen, K. Haupfear, J.D. Dalton, W. Orisme, J. Wen, M. Hubank, K.M. Kurian, C. Rowe, M. Maybury, S. Crosier, J. Knipstein, U. Schüller, U. Kordes, D.E. Kram, M. Snuderl, L. Bridges, A.J. Martin, L.J. Doey, S. Al-Sarraj, C. Chandler, B. Zebian, C. Cairns, R. Natrajan, J.K.R. Boulton, S.P. Robinson, M. Sill, I.J. Dunkel, S.W. Gilheeny, M.K. Rosenblum, D. Hughes, P.Z. Proszek, T.J. Macdonald, M. Preusser, C. Haberler, I. Slavc, R. Packer, H.-K. Ng, S. Caspi, M. Popović, B.F. Kotnik, M.D. Wood, L. Baird, M.A. Davare, D.A. Solomon, T.K. Olsen, P. Brandal, M. Farrell, J.B. Cryan, M. Capra, M. Karremann, J. Schittenhelm, M.U. Schuhmann, M. Ebinger, W.N.M. Dinjens, K. Kerl, S. Hettmer, T. Pietsch, F. Andreiuolo, P.H. Driever, A. Korshunov, L. Hiddingh, B.C. Worst, D. Sturm, M. Zuckermann, O. Witt, T. Bloom, C. Mitchell, E. Miele, G.S. Colafati,



F.Diomedì-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. Singhanía, 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. Pozniak, J.M.S. Díaz, 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.

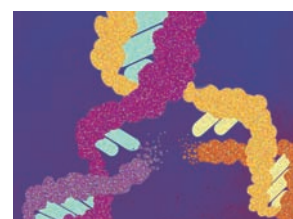
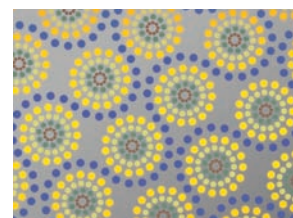
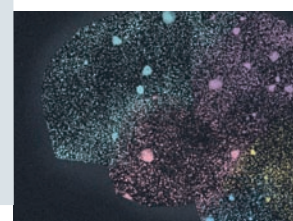
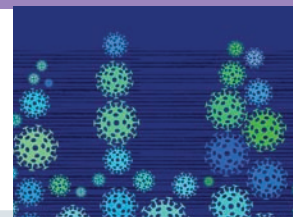
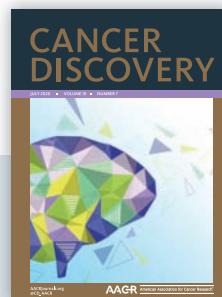
See commentary, p. 910

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.



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