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Infant High-Grade Gliomas Comprise Multiple Subgroups Characterized by Novel Targetable Gene Fusions and Favorable Outcomes ..........942
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Tumor Microenvironment Is Critical for the Maintenance of Cellular States Found in Primary Glioblastomas ...... 964
Precis: 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.
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Gain-of-Function Genetic Alterations of G9a Drive Oncogenesis ............. 980
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EZH2-Deficient T-cell Acute Lymphoblastic Leukemia Is Sensitized to CHK1 Inhibition through Enhanced Replication Stress ... 998
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Selective Alanine Transporter Utilization Creates a Targetable Metabolic Niche in Pancreatic Cancer ................. 1018
Precis: 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.

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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.