## RESEARCH BRIEFS

**Radiotherapy and Immunotherapy Promote Tumoral Lipid Oxidation and Ferroptosis via Synergistic Repression of SLC7A11** … 1673  
Précis: In multiple mouse cancer models, ferroptosis plays a pivotal role in tumor response to radiotherapy and may be partially responsible for the observed synergy between radiotherapy and immunotherapy.

**Acquired On-Target Clinical Resistance Validates FGFR4 as a Driver of Hepatocellular Carcinoma** … 1686  
Précis: Resistance mutations seen in a clinical trial of the fibroblast growth factor receptor 4 (FGFR4) inhibitor fisogatinib validate FGFR4 activation as a driver of hepatocellular carcinoma.  
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## RESEARCH ARTICLES

**First-in-Human Phase I Study of Fisogatinib (BLU-554) Validates Aberrant FGFR19 Signaling as a Driver Event in Hepatocellular Carcinoma** … 1696  
Précis: In a first-in-human, phase I clinical trial, the fibroblast growth factor receptor 4 (FGFR4) inhibitor fisogatinib was tolerable and demonstrated preliminary evidence of efficacy in patients with FGFR19-positive hepatocellular carcinoma.  
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## VIEWS

**In The Spotlight**

**Precision Oncology for Hepatocellular Cancer: Slivering the Liver by FGFR19–FGFR4–KLB Pathway Inhibition** … 1646  
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The Phenotypes of Proliferating Glioblastoma Cells Reside on a Single Axis of Variation .......................... 1708


Précis: A proneural–mesenchymal axis in glioma stem cells was sufficient to account for intratumor heterogeneity in tumor samples from patients with glioblastomas.

See commentary, p. 1650

Polysaturated Fatty Acids from Astrocytes Activate PPARγ Signaling in Cancer Cells to Promote Brain Metastasis ............... 1720


Précis: PPARγ signaling was associated with an increase in brain metastasis in mouse models of melanoma and breast cancer, an effect that was mediated by release of polysaturated fatty acids by astrocytes.

Ontogenic Changes in Hematopoietic Hierarchy Determine Pediatric Specificity and Disease Phenotype in Fusion Oncogene–Driven Myeloid Leukemia .......... 1736


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In a first-in-human, phase I clinical trial, Kim and colleagues investigated the use of the fibroblast growth factor receptor 4 (FGFR4) inhibitor fisogatinib in patients with hepatocellular carcinoma, demonstrating that it is generally tolerable and may be of clinical utility in patients positive for fibroblast growth factor 19. By investigating mechanisms of resistance to fisogatinib in select patients in the trial as well as by conducting further in vitro and in vivo studies, Hatlen, Schmidt-Kittler, and colleagues found evidence that FGFR4 is, as has been suspected but never proven, a driver of hepatocellular carcinoma. For details, please see the article by Kim and colleagues on page 1696 and the article by Hatlen, Schmidt-Kittler, and colleagues on page 1686.