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Unique Neoantigens Arise from Somatic Mutations in Patients with Gastrointestinal Cancers 1022
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First-in-Human RNA Polymerase I Transcription Inhibitor CX-5461 in Patients with Advanced Hematologic Cancers: Results of a Phase I Dose-Escalation Study 1036
Précis: A phase I dose-escalation study evaluates the safety and pharmacokinetics of the RNA Polymerase I inhibitor CX-5461 in patients with advanced hematologic cancers.

Clonal Selection with RAS Pathway Activation Mediates Secondary Clinical Resistance to SelectiveFLT3 Inhibition in Acute Myeloid Leukemia 1050
Précis: Targeted next-generation sequencing of matched pretreatment and progressive samples from patients with AML on gilteritinib identified multiple secondary gilteritinib resistance mechanisms.
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TAS-120 Overcomes Resistance to ATP-Competitive FGFR Inhibitors in Patients with FGFR2 Fusion–Positive Intrahepatic Cholangiocarcinoma .................1064


Précis: The irreversible FGFR inhibitor TAS-120 has clinical activity against FGFR2 mutations that confer resistance to FGFR inhibitors in patients with FGFR2-altered intrahepatic cholangiocarcinoma.

Aging Human Hematopoietic Stem Cells Manifest Profound Epigenetic Reprogramming of Enhancers That May Predispose to Leukemia ...............1080


Précis: Human hematopoietic stem cells undergo age-associated genome-wide epigenomic changes that target developmental and cancer-related pathways and may increase susceptibility to myeloid malignancies.

Cross-Species Single-Cell Analysis of Pancreatic Ductal Adenocarcinoma Reveals Antigen-Presenting Cancer-Associated Fibroblasts ...............1102


Précis: A previously unknown class of cancer-associated fibroblasts with unique immune properties may contribute to the immunosuppressive PDAC microenvironment.

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ß-Catenin Activation Promotes Immune Escape and Resistance to Anti–PD-1 Therapy in Hepatocellular Carcinoma ...... 1124


Précis: A mouse model of hepatocellular carcinoma reveals that ß-catenin activation leads to anti–PD-1 resistance via faulty immune surveillance.

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Editor’s Note

Editor’s Note: Increased Levels of COX-2 and Prostaglandin E2 Contribute to Elevated Aromatase Expression in Inflamed Breast Tissue of Obese Women ......... 1142

Elyada and colleagues profiled human pancreatic ductal adenocarcinoma tumors and adjacent normal tissue along with mouse pancreatic tumors and discovered a previously unknown class of cancer-associated fibroblasts (CAF) they named antigen-presenting CAFs (apCAF). These CAFs are unique in their expression of MHC class II-related genes, which implies they may interact with CD4⁺ T-cells; supporting this idea, apCAFs activated CD4⁺ T-cells ex vivo in an antigen-dependent fashion. Also unlike other CAFs, apCAFs upregulate MYC targets and antigen presentation, antigen processing, fatty-acid metabolism, and MTORC1 signaling pathways. Hinting that apCAFs may contribute to immune suppression in PDAC, they do not produce costimulatory molecules needed for induction of T-cell proliferation. For details, please see the article by Elyada and colleagues on page 1102.