**RESEARCH BRIEF**

Unique Neoantigens Arise from Somatic Mutations in Patients with Gastrointestinal Cancers ....... 1022

Précis: Neoantigens in cancers with low numbers of mutations are similarly recognized by tumor-infiltrating lymphocytes, with implications for improving immunotherapy.

**RESEARCH ARTICLES**

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 Selective FLT3 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.

See commentary, p. 998

**IN THIS ISSUE**

Highlighted research articles .................. 983

**NEWS IN BRIEF**

Important news stories affecting the community .......... 988

**NEWS IN DEPTH**

IDH Inhibitors Target Common Glioma Mutation ............ 992

**RESEARCH WATCH**

Selected highlights of recent articles of exceptional significance from the cancer literature .......... 993

**ONLINE**

For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/CDNews.

**VIEWS**

In The Spotlight

Polyclonal Heterogeneity: The New Norm for Secondary Clinical Resistance to Targeted Monotherapy in Relapsed Leukemia? ........ 998
A.H. Wei and A.W. Roberts

See article, p. 1050

A Single-Cell Window into Pancreas Cancer Fibroblast Heterogeneity ............. 1001
J.J. Belle and D.G. DeNardo

See article, p. 1102

Immune Desertic Landscapes in Hepatocellular Carcinoma Shaped by β-Catenin Activation .... 1003
P. Berraondo, M.C. Ochoa, I. Olivera, and I. Melero

See article, p. 1124

**REVIEW**

The Metabolic Basis of Kidney Cancer .............. 1006
W.M. Linehan, L.S. Schmidt, D.R. Crooks, D. Wei, R. Srinivasan, M. Lang, and C.J. Ricketts

Downloaded from cancerdiscovery.aacrjournals.org on March 17, 2021. © 2019 American Association for Cancer Research.
TAS-120 Overcomes Resistance to ATP-Competitive FGFR Inhibitors in Patients with FGFR2 Fusion–Positive Intrahepatic Cholangiocarcinoma


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


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

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 (CAFs) 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.

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


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

See commentary, p. 1001

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

AC icon indicates AuthorChoice

For more information please visit http://www.aacrjournals.org

See commentary, p. 1003

ON THE COVER

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 (CAFs) 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.