IN THIS ISSUE
Highlighted research articles ........................................ 1

NEWS IN BRIEF
Important news stories affecting the community ........... 6

NEWS IN DEPTH
Dueling KRASG12C Inhibitors Achieve Responses ............. 10

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ......... 11

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

VIEWS
In The Spotlight
Lessons from the A2A Adenosine Receptor Antagonist-Enabled Tumor Regression and Survival in Patients with Treatment-Refractory Renal Cell Cancer . . . 16
M.V. Sitkovsky
See article, p. 40

Can the Help Match the Hype? KRASG12C-Specific Inhibitors and Beyond ....................... 20
S.J. Klempner and A.N. Hata
See article, p. 54

Personalizing KRAS-Mutant Allele-Specific Therapies ...... 23
C. Falcomatà, G. Schneider, and D. Saur
See article, p. 104

RESEARCH ARTICLES
Adenosine 2A Receptor Blockade as an Immunotherapy for Treatment-Refractory Renal Cell Cancer .................. 40
Précis: The adenosine 2A receptor antagonist ciforadenant was well tolerated and exhibited clinical activity in patients with refractory renal cell carcinoma in a first-in-human, phase I clinical trial.
See commentary, p. 16

The KRASG12C Inhibitor MRTX849 Provides Insight toward Therapeutic Susceptibility of KRAS-Mutant Cancers in Mouse Models and Patients ................ 54
Précis: The KRASG12C inhibitor MRTX849 exhibited antitumor efficacy alone and in combination in multiple KRASG12C-mutant mouse models as well as in two representative patients in a phase I clinical trial with KRASG12C-mutant tumors.
See commentary, p. 20

PTEN Loss Mediates Clinical Cross-Resistance to CDK4/6 and PI3Kα Inhibitors in Breast Cancer .......... 72
See article, p. 82

Selected highlights of recent articles affecting the community

http://cancerdiscovery.aacrjournals.org

AACR Journals

CANCER DISCOVERY

JANUARY 2020 • VOLUME 10 • NUMBER 1

aacrjournals.org

Downloaded from cancerdiscovery.aacrjournals.org on August 1, 2021, © 2020 American Association for Cancer Research.
Précis: Loss of PTEN causes resistance to CDK4/6 inhibitors in ER+ breast cancer via reducing localization of p27 to the nucleus, increasing CDK4/6 and CDK2 activity in PTEN-deficient cells.

Circulating Tumor Cells Exhibit Metastatic Tropism and Reveal Brain Metastasis Drivers .......... 86

Précis: The axon-guiding protein SEMA4D enabled human circulating breast cancer cells to cross the blood-brain barrier in mice, where MYC promoted their survival by upregulating the antioxidant enzyme GPX1, providing a molecular basis for brain metastasis.

Atypical KRASG12R Mutant Is Impaired in PI3K Signaling and Macropinocytosis in Pancreatic Cancer .......... 104

Précis: KRASG12R, a mutation common in pancreatic ductal adenocarcinoma (PDAC) but not in other cancers driven by KRASG12 mutations, causes defects in PI3K signaling and KRAS-independent macropinocytosis, a metabolic process required for PDAC growth.

See commentary, p. 23

MAIT Cells Promote Tumor Initiation, Growth, and Metastases via Tumor MR1 .......... 124

Précis: In vivo experiments showed that mucosal-associated invariant T cells promoted lung metastasis in mice in a mechanism dependent on tumor-expressed MHC class I–related protein and suppression of lymphocyte function.

ID1 Mediates Escape from TGFβ Tumor Suppression in Pancreatic Cancer .......... 142

Précis: Dysregulated expression of inhibitor of differentiation 1, an inhibitor of progenitor-cell differentiation, may explain how pancreatic ductal adenocarcinoma cells that maintain normal TGFβ-pathway function escape apoptosis.

Acknowledgment to Reviewers ....... 158

AC icon indicates AuthorChoice
For more information please visit http://www.aacrjournals.org

ON THE COVER Genetic inactivation of the TGFβ pathway is observed in only about half of pancreatic ductal adenocarcinomas (PDAC), yet preventing TGFβ-mediated apoptosis of premalignant cells is thought to be important for PDAC development. Huang and colleagues found that dysregulated expression of inhibitor of differentiation 1 (ID1) may explain this phenomenon. Many PDAC cells exhibited high ID1 expression despite retaining TGFβ-pathway activity, and ID1 downregulation in PDAC cells led to apoptosis. The pathologically sustained expression of ID1 appears to uncouple the TGFβ-mediated epithelial-mesenchymal transition from apoptosis, enabling PDAC cells to survive without genetic inactivation of the TGFβ pathway. For details, please see the article by Huang and colleagues on page 142.