**IN THIS ISSUE**

Highlighted research articles ..........................115

**NEWS IN BRIEF**

Important news stories affecting the community ..........118

**RESEARCH WATCH**

Selected highlights of recent articles of exceptional significance from the cancer literature ...............123

**ONLINE**

For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/content/early/by/section.

**VIEWS**

In The Spotlight

JAK Mutations as Escape Mechanisms to Anti-PD-1 Therapy ...................................128

A. Marabelle, S. Aspeslagh, S. Postel-Vinay, and J.-C. Soria

See article, p. 188

Epigenomic Inactivation of RasGAPs Activates RAS Signaling in a Subset of Luminal B Breast Cancers ......131

R. Sears and J.W. Gray

See article, p. 202

Tuning Chromosomal Instability to Optimize Tumor Fitness .............................134

M.E. Burkard and B.A. Weaver

See article, p. 218

**REVIEW**

Targeting ALK: Precision Medicine Takes on Drug Resistance .............................137

J.J. Lin, G.J. Riely, and A.T. Shaw

**RESEARCH BRIEFS**

Blastic Plasmacytoid Dendritic Cell Neoplasm Is Dependent on BCL2 and Sensitive to Venetoclax .................156


Précis: The hematologic malignancy blastic plasmacytoid dendritic cell neoplasm is characterized by sensitivity to BCL2 inhibition with venetoclax in vitro, in patient-derived xenografts, and in patients with relapsed/refractory disease.

Cellular Senescence Promotes Adverse Effects of Chemotherapy and Cancer Relapse ..........................165


Précis: Chemotherapy-induced senescent noncancerous cells promote therapy-associated side effects, tumor metastasis, and relapse.

The Rodent Liver Undergoes Weaning-Induced Involution and Supports Breast Cancer Metastasis ......................177


Précis: Weaning-induced liver involution establishes a prometastatic liver microenvironment in rodents, which may explain the increased risk for liver metastasis in patients with postpartum breast cancer.
Shin and colleagues performed whole-exome sequencing of pretreatment biopsies from 23 patients with metastatic melanoma and 16 patients with metastatic colon cancer treated with anti–PD-1 therapy and identified a concomitant loss-of-function JAK1 mutation and amplification of the JAK locus in one of the patients with melanoma and a concomitant homozygous truncating JAK1 mutation and LOH at the JAK1 locus in one of the patients with colon cancer. Loss-of-function JAK1/2 mutations abrogated IFN-γ-mediated signaling and subsequent upregulation of PD-L1 in patient-derived melanoma cell lines. Analysis of the Cancer Cell Line Encyclopedia and The Cancer Genome Atlas databases revealed that truncating JAK1/2 mutations occurred in multiple types of cancer and were associated with significantly decreased overall survival in patients with melanoma or breast, prostate, and lung cancers. These findings describe the mechanism by which loss-of-function kinase mutations induce primary resistance to anti–PD-1 therapy. For details, please see the article by Shin and colleagues on page 188.
CANCER DISCOVERY

7 (2)


Updated version  Access the most recent version of this article at: http://cancerdiscovery.aacrjournals.org/content/7/2

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, use this link http://cancerdiscovery.aacrjournals.org/content/7/2. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site.