ARID1A Mutations in Cancer: Another Epigenetic Tumor Suppressor? ..........35
J.N. Wu and C.W.M. Roberts

Opposing Effects of Androgen Deprivation and Targeted Therapy on Prostate Cancer Prevention ..........44
Précis: Antiandrogen therapies promote prostate cancer progression, whereas blockade of PI3K and MAPK signaling suppresses tumor growth in the context of PTEN deficiency.

Genotype-Selective Combination Therapies for Melanoma Identified by High-Throughput Drug Screening ..........52
See commentary, p. 14
Précis: A systematic screening approach was used to characterize inhibitor combinations that are effective in melanomas driven by specific oncogenic mutations.

Loss of 53BP1 Causes PARP Inhibitor Resistance in Brca1-Mutated Mouse Mammary Tumors ..........68
See commentary, p. 20
Précis: PARP inhibitor resistance can arise in vivo through partial restoration of homologous recombination caused by 53BP1 inactivation.

Unpicking the Combination Lock for Mutant BRAF and RAS Melanomas ..........14
B. Al-Lazikani and P. Workman
See article by Held et al., p. 52
Mechanisms of Resistance to PARP Inhibitors—Three and Counting ..........20
T. Fojo and S. Bates
See article by Jaspers et al., p. 68
Mutant and Wild-type Ras: Co-conspirators in Cancer ..........24
T.K. Hayes and C.J. Der
See article by Young et al., p. 112

The Genomic Landscape of Breast Cancer as a Therapeutic Roadmap ..........27
M.J. Ellis and C.M. Perou

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org.
The mTORC1 Inhibitor Everolimus Prevents and Treats Eμ-Myc Lymphoma by Restoring Oncogene-Induced Senescence


Précis: mTORC1-dependent bypass of MYC-induced senescence is required for the initiation and maintenance of Eμ-Myc B-cell lymphoma.

Targeting C4-Demethylating Genes in the Cholesterol Pathway Sensitizes Cancer Cells to EGF Receptor Inhibitors via Increased EGF Receptor Degradation


Précis: Sterol biosynthesis genes regulate EGFR endocytosis and signaling, and inhibition of these genes increases the efficacy of anti-EGFR therapies.

Oncogenic and Wild-type Ras Play Divergent Roles in the Regulation of Mitogen-Activated Protein Kinase Signaling

A. Young, D. Lou, and F. McCormick

See commentary, p. 24

Précis: Wild-type RAS isoforms regulate growth factor signaling in the context of oncogenic RAS and are required for optimal growth of cells harboring RAS mutations.

Correction

IDO Is a Nodal Pathogenic Driver of Lung Cancer and Metastasis Development

Young and colleagues show that oncogenic and wild-type RAS isoforms have nonredundant, independent roles in cancer cells. Oncogenic RAS isoforms desensitize cells to receptor tyrosine kinase (RTK) stimulation and promote basal mitogen-activated protein kinase (MAPK) signaling, whereas wild-type RAS isoforms are required for RTK-dependent activation of MAPK signaling and optimal growth of cancer cells expressing oncogenic RAS. Depletion of oncogenic RAS sensitizes cells to wild-type isoform-mediated growth factor signaling, uncovering a potential resistance mechanism employed by RAS-mutant cells. Combined inhibition of RAS and RTK signaling effectively blocks growth of cells expressing oncogenic RAS and may therefore be a potential approach to circumvent resistance. For details, please see the article by Young and colleagues on page 112.

ON THE COVER

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:

- New ADC Effective against Prostate Cancer
- Proposals Aim to Make Trials More Efficient
- Triple Jeopardy for Triple-Negative Breast Cancers
- Sandy Underlines Need for Disaster Preparation
- Inhibiting JAK2 for Inflammatory Breast Cancer
- Bevacizumab Fails to Up Breast Cancer Survival

Downloaded from cancerdiscovery.aacrjournals.org on February 12, 2021. © 2013 American Association for Cancer Research.
## CANCER DISCOVERY

### 3 (1)


| Updated version | Access the most recent version of this article at: http://cancerdiscovery.aacrjournals.org/content/3/1 |

| 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/3/1. Click on "Request Permissions" which will take you to the Copyright Clearance Center's (CCC) Rightslink site. |