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### RESEARCH BRIEF
**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.

### RESEARCH ARTICLES
**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.
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.

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

Y oung 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.

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