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Précis: Antiandrogen therapies promote prostate cancer progression, whereas blockade of PI3K and MAPK signaling suppresses tumor growth in the context of PTEN deficiency.

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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.

Published Online January 10, 2013; Received May 27, 2012; Revised September 10, 2012; Accepted September 25, 2012.
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.