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


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


Précis: A systematic screening approach was used to characterize inhibitor combinations that are effective in melanomas driven by specific oncogenic mutations.

IN THIS ISSUE  Highlighted research articles

NEWS IN BRIEF  Important news stories affecting the community

NEWS IN DEPTH  Q&A: Mina Bissell on Tumors as Organs

Putting the Brakes on Cancer in Africa

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

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

VIEWS  In The Spotlight

Unpicking the Combination Lock for Mutant BRAF and RAS Melanomas  B. Al-Lazikani and P. Workman

See article by Held et al., p. 52

Mechanisms of Resistance to PARP Inhibitors—Three and Counting  T. Fojo and S. Bates

See article by Jaspers et al., p. 68

Mutant and Wild-type Ras: Co-conspirators in Cancer  T.K. Hayes and C.J. Der

See article by Young et al., p. 112

Prospective

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


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.

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


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

ON THE COVER

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.

ONCOCGENIC RAS

ONCOCGENIC RAS

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

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• 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