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Highlighted research articles

Important news stories affecting the community

Q&A: Crystal Mackall, John Maris on Pediatrics

Stopping Breast Cancer Before It Starts

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

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

In The Spotlight

Epigenetic Approaches for Chemosensitization of Refractory Diffuse Large B-Cell Lymphomas

J.J. Steinhardt and R.B. Gartenhaus

See article, p. 1002

Resistance Emerges to Second-Generation Antiandrogens in Prostate Cancer

W.G. Nelson and S. Yegnasubramanian

See article, p. 1020

See article, p. 1030

Say What? The Activity of the Polyamine Biosynthesis Inhibitor Difluoromethylornithine in Chemoprevention Is a Result of Reduced Thymidine Pools?

R.A. Casero Jr

See article, p. 1072

Cell-Autonomous and Non-Cell-Autonomous Mechanisms of HGF/MET-Driven Resistance to Targeted Therapies: From Basic Research to a Clinical Perspective

S. Corso and S. Giordano

Dominant Role of Oncogene Dosage and Absence of Tumor Suppressor Activity in Nras-Driven Hematopoietic Transformation


Précis: Increased expression of mutant Nras, not loss of wild-type Nras, drives transformation in the hematopoietic lineage.

Mechanism-Based Epigenetic Chemosensitization Therapy of Diffuse Large B-Cell Lymphoma


Précis: Treatment with DNA methyltransferase inhibitors overcomes chemoresistance in high-risk DLBCL via demethylation and reactivation of SMAD1.

See commentary, p. 968

A Clinically Relevant Androgen Receptor Mutation Confers Resistance to Second-Generation Antiandrogens Enzalutamide and ARN-509


Précis: An ARART mutation confers ligand-specific resistance and is found in the circulating tumor DNA of ARN-509-treated patients with progressive castration-resistant prostate cancer.

See commentary, p. 971

Say What? The Activity of the Polyamine Biosynthesis Inhibitor Difluoromethylornithine in Chemoprevention Is a Result of Reduced Thymidine Pools?

R.A. Casero Jr

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Précis: A recurring androgen receptor (AR) mutation identified in enzalutamide-resistant prostate cancer cells converts enzalutamide from an AR antagonist to an AR agonist.
See commentary, p. 971

Parallel RNA Interference Screens Identify EGFR Activation as an Escape Mechanism in FGFR3-Mutant Cancer ...........................1058
Précis: Activation of EGFR signaling specifically limits the sensitivity of FGFR3-activated bladder cancer cells to FGFR inhibitors.

Systematic Interrogation of 3q26 Identifies TLOC1 and SKIL as Cancer Drivers .......... 1044
Précis: The coamplified genes TLOC1 and SKIL cooperate to induce transformation via regulation of distinct tumor phenotypes.

Unbiased Metabolite Profiling Indicates that a Diminished Thymidine Pool Is the Underlying Mechanism of Colon Cancer Chemoprevention by Alpha-Difluoromethylornithine ............1072
Précis: The cytostatic effects of α-difluoromethylornithine (DFMO) are attributable to reduced cellular thymidine levels caused by depletion of an essential cofactor of thymidine synthase.
See commentary, p. 975

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

• Prostate Cancers Get Nerved Up
• Aftatinib Approved for Advanced NSCLC
• UK Launches 100,000-Genome Initiative
• Myriad Genetics Sues BRCA Diagnostic Rivals
• MGN1703 Maintenance Therapy Extends PFS in Colorectal Cancer
• FDA Exercises Its Authority to Regulate Tobacco Products

ON THE COVER
Clozel and colleagues found that low-dose DNA methyltransferase (DNMT) inhibitor treatment induced DNA hypomethylation and a senescence-like phenotype in chemorefractory diffuse large B-cell lymphoma (DLBCL) cells and enhanced the sensitivity of these cells to doxorubicin. In addition, DNMT inhibition upregulated the expression of several hypermethylated genes including SMAD1 in refractory DLBCL cell lines and primary tumors, indicative of epigenetic reprogramming. SMAD1 reactivation sensitized resistant cells to growth inhibition by doxorubicin, whereas SMAD1 depletion augmented chemoresistance. Furthermore, in a phase I clinical trial of newly diagnosed, high-risk patients with DLBCL, DNMT inhibitor pretreatment prior to standard chemoimmunotherapy was well tolerated and resulted in a high rate of complete remission, supporting further investigation of this therapeutic combination in DLBCL. For details, please see the article by Clozel and colleagues on page 1002.