In The Spotlight

Immunotherapy for Pancreatic Cancer: More Than Just a Gut Feeling
E. Riquelme, A. Maitra, and F. McAllister
See article, p. 403

Advances on the BRAF Front in Colorectal Cancer
F. Janku
See article, p. 417
See article, p. 428

Plasma DNA and Metastatic Castration-Resistant Prostate Cancer: The Odyssey to a Clinical Biomarker Test
A. Jayaram, D. Wetterskog, and G. Attard
See article, p. 444

Prospective

Tissue-Specific Immunoregulation: A Call for Better Understanding of the “Immunostat” in the Context of Cancer

RESEARCH BRIEFS

The Pancreatic Cancer Microbiome Promotes Oncogenesis by Induction of Innate and Adaptive Immune Suppression
See commentary, p. 386

Convergent Therapeutic Strategies to Overcome the Heterogeneity of Acquired Resistance in BRAFV600E Colorectal Cancer
See commentary, p. 389
See article, p. 428

RESEARCH ARTICLES

Combined BRAF, EGFR, and MEK Inhibition in Patients with BRAFV600E-Mutant Colorectal Cancer
See commentary, p. 389
See article, p. 417
Circulating Tumor DNA Genomics Correlate with Resistance to Abiraterone and Enzalutamide in Prostate Cancer


Précis: Analysis of ctDNA from patients with metastatic castration-resistant prostate cancer treated with androgen receptor (AR)-targeted therapy identifies genetic alterations that predict response to AR-targeted inhibitors.

See commentary, p. 392

BRD4 Profiling Identifies Critical Chronic Lymphocytic Leukemia Oncogenic Circuits and Reveals Sensitivity to PLX51107, a Novel Structurally Distinct BET Inhibitor


Précis: BRD4 is overexpressed in CLL and enriched at transcriptionally active genes, and disrupting BRD4 with PLX51107 downregulates CLL driver genes and reduces CLL cell proliferation in vitro and in vivo.

MEF2C Phosphorylation Is Required for Chemotherapy Resistance in Acute Myeloid Leukemia


Précis: In acute myeloid leukaemia, phosphorylation of MEF2C S222 by MARK is required for leukemic stem cell maintenance and chemoresistance, suggesting the potential for MARK inhibitors to restore chemosensitivity.

E-Cadherin/ROS1 Inhibitor Synthetic Lethality in Breast Cancer


Précis: Clinical ROS1 inhibitors elicit a synthetic lethal interaction in preclinical models of E-cadherin–deficient breast cancer by further impairing p120 catenin function, thereby inducing defects in cytokinesis.

In an open-label phase I trial of 142 patients with BRAFV600-mutant colorectal cancer, Corcoran and colleagues assess the safety and efficacy of BRAF plus EGFR inhibition (in 20 patients receiving dabrafenib and panitumumab; D+P), MEK plus EGFR inhibition (in 31 patients receiving trametinib and panitumumab; T+P), or “triplet” BRAF, MEK, and EGFR inhibition (in 91 patients receiving dabrafenib, panitumumab, and trametinib; D+T+P) to determine if EGFR inhibition would suppress MAPK reactivation to enhance the efficacy of BRAF inhibition. Overall response rates were 10% for D+P, 0% for T+P, and 21% for D+T+P achieving the greatest reduction in MAPK pathway activity. Serial cfDNA analysis identified potential resistance mutations linked to disease progression. The results of this trial indicate that combined targeting of BRAF, EGFR, and MEK may suppress adaptive feedback pathways to improve responses in patients with BRAFV600-mutant colorectal cancer. For details, please see the article by Corcoran and colleagues on page 428.