In this issue

Highlighted research articles

Important news stories affecting the community

Q&A: Brian Kennedy on Aging and Cancer

New Nanomedicines May Better Target Tumors

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.

Research Watch

Immune Cell–Poor Melanomas Benefit from PD-1 Blockade after Targeted Type I IFN Activation

NFATC1 expression is induced by inflammation and cooperates with KRASG12D in pancreatic carcinogenesis by forming complexes with STAT3 at enhancer regions that regulate oncogenic gene networks.

Research articles

Blood-Based Analyses of Cancer: Circulating Tumor Cells and Circulating Tumor DNA

D.A. Haber and V.E. Velculescu

Ceritinib, a next-generation ALK inhibitor, has potent activity in preclinical models of crizotinib-naïve and crizotinib-resistant ALK-rearranged non–small cell lung cancer.

Précis: Ceritinib, a next-generation ALK inhibitor, has potent activity in preclinical models of crizotinib-naïve and crizotinib-resistant ALK-rearranged non–small cell lung cancer.

See commentary, p. 634

Type I IFN–associated inflammatory pathway activation combined with antibody blockade of the T-cell immunoinhibitory receptor PD-1 improves immune surveillance of melanomas.

Précis: Type I IFN–associated inflammatory pathway activation combined with antibody blockade of the T-cell immunoinhibitory receptor PD-1 improves immune surveillance of melanomas.

Inflammation-Induced NFATc1–STAT3 Transcription Complex Promotes Pancreatic Cancer Initiation by Kras

EML4–ALK Fusions: Propelling Cancer but Creating Exploitable Chaperone Dependence

Surviving Metabolic Stress: Of Mice (Squirrels) and Men

In the spotlight

Second-Generation ALK Inhibitors: Filling the Non"MET" Gap

Soil Amendments That Slow Cancer Growth

VEGFA Genomic Amplification Tailors Treatment of HCCs with Sorafenib

In Focus

Surviving Metabolic Stress: Of Mice (Squirrels) and Men
Epithelial-to-Mesenchymal Transition Activates PERK-eIF2α and Sensitizes Cells to Endoplasmic Reticulum Stress ....... 702
Précis: Elevated ECM synthesis and secretion activates the PERK arm of the UPR and renders cells that have undergone EMT vulnerable to ER stress-inducing agents.

p38MAPK Plays a Crucial Role in Stromal-Mediated Tumorigenesis .... 716
Précis: The secretory phenotype of cancer-associated fibroblasts that promotes tumor growth is post-transcriptionally controlled by p38MAPK.
See commentary, p. 637

Human and Mouse VEGFA-Amplified Hepatocellular Carcinomas Are Highly Sensitive to Sorafenib Treatment ............ 730
Précis: VEGFA amplifications frequently occur in mouse and human hepatocellular carcinomas and drive dependence on VEGFA signaling via manipulation of the tumor microenvironment.
See commentary, p. 640

ON THE COVER
Friboulet and colleagues report that ceritinib, a next-generation ALK inhibitor that is more selective and potent than crizotinib, is active in preclinical models of both crizotinib-naïve and crizotinib-resistant non-small cell lung cancer (NSCLC). Ceritinib retained activity against the most common crizotinib-resistant ALK mutants, although some secondary ALK mutations did confer resistance to both crizotinib and ceritinib. Structural analyses provided a mechanistic basis for these findings, as the most common secondary ALK mutations that inhibit binding of crizotinib are not predicted to impair ceritinib binding, but other mutations, which the authors have identified in patients with acquired resistance to ceritinib, are predicted to reduce ceritinib binding through steric hindrance or conformational changes of the ALK catalytic domain. For details, please see the article by Friboulet and colleagues on page 662.

AC icon indicates Author Choice
For more information please visit http://www.aacrjournals.org

Research