IN THIS ISSUE
Highlighted research articles .................................. 621

NEWS IN BRIEF
Important news stories affecting the community .................. 624

NEWS IN DEPTH
Q&A: Brian Kennedy on Aging and Cancer ......................... 627

New Nanomedicines May Better Target Tumors ............. 628

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature .................. 629

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

REVIEW
Blood-Based Analyses of Cancer: Circulating Tumor Cells and Circulating Tumor DNA .......... 650
D.A. Haber and V.E. Velculescu

The ALK Inhibitor Ceritinib Overcomes Crizotinib Resistance in Non–Small Cell Lung Cancer .... 662

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

Immune Cell–Poor Melanomas Benefit from PD-1 Blockade after Targeted Type I IFN Activation .............. 674

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 KrasG12D ................ 688

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.

VEGFA Genomic Amplification Tailors Treatment of HCCs with Sorafenib ......................... 640
X. Luo and G.-S. Feng

See article, p. 730

EML4–ALK Fusions: Propelling Cancer but Creating Exploitable Chaperone Dependence ....... 642
P. Workman and R. van Montfort

In Focus
Surviving Metabolic Stress: Of Mice (Squirrels) and Men ...... 646
W.N. Hait, M. Versele, and J.-M. Yang

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