CONTENTS
JUNE 2013
VOLUME 3
NUMBER 6

IN THIS ISSUE
Highlighted research articles .................................. 591

NEWS IN BRIEF
Important news stories affecting the community ............. 594

NEWS IN DEPTH
Q&A: Ashok Venkitaraman on “Undruggable” Targets .... 597

RESEARCH BRIEFS
Second Chances for Shelved Compounds ................. 598

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature .......... 599

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

REVIEW
Illuminating Cancer Systems with Genetically Engineered Mouse Models and Coupled Luciferase Reporters In Vivo ................. 616
B. Kocher and D. Piwnica-Worms

RESEARCH BRIEFS
Response to Cabozantinib in Patients with RET Fusion-Positive Lung Adenocarcinomas ................. 630

Précis: Preliminary data from a prospective phase II trial shows cabozantinib elicits prolonged partial responses and disease stabilization in non-small cell lung cancers harboring RET fusions.

Identification of Targetable FGFR Gene Fusions in Diverse Cancers ................. 636

Précis: FGFR gene fusions that encode for active kinases are present in multiple cancer types and confer enhanced sensitivity to FGFR inhibitors.

Succinate Dehydrogenase Mutation Underlies Global Epigenomic Divergence in Gastrointestinal Stromal Tumor ................. 648

Précis: SDH-deficient tumors of various lineages are characterized by a divergent DNA hypermethylation profile comparable to that of other Krebs cycle-defective tumors.
Amplification of the MET Receptor Drives Resistance to Anti-EGFR Therapies in Colorectal Cancer ........... 658
Précis: MET amplification underlies acquired resistance to cetuximab or panitumumab in colorectal cancers that have not developed secondary KRAS mutations.

Canonical Wnt/β-catenin Signaling Drives Human Schwann Cell Transformation, Progression, and Tumor Maintenance ............. 674
Précis: WNT pathway activation induces oncogenic properties in Schwann cells and promotes growth of malignant peripheral nerve sheath tumors.

GSK-3α Promotes Oncogenic KRAS Function in Pancreatic Cancer via TAK1–TAB Stabilization and Regulation of Noncanonical NF-κB .............. 690
D. Bang, W. Wilson, M. Ryan, J.J. Yeh, and A.S. Baldwin
Précis: GSK3α but not GSK3β enhances pancreatic cell growth downstream of mutant KRAS via coordinate activation of both canonical and noncanonical NF-κB signaling.

Killian and colleagues found that gastrointestinal stromal tumors (GIST) with mutations in succinate dehydrogenase (SDH) complex genes exhibited a distinct methylation signature relative to the profile of KIT-mutant tumors and normal reference tissues. This methyl-divergent profile was distinguished by increased global DNA hypermethylation, particularly at DNase hypersensitive sites, and was also present in other SDH-mutant tumor lineages, including paraganglioma and pheochromocytoma, supporting the oncogenotype dependence of this signature. In addition, a similarly perturbed methylation profile was detected in gliomas harboring mutations in another Krebs cycle enzyme, isocitrate dehydrogenase (IDH). These findings identify a strong association between the mitochondrial Krebs cycle and cancer epigenomic reprogramming. For details, please see the article by Killian and colleagues on page 648.