IN THIS ISSUE
Highlighted research articles                      826

NEWS IN BRIEF
Important news stories affecting the community          830

NEWS IN DEPTH
Q&A: Eric Winer on Neoadjuvant Clinical Trials          832
Seeking Value as Cancer Drug Costs Soar                  833

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature 835

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

VIEWS
In The Spotlight
Targeting BRAF in Multiple Myeloma               840
E. O'Donnell and N.S. Raje
See article, p. 862

Energizing the Search to Target LKB1-Mutant Tumors         843
A.I. Marcus and F.R. Khuri
See article, p. 870

Myeloid TGF-β Responsiveness Promotes Metastases           846
F. Souza-Fonseca-Guimaraes and M.J. Smyth
See article, p. 936

RESEARCH BRIEFS
Targeting the BRAF V600E Mutation in Multiple Myeloma 862
Précis: A patient with BRAFV600E-mutant multiple myeloma experienced a rapid, stable response to the BRAF inhibitor vemurafenib.
See commentary, p. 840

Metabolic and Functional Genomic Studies Identify Deoxynucleotide Kinase as a Target in LKB1-Mutant Lung Cancer 870
Précis: Inhibition of DTYMK, a critical enzyme for nucleotide metabolism, is synthetically lethal with LKB1 deficiency in KRAS-driven lung cancer.
See commentary, p. 843

RESEARCH ARTICLES
Identifying the Ubiquitin Ligase Complex that Regulates the NF1 Tumor Suppressor and Ras 880
P.E. Hollstein and K. Cichowski
Précis: CUL3 and the adaptor protein KBTBD7 enhance RAS activation by promoting both the regulated ubiquitin-mediated degradation of neurofibromin and its pathogenic destruction in glioblastoma.
Autophagy Opposes p53-Mediated Tumor Barrier to Facilitate Tumorigenesis in a Model of PALB2-Associated Hereditary Breast Cancer


Précis: Autophagy promotes cell survival and tumorigenesis in a model of hereditary breast cancer driven by conditional knockout of Poib2 in the mammary gland.

Pten-Null Tumors Cohabiting the Same Lung Display Differential AKT Activation and Sensitivity to Dietary Restriction


Précis: Heterogeneous AKT activation in Pten-null murine lung tumors and PTEN-deficient human NSCLCs suggests that PTEN loss does not always correlate with AKT activity.

Stromal EGF and IGF-I Together Modulate Plasticity of Disseminated Triple-Negative Breast Tumors


Précis: Expression of EGF and IGF-I in the tumor microenvironment is required for malignant conversion of certain indolent cancer cells and accelerates recurrence of triple-negative breast cancer.

TGF-β Signaling in Myeloid Cells Is Required for Tumor Metastasis


Précis: Disruption of TGFβ signaling in myeloid cells enhances IFNγ production and CD8+ T-cell–mediated antitumor immunity and inhibits metastasis.

See commentary, p. 846

Correction

Telomeric Allelic Imbalance Indicates Defective DNA Repair and Sensitivity to DNA-Damaging Agents

Curry and colleagues made the surprising observation that two adjacent tumor types with either low or high AKT activity can develop in Pten-null lungs. Heterogeneous AKT activation was cell autonomous and associated with differential expression of ectonucleoside triphosphate diphosphohydrolase 5 (ENTPD5), a UDPase that promotes receptor tyrosine kinase folding in the endoplasmic reticulum. Knockdown of ENTPD5 led to a reduction in levels of insulin growth factor receptor β (IGFIRβ), an upstream activator of AKT. In human non–small cell lung cancers (NSCLC), AKT phosphorylation was directly correlated with ENTPD5 expression, but not always with loss of PTEN expression. Together, these findings suggest that PTEN loss may not be sufficient to activate AKT and may not be an appropriate biomarker of PI3K/AKT activation or response to PI3K/AKT-targeted therapies. For details, please see the article by Curry and colleagues on page 908.