## 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

## Research Articles
**Metabolic and Functional Genomic Studies Identify Deoxynucleoside 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

**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.

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


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.


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.


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

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.