## IN THIS ISSUE
Highlighted research articles .......................................... vi

## NEWS IN BRIEF
Important news stories affecting the community. ...................... 458

## NEWS IN DEPTH
Q&A: Michael Stratton on What’s Next in Sequence .......... 460

Broadening Trial Recruitment for Minorities, the Elderly .......... 461

Placing Bets on Biotech .................................................. 462

## RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ......................... 463

## ONLINE
For more News and Research Watch, visit Cancer Discovery online at www.AACR.org/CDnews.

## VIEWS
**In The Spotlight**
Understanding the Lethal Variant of Prostate Cancer: Power of Examining Extremes ......................... 466
A. Aparicio, C. J. Logothetis, and S.N. Maity
Commentary on Beltran et al., p. 487

**NF-κB in Cancer: A Matter of Life and Death ................. 469**
B.B. Aggarwal and B. Sung
Commentary on Ezzler et al., p. 496

**HER2 Signaling and Resistance to the Anti-EGFR Monoclonal Antibody Cetuximab: A Further Step toward Personalized Medicine for Patients with Colorectal Cancer .......... 472**
F. Ciardiello and N. Normanno
Commentary on Bertotti et al., p. 508

## REVIEW
**PI3K and STAT3: A New Alliance ......................... 481**
P.K. Vogt and J.R. Hart

## RESEARCH BRIEF
**Molecular Characterization of Neuroendocrine Prostate Cancer and Identification of New Drug Targets .......... 487**
Précis: Frequent AURKA and MYCN amplification is identified in an aggressive prostate cancer subtype.

## RESEARCH ARTICLES
**mTORC 2:1 for Chemotherapy Sensitization in Glioblastoma ............... 475**
W. Wick, J. Blaes, and M. Weiler
Commentary on Tanaka et al., p. 524

**Prospective**
Curing “Incurable” Cancer ............... 477
J.D. Watson

**Cell-Selective Inhibition of NF-κB Signaling Improves Therapeutic Index in a Melanoma Chemotherapy Model ...................... 496**
T. Enzler, Y. Sano, M-K. Choo, H.B. Cottam, M. Karin, H. Tsao, and J.M. Park
Précis: Host- and tumor-specific cellular responses, respectively, underlie the adverse and therapeutic effects of NF-κB blocking agents.
A Molecularly Annotated Platform of Patient-Derived Xenografts (“Xenopatients”) Identifies HER2 as an Effective Therapeutic Target in Cetuximab-Resistant Colorectal Cancer .......................... 508

Précis: Population-based preclinical testing identifies HER2 amplification as a novel biomarker of cetuximab resistance in metastatic colon cancer and indicates dual targeting of HER2 and EGFR may be a more effective therapeutic approach.

Oncogenic EGFR Signaling Activates an mTORC2–NF-κB Pathway That Promotes Chemotherapy Resistance ............... 524

Précis: mTORC2 is identified as a novel mediator of drug resistance and regulator of NF-κB signaling in glioblastoma.

On the Cover: Tanaka and colleagues demonstrate that mTORC2 is activated in the majority of glioblastomas and mediates chemoresistance in an AKT-independent manner via NF-κB pathway activation. Surprisingly, they show increased activity of this mTORC2–NF-κB signaling pathway in GBM cells in response to rapamycin, which may provide an explanation for the failure of rapamycin to demonstrate efficacy in GBM clinical trials. Instead, dual mTOR kinase inhibitors that block the activity of both mTORC1 and mTORC2 may improve clinical outcome, particularly when combined with other chemotherapeutic agents. For details, please see the article by Tanaka and colleagues on page 524.