IN THIS ISSUE
Highlighted research articles.............................. viii

NEWS IN BRIEF
Important news stories affecting the community.................... 277

NEWS IN DEPTH
Q&A: Stephen Baylin and Peter Jones on Team Science .............. 279
Nanoparticle Theories Slowly Turn into Practice .................. 280
Chinese, American Researchers Expand Collaborations ............ 281

RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature .................. 282

VIEWS
In The Spotlight
On the Road to Combinations of Targeted Therapies: PPM1H Phosphatase as a Suppressor of Trastuzumab Resistance .................. 285
N. Aceto and M. Bentires-Alj
Commentary on Lee-Hoeflich et al., p. 326
ER and PI3K Independently Modulate Endocrine Resistance in ER-Positive Breast Cancer .................. 287
B.A. Van Tine, R.J. Crowder, and M.J. Ellis
Commentary on Miller et al., p. 338

RESEARCH ARTICLES
The Potential Benefits of BIM in the Further Pursuit of Biomarker Discovery in Cancer Therapeutics ............. 289
T. Yoshida and E.B. Haura
Commentary on Faber et al., p. 352

In Focus
Targeting the Tumor Microenvironment in Cancer: Why Hyaluronidase Deserves a Second Look ............. 291
C.J. Whatcott, H. Han, R.G. Posner, G. Hostetter, and D.D. Von Hoffman

REVIEW
Clinical Implementation of Comprehensive Strategies to Characterize Cancer Genomes: Opportunities and Challenges .......... 297
L.E. MacConaill, P. Van Hummelen, M. Meyerson, and W.C. Hahn

Discovery of Mdm2-MdmX E3 Ligase Inhibitors Using a Cell-Based Ubiquitination Assay ............. 312
Précis: A novel class of small-molecule inhibitors of the Mdm2-MdmX E3 ligase heterocomplex is identified using a high-throughput cell-based Mdm2 auto-ubiquitination assay.
PPM1H Is a p27 Phosphatase Implicated in Trastuzumab Resistance


Précis: PPM1H is a p27 phosphatase required for trastuzumab sensitivity in vitro that may be useful for predicting which HER2+ breast cancers are more likely to respond to trastuzumab therapy.

ERα-Dependent E2F Transcription Can Mediate Resistance to Estrogen Deprivation in Human Breast Cancer


Précis: ER drives CDK4/E2F-mediated cell cycle progression and cooperates with PI3K hyperactivation in estrogen-deprived ER+ breast cancer cells.

BIM Expression in Treatment-Naïve Cancers Predicts Responsiveness to Kinase Inhibitors


Précis: Quantitation of pretreatment RNA levels of the pro-apoptotic factor BIM can predict the efficacy of tyrosine kinase inhibitor therapy in oncogene-addicted cancers.

ON THE COVER

Faber and colleagues demonstrate that expression of the pro-apoptotic Bcl-2 family member BIM predicts the capacity of selective kinase inhibitors to induce apoptosis in cancers addicted to EGFR, HER2, PI3K, or BRAF signaling. Evaluating BIM levels in tumor biopsies prior to chemotherapy therefore has the potential to predict which patients are most likely to respond to single-agent kinase inhibitor therapy. For details, please see the article by Faber and colleagues on page 352.