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The Potential Benefits of BIM in the Further Pursuit of Biomarker Discovery in Cancer Therapeutics

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

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**Clinical Implementation of Comprehensive Strategies to Characterize Cancer Genomes: Opportunities and Challenges**

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**


**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.

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.