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HER2 Amplification: A Potential Mechanism of Acquired Resistance to EGFR Inhibition in EGFR-Mutant Lung Cancers That Lack the Second-Site EGFR<sup>T790M</sup> Mutation ................. 922


Précis: Increased HER2 expression confers resistance to EGFR tyrosine kinase inhibitors in non-small cell lung cancers with EGFR mutations.

Reactivation of ERK Signaling Causes Resistance to EGFR Kinase Inhibitors .................... 934


Précis: Acquired resistance to EGFR inhibitors can occur through aberrant activation of ERK signaling via MAPK1 amplification or downregulation of ERK negative regulators.

Correction


For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:

- Setting the Stage for Cancer Startups
- NCI Trials Program Looks for Net Gains
- Zaltrap Approved for Metastatic Colorectal Cancer
- UPenn, Novartis Team Up on Adaptive T-Cells
- Genomics Venture Sets Sights on Clinical Trials
- More NIH Grants to Undergo Second Review

ON THE COVER

Harbinski and colleagues performed a high-throughput screen of the human secretome to identify proteins capable of rescuing growth of receptor tyrosine kinase (RTK)-addicted cells following RTK inhibition and observed numerous potential ligand-mediated resistance mechanisms. Multiple human epidermal growth factor (HER) and fibroblast growth factor (FGF) ligands could rescue growth of hepatocyte growth factor (HGF) receptor (MET)-addicted cancer cells following MET inhibition, and FGFR-addicted cell lines treated with FGFR inhibitors could be rescued by HER ligands or HGF. Combination therapy modalities targeting the broad compensatory relationship between MET, FGFR, and HER ligands may thus have improved clinical efficacy. For details, please see the article by Harbinski and colleagues on page 948.