Background
Recent studies have shown that mutations in the Epidermal Growth Factor Receptor (EGFR) may be responsible for some patient sensitivity to EGFR kinase inhibitors such as Iressa and Tarceva; therefore, potential cell signaling biomarkers for mutant EGFR would be clinically useful.

Results
• High EGFR phosphorylation of all the tyrosine sites probed and phosphorylated Akt were detected in mutant EGFR cell xenografts but not in xenografts with wild type EGFR.
• IHC analysis of general phospho-tyrosine, phospho-EGFR and phospho-Akt on a NSCLC TMA found phosphorylated EGFR in 15%-25% of patient samples, depending on the tyrosine site. Phosphorylated EGFR was more frequent in adenocarcinomas (20%-30%) and in bronchial small carcinomas (80%-85%) than in squamous cell carcinomas (SCC) (5%-10%).
• The phospho-EGFR reactivity was closely correlated with high general phospho-tyrosine reactivity. There was also a strong correlation between high phospho-EGFR staining and high phospho-Akt staining in patient tissue samples.
• EGFR kinase domain DNA sequencing revealed that a majority of these samples with high EGFR and Akt phosphorylation were mutant.

Conclusion
These results suggest that mutant EGFR is constitutively phosphorylated and activates downstream Akt in NSCLC; therefore, IHC analysis of phosphorylated EGFR and Akt may reflect the activation of mutant EGFR signaling in patient samples.