Protein Changes

It has been reported that cell lines that are sensitive to erlotinib undergo G1/S cell cycle arrest that may be mediated through a reduction in cyclin A/CDK2 protein level and an increase in p27\(^{kip1}\) protein level, preventing G1 cell cycle progression\(^1,4\).


Using the SOMAscan\textsuperscript{TM} assay, we investigated the proteomic changes in NSCLC HCC827 (sensitive) or H1299 (resistant) cell lines exposed to erlotinib, and in NOD/SCID mice implanted with HCC827 cells and exposed to erlotinib. We demonstrate that erlotinib sensitivity and resistance correlate with cyclin A and p27\(^{kip1}\) protein changes in HCC827 and H1299 cell lines, and we detect additional protein changes that correlate with erlotinib sensitivity and resistance. We also show there is good concordance of the protein changes observed in the HCC827 cells treated with erlotinib and the HCC827 cells implanted in NOD/SCID mice dosed with erlotinib.

Conclusions

1001 proteins were quantified in cells and tumor xenografts exposed to erlotinib and no-drug controls. Concentration-dependent changes were seen for 93 proteins in erlotinib-sensitive HCC827 cells, 57 proteins in tumors, and 26 proteins in erlotinib-resistant H1299 cells. Twenty-two changes were shared between HCC827 cells and tumors, which included p27\(^{kip1}\) and cyclin A (previously associated with erlotinib sensitivity) and 21 newly associated proteins with highly plausible connections to erlotinib’s mode of action. These new proteins may have implications for treating patients that develop resistance to erlotinib in the clinic, and new technologies for early detection of lung cancer.

References


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