SUMMARY

Lung adenocarcinoma sensitivity or resistance to inhibitor therapy is dependent on other mutations such as the Δ746-750, T790M and other deletions. Exploring phosphorylation dynamics of proteins is necessary to understand and apply these global changes to develop a network map to determine causes of resistance/sensitivity. A phospho profile of cancer cell lines such as H1975, 11-18, A549 and others are needed to for the development of such a map. The development of next generation non-reversible inhibitors of EGFR such as the drug released by Boehringer Ingelheim BIBW 2992 (Afatinib) also need to be investigated for their effectiveness in treating cancer.

Mass spectrometry is not an absolute method and there are possibilities for us to not detect certain molecules that have a lower stoichiometry or have a PTM that is very transient and cannot be grabbed by conventional methods. We were limited by the availability of good antibodies and specifically phospho specific antibodies. Further most of the novel molecules that were identified do not have antibodies available as of yet. The poor quality of antibodies is another issue that has to be dealt with. Global initiatives such as the Human Protein Atlas (HPA) are generating such high quality Pan antibodies but more resources need to be developed in order to investigate post translational modifications specifically.

There is a general assumption that the EGFR pathway is well characterised but identification of even more molecules that are modulated also indicate the complexity of the pathway and that there are more proteins/cross talks with other pathways that also need to be investigated. Besides, we have looked at only phosphorylation and more experiments need to be done to investigate other PTMs other than phosphorylation, such as oxidation, acetylation, sumoylation, glycosylation etc. Directed experiments need to be also done with specific cellular components/cellular fractions to determine signaling specificity.

More directed studies need to be done in case of certain molecules that have been identified as they could be possible therapeutic targets for which the next generation drugs could be developed. The role of several of the autophagy or transcription and translation related molecules needs to be investigated in order more in detail specifically using Selective Reaction monitoring (SRM) type studies to investigate change in real time.