FGFR and FGF ligand overexpression in lung cancer: Implications for targeted therapy

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Abstract

Background: Fibroblast growth factor receptor (FGFR) pathway has been shown to be important for targeted therapy in non-small cell lung cell carcinoma (NSCLC). To determine the expression of FGFR and FGFs in NSCLC, we profiled 207 NSCLC specimens using a gene expression assay.

Methods: FGFR and FGF gene expression in formalin fixed paraffin-embedded (FFPE) samples was performed using an quantitative nucleic acid protection assay. This gene expression panel includes all four FGFRs, all 22 FGF ligands and known FGF interacting proteins KLOTHO and KLK4 in FFPE tissue. Using this assay we profiled 207 NSCLC samples (85 squamous, 102 non-­‐squamous). In addition 20 samples characterized by FISH for FGFR1 amplification were analyzed for FGFs mRNA expression.

Results: Gene expression analysis of the FGFR family in lung cancer showed that FGFR1 amplification by FISH does not have a one to one correlation with FGFR1 mRNA expression unlike Her2 amplification and expression in breast cancer. Furthermore, subsets of squamous and non-­‐squamous NSCLC show high level of receptor expression with or without ligand overexpression encompassing all FGFRs and a subset of FGFR4. This study suggests that DNA amplification may not result in transcriptional overexpression in some cases. However, we detected high level of expression of both receptor and ligand in a subset of squamous and non-­‐squamous lung cancer suggesting a paracrine/autocrine loop. Expression profiling data support frequent FGFR pathway dysregulation in lung cancer and highlight that gene expression profiling is likely to identify potential responders to novel anti-­‐FGFR therapies beyond FGFR1 gene amplification.

Conclusions: We report for the first time a comprehensive FGFR and FGF gene expression analysis of 207 lung cancer samples. Our expression profiling did not confirm preferential overexpression of FGFRs in squamous NSCLC in contrast to frequent gene amplification at this locus suggesting that DNA amplification may not result in transcriptional overexpression in some cases. However, we detected high level of expression of both receptor and ligand in a subset of squamous and non-­‐squamous lung cancer suggesting a paracrine/autocrine loop. Expression profiling data support frequent FGFR pathway dysregulation in lung cancer and highlight that gene expression profiling is likely to identify potential responders to novel anti-­‐FGFR therapies beyond FGFR1 gene amplification.

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