WES and Roche SeqCap EZ Exome V3

[Abstract]

6,318 SNVs and 56,686 mutation events in 3864 genes were observed in 13 paired lung cancer and brain metastasis samples. We identified 46 lung cancer most frequently driven gene mutations were identified in our samples. Furthermore, we identified several lung cancer metastasis associated genes (KMT2C, BAGE2 and FER1L4) and epigenetic factors (CHEK2P2, miR-4436A, miR-6077). We identified a mean of 3.1 driver mutation events per tumor with the dN/dS of 2.06 (95%CI: 1.73-2.4) indicating a significant enrichment for the cancer driven mutations. Mutation spectrum analysis found lung-brain metastasis samples have more similar transition (Ti) and transversion (Tv) profile with brain cancers in which C->T transitions is more frequently while lung cancer have higher frequency of C->A transversion. We also found the most important tumor onset and metastasis pathways such as focal adhesion,PI3K-Akt signaling pathway, MAPK signaling pathway. What’s more, Glioma pathway were also identified which highly indicating the solid finding of the study. In summary, we conducted a pairwise lung-brain metastasis based exom-wide sequencing and identified some novel cancer and metastasis related mutation which provided potential biomarkers for prognosis and targeted therapeutics.

Result:

COSMIC database showed KMT2C mutation frequency in cancer samples is 5.7%

1). dN/dS in different sample types

Average: dN/dS 2.06 (95%CI: 1.73-2.4)

Primary tumor tissue: dN/dS: mean=2.14, 95% CI: 1.65-2.64

Brain tumor tissue: dN/dS: mean=1.99, 95% CI: 1.42-2.56

Shared mutation between lung and brain: dN/dS: mean=2.2, 95%CI: 1.39-3.0

2). Mutation ratio perl Million basepair

I need raw data so that I can make this analysis.

3) Transition (Ti) and transversion (Tv) profile showed our mutation profile is more close to brain cancer mutation profile since brain cancer have high C->T transitions is more frequently while lung cancer have higher frequency of C->A transversion (see nature, cyriac kandoth, vol 502, page 333)

4) Common Mutations in cancer and brain metastasis samples

Table 1. Clinical Information of lung cancer samples

Table 2. Common mutation genes in our lung-brain metastasis cancer samples

Table 3. Enriched pathway of frequently mutated genes

Table 4. Keywords Enriched analysis of frequently mutated genes

Supplementary Table 8. Gene Ontology analysis to frequently mutated genes.

Supplementary Table 9. 16 tumor mutation driven genes validated by our study.

Supplementary Table 10. Enriched pathways (Benjamini<0.05) indicates brain metastasis trending.

Supplementary Table 11. Keyword enrichment (Benjamini<0.05) indicates important metabolic abnormal for the lung-metastasis cancers including Alternative splicing, Methylation and EGF-like domain.