Comparison between circulating tumor DNA and tumor tissue multiple gene detection in non-small cell lung cancer patients by targeted sequencing with the Ion PGM and AmpliSeq Cancer Panel

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OBJECTIVES

- Circulating tumor DNA (ctDNA) is a noninvasive assessment that can be used as an alternative method to detect gene mutations in lung cancer patients. However, previous studies have analyzed only a small subset of genes like EGFR and KRAS using a variety of detection methods. Feasibility to evaluate concordance between tumor tissue DNA(tDNA) and plasma ctDNA mutations in a large number of genes need to be assessed. We used a relatively inexpensive targeted sequencing method to analyze and compare mutations between tumor tissue and plasma.

METHODS

- Fresh tumor tissue, peripheral blood lymphocytes and plasma samples were collected prospectively from 167 non-small-cell lung cancer(NSCLC) patients before treatment. We utilized the Ion PGM and AmpliSeq Cancer Panel which covers 739 mutational hotspot loci in 50 oncogenes and tumor suppressor genes in matched tDNA and plasma ctDNA samples with matched white blood cell DNA as a control.

RESULTS

- Of the 167 NSCLC sample pairs analyzed, 118 contained mutations in one or more of the 50 genes screened in our cancer panel in tDNA. The majority of all mutations identified in both tDNA and plasma ctDNA were single nucleotide polymorphisms (SNPs) (112 and 162, respectively), insertions and deletions (Indels) accounted for 31 of tDNA mutations and 28 plasma ctDNA mutations, and 1 of tDNA and 2 of plasma ctDNA mutations were multi-nucleotide polymorphisms (MNPs). EGFR was most common mutation found in 60 of tDNA samples and 54 of plasma ctDNA samples. Overall study concordance is 70.66%, with a sensitivity and specificity of blood test were 77.53% and 62.82%, respectively. The concordance, sensitivity and specificity was (62.32%,68.42%,54.84%) in stage Ⅰ,(68.00%,81.82%,57.14%) in stage Ⅱ,(80.36%,85.19%,75.86%)in stage Ⅲ, and (76.47%,84.62%,50%) in stage Ⅳ patients, respectively.

Ⅰ		plasma positive	plasma negative	count
tumor	positive	26	12	38
	negative	14	17	31
	counts	40	29	69

Ⅱ		plasma positive	plasma negative	count
tumor	positive	9	2	11
	negative	6	8	14
	counts	15	10	25

Ⅲ		plasma positive	plasma negative	count
tumor	positive	23	4	27
	negative	7	22	29
	counts	30	26	56

Ⅳ		plasma positive	plasma negative	count
tumor	positive	11	2	13
	negative	2	2	4
	counts	13	4	17

CONCLUSION

- Target sequencing with the Ion PGM and AmpliSeq cancer panel can detect ctDNA mutations in plasma from NSCLC patients with high concordance to mutations found in the primary tumor, even in early stage patients. This approach could easily be implemented and standardized for clinical use.

Fig.1 Comparison of number of tDNA and plasma ctDNA samples with concordant and discordant mutations A (No. of samples,) B(Rate of Samples)

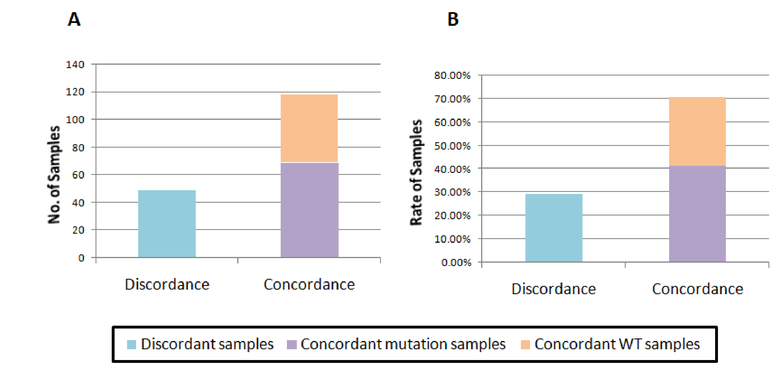
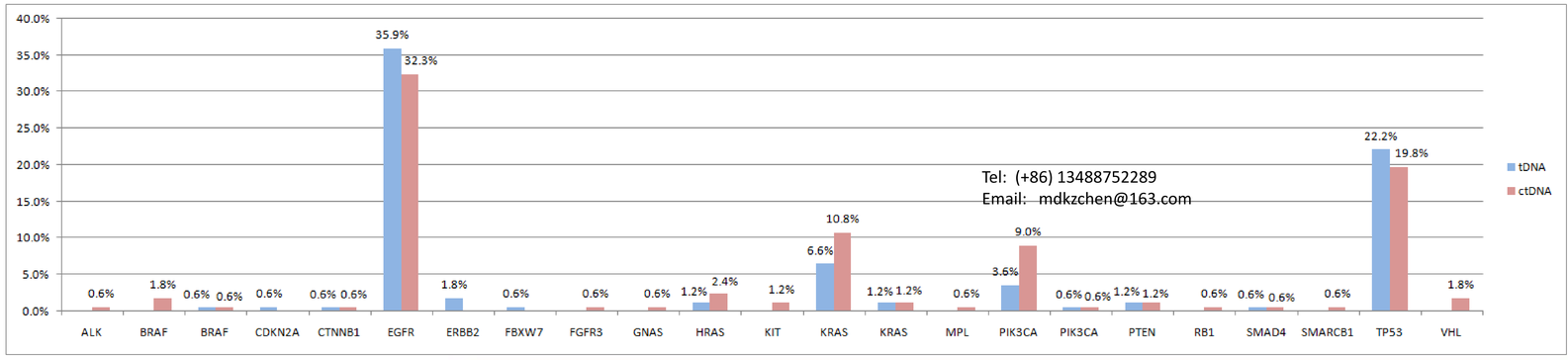


Fig.2 Rates of gene mutations in tDNA vs. plasma ctDNA from matched sample pairs



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