Non-invasive patient stratification and treatment follow-up using ctDNA in colo-rectal cancer patients

an ultra-sensitive multiplex mutation detection method using flow cytometer readout

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Introduction

ctDNA in liquid biopsies is an emerging biomarker class that enables less cumbersome and less costly sampling, and many times also less discomfort for patients. However, the analytical challenges with current methodologies are a lack of sensitivity, specificity and sample amount to measure several mutations. This study aims at investigating the utility of ctDNA in plasma samples in colorectal cancer patients and relate it to normal and tumour solid biopsies, and to clinical outcome. The innovative superRCA technology is used to achieve the sensitivities needed. A 44-plex panel is applied to each sample using only 1.8mL plasma. The results are published. (DOI: 10.3390/cancers16030549)

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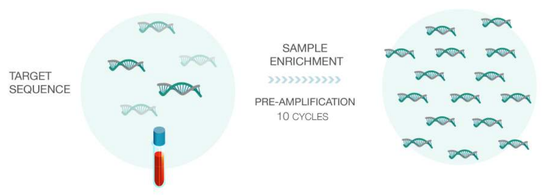
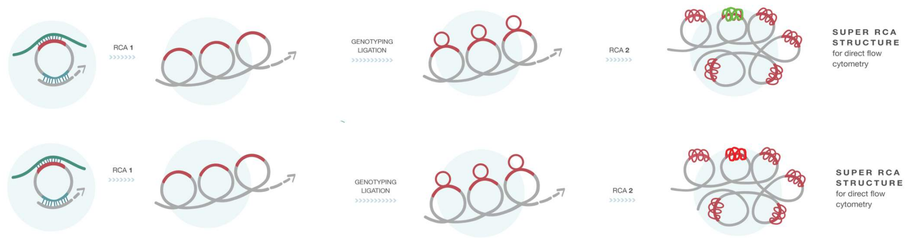
Sensitive. Efficient. Multiplex.

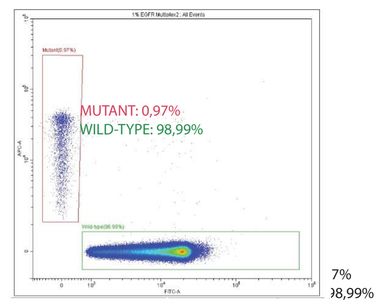
Sample enrichment



Single tube/well genotyping



Simple Data Read-out



The technology outlined in Nature: https://www.nature.com/articles/s41467-022-31397-y

Published Data - Sensitive and Specific Analyses of Colorectal Cancer Recurrence through Multiplex superRCA Mutation Detection in Blood Plasma

Assay performance

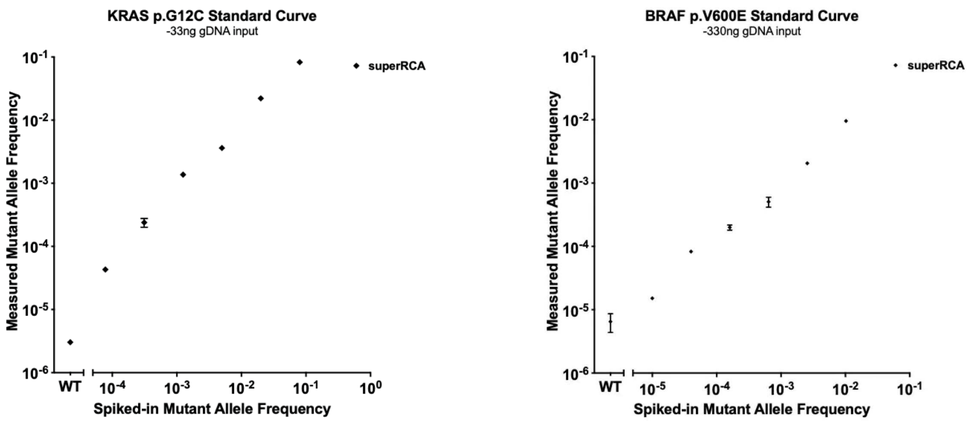


Figure 2 : Example assay performance of the 44-plex ctDNA panel. 4-fold dilution curve of superRCA mutation assay for KRAS p.G12C and BRAF p.V600E, using mutation positive genomic DNA samples spiked into wild-type genomic DNA, total 330ng or 33ng assay input. Mean and SD from 3 replicates.

Mutation detection in normal and tumour tissue and ctDNA collected at operation

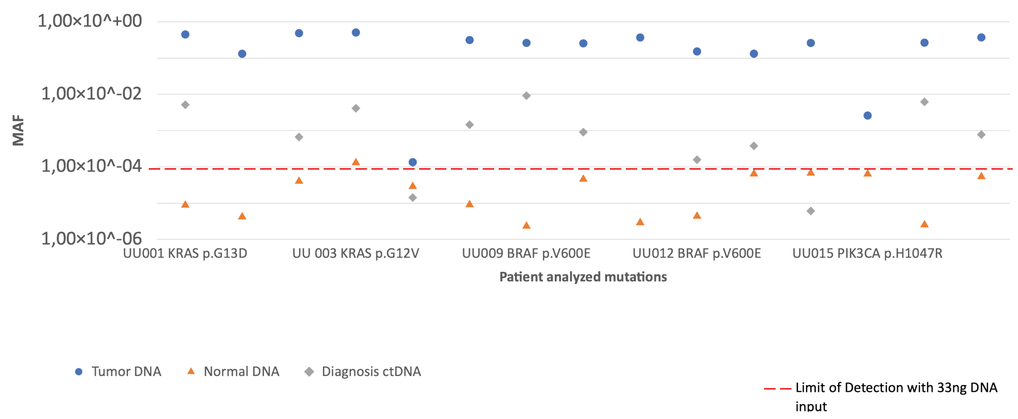


Figure 3 : Mutant allele frequency of tumor and normal gDNA samples analyzed with sRCA assay. MAF, mutant allele frequency; gDNA, genomic DNA; LOD, limit of detection

ctDNA monitoring and clinical outcome

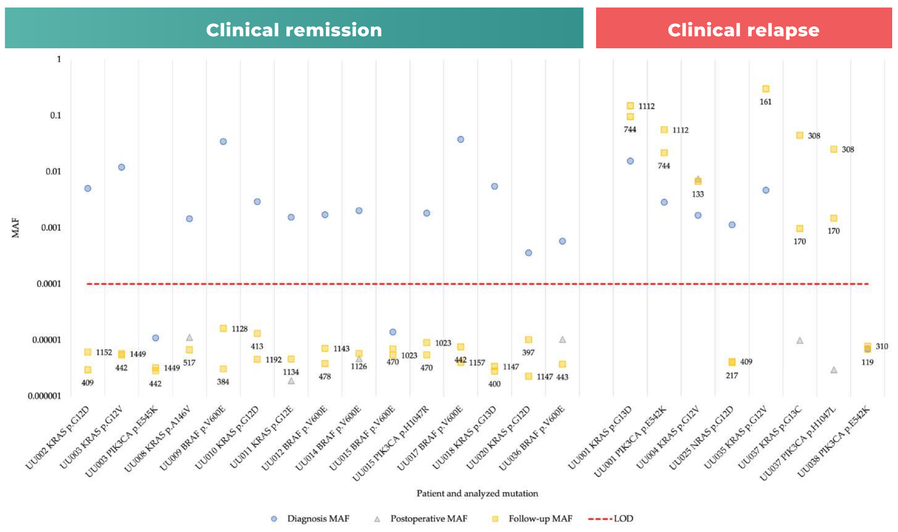
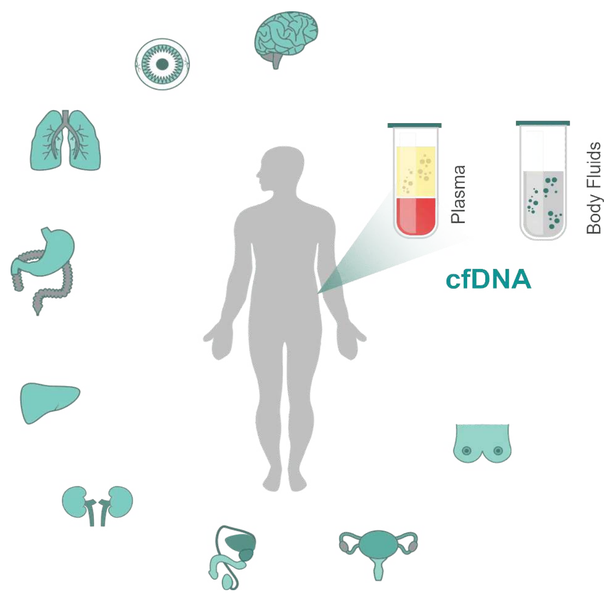


Figure 4: sRCA analysis on the longitudinal ctDNA samples from stage III &IV CRC patients. Round blue symbol stands for samples collected at diagnosis , grey trangle sample were colleted at post operative check up and yellow square samples are collected at a long-time follow-up.

More Applications



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Conclusion

Conclusion: The data indicate that superRCA cfDNA mutation assays can detect several mutations in the same blood sample at high sensitivity and specificity using existing devices in hospital laboratories and CROs, and with very short turn-around-times (TAT). The high sensitivity of the assay and non-invasive nature of the sampling allows for more frequent monitoring of patients post treatment and possibly earlier detection of relapse. The utility of the technology for standardized estimation of total tumour burden in metastatic patients is an interesting future aspect.