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Correlation of tumor size and -biology with ctDNA release in early colorectal cancer

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Background/Aims

The analysis of circulating tumor DNA (ctDNA) from plasma has evolved into a promising clinical tool for monitoring advanced cancer patients. More recently, early detection of localized tumors is intensively investigated, but is highly challenged by minute amounts of ctDNA in plasma in these early stages. Except for tumor burden, biological factors contributing to the release of ctDNA are largely unknown. Since knowledge about the earliest time point in tumorigenesis, at which ctDNA becomes detectable in the circulation, is crucial for the development and assessment of noninvasive screening tests, we aim to shed light onto ctDNA release kinetics.

Methods/Results

In a cohort of 22 treatment naïve early stage (I-II) colorectal cancer patients, we performed matched targeted sequencing of tissue and plasma samples using a gene panel enriching for 523 cancer associated genes (TSO500, lllumina). Phenotypic properties of the tumor were determined using a novel spatial transcriptomics method called in situ sequencing (ISS), where a marker panel of 220 genes involved in common biological pathways was spatially resolved. To support the spatial analysis data, total RNA-Seq of the tissue samples is still ongoing. We were able to detect mutations identified in tumor tissues in 18/22 (~82%) of corresponding plasma samples. In addition, unique variants in plasma and tissue have been observed but with significantly lower variant allele frequencies. Preliminary phenotypic ISS data revealed that subsets of genes involved in apoptosis, autophagy, invasion, proliferation and stemness/differentiation were significantly upregulated in the ctDNA releasing- compared to the non-releasing patients.

Conclusion

Further analysis of ISS and RNA-Seq data will allow to extend our already established phenotypic correlation. The next steps will focus on targeting the distribution of immune cells within the tissue as well as looking at metabolic and stress related pathways.