Personalised analysis of circulating tumor DNA as a novel biomarker in neuroblastoma

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Background & objectives

Neuroblastoma is a childhood cancer most commonly affecting younger children, and accounts for 6-10% of all childhood cancers. It stems from the development of the sympathetic nervous system, originating from neuroblasts. Thus, the tumors can be found anywhere along this path, most frequently in the adrenal glands but also where groups of nerve cells exist such as the neck, thorax, and abdomen. Neuroblastoma is a heterogenous disease showing great diversity both clinically and genetically. Differing genetic alterations as well as anatomic positions poses great clinical challenges in monitoring and treating the disease. Discovering clinically relevant biomarkers and new therapeutic methods is a priority for successful treatment of neuroblastoma. Circulating tumor DNA (ctDNA) analysis is a emerging potential biomarker

for neuroblastoma. We aim to develop personalised ctDNA analysis for monitoring treatment response and detecting disease relapse in neuroblastoma patients.

Methods

Previous studies generally use generic sequencing panels for ctDNA analysis, which is difficult in childhood tumors due to their low number of recurrent mutations. We develop personalised multiplex assays for detection of 10 tumor specific mutations, and use a PCR based method for ultra-sensitive sequencing in a longitudinal fashion as a proxy for measuring ctDNA levels in children with neuroblastoma. CtDNA levels are measured in plasma samples taken at diagnosis, during treatment and follow up in 12 patients with neuroblastoma.

Results

We detect ctDNA in all of 12 of patients with neuroblastoma, and ctDNA levels are associated with tumor stage at diagnosis. Levels of ctDNA decrease gradually and eventually become undetected in children with successful treatment and is elevated at the time of relapse. Our personalized ctDNA assays seem to outperform tumor markers used in the clinic today, although more patients are needed to assess the method for detection of relapse.

Conclusion

Personalized ctDNA analysis appears promising for estimation of tumor burden in children with neuroblastoma, but more data is needed before clinical implementation.