00506 Isolation of Circulating Tumor Cells Using Spiral Microfluidic Chip for Disease Monitoring and Prognostication in Neuroblastoma

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Aims: Among pediatric tumors, minimal residual disease (MRD) has been explored only in neuroblastoma. Current disease and treatment response evaluations in neuroblastoma are limited to imaging, tumor histology and bone marrow morphology. Recently, single cell capture techniques have allowed circulating tumor cells (CTCs) to be isolated from peripheral blood. One of these is via label-free, size-based separation. Hence, this study aims to isolate and characterize CTCs from peripheral blood of neuroblastoma patients at 5 key disease evaluation timepoints in current treatment protocols. This proof-of-concept study will establish the utility of this 'liquid biopsy' approach for neuroblastoma prognostication and disease monitoring.

Methodology: Isolated CTCs, using a spiral microfluidic chip (Clearbridge Biomedics, Singapore), will be validated using established MRD marker, PHOX2B, by RT-PCR and characterized using multiplex gene expression analysis such as nanoString. PHOX2B and other genomic markers of interest expression will be correlated with clinical covariates.

Result: Patients of varying stage and histological grade were recruited from KK Women's and Children's Hospital. PHOX2B appeared to be the most reliable marker and sufficient for confirming the presence of CTCs. From blood samples taken at diagnosis, PHOX2B expression was significantly associated with liver, marrow and bone metastases ($P<0.05$), and number of isolated CTCs – characterized by cellular atypia – were significantly associated with metastases to marrow and bone ($P<0.05$). Interestingly, PHOX2B expression was present in the CTC fractions of peripheral blood and bone marrow aspirate of a patient with metastasis to multiple sites. Moreover, expression of other neuroblastoma markers quantified using nanoString confirms the presence of CTCs at different timepoints.

Conclusion: Quantification, characterization and profiling of isolated CTCs from peripheral blood of neuroblastoma patients using spiral microfluidic chip at various disease evaluation points could be a less invasive, low-cost, upfront and more predictive approach in prognostication and disease monitoring.