

Multimodal liquid biopsy analysis in children with cancer using long-read sequencing on a national scale

Paediatric cancers are the leading cause of death in children post infancy in the Western world. Comprehensive molecular profiling is essential to elucidate the molecular basis of treatment resistant disease and to guide clinical decision making. Access to high-quality tumour material for genomic profiling is a challenge in children where tissue biopsies are small. The analysis of cell-free DNA (cfDNA) from liquid biopsies for the detection of circulating tumour DNA (ctDNA) offers a powerful, minimally invasive alternative to tumour profiling. However, ctDNA analysis is currently limited in sensitivity, scalability, turnaround time and cost, hindering its implementation into standard clinical care. Emerging Nanopore sequencing can report on native DNA, is rapid and scalable at low cost, making this technology highly attractive in the clinical setting.

In this talk, I will introduce the UK Stratified Medicine Paediatrics study which has recruited >800 paediatric patients with solid tumours, and present our Nanopore sequencing approaches for sequencing native cfDNA from these patients. I will then show bioinformatic approaches and tools developed in our laboratory for the analysis of Nanopore sequencing data from cfDNA. Finally, I will present research results to illustrate how Nanopore-based multi-modal cfDNA analysis (including copy number, methylation and fragmentomics) could be utilised to improve disease management in children with cancer by facilitating early detection, accurate diagnosis, and efficient serial monitoring of disease progression.