

# Circulating tumor DNA in Genetic Profiling and Monitoring of Pediatric Hodgkin Lymphoma

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## Introduction

Hodgkin Lymphoma (HL) comprises 6% of all pediatric cancers. By using response-based therapies, the overall survival of HL is >90%; however, children remain at risk for long-term treatment-related morbidity. Currently, response to therapy in HL is assessed by PET-CT scan. However, a more sensitive and specific assessment method would have improved predictive value to more appropriately tailor therapy to prevent both relapse and long-term morbidity. We have developed an ultra-sensitive method for detecting circulating tumor DNA (ctDNA) called Cancer Personalized Profilng by Deep Sequencing (CAPP-Seq). CAPP-Seq uses selective sequencing of specific regions of DNA that are commonly mutated in a given malignancy to assess the presence and quantity of cell free DNA (cfDNA) that has tumor-associated mutations [1].

## Methods

For this study, we will use the CAPP-Seq selector that was developed for adult HL, which contains a library of genes curated using genomic studies of B-cell malignancies [1, 2]. We will begin by performing CAPP-Seq analysis on a discovery set of 25 pediatric patients. We will extend to whole exome sequencing on a subset of patients to allow for the detection of additional mutations. We will use the results of this discovery set to refine our selector library and then expand our analysis to longitudinal ctDNA samples collected prospectively as part of the Pediatric Hodgkin Consortium cHOD17 study. Treatment response will be measured by fold ctDNA change from baseline. We will observe the dynamics of tumor response to treatment and correlate these to patient outcomes.

## Results

Preliminary results from a CAPP-Seq analysis on a cohort of 50 adult patients with HL undergoing treatment showed that ctDNA mean variant allele frequency (VAF) and mutation number did not differ between HL and other aggressive lymphoma histologies despite the relatively low presence of tumor cells in HL. CAPP-Seq was also used in genotyping single nucleotide variants and somatic copy number alterations. In longitudinal studies, patients with log fold decrease in ctDNA of 2 or greater after 2 cycles of chemotherapy had better outcomes [2, 3].

## Conclusion

Targeted next-generation sequencing of ctDNA by CAPP-Seq allows for biopsy-free genotyping and disease monitoring in adults with HL. In order to demonstrate the feasibility of this method in pediatrics, samples from pediatric patients with HL are currently being profiled and the results of the analysis will be presented at the meeting.

**Affix****References**

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