#2064: Ultrasensitive detection and monitoring of central nervous system tumors from plasma using personalized whole-genome ctDNA profiling

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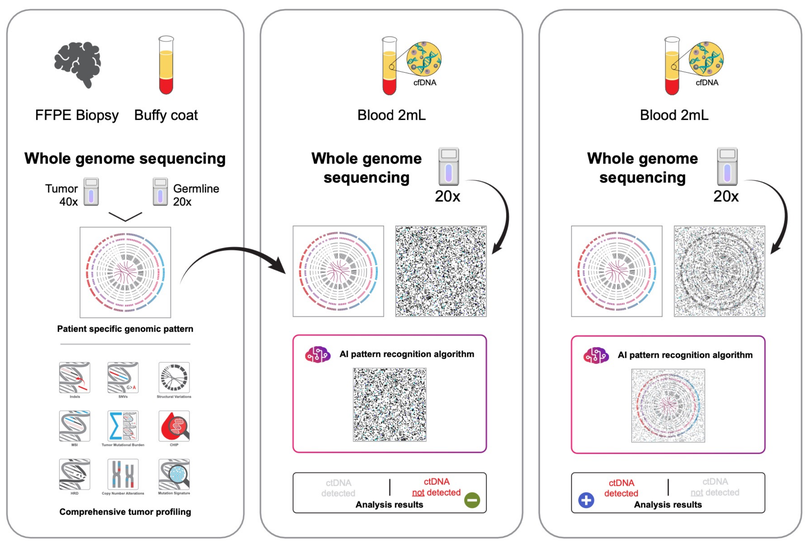
BACKGROUND

Patients with central nervous system (CNS) tumors are largely followed up by imaging. Current plasma-based liquid biopsy techniques have limited utility in neurooncology due to a low circulating cell-free tumor DNA (ctDNA) burden, blood-brain barrier, and low number of mutations in coding regions. Whole genome sequencing (WGS)-derived patient specific mutation signatures from matched tumor-normal samples can provide a personalized, highly sensitive and specific approach to detect mutations in ctDNA and provide blood-based monitoring in brain tumor patients.

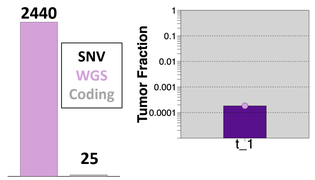
METHODS



Using an AI-based error suppression model, we derived a personalized mutation pattern using SNVs and copy number for quantification and ultra-sensitive detection of ctDNA in plasma samples. The ctDNA tumor fraction (TF) was compared to the clinical status and MRI-based imaging.

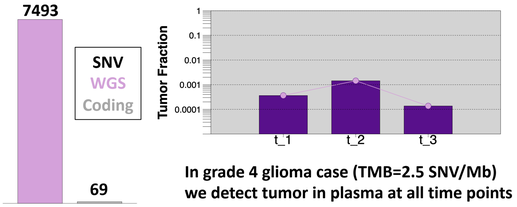
RESULTS

Case Study: Ependymoma – 2 y.o. male



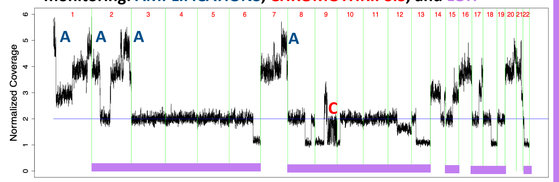
Successfully detects evidence of grade 3 anaplastic ependymoma with low TMB (0.8 SNV/MB) in plasma at time of diagnosis

Case Study: Glioma – 14 y.o. male

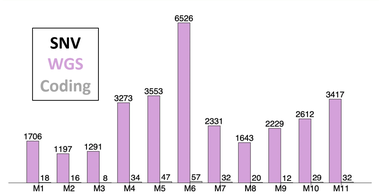


In grade 4 glioma case (TMB=2.5 SNV/Mb) we detect tumor in plasma at all time points

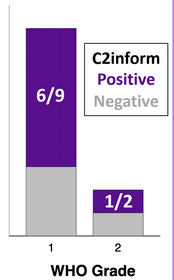
By using WGS we can expand variant types used in C2inform for monitoring: AMPLIFICATIONS, CHROMOTHRIPSIS, and LOH



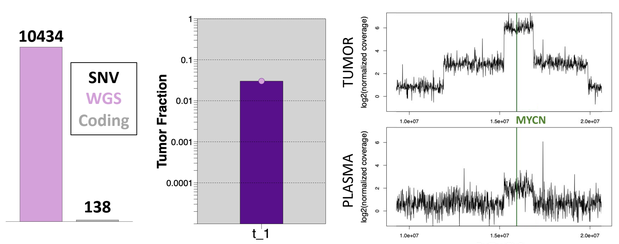
Cohort Study: Meningioma – 11 samples - adult



Low TMB cancer (median 0.8 SNV/Mb, 2331 total mutations; 29 coding) able to detect at resection in 6/9 grade 1 tumors and 1/2 grade 2 tumors



Case Study: Recurrent Adult Medulloblastoma



De novo detection of MYCN amplification in matched tumor and plasma

This demonstrates utility of CNV in monitoring

CONCLUSIONS

We demonstrate ultrasensitive detection and monitoring of CNS tumors across several subtypes, across all WHO grades 1-4, in both adult and pediatric samples, and in benign and metastatic disease. We show how WGS allows for a 100x fold increase in the number of mutations for detection as well as how WGS allows for the use of other variant types (e.g. amplifications, chromothripsis, LOH) in monitoring.

Whole genome sequencing (WGS) of cfDNA enables sensitive monitoring of primary CNS tumors in adults and children by detecting tumor mutation signatures in blood samples

C2i Genomics

NYU Langone Health

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