

Clinical Whole Exome Sequencing with Somatic Analysis

PRODUCT OVERVIEW

The Broad clinical research sequencing lab is a clinical laboratory accredited by the College of American Pathologists (CAP), licensed by the State of Massachusetts and registered with the Centers for Medicare and Medicaid Services to provide testing under the CLIA regulations¹. The clinical research sequencing lab was created to further the Broad Institute mission of creating and making available tools for genomic medicine, and applying them to human disease.

The clinical research lab provides Whole Exome Sequencing that leverages the Broad-developed solution-phase hybridization assay² and a co-developed with Illumina® whole exome content bait set (38Mb target territory). This content includes all of our previous exome content plus additional coding content that brings the total coverage of the RefSeq and GENCODE v12 databases to >98%. Table 1 outlines the technical specifications of our Somatic Whole Exome Sequencing Test, which provides the necessary depth of coverage for somatic variant calling across Tumor/Normal pairs including SNV, indel and CNV calls.

Table 1. Technical Specifications of Broad CLIA Somatic Exome

Targeted Territory	38 Mb		
Coverage Deliverable	≥150X MTC		
Sample Format	Tumor/Normal Pairs		
Input Materials*	500ng Genomic DNA, Whole Blood, Cells, FFPE, Fresh-frozen Tissue, Buffy Coat		
Sample Prep Method	Broad With-Bead ³		
Analytical Sensitivity ⁺	Specification	Observed	
	SNV	95%	97.1%
Indel	80%	89.3	
Analytical Specificity (FPR/Mb)	SNV	<1	0.304
	Indel	<1	0.088

⁺Performance metrics represent mean sensitivity across targeted regions with 50bp padding based on 20% Allele Fraction.

*Please contact for additional detail on input material requirement

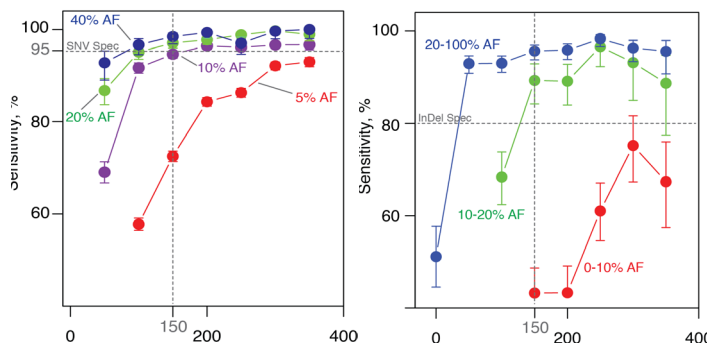


Figure 1. Somatic SNV (left) and Indel (right) sensitivity at varying allele fractions.

DELIVERABLES, REPORTING AND DATA DELIVERY

The deliverables for the Somatic test is a technical report, Picard-generated aggregated, aligned BAM files, somatic SNV (VCF) and Indel mutation annotation format (MAF) files through the Broad’s cancer analysis Firehose pipeline, as well as CNV calls (.called & .called.seg.annotated) delivered through the ReCapSeg algorithm. The technical report outlines process specifications and performance of the sample relative to these specifications. The variant files list all variants identified by the analytics pipeline.

DATA ACCESS AND RETENTION

All files are accessible via a dedicated, secure data portal. Data is stored in accordance with relevant federal and state regulations for CLIA or clinical trials testing as appropriate.

References

1. CLIA # 22D2055652; MA License # 5347; CAP # 8707596
2. Gnirke *et al.* Solution hybrid selection with ultra-long oligonucleotides for massively parallel targeted sequencing. *Nature Biotechnology* 27, 182 - 189 (2009).
3. Fisher *et al.* A scalable, fully automated process for construction of sequence-ready human exome targeted capture libraries. *Genome Biology* 12:R1 (2011).
4. Cibulskis *et al.* Sensitive detection of somatic point mutations in impure and heterogeneous cancer samples. *Nature Biotechnology* 31, 213–219 (2013).
5. Allen *et al.* Whole-exome sequencing and clinical interpretation of FFPE tumor samples to guide precision cancer medicine *Nature Medicine* 20. 682-8. (2014).



FOR MORE INFORMATION

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