

Clinical Whole Exome Sequencing Germline Analysis

PRODUCT OVERVIEW

Clinical Whole Exome Sequencing with Germline Analysis is a technical exome product useful for discovery of variants that do not have well-characterized associations with disease biology, including rare coding variants. Sequenced in our Clinical Research Sequencing 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 CLIA regulations. The lab was specifically developed to further the Broad Institute's mission of creating and making tools available for genomic medicine that will be applied to human disease research.

The Clinical Whole Exome for Germline Analysis leverages Broad Institute developed solution-phase hybridization assay* and includes whole exome content bait set (38Mb target territory) which includes all of our previous exome content plus additional coding content bringing the total coverage of RefSeq and GENCODE v12 databases to >98%. Analytical sensitivity includes 95% specification, observed at 98.8% for SNVs and 80% specification, 88.4% observed for Indels.

The assay for Clinical WES may identify mutations for which clinical significance has not been determined. It does not detect genomic rearrangements, epigenetic changes, or other structural genomic changes and is not validated for copy number detection or germline mosaicism. It is not suitable for analysis of the mitochondrial genome.

WHAT'S INCLUDED:

- Targeted territory of 38Mb
- Sample Receipt, Quantification & Plating, Sample Preparation
- Sample Fidelity QC (96 SNP fingerprinting)

PRODUCT REQUIREMENTS:

- 500ng of genomic DNA (per sample)
- Fresh/frozen tissue, FFPE, and blood preferably yielding >500ng of DNA
- Minimum sample data including collaborator participant ID, collaborator ID, gender

GERMLINE SENSITIVITY AS FUNCTION OF READ DEPTH

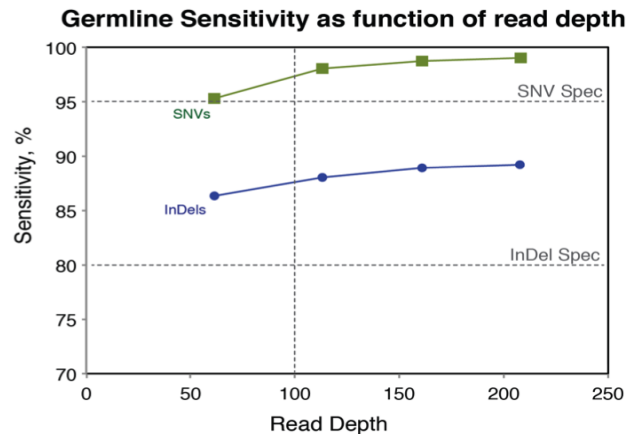


Figure 1. Germline SNV and Indel sensitivity as a function of read depth

DATA DELIVERABLE:

- Technical report outlining process specifications and performance of the samples
- Standard 21-day turnaround time after sample receipt
- De-Multiplexed, aggregated Picard BAM file for the germline exome test
- Coverage deliverable >100X MTC
- Analytical sensitivity of SNV - Specification: 95%, Observed: 98.8%
- Analytical sensitivity of Indels - Specification: 80%, Observed: 88.4%
- Germline Variant Call Format (VCF) files list all single nucleotide and Indel variants
- Data accessed via secure online digital transfer

*Gnirke et al. Solution hybrid selection with ultra-long oligonucleotides for massively parallel targeted sequencing. Nature Biotechnology 27, 182 - 189 (2009).

TURNAROUND TIME

Processing times is 21 calendar days from sample receipt to delivery of the technical report, VCF/MAF, aggregated Picard BAM files, and ReCapSeg data.