Clinical Blended Genome-Exome

A combined genome & exome product that supports GWAS and rare variant calling at the clinical level

Clinical Blended Genome-Exome starting at $150

Pricing dependent on number of samples and project details

Product Overview

Clinical Blended Genome-Exome (BGE) is a qualitative assay intended for low pass genome and deeper exome sequencing of single nucleotide variants (SNVs) and small insertions and deletions (InDels), in human genome DNA extracted from saliva and blood samples. The sequencing data generated by BGE is intended as an input for clinical germline assays that have been appropriately validated for use with this data type. If interested in an interpreted clinical report from BGE, please refer to the Clinical Blended Genome Exome with Resulting product.

From a single blood or saliva sample, a PCR-free whole genome library is constructed, and an aliquot is taken through PCR amplification and exome selection. The libraries are recombined and sequenced on the Illumina NovaSeqX Plus platform. A single CRAM file is generated containing low-coverage whole genome data (on average 2-4x) and higher coverage exome data (on average >85x). Alignment and variant calling are performed using the Illumina DRAGEN™ platform.

In the research space, BGE is being used at high scale for germline gene-disease discovery studies in which the low pass genome region is used as an unbiased alternative to microarray genotyping in GWAS applications[1]. Low pass genome data can also be used post-imputation for polygenic risk score (PRS) calculations. We have confirmed that BGE-based imputation is superior to microarray-based data, in terms of low allele frequency sensitivity across genetic ancestries. The exome region coverage of BGE has been assessed for performance in germline variant calling. Coverage and callability (min. 20X depth, Q20 base quality, and Q20 mapping quality, ***Table. 3***) have been measured over the exome target region.
All samples are processed in Broad Clinical Labs' CLIA-certified/CAP-accredited laboratory.

Table 1. *Clinical validation performance metrics from a cohort of blood, saliva, and cell line samples (n=189)*

Mean WES coverage	Mean WGS coverage	% Exome ≥ 20X	% Mapped
96.50	3.23	97.94	99.25

Table 2. *Precision & sensitivity across the exome (+/-16bp padding)*

	Average precision	Average sensitivity	Average F-Measure
SNP	99.90%	99.44%	99.67%
INDEL	97.53%	97.02%	97.27%
All	99.78%	99.32%	99.55%

Table 3. *Callability Analysis of matched BGE and clinical WGS samples*

BGE undercovered* bases (%)	WGS undercovered bases (%)
765,138 (2.19%)	924,927 (2.65%)

* *a base is considered undercovered when in 80% of samples the base does not achieve ≥20 for depth, base quality, and mapping quality. Analysis over the exome region in 27 samples.*

Input Requirements

- Genomic DNA: 15ng/µL - 110ng/µL concentration; 50 - 300µL preferred volume, 30µL minimum acceptable volume. Whole blood, saliva.
- Minimum sample metadata, including collaborator participant ID, collaborator sample ID, biological sex of participant.

Data Deliverables

- Raw data (CRAM files aligned to HG38)
- Single sample hard-filtered VCF, gVCF
- Technical report (PDF)

Product Specifications

- Mean Genome Coverage: ≥1x
- Exome Mean Target Coverage: ≥ 60x
- Percent Exome Bases @ 20x: ≥ 90%
- Percent Mapped Bases: ≥ 75%
- Percent Exome Callability: ≥ 95%
- Percent Contamination: ≤ 2.5%
- Percent Reads Not Properly Paired: ≤ 5%

[1]DeFelice M, Grimsby JL, Howrigan D, et al. Blended Genome Exome (BGE) as a Cost Efficient Alternative to Deep Whole Genomes or Arrays. Preprint. bioRxiv. 2024;2024.04.03.587209. Published 2024 Jul 30. doi:10.1101/2024.04.03.587209