BROAD CLINICAL LABS

PRODUCT DATASHEET

Available for as low as $99 per sample

Blended Genome-Exome (BGE)

A combined genome & exome product that supports GWAS and rare variant calling.

Product Overview

Complex disease requires large, diverse populations to detect associated common and rare variants. The probe content of current genotyping arrays makes unbiased discovery difficult, as rare population-specific variants rarely make it on to commercial arrays. Development of the unbiased, cost-competitive BGE product allows for expanded studies into additional global populations and existing biobanks, driving equity to populations historically underrepresented in genetic studies. BGE allows for high quality imputation of common variants across the genome as well as detection of rare coding variants across the exome region. Applications of BGE include global population genome-wide association studies and polygenic risk score determination, as well as rare variant calling and monogenic risk determination.

From a single sample, a PCR-free whole genome library is constructed and a sub-aliquot is taken through PCR amplification and exome selection. Genome and exome libraries are then blended together (exome 38%, PCR-free genome 62%) into one tube. The blended sample is sequenced on the Illumina® NovaSeq X Plus platform, and a single CRAM file is generated containing low-coverage (1-3x) whole genome and higher coverage (30-40x) exome data. Alignment and variant calling are performed using the Illumina DRAGEN™ platform. Data can be further processed through the GLIMPSE2 analytical pipeline, a phasing and imputation method for large-scale low-coverage sequencing studies. Broad Clinical Labs' current BGE processing capacity is >500,000 samples annually.

Input Requirements

- ≥ 50µL volume per sample
- ≥ 40ng/µL concentration per sample

Product Performance

Exome Variant Calling

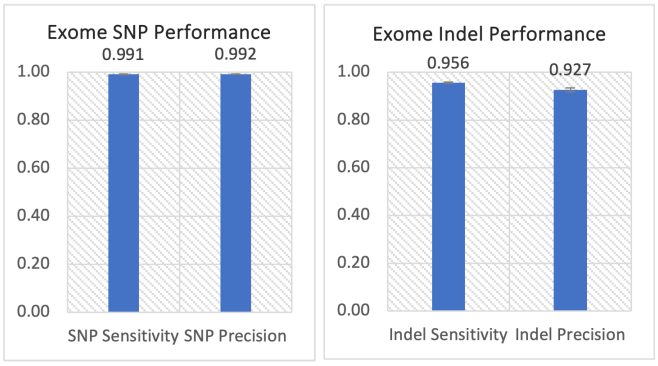

Figure 1. BGE sequencing on samples HG001 and HG002 to an average mean target exome coverage of 36x. Variant calling for SNPs and Indels performed using DRAGEN™ V4.2 and calls compared to high confidence truth data from NIST GIAB v4.2.

Low Pass WGS Imputation

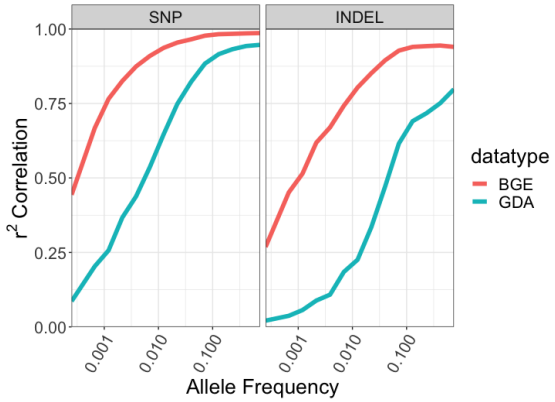

Figure 2. R^2 correlation of overlapping sites between BGE imputation and the Illumina® Global Diversity Array, compared with matched 30X whole genome sequencing, demonstrating that BGE outperforms GDA across a range of allele frequencies.

Performance Deliverables

- ≥ 90% of exome covered to ≥10X
- ≥ 9.5B PF aligned bases

Data Deliverables

- Raw data (CRAM files aligned to HG38)
- Single sample VCF