Human Low-pass Whole Genome Sequencing (LPWGS)

BGI

gencove

High-throughput, Cost-Effective Sequencing from BGI and Gencove

The unique combination of DNBSEQ™ sequencing and Gencove's low-pass sequencing software platform enables researchers to efficiently obtain fully-imputed, analysis-ready VCF files from DNA in a single service.

Low-pass whole genome sequencing (LPWGS) is commonly defined as sequencing a genome to an average depth less than 1x coverage. LPWGS, combined imputation, offers a solution to the limitations of genotyping arrays and the high cost of WGS (30x). LPWGS has been shown to provide a substantial increase in statistical power for genome wide association studies (GWAS), and increased accuracy for polygenic risk prediction (PRS) at effective coverages of 0.5x and higher[1].

LPWGS advantages:

· Accuracy with less ascertainment bias
· Complete genomic information to discover novel variation at the population level
· Fast and high-volume achieved by multiplexing large numbers of samples
· Easy to set up and future-proofed by updating the reference panel

LPWGS is the perfect solution for:

· **Biobanks** - easily and cost-effectively sequence all samples
· **Clinical research** - ensure accurate results with genome level insight for large cohorts
· **GWAS** - predict genotype to phenotype associations with greater certainty
· **Pharmacogenomics** - get fast and expanded profiling

Sequencing Service Specification

BGI's Human Whole Genome Sequencing Services are performed with DNBSEQ™ sequencing technology.

Superior Data Quality

· PCR and PCR-free library methods are available
· 100bp/150bp Paired end sequencing
· Choice of sequencing depth: low pass WGS (1x, 4x, or custom)
· CAP/CLIA laboratory services available

Sequencing Quality Standard

· Guaranteed ≥80% of bases with quality score of ≥Q30

Turn Around Time

· Typically, 18 working days from sample QC acceptance to Data Analysis Report availability
· Expedited services are available, contact your local BGI specialist for details

Project Workflow

We care for your samples from the start through to the result reporting. Highly experienced laboratory professionals follow strict quality procedures to ensure the integrity of your results.
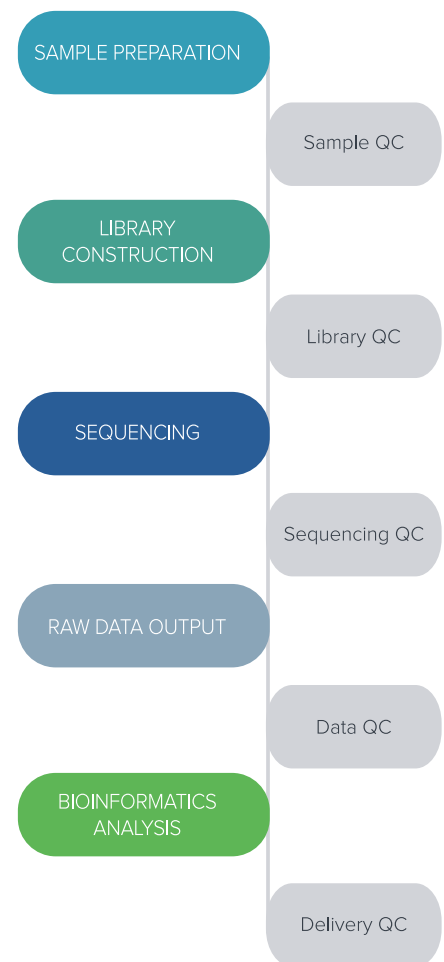
SAMPLE PREPARATION

Sample QC

LIBRARY CONSTRUCTION

Library QC

SEQUENCING

Sequencing QC

RAW DATA OUTPUT

Data QC

BIOINFORMATICS ANALYSIS

Delivery QC

DNBSEQ™ Sequencing Technology

DNBSEQ™ is an innovative high-throughput sequencing technology, first developed by BGI's Complete Genomics subsidiary in Silicon Valley. The system is powered by combinatorial Probe-Anchor Synthesis (cPAS), linear isothermal Rolling-Circle Replication and DNA Nanoballs (DNB™) technology, followed by high-resolution digital imaging.

The combination of linear amplification and DNB technology reduces the error rate while enhancing the signal. The size of the DNB is controlled in such a way that only one DNB is bound per active site on the flow cell. This densely patterned array technology provides optimal sequencing accuracy and increases flow cell utilization.
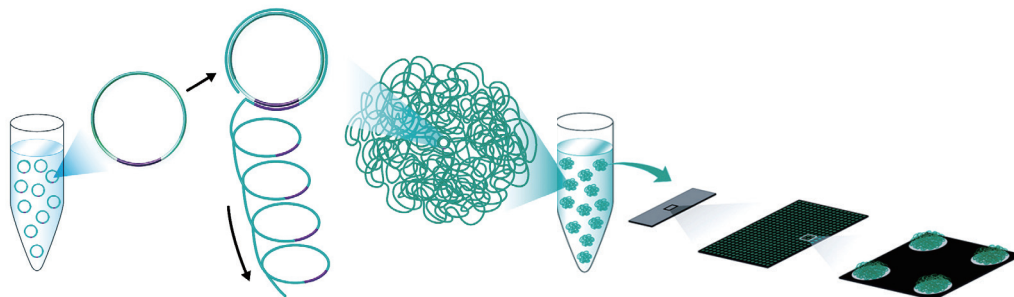
Sample Requirements

We can process your gDNA, saliva, blood, fresh frozen tissue, cell pellets and FFPE samples, with the following general requirements:

	DNA Amount and Concentration	Minimum Sample Volume
Regular Samples For PCR libraries	Intact genomic DNA ≥1µg, Concentration ≥12.5ng/µl	15µl
Low Input Samples For PCR Libraries	Intact genomic DNA ≥200ng, Concentration ≥2.5ng/µl	15µl
Samples For True PCR-Free Sequencing	Intact genomic DNA ≥2µg, Concentration ≥12.5ng/µl	15µl

Gencove's Imputation and Analysis Platform

Out-performs genotyping arrays and reduces bias

Gencove's low-pass sequencing at 0.4x and 1x coverage consistently yields higher imputation quality than genotyping arrays in European and African populations, but the difference is especially pronounced in African samples.
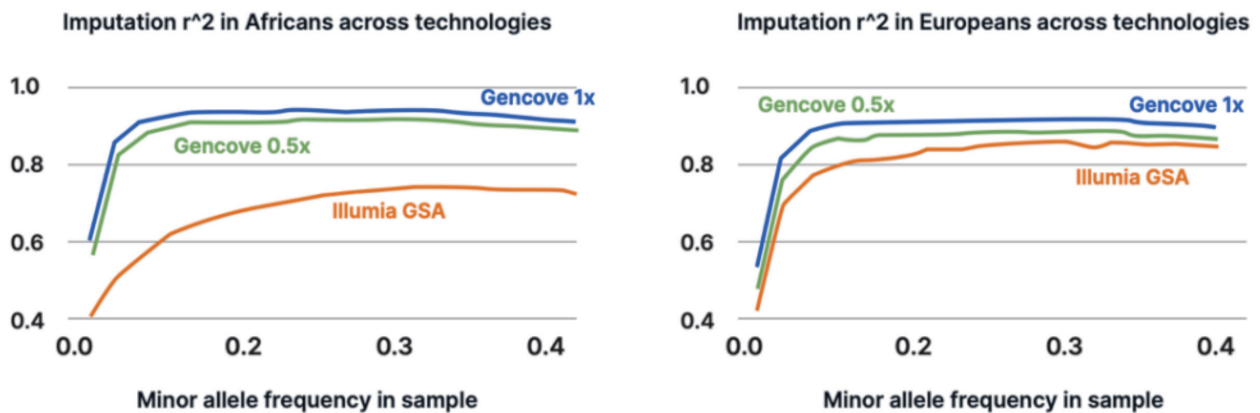
Moreover, based on the experiment design as shown in Table1, low-pass sequencing at an effective coverage of ~0.4x or higher consistently yields more accurate imputed genotype calls at sites of common variation than the Illumina GSA and that this pattern holds across both EUR and AFR cohorts (Figure 1). DNBSEQ™ LPWGS performs the best among all the experiments.

Table 1. Details of experiments conducted. Experiments A-D were based on low-pass sequencing, while experiment E used the Illumina GSA v3.0.

Experiment	Mean Coverage	Samples	Assay	Library Prep	Sequencer
A	0.67	120 (3 replicates)	lpSeq	KAPA HyperPlus	Illumina HiSeqX
B	1.25	120 (3 replicates)	lpSeq	KAPA HyperPlus	Illumina HiSeqX
C	1.20	1 (30 replicates)	lpSeq	KAPA HyperPlus	Illumina HiSeqX
D	1.26	60 (1 replicate)	lpSeq	MGIEasy	BGIseq 500
E(array)	NA	120 (3 replicates)	Illumina GSA v3.0	NA	NA

Average NRC by non-reference allele frequency for unfiltered sites
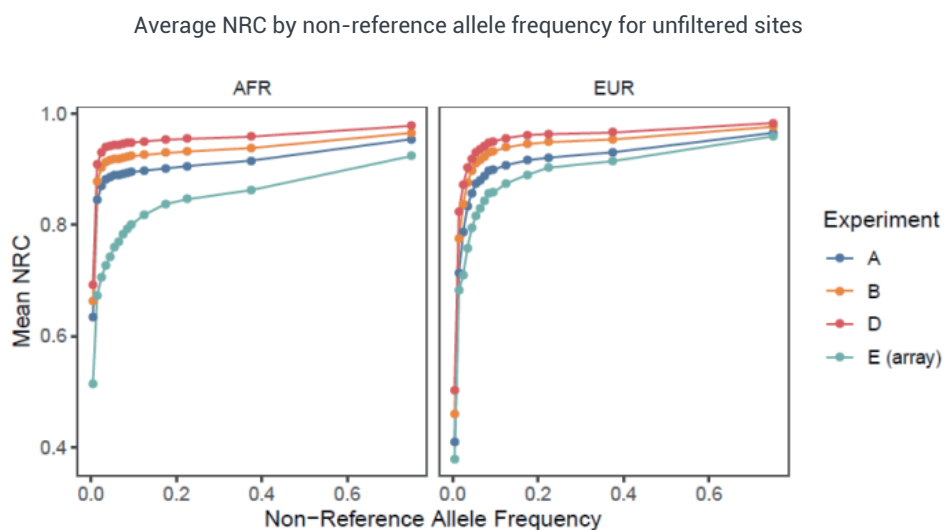

Figure 1. Average non-reference concordance for unfiltered SNPs by superpopulation by non-reference allele frequency in 1KGP3.

[1] Li, J. et. al. (2020). Low-pass sequencing increases the power of GWAS and decreases measurement error of polygenic risk scores compared to genotyping arrays. 10.1101/2020.04.29.068452.

Request for Information or Quotation

Contact your BGI account representative for the most affordable rates in the industry and to discuss how we can meet your specific project requirements or for expert advice on experiment design, from sample to bioinformatics.

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