APPLICATION NOTE

Advancing Human Population Genomics with Twist Bioscience and Gencove

A Scalable Solution for High-Throughput Genotyping

INTRODUCTION

Population genomics studies are uniquely suited to identifying rare and polygenic patterns in the human genome, shining valuable light on both the genetic drivers of disease and our complex evolutionary history. Such studies have traditionally relied on data collected using either microarrays or low-pass whole genome sequencing (lpWGS). Though valuable, the genetic content of these assays may not be easily customized and can result in poor coverage over key variants (thereby affecting assay sensitivity). As a result, the breadth of insights gained from population genomics studies is severely limited by these tools.

APPLICATION SPOTLIGHT

- Conversion to NGS has advantages over arrays for data completeness and scalability
- NGS enables easy customization of content
- Novel library preparation overcomes barriers to cost per sample and throughput
- Gencove imputation pipeline provides high-confidence SNP variant calling

To address this, Twist Bioscience has developed a comprehensive suite of population genomics tools that enable exceptional assay flexibility, performance, and economy at scale.

TRADITIONAL POPULATION GENOMICS TOOLS

Microarrays have played an invaluable role in the rise of population genomics. By providing narrow and fixed coverage over specific genetic loci, microarrays have enabled researchers to interrogate genomes without breaking the bank. However, the shrinking cost of next-generation sequencing (NGS) and an increasing demand for more data has highlighted limitations to microarray technology: it is inflexible, difficult to customize, and it fails to detect unique and novel variant types.

While lpWGS offers a low-cost and broad survey of genomic variants, the amount of data that is often needed to make sensitive variant calls can still be cost prohibitive for ultra-high throughput population genomics studies. Therefore, researchers often compromise by reducing assay coverage at the cost of sensitivity.

In short, current tools force researchers to compromise between breadth of coverage, depth of coverage, and cost—generating a need among researchers for more genotyping solutions that can scale without sacrificing data breadth or quality.

For Research Use Only. Not for use in diagnostic procedures.

MODERNIZING THE POPGEN TOOLKIT

Twist Bioscience's comprehensive suite of products is designed to meet these needs by enabling efficient and informative workflows. This is done through two key technologies:

Twist FlexPrep™ UHT Library Preparation Kit
Regardless of the researcher's sequencing approach, library preparation is a common bottleneck, specifically the process of sample normalization. Twist Bioscience has developed a proprietary Normalization By Ligation™ (NBL) technology, found in the FlexPrep UHT Library Preparation Kit, which eliminates the need for sample-by-sample normalization during library preparation. Additionally, Twist's FlexPrep UHT Library Preparation Kit includes inline barcodes which enable samples to be pooled immediately post-ligation, reducing reagent needs and saving considerable time when used in large-scale applications. Such savings are critical to make ultra-high throughput sequencing feasible.

Twist Catalog and Custom Genotyping Panels
For many genomics applications, such as running genome-wide association studies (GWAS), it isn't necessary to have high coverage sequencing data of every base in the genome. One strategy for reducing the amount of sequencing coverage needed is sequencing only the DNA captured with custom hybridization probes targeting specific loci. Twist target enrichment panels enable you to capture the DNA regions that contain the information you need. Tailoring sequencing depth like this allows researchers to reduce sequencing coverage (and costs) while still enabling accurate and sensitive variant calling.

Twist Bioscience has developed a genotyping panel design pipeline using a novel and proprietary design algorithm that optimizes capture efficiency according to target binding thermodynamics.

The Twist Genotyping Panel–Human 600k has been optimized to enrich over 600,000 genetic variants (covering commonly used variants in genotyping assays for population screening studies). Twist Bioscience also offers custom target enrichment panels and design support to enable the capture of your primary target loci.

Together, Twist Bioscience's FlexPrep UHT Library Preparation Kit and updated target enrichment panel pipeline enables far more efficient population genomics studies by streamlining sample preparation and reducing sequencing costs. This solution is powerful on its own, but it becomes even more so when combined with Gencove's data analysis and imputation software.

REVOLUTIONIZING DATA ANALYTICS WITH GENCOVE

Gencove's software analytics platform enables researchers to impute and analyze genotyping data with high accuracy. When imputation is paired with target enrichment data, total sequencing coverage can be reduced to as low as 1 Gb of sequencing while still enabling high-quality variant calling. By leveraging Gencove's software, researchers can reduce sequencing costs without compromising data quality, as shown in Figure 1a and 1b.

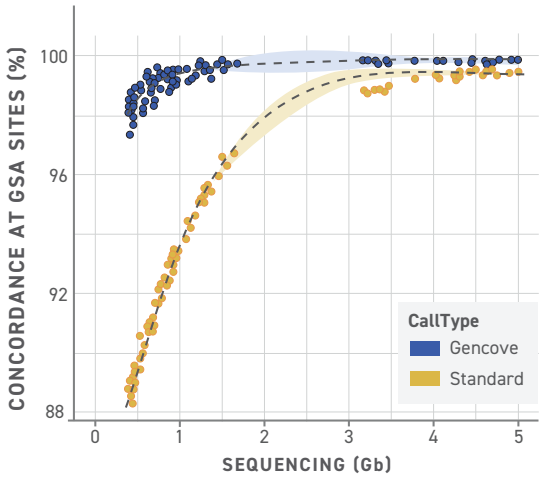

Figure 1a. Twist Genotyping Panel - Human 600k achieves high concordance with deep WGS data. At 1 Gb, the hybrid capture approach achieved 99.46% (IQR: 99.18-99.74%) concordance to deep whole genome sequencing data. Standard variant calling yielded a concordance of 93.56% (IQR: 93.32-93.80%).

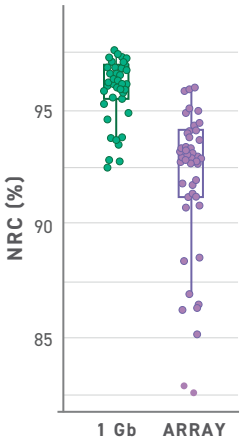

Figure 1b. Twist Genotyping Panel - Human 600k achieves high concordance with array data. Genome-wide non-reference concordance (NRC) obtained after imputing all data (sequencing or array) to the Gencove v6.1 imputation reference panel.

Get in touch with us to explore the future of population genomics.

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ORDERING INFORMATION

Twist Genotyping Panel - Human 600k
110522: Twist Genotyping Panel - Human 600k, 2 Reactions
110523: Twist Genotyping Panel - Human 600k, 12 Reactions
110619: Twist Genotyping Panel - Human 600k, 96 Reactions

FlexPrep UHT Library Preparation Kit
109220: Twist FlexPrep UHT Library Preparation Kit, 192 Samples
109223: Twist FlexPrep UHT LP and Hybridization Kit, 192 Samples
109224: Twist FlexPrep UHT Library Preparation Kit, 1152 Samples
109226: Twist FlexPrep UHT LP and Hybridization Kit, 1152 Samples

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