TruPath™ Genome

Infer inheritance with long-range phasing

TruPath Genome enables variant phasing to deliver long-range haplotypes, compound-heterozygous clarity, and more accurate variant calls for critical inheritance context within rare disease and hereditary disorder research.

Phasing

TruPath Genome delivers long-range phasing from standard short-read WGS by preserving the original DNA template structure, enabling proximity-linked reads and long haplotypes from a single sample. By revealing whether variants occur on the same chromosome or on opposite chromosomes, phasing provides essential inheritance context, including:

- Clear distinction of in-*cis* vs. in-*trans* variant relationships
- Confident resolution of compound heterozygosity without parental sequencing or long-read assays
- More accurate interpretation across key genomics applications, including hereditary disease research, rare disease analysis, carrier screening, structural variant analysis, and population genomics

Infer inheritance in singleton and trio-based analyses

Clear resolution of compound heterozygosity

Standard NGS without phasing leaves variant relationships unresolved, often requiring parental samples or long-read assays for confirmation. TruPath Genome resolves these relationships by clarifying inheritance patterns and compound heterozygosity, enabling confident interpretation from singleton samples as well as traditional trio studies (see Figure 1).

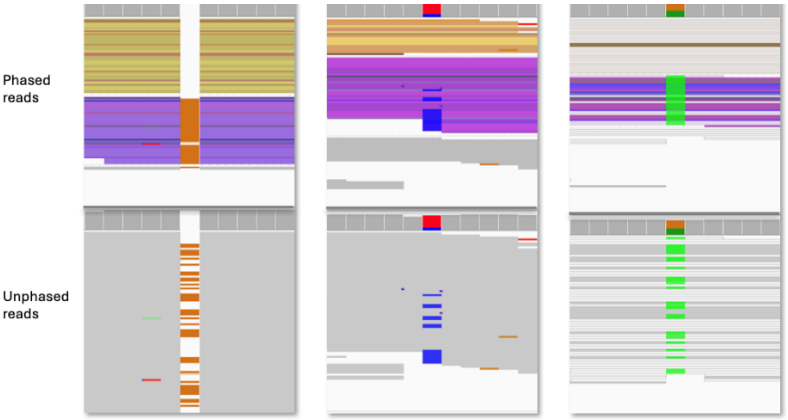
This enables:

- Clear determination of compound heterozygous status
- Confident inheritance interpretation from singleton or trio analyses
- Reduced reliance on parental sequencing or long-read methods

Infer inheritance in singleton and trio-based analyses, delivering definitive clarity for compound heterozygosity

TruPath Genome phases 98% of high-molecular-weight (HMW) DNA and is the only technology that phases small-molecular-weight DNA

Higher variant calling accuracy through early, probabilistic phasing of reads



Phased & unphased TP

Unphased FP (0/1)

Phased TP (0|1), unphased FP (1/1)

Figure 1: Phased genotyping

Phased pile-ups organize sequencing reads by haplotype, preserving variant relationships that are unresolved in unphased data. In the first example, phased and unphased genotyping yield a concordant call while retaining haplotype context; in the second, conflicting spurious alleles are resolved using phased evidence; and in the third, haplotype-consistent low-confidence alleles enable a heterozygous call that is ambiguous in the unphased pile-up, illustrating how phasing supports confident inheritance and compound heterozygosity interpretation.

High phasing completeness and long-range continuity

TruPath Genome fully phases 98.4% of genes with high-molecular-weight DNA and delivers long, contiguous phase blocks that enable gene-length haplotypes across large genomic regions (see Figure 2). This combination of high phasing completeness and extended continuity preserves inheritance context over long genomic distances, strengthening variant interpretation in rare disease, hereditary conditions, and complex genomic regions—without requiring specialized extraction methods.

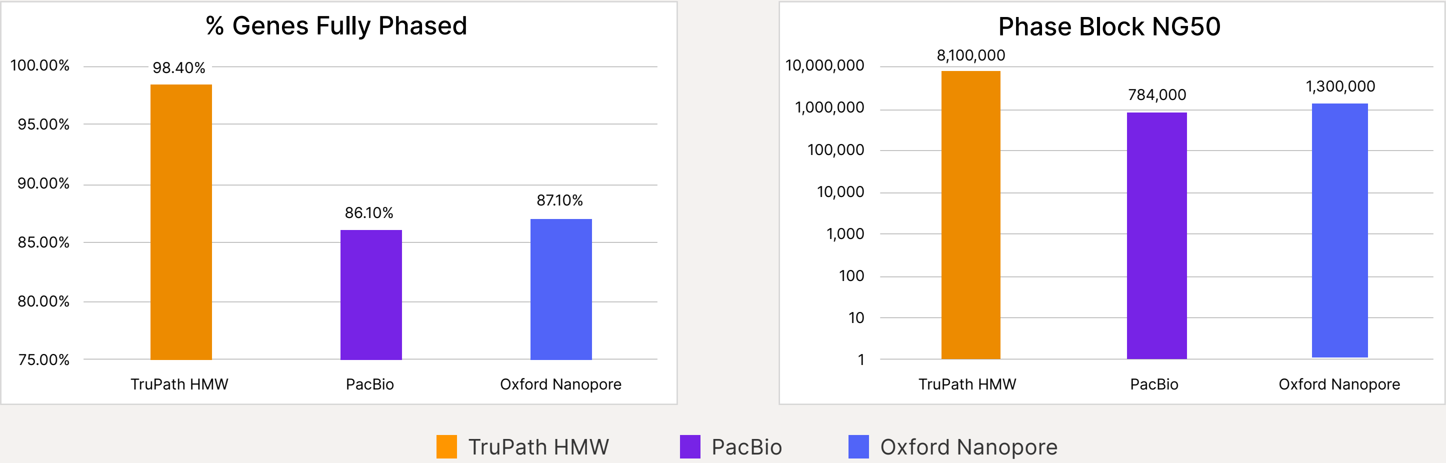


Figure 2: TruPath Genome phasing outperforms long reads

Gene-level phasing completeness (left) and phase block continuity measured by NG50 (right) are shown for TruPath Genome compared with long-read technologies, demonstrating stronger phasing performance across both metrics.

Higher variant calling accuracy through early phasing

TruPath Genome improves variant calling accuracy by assigning reads to maternal and paternal haplotypes before variants are called, rather than attempting to phase results after the fact. This early phasing approach suppresses spurious reads, reduces false positives, and delivers high-confidence, pre-phased variant calls from short-read WGS.

With <1% error rates and >98% of genes fully phased, TruPath Genome sets a new standard for accurate phased variant calling without the need for long-read sequencing.

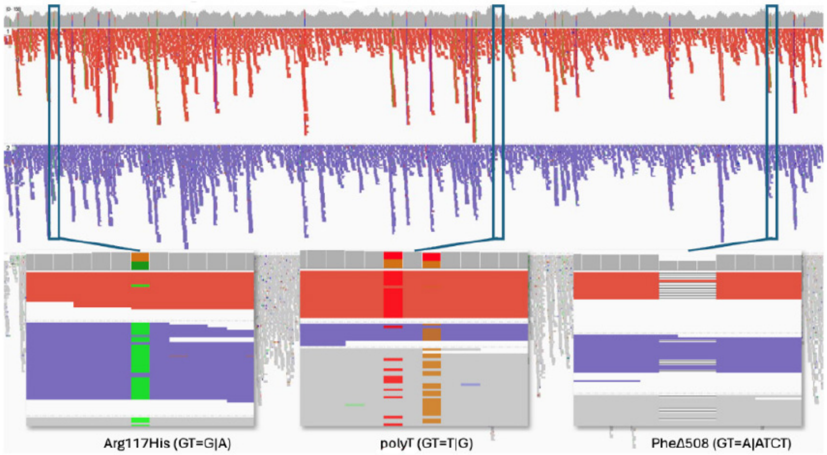


Figure 3: Long-range variant phasing using proximity-based read links

Using TruPath Genome, three variants on chromosome 7 relevant to cystic fibrosis genetics are phased into a single phase set. Despite being separated by tens of kilobases, proximity-mapped reads enable these variants to be confidently linked to the same haplotype, preserving haplotype assignment across large genomic gaps that are typically unresolved by standard short-read approaches.

Learn more about TruPath Genome

FAQs, product documentation, and ready-to-order bundled solutions

- **Visit** illumina.com/trupath
- **Contact** your Illumina representative for evaluation options
- **Learn** more about mapped read technology and NovaSeq™ X systems

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