Oxford Nanopore Technologies

Pharmacogenomic Oxford Nanopore sequencing of the Twist Alliance Long-Read PGx Panel

Comprehensive characterisation of pharmacogenomic (PGx) targets with Oxford Nanopore sequencing

Conventional microarray and short-read sequencing technologies limit the resolution of PGx variants to a small subset, sacrificing allele coverage and performance to deliver a cost-effective solution.

Oxford Nanopore reads of unrestricted length — from short to ultra long — overcome these limitations, providing the ability to disambiguate pseudogene homology, detect and characterise complex structural variants (SVs) and gene-pseudogene conversions, and phase haplotypes.

Utilising Twist Bioscience hybridisation capture with the Twist Alliance Long-Read PGx Panel, Oxford Nanopore delivers a practical, single-assay research workflow for PGx sequencing without compromise.

The Oxford Nanopore and Twist Bioscience PGx workflow delivers:

- High-confidence, unambiguous allele and variant calling for all alleles in all Clinical Pharmacogenetics Implementation Consortium (CPIC) genes
- Phased haplotypes, even for hybrid alleles and complex copy numbers
- A complete, sample-to-star-allele workflow
- Full resolution of *CYP2D6* from a single assay
- Flexible sequencing options to suit every lab, from small-batch to high-throughput solutions

Unambiguous calling and phasing of PGx variants

PGx with short-read sequencing technology	PGx with the Oxford Nanopore and Twist Bioscience workflow
High sequence homology between the gene *CYP2D6* and its pseudogene, *CYP2D7*, results in ambiguous alignments and low-confidence allele calling.	Oxford Nanopore reads of unrestricted length easily distinguish *CYP2D6* from *CYP2D7*, delivering unambiguous, high-confidence alignments.
The high density of variants in PGx genes often results in ambiguous allele calling, precluding the confident assignment of variants to maternal and paternal chromosomes.	Long Oxford Nanopore reads enable unambiguous haplotyping of all the variants in a gene.
The proximity and homology of *CYP2D6* and *CYP2D7* can cause conversion events, producing hybrid genes that are challenging to distinguish from the gene and pseudogene with high confidence.	The entire *CYP2D6* gene, *CYP2D7* pseudogene, and any hybrids are sequenced with long nanopore reads and can be easily and unambiguously aligned with high confidence.
Full-gene deletions and duplications are common in PGx genes, especially *CYP2D6*. Resolution of these SVs is limited with short reads.	Unambiguous allele calling, delivered by long nanopore reads combined with consensus sequencing reads for each allele, allows for high-confidence detection of copy gains and losses.

Coverage of all CPIC genes

The Oxford Nanopore workflow with Twist Bioscience covers mitochondrial DNA (mtDNA) and 49 PGx genes, comprising 39 entire gene sequences and 10 genes covering key PGx variants.

ABCB1	*ABCG2*	*ADD1*	*ADRA2A*	*ANKK1*	*APOL1*	*BCHE*	*CACNA1S*
CFTR	*COMT*	*CTBP2*	*CYP1A2*	*CYP2B6*	*CYP2C8*	*CYP2C9*	*CYP2C19*
CYP2D6	*CYP3A4*	*CYP3A5*	*CYP4F2*	*DPYD*	*DRD2*	*F2*	*F5*
GBA	*GRIK4*	*G6PD*	*HLA-A*	*HLA-B*	*HLA-DRB1*	*HLA-DQA1*	*HTR2C*
IFNL3	*MTHFR*	*NAGS*	*NAT2*	*NUDT15*	*OPRD1*	*OPRK1*	*OPRM1*
POLG	*RYR1*	*SLC6A4*	*SLCO1B1*	*TPMT*	*UGT1A1*	*UGT2B15*	*VKORC1*
YEATS4	*MT-RNR1*						

Full-length gene targeted

Hot spots targeted

Flexible, sample-to-star-allele workflow

Prepare: following extraction of DNA from human blood or saliva research samples, genes of interest are enriched using the Twist Alliance Long-Read PGx Panel, then sequencing libraries are prepared with the Oxford Nanopore Ligation Sequencing Kit.

Sequence: up to eight samples can be sequenced per MinION™ Flow Cell on a MinION or GridION™ device for on-demand sequencing of smaller batches. For high-throughput needs, up to 48 samples can be sequenced per PromethION™ Flow Cell on a PromethION 2 Solo, PromethION 2 Integrated, or PromethION 24 device.

Analyse: after live basecalling, the dedicated EPI2ME™ data analysis workflow, wf-pgx, performs alignment, variant calling, and star allele calling — without requiring prior bioinformatics experience.

Find out more about pharmacogenomics with Oxford Nanopore:
nanoporetech.com/pgx

Oxford Nanopore Technologies

T W I S T BIOSCIENCE twistbioscience.com

oxford-nanopore-technologies
@nanopore
@nanoporetech.com
www.nanoporetech.com

FL_1258(EN)_V3_02Apr2025