OeXome® Whole Exome Sequencing (WES)

Deep dive for exome analysis

Exons comprise approximately 1% of the genome (~30 Mb) [1], yet they harbor 85% of known pathogenic variants [2]. Therefore, whole exome sequencing (WES) is often used to investigate complex conditions suspected to have a genetic basis, where sequencing a small portion of the genome is likely to yield meaningful findings.

OeXome WES provides a highly accurate and in-depth solution for physicians and researchers to investigate genetic factors that may be relevant to a patient's phenotype, fetal abnormalities, or provide additional insights. With our self-developed experimental and bioinformatics pipeline, combined with the expertise of our team, we deliver high-quality, reliable results to support your work with confidence.

Test information

Technology and Platform
Illumina NGS system, paired-end
Data and Coverage
Standard Data Volume ~8-10 Gb*
≥97.5% coverage of target regions at a depth of ≥20x
Test Design
Proband, Duo or Trio analysis
Reanalysis
Turnaround Time
Prenatal OeXome: 15 working days
General OeXome: 23 working days

*Can be customized under special request.
Note: TAT starts from the date of sample arrival at the testing laboratory

Comprehensive coverage

NanoWES, our patented DNA capture probe, is designed to target protein-coding regions (~25,000 genes), regulatory elements and intronic regions with defined pathogenicity, the mitochondrial genome, and other relevant genomic regions.

Reporting variants:

- Single nucleotide variants (SNVs)
- Insertions and deletions (InDels) < 50 bp
- Aneuploidy
- Mitochondrial SNVs > 1% heteroplasmy
- Exon CNVs (WES-CNVs) ≥ 3 exons
- UPD in clinically relevant chromosomal regions
- Dynamic mutations (trinucleotide repeats) of clinically relevant genes

Superior sequencing quality powered by patented technology

NanoWES-based workflow eliminates the PCR step before capturing, reducing amplification biases, errors, and duplication rates.

- Delivers highly uniform coverage across target regions for accurate variant detection
- Particularly well-suited for high-resolution pathogenic exonic-CNVs detection, offering a distinct advantage over low-coverage whole-genome sequencing with its high sequencing depth

Additional services and supports

Bundled Services for Enhanced Insights:

- **Xromate CNV-seq**: Precise detection of aneuploidy, and genomic CNVs >100 kb with mosaicism using whole-genome NGS
- **Sanger Sequencing & Molecular Assays** (such as MLPA and PCR): Reliable variant confirmation
- **LRS Test**: Powered by PacBio HiFi technology for detecting difficult-to-map regions (e.g. structural variants, homologous sequences) beyond the technical limitations of NGS

Long-Term Support:

- Free reanalysis within 3 years
- Raw data (BAM, VCF, FASTQ, LEVEL) provided at no extra charge
- Opt-in reporting for additional findings (Please refer to the table on the next page)

OeXome Leads in Quality: Proficiency Testing

To systematically assess the comparability of clinical WES testing results under routine conditions, the National Center for Clinical Laboratories (NCCL) conducted a proficiency test across 24 participating laboratories [3]. Two of Berry Genomics' laboratories (BerryExon, lab 9 and 10) outperformed other commercial laboratories in terms of breadth of coverage, coverage uniformity, and bioinformatic reproducibility.

- The top performer in uniformity of coverage and coverage at depth ≥ 20x over the years
- Covering the listed ACMG genes with >95% coverage at depth ≥ 20x
- High bioinformatic reproductivity on small variant detection compared with the NCCL pipeline

Enhance Diagnosis with OeXome Exon-CNVs Analysis

In a retrospective analysis on 75 children with neurodevelopmental disorders, OeXome demonstrated an overall diagnostic yield of 54.05% (40/74) when combining SNVs/InDels and CNVs analysis. Specifically, 35.13% (26/74) of diagnoses were from SNVs/InDels analysis, and 18.92% (14/74) were from exon CNVs (WES-CNVs) analysis. [4]

Reporting

Session	Description
Main Findings	Pathogenic (P) or Likely Pathogenic (LP) variants with the expected inheritance pattern, including incomplete penetrance
	Compound heterozygote where one variant is rated as P or LP while the other is rated as Variant of Uncertain Significance (VUS)
	Heterozygous P or LP variants potentially forming compound heterozygotes with WES-CNVs
	X-linked recessive (XLR) or X-linked dominant (XLD), P or LP hemizygous/ heterozygous variants
	Phenotypically related and highly pathogenic WES-CNVs, mitochondrial variants, dynamic mutations in the *ATXN1*, *ATXN2*, *ATXN3*, *CACNA1A*, *ATXN7*, *PPP2R2B*, *ATXN8OS/ATXN8*, *ATN1*, *AR*, *DMPK*, *HTT*, *JPH3*, and *PABPN1* genes, or uniparental disomy (UPD) located in critical regions of chromosomes 6, 7, 11, 14, 15, and 20
Potential Relevant Findings	Phenotypically related VUS variants with the expected inheritance pattern (which classification might change if more information provided, incomplete penetrance)
	Phenotypically related, XLR or XLD, VUS hemizygous/ heterozygous single variant
	Phenotypically related, P or LP or VUS variants but does not confirm to family co-segregation
	Phenotypically related, autosomal recessive (AR) variants
	Specific variants or genes of interest by the physicians
	Unexcluded diseases/phenotypes susceptibility, highly suspected P, LP or VUS variants with the expected inheritance pattern
ACMG Secondary Findings	P or LP variants identified from the ACMG Secondary Findings gene list are unrelated to the patient's primary phenotype and do not overlap with the Main Findings or Potentially Relevant Findings

Appendix (Opt-in):

Customized insights beyond the standard WES report are available on request to deliver a more comprehensive analysis.

For example:

- Carrier status
- Partially phenotypically related AR heterozygous single variant
- Partially phenotypically related autosomal dominant (AD) VUS variants, with a significant population carrying that heterozygous variants according gnomAD
- Selected top causative variants

References:
[1] Ng SB, Turner EH, Robertson PD, et al. Targeted capture and massively parallel sequencing of 12 human exomes. *Nature*. 2009;461(7261):272-276.
[2] Choi M, Scholl UI, Ji W, et al. Genetic diagnosis by whole exome capture and massively parallel DNA sequencing. *Proc Natl Acad Sci U S A*. 2009;106(45):19096-19101.
[3] Zhang K, Yu L, Lin G, Li J. A multi-laboratory assessment of clinical exome sequencing for detection of hereditary disease variants: 4441 ClinVar variants for clinical genomic test development and validation. *Clin Chim Acta*. 2022;535:99-107.
[4] Zhai Y, Zhang Z, Shi P, Martin DM, Kong X. Incorporation of exome-based CNV analysis makes trio-WES a more powerful tool for clinical diagnosis in neurodevelopmental disorders: A retrospective study. *Hum Mutat*. 2021;42(8):990-1004.

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