CENTOGENE
THE RARE DISEASE COMPANY

Whole Exome Sequencing

CentoXome®

Turning Years Into Days

CentoXome®
Whole Exome Sequencing

With more than 7,000 identified rare diseases and approximately 80% being linked to genetic causes, diagnosing rare disease patients can often be difficult – resulting in lengthy, expensive, and emotional diagnostic odysseys.

With Whole Exome Sequencing (WES), you have the genetic testing tool in hand to diagnose your patients in less time with high levels of certainty. CENTOGENE's enhanced WES – CentoXome®, provides highly uniform coverage of the entire exome and mitochondrial genome, and nearly complete coverage of all known disease-causing regions throughout the genome in a single test. The improved test design includes scientific knowledge and unique insights based on the CENTOGENE Biodatabank, the world's largest real-world data repository for rare and neurodegenerative diseases, paired with life-long support from the leader and trusted partner in diagnostics. With CentoXome, we help you provide patients with the answers they need today for a better tomorrow.

The CENTOGENE Advantage

Turn Your Open Questions Into Answers

Superior technology from experts in multiomic testing for rare and neurodegenerative diseases combined with outstanding clinical coverage and unmatched diagnostic power in a single test

Turn Our Expertise Into Your Advantage

Best-in-class insights powered by CENTOGENE's CE-IVD Bioinformatics pipeline and the CENTOGENE Biodatabank

Turn Our Commitment Into Your Promise

Life-long support by a team dedicated to improving the lives of patients with rare diseases

Outstanding Clinical Coverage and Diagnostic Power

The CentoXome design and service delivers ideal quality and performance from the world leader and trusted partner in rare and neurodegenerative disease diagnostics with outstanding clinical coverage and unmatched clinical diagnostic power in a single test. Coupling insights from the CENTOGENE Biodatabank for rare and neurodegenerative diseases with superior omics technology, you benefit from a solution that delivers a higher diagnostic yield compared to standard WES.[1–10]

Key Features and Performance

Broad and Uniform Exome & Mitochondrial Genome Coverage	• Highly uniform coverage of the entire exome (~20,000 genes), +/-10 bp exon-intron boundaries, and complete mitochondrial genome (37 genes) • ≥98 % target regions covered at ≥20 x
Enhanced Coverage of Clinically Relevant Regions	• Enhanced coverage of disease-associated genes (OMIM®, HGMD®, CENTOGENE Biodatabank), with ≥99 % target regions covered at ≥20 x • Coverage of known clinically relevant variants in coding and non-coding regions (HGMD®, ClinVar, CENTOGENE Biodatabank for rare and neurodegenerative diseases)
Advanced and Sensitive Variant Detection	• Detection of SNVs, InDels, SVs, including CNVs of exon-level to cytogenomic-level changes, and mtDNA with heteroplasmy ≥ 15% • Sensitivity: - SNVs and InDels (≤ 50 bp) >99.6 % - CNVs* >95 % • Specificity of > 99.9 % is guaranteed for all reported variants** • UPD detection*** for the well-known clinically relevant chromosomal regions: 6q24, 7, 11p15.5, 14q32, 15q11q13, 20q13, and 20
Technical Details	• Exome capture with custom-designed reagents based on Twist® Human Core Exome, with 18 – 20 Gb of sequencing data generated per patient • Illumina paired-end Next Generation Sequencing (NGS) technology (2 x 150 bp) • Nuclear genome aligned to Genome Reference Consortium Human Build 37 (GRCh37/hg19) • Mitochondrial genome aligned to the revised Cambridge Reference Sequence (rCRS) of the Human Mitochondrial DNA (NC_012920)

SNVs: single nucleotide variants; **InDels:** small insertions/deletions; **CNVs:** copy number variations; **UPD:** uniparental disomy; **mtDNA:** mitochondrial DNA

* CNV detection software sensitivity > 95 %; however, this sensitivity may be decreased for repetitive and homologous regions, such as pseudogenes, as well as for events spanning two or fewer exons.

** Variants with low quality and/or unclear zygosity are confirmed by orthogonal methods: SNVs and InDels by Sanger sequencing; CNVs by Multiplex ligation-dependent probe amplification (MPLA), quantitative polymerase chain reaction (qPCR) or chromosomal microarray (CMA)

*** Screening of UPD is performed using an in-house algorithm for Mendelian Inheritance Errors (MIE) to detect runs of homozygosity (ROH) for the well-known clinically relevant chromosomal regions Guaranteed internal confirmatory testing using CMA when necessary.

Tailored Testing and Life-Long Diagnostic Support

We offer flexible testing options and additional services to provide a CentoXome analysis tailored to your patient's needs, such as WES for ongoing pregnancies with fetal abnormalities for prenatal diagnostics (CentoXome Prenatal) and our multiomic WES solutions (CentoXome MOx 1.0 and 2.0) integrating different data sets to capture the most complete clinical picture. Committed to improving the lives of patients, our CentoXome testing solutions are paired with life-long diagnostic support via a free-of-charge reclassification program, as well as an affordable case-level reanalysis.

Options & Additional Services

Testing Design*		• Solo, Duo, Trio, and PLUS • Mitochondrial genome analysis is performed only for the index patient and maternal samples
Testing Solutions	**CentoXome**	• WES for postnatal diagnostic testing of rare and neurodegenerative diseases • TAT: ≤ 30 business days
	CentoXome MOx**	• Multiomics single-test solutions integrating WES with biochemical testing and/or RNA-seq for splicing variants • CentoXome MOx 1.0 and 2.0 for postnatal testing of rare and neurodegenerative diseases • CentoXome MOx 1.0 TAT: ≤ 30 business days • CentoXome MOx 2.0 TAT: ≤ 35 business days
	CentoXome Prenatal***	• WES for prenatal diagnostics (ongoing pregnancy) when fetus structural abnormalities are detected on ultrasound, or a diagnosis cannot be obtained using routine prenatal methods • Expedited and prioritized testing and includes cell culture and maternal cell contamination (MCC) analysis • TAT: ≤ 15 business days
	CentoXome POC***	• WES for diagnostic testing of product of conception (pregnancy loss) in cases of intrauterine fetal demise or stillbirth to better understand cause of fetal loss and risk for recurrence, or when a diagnosis cannot be obtained using routine methods • Includes cell culture and MCC analysis • TAT: ≤ 30 business days
	CentoXome Variants	• WES raw and processed data (files in FASTQ, BAM and VCF format along with filtered and annotated variant files in XLS format) for further research available • Free of charge for download via CentoPortal for a period of 30 days • TAT: ≤ 20 business days
Additional Options	**FAST Processing**	• ≤ 15 business days (not applicable with CentoXome MOx 2.0)
	Free of Charge Raw Data	• For all testing solutions accompanied by medical reports, both raw and processed data are available as options. These data include files in FASTQ, BAM, and VCF formats, as well as a filtered and annotated variant file in XLS format. • This data can be downloaded via CentoPortal free of charge for a period of 30 days
Life-long diagnostic support****		• Proactive variant-level reclassification; reclassification report issued at no extra cost • Case-level reanalysis for uncertain/negative results (e.g., new clinical information, one-year intervals) at an affordable cost

TAT: Turnaround time

* **Solo**: only affected index patient is tested; **Duo**: index patient and affected or unaffected family member are tested; **Trio**: index patient and two family members, affected or unaffected are tested; **PLUS**: additional family member beyond Trio is tested.

** More details about our Multiomic Solutions at centogene.com/mox

*** WES-based mitochondrial genome analysis and screening for UPD is not offered due to technical limitations. More details about Prenatal Testing: centogene.com/prenatal-testing

**** Case reanalysis is available only for orders with original sequencing data from August 2020 onwards. More details about Variant Reclassification Program: centogene.com/diagnostics/benefits-of-genetic-testing/variant-reclassification-program

Best-in-Class Medical Reporting and Extra Insights

When choosing our WES services, patients, physicians, and partners can feel confident that they will receive high-quality sequencing paired with advanced data analysis and interpretation. By combining deep phenotype and genotype data using our CE-IVD bioinformatics pipeline, CENTOGENE accurately identifies disease-causing variants to deliver best-in-class clinical reporting. A team of highly trained clinical geneticists and scientists interpret the data and cross-check every medical report.

Medical Reports and Extra Expertise Insights

Main Findings	• Diagnostic findings related to patients' phenotype • Optional research findings* related to patient's phenotype providing information on potential diagnoses
Potential Relevant Findings	• Findings not directly related to patients' phenotype that might be clinically relevant to help close diagnostic gaps • List of variants for the index patient related to disorders without an apparent overlap with the described phenotype and/or variants with a zygosity inconsistent with the expected mode of inheritance
Secondary Findings*	• Optional findings unrelated to patients' phenotype • Medically actionable variants based on the American College of Medical Genetics and Genomics (ACMG) guidelines available for all tested individuals
Carriership Findings*	• Optional carriership status findings not related to patients' phenotype but potentially clinically relevant for family planning are provided upon request for both index and non-index individuals, except for fetuses of ongoing pregnancies • A list of sequence variants classified as pathogenic or likely pathogenic in the CENTOGENE Biodatabank for selected genes associated with recessive severe and early-onset Mendelian diseases is reported
Extra Disease Confirmation & Insights	• Internal confirmatory testing by an orthogonal method for reported variants when necessary • Extra insights supported by the CENTOGENE Biodatabank are used to confirm results and provide evidence about the pathogenicity of the variants found

* Please note that for testing index patients in the following cases: 1) prenatal diagnostics (ongoing pregnancy), research, secondary, and carriership findings are not reported; 2) products of conception diagnostics (pregnancy loss), secondary findings are not reported.

For more infromation about our medical reporting, please visit centogene.com/reporting; more details about our carriership findings reported in our WES at centogene.com/carriership

References

1 Cheema et al. 2020, PMID: 33083013
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5 Posey et al. 2019, PMID: 31234920
6 Schon et al. 2020, PMID: 32674947
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10 Wagner et al. 2019, PMID: 31059585

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