

CENTOGENE  
THE RARE DISEASE COMPANY



Centoxome<sup>®</sup>

Turning Years Into Days

PRODUCT SHEET

# CentoXome<sup>®</sup>

## 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<sup>®</sup>, 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 the most up-to-date scientific knowledge and unique insights based on 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.

**Have you heard about our multiomic add-on?** CentoXome MOx – By combining genetic and biochemical testing, we now deliver an even quicker and more accurate diagnosis of rare, metabolic, and neurodegenerative diseases. We are going beyond genetics for a higher diagnostic yield.

### The CENTOGENE Advantage



#### Turn Your Open Questions Into Answers

Superior technology from the experts in omics testing for rare 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 Biodatabank, the world's largest real-world data repository for rare and neurodegenerative diseases



#### 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 the ideal quality and performance from the world leader and trusted partner in rare disease diagnostics with outstanding clinical coverage and unmatched clinical diagnostic power in a single test. Coupling insights from CENTOGENE's Biodatabank for rare and neurodegenerative diseases with superior omics technology, you benefit from a unique approach that increases diagnostic yield by up to 20% compared to standard WES.<sup>1-10</sup>

## Key Features and Performance

### Broad and Uniform Exome & Mitochondrial Genome Coverage

- Mean depth  $\geq 100x$
- Highly uniform coverage of the entire exome (~20,000 genes), +/- 10bp exon-intron boundaries, and complete mitochondrial genome (37 genes); with  $\geq 98\%$  target regions covered at  $\geq 20x$

### Enhanced Coverage of Clinically Relevant Regions

- ~8000 disease-associated genes (OMIM®, HGMD®, the CENTOGENE Biodatabank), with  $\geq 99\%$  target regions covered at  $\geq 20x$
- >99% of all known clinically relevant variants in coding and non-coding regions (HGMD®, ClinVar, CENTOGENE's Biodatabank for rare and neurodegenerative diseases)

### Variant Types

- Highly sensitive and specific detection of SNVs, InDels, and CNVs to cytogenomic-level changes, UPD\*, and mtDNA with heteroplasmy  $\geq 15\%$
- Sensitivity
  - SNVs and InDels ( $\leq 55bp$ ) >99.6%
  - CNVs\*\* >95%
- Specificity of >99.9% is guaranteed for all reported variants\*\*\*

### Technical Details

- Illumina paired-end next-generation sequencing (NGS) technology (2x150bp)
- Exome capture with custom-designed reagents based on Twist® Human Core Exome, with 18–20Gb of sequencing data generated per patient
- Nuclear genome aligned to GRCh37/hg19 Human genome assembly
- 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

\* UPD screening is performed using an in-house specific algorithm for the following well-known clinically relevant chromosomal regions: 6q24, 7, 11p15.5, 14q32, 15q11q13, 20q13 and 20

\*\* CNV detection software has a sensitivity >95% for all homozygous/hemizygous and mitochondrial deletions, as well as heterozygous deletions/duplications and homozygous/hemizygous duplications spanning at least three consecutive exons

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

# 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 a multiomic WES solution, CentoXome MOx, that integrates deep exomic and biochemical insights in a single test, enabling early diagnosis, better prognosis, and optimized treatments for rare and metabolic diseases. Committed to improving the lives of patients, our CentoXome testing solutions are paired with life-long diagnostic support via a free-of-charge and proactive reclassification program, as well as an affordable case-level reanalysis.

## Options & Additional Services

<b>Turnaround Time</b>	<ul style="list-style-type: none"><li>• Regular: <math>\leq 30</math> business days</li><li>• FAST: <math>\leq 15</math> business days</li></ul>
<b>Testing Design*</b>	Solo, Duo, Trio, and Trio PLUS
<b>Raw Data</b>	Raw data available free-of-charge for download (FASTQ, BAM, VCF files) along with filtered and annotated variant table (XLS file) for further research
<b>Genome-Wide Analysis of Structural Variants</b>	CentoArray (chromosomal microarray analysis, CMA)
<b>Life-Long Reclassification And Re-Analysis</b>	<ul style="list-style-type: none"><li>• Proactive variant-level re-evaluation and reclassification at no extra cost**</li><li>• Case-level reanalysis and medical reinterpretation at an affordable cost in case of uncertain or negative results (i.e., new clinical information, one-year intervals)</li></ul>
<b>CentoXome Prenatal***</b>	<ul style="list-style-type: none"><li>• Expedited and prioritized testing (<math>\leq 15</math> business days) specifically designed for ongoing pregnancies</li><li>• Includes cell culture and maternal contamination testing</li></ul>
<b>CentoXome MOx</b>	<ul style="list-style-type: none"><li>• Integrates WES with biochemical testing for inherited metabolic disorders (IMDs) and hereditary angioedema (HAE), including proprietary biomarkers, in a single solution</li><li>• Biochemical testing allows for orthogonal confirmation of disease accelerating the diagnosis path by avoiding stepwise testing</li><li>• Indicated for patients with complex and overlapping symptoms, varying age of onset and severity, or symptoms suggestive of IMDs or HAE (e.g., babies and children critically ill that need a fast diagnosis, babies with abnormal newborn screening results, patients with symptoms related to neurological conditions of unknown etiology)</li></ul>

We are ready to go beyond genetics, to go beyond diagnostics. Learn now more about our Multiomic Solutions: [centogene.com/mox](https://centogene.com/mox)

\* **Solo**: only the 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. Mitochondrial genome analysis is performed only for the index patient and maternal samples

\*\* More details about Variant Reclassification Program ([link.centogene.com/variant-reclassification](https://link.centogene.com/variant-reclassification))  
\*\*\* We do not offer WES-based CNV and mitochondrial genome analysis with CentoXome Prenatal due to technical limitation. More details about Prenatal Testing ([link.centogene.com/prenatal-testing](https://link.centogene.com/prenatal-testing))

# 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 combined with best data analysis and interpretation, documented in comprehensive medical reports. By combining deep phenotype data with genotype data using our advanced bioinformatic pipeline and artificial intelligence, CENTOGENE accurately identifies and prioritizes disease-causing variants to deliver best-in-class clinical interpretation and reporting. A team of highly trained clinical geneticists and scientists interpret the data and cross-check every medical report. We perform additional testing using CENTOGENE's Biodatabank to confirm results and validate variant pathogenicity.

## Medical Reports and Extra Expertise Insights

### Main Findings

- Diagnostic findings related to patients' phenotype
- Research findings related to patients' phenotype providing information on potential diagnoses in cases where no definitive diagnosis can be found

### 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

### Potential Relevant Findings

- Findings unrelated 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

### Carriership Findings

- Optional carriership status findings not related to patients' phenotype that are potentially clinically relevant for family planning
- List of sequence variants for the index patient classified as pathogenic/likely pathogenic in CENTOGENE's Biodatabank for selected genes associated with recessive severe and early-onset Mendelian diseases

### Extra Insights

Extra insights supported by the CENTOGENE Biodatabank, which contains curated unique variants and omics data from a wide range of ethnicities from more than 120 countries, are used to confirm results and validate pathogenicity of the variants found.

More details about Medical Reporting ([link.centogene.com/reporting](http://link.centogene.com/reporting)) and Carriership findings reported in WGS and WES ([link.centogene.com/tabularlist](http://link.centogene.com/tabularlist)). Please note that for prenatal diagnostics research, secondary and additional carriership are not reported.

#### References

1 Cheema et al. 2020, PMID: 33083013  
2 Clark et al. 2018, PMID: 30002876

3 Data on file at CENTOGENE  
4 Gross et al. 2018, PMID: 30293986

5 Posey et al. 2019, PMID: 31234920  
6 Schon et al. 2020, PMID: 32674947

7 Scuffins et al. 2021, PMID: 33495530  
8 Stark et al. 2016, PMID: 26938784

9 Trujillano et al. 2017, PMID: 27848944  
10 Wagner et al. 2019, PMID: 31059585

FOR ORDERING

**[www.centoportal.com](http://www.centoportal.com)**

FOR MORE INFORMATION

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