CENTOGENE
THE RARE DISEASE COMPANY

CentoGenome®

See Diagnostics In a New Way

PRODUCT SHEET

CentoGenome®
Whole Genome 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 Genome Sequencing (WGS), you have the most comprehensive genetic tool to diagnose your patients with the highest level of certainty. CENTOGENE's WGS service – CentoGenome®, provides an unparalleled coverage of the human genome, including the coding, non-coding regions, and the mitochondrial genome, and detects nearly all types of genetic variants in a single test.This comprehensive service gives not only a more complete picture, but also offers flexible testing options tailored to your patient's needs, paired with life-long support from the leader and trusted partner in diagnostics. With CentoGenome, we help you provide patients with the answers they need today for a better tomorrow.

Have you heard about our newest multiomic add-on? CentoGenome 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

Your Questions Answered
Unparalleled genome coverage and diagnostic power in a single test, providing fast track to diagnosis and optimized therapies

Our Expertise
Best-in-class insights powered by CENTOGENE's Biodatabank, the world's largest real-world data repository for rare and neurodegenerative diseases

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

Unparalleled Genome Coverage and Diagnostic Power

CentoGenome offers unparalleled genome coverage and captures one of the most extensive range of genetic variants in a single test. CentoGenome is a highly effective diagnostic tool — delivering high diagnostic yields across a variety of rare genetic conditions.[1,2] CentoGenome is especially valuable in patients for whom previous WES produced negative results, with our latest studies showing its ability to solve up to 30% of WES negative cases.[1] For more information, please see the table below and consult the CentoGenome Webpage.

Key Features and Performance

UNIFORM NUCLEAR AND MITOCHONDRIAL GENOME COVERAGE

- Mean depth >30x
- Highly uniform coverage of the entire nuclear genome (>20,000 genes), including both protein-coding and non-coding regions, and full mitochondrial genome (37 genes), with >97% of the genome covered at ≥10x

ADVANCED DETECTION OF NEARLY ALL TYPES OF VARIANTS IN ONE SINGLE TEST

- Highly sensitive and specific detection of SNVs, InDels, CNVs of exon-level to cytogenomic-level changes, complex SVs, and mtDNA with heteroplasmy ≥15%
- Sensitivity

SNVs and InDels (≤55bp)	>99.7%
SVs/CNVs	>98.0%

- Specificity of >99.9% is guaranteed for all reported variants*

TECHNICAL DETAILS

- Illumina paired-end next-generation sequencing (NGS) technology (2x 150bp)
- Genome is enzymatically fragmented, and libraries are generated using Illumina Nextera DNA Flex kit, with 100 – 110 Gb of sequencing data generated for each patient
- Nuclear genome aligned to GRCh37/hg19 Human genome assembly
- Mitochondrial genome aligned to revised Cambridge Reference Sequence (rCRS) of the Human Mitochondrial DNA (NC_012920)

Single nucleotide variants; InDels: small insertions/deletions; CNVs: copy number variations; SVs: structural variants (includes CNVs); mtDNA: mitochondrial DNA

* 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 CentoGenome analysis tailored to your patient's needs, such as WGS for ongoing pregnancies with fetal abnormalities for prenatal diagnostics, CentoGenome Prenatal, and a multiomic WGS solution, CentoGenome MOx, that integrates deep genomic 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 CentoGenome 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 and Additional Services

TURNAROUND TIME	• Regular: ≤20 business days • FAST: ≤15 business days
TESTING DESIGN*	Solo, Duo, Trio and Trio PLUS
GENOME WIDE ANALYSIS OF STRUCTURAL VARIANTS	CentoArray® (chromosomal microarray analysis, CMA)
RAW DATA	Raw data available free of charge for download (FASTQ, BAM, VCF files) along with filtered and annotated variant table (XLS) for further research
LIFE-LONG RECLASSIFICATION AND RE-ANALYSIS	• Proactive variant-level re-evaluation and reclassification at no extra cost** • 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)
CENTOGENOME PRENATAL* **	• Expedited and prioritized testing (≤15 business days) specifically designed for ongoing pregnancies • Includes cell culture and maternal contamination testingprenatal sample
CENTOGENOME MOX	• Integrates WGS with biochemical testing for inherited metabolic disorders (IMDs) and hereditary angioedema (HAE), including proprietary biomarkers, in a single solution • Biochemical testing allows for orthogonal confirmation of disease accelerating the diagnosis path by avoiding stepwise testing • 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)

We are ready to go beyond genetics, to go beyond diagnostics. Learn now more about our Multiomic Solutions: 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

*** We do not offer WGS-based CNV and mitochondrial genome analysis with CentoGenome Prenatal due to technical limitation. More details about Prenatal Testing

Best-in-Class Medical Reporting and Extra Insights

When choosing our WGS, physicians, patients, 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 Biodatabank to confirm results and validate variant pathogenicity.

Medical Reports and Extra Expertise Insights

MAIN FINDINGS	• Diagnostic findings related to patient's phenotype • Research findings related to patient's phenotype providing information on potential diagnoses in cases where no definitive diagnosis can be found
POTENTIALLY 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
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 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 CENTOGENE's 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 at CENTOGENE and Carriership Findings reported in our WGS and WES.
Please note that for prenatal diagnostics research, secondary and additional findings are not reported.

References:
[1] Bertoli-Avella et al. 2020, PMID: 32860008
[2] Cheema et al. 2020, PMID: 33083013