CENTOGENE
THE RARE DISEASE COMPANY

NEW
CentoGenome®
Whole Genome Sequencing

PRODUCT SHEET

NEW CentoGenome® – Whole Genome Sequencing

Establishing a rapid and reliable diagnosis for rare and neurodegenerative diseases can be difficult, even for the most skilled physicians. Thanks to the latest technologies and scientific insights into genetic factors, this no longer has to be the case! Introducing the world's most comprehensive Whole Genome Sequencing (WGS) tool for diagnosis of rare and neurodegenerative diseases – NEW CentoGenome®.

This first-line test combines superior technology powered by a streamlined CE-IVD bioinformatics pipeline and the CENTOGENE Biodatabank, with approximately 700,000 patients from over 120 highly diverse countries.

With NEW CentoGenome, you can significantly reduce time and resources to deliver a rapid and reliable diagnosis and identification of treatment options for your patients.

The NEW CentoGenome Advantage

Advanced Technology for Greater Insights

By implementing Polymerase Chain Reaction (PCR)-free technology, NEW CentoGenome significantly reduces bias and provides high-quality sequence information for difficult-to-sequence genetic regions – enabling greater insights into coding, regulatory, and intronic regions

Superior Performance for Enhanced Disease Coverage

In leveraging advanced data analysis with CE-IVD bioinformatics and medical expert-based interpretation powered by the CENTOGENE Biodatabank, NEW CentoGenome delivers superior variant detection

Integrated Variant Reclassification and Confirmatory Testing for a Life-Long Commitment

As a world leader and trusted partner, CENTOGENE provides a free-of-charge and proactive diagnosis confirmation and variant reclassification program

Unparalleled Genome Coverage and Diagnostic Power

NEW CentoGenome is your first-line diagnostic tool — delivering a high diagnostic yield for genetically linked diseases.[1-3]

Genome Coverage	• Average depth coverage ≥ 30 x • Highly uniform and nearly complete coverage of the nuclear genome (>20,000 genes), and complete mitochondrial genome (37 genes), with >97% of the genome covered at ≥10x
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) 99.9% 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 • Repeat expansion detection ** in 23 well-known genes associates with neurological diseases: *AR, ATN1, ATXN1, ATXN2, ATXN3, ATXN7, ATXN8OS, ATXN10, CACNA1A, CNBP, CSTB, C9ORF72, DMPK, FMR1, FXN, HTT, JPH3, NOP56, PABPN1, PHOX2B, PPP2R2B, PRNP,* and *TBP*
Enhanced Detection of Variants Associated to SMA & GD/ PD * **	• Spinal Muscular Distrophy (SMA): *SMN1/SMN2* CNV analysis • Gaucher Disease (GD)/Parkinson's Disease (PD): *GBA1* including conversion analysis with its pseudogene *GBAP1*
Extra Diagnostic Confirmation**	• Guaranteed internal confirmatory testing using an orthogonal method for all reported variation associated with repeat expansion diseases, UPD, SMA, and GD/PD • CENTOGENE's fully automated CE-IVD bioinformatics software covers all known disease-causing variants published in public databases (HGMD®, ClinVar, Mastermind) and the CENTOGENE Biodatabank
Technical Details	• Illumina paired-end next-generation sequencing (NGS) technology (2x150 bp) • Genome is enzymatically fragmented and libraries are generated using Illumina DNA PCR-Free Library Prep kit, with 100 – 110 Gb of sequencing data generated for each patient • Nuclear genome aligned to Genome Reference Consortium Human Build 37 (GRCh37/hg19) • Mitochondrial genome aligned to revised Cambridge Reference Sequence (rCRS) of the Human Mitochondrial DNA (NC_012920)

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

* 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 repeat expansions is performed by the ExpansionHunter. 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

*** Spinal muscular atrophy (SMA) screening is performed using SMN Caller algorithm to detect *SMN1/SMN2* CNVs. *GBA1* screening is performed using Gauchian algorithm to detect recombination events affecting the region encompassing exons 9-11 (NM_000157.3), a region which has the highest homology to *GBAP1*

****Internal confirmatory testing are obtained by orthogonal methods: fragment length analysis (FLA) for repeat expansions, CMA for UPD, MLPA for *SMN1/SMN2* CNVs, and qPCR for conversion events between *GBA1* and *GBAP1*.

Tailored Testing and Life-Long Diagnostic Support

We offer flexible testing options and additional services tailored to your patient's needs, paired with life-long diagnostic support via a free-of-charge and proactive reclassification program.

Turnaround Time	• Regular: ≤ 20 business days • FAST: ≤ 15 business days
Testing Design*	Solo, Duo, Trio, and Trio PLUS
Genome Wide Analysis of SVs / Large CNVs	CentoArray (chromosomal microarray analysis, CMA)
Raw Data	Raw and processed data (files in FASTQ, BAM and VCF format along with filtered and annotated variant file(s) in XLS format) for further research available, free of charge for download via CentoPortal for a period of 30 days
Life-Long Diagnostic Support**	• Proactive variant-level reclassification at no extra cost • Case-level reanalysis and medical reinterpretation at an affordable cost (e.g., new clinical information, one-year intervals)
CentoGenome Prenatal***	• Powerful cutting-edge genomic test for prenatal diagnostics (ongoing pregnancy) when fetus structural abnormalities detected on ultrasound, or a diagnosis cannot be obtained using routine prenatal methods • Expedited and prioritized testing (≤ 15 business days) includes cell culture and maternal contamination testing
CentoGenome MOx****	• Cutting-edge multiomic WGS testing solution indicated for patients with suspicion of rare genetic diseases, especially when presenting complex and overlapping symptoms • Multiomics (MOx) allows for orthogonal confirmation of disease, accelerating the diagnostic path by avoiding stepwise testing

* **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, and CMA analysis is only performed for the index patient

** Case reanalysis is available only for orders with original sequencing data from August 2020 onwards. More details about Variant Reclassification Program

*** We do not offer WGS-based CNV, mitochondrial genome, UPD, repeat expansions, SMN1/SMN2 CNV and GBA1 conversion analysis with CentoGenome Prenatal due to technical limitations. More details about Prenatal Testing

**** More details about our Multiomic Solutions at MOx

Best-in-Class Medical Reporting and Advanced Insights

A team of highly trained medical experts interpret the data and verify every medical report. We perform internal confirmatory testing free-of-charge using orthogonal methods if applicable and use the CENTOGENE Biodatabank to confirm results and validate variant pathogenicity.

Main Findings	• Diagnostic findings related to patient's phenotype • Research findings related to patient's phenotype providing information on potential diagnoses
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 with no 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' phenotypes • 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' phenotypes that are potentially clinically relevant for family planning • List of sequence variants for the index patient classified as pathogenic/likely pathogenic in the CENTOGENE Biodatabank for selected genes associated with recessive severe and early-onset Mendelian diseases
Extra Disease Confirmation & Insights	• Internal confirmatory testing by an orthogonal method for reported variants when necessary and for all reported variants associated with repeat expansion diseases, UPD, SMA, and GD/PD • Extra insights supported by the CENTOGENE Biodatabank, which contains curated unique variants and omics data from approximately 700,000 patients from over 120 highly diverse 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.

Please note that for prenatal and products of conception diagnostics the following findings are not reported: research, secondary and carriership findings for prenatal and secondary finding for product of conception.

References

1 Data on file at CENTOGENE

2 Bertoli-Avella et al. 2020, PMID: 32860008

3 Cheema et al. 2020, PMID: 33083013

FOR ORDERING
www.centoportal.com

FOR MORE INFORMATION
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