CENTOGENE
THE RARE DISEASE COMPANY

CentoGenome®
See Diagnostics In a New Way

PRODUCT SHEET

CentoGenome®
Whole Genome Sequencing

CENTOGENE's Whole Genome Sequencing (WGS) testing solution – CentoGenome® – identifies virtually all changes in a patient's DNA by sequencing both the entire protein coding and non-coding regions of the genome. Combined with our world-class expertise in rare disease diagnostics, experience in genomic testing, and clinical interpretation, CentoGenome is the ideal solution to diagnose complex cases rapidly and with the highest levels of diagnostic success.

The CENTOGENE Advantage

1. **Unparalleled nuclear & mitochondrial genome coverage**, with reliable detection of virtually all types of genetic variants
2. **Highest diagnostic power in a single test,** providing quick & precise answers to avoide diagnostic delays
3. **High-quality analysis for precise clinical interpretation** using advanced bioinformatics and artificial intelligence-powered tools
4. **Best-in-class insights** powered by the world's largest rare disease-centric Bio / Databank from the leader and trusted partner in rare disease diagnostics
5. **Dedicated team of rare disease experts** to provide best clinical interpretation and life-long support

Key Features and Performance

CentoGenome offers unparalleled genome coverage and captures one of the most extensive ranges of disease-causing genetic variants in a single test. This includes single nucleotide variants (SNVs), small insertions/deletions (InDels), structural variants (SVs) including copy number variations (CNVs), and heteroplasmic mitochondrial variants. For more information, please see the table below and consult the CentoGenome Webpage.

Key Features and Performance

GENOME COVERAGE

- Almost complete and uniform coverage of the genome (nuclear and mitochondrial), including both protein-coding and non-coding regions (> 20,000 genes)
- Average depth coverage > 30 x
- > 97 % genome covered at ≥ 10 x
- ≥ 97 % of MitoGenome at 200 x

VARIANT TYPES

- Highly sensitive and specific detection of SNVs, InDels, CNVs of exon-level to cytogenomic-level changes, complex SVs, repeat expansions, and variants in mtDNA at ≥ 15 % heteroplasmy*
- Sensitivity

SNVs and InDels (≤ 50 bp)	> 99.9 %
Deletions	
51 bp – 1 kb	> 70.0 %
1 kb – 10 kb	> 60.0 %
Copy number deletion > 10 kb	> 70.0 %
Insertions	
51 bp – 99 bp	> 70.0 %
100 bp – 199 bp	> 80.0 %
200 bp – 299 bp	> 75.0 %
> 300 bp	> 65.0 %
Duplications	
Tandem Duplication 100 bp – 1 kb	> 85.0 %
Tandem Duplication 1 kb – 10 kb	> 65.0 %
Copy number duplication > 10 kb	> 70.0 %

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

TECHNICAL DETAILS

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

* SNVs: single nucleotide variants; InDels: small insertions/deletions; CNVs: copy number variations; SVs: Structural variants (includes CNVs) mtDNA variants: mitochondrial DNA variants

** 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-depedent probe amplification (MPLA), quantitative polymerase chain reaction (qPCR) or chromosomal microarray (CMA)

Tailored Testing

We offer flexible testing options and additional services that allow healthcare providers to tailor the CentoGenome analysis to their patients' needs, such as WGS for ongoing pregnancies with fetal abnormalities for prenatal diagnostics and expedited WGS for critically ill patients that need rapid and precise genetic diagnosis.

Options and Additional Services

TURNAROUND TIME	• Regular: ≤ 20 business days • FAST: ≤ 15 business days
TESTING DESIGN	Solo, Duo, Trio and Trio PLUS
PRENATAL TESTING	Expedited and prioritized testing (≤ 15 business days) specifically designed for ongoing pregnancies
LIFE-LONG RECLASSIFICATION AND RE-ANALYSIS	• Variant-level reevaluation and reclassification at no extra cost • Case-level reanalysis and medical reinterpretation in case of uncertain or negative results

Medical Reporting

When choosing our WGS services, 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 high quality 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. For more information, please see the table below and consult the designated Medical Reporting and 'Tabular List' webpages.

Medical Reports and Data

MAIN FINDINGS	• Diagnostic findings related to patient's phenotype • Optional research findings related to patient's phenotype providing information on potential diagnoses in cases where no definitive diagnosis can be found
OPTIONAL SECONDARY FINDINGS	Medically actionable variants based on American College of Medical Genetics and Genomics (ACMG) guidelines available for all tested individuals
ADDITIONAL FINDINGS	CENTOGENE's 'Tabular List' variant section for the index patient, which includes known gene variants in CentoMD® classified as pathogenic/likely pathogenic. Our list makes often unreachable information accessible to physicians/genetic counselors, which may lead to further diagnostics and medical management of the patient and/or their family
RAW DATA	Raw data available free of charge for download (FASTQ, BAM, VCF files) along with filtered and annotated variant table for further research