CentoGenome®
The complete diagnostic solution
Often, after months, years and many costly tests, patients and physicians find themselves back where they started – sometimes with a dramatic deterioration of patients’ quality of life.

Now you can escape the maze with a single test – one which provides a comprehensive view into genetic information paired with highest quality of medical interpretation.

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Introducing the diagnostic solution

CENTOGENE is revolutionizing genetic diagnostics with CentoGenome® – our premium whole genome analysis service for the diagnosis of complex diseases.

Whole genome sequencing (WGS) with CentoGenome® provides the most comprehensive genetic testing available for the detection of rare diseases. It identifies more different types of DNA sequence variation and offers greater sensitivity than any other technology available.

Together with CENTOGENE’s proprietary mutation database (CentoMD®) and the highest level of medical interpretation and reporting, CentoGenome® provides definite answers for patients with unresolved diagnoses.

CentoGenome® is

› Sensitive analysis
  unparalleled genome coverage and multi-variant detection

› Reliable interpretation
  proven success from over 10 years of medical-focused diagnostic work

› Fast results
  guaranteed rapid turnaround times through optimized workflows

› Accessible logistics
  easy sample shipment using CentoCard®, our unique, CE-labeled filtercard technology

› Affordable pricing
  as the leading provider of this technology, we offer WGS analysis at a cost that enables physicians to provide the best solutions for their patients from the start

Why whole genome sequencing?

WGS identifies nearly all changes in a patient’s DNA by sequencing the entire coding and non-coding regions of the genome. It provides detailed information on the thousands of genes involved in normal growth and development and all of the ‘silent’ genome regions simultaneously.

Existing research and diagnosis of genetic diseases have been heavily biased towards mutations in gene coding regions, but this is only 1% of a patient’s entire genome. Numerous clinical studies now exist which reveal the critical role of non-coding sequence variants in diseases.

WGS opens the door to greater research and diagnostic power for all genetic diseases.

All genetic tests in one

Single variant testing, panel testing and microarrays all identify known variants in pre-determined genes, and whole exome sequencing (WES) analyses only regions that encode functional proteins. Although in many cases these tests are sufficient to identify the cause of a disease, these analyses are ultimately limited and can fail to reveal the full genetic cause.

Millions of patients today suffer from wrongly or undiagnosed genetic diseases because the best technology has not been applied. WGS can perform all of these tests and provide analysis of many more variants at the same time all in a single method.

Better sensitivity in coding and non-coding regions

WGS gives nearly complete coverage of a patient’s genome sequence with better resolution than WES in both the gene coding or non-coding regions. This means that WGS detects more disease-causing variants and gives a more complete picture of the genetic landscape for a precise diagnostics to aid diagnosis.

In a recent study, next-generation sequencing for WGS and WES both identified the vast majority of single nucleotide variations (SNVs) and insertions/deletions (indels), but WES missed about 3% potential ‘high-quality’ variants, demonstrating that WGS was more powerful than WES for detecting potential disease-causing mutations within WES regions. The study concluded that compared to WES, only WGS is able to provide hitherto unprecedented complete coverage of the coding region of the genome."

CentoGenome® – Whole genome sequencing and analysis at CENTOGENE

CENTOGENE performs whole genome sequencing in the index patient as well as in two family members (TRIO); or in affected relatives to provide the most complete diagnostic solution.

A comprehensive view on genetic information paired with conclusive medical interpretation

The large amount of data generated by WGS requires filtering and verification to accurately identify high-quality candidate variants and pinpoint the correct one, a skill that few variant physicians or analysts possess. This is where CENTOGENE provides exceptional assistance, with its proprietary database (CentoMD®) and its expert analysis team who have performed thousands of patient WES/WGS analyses and assessments.

Our genome pipeline includes all of the following in a single, in-house workflow:

- Validated sequencing of all coding and non-coding genome regions with Illumina next generation sequencing
- Filtering, analysis and interpretation of single-nucleotide variants (SNVs), indels, structural variants, and CNVs both in the ~1% portion of the genome that encodes protein sequences and in non-coding sequences
- End-to-end bioinformatics analysis of raw data with clinical reporting
- Streamlined processes

Sequencing of the genome *  
End-to-end bioinformatics analysis of raw data  
Validation of sequencing results  
Medical reports

* mean coverage of 30X (>98% of the genome is covered at >10X)

Our experts highly recommend the use of CentoGenome® for diagnosis when the patient presents:

- Complex and heterogeneous syndromes with an unclear or atypical phenotype
- A phenotype with significant genetic heterogeneity, where mutations in several genes may lead to the same clinical presentation (for example, neuropsychiatric, ataxias, intellectual disability, and muscular disorders)
- Causative cancer mutation in tumors at every stage of treatment

Key benefits of whole genome sequencing

- CentoGenome® produces a more comprehensive dataset for known human mutations in exons, introns and regulatory regions (5’ untranslated regions/promoter regions).
- CentoGenome® detects CNVs, translocations, splice site variants, regulatory region variants and insertions/deletions, including their position on the genome to help interpret their downstream effects in coding regions.
- CentoGenome® outperforms WES in terms of overall sequencing coverage but also for the non-coding region as well as for the WES targeted exonic regions.
- CentoGenome® datasets show fewer artefacts and are more accurate than WES because there is no need for a PCR enrichment step.

Key applications of CentoGenome®

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Role of whole genome sequencing for detection of variants in intellectual disability

Intellectual disability (ID), also referred to as mental retardation, occurs in ~0.5% of newborns and is closely connected to a genetic cause; 15% are due to chromosomal abnormalities, 10% are due to microdeletions, and 10% in males are due to monogenetic alterations. The likelihood of a genetic cause for ID in a patient increases with severity of the symptoms.

A detailed clinical analysis with comprehensive genetic testing is known to be the best way to achieve a diagnosis in this disorder, which often has a high level of genetic heterogeneity. WGS analysis with CentoGenome® can be applied as the primary analysis needed to reliably identify and characterize the comprehensive spectrum of genetic variation and provide a genetic diagnosis in the majority of patients with ID.

Microarray and WES studies have shown the prevalence of de novo copy number variations and SNVs in ID, but are not able to diagnose the majority of cases that come to the clinic. A recent paper published in Genomic Medicine revealed that WGS analyses of pediatric populations have shown identification of clinically relevant variants in ~40% of those with autism and ~60% of those with intellectual disability. Another scientific group showed that out of a cohort of 170 individuals (85 quartet families), 69.4% carried different ASD-relevant mutations. Whole genome sequencing was applied to analyze de novo and rare inherited single-nucleotide and structural variations that were previously connected with ASD or other neurodevelopmental disorders.

Furthermore, WGS analysis provided a conclusive diagnosis in 42% of the 50 patients where array-CGH and WES had failed to provide a diagnosis. This demonstrates that WGS is superior for diagnosis this genetically complex disorder, as described in a study of how whole genome sequencing was used to identify the cause of severe intellectual disability.

The increased yield of diagnosis for cases with intellectual disability and the single analysis for the different possible pathogenetic variants highlights CentoGenome® as the first tier diagnosis for ID, providing the best way to identify variants with expert interpretation and reporting in one complete package.
CentoGenome® – for detection of somatic variants in cancer

The genetics underlying any given cancer can be complex and highly individual, involving a number of genes in coding and non-coding regions, in both germline and somatic cells. CentoGenome® is the state-of-the-art technology for identifying variants to guide diagnosis and treatment of somatic cancers.

Somatic mutations are found exclusively in tumor cell genomes; their frequency varies across different cancer types as do the relative proportions of non-coding and coding variants. A high proportion of somatic variants in tumors are structural variants including large genomic rearrangements. Somatic mutations in tumors often fall within known driver genes and hotspots but virtually all solid tumors have additional mutations which have an effect outside the known hotspot region.

A recent review in Nature Genetics1 compares the genetics of germline versus somatic cancers and highlights the importance of non-coding variants in somatic cancer.

Only WGS is capable of detecting the full range of variants possible in a genome, making it the best option for detecting causative cancer mutation in tumors at every stage of treatment.

Tracking tumour progression

Any changes within the tumor genome can be carefully monitored with CentoGenome®, so de novo somatic mutations that occur in response to tumor therapy can be identified and treatment modified accordingly. Analysis includes tumor plus normal tissue pair-analysis for a state-of-the-art cancer monitoring.

In somatic cancer investigations, identifying the causative mutations with WGS can be difficult and success relies on specialist expertise in variant filtering as well as access to a broad variant database; CentoGenome® incorporates all of this, enabling you to provide precision medicine treatments for your patient.

CentoGenome® – pioneering WGS data interpretation

CentoGenome® enhances state-of-the-art WGS technology with expert filtering and interpretation of data by experienced professionals with reference to CENTOGENE’s comprehensive disease-linked mutation database (CentoMD®).

Conclusive clinical reports:

› Validated by certified human genetics consultants and geneticists
› Detailed descriptions and explanations of the applied testing methods
› Differential diagnosis and detailed assessment of the clinical information received
› Clear results, recommendations, and genetic counseling

Clinical anamnesis

For high quality interpretation of the data it is crucial to obtain specific and detailed clinical information from the index patient and the family (TRIO) when performing whole genome sequencing. This increases the diagnostic yield from roughly 20% to over 40%.

Incidental findings

CENTOGENE does not report on findings not directly related to the cause of a disease and not listed in the ACMG guidelines (Green RC et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing, Genet Med. [2013]).

Please visit our website for more information:

www.CENTOGENE.com

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