



Dr.

Order no.: XXXXXXXX

Order received:

Sample type: blood, filter card

Sample collection date:

Report date:

Report type: Final report



Country

Patient no.: XXXX, First Name: XXXX, Last Name: XXXX  
DOB: XXXX, Sex: male, Your ref.: XXXX

**Test(s) requested: CentoLCV™ - Whole Genome NGS-based Large Copy number Variation analysis**

### CLINICAL INFORMATION

Anxiety; Obsessive-compulsive behavior  
(Clinical information indicated above follows HPO nomenclature.)

Family history: Unknown.  
Consanguineous parents: No.



**NEGATIVE RESULT**

### INTERPRETATION

**We did not detect any clinically relevant copy number variation (CNV) for the described phenotype of the patient in the analyzed sample.**

The detected genetic sex is: male.

### RECOMMENDATIONS

- We recommend proceeding to whole exome sequencing together with the parents (WES-trio) for segregation analysis.
- Genetic counselling is recommended.

#### > Contact Details

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## ANALYSIS STATISTICS

The target sequence was covered >3x (average coverage was 5.9x).

## CENTOGENE CLASSIFICATION OF DETECTED COPY NUMBER VARIANTS

**PATHOGENIC** – CNV with sufficient evidence to classify as pathogenic

**LIKELY PATHOGENIC** – CNV with strong evidence in favor of pathogenicity

**UNCERTAIN SIGNIFICANCE** – CNV with limiting and/or conflicting evidence regarding pathogenicity

**LIKELY BENIGN** – CNV with strong evidence against pathogenicity

**BENIGN** – CNV with sufficient evidence to classify as benign; polymorphism

Additionally, other types of clinical relevant variants can be identified (e.g. risk factors, modifiers).

The classification of copy number variants at CENTOGENE is based on the ACMG standards and guidelines for interpretation and reporting of postnatal constitutional copy number variants (2011). Copy number variants are evaluated based on the patient's reason for referral for this genomic screening. Comprehensive reporting of heterozygous recessive variants is outside the scope of the intended use of this test. Therefore, recessive carrier status might not be disclosed. Any clinical concern for recessive disorders should be communicated to the reporting laboratory for appropriate consideration.

**1 copy loss** – heterozygous/hemizygous deletion

**1 copy gain** – heterozygous/hemizygous gain

**2 copy loss** – homozygous deletion

**2 copy gain** – homozygous gain

## METHODS

Genomic DNA is enzymatically fragmented and libraries are generated by PCR-mediated addition of Illumina compatible adaptors. Final libraries are sequenced at 2 x 150 bp paired-end ~500bp insert sizes on an Illumina platform (HiSeq X or HiSeq 4000) with a mean coverage of >3x. Alignment to the human reference genome (GRCh37/hg19) and CNV calling is performed based on an internal pipeline including multiple callers. Bioinformatic analysis is restricted to potentially clinically relevant genomic regions encompassing the complete nuclear genome. Interrogated regions do not include highly repetitive DNA sequences, such as the short arm of acrocentric chromosomes, centromeres, telomeres and other heterochromatin blocks. Copy number variations with a minimum size of 50 kb for deletions and 200kb for duplications are analyzed. A lower size threshold is considered for homo/hemizygous deletions. The provided clinical information and family history and the current knowledge of genes and alterations at the time of reporting are used to evaluate the identified copy number variants in respect to their pathogenicity and causality which leads to classification into 5 classes (see above). All variants related to the phenotype of the patient, except benign or likely benign variants, are reported. CENTOGENE has established stringent quality criteria and validation processes for variants detected by shallow WGS. Lower quality aberrations are confirmed by MLPA, qPCR or microarray for reported variants.

## LIMITATIONS

CentoLCV™ method is recommended for the purpose of identifying DNA copy number variations (CNVs) associated with large chromosomal imbalances, microdeletion/duplication syndromes, and partial or complete gene deletions/duplications based on shallow whole genome sequencing. CentoLCV™ can only detect large genomic copy number imbalances in the nuclear genome. It cannot detect balanced chromosomal rearrangements such as translocations and inversions, imbalances in the mitochondrial genome, repeat sequences such as segmental duplications or repeat expansions, regions with absence of heterozygosity, uniparental heterodisomy, point mutations and delins, chromosomal mosaicism, sample contamination, complete ploidy changes, methylation aberrations, or copy number changes in the regions of the genome that are not targeted/covered. CentoLCV™ may not reliably detect CNV within or encompassing the pseudoautosomal regions of the sex chromosomes. Failure to detect an alteration at a specific locus does not exclude the diagnosis of a genetic disorder associated with that locus. There might be abnormalities present in that region that are not detectable by the CentoLCV™ technology.

## ADDITIONAL INFORMATION

This test was developed and its performance validated by CENTOGENE AG. The US Food and Drug Administration (FDA) has determined that clearance or approval of this method is not necessary and thus neither have been obtained. This test has been developed for clinical purposes. All test results are reviewed, interpreted and reported by our scientific and medical experts.

To exclude mistaken identity in your clinic, several guidelines recommend testing a second sample that is independently obtained from the proband. Please note that any further analysis will result in additional costs.

The classification of variants can change over the time. Please feel free to contact CENTOGENE ([customer.support@centogene.com](mailto:customer.support@centogene.com)) in the future to determine if there have been any changes in classification of any reported variants.

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## DISCLAIMER

Any preparation and processing of a sample from patient material provided to CENTOGENE by a physician, clinical institute or a laboratory (by a "Partner") and the requested genetic and/or biochemical testing itself is based on the highest and most current scientific and analytical standards. However, in very few cases genetic or biochemical tests may not show the correct result, e.g. because of the quality of the material provided by a Partner to CENTOGENE or in cases where any test provided by CENTOGENE fails for unforeseeable or unknown reasons that cannot be influenced by CENTOGENE in advance. In such cases, CENTOGENE shall not be responsible and/or liable for the incomplete, potentially misleading or even wrong result of any testing if such issue could not be recognized by CENTOGENE in advance.

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