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CENTOGENE
THE RARE DISEASE COMPANY

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Date: 19.04.2017

Patient name: **Taneja, Sohini Singh**
Your ref.: **011608060042**
DOB (dd.mm.yyyy): **14.06.1982**
Sample collection date (dd.mm.yyyy): **05.04.2017**
Order received (dd.mm.yyyy): **11.04.2017**

Sex: **female**
Patient no.: **1197714**
Sample type: **blood, filter card**
Order no.: **62373417**

Request for sequencing of the BRCA1, BRCA2 panel

Clinical information: patient with infiltrating ductal carcinoma, grade 3.

Result summary

BRCA1, BRCA2 panel (sequencing)

BRCA1, BRCA2	**no pathogenic variant**

A diagnosis of familial breast and ovarian cancer syndrome (HBOC) cannot be genetically confirmed.

Interpretation

We did not detect any pathogenic variant in the BRCA1 or BRCA2 genes by sequencing. As large deletions/ duplications not detectable by sequencing have been described in the BRCA1 and BRCA2 genes, you might consider MLPA analysis. Alternatively, depending on the patient's disease status and the family history you might consider analysis with specific extended gene panels such as the CentoBreast panel. Genetic counselling is recommended.

Best regards,

Prof. Arndt Rolfs, MD
Chief Medical Director

Oliver Brandau, MD
Medical Director, Director Medical Reporting

Franziska Gustke, PhD
Clinical Scientist

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CENTOGENE variant classification (based on ACMG recommendations)
Class 1 – Pathogenic
Class 2 – Likely pathogenic
Class 3 – Variant of uncertain significance (VUS)
Class 4 – Likely benign
Class 5 – Benign
Class 6 – Disease-associated variant

Methods

The sample has been processed by enriching of targeted sequences and sequencing was done by using Next Generation Sequencing Technologies.
For the BRCA1, BRCA2 panel, the entire coding region of the BRCA1, BRCA2 genes including 10 bp of intronic flanking sequences were targeted. Due to limitations of the method, the target sequences of the requested panel might not be covered 100%. Missing fragments were therefore completed with classical Sanger sequencing to achieve 100 % coverage of all genes of this panel. Raw sequence data analysis, including base calling, demultiplexing, alignment to the hg19 human reference genome (Genome Reference Consortium GRCh37) and variant calling was performed using validated in-house software. All identified variants were evaluated regarding their pathogenicity and causality, and these were classified in classes 1 - 6 (see above). All variants except benign or likely benign variants are reported. Analysis does not include copy number variations (CNV) or large deletion/duplications.

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.
Of note:
- unless reported or predicted to cause disease, alterations found deep in the intron or variants that do not result in an amino acid substitution are typically not reported by CENTOGENE. These and common polymorphisms identified for this patient are available upon request.
- test results have to be always interpreted in the context of clinical findings, family history, and other laboratory data. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. Rare polymorphisms exist that could lead to false negative or positive results. If results obtained do not match the clinical findings, additional testing should be considered.
- we cannot exclude allele drop off. Polymorphic/normal genomic variation in the patient sample may interfere with mutation detection.

The classification of variants of uncertain clinical significance can change over the time. Please feel free to contact CENTOGENE (testing@centogene.com) in the future to determine if there have been any changes in classification of these variants. CENTOGENE performs confirmatory testing by an independent DNA aliquot in all cases with a mutation (class 1), in all cases with a likely pathogenic variant (class 2) and in most cases with variants of uncertain significance (class 3). We will only contact you if the results are inconsistent. To also 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. If you would like to enquire about additional analyses, please do not hesitate to contact us (office@centogene.com).

Disclaimer
Any preparation and processing of a sample from patient material provided to CENTOGENE by a physician, clinical institute or a laboratory (each 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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