

Booked on	07/02/2017	Patient Id	011702070252	Printed on	27/02/2017
Name	Mr Ranjan Kumar Srivastava	Age	49 Years	Sex	M
Ordering Physician					

BRCA1 and BRCA2 Gene Analysis

Sample Information

Sample Type: Whole Blood, EDTA

Clinical Indications

In the proband's family there is a positive history of breast cancer and head and neck cancer.

Results

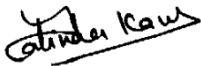
BRCA1 (sequencing)	no pathogenic variant
BRCA2 (sequencing)	no pathogenic variant

A diagnosis of familial susceptibility to a *BRCA1* or *BRCA2*-related cancer syndrome cannot be 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. Depending on the patient's disease status and the family history you might consider analysis with specific extended gene panels such as the Breast ovarian cancer panel (*TP53*, *PTEN*, *STK11* and *CDH1*) in the case of tumors in multiple different tissues. Genetic counseling is recommended.

Report Released by:



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Supplement Information Sheet

Comment

The classification of variants of uncertain clinical significance can change over time. Please feel free to contact MolQ Laboratory (contact@molq.in) in the future to determine if there have been any changes in classification of these variants. If you would like to enquire about any additional analyses, please do not hesitate to contact us (contact@molq.in).

Classification of the variants (based on ACMG recommendations):

- Class 1 – Pathogenic
- Class 2 – Likely pathogenic
- Class 3 – Variant of uncertain clinical significance (VUS)
- Class 4 – Likely benign
- Class 5 – Benign
- Class 6 – Disease-associated variant

Methodology

- 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.
- The *BRCA1* gene (intron 14) was analysed by PCR and Sanger sequencing of both DNA strands of the entire coding region and the highly conserved exon-intron splice junctions. The reference sequence is: **BRCA1: NM_007300.3**. The reference sequences of the *BRCA2* gene is: **NM_000059.3**

Analytical Sensitivity

The analytical sensitivity of DNA sequencing performed in both directions is estimated to be >99.98%. Failure to detect a genetic variant or mutation in the analyzed DNA regions may result from errors in specimen handling and tracking, amplification and sequencing reactions or computer-assisted analysis and data review. The rate of such errors is estimated from validation studies to be less than one Percent (<1%)

Overall Test Accuracy

For a patient with at least a 10 % probability of a positive test based on a personnel or family history of cancer, the chance of an incorrect test result is less than 1%.

Description of Nomenclature

All mutations and genetic variants are named according to the convention of Beaudet and Tsui. (Beaudet AL, Tsui LC. A suggested nomenclature for designating mutations. Hum Mut 1993; 2:245- 248). Nucleotide numbering starts at the first transcribed base of *BRCA1* and *BRCA2* based on Gen Bank entries U14680 and U43746, respectively.

Interpretive Criteria

The classification and interpretation of all variants identified in the assay reflects the current state of scientific understanding at the time the report is issued. In some instances, the classification and interpretation of variants may change as scientific information becomes available.

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Positive for a deleterious mutation

Includes clinically significant nonsense and frame shift mutations that prematurely truncate the protein. In addition, specific missense mutations and non- coding intervening sequence (IVS) mutations are recognized as deleterious on the basis of data derived from linkage analysis of high Risk families, functional assays, statistical analysis, biochemical evidence and / or demonstration of abnormal mRNA transcript processing.

Genetic variant, suspected deleterious

Includes genetic variants for which the available evidence indicates a likelihood, but not proof , that the mutation is deleterious . The specific evidence supporting such an interpretation will be summarized for individual variants on each such report.

Genetic variant favor polymorphism

Includes genetic variants for which available indicates that the variant is highly unlikely to contribute substantially to cancer. The specific evidence supporting such as interpretation will be summarized for individual variants on each such report.

Genetic variant of uncertain significance

Includes missense mutations and mutations that occur in analyzed intronic regions whose clinical significance has not yet been documented (Mazoyer S et al., Nature Genetics 1996: 14:253-254).

No deleterious mutation detected

Includes genetic variants for which published data demonstrate absence of substantial clinical significance. Includes truncating mutations in *BRCA* that occur at and distal to amino acid 3326 (Mazoyer S et al. Nature Genetics 1996: 14:253-254). Also includes mutations in the protein-coding region that neither alter the amino acid sequence nor are predicated to significantly affect exon splicing, and base pair alternations in non – coding portions of the gene that have been demonstrated to have no deleterious effect on the length or stability of the mRNA transcript.

Specific variant / mutation not identified

Indicates that specific and designed mutations or variants are not present in the individual being tested.