Booked on	30/01/2016	**Patient Id**	011601300132	**Printed on**	06/03/2016
Name	Mrs. Suchi Sangal	**Age**	30 Years	**Sex**	F
Ordering Physician	Dr Amit Verma Max Hospital				

BRCA1 and *BRCA2* Gene Analysis

Sample Information

Sample Type: Whole Blood, EDTA

Results

BRCA1 & BRCA2 (sequencing)	**no pathogenic variant detected**

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

Recommendations

We recommend

- deletion/duplication testing

- genetic counselling of the patient and further family members

- if possible, testing other family members to establish the segregation of the variant in the family

Interpretation:
We did not detect any pathogenic variant in the BRCA1 or BRCA2 genes by sequencing, including the known variant in the BRCA1 gene, c.4158_4162del.
Hereditary breast cancer is responsible for 5-10% of all breast cancer cases. Germline pathogenic variants in BRCA1 and BRCA2 lead to familial/hereditary breast and ovarian cancer (HBOC) that is characterized by an increased life time risk for breast cancer (40 – 80%), ovarian cancer (11-40%), prostate cancer (1-10%), and pancreatic cancer (1-7%), and possibly also melanoma.
Dependent on an eventual tumor disease of the patient, further analysis might be considered, such as analysis with the Breast panel (BRCA1, BRCA2, TP53, PTEN, STK11, CDH1, ATM, CHEK2, PALB2, NBN, BRIP1, BARD1 and RAD51C).

Report Released by:

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Supplement Information Sheet

Comment

This result does not eliminate the possibility of hereditary cancer susceptibility. Further, genetic susceptibility to breast/ovarian cancer has also been suggested to be associated with mutations in genes other than *BRCA1* and *BRCA2* (at least 22 other genes, including *RAD51C (BROVCA3)* and *RAD51D (BROVCA4)*, and other susceptibility loci).

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 – Previously reported as disease-causing
Class 2 – Previously unreported, but of the type which can cause the disorder
Class 3 – Previously unreported, may or may not be the cause of the disorder (Variant of uncertain clinical significance)
Class 4 – Previously unreported and is likely neutral
Class 5 – Previously reported as neutral
Class 6 – Disease-associated SNPs

Methodology

The sample has been processed by enriching of targeted sequences and sequencing was done by using Next Generation Sequencing Technologies. Following the base calling and primary filtering of low quality reads, standard Bioinformatics pipeline was implemented to annotate detected variants and to filter out probable artefacts. 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. For the BRCA1, BRCA2 Panel (Ion Torrent), the entire coding region of the BRCA1, BRCA2 genes including 10 bp of intronic flanking sequences were amplified and sequenced. 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 0 - 7 (see above). All variants except benign or likely benign variants are reported. Analysis does not include copy number variations (CNV) or large deletion/duplications.

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.

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.