Booked on	20/09/2016	**Patient Id**	011609200010	**Printed on**	15/10/2016
Name	Mrs. Suman Gupta	**Age**	50 Years	**Sex**	F
Ordering Physician	Dr Amit Verma Max Hospital				

BRCA1 and *BRCA2* Gene Analysis

Sample Information

Sample Type: Whole Blood, EDTA

Clinical Indications

Ovarian Cancer.

Results

BRCA1 (NM_007294.3, sequencing)	**no pathogenic variant**
BRCA2 (sequencing)	**no pathogenic variant**

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

Recommendation

Given the results we recommend
-Genetic Counselling
-Deletion/duplication analysis of the *BRCA1* and *BRCA2* genes
-analysis of further relevant genes in Ovarian cancer panel.

Interpretation
We did not detect any pathogenic variant in the *BRCA1* or *BRCA2* genes by sequencing.

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. In addition, further genes have been identified which can confer an increased risk for ovarian cancer.
Based on the patient's clinical history you might consider further analysis. As large deletions/duplications not detectable by sequencing have been described in the *BRCA1* and *BRCA2* genes, you might consider MLPA analysis. As well, you might consider analysis with specific extended gene panel for ovarian cancer (The Ovarian cancer panel*: BRCA1, BRCA2, TP53, STK11, NBN, BRIP1, BARD1, RAD51C, RAD51D, MLH1, MSH2, MSH6, EPCAM, PMS1*)

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 ***BRCA1, BRCA2*** genes were analyzed by PCR and sequencing of both DNA strands of the entire coding region and the highly conserved exon-intron splice junctions. The reference sequences of the ***BRCA2*** gene is: **NM_000059.3**
- There may be limited portions of either *BRAC1* or *BRACA*2 for which sequence determination can be performed only in the forward or reverse direction. Unequal allele amplification may result from rare polymorphisms under primer sites.

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.

contd...

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.