Booked on	19/03/2018	**Patient Id**	011803190160	**Printed on**	23/04/2018
Name	Mrs Nidhi Mathur	**Age**	40 Years	**Sex**	F
Ordering Physician	Dr Amit Verma Max Hospital				

Germline Mutation Analysis Panel for Cancer Predisposition

Sample Information

Sample Type: Blood

Clinical Indications

Risk prediction. Family history of cancer: Mother affected with ovarian cancer (age at diagnosis: 60+ years) and grandmother (lineage: unknown) affected with breast cancer (age at diagnosis: 60+ years).

Test Details

Inherited cancer: All 86 genes in the germline cancer predisposition panel (listed in attached Appendix) were assessed for any key and incidental findings in the genes recommended by ACMG (American College of Medical Genetics and Genomics).

Results

Negative (uninformative) for disease-causing or likely disease-causing variants in the genes tested in this cancer.

Interpretation

- This individual does not carry any germline pathogenic (disease-causing) or likely pathogenic (likely disease causing) variant in the genes associated with hereditary breast and ovarian cancer predisposition.
- The probability that a pathogenic or likely pathogenic variant, inclusive of SNVs (single nucleotide variants), indels (small deletions, duplications or insertions) and structural variants (large deletions/duplications or complex rearrangements), in the tested genes was not detected by the test is extremely small and is close to 0%.
- A negative test result reduces but does not exclude the possibility that this individual's family history of cancer has a genetic cause, as it may be due to variation in a genomic region not covered by the test (such as weakly associated genes or due to poorly understood polygenic variants) or due to absence of disease-causing or likely disease-causing variants in this individual.
- Although the individual is unaffected at present, according to risk estimation model (BRCAPRO from BayesMendel); with a negative finding in the test and considering the family history of cancer, the lifetime risk for developing breast cancer and ovarian cancer are: ~7.9% and ~0.9%, respectively.

Recommendations

- Genetic counseling is recommended to discuss the implications of this test result for this individual.
- The physician can request reanalysis of the data and this is recommended on an annual basis. Data from this test is based on currently available scientific information. This data can be re-assessed for the presence of any variants that may be newly linked to established genes associated with the individual's family history of cancer or to newly identified disorders since the date of this report. A charge may apply for reanalysis.
- For further details, kindly contact: contact@molq.in

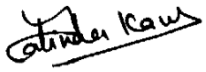
Limitations of Gene Coverage

For each test gene, the fraction of the gene covered by less than 20 reads is indicated below.

Gene	HGMD variants not covered	% of Coding Region under covered
MSH2	2/686	0.07%
MSH6	2/363	1.93%

******End of the report******

Report Released by:



Dr. Jatinder Kaur, PhD
Head, Molecular Biology & Genomics

Appendix

Test Description

The MolQ Germline Cancer Predisposition Panel include genes associated with both common (e.g., breast, colorectal) and rare cancers. The test involves preparation of a target sequence enrichment based library from the patient's genomic DNA (gDNA) using Illumina's Nextera's technology. The panel covers 86 unique genes and includes variation coverage for all coding exons (>97%) and essential splice sites.

Genes evaluated: 86 genes

AIP, ALK, APC, ATM, BLM, BMPR1A, BRCA1, BRCA2, BRIP1, BUB1B, CDC73, CDH1, CDK4, CDKN2A, CEP57, CHEK2, CYLD, DDB2, DICER1, DIS3L2, EGFR, EPCAM, ERCC2, ERCC3, ERCC4, ERCC5, EXT1, EXT2, EZH2, FANCA, FANCB, FANCC, FANCD2, FANCE, FANCF, FANCG, FANCI, FANCL, FANCM, FH, FLCN, GPC3, HNF1A, HRAS, KIT, MAX, MEN1, MET, MLH1, MSH2, MSH6, MUTYH, NBN, NF1, NF2, NSD1, PALB2, PMS1, PMS2, PRF1, PRKAR1A, PTCH1, PTEN, RAD51C, RAD51D, RB1, RECQL4, RET, SBDS, SDHAF2, SDHB, SDHC, SDHD, SLX4, SMAD4, SMARCB1, STK11, SUFU, TP53, TSC1, TSC2, VHL, WRN, WT1, XPA, XPC.

Methodology

Sample preparation: Genomic DNA from saliva, blood or any other standard tissue source is used to make the library. "Nextera" library preparation uses a transposon based shearing of the genomic DNA and allows the DNA to be "tagmented" (fragmented and tagged simultaneously in the same tube). Limited cycle PCR step allows the incorporation of adaptors, platform-specific tags and barcodes to prepare the DNA sequencing libraries.

Target Enrichment: Approximately 500 ng of each library is used for target enrichment. For this panel, up to 12 libraries can be combined into a single tube and set up for enrichment, to generate adequate coverage on a Miseq sequencer. Two simultaneous enrichment steps are performed to optimize the pull down of regions of interest using target specific probes.

Sequencing Details: Sequencing is performed using a standard v2 kit on Illumina Miseq with the expected data output of 4.0-5 GB. For this panel, the output size is 0.253 MB, optimum cluster density to be achieved during sequencing is 750-1000 clusters/mm^2.

Analysis

The trimmed FASTQ files were generated using MiSeq Reporter from Illumina. The reads were aligned against the whole genome build hg19. Five bas e-pairs from the 3' end of the reads were trimmed, as were 3' end bases with quality below 10. Reads which had length less than 25bp after trimming were not considered for alignment. A maximum of 5 matches of alignment score at least 90% were computed. The reads were realigned using the local realignment tool. Reads that failed vendor QC, reads with average quality less than 20, reads with ambiguous characters were all filtered out. The NGS variant caller was used to detect variants at locations in the target regions covered by a minimum of 10 reads with at least 2 variants reads. Variants with a decibel score of at least 50 were reported.

Limitations

This test is based on a research protocol. At present FDA has determined that clearance or approval is not necessary for this test. Variants that have not been confirmed by an independent analysis could represent technical artifacts. Some types of genetic abnormalities may not be detectable by this test. It is possible that the genomic region where a disease causing variation exists in the proband was not captured using the current technologies and therefore was not detected. Additionally, it is possible that a particular genetic abnormality may not be recognized as the underlying cause of the genetic disorder due to incomplete scientific knowledge about the function of all genes in the human genome and the impact of variants on those genes. The quality of sequencing varies between regions. Many factors such as homopolymers, GC-rich regions etc. influence the quality of sequencing. This may result in an occasional error in sequence reads.