

Booked on	02/01/2010	Patient Id	011901020065	Printed on	14/02/2019
Name	Ms Shweta Agarwal	Age	36 Years	Sex	F
Ordering Physician	Dr Amit Verma Max Hospital				

Germline Mutation Analysis Panel for Cancer Predisposition

Sample Information
Sample Type: Blood
Clinical Indications
Diagnosed with retroperitoneal leiomyosarcoma (age at diagnosis: 32 years). Family history of breast cancer.
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
<i>No disease-causing or likely disease-causing variant was detected in the genes (as mentioned below) tested in this sample.</i>
Interpretation
<ul style="list-style-type: none"> This individual does not carry any germline pathogenic (disease-causing) or likely pathogenic (likely disease-causing) variant in the 35 genes associated with hereditary breast, ovarian and other cancers predisposition. A negative test result reduces but does not exclude the possibility that this individual's personal and family history of cancer has a genetic cause, as it may be due to variation in a genomic region not covered by the test or it can also be due to the inherent technical limitations of the test.
Recommendations
<ul style="list-style-type: none"> 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 patient's phenotype 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, all gene target regions were adequately covered by greater than 20 reads.



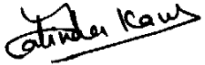
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****End of the report****

Report Released by:



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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, BMPRIA, 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, PRKARIA, 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 isolated from saliva, blood or any other standard tissue source is used for preparation of the 'DNA sequencing ready' library. The DNA is quantified using Qubit Fluorometer and 50 ng is taken for library preparation. "Nextera" library preparation uses transposon-based shearing of the genomic DNA. The Nextera protocol allows the DNA to be "tagmented" (fragmented and tagged simultaneously in the same tube). A limited cycle PCR step allows the incorporation of adaptors, platform-specific tags and barcodes to prepare the DNA sequencing libraries.

Target Enrichment: The tagged and amplified sample libraries are checked for quality and quantified. Approximately 500 ng of each library is used in this step and any deviation from the recommended amount results in over or under representation of the sample and greater or less mean coverage. For this panel, up to 12 libraries can be combined into a single tube and set up for enrichment, to generate adequate coverage total sequencing for each sample on a MiSeq sequencer. Two simultaneous enrichment steps are performed to optimize the pull down of the regions of interest using biotinylated target specific probes. Target libraries are amplified using limited PCR steps and 6-10 pM are loaded for sequencing on the MiSeq.

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/mm².

Analysis

The trimmed fastq files were generated using MiSeq Reporter from Illumina. The reads were aligned against the whole genome build hg19. Five base 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 variant reads. Variants with a depth 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



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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.