Patient Name:	Mrs.Dummy	**CRM ID:**	XXX
Age:	41 Years	**Sample Type:**	Whole Blood EDTA
Sex:	Female	**Sample collection date:**	03-05-2024
Referring Clinician:	Dr. TarunKumar(BHU)	**Sample receiving date:**	04-05-2024
Test Requested:	Homologous Recombination Repair (HRR) Germline By Ngs	**Reporting date:**	01-06-2024

HOMOLOGOUS RECOMBINATION REPAIR (HRR) GERMLINE PANEL BY NGS

CLINICAL INDICATION/DIAGNOSIS

C/o Carcinoma right ovary, Post NACT

TEST RESULT SUMMARY

NEGATIVE

(No significance variant detected related to the phenotype)

KEY FINDINGS

Genes & Transcript	Exon	Variant	Zygosity/ Inheritance	OMIM Phenotype	ACMG Classification
None					

*Genetic test results are reported based on the recommendations of ACMG guidelines.

Variant Interpretation & Clinical correlation

NA

RECOMMENDATION

- ✓ Please correlate clinically.
- ✓ Genetic counseling for accurate interpretation of test results is recommended.
- ✓ MLPA is recommended to rule out the large deletion/duplication analysis of BRCA1&2 gene.
- ✓ Homologous Recombination Repair (HRR)/HRD somatic panel by NGS on tissue block is recommended, if available.
- ✓ For questions about this report, or for assistance in locating nearby genetic counseling services, please contact the Laboratory: geneticcounselors@redcliffelabs.com, ccsupport@redcliffelabs.com.

TEST DESCRIPTION

This Homologous Recombination Repair (HRR) germline extended panel includes 154 genes, is a Next Generation Sequencing (NGS) based assay that identifies clinically relevant genomic alterations (SNVs, indels, and CNVs) within these genes (genes list table attached at end of the report) that are most frequently altered.

METHODOLOGY & VARIANT ANALYSIS

Next Generation Sequencing: DNA extracted from Blood sample is used for targeted capture-based Library preparation. Targeted capture provides an efficient and sensitive means for sequencing specific genomic regions in a high-throughput manner. The libraries were sequenced to mean >85-100x coverage on Illumina Novaseq 6000 sequencing platform with Paired End 2x150 chemistry. We follow the Illumina DRAGEN Bio-IT Platform for identification of variants in the sample. The sequences obtained are assembled and aligned to reference sequences based on NCBI RefSeq transcripts and human genome build (GRCh38). Haplotype caller has been used to identify variants which are relevant to the clinical indication. In addition to SNVs and small Indels, copy number variants (CNVs) are detected from targeted sequence data using the commercially available algorithm. This algorithm detects rare CNVs based on comparison of the read-depths of the test data with the matched aggregate reference datasets.

Clinically relevant mutations were annotated using published variants in literature, Commercial datasets and a set of diseases databases. Common variants are filtered based on allele frequency in 1000Genome, ExAC, gnomAD, dbSNP & our internal database. Non- synonymous variants effect is calculated using multiple algorithms such as PolyPhen-2, SIFT, MutationTaster2.

Variants are labeled as per Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer, by American College of Medical Genetics and Genomics (ACMG) published guideline.

TEST LIMITATIONS

- ✓ It should be noted that this test is limited to a limited number of genes and does not include all intronic and non-coding regions.
- ✓ This report only includes variants that meets a level of evidence threshold for cause or contribute to disease. Test results are interpreted in the context of clinical & pathological findings and laboratory data.
- ✓ The accuracy and completeness may vary due to variable information available in different databases. Synonymous mutations were not considered while preparing this report.
- ✓ The variants have not been confirmed using Sanger sequencing and/or alternate technologies.
- ✓ The sensitivity of this assay to detect small deletions/duplication is upto certain number of bases only. The CNVs if detected with this assay have to be confirmed by alternate method such as MLPA.
- ✓ Variations with high minor allele frequencies which are benign/likely benign will be given upon request if required. Certain genes may not be covered completely, and few mutations could be missed.
- ✓ Due to inherent technology limitations, coverage is not uniform across all regions. Hence, pathogenic variants present in areas of insufficient coverage as well as those variants which currently do not correlate with the provided phenotype may not be analyzed/ reported. Additionally, it may not be possible to fully resolve certain details about variants, such as mosaicism, phasing, or mapping ambiguity.
- ✓ This assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements. Incidental or secondary findings (if any) that meet the ACMG guidelines can be given upon request.
- ✓ Genes with pseudo-genes, para-log genes and genes with low complexity may have decreased sensitivity and specificity of variant detection and interpretation due to inability of the data and analysis tools to unambiguously determine the origin of the sequence data in such regions. Sequence and copy number variants are reported according to the Human Genome Variation Society (HGVS).
- ✓ The transcript used for clinical reporting generally represents the canonical transcript, which is usually the longest coding transcript with strong/multiple supporting evidence. However, clinically relevant variants annotated in alternate complete coding transcripts could also be reported.

DISCLAIMER

- Test has been performed assuming that the sample received belongs to the above-named individual(s) and that any stated relationships between individuals are accepted as true. It is also assumed that consent for the same was provided after pre- test counseling at the point of collection/referral.
- The results should be interpreted in the context of the patient's medical evaluation, family history and racial/ethnic background. Please note that variant classification and/or interpretation may change over time if more information available. Re-interpretation of multi gene next generation sequencing data is recommended on an annual basis and may be requested by a medical provider.
- More evidence for disease association of genes and causal pathogenic variants are discovered every year, and it is recommended that genetic variants are re-interpreted with updated software and annotations periodically.
- Rare polymorphisms may lead to false negative or positive results. False negative results may be due to sampling error/errors in sample handling as well as clonal density below the limit of detection. Misinterpretation of results may occur if the information provided is inaccurate or incomplete. Identification of a mutation in one or more of these genes does not guarantee activity of the drug in a given indication due to the presence of contraindicated mutation in the gene not covered by the panel.
- The information provided should only be utilized as a guide or aid and the decision to select any therapy option based on the information reported here resides solely with the discretion of the treating physician.
- Patient care and treatment decisions should only be made by the physician after taking into account all relevant information available including but not limited to the patient's condition, family history, findings upon examination, results of other diagnostic tests, and the current standards of care.
- This report should only be used as an aid and the physician should employ sound clinical judgment in arriving at any decision for patient care or treatment.
- By providing drug information for the reported diagnosis, Redcliffe Lab Pvt. Ltd. is not guaranteeing that any drug or clinical trial is necessarily appropriate for this patient.
- Healthcare providers should evaluate and interpret the information provided in this report, along with all other available clinical information about this patient, to determine the best treatment decisions in their own independent medical judgment. Patient management decisions should not be based on a single test, including this one, nor solely on the information contained in this report.

VARIANT REPORTING CLASSIFICATION BASED ON AMP-ASCO-CAP RECOMMENDATIONS

Variant	A change in a gene. This could be disease causing (pathogenic) or not disease causing(benign).
Pathogenic	A disease-causing variation in a gene which can explain the patient's symptoms.
Likely pathogenic	A variant which is very likely to contribute to the development of disease. However, the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of Pathogenicity
Variant of uncertain significance	A variant which is difficult to classify either as pathogenic (disease causing) or benign (non disease causing) based on current available scientific evidence.
Likely Benign	A variant which is very unlikely to contribute to the development of disease, however,the scientific evidence is currently insufficient to prove this conclusively. Additional evidence is expected to confirm this assertion of Pathogenicity.
Benign	A variant which is known not to be responsible for disease has been detected.

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APPENDIX: LIST OF INCLUDED GENES

Gene	Region covered	Gene	Region cover	Gene	Region covered
AIP	100.00%	ALK	100.00%	ANKRD26	100.00%
APC	100.00%	ATM	100.00%	AXIN2	100.00%
BAP1	100.00%	BARD1	100.00%	BLM	100.00%
BMPR1A	100.00%	BRAF	100.00%	BRCA1	100.00%
BRCA2	100.00%	BRIP1	100.00%	BUB1B	100.00%
CBL	100.00%	CD70	100.00%	CDC73	100.00%
CDH1	100.00%	CDK4	100.00%	CDKN1B	100.00%
CDKN1C	100.00%	CDKN2A	100.00%	CEBPA	100.00%
CEP57	100.00%	CHEK2	100.00%	CTNNA1	100.00%
CYLD	100.00%	DDB2	100.00%	DDX41	100.00%
DICER1	100.00%	DIS3L2	100.00%	DKC1	100.00%
EFL1	100.00%	EGFR	100.00%	ELANE	100.00%
EPCAM	100.00%	ERCC1	100.00%	ERCC2	100.00%
ERCC3	100.00%	ERCC4	100.00%	ERCC5	100.00%
ETV6	100.00%	EXO1	100.00%	EXT1	100.00%
EXT2	100.00%	EZH2	100.00%	FAM111B	100.00%
FANCA	100.00%	FANCB	100.00%	FANCC	100.00%
FANCD2	100.00%	FANCE	100.00%	FANCF	100.00%
FANCG	100.00%	FANCI	100.00%	FANCL	100.00%
FANCM	100.00%	FH	100.00%	FLCN	100.00%
GALNT12	100.00%	GATA2	100.00%	GPC3	100.00%
GPR101	100.00%	GREM1	100.00%	HAVCR2	100.00%
HNF1A	100.00%	HOXB13	100.00%	HRAS	100.00%
IKZF1	100.00%	KIF1B	100.00%	KIT	100.00%
KITLG	100.00%	KRAS	100.00%	LZTR1	100.00%
MAP2K1	100.00%	MAP2K2	100.00%	MAX	100.00%
MEN1	100.00%	MET	100.00%	MITF	100.00%
MLH1	100.00%	MLH3	100.00%	MRE11	100.00%
MSH2	100.00%	MSH3	100.00%	MSH6	100.00%
MUTYH	100.00%	NBN	100.00%	NF1	100.00%
NF2	100.00%	NRAS	100.00%	NSD1	100.00%
NSUN2	100.00%	NTHL1	100.00%	PALB2	100.00%
PAX5	100.00%	PDGFRA	100.00%	PHOX2B	100.00%
PMS1	100.00%	PMS2	100.00%	POLD1	100.00%
POLE	100.00%	POLH	100.00%	POT1	100.00%
PPM1D	100.00%	PRF1	100.00%	PRKAR1A	100.00%
PTCH1	100.00%	PTEN	100.00%	PTPN11	100.00%
RAD50	100.00%	RAD51C	100.00%	RAD51D	100.00%
RAF1	100.00%	RASA2	100.00%	RB1	100.00%
RECQL	100.00%	RECQL4	100.00%	REST	100.00%

RET	100.00%	RHBDF2	100.00%	RIT1	100.00%
RPS20	100.00%	RRAS	100.00%	RUNX1	100.00%
SAMD9	100.00%	SAMD9L	100.00%	SBDS	100.00%
SDHA	100.00%	SDHAF2	100.00%	SDHB	100.00%
SDHC	100.00%	SDHD	100.00%	SHOC2	100.00%
SLX4	100.00%	SMAD4	100.00%	SMARCA4	100.00%
SMARCB1	100.00%	SMARCE1	100.00%	SOS1	100.00%
SOS2	100.00%	SPRED1	100.00%	SRP72	100.00%
STK11	100.00%	SUFU	100.00%	TERC	100.00%
TERT	100.00%	TINF2	100.00%	TMEM127	100.00%
TP53	100.00%	TRIP13	100.00%	TSC1	100.00%
TSC2	100.00%	VHL	100.00%	WRN	100.00%
WT1	100.00%	XPA	100.00%	XPC	100.00%
XRCC2	100.00%				

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.....End of Report .....

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