Patient Name	Centre
Age/Gender	OP/IP No/UHID
MaxID/Lab ID	Collection Date/Time
Ref By	Reporting Date/Time

TEST REQUESTED: **Hereditary Cancer Gene Panel, 57 ACMG Genes**

METHOD USED

Next Generation Sequencing

CLINICAL INFORMATION / FAMILY INFORMATION

52-year-old female patient with recurrent high grade serous carcinoma of fallopian tube. She has been evaluated for genes related to hereditary cancer predisposition.

TEST RESULTS

No significant variant related to patient phenotype has been detected
No clinically relevant Copy Number Variation (CNV) has been detected
No clinically relevant mtDNA variant has been detected

SECONDARY FINDINGS

No pathogenic or likely pathogenic variants identified in the genes for which incidental findings are to be reported based on the ACMG-AMP guidelines.

Gene	Variant	Chromosomal Coordinates	Exon	Zygosity	Disease	Inheritance	Classification

NONE

RECOMMENDATIONS

- Genetic Counselling is recommended.

Laboratory Investigation Report

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QUALITY THRESHOLDS

Total data generated (Gb)	8.78
Reads aligned (%)	99.65
Q30 data (%)	95.79
Mean Depth	91.36

TEST METHODOLOGY

ereditary cancer test is a comprehensive gene panel sequencing test that sequences the protein-coding regions including 57 ACMG recommended hereditary genes. As per ACMG 57 recommended genes should be screened regardless of the indication so that clinician can re-evaluate the patient's family history and personal risk.

This test uses next generation sequencing (NGS) technology to detect the variations/mutations in these genes. DNA from the sample was subjected to library preparation. The enrichment of the coding regions for the genes of interest was performed with the use of target specific probes. The enriched libraries were sequenced to generate required sequence data.

The variants were called using in-house pipeline. In brief, the sequence data was processed to remove low quality bases, map to hg38 reference sequence, remove duplicate reads and call variants. The variants were prioritized and reported based on ACMG [1,2] guidelines. The DNA sequence was mapped to, and analysed in comparison with, the published human genome build UCSC hg38 reference sequence. The targeted coding exons and splice junctions of the known protein-coding RefSeq genes were assessed for the average depth of coverage and data quality threshold values. The possible causative variants were prioritised based on the variant's predicted pathogenicity, frequency of occurrence in population and patient's phenotype with known disease-causing genes from human and model organism data. Analysis results are reported based on the recommendations of American College of Medical Genetics and Genomics and the Association for Molecular Pathology (ACMG-AMP), as described below:

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Class 1	Pathogenic	This variant may directly contribute to the development of disease.
Class 2	Likely Pathogenic	There is a high likelihood that this variant is disease-causing. Additional evidence is expected to confirm this assertion of pathogenicity
Class 3	Variant of Uncertain Significance (VUS)	There is not enough scientific evidence at this time to support a more definitive classification of this variant.
Class 4	Likely Benign	As per current scientific evidence, this variant is not expected to have a major effect on disease. Additional evidence is expected to confirm this assertion. New evidence may demonstrate that this variant can contribute to disease.
Class 5	Benign	The variant does not cause disease.

In line with ACMG-AMP recommendations for reporting of secondary findings in clinical exome and genome sequencing, we report pathogenic variants and likely pathogenic variants only in the recommended genes for the recommended phenotypes.

TESTED GENES								
ACMG Recommended Hereditary Genes (57 genes)								
ACTA2	*ACTC1*	*APC*	*APOB*	*BRCA1*	*BRCA2*	*CACNA1S*	*COL3A1*	*DSC2*
DSP	*FBN1*	*GLA*	*KCNH2*	*KCNQ1*	*LDLR*	*LMNA*	*MEN1*	*MLH1*
MSH2	*MSH6*	*MUTYH*	*MYBPC3*	*MYH11*	*MYH7*	*MYL2*	*MYL3*	*MYLK*
NF2	*NTRK1*	*PCSK9*	*PKP2*	*PMS2*	*PRKAG2*	*PTEN*	*RB1*	*RET*
RYR1	*RYR2*	*SCN5A*	*SDHAF2*	*SDHB*	*SDHC*	*SDHD*	*SMAD3*	*STK11*
TGFBR1	*TGFBR2*	*TMEM43*	*TNNI3*	*TNNT2*	*TP53*	*TPM1*	*TSC1*	*TSC2*
VHL	*WT1*							

LIMITATIONS

Inaccurate and/or incomplete clinical information might lead to misinterpretation of results. The analysis results are interpreted in the context of clinical observations, family history, and other lab reports provided. Only the variants located in genes that are potentially related to the proband's clinical phenotype are reported. Intronic variants, repeat expansions, copy number variations or chromosomal rearrangements may not be reliably detected with this test.

DISCLAIMERS

This report provides information about the patient's mutations that may aid the physician's decision-making processand should not be the sole source of information for making decisions on patient care and treatment. These tests should be interpreted in the context of standard clinical, laboratory, and pathological findings. Benign mutations and mutations in intronic regions have not been included in this report. Genetic counselling is recommended**.** The information provided in this report was collected from various sources that we believe to be reliable and quality control procedures have been put in place to ensure the information provided is as accurate, comprehensive, and as current as possible. The information provided should only be utilized as a guide or aid and

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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 clinical judgment in arriving at any decision for patient care or treatment.

REFERENCES

1. Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genetics in Medicine. 2015 May;17(5): 405-24.
2. David T. Miller et. al. Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2021 update: a policy statement of the American College of Medical Genetics and Genomics (ACMG). Genetics in Medicine 2021; 23:1391–1398

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