CÖRE DIAGNOSTICS™

Case Number:	**24010002000**
Patient Name:	**Priyalakshmi De Silva**
Age/Sex:	**59 Yrs/Female**
Patient Location:	**Colombo**
Hospital Name:	**Aegle Omics Private Limited**
Physician Name:	**Dr. Mahendra Perera**
Date & Time of Accessioning:	**04/07/2024 13:21 Hrs**
Date & Time of Reporting:	**23/07/2024 15:04 Hrs**

Your Test Results

TEST INFORMATION

***gene*CORE somatic endometrial panel** is a **Next Generation Sequencing (NGS)** assay that enables the detection of clinically relevant genomic alterations (**SNVs**, **indels** and **gene fusions**) from both **DNA** & **RNA**, within the 38 unique genes for optimum therapy selection, prognostication and additionally aids in drug discovery research and clinical trial research programs.

SPECIMEN INFORMATION

Received 01 paraffin block labelled as IN/2947/ A11. Tumor content: 30%.

CLINICAL HISTORY

Outside HPE (Large pelvic mass): High grade carcinoma. MSI-S (MSI-Stable) by PCR.

MOLECULAR CLASSIFICATION RESULTS

GENOMIC FINDINGS	MOLECULAR CLASSIFICATION
Pathogenic mutation detected in TP53 gene (NGS) **No Pathogenic mutation detected in POLE gene (NGS)** **MSI stable (PCR)**	**Please refer to page no. 2 for NCCN guidelines** (MMR status by IHC is unknown)

RESULTS

CLINICALLY RELEVANT GENOMIC FINDINGS (Variants summary)

Gene (Exon) [Transcript]	Variant (Amino acid Alteration)	Variant (Coding)	Variant Allele Frequency (VAF)	Variant Effect*	Variant Classification (AMP)**	Variant Classification (ACMG)#	Associated FDA Approved Therapies
TP53 (8) [NM_000546.6]	p.Arg282Trp [**p.R282W**]	c.844C>T	63.2%	LOF	Tier1	Pathogenic	NA

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AU-ID-2010258

Aditi Aggarwal, Molecular Scientist

Dr. Shivani Sharma
DCP, DNB, DipRCPath. Reg. No. 1906

Dr. Rahul Katara, Ph.D.

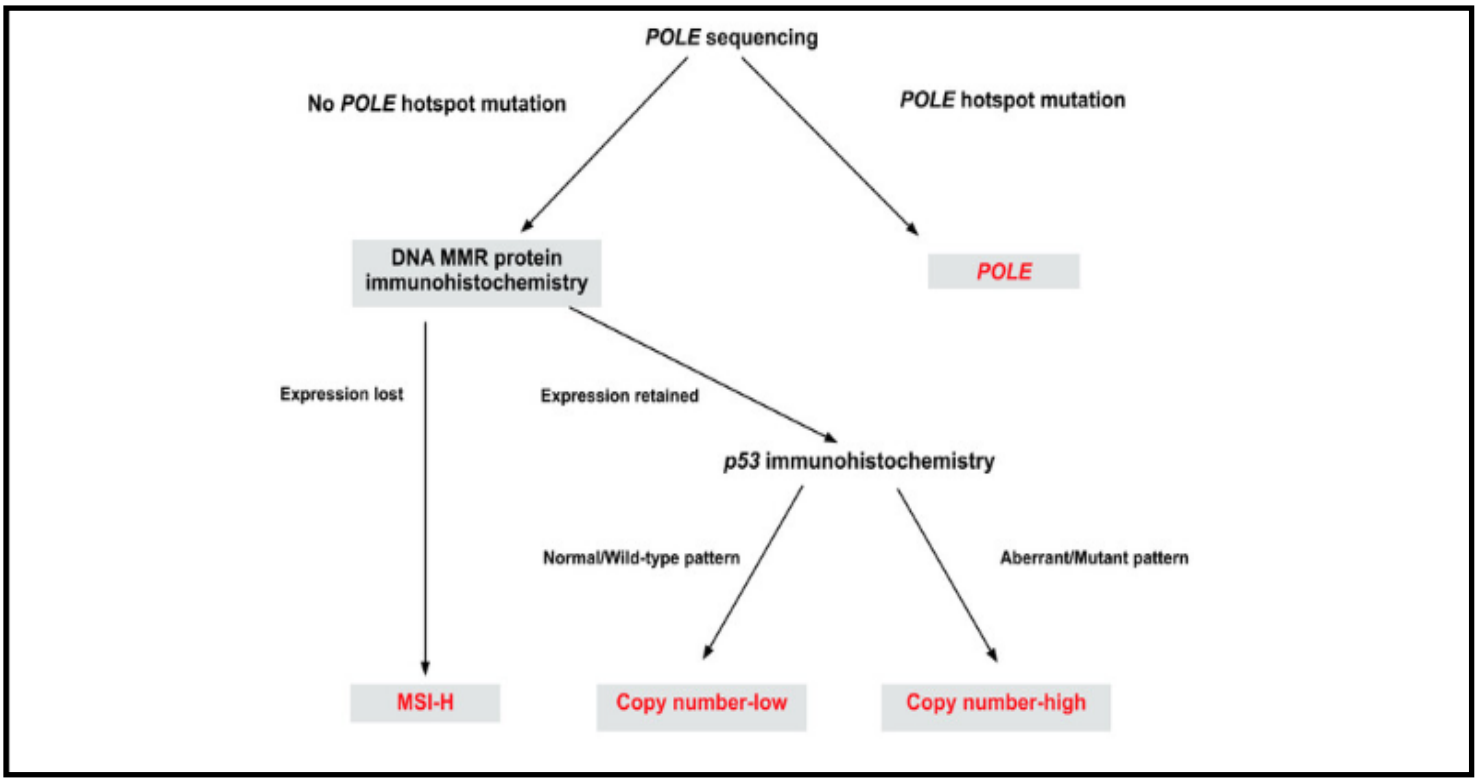
Case Number: **24010002000** Patient Name: **Priyalakshmi De Silva** Ordering Physician Name: **Dr. Mahendra Perera**

RESULTS

MISMATCH REPAIR (MMR) PATHWAY RESULTS

Assay Biomarker	Result	Interpretation
MMR Pathway Genes Status (MSH2, MSH3, MSH6, MLH1, PMS1, MLH3, PMS2)	Negative	No clinically significant variant detected in MMR pathway genes.

NCCN Guidelines for Endometrial Molecular Classification



Uterine Neoplasms, Version 1.2023, NCCN Clinical Practice Guidelines in Oncology.

VARIANTS OF UNKNOWN FUNCTIONAL/THERAPEUTIC SIGNIFICANCE (VUS)

Gene (Exon) [Transcript]	Variant details	VAF
BRCA1 (10) [NM_007294.4]	p.Asp295Gly (c.884A>G)	22.4%
ESR1 (9) [NM_001122740.2]	p.Val560Met (c.1678G>A)	47.7%

ESR1 V560M is present in 0.01% of AACR GENIE cases, with ampulla of vater carcinoma, colorectal neuroendocrine carcinoma, endometrial endometrioid adenocarcinoma, lung adenocarcinoma, and salivary gland adenoid cystic carcinoma having the greatest prevalence [MCG].

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METHODOLOGY

geneCORE somatic endometrial panel is a multibiomarker NGS assay that enables detection of variants in 38 genes relevant to Endometrial Cancer. The test utilizes AmpliSeq technology based NGS assay. DNA and RNA from FPPE samples were extracted and subjected to Next Generation Sequencing (NGS) using the Ion System. High quality nucleic acids that passed QC checks were subjected to library preparation and analysed for relevant genomic alterations in both the DNA and RNA to simultaneously detect multiple types of variants, including hotspots, single-nucleotide variants (SNVs), indels and gene fusions as mentioned below:

Hotspot genes (SNVs and short indels): AKT1, ARID1A, BRAF, BRCA1, BRCA2, CCND1, CDH1, CDKN2A, CHEK2, CTNNB1, ERBB2, ESR1, FBXW7, FGFR1, FGFR2, FGFR3, KRAS, L1CAM, MLH1, MLH3, MSH2, MSH3, MSH6, MUTYH, MYC, NRAS, NTRK1, NTRK2, NTRK3, PIK3CA, PIK3R1, PMS1, PMS2, POLD1, POLE, PTEN, RET and TP53

Gene Fusions: NTRK1, NTRK3, FGFR1, FGFR2, FGFR3 and RET

Mismatch repair genes: MSH2, MSH3, MSH6, MLH1, PMS1, MLH3, PMS2

Sequencing was performed to achieve a minimum 500X depth of coverage. The output sequences were aligned to the human reference genome hg19(GRCh37). Raw data analysis, alignments, and variant calling was done using the Torrent Variant Caller. High quality sequencing data was then analysed using the optimized ION Torrent Suite and the ION Reporter software to accurately detect rare somatic variants. The hotspots, indels and fusions were analyzed with the help of the ION Reporter Software and variants were annotated according to the American College of Medical Genetics (ACMG) and AMP guidelines. NCBI dbSNP, Catalogue of Somatic Mutations in Cancer (COSMIC), The Exome Aggregation Consortium and ClinVar as well as protein function prediction and classification algorithms FATTHM, SIFT, PolyPhen-2 and Grantham score were used for variant annotation.

For the index patient, on target was 97.06% with 91.70% target base coverage at 500X.

LIMITATIONS AND DISCLAIMER

Despite all precautions taken, the error (administrative and technical) associated with these types of molecular diagnostic tests can be as high as 1% to 2%. Rare polymorphisms may be present that could lead to false negative or false positive results. The quality of sequencing and coverage varies between regions; many factors such as homopolymers, GC-rich regions etc. influence the quality of sequencing and coverage. This may result in an occasional error in sequence reads or lack of detection of a particular genetic variant. Furthermore, A negative (wild type) result does not rule out the presence of a mutation or rearrangement resulting in targeted fusion, that may be present but below the limits of detection of this assay. Variants that have not been confirmed by an independent analysis could represent technical artifacts. Not all variants detected may be listed in the report. Inclusion of variants is dependent upon our assessment of their clinical significance. Additionally, the presence of a mutation may not be predictive of response to therapy in all patients. The selection of any potential treatment/course of action based on this report rests solely within the decision and judgment of the treating physician and patient. Decisions on patient care should be based on the independent medical judgment of the treating physician based upon all available clinical information, according to the applicable standard of care and should not be based solely on the tests and information contained in this report. Accurate interpretation of this report is dependent on provided detailed clinical history of the patient. In the event of unavailability of detailed clinical history, the lab cannot guarantee the accuracy of the interpretation. The results and interpretation are based on current knowledge and might change in the future. Some findings listed in this report may be based on pre-clinical studies or studies not in the given patient's tumor type.

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Hospital Name	: Aegle Omics (Private) Limited, Colombo
Physician Name	: Dr. Mahendra Perera
Registration On	: 04-Jul-2024 13:21
Collection On	: 02-Jul-2024 00:00
Reported On	: 08-Jul-2024 19:56
Process AT	: CORE-Gurugram
Ref ID	:
Sample Type	: FFPE Block
Report Status	: Final

MC-2256

UNIQUE PATIENT ID : 5501

TEST NAME

MSI

SPECIMEN INFORMATION

Received 01 paraffin block labelled as IN/2947 A11. Peripheral blood in EDTA collected on 02/07/2024.

CLINICAL HISTORY

High grade carcinoma.

METHODOLOGY

PCR, Fragment Analysis

RESULTS

Test Details	Results
NR-21	Stable
NR-24	Stable
BAT-25	Stable
BAT-26	Stable
MONO-27	Stable
Impression	MSI-S(MSI-Stable)

INTERPRETATION

Microsatellite instability	Remarks
MSI-H(MSI-High)	≥40% of the loci studied are unstable.
MSI-L(MSI-Low)	<40% of the loci studied are unstable.
MSI-S(MSI-Stable)	None of the loci studied are unstable.

COMMENTS

1. This test examines instability of microsatellites as per National Cancer Institute guidelines1 .
2. The mononucleotide markers are quasi-monomorphic and used to determine MSI.
3. The profiles of the normal tissue (blood) have been compared to the tumor tissue to elucidate results.
4. Results are meant to be interpreted in context of clinical findings, and other laboratory data.
5. Genetic counseling is recommended.

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Dr.Sanjay Kumar
Ph.D

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APPENDIX

Microsatellite instability (MSI) is a sign of DNA mismatch repair (MMR) deficiency, presenting as accumulation of mutations in DNA 'microsatellites' (1-9 nucleotides). The MMR system involves at least ten proteins, including MLH1, MSH2, MSH6, and PMS2 as among the most frequently mutated or epimutated (MLH1) genes in cancer 2 . MSI has recently been shown to occur at a frequency of 1-30% in most types of cancers. MSI -High indicates a tumor with instability in two or more microsatellites.

Nearly 15 % of colorectal carcinomas (CRC) display high level microsatellite instability (MSI-H) including 3% occurrence of hereditary non-polyposis colorectal cancer (HNPCC) or Lynch syndrome(LS) 3,4 . More than 90% of LS with MSI-H/L have been reported to have MMR deficiency 5 . MSI-Low (L) indicates a tumor with instability in one of five microsatellite repeats. Since instability in even a single marker can be indicative of MMR deficiency, in such cases it is recommended to use additional techniques such as immunohistochemistry (IHC) staining for mismatch repair proteins. MSI-Stable indicates a lack of microsatellite instability in a tumor.

A lack of microsatellite instability would be unusual in colorectal cancers from individuals with Lynch syndrome (HNPCC), although it does not completely exclude this possibility. Evaluation of mismatch repair deficiency by Microsatellite Instability by IHC may be helpful in this determination. This interpretation may not apply to tumors other than colon cancers. The lack of microsatellite instability does not rule out the possibility of other colon cancer-associated genetic disorders.

REFERENCES

- Murphy KM, Zhang S, Geiger T, Hafez MJ, Bacher J, Berg KD, et al. Comparison of the Microsatellite Instability Analysis System and the Bethesda Panel for the Determination of Microsatellite Instability in Colorectal Cancers. J Mol Diagn JMD. 2006 Jul; 8 (3):305–11.
- Baudrin LG, Deleuze J-F, How-Kit A. Molecular and Computational Methods for the Detection of Microsatellite Instability in Cancer. Front Oncol [Internet]. 2018 Dec 12
- Gatalica Z, Vranic S, Xiu J, Swensen J, Reddy S. High microsatellite instability (MSI-H) colorectal carcinoma: a brief review of predictive biomarkers in the era of personalized medicine. Fam Cancer. 2016; 15:405–12.
- Kašubová I, Kalman M, Jašek K, Burjanivová T, Malicherová B, Vanochová A, et al. Stratification of patients with colorectal cancer without the recorded family history. Oncol Lett. 2019 Apr; 17(4):3649–56.
- Latham A, Srinivasan P, Kemel Y, Shia J, Bandlamudi C, Mandelker D, et al. Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. J Clin Oncol Off J Am Soc Clin Oncol. 2019 Feb 1; 37(4):286–95.

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Report Status	: Final

MC-2256

UNIQUE PATIENT ID : 5501

TEST NAME

P53

SPECIMEN INFORMATION

Received one paraffin block labeled as 2947 A11.

CLINICAL HISTORY

Large pelvic cystic mass, septated with cystic & solid areas.

METHODOLOGY

Immunohistochemistry

IMMUNOHISTOCHEMISTRY STUDIES

P53 (BP53-12): Abnormal (mutant)

TECHNICAL NOTE

All immunohistochemistry markers have been evaluated in the context of appropriate positive and negative controls. A result is considered uninterpretable as a result of the type of fixative used (non 10% neutral buffered formalin), time to fixation (> 1 hour), duration of fixation (< 6 hr or > 72 hour), strong decalcification, or inappropriate staining of normal internal or external assay controls. An alternative sample for retesting is then usually recommended. These assays have not been validated on decalcified specimens.

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If you have any questions about this report or would like to have a conversation about the test results, please feel free to reach out to us at

+91 88828 99999 or **info@corediagnostics.in**

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2. The test results relate specifically to the sample received in the lab and are presumed to have been generated and transported per specific instructions given by the physicians/laboratory.
3. The reported results are for information and are subject to confirmation and interpretation by the referring doctor.
4. Some tests are referred to other laboratories to provide a wider test menu to the customer.
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