Lynch Syndrome/ HNPCC Gene Panel-Focused

Test Description

Lynch syndrome is a hereditary cancer arising from loss of function mutations in DNA mismatch repair genes, such as *MLH1*, *MSH2*, *MSH3*, *MSH6*, *PMS2*, and *EPCAM.* MolQ Lynch Syndrome panel includes next-generation sequencing of these genes for mutations and large deletions/duplications.

Patient Demographic

Name: Ms. Meenakshi Sachdeva
Sex: Female
Date of Birth/Age: 22 years
Disease: Healthy Individual

Clinician

Clinician Name: Dr Amit Verma
Medical Facility: Max Hospital
Pathologist: Not Provided

Specimen

Booking ID: 011906270350
Site: NA
Sample Type: Blood
Date of Collection: 27-06-2019
Date of Booking: 27-06-2019

CLINICAL SYNOPSIS

The index patient, Ms. Seema Sachdeva is a case of moderately differentiated endometrioid adenocarcinoma. She was found to harbor a heterozygous variation in *MLH1* gene. Her daughter is being evaluated for the same variation.

RESULTS

The same likely pathogenic variation was detected in heterozygous condition in the asymptomatic daughter of the index patient, Ms. Meenakshi Sachdeva.

Gene	Location	Variation reported in the index patient	Zygosity	Clinical condition of family member	Classification	Variation reported in family member
MLH1 (ENST00000231790.2)[1]	Exon 3	Chr3:37042544G>T (HET); c.306G>T (p.Glu102Asp)	Heterozygous	Asymptomatic	Likely Pathogenic	Present

CLINICAL CORRELATION AND VARIANT INTERPRETATION

Variant description: A heterozygous missense variation in exon 3 of the *MLH1* gene (chr3:37042544G>T; c.306G>T) that results in the amino acid substitution of Aspartic Acid for Glutamic Acid at codon 102 (p.Glu102Asp) was detected in the index patient, Ms. Seema Sachdeva (Sample ID: 218474) by NGS and was further validated by Sanger sequencing.

The same likely pathogenic variation was detected in heterozygous condition in the asymptomatic daughter of the index patient, Ms. Meenakshi Sachdeva (Figure 1). Incomplete penetrance and variable age of cancer development has been reported for Lynch Syndrome[2].

RECOMMENDATIONS

Careful correlation with clinical and investigational findings is recommended for the daughter of index case.

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APPENDIX 1: TEST METHODOLOGY

Method

Exon 3 of the *MLH1* gene was PCR-amplified and the product was sequenced using Sanger sequencing. In case of mosaicism in leucocytes, the detection limits of Sanger sequencing for presence of variation is ~12%. The sequence was aligned to available reference sequence ENST00000231790.2[1] to detect variation using variant analysis software programs. Variant classification follows the tenets of American College of Medical Genetics (ACMG) guidelines[3].

REFERENCES

1. ENSEMBL: http://www.ensembl.org
2. Kohlmann W, Gruber SB. Lynch Syndrome. 2004 Feb 5 [Updated 2018 Apr 12]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019.
3. Green R. C., et al., American College of Medical Genetics and Genomics. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med. 2013 Jul;15(7):565-74.

Figure 1: Sequence chromatogram and alignment to the reference sequence showing the variation in exon 3 of the *MLH1* gene (chr3:37042544G>T; c.306G>T; p.Glu102Asp) detected in heterozygous condition in the daughter of the index patient, Ms. Meenakshi Sachdeva.