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: Mr. Mridul Sachdeva
Sex: Male
Date of Birth/Age: 18 years
Disease: Healthy Individual

Clinician

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

Specimen

Booking ID: 011906280076
Site: NA
Sample Type: Blood
Date of Collection: 28-06-2019
Date of Booking: 28-06-2019

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 son is being evaluated for the same variation.

RESULTS

The same likely pathogenic variation was not detected in the asymptomatic son of the index patient, Mr. Mridul 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	Absent

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 not detected in the asymptomatic son of the index patient, Mr. Mridul Sachdeva (Figure 1).

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APPENDIX 1: TEST METHODOLOGY

Method

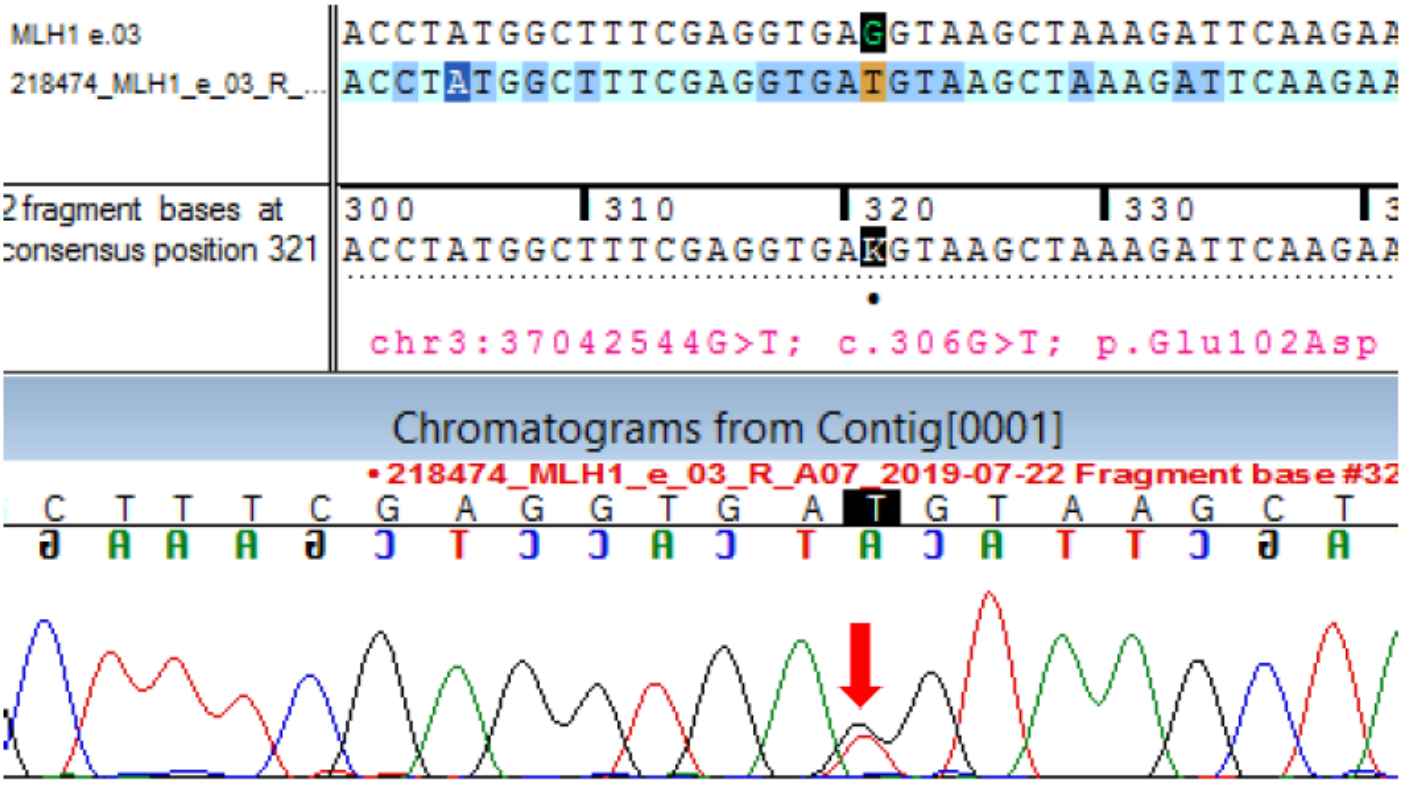
Exon 3 of the *MLH1* gene was PCR-amplified and the product was sequenced using Sanger sequencing. In case of mosaicism in leucocytes, the detection limits of Sanger sequencing for presence of variation is ~12%. The sequence was aligned to available reference sequence ENST00000231790.2[1] to detect variation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

REFERENCES

1. ENSEMBL: http://www.ensembl.org
2. 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 the index patient, Ms Seema Sachdeva (A) and not detected in the son of the index patient, Mr. Mridul Sachdeva (B).

(A) 218474-Index patient Ms. Seema Sachdeva



(B) 283182-Sibling of the index patient Mr Mridul Sachdeva