

# Lynch Syndrome/ HNPCC Gene Panel-Focused

PATIENT	REPORT DATE	BOOKING ID
Naresh Chadha	13 August 2019	#011906270369

#### **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. Naresh Chadha Sex: Male Date of Birth/Age: 55 years Disease: Healthy Individual

#### Clinician

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

#### **Specimen**

Booking ID: 011906270369 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 sibling is being evaluated for the same variation.

## **RESULTS**

The same likely pathogenic variation was detected in heterozygous condition in the asymptomatic sibling of the index patient, Mr. Naresh Chadha.

Gene	Location	Variation reported in the index patient	Zygosity	Clinical condition of family member	Classification	Variation reported in family member
MLH1 (ENST0000 0231790.2) <sup>1</sup>	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 sibling of the index patient, Mr. Naresh Chadha (Figure 1). Incomplete penetrance and variable age of cancer development has been reported for Lynch Syndrome<sup>2</sup>.

## **RECOMMENDATIONS**

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

atinda Kaus

Jatinder Kaur, PhD Head, Molecular Biology & Genomics

with

Dr. Gulshan Yadav, MD Head, Pathology



# **APPENDIX 1: TEST METHODOLOGY**

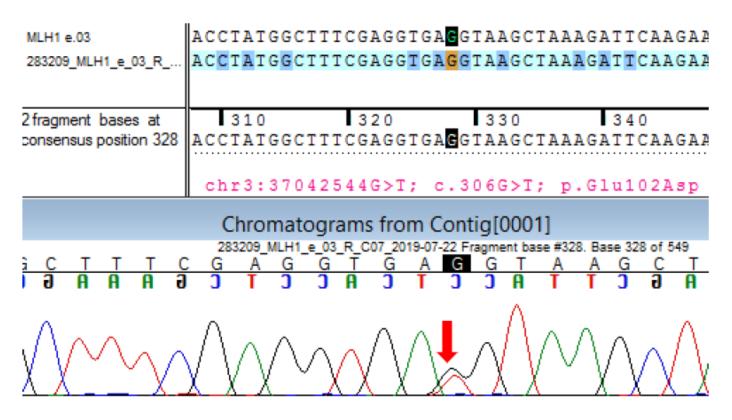
#### Method

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<sup>1</sup> to detect variation using variant analysis software programs. Variant classification follows the tenets of American College of Medical Genetics (ACMG) guidelines<sup>3</sup>.

# 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 sibling of the index patient, Mr. Naresh Chadha.



MolQ Laboratory (A Unit of Molecular Quest Healthcare Pvt. Ltd.)

Reference Laboratory: 28-29, Sector-18 (P) I Gurgaon, Haryana, 122015 I Phone 0124 - 4307906, Fax 0124 - 4278596 I Email: contact@molq.in