Germline Cancer Predisposition-Additional Family Member (Investigational) Testing

Test Description

The MolQ Germline Cancer Predisposition-Additional Family Member (Investigational) Testing analyse variant(s) observed in other family members by targeted gene Sanger sequencing.

Patient Demographic

Name: Mr Preetendra Singh
Sex: Male
Date of Birth/Age: 50 years
Disease: Asymptomatic

Clinician

Clinician Name: Dr Amit Verma
Medical Facility: Dr AV Institute of Personalized Therapy and Cancer Research (IPTCR)
Pathologist: Not Provided

Specimen

Booking ID: 012202240054
Site: NA
Sample Type: Blood
Date of Collection: 24-02-2022
Date of Booking:24-02-2022

CLINICAL SYNOPSIS

The index patient, Ms. Puneet Pawan, case of colon cancer, was found to harbor a heterozygous variant (c.2246T>C) in the *MLH1* gene. Her brother is being evaluated for the same variant.

RESULTS

Variant is detected

Gene#	Location	Variant	Zygosity	Clinical condition of family member	Variation reported in family member*
MLH1	Exon 19	chr3:37092119T>C (HET); c.2246T>C (p.Leu749Pro)	Heterozygous	? Symptomatic	Present

*The variant analysis in Sanger sequencing is based on the *MLH1* reference sequence NM_000249.3[1]. The exon number and nucleotide numbers will differ based on the reference file chosen and the database used.

CLINICAL CORRELATION AND VARIANT INTERPRETATION

Variant description: A heterozygous variant in exon 19 of the ***MLH1*** gene (**chr3:37092119T>C; c.2246T>C; p.Leu749Pro**) was detected in the index patient (Tested outside of MolQ Laboratory, Report Dated: 10th February 2022) by NGS.

The same pathogenic variant was detected in heterozygous condition in the brother of the index patient, Mr. Preetendra Singh (Figure 1).

The variant detected in the test and its significance needs to be carefully correlated with the clinical indications of the individual tested.

RECOMMENDATIONS

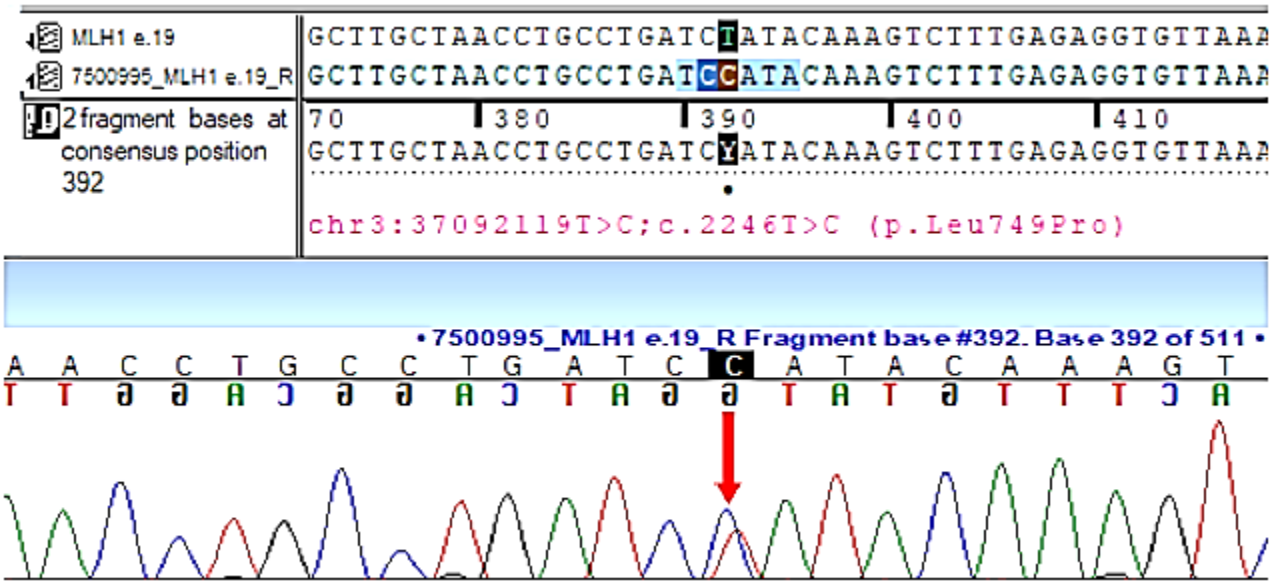
Genetic counselling is advised to discuss and interpret the significance of the results. Kindly email us at contact@molq.in for post-test counselling.

REFERENCES

1. ENSEMBL: http://www.ensembl.org.

Germline Cancer Predisposition-Additional Family Member (Investigational) Testing

Figure 1: Sequence chromatogram and alignment to the reference sequence showing the variant in exon 19 of the *MLH1* gene (chr3:37092119T>C; c.2246T>C; p.Leu749Pro) detected in heterozygous condition in the brother, Mr. Preetendra Singh.



Jatinder Kaur, PhD
Head, Molecular Biology & Genomics

Dr. Gulshan Yadav, MD
Head, Pathology

Germline Cancer Predisposition-Additional Family Member (Investigational) Testing

APPENDIX 1: TEST METHODOLOGY

METHOD

Targeted Gene Sanger Sequencing: Exon 19 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 variants are ~20%. The sequence was aligned to available reference sequence NM_000249.3[1] to detect variant using variant analysis software programs. Variant classification follows the tenets of American College of Medical Genetics (ACMG) guidelines[2].

DISCLAIMER

About 0.44% of total cases are susceptible to allele dropout/dropin phenomenon, which can lead to misdiagnosis[3].

REFERENCES

1. ENSEMBL: http://www.ensembl.org.
2. Green RC et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med. 2013, 15(7):565-74.
3. Blais J et al. Risk of Misdiagnosis Due to Allele Dropout and False-Positive PCR Artifacts in Molecular Diagnostics: Analysis of 30,769 Genotypes. J Mol Diagn. 2015, 17(5): 505-14.