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 Mayank Singh
Sex: Male
Date of Birth/Age: 27 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: 012309090104
Site: NA
Sample Type: Blood
Date of Collection:09-09-2023
Date of Booking:09-09-2023

CLINICAL SYNOPSIS

The index patient, Ms. Urmesh Lata, is suspected to be affected with carcinoma sigmoid colon with carcinoma ovary and endometrium. She was found to harbor a heterozygous pathogenic variant, c.793C>A in the *MLH1* gene. The son of the index patient is being evaluated for the same variant.

RESULTS

Variant is not detected

Gene#	Location	Variant	Zygosity	Clinical condition of family member	Variation reported in family member*
MLH1	Exon 10	chr3:g.37058999C>A; c.793C>A (HET); (p.Arg265Ser)	Heterozygous	Asymptomatic	Absent

*The variant analysis in Sanger sequencing is based on the *MLH1* reference sequence ENST00000231790.2 (GRCh37)[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 splice site proximal missense variation in exon 10 of the ***MLH1*** gene (**chr3: g.37058999C>A; c.793C>A; p.Arg265Ser**) was detected in the index patient (Sample ID: 364264; Date of report: 25th April 2020) by NGS and was further validated by Sanger sequencing.

The same pathogenic variant is not detected in the asymptomatic son of the index patient, Mr. Mayank Singh (Figure 1).

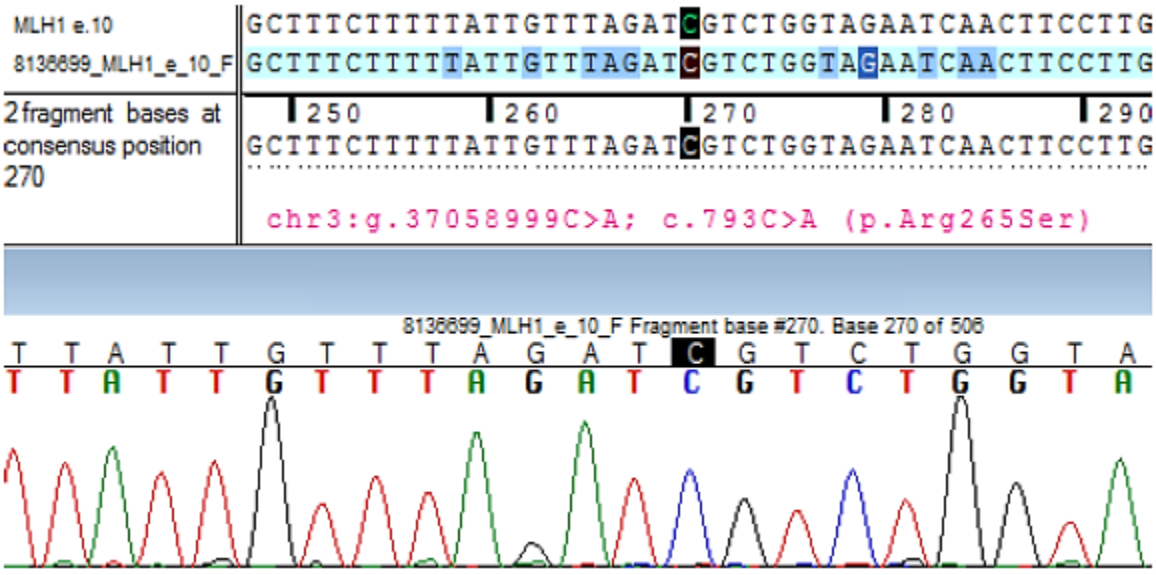
RECOMMENDATIONS

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.

Figure 1: Sequence chromatogram and alignment to the reference sequence showing the respective area in exon 10 of the *MLH1* gene (chr3:g.37058999C>A; c.793C>A (HET); p.Arg265Ser) wherein variant was not detected in the son of the index patient, Mr. Mayank Singh.



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APPENDIX 1: TEST METHODOLOGY

METHOD

Targeted gene Sanger sequencing: Genomic DNA was extracted from the blood samples and subsequently subjected to targeted PCR amplification. The amplified DNA was then subjected to bi-directional Sanger sequencing using an ABI Sanger sequencing instrument. The resulting data was analyzed using the Sequencher software. Variant classification follows the tenets of American College of Medical Genetics (ACMG) guidelines[1].

DISCLAIMER

1. This is a laboratory developed test and the development and the performance characteristics of this test was determined by the reference laboratory.
2. Please note that the tests are performed only after approval of referring/ ordering clinician/physician. Above recommendations /results should not be viewed as only source of information on which treatment or other clinical decisions are made. Clinical correlation is highly recommended.
3. The classification of variants of unknown significance can change over time and MolQ Laboratory cannot be held responsible for this. Please contact MolQ Laboratory later to inquire about any changes.
4. This sanger custom test is not a clinically validated assay for each and every primer set. No form of test can guarantee 100% accuracy. This assay is no such exception, and it has some Inherent pitfalls.
5. The PCR based assay will not amplify genic regions outside primer binding site, may not detect the exact size for the deletion or duplication which is more than 50bp.
6. Pseudogenes can present challenges during sequencing and analysis, which may impact the accuracy and interpretation of the results.
7. Though PCR is a highly sensitive and specific technique, performance may vary based on several factors including allelic dropout and preferential amplification (Chance phenomenon) causing a potential source of misdiagnosis for both dominant and recessive diseases. About 0.44% of total cases are susceptible to allele dropout phenomenon, which can lead to misdiagnosis[2].
8. Testing of affected/carrier index/proband samples parallel with test samples is highly recommended to rule out false negative/positive results.
9. The accuracy of the results assumes that samples received were correctly identified, family relationships are true and clinical diagnosis of relatives is correct.
10. In a very few cases genetic tests may not show the correct results leading to false positives and negatives, e.g., because of the quality of the sample provided to MolQ Laboratory. In case where any test provided by MolQ Laboratory fails for unforeseeable or unknown reason that cannot be influenced by MolQ Laboratory in advance, MolQ Laboratory shall not be responsible for the incomplete, potentially misleading, or even wrong result of testing if such could not be recognized by MolQ Laboratory in advance.
11. Negative results do not negate the absence of mutations that are not covered by the test.
12. The report shall be generated within turnaround time (TAT), however, such TAT may vary depending upon the complexity of test(s) requested. MolQ Laboratory under no circumstances will be liable for any delay beyond afore mentioned TAT.
13. If results obtained do not match the clinical findings, additional testing should be considered as per the referring clinician's recommendations.
14. MolQ Laboratory hereby recommends the patients and/ or guardians of the patients, as the cause may be, to take assistance of the clinician or a certified physician or doctor, to interpret the report(s) thus generated. MolQ Laboratory hereby disclaims all liability arising in connection with the report (s).

REFERENCES

1. Green RC et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med. 2013, 15(7):565-74.
2. Blais, Jonatan et al. Risk of Misdiagnosis Due to Allele Dropout and False-Positive PCR Artifacts in Molecular Diagnostics. The Journal of Molecular Diagnostics, Volume 17, Issue 5, 505 – 514.