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 Sharad Vats
Sex: Male
Date of Birth/Age: 40 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: 012303270030
Site: NA
Sample Type: Blood
Date of Collection:27-03-2023
Date of Booking:27-03-2023

CLINICAL SYNOPSIS

The index patient, Mr. Anil Sharma (Sample ID: 7752274), is a case of metastatic, small cell, neuroendocrine carcinoma, prostate. He has a family history of prostate cancer with his brother diagnosed at the age of 48 years. He was found to harbor a heterozygous pathogenic variant, c.2317del in the *PALB2* gene. His son 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*
PALB2	Exon 5	chr16:g.23629837del (GRCh38); c.2317del (HET); (p.Thr773LeufsTer78)	Heterozygous	Asymptomatic	Present

*The variant analysis in Sanger sequencing is based on the *PALB2* reference sequence ENST00000261584.8[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 single base pair deletion in exon 5 of the ***PALB2*** gene (**chr16:g.23629837del; c.2317del**) that results in a frameshift and premature truncation of the protein 78 amino acids downstream to codon 773 (**p.Thr773LeufsTer78**) was detected in the index patient (Sample ID: 7752274; Report Dated: 1st December 2022) by NGS.

The same variant is detected in heterozygous condition (Alt. Allele 46.1%) in the asymptomatic son of the index patient, Mr. Sharad Vats (Figure 1).

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

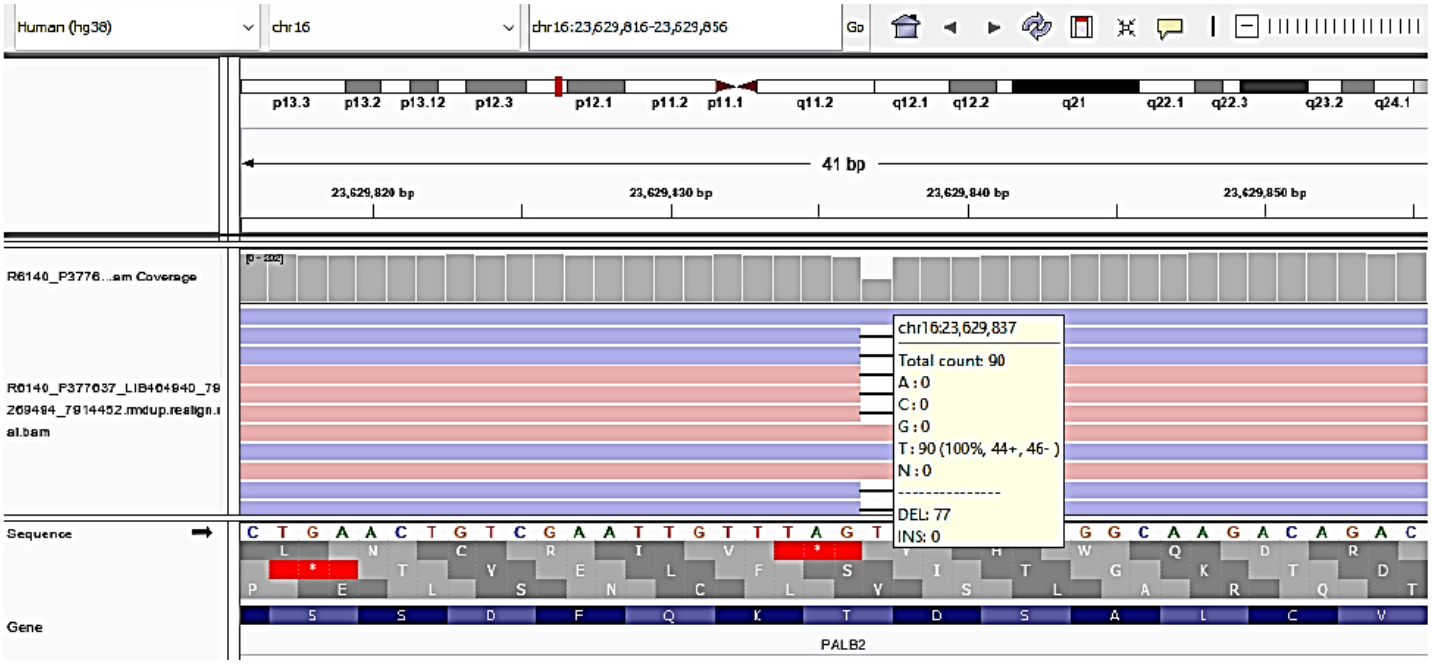
RECOMMENDATIONS

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 variant in exon 5 of the *PALB2* gene (chr16:g.23629837del; c.2317del; p.Thr773LeufsTer78) detected in heterozygous condition in the son of the index patient, Mr. Sharad Vats.



Jatinder Kaur, PhD
Head, Molecular Biology & Genomics

Dr. Gulshan Yadav, MD
Head, Pathology

APPENDIX 1: TEST METHODOLOGY

METHOD

Targeted gene sequencing by Next Generation Sequencing: Selective capture and sequencing of the protein coding regions of the genome/genes is performed using NGS platform. The sequences obtained are aligned to human reference genome (GRCh38) using BWA program and analyzed using Picard and GATK-version 3.6 to identify variants detected in the individuals tested in NGS. 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. Testing of affected/carrier index/proband samples parallel with test samples is highly recommended to rule out false negative/positive results.
5. The accuracy of the results assumes that samples received were correctly identified, family relationships are true and clinical diagnosis of relatives is correct.
6. The sensitivity of this assay to detect large deletions/duplications of >10 bp or copy number variations (CNV) is 80-90%.
7. Possibility of false positive due to presence of pseudogene cannot be ruled out by NGS methodology.
8. 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.
9. Negative results do not negate the absence of mutations that are not covered by the test.
10. 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.
11. If results obtained do not match the clinical findings, additional testing should be considered as per the referring clinician's recommendations.
12. 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).
13. **The results generated after Sanger sequencing for the variation in exon 5 of the *PALB2* gene (chr16:g.23629837del) remains inconclusive, so we have performed Next generation sequencing for the same.**

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.