Patient Name:	Dummy	**CRM ID:**	XXX
Age/DOB:	33 Years	**Sample Type:**	EDTA Whole Blood
Sex:	Female	**Collection date:**	24.02.2024
Referring Clinician:	Dr. XXX	**Receiving Date:**	26.02.2024
Test Requested:	Methylenetetrahydrofolate Reductase (MTHFR)-2 Variants(C677T,A1298C)	**Reporting Date:**	02.03.2024

MTHFR GENE MUTATION (C677T, A1298C) BY PCR, SANGER

CLINICAL DIAGNOSIS & SYMPTOMS

N/A

RESULTS

	POSITIVE
***MTHFR*: c.1298A>C (p.Glu429Ala)**	Heterozygous mutation detected
***MTHFR*: c.677C>T (p.Ala222Val)**	Heterozygous mutation detected

Result classification	**Comment**
Homozygous mutation detected	Both copies of the gene carry mutation
Heterozygous mutation detected	One copy of the gene carries mutation
Not Detected	Mutation not detected

CLINICAL SIGNIFICANCE

The mutation for MTHFR (Methyltetrahydrofolate reductase) is associated with hyperhomocysteinemia which is an independent risk factor for Stroke, Myocardial infarction, Peripheral arterial disease and venous thrombosis. Indian studies suggest that heterozygosity for MTHFR C 677T is also associated with elevated homocysteine levels. MTHFR C677T or A1298C carriers are not at increased risk for thrombosis in the absence of hyperhomocysteinemia.

Homozygous MTHFR C 677T or A1298C carriers are at increased risk for hyperhomocysteinemia if they become deficient in vitamins B6, B12 or folic acid. Hyperhomocysteinemia is a relatively weak risk factor for both venous thromboembolism and arterial thrombosis.

METHODOLOGY

Targeted sequencing and mutation analysis was performed by Polymerase Chain Reaction (PCR) followed by automated DNA sequencing of the amplicon using BigDye Terminator Chemistry on an ABI Genetic Analyzer 3500XL platform. Sequencing data were aligned to NCBI database to analyze the mutations

COMMENT

A genetic polymorphism commonly associated with severe MTHFR deficiency is defined by a C to T substitution (cytosine to thymine) at position 677 (C677T) of the MTHFR gene, which leads to the incorporation of amino acid alanine (A) instead of valine (V) at position 222 of the MTHFR protein. The altered MTHFR is known as “thermolabile MTHFR”. Homozygous and heterozygous carriers of this mutation both show reduced MTHFR activity. In particular, homozygous carriers suffer from significantly increased blood levels of homocysteine. C677T mutation in its homozygous form alone or as a compound heterozygote, which involves both C677T and an A1298C condition (where an Adenine (A) residue changes to a Cytosine (C) residue at the 1298th position) lead to the disruption of the MTHFR gene and causes a drastic reduction of the MTHFR enzyme. This in turn, leads to an elevation of Homocysteine in the blood. Homocysteine is an important substance in the blood as elevated levels of Homocysteine has been found to be the causative agent of various diseases such as; Cerebrovascular disease cerebral vein thrombosis, coronary artery disease, myocardial infarction, venous thrombosis neural tube defects leading to dementia and Alzheimer’s disease osteoporosis, diabetes, complications in pregnancy.

LIMITATIONS

- A positive result is specific for a particular MTHFR C677T & A1298C variant, diagnosis and clinicopathologic correlation is necessary in all cases.

- The sensitivity of detection for Sanger sequencing is generally recognized as being approximately 15%to20%mutantallelefrequency.

- PCR is a highly sensitive technique; common reasons for paradoxical results are contamination during specimen collection, selection of inappropriate specimen and inherent PCR inhibitors in the sample.

REFERENCES:

1. Arruda, VR, et al. The mutation Ala677. Val in the Methylene Tetrahydro Folate Reductase gene: a risk factor for arterial disease and venous thrombosis. Thrombosis and Haemostasis 77(5) (1997).
2. . Dahlback B et al. Resistance to activated protein C, the FV: Q506 allele, and venous thrombosis. Ann Hematol. 1996; 72:166-176.
3. Bagley PJ et al. Proc Natl Acad Sci U S A 1998; 95:13217- 13220.
4. Botto LD, Yang Q. 5,10-Methylenetetrahydrofolate reductase gene variants and congenital anomalies: a HuGE review. Am J Epidemiol. 2000 May 1; 151 (9): 862 – 877.

CONDITIONS OF REPORTING

- Test results released pertain to the specimen submitted .
- All test results are dependent on the quality of the sample received by the Laboratory .
- Laboratory investigations are only a tool to facilitate in arriving at a diagnosis and should be clinically correlated by the Referring Physician .
- Certain tests may require further testing at additional cost for derivation of exact value. Kindly submit request within 72 hours postreporting.
- Test results may show inter laboratory variations.
- If Sample collection date is not stated on test requisition form, the current date will be printed by default as the date of collection.
- Test results are not valid for medico legal purposes.

Disclaimer: Method given in report are only indicative and can be changed depending upon type of machine and kit available at time of testing.

Not all tests at all locations are under NABL scope. Availability of tests under NABL scope varies from lab to lab.

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2. It is to be presumed that the tests performed pertain to the specimen/sample attributed to the Customer's name or identification. It is presumed that the verification particulars have been cleared out by the customer or his/her representation at the point of generation of said specimen / sample. It is hereby clarified that the reports furnished are restricted solely to the given specimen only.

3. It is to be noted that variations in results may occur between different laboratories and over time, even for the same parameter for the same Customer. The assays are performed and conducted in accordance with standard procedures, and the reported outcomes are contingent on the specific individual assay methods and equipment(s) used, as well as the quality of the received specimen.

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