Methylenetetrahydrofolate Reductase (MTHFR) 2 Variants

ARUP test code 0055655

MTHFR PCR Specimen: Whole Blood

MTHFR Mutation: c.665C>T
- Heterozygous *

MTHFR Mutation: c.1286A>C
- Negative

MTHFR Interpretation

Indication for testing: Determine genetic contribution to hyperhomocysteinemia.

Heterozygous MTHFR c.665C>T: One copy of the MTHFR variant c.665C>T (previously designated C677T) was detected; the c.1286A>C (previously designated A1298C) variant was not identified. The common variant is present in 12 percent of African Americans, 35 percent of Caucasians, and 50 percent of Hispanic individuals. Although MTHFR enzyme activity may be mildly reduced, this genotype is not predicted to have clinical significance.

This result has been reviewed and approved by Rong Mao, M.D.
Background Information: Methylenetetrahydrofolate Reductase (MTHFR) 2 Variants

Characteristics: Variants in the MTHFR gene may reduce enzyme activity contributing to hyperhomocysteinemia. Although hyperhomocysteinemia was previously reported to be a risk factor for many conditions, especially venous thrombosis and cardiovascular disease, recent meta-analysis casts doubt on whether lifelong moderate homocysteine elevation has an effect on cardiovascular disease. The American College of Medical Genetics Practice Guidelines indicate that individuals with elevated homocysteine and two copies of the c.665C>T variant have an odds ratio of 1.27 for venous thromboembolism. Thus, they recommend MTHFR genotyping not be ordered as part of a routine evaluation for recurrent pregnancy loss or thrombophilia due to questionable clinical significance.

Incidence: The allele frequency of the c.665C>T variant is 0.35 in European Caucasians, 0.5 in Hispanics, and 0.12 in African Americans.

Inheritance: Autosomal recessive; two copies of the c.665C>T variant may be a contributing factor to hyperhomocysteinemia. Variants Tested: c.665C>T(p.Ala222Val) and c.1286A>C(p.Glu429Ala). (legacy names C677T and A1298C, respectively).

Clinical Sensitivity: Undefined; hyperhomocysteinemia is caused by genetic, physiologic and environmental factors. MTHFR variants are only one contributing factor.

Methodology: Polymerase chain reaction (PCR) and fluorescence monitoring.

Analytical Sensitivity & Specificity: 99 percent.

Limitations: Only two MTHFR gene variants (c.665C>T and c.1286A>C) are tested. Diagnostic errors can occur due to rare sequence variations.

Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement C: aruplab.com/CS

VERIFIED/REPORTED DATES

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