ARUP LABORATORIES
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Tracy I. George, MD, Chief Medical Officer

Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	3/16/1981
Gender:	Female
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	01/01/2017 12:34

Methylenetetrahydrofolate Reductase (MTHFR) 2 Variants

ARUP test code 0055655

MTHFR PCR Specimen	Whole Blood
MTHFR Mutation: c.665C>T	**Homozygous** *
MTHFR Mutation: c.1286A>C	Negative
MTHFR Interpretation	See Note

Indication for testing: Determine genetic contribution to hyperhomocysteinemia.

Homozygous MTHFR c.665C>T: Two copies of the MTHFR gene variant c.665C>T (previously designated C677T) were detected; the c.1286A>C (previously designated A1298C) variant was not detected. Homozygosity for the common c.665C>T variant is observed in 12 percent of Caucasians and 25 percent of individuals of Hispanic ancestry. Since this genotype may be associated with mild to moderate increased plasma homocysteine levels, fasting total plasma homocysteine levels should be measured. Genetic consultation is recommended.

This result has been reviewed and approved by [redacted]

H=High, L=Low, *=Abnormal, C=Critical

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 thromobophilia 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

Procedure	Accession	Collected	Received	Verified/Reported
MTHFR PCR Specimen	20-057-400719	2/25/2020 11:10:00 AM	2/27/2020 9:07:58 PM	3/1/2020 8:07:00 PM
MTHFR Mutation: c.665C>T	20-057-400719	2/25/2020 11:10:00 AM	2/27/2020 9:07:58 PM	3/1/2020 8:07:00 PM
MTHFR Mutation: c.1286A>C	20-057-400719	2/25/2020 11:10:00 AM	2/27/2020 9:07:58 PM	3/1/2020 8:07:00 PM
MTHFR Interpretation	20-057-400719	2/25/2020 11:10:00 AM	2/27/2020 9:07:58 PM	3/1/2020 8:07:00 PM

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical