



TEST UPDATE

FROM YOUR LABORATORY SERVICES PROVIDER

MTHFR Mutation Analysis for Hyperhomocysteinemia, Increased Risk of Coronary Artery Disease, and Thrombophilia Is Now Available at PAML

Marcy L. Hoffmann, Ph.D., Technical Director, Molecular Diagnostic Laboratory

Elevated plasma homocysteine levels (hyperhomocysteinemia) have been linked to an increased risk for coronary artery disease (CAD) and thrombophilia. Hyperhomocysteinemia can be attributed to a variety of causes such as folate or vitamin B₆/B₁₂ deficiency, kidney disease, hypothyroidism, psoriasis, certain medications, or genetic predisposition.

The most commonly known genetic risk factors for elevated plasma homocysteine levels are mutations in the gene methylenetetrahydrofolate reductase (MTHFR). The MTHFR gene encodes for the MTHFR protein, an enzyme involved in folate and homocysteine metabolism. A specific mutation or combination of mutations in the MTHFR gene is associated with reduced enzyme activity and elevated homocysteine levels. One mutation - a C-to-T transition at nucleotide position 677 (C677T) of the gene - causes a substitution of a valine for an alanine in the protein, a thermolabile variant of the MTHFR enzyme. A second mutation, an A-to-C transition at nucleotide position 1298 (A1298C) of the gene, causes a substitution of a glutamic acid for an alanine in the protein. An individual with two copies the C677T mutation (homozygosity) or one copy each of the C677T and A1298C mutations (compound heterozygosity) may have elevated homocysteine levels and an increased risk for CAD or thrombophilia.

PAML now offers a molecular-based test for the detection of the C677T and A1298C mutations.

References

Kang, et al. *Am J Hum Genet* 48:536-545, 1991.
Klerk et al. *JAMA* 288:2023-2031,2002.
Varga et al. *Circulation* 111:289-293, 2005.
Weisberg et al. *Atherosclerosis* 156:409-415,2001

Test Information

DESCRIPTION	MTHFR MUTATIONS MTHFR C677T and A1298C, INVADER
METHOD	Invader
ORDER CODE	MTINV
CPT CODE	83891, 83892 X 2, 83896 X 2, 83912
SAMPLE	3 mL EDTA whole blood (lavender-top tubes). Due to the sensitivity of this test, submit the entire specimen in the original collection tube. Store and transport at room temperature. Do not freeze sample.
COMMENTS	Minimum amount: 1 mL or one full EDTA microtainer Other acceptable samples: sodium citrate or ACD whole blood (blue or yellow tube). Unacceptable conditions: heparinized whole blood, serum, grossly hemolyzed or frozen samples, samples not in original collection tubes, over 5 days old, or in leaking containers. Stability: 72 hours at room temperature, 5 days refrigerated, unstable frozen.
SCHEDULE	Weekly
TURNAROUND	2-8 days
RANGES	

Fast Facts

Indications for MTHFR Mutation Analysis:

- ▶ Patients with hyperhomocysteinemia of unknown cause.
- ▶ Patients with a family history of hyperhomocysteinemia due to MTHFR mutations
- ▶ Patients with early onset atherosclerosis or venous thrombosis (not to be used as a first line test for inherited thrombophilia).

The C677T and A1298C mutations are common in the general population:

- ▶ Homozygosity for the C677T mutation ranges from 5-15% in Caucasians of European descent, depending on the population studied.
- ▶ Homozygosity for the C677T mutation is estimated to occur in 1.4% of the African-American population.
- ▶ Homozygosity for the A1298C mutation occurs in approximately 10% of the general population.

For more information, please contact Client Services or see us on the Web at



Provided for the clients of

PATHOLOGY ASSOCIATES MEDICAL LABORATORIES • PACLAB NETWORK LABORATORIES
TRI-CITIES LABORATORY TREASURE VALLEY LABORATORY ALPHA MEDICAL LABORATORY

For more information, please contact your local representative.