**MTHFR Mutation (Methylene-tetrahydrofolate Reductase) (C677T)**

**Test Code:** 2040

**Department:** Molecular Genetics

**Test Synonyms:**
- Homocysteine, DNA Test;
- Methylene Tetrahydrofolate Reductase
- MTHFR (C677T)

**CPT Code(s):**
- 83890
- 83892
- 83894
- 83898

**Background:**
The MTHFR gene provides instructions for making an enzyme called methylenetetrahydrofolate reductase. This enzyme plays a role in processing amino acids, the building blocks of proteins. Methylene tetrahydrofolate reductase is important for a chemical reaction involving forms of the B-vitamin folate (also called folic acid or vitamin B9). Specifically, this enzyme converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate. This reaction is required for the multistep process that converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds.

Elevated levels of homocysteine have been shown to be an independent graded risk factor for the development of both arteriosclerotic vascular disease (coronary artery disease, stroke, and peripheral vascular disease) and venous thrombosis. The remethylation of homocysteine to methionine requires the carbon donor 5-methyltetrahydrofolate, formed by the action of the enzyme methylenetetrahydrofolate reductase (MTHFR). Hereditary deficiencies of MTHFR are thus a common cause of hyperhomocysteinemia. A common thermolabile variant of MTHFR with decreased enzyme activity has recently been found in a large proportion of both normal (5%) and vascular disease (17%) patients. This common thermolabile MTHFR is a significant risk factor for coronary artery disease. The genetic mutation responsible for this thermolability, a C to T substitution at MTHFR nucleotide 677 (changing alanine to valine), has been found to be extremely prevalent with an allele frequency of ~36% in the normal population. Approximately 10% of the population is therefore homozygous for this mutation which predisposes to significant elevations in plasma homocysteine levels. This prevalent MTHFR mutation may therefore be the most common genetic deficit predisposing to vascular disease.

Changes in the MTHFR gene have been associated with health conditions such as homocystinuria, anencephaly, and spina bifida.

**Clinical Utility:**
The MTHFR mutation assay is clinically indicated for the evaluation of:
- Patients with early onset or significant family histories of atherosclerotic vascular disease - coronary artery disease, cerebrovascular disease, or peripheral vascular disease.
- Patients with clinically confirmed venous thromboembolism, especially those with recurring episodes or those with a strong family history.
- Patients with known or suspected hyperhomocysteinemia.
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- Family members of individuals with hyperhomocysteinemia or *MTHFR* gene mutations.
- Patients with ambiguous or variable homocysteine levels.
- At the present time, this test should **not** be used to screen asymptomatic individuals for predisposition to vascular disease.

**Methodology:**
Direct detection (by PCR) of a common thermolabile variant of the *MTHFR* gene at nucleotide 677. The mutation in the gene predisposes to increased homocysteine levels and vascular disease.

The presence of the mutation at nucleotide 677 of the *MTHFR* gene is directly determined by PCR amplification of peripheral blood leukocyte DNA followed by digestion with a restriction enzyme. The mutant and wild type alleles are easily distinguished on a size-separating gel.

**Specimen Requirements:**
- **Blood**: 6.0 mL in EDTA (purple-top) or ACD (yellow-top) tube

**A REQUISITION FORM MUST ACCOMPANY ALL SAMPLES.** Please include detailed clinical information, including ethnicity, clinical history, and family history.

**Test Performed (Days):**
Weekly

**Turn Around Time:**
7 – 10 Days

**Shipment Sensitivity Requirements:**
Keep specimen cold during transit, but do not ship on dry ice. Please use the cold pack provided in the KDL shipping kit. Contact Client Services at (855) 535-1522 for shipping kits and instructions. Ship the specimen overnight express, using the FedEx priority overnight label provided. The specimen must arrive at the lab no more than 24 hours after collection.

**References:**