Summary: The MTHFR 677C>T mutation is the most common single nucleotide polymorphism in 5,10-methylenetetrahydrofolate reductase (NADPH) leading to a theremolabile variant of protein (p.A222V). MTHFR is a key enzyme in the metabolism of homocysteine during amino acid synthesis. Mutations in the MTHFR gene have been linked to the build up of homocysteine.

Indications for MTHFR:p.A222V (677C>T) Thermolabile Test

- Hyperhomocysteinemia
- History of venous thromboembolism, coronary artery disease, and/or stroke
- History of pregnancy complications including neural tube defects, stillbirths, and/or recurrent pregnancy loss
- Individuals with other genetic hypercoagulabilites (e.g. factor V Leiden)

Specimen Requirements: 4 ml of whole blood in an EDTA Vacutainer (lavender top) or buccal swab, and completed requisition form.

Turnaround time: 2-5 business days. Urgent testing with one business day turn-around can be provided at 25% additional cost.

Interfering substances: Bone marrow recipients, or recipients of blood transfusion within the past 6 months, may show the genotype of the donor. In such patients, buccal swab specimen is preferred for testing. Additionally, substances that may inhibit nucleic acid amplification (e.g. some lipsticks) may prohibit us from performing the test.

Hyperhomocysteinemia is a widely recognized risk factor for coronary artery disease, venous thrombosis, and stroke. It is also involved in the pathogenesis of neural tube defects, stillbirths, and recurrent pregnancy loss. The leading cause of hyperhomocysteinemia is folate deficiency. Other determinants include insufficient B12 intake, impaired renal function, and genetic variations including those in the MTHFR gene. Folate supplementation can correct for most causes of hyperhomocysteinemia.

Mutations in the MTHFR gene have been reported as causes of hyperhomocysteinemia. The most common MTHFR mutation, 677C>T, is present in the homozygous state in 5-40% of the general world population (Wilkens 2004). In homozygous individuals, this results in a thermolabile variant of the enzyme with decreased activity. Individuals homozygous for the 677C>T mutation are predisposed to developing hyperhomocysteinemia, particularly when deficient in folate. The frequency of 677C>T homozygosity is increased in individuals with coronary artery disease (to 17%), arterial disease (to 19%), and venous thromboembolism (to 11%).