



Methylenetetrahydrofolate Reductase (MTHFR) Thermolabile Variant (677C>T)

Elevated homocysteine level has been identified as a risk factor for thrombosis and vascular disease. Homocysteine is normally metabolized by remethylation to methionine or by transsulfuration to cysteine. Elevated levels of homocysteine may occur because of inherited disorders which alter the enzyme activity of metabolism or because of nutritional deficiencies of vitamin B12, folate, or vitamin B6 that are necessary as cofactors. One inherited disorder that affects metabolism involves a sequence change in a single nucleotide of the enzyme methylenetetrahydrofolate reductase (MTHFR) resulting in a thermolabile variant. The thermolabile variant has been identified as a 677C>T transition. Nine different variants have been identified. The thermolabile variant MTHFR is the most common inherited disorder of folic acid metabolism.

Homocysteine levels appear to be very mildly elevated in population studies of individuals homozygous for the 677T allele, although these elevations are not the very high levels identified in some other disorders of methionine metabolism associated with vascular disease. Relative risk levels for thrombosis appear to be slightly elevated in homozygous 677T individuals. However, there is no convincing evidence that heterozygosity by itself contributes to increased risk for thrombosis. The 677T allele is present at a gene frequency of 15-20%, so 35-45% of randomly sampled individuals will be heterozygous for this marker.

This assay is performed using the Invader® platform from Third Wave Technologies (<http://www.twt.com>) which applies two hybridization probes for normal and mutant sequences to non-amplified DNA isolated from peripheral blood white cells. The formation of distinctive structures between probe and patient DNA in the presence of the target sequence allows enzymatic digestion and release of a fluorescent marker. A customized report is generated which takes into account family history (if provided) and the inheritance pattern of this disorder

Turnaround Time: 5-7 business days.

Specimen Requirements: See Oncology/Genetics Specimen Handling Protocol or Molecular Diagnostics Genetics Requisition Form.

Informed Consent: It is the responsibility of the referring health care professional to obtain proper informed consent from the patient for genetic testing. Test results are released only to the primary referring physician and/or genetic counselor. The laboratory report contains information that may be useful for genetic counseling of the patient and/or family members, although adjunct use of an experienced genetic counselor or medical geneticist may be beneficial for this genetic disorder.