

Genetic Thrombotic Risk Factors

The diagnosis of the etiologic causes of thrombosis can be challenging. Thrombotic disease is typically characterized by the presence of any number of acquired and *genetic* factors. Factor V Leiden, Prothrombin 20210A and the MTHFR C677T mutations represent a majority of the identifiable *genetic* causes of thrombotic disease and should be considered in the diagnosis and thrombotic risk assessment in patients with a personal or familial history of recurrent thrombosis.

Genotypic analysis for the Factor V Leiden and Prothrombin 20210A mutations is performed on chromosomal DNA isolated from whole blood using real-time polymerase chain reaction (RT-PCR) methodology by CPAL. Test runs are batched once a week and results reported out the same day as *Wildtype (Normal)*, *Heterozygous* or *Homozygous* for each allele. The MTHFR C677T genotyping is performed at Quest Diagnostics Nichols Institute in Chantilly, Virginia by the Invader Assay/Signal amplification methodology. Test results are reported within 5-7 days as *Negative*, *Heterozygous-Positive* or *Homozygous-Positive* for each allele.

Factor V Leiden

The Factor V Leiden allele is represented by a single nucleotide change in the normal DNA sequence of either one or both copies (alleles) for G1691A of the factor V gene. This mutation renders the factor V protein resistant to cleavage by activated protein C. Heterozygotes for the Factor V Leiden allele are at 7 fold increased relative risk for thrombosis, homozygotes are at 80-fold increased relative risk.

Prothrombin 20210A

The prothrombin 20210A allele is represented by a mutation in the 3'untranslated region of the prothrombin (factor II) gene. This mutation leads to increased prothrombin levels and increased relative risk for thrombosis. Individuals heterozygous for the prothrombin 20210A mutation are reported to be at 2.8 fold increased risk over individuals who are homozygous-positive.

MTHFR C677T Mutations

The methylenetetrahydrofolate reductase (MTHFR) C677T mutation is a specific mutation in the MTHFR gene that renders its associated enzyme less active than the normal version of the enzyme. This enzyme is integral in homocysteine metabolism and the MTHFR C677T mutation is associated with increased risk for thrombosis, hyperhomocystinemia and possibly neural tube defects.

SAMPLES

Blood: Draw 3 mL blood in a lavender top tube containing potassium EDTA.

INDICATIONS FOR TESTING

- History of recurrent thrombotic events
- Family history of recurrent thrombosis or a known mutation in a relative
- Certain maternal/fetal complications
- Prior to certain high risk situations, if there is a personal or family history of thrombosis.
- Thrombosis at a young age (<45 years).

CLINICAL BENEFITS OF TESTING

Identification of a mutation:

- Establishes an etiology for an individual's thrombosis
- Identifies individuals and families at increased risk for future thrombosis
- Can contribute towards prevention of thrombosis by influencing patient management (e.g. avoidance of oral contraceptive in homozygotes, prolonged aggressive anticoagulation after major surgery)