Unipath
SPECIALTY LABORATORY Ltd.

THROMBOPHILIC POLYMORPHISM PANEL (Factor V Leiden G1691A, PROTHOMBIN G20210A, MTHFR C677T, MTHFR A1298C)

Department of Molecular Biology

INHERITED THROMBOPHILIA:

Factor V Leiden (FVL), Factor II (Prothrombin) G20210A mutation, and methylene-tetrahydrofolate reductase (MTHFR C677T & MTHFR A1298C) mutation are the three most common inherited disorders of blood clotting that predispose individuals to venous thrombosis.

FACTOR V LEIDEN (G1691A) MUTATION

This mutation is associated with resistance to activated protein C. Individuals who are heterozygous for FVL have a 2-8 fold risk of developing venous thrombosis. When coupled with oral contraceptive use or estrogen therapy, heterozygotes have an estimated 30-fold risk of venous thrombosis. Individuals who are homozygous for FVL have a 50-100 fold risk of developing venous thrombosis. Up to 20% of individuals with venous thrombosis have FVL. The frequency of heterozygous FVL in individuals of Caucasian descent is about 5% and about 1% in individuals of African-American descent.

PROTHOMBIN G20210 MUTATION

The Prothrombin G20210A mutation is the second-most common cause of inherited thrombosis and results in elevated levels of prothrombin which mildly increases the risk of venous thrombosis. An increased risk of cerebral vein thrombosis and of myocardial infarctions in women less than 50 years of age may also be associated with this mutation, especially in conjunction with other environmental risk factors. The G20210A mutation results in approximately 30% higher levels of prothrombin, which can cause a mild hypercoagulable condition associated with deep vein thrombosis.

Clinical Utility: Heterozygosity for the G20210A mutation results in a 3 to 10-fold higher risk of thrombosis. Combined heterozygosity for Factor V Leiden and Prothrombin G20210A results in up to a 20-fold increased risk of thrombosis. The population frequency of Prothrombin G20210A mutation is between 1% and 4% in Caucasians and about 0.2% in African-Americans.

MTHFR GENE MUTATION (C677T & A1298C)

The MTHFR C677T mutation lowers the levels of the functional enzyme MTHFR resulting in higher levels of homocysteine. Hyperhomocysteinemia is associated with an increased risk of arterial and venous thrombosis. Homozygosity of the C677T mutation results in elevated homocysteine levels and may mildly increase the risk of arterial and venous thrombosis.

Clinical Utility: Individuals with both the MTHFR C677T mutation and the Factor V Leiden mutation may be at a significantly greater risk of developing venous thrombosis than those with either mutation alone. The homozygous MTHFR C677T mutation is quite common, occurring in about 5-15% of individuals of European, Middle Eastern and Asian descent. The frequency of the homozygous mutation in individuals of African-American descent is approximately 1-2%. Compound heterozygosity of C677T and A1298C occurs in approximately 20% of the Caucasian population and is also a risk for increased homocysteine levels. In addition, homozygosity of C677T and compound heterozygosity of C677T and A1298C result in a 2-3 fold risk of folate-sensitive neural tube defects.

INDICATIONS OF TESTING:

- Evaluation of all patients with venous thrombosis, coronary artery disease, and/or stroke of unknown etiology.
- Evaluation of asymptomatic individuals with a family history of venous thrombosis.
- Evaluation of individuals with family members known to have Factor V Leiden, Prothombin G2010A, MTHFR C677T or MTHFR A1298C mutations.
- Evaluation of women with recurrent pregnancy loss, unexplained severe pre-eclampsia, placental abruption, fetal growth retardation, still birth or neural tube defects in offspring.

METHEDOLOGY OF TESTING:

Allelic Discrimination by TaqMan Assay (Applied Biosystems) is used to determine the genotype at each of the above loci. End-products are analyzed using the ABI 7500 Real-Time PCR System for genotype detection.

SENSITIVITY OF ASSAY:

This test methodology detects >99% of instances of these mutations.

SPECIMEN REQUIREMENT:

At least 2ml whole blood in lavender top (EDTA) tube. Label tube with patient's name, age and date of collection. Phlebotomist must initial tube to verify patient's identity.

TAT AND ORDERING INFORMATION:

TEST NAME	METHOD	SPECIMEN	REPORTING TIME
FACTOR V LEIDEN MUTATION DETECTION	REAL TIME PCR	EDTA WB	48 Hours
MTHFR GENE MUTATION DETECTION	REAL TIME PCR	EDTA WB	48 Hours
PROTHOMBIN GENE MUTATION	REAL TIME PCR	EDTA WB	48 Hours
THROMBOPHILLIA PCR PANEL*	REAL TIME PCR	EDTA WB	48 Hours

* Thrombophillia PCR panel includes Factor V Leiden G1691A Mutation, MTHFR C677T & A1298C Mutations and Prothombin G20210A Mutation.

RESULTS:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

ISO 9001 International Standard Certification LIC No QAC/R91/3585
NABL M-0520
Unipath SPECIALTY LABORATORY Ltd.
Unipath specialty Laboratories ltd
102 Sanoma Plaza, B/S JMC House, Opp. Parimal Garden, Ellis Bridge, Ahmedabad – 380006
Phone No -079-49006800/31
Mail to: unipathmdx@gmail.com