Prothrombin Gene Mutation (G20210A)

Versiti offers targeted testing for the prothrombin variant *F2* c.*97G>A (prothrombin gene mutation, legacy nomenclature G20210A)

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common yet complex disorder. Risk factors involved in the pathogenesis of this disorder include inherited thrombophilias that are caused by loss-of-function of anticoagulant proteins, gain-of-function of procoagulants, or defects in the fibrinolytic pathways. These inherited risk factors, together with acquired risk factors, predispose an individual to thrombosis. Not all individuals with a genetic predisposition to thrombosis will develop VTE; the relative risk for thrombosis may be influenced by the specific variant present, whether the variant(s) is heterozygous, compound heterozygous or homozygous, the concomitance of other pathogenic variants, a family history of DVT, as well as the presence of other inherited and/or acquired risk factors. Identifying individuals who have an increased genetic susceptibility for VTE may assist providers in establishing an individualized risk assessment, which in some cases may guide management decisions, assist with the identification of affected family members, and allow for accurate genetic recurrence risk assessment.

Conversion of prothrombin to thrombin is a central event in fibrin clot formation and platelet activation. The F2 c.*97G>A variant in the 3' untranslated region of the prothrombin gene leads to increased concentration of prothrombin in circulation. This variant is associated with an increased risk increase for venous thromboembolism, a risk which is further increased by coexisting genetic thrombophilias, acquired hypercoagulable states, and circumstantial risk factors such as obesity, immobilization, age, surgery or other medical conditions.

Indications for testing:

- Evaluation of individuals with thrombosis or a family history of thrombosis
- Evaluation of carriers of the prothrombin variant F2 c.*97G>A ,where identification of the risk allele changes clinical management

Informed Consent

It is recommended that healthcare providers obtain informed consent from the patient when genetic testing is ordered, consistent with any applicable state laws and regulations, documenting that the patient has been advised of and understands the indications for and implications of the genetic test. If needed, an informed consent form for Versiti Hematology Genetics testing can be found at http://www.versiti.org/hg under forms.

Test method:

Gene amplification followed by detection of wild type, heterozygous or homozygous prothrombin gene variant (*F2* c.*97G>A) with sequence-specific fluorescent resonance energy transfer (FRET) hybridization probes.

Assay sensitivity and limitations:

Specificity and sensitivity for detection of the *F2* c.*97G>A (G20210A) variant is > 99%. Specificity may be affected by variants in the PCR priming sites.

Reporting of Results

Wild type (normal) sequence at the F2 97 position will be interpreted as negative. Abnormal results will be interpreted as heterozygous or homozygous.

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Specimen requirements:

5 mL Whole blood (EDTA tube, lavender top), 3-4 Buccal swabs, or ≥1ug of DNA at ≥50ng/uL of High Quality DNA.

SHIP

Shipping requirements:

Ship on an ice pack or at room temperature. Protect from freezing. Place the specimen and the requisition into plastic bags and seal. Insert into a Styrofoam container, seal and place into a sturdy cardboard box, and tape securely. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Client Services/Diagnostic Laboratory
Versiti
638 N. 18th Street
Milwaukee, WI 53233

ORDER

Required forms:

Please complete all pages of the requisition form.

CPT Codes/Billing/Turnaround time:

Order Code: 1024

CPT Code: For CPT code information, visit the Versiti.org online catalog.

Turnaround Time: 3-6 days

References:

1. Gohil R, Peck G, Sharma P. The genetics of venous thromboembolism. A meta-analysis involving approximately 120,000 cases and 180,000 controls. Thromb Haemost. 2009 Aug;102(2):360-70. doi: 10.1160/TH09-01-0013. PMID: 19652888.
2. Mannucci PM, Franchini M. Classic thrombophilic gene variants. Thromb Haemost. 2015 Nov;114(5):885-9. doi: 10.1160/TH15-02-0141. Epub 2015 May 28. PMID: 26018405.
3. Poort SR, Rosendaal FR, Reitsma PH, Bertina RM. A common genetic variation in the 3'-untranslated region of the prothrombin gene is associated with elevated plasma prothrombin levels and an increase in venous thrombosis. Blood. 1996 Nov 15;88(10):3698-703. PMID: 8916933.

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