



Molecular Diagnostic Laboratory
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Prothrombin Mutation Analysis

Prothrombin (F2) point mutation G20210A

Indications for Molecular Testing

- Family history of venous thromboembolism (VTE)
- Unprovoked thrombotic event at age of <45
- Women with multiple stillbirths or spontaneous abortions

Testing Methodology

Screening utilizes polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) techniques to detect the Prothrombin point mutation (G20210A). A nucleotide change from G to A at position 20210 on the Prothrombin Gene is detected using a mutagenic primer, which changes the adjacent normal sequence of the gene in the PCR product. The primer change in the presence of the mutation in the prothrombin gene, creates a second *Hind* III digestion site. (PCR is utilized pursuant to a license agreement with Roche Molecular Systems, Inc.)

Interpretation of DNA analysis

Prothrombin (coagulation factor II) is the precursor of thrombin, which participates as a serine protease in the coagulation cascade. The Pro G-20210-A mutation is present in 1-2% of the general Caucasian population and has been associated with an increased risk of venous thrombosis similar to that of factor V Leiden (FVL). For individuals presenting with venous thromboembolism (VTE), Pro G-20210-A occurs in 6-8% of those of all ages. About 10% of FVL carriers with first VTE will also have the prothrombin variant. In addition, Pro G-20210-A has been associated with myocardial infarction in young women, cerebral vein thrombosis in oral contraceptive users, preeclampsia and pregnancy complications and infarctions at other sites. The relative risk for thrombosis in the Pro G-20210-A heterozygous state (AG) is increased by a factor of 2.8. Patients with both FVL and this F2 mutation have a 20-fold increased risk for recurrent VTE.

Specimen Requirements

Peripheral blood--1 lavender-top (EDTA) tube. Invert several times to mix blood. **Blood Spot Cards**--one 10mm punch from a spotted and dried FTA[®] Card (cat# WB 120208, Whatman[®] Bioscience Ltd.). Forward card, enclosed in envelope or plastic, at ambient temperature. **Buccal Swabs**--Please contact Barnes-Jewish Molecular Diagnostics lab at 314-454-8685 for details. Do not freeze. Forward at ambient temperature to:

Molecular Diagnostic Laboratory
Barnes-Jewish Hospital North, Room 2445
Mail Stop 90-28-372
216 South Kingshighway
St. Louis, MO 63110

Clinical information must be provided with specimen referral in order to correctly interpret test results.

Current Pricing

Contact Lab Customer Service for current pricing 314 362-1470.
CPT codes: 83907, 83890, 83898, 83892, 83894, 83912

Degen SJF, Davie EW. Nucleotide Sequence of the Gene for Human Prothrombin. *Biochemistry* 1987;26:6165-6177

Poort SR, Rosendaal FR, Reitsma PH, and Bertina MB. 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* 15 November 1996;88(10): 3698-3703

Reich L, Bower M, Key N. Role of the geneticist in testing and counseling for inherited thrombophilia. *Genetics IN Medicine* May/June 2003; 5(3):133-143