



Prothrombin (Factor II) 20210 G→A Polymorphism Detection by PCR

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PAML AND SHMC ARE NOW OFFERING a polymerase chain reaction (PCR)-based test to detect the prothrombin 20210 G→A polymorphism, a common genetic risk factor for venous thromboembolic disease.

The prothrombin 20210 G→A polymorphism causes elevated plasma prothrombin levels. This increased prothrombin level is associated with increased tendency toward coagulation and venous thrombosis.¹ On a worldwide basis, the prevalence of this polymorphism varies greatly with ethnic origin. Prevalence within Caucasian populations ranges from 1% to 3%, although it is very uncommon in individuals of Asian or African descent. For those patients with a personal and family history of venous thromboembolic disease, the prevalence of the prothrombin 20210 G→A polymorphism reportedly ranges up to 20%.

Not all individuals heterozygous for the prothrombin 20210 A allele will develop thrombosis, although they have a 3-7 fold increased risk compared to individuals without the polymorphism. Homozygotes have been described but are very uncommon. The risk of thromboembolic disease is further increased in those patients who are also carriers of Factor V Leiden² or who have other inherited abnormalities predisposing to thrombosis.

The prothrombin 20210 G→A polymorphism is a single base mutation (guanine to adenine transition) in the 3'-untranslated region of the prothrombin gene.¹ The mechanism whereby this polymorphism results in increased prothrombin levels is unknown. The laboratory diagnosis for the presence of the prothrombin 20210 A allele relies completely on DNA analysis. In fact, this mutation is the first example of a genetic risk factor for venous thrombosis that cannot be reliably diagnosed by standard functional or immunological hemostatic tests.³

The prothrombin 20210 G→A polymorphism should be evaluated in patients for whom testing is undertaken to identify other risk factors for venothrombotic disease, including activated protein C resistance (Factor V Leiden), and deficiencies of protein S, C and antithrombin.

After isolation of DNA from patient cells, the prothrombin 20210 A allele is identified by PCR using DNA sequences specific for the normal and abnormal gene. In normal individuals no 20210 A allele is detected. Heterozygotes express one normal and one abnormal gene and homozygotes, although rarely encountered, express two abnormal genes.

References

1. **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. **88**:3698-3703.
2. **Margaglione M, Brancaccio V, Giuliani N, D'Andrea G, Cappucci G, Iannaccone L, Vecchione G, Grandone E, Di Minno G.** Increased risk for venous thrombosis in carriers of the prothrombin G→A gene variant. *Ann Intern Med* 1998. **129**:89-93.
3. **Bertina RM.** Factor V Leiden and other coagulation factor mutations affecting thrombotic risk. *Clin Chem* 1997. **43**(9):1678-1683.

Test Information

DESCRIPTION **PROTHROMBIN 20210 BY PCR**

METHOD PCR

WORKPAR PTPCR

CPT CODE 83890, 83894, 83901×2, 83912

SPECIMEN 5 mL EDTA whole blood (lavender-top tube). Store and transport at room temperature. If delayed more than 72 hours, store and transport refrigerated. Do not freeze specimen.

COMMENTS *Minimum amount:* 1 mL or a full EDTA microtainer.

Other acceptable specimens: sodium citrate or ACD whole blood (blue or yellow-top tube).

Unacceptable conditions: heparinized whole blood, serum, grossly hemolyzed, frozen specimens, or specimens over 5 days old. Also, specimens in leaking containers.

Stability: 72 hours at room temperature, 5 days refrigerated, unstable frozen.

SCHEDULE Variable

TURNAROUND Variable

RANGES PT 20210 by PCR Negative
Interpretation
Comment
Comment

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