Plasminogen Activator Inhibitor-1 (SERPINE1) Genotyping

Last Literature Review: December 2020 Last Update: December 2023

The plasminogen activator inhibitor 1 (PAI-1) protein, which is encoded by the *SERPINE1* gene, is involved in hemostasis, or the normal blood clotting pathway. The 4G/5G polymorphism in the promoter region of this gene is a major determinant of PAI-1 expression. Individuals who are heterozygous or homozygous for the 4G allele may have an increased risk for venous thromboembolism (VTE), especially when there are other risk factors for thrombophilia.[1,2,3] This genotype may also confer an increased risk for myocardial infarction (MI).[4]

Featured ARUP Testing

Plasminogen Activator Inhibitor-1, PAI-1 (SERPINE1) Genotyping 2004980

Method: Polymerase Chain Reaction (PCR) Fluorescence Monitoring

- Use to screen for genetic susceptibility for VTE or MI in individuals with a personal or family history of thrombotic events
- Aids in risk/benefit assessment for preventive or therapeutic interventions for VTE or MI

Genetics

Gene/Variants

The 4G/5G polymorphism is located at c.-817dupG (from start of translation) in the promoter region of the *SERPINE1* gene.

Inheritance

Autosomal dominant

Frequency of the 4G allele varies by ethnicity:

- White: 0.52
- Hispanic: 0.38
- African American: 0.13-0.28

Test Interpretation

Sensitivity/Specificity

Analytic sensitivity/specificity: 99%

Clinical sensitivity: unknown

Results

Genotype	Allele(s) detected	Clinical significance
5G/5G genotype	2 copies of 5G allele	Not at increased risk of VTE and MI Does not exclude other genetic or nongenetic causes of thrombosis
4G/5G genotype	1 copy of 4G allele	Associated with increased risk of VTE and MI, particularly in individuals with other thrombotic risk factors
4G/4G genotype	2 copies of 4G allele detected	

Limitations

- Variants other than the 4G/5G polymorphism in the *SERPINE1* gene are not evaluated.

- Test does not evaluate risk for complete PAI-1 deficiency.
- Diagnostic errors can occur due to rare sequence variations.

References

1. Sundquist K, Wang X, Svensson PJ, et al. Plasminogen activator inhibitor-1 4G/5G polymorphism, factor V Leiden, prothrombin mutations and the risk of VTE recurrence. *Thromb Haemost*. 2015;114(6):1156-1164.

2. Wang J, Wang C, Chen N, et al. Association between the plasminogen activator inhibitor-1 4G/5G polymorphism and risk of venous thromboembolism: a meta-analysis. *Thromb Res*. 2014;134(6):1241-1248.

3. Zhang Q, Jin Y, Li X, et al. Plasminogen activator inhibitor-1 (PAI-1) 4G/5G promoter polymorphisms and risk of venous thromboembolism - a meta-analysis and systematic review. *Vasa*. 2020;49(2):141-146.

4. Song C, Burgess S, Eicher JD, et al. Causal effect of plasminogen activator inhibitor type 1 on coronary heart disease. *J Am Heart Assoc*. 2017;6(6):e004918.

Related Information

Venous Thromboembolism
Fibrinolytic Disorders
Hereditary Thrombophilia - Hypercoagulability

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