



TECHNICAL NOTICE

SOUTH BEND MEDICAL FOUNDATION

Plasminogen Activator Inhibitor-1 (PAI-1) 4G/5G Polymorphism Detection

Effective Date: April 1, 2010

Performing Department: Molecular Pathology

Use: Evaluation of patients who have a history of unexplained arterial thrombosis, particularly starting at a relatively young age.

Clinical Significance: Plasminogen activator inhibitor-1 (PAI-1) is the major inhibitor of tissue type plasminogen activator (tPA), which is necessary for appropriate fibrinolysis (clot lysis). In fibrinolysis, tPA converts plasminogen to plasmin, and plasmin degrades fibrin. Reduced fibrinolytic capacity due to increased plasma PAI-1 levels is postulated to play an important role in the delicate balance between fibrin formation and fibrin degradation. Too much PAI-1 prevents fibrinolysis and promotes thrombophilia, while too little PAI-1 promotes bleeding. Recently, a common functional deletion/insertion polymorphism (4G/5G) in the promoter of the PAI-1 gene located 675 base pairs upstream from its transcription start site was reported to result in elevated expression of the gene and increased plasma levels of PAI-1. Individuals with the 4G allele may have an increased plasma PAI-1 concentration compared to those with the 5G allele.

When the identified PAI-1 genotype is associated with an increased level of PAI-1 activity, this may predispose the patient to an increased risk for arterial thrombotic events such as myocardial infarction. Consultation with a hematologist is suggested for such patients as an adjunct to management of their cardiovascular disease.

Limitations of test: It is possible that a spontaneous polymorphism within the amplified sequence will render an erroneous genotype or an inability to amplify the patient's DNA; however, such polymorphisms are likely to be rare. Other mutations within the PAI-1 gene or other genes could result in a similar clinical phenotype but will not be detected by this method.

Reference Range:

- a. 4G/4G genotype: This is associated with increased level of PAI-1 activity.
- b. 4G/5G genotype: This is associated with mildly increased level of PAI-1 activity.
- c. 5G/5G genotype: This is not associated with increased level of PAI-1 activity.

Specimen and Collection Requirement:

Specimen Type: Whole Blood

Primary : 1 Whole Blood EDTA 5 (3) mL Ambient – 3 Day(s), Refrigerated -14 Day(s)

Alternate Type: Whole Blood ACD 5 (3) mL Ambient - 3 Day(s), Refrigerated -14 Day(s)

5 (3) mL Ambient - 3 Day(s), Refrigerated – 14 Day(s)

Preferred Volume: 5.0 mL

Minimum Volume: 3.0 mL

Collection: Routine venipuncture

Stability: Ambient – 3 Day(s), Refrigerated -14 Day(s)

Testing Schedule: Thursday morning

Order: Test #: 36160.....CPT: 83891-3Z; 83896-3Zx2; 83898-3Z; 83912-3Z

Please direct any questions, or comments regarding this notice to Dr. Bobbie C. Sutton (bsutton@sbmf.org), Deborah H. Sun, Ph.D. (dsun@sbmf.org), or Sally Cornwall (scornwall@sbmf.org) or call South Bend Medical Foundation, (574) 234-4176 or (800) 544-0925.

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530 N. Lafayette Boulevard • South Bend, IN 46601 • (574) 234-4176

Elkhart (574) 293-8441 • (800) 544-0925

Robert J. Tomec, M.D. • *Medical Director*