

Factor XIII (*F13A1*) V34L Variant

TO HELP ASSESS THROMBOTIC RISK IN CAUCASIANS

Clinical Background

- Factor XIII (FXIII), or fibrin stabilizing factor, is an enzyme that cross-links fibrin during clot formation.
- FXIII circulates in the plasma as tetramer of two catalytic A subunits and two carrier B subunits.
- FXIII is activated by thrombin and calcium into factor XIIIa, which is involved in wound repair, cytoskeletal remodeling, phagocytosis, placental attachment, and inflammatory processes.
- The *F13A1* gene encodes the FXIII A subunit. A common *F13A1* sequence variant, V34L, increases the rate of FXIII activation by thrombin, resulting in prematurely depleted FXIIIa.
- V34L also affects the structure of the cross-linked fibrin clot. At high fibrinogen concentrations, fibrin clots of V34L carriers have looser structure and thicker fibers and are degraded faster by fibrinolysis, thus offering protection against thrombotic events.

Epidemiology

Allele frequency for the V34L sequence variant is 0.27 in Caucasians, 0.17 in Africans, 0.01 in Asians, and 0.29 in American Indians.

Genetics

- Autosomal dominant inheritance.
- The V34L sequence variant results from a G>T substitution at position 103 in the *F13A1* gene, which is located on chromosome 6p24-25.
- In Caucasians, V34L is associated with a reduced risk for pulmonary embolism and deep-vein thrombosis, a modest reduction in risk for MI, and a slight protective effect against CAD.
- A single study suggests V34L may also be associated with idiopathic spontaneous subconjunctival hemorrhage (SSH); however, this finding has not been confirmed.
- Gene-environment and gene-gene interactions may influence the protective effect of V34L:
 - In a UK Asian population, insulin resistance negated the protective effect of V34L.
 - A variant allele (4G/4G) of the plasminogen activator inhibitor 1 gene (*PAI-1*) may also reduce the protective effect of V34L.

Indications for Ordering

- To assess genetic susceptibility for VTE, MI, or CAD in Caucasians with a personal or family history of thrombotic events.
- Risk-benefit assessment for preventive or therapeutic interventions for VTE, MI, or CAD in Caucasians.

Contraindication

Fetal testing.

Interpretation

- Negative: The *F13A1* V34L sequence variant was not detected.
- Heterozygous: One copy of the V34L sequence variant was detected; this is associated with a reduced risk for VTE, MI, and CAD in Caucasian individuals.
- Homozygous: Two copies of the V34L sequence variant were detected; this is associated with a reduced risk for VTE, MI, and CAD in Caucasian individuals.
- Results of V34L genotyping should be interpreted in the context of other laboratory tests and clinical information. The protective effect of the V34L variant has only been established in Caucasian populations and may be altered by other genetic and non-genetic factors not assessed by this assay.
- The presence of the V34L variant in the sample is associated with decreased/reduced risk for VTE, MI, and CAD.

Methodology

- Polymerase chain reaction (PCR) and fluorescence monitoring to detect the *F13A1* variant c.103G>T (p.Val34Leu).
- Analytical sensitivity and specificity are 99 percent.

Limitations

- Mutations in the *F13A1* or *F13B* genes, other than the V34L sequence variant, are not evaluated.
- Rare diagnostic errors may occur due to primer- or probe-site mutations.

Related Tests

- [Thrombotic Risk, DNA Panel \(0056200\)](#)
- [Thrombotic Risk, Inherited Etiologies \(Most Common\) with Reflex to Factor V Leiden \(0030133\)](#)
- [Thrombotic Risk \(Acquired\) Reflexive Panel \(0030268\)](#)

References

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- Parmeggiani F, et al. Prevalence of factor XIII Val34Leu polymorphism in patients affected by spontaneous subconjunctival hemorrhage. *Am J Ophthalmol* 2004;38:481–4.
- Shafey M, et al. Factor XIII Val34Leu variant and the risk of myocardial infarction. A meta-analysis. *Thromb Haemost* 2007;97:635–41.
- Voko Z, et al. Factor XIII Val34Leu variant protects against coronary artery disease. *Thromb Haemost* 2007;97:458–63.
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Test Information

2003220

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.