Factor XIII (*F13A1*) V34L Variant for Thrombosis Risk Assessment

Indications for Ordering

- Assessment of genetic susceptibility for pulmonary embolism and deep vein thrombosis (VTE), myocardial infarction (MI), or coronary artery disease (CAD) in the White population with a personal or family history of thrombotic events
- Assessment of risk/benefit for preventive or therapeutic interventions for VTE, MI, or CAD in White individuals

Test Description

Polymerase chain reaction (PCR) and fluorescence monitoring

Tests to Consider

Primary test

Factor XIII (*F13A1*) V34L Variant 2003220
- Assess genetic risk for thrombosis
- Risk-benefit assessment for preventive or therapeutic interventions for VTE, MI, or CAD in White individuals

Related tests

Thrombotic Risk, Inherited Etiologies (Most Common) with Reflex to Factor V Leiden 0030133
- Acceptable screening panel for the most common inherited thrombophilias

Thrombotic Risk, DNA Panel 0056200
- Acceptable panel to detect the two most common inherited thrombophilias (prothrombin related and factor V Leiden related)

Thrombotic Risk, Inherited Etiologies (Uncommon) 0030177
- Acceptable panel to screen for uncommon inherited thrombophilias

Thrombotic Risk Reflexive Panel 2006385
- Panel to evaluate for inherited and acquired thrombophilias

Disease Overview

Prevalence

Allele frequency by ethnicity for V34L sequence variant
- White: 0.27
- African American: 0.17
- American Indian: 0.29
- Asian: 0.01

Clinical importance

- *F13A1* gene encodes the factor XIII (FXIII) A subunit
- Functions of *F13A1* sequence variant V34L
  - Increases the rate of FXIII activation by thrombin, resulting in prematurely depleted FXIIIa
  - Affects the structure of the cross-linked fibrin clot
- At high fibrinogen concentrations, fibrin clots of V34L carriers have a looser structure and thicker fibers, and are degraded faster by fibrinolysis
  - Offers protection against thrombotic events

Genetics

Gene: *F13A1* V34L variant

Inheritance: autosomal dominant

Variants

- V34L variant in White individuals confer:
  - Reduced risk for VTE
  - Modest reduction in risk for MI and a slight protective effect against CAD
  - Gene-environment and gene-gene interactions may influence the protective effect of V34L
- Variant allele (4G/4G) of the plasminogen activator inhibitor 1 gene (*SERPINE1*) may also reduce the protective effect of V34L
- Insulin resistance negated the protective effect of V34L in a UK Asian population

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity: varies by ethnicity
- Analytical sensitivity and specificity: 99%

Results

Positive: one or two copies of the V34L sequence variant detected
- Variant associated with a reduced risk for VTE, MI, and CAD in White individuals

Limitations

- Variants in the *F13A1* or *F13B* genes, other than the V34L sequence variant, are not evaluated
- Diagnostic errors can occur due to rare sequence variations
- The protective effect of the V34L sequence variant has not been established for ethnicities other than White individuals and may be altered by other genetic and nongenetic factors not assessed by this test