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 Caucasians with a personal or family history of thrombotic events
- Assessment of risk/benefit for preventive or therapeutic interventions for VTE, MI, or CAD in Caucasians

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 Caucasians

Related tests

Thrombotic Risk, Inherited Etiologies (Most Common) with Reflex to Factor V Leiden 0030133
- Acceptable panel to detect 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

Disease Overview

Prevalence

- Allele frequency for V34L sequence variant
  - Caucasians – 0.27
  - Africans – 0.17
  - Asians – 0.01
  - American Indians – 0.29

Clinical importance

- *F13A1* gene encodes the 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

Muations

- V34L variant in Caucasians confers
  - 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 – 1 or 2 copies of the V34L sequence variant detected
- Variant associated with a reduced risk for VTE, MI, and CAD in Caucasian individuals

Limitations

- Variants 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 variants
- The protective effect of the V34L variant has only been established in Caucasian populations and may be altered by other genetic and nongenetic factors not assessed by this test