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
Mutations
- 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.