

## Factor V Leiden (F5) R506Q Variant

Factor V Leiden (FVL) thrombophilia is a blood-clotting disorder caused by an inherited genetic variant, c.1601G>A; p.Arg534Gln in the Factor 5 (F5) gene that may result in abnormal blood clots that can block blood vessels (venous thromboembolism [VTE]). Individuals with FVL thrombophilia have a higher risk of developing deep venous thrombosis (DVT), which occurs most often in the legs. However, DVTs can occur in other areas of the body, including the brain, eyes, liver, and kidneys.

### DISEASE OVERVIEW

#### Prevalence

Most common genetic risk factor for VTE

- Heterozygosity for R506Q
- Caucasians – 5%
- Hispanics – 2%
- African-Americans – 1%
- Asians – 0.5%
- Homozygosity for R506Q – 1/1,500 Caucasians

#### Risk Estimates

- Lifetime risk of VTE
  - Heterozygotes – 10%
  - Homozygotes – 80%
- Risk of thrombosis among individuals with FVL is impacted by
  - Coexisting genetic thrombophilic disorders (eg, factor II G20210A variant, protein C deficiency, homocystinemia)
  - Acquired thrombophilic disorders (eg, malignancy, hyperhomocysteinemia, high factor VIII levels)
  - Nongenetic risk factors (eg, pregnancy, oral contraceptive use, HRT, selective estrogen-receptor modulators, travel, immobilization, central venous catheters, surgery, transplantation, advanced age)

### GENETICS

#### Variant

Factor V (F5) c.1601G>A; p.Arg534Gln. Legacy nomenclature R506Q (1691G>A).

#### Inheritance

Semidominant; both heterozygotes and homozygotes are at increased risk for VTE.

#### Penetrance

Lifetime risk of VTE is 10 percent for heterozygotes and 80 percent for homozygotes.

### TEST INTERPRETATION

#### TESTS TO CONSIDER

##### Factor V Leiden (F5) R506Q Mutation 0097720

Method: Polymerase Chain Reaction/Fluorescence Monitoring

- Order for individuals at risk for VTE when results will impact clinical management.
- Results of F5 genotyping can be accurately determined for individuals on oral anticoagulant and standard heparin therapy.

#### Testing Strategy

- FVL testing is recommended in individuals with
  - One unprovoked VTE, particularly before age 50
  - Recurrent VTE
  - VTE in unusual locations
  - Personal history of VTE and one family member with VTE before age 50 or two or more family members with VTE
  - Individuals with low activated protein C (APC) resistance activity
- Consider FVL testing in any individual whose sibling is homozygous for FVL or specifically in females who are
  - Smokers <50 years of age with history of acute myocardial infarction
  - Planning pregnancy and have a relative with unprovoked VTE or VTE linked to contraceptive use or pregnancy
  - Planning pregnancy or HRT and have a first degree relative with VTE who is carrier of FVL or factor II variant
  - Planning pregnancy and have a previous unprovoked VTE
- Contraindications for FVL testing:

## Sensitivity/Specificity

Analytical sensitivity/specificity – 99.9%

## Limitations

- *F5* gene variants, other than R506Q, are not evaluated by this assay.
- Results of *F5* genotyping can be accurately determined for individuals on oral anticoagulant and standard heparin therapy.
- Rare diagnostic errors may occur due to primer-site variants.
- Not recommended for
  - Population screening and testing of asymptomatic minors for FVL
  - Routine testing for individuals with a personal or family history of arterial thrombotic disorders
  - Exceptions may include young female smokers who have experienced myocardial infarction or individuals <50 years with acute arterial thrombosis in the absence of other risk factors

## REFERENCES

Kujovich J. [Factor V Leiden Thrombophilia](#). In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews, University of Washington, 1993-2018. Seattle, WA [Updated: Jan 2018; Accessed: Feb 2019]

Zhang S, Taylor AK, Huang X, Luo B, Spector EB, Fang P, Richards S, ACMG Laboratory Quality Assurance Committee. [Venous thromboembolism laboratory testing \(factor V Leiden and factor II c.\\*97G>A\), 2018 update: a technical standard of the American College of Medical Genetics and Genomics \(ACMG\)](#). Genet Med. 2018; 20(12): 1489-1498. PubMed

## RELATED INFORMATION

[Hypercoagulable States - Thrombophilia](#)

[Deep Vein Thrombosis - Pulmonary Embolism](#)

## RELATED TESTS

[APC Resistance Profile 0030127](#)

Method: Electromagnetic Mechanical Clot Detection

[APC Resistance Profile with Reflex to Factor V Leiden 0030192](#)

Method: Electromagnetic Mechanical Clot Detection/Polymerase Chain Reaction/Fluorescence Monitoring

[Thrombotic Risk, DNA Panel 0056200](#)

Method: Polymerase Chain Reaction/Fluorescence Monitoring

[Thrombotic Risk, Inherited Etiologies \(Most Common\) with Reflex to Factor V Leiden 0030133](#)

Method: Electromagnetic Clot Detection/Quantitative Enzymatic/Polymerase Chain Reaction/Fluorescence Monitoring

[Factor V, R2 Mutation Detection by PCR 2014248](#)

Method: Polymerase Chain Reaction

- Asymptomatic adult family members of individuals known to have a FVL variant
- Adults with VTE provoked by major transient risk factors
- Adult with unprovoked VTE while on long-term anticoagulation
- Individuals with arterial thrombosis
- Infants and children with asymptomatic central venous catheter-related thrombosis
- Women with unexplained pregnancy loss
- Routine testing of asymptomatic minors for FVL
- Routine testing during pregnancy or prior to the use of oral contraceptives or hormone replacement therapy
- Appropriate testing is customized based on the patient's personal and family history. See ARUP Consult<sup>®</sup> topic, [Hypercoagulable States](#), for more information.

See [Related Tests](#)