

# Factor V Leiden (F5) R506Q Variant

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Factor V Leiden (FVL) thrombophilia is a blood-clotting disorder caused by an inherited genetic variant, c.1601G>A; p.Arg534Gln (also known as R506Q) in the coagulation factor V (*F5*) gene, that increases the risk of abnormal clotting and venous thromboembolism (VTE). Individuals with FVL thrombophilia are at greater risk of developing deep vein thrombosis (DVT), which occurs most often in the legs. However, DVT can occur in other areas of the body, including the brain, eyes, liver, and kidneys.

## Testing Strategy

Testing for FVL is recommended<sup>1</sup> for individuals with any of the following criteria when results will affect patient management:

- 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
- Low activated protein C (APC) resistance activity

Testing for FVL can be considered<sup>1</sup> for individuals who:

- Have a sibling homozygous for FVL
- Are pregnant or plan to become pregnant and have a first-degree relative with unprovoked VTE or VTE linked to contraceptive use or pregnancy
- Are pregnant, plan to become pregnant, or plan to use estrogen-containing oral contraceptives or hormone replacement therapy and have a first-degree relative with VTE who carries FVL
- Plan to become pregnant and have a previous unprovoked VTE
- Are female smokers <50 years of age and have a history of acute myocardial infarction

Testing for FVL is currently not recommended in other clinical contexts, such as history of fetal loss or other pregnancy complications, family or personal history of arterial thrombosis, or population screening, particularly of asymptomatic minors.<sup>1</sup>

For detailed clinical recommendations for FVL, refer to [the American College of Medical Genetics and Genomics' 2018 Technical Standard](#).<sup>1</sup>

For more on the recommended testing for inherited thrombophilia, see the [Hereditary Thrombophilia](#) Consult topic.

## Disease Overview

### Prevalence

Most common genetic risk factor for VTE

- Heterozygosity for FVL by ethnicity
  - White: 5%
  - Hispanic: 2%
  - Black/African American: 1%
  - Asian: 0.5%
- Homozygosity for FVL: 1/1,500 White individuals

## Featured ARUP Testing

### [Factor V Leiden \(F5\) R506Q Mutation 0097720](#)

**Method:** Polymerase Chain Reaction (PCR)  
Fluorescence Monitoring

- Use to identify 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.

See [Testing Strategy](#)

## 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

### Gene

Coagulation factor V (*F5*)

### Variant

c.1601G>A; p.Arg534Gln; legacy nomenclature is R506Q (1691G>A).

### Inheritance

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

## Test Interpretation

### Sensitivity/Specificity

Analytic sensitivity/specificity: 99.9%

### Limitations

- *F5* gene variants other than FVL (c.1601G>A) 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.

### References

1. Zhang S, Taylor AK, Huang X, et al. [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.

## Additional Resources

Kujovich JL. [Factor V Leiden thrombophilia](#). In: Adam MP, Ardinger HH, Pagon RA, et al, eds. *GeneReviews*. University of Washington, Seattle. Updated Jan 2018; accessed Nov 2021.

## Related Information

[Hereditary Thrombophilia - Hypercoagulability](#)  
[Venous Thromboembolism](#)

