

## **Factor V Leiden Mutation Detection by PCR**

## **Test Update**

May 27, 2005

### **Overview**

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PathGroup Labs is now offering a polymerase chain reaction (PCR)-based test to detect the most common hereditary defect predisposing to venothromboembolic disease, *Factor V Leiden*.

Factor V Leiden is the name given to the mutation in the coagulation Factor V gene that is the most common cause of inherited predisposition to thrombosis (1). Factor V Leiden occurs in 3%-5% of the general population and in 20%-40% of patients with venous thromboembolic disease (2). In contrast, abnormalities of protein C, protein S and antithrombin III are identified in approximately 5% of patients with thrombotic disease. Individuals who are heterozygous for the Factor V Leiden defect have a 5-10 fold increased risk of thrombosis compared to the general public, while homozygotes have a 50-100 fold increased risk (3).

Factor V Leiden is a single base mutation in the gene for coagulation Factor V (4). This results in a substitution of glutamic acid for an arginine at amino acid 506 in the Factor V protein molecule. Because this is a normal cleavage site for activated protein C to inactivate Factor V, the net effect of the substitution is relative increased Factor V activity with increased coagulation. The biological effect of

Factor V Leiden is relative resistance to activated protein C, the basis of assays for activated protein C resistance (APCR), an alternative means of diagnosing of this hypercoagulable state.

Nearly all activated protein C resistance as diagnosed by APCR assays is due to Factor V Leiden. APCR testing cannot distinguish between heterozygotes and homozygotes with Factor V Leiden, and since treatment may differ for the two genotypes, it is appropriate to test all patients with a low APCR ratio (i.e., increased APC resistance) for the Factor V Leiden mutation. Some physicians prefer to use DNA based testing initially and will order Factor V Leiden by PCR in all patients with suspected inherited hypercoagulable states instead of APCR.

After isolation of DNA from patient cells, Factor V Leiden is identified by PCR using a specific pair of Hybridization Probes for the normal and mutated (abnormal) Factor V gene. In normal individuals, no Factor V Leiden (mutated) allele is detected. Heterozygotes express one normal and one abnormal allele, and homozygotes express two abnormal alleles.

### **Clinical Utility**

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- Venous thromboembolism
- Pulmonary embolism
- Recurrent miscarriages
- Other Thrombotic problems

### **Method**

Real-Time Polymerase Chain Reaction (PCR)

### **Specimen Collection & Storage**

3-5 ml EDTA whole blood (lavender-top tube). Store and transport at room temperature. If delayed more than 72 hours, store and transport refrigerated. Do not freeze specimen.

### **Reference Ranges**

Mutation not detected

### **Turnaround Time**

3-5 days

### **References**

1. Price, D.T. and Ridker, P.M. Factor V Leiden mutation and the risks for thromboembolic disease: a clinical perspective. *Ann Intern Med*, 1997. **127**(10): p. 895-903.
2. Dahlback, B., Inherited thrombophilia: resistance to activated protein C as a pathogenic factor of venous thromboembolism. *Blood*, 1995. **85**(3): p. 607-14.
3. Rosendaal, F.R., et al., High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistance). *Blood*, 1995. **85**(6): p. 1504-8.
4. Bertina, R.M., et al., Mutation in blood coagulation factor V associated with resistance to activated protein C. *Nature*, 1994. **369**(6475): p. 64-7.