Factor V Leiden

The diagnosis of the etiologic causes of thrombophilia can be challenging. Thrombotic disease is typically characterized by the presence of any number of acquired and genetic risk factors. The Factor V Leiden allele represents a majority of identifiable genetic causes of thrombotic disease and should be considered in the diagnosis and thrombotic risk assessment in patients with a personal or familial history of recurrent thrombosis. The Factor V Leiden is typically present in 5-10% of the population. In one study of local interest, 7.9% of the South Central Pennsylvania population was identified as having the Factor V Leiden allele.

The Factor V Leiden assay allows the detection and genotyping of a single point mutation (G to A at position 1691) of the human Factor V gene (Factor V Leiden mutation) from DNA isolated from human whole peripheral blood. The test is performed on the LightCycler instrument utilizing real-time polymerase chain reaction (PCR) for the amplification of Factor V DNA recovered from clinical specimens and fluorogenic target-specific hybridization for the detection and genotyping of the amplified Factor V DNA. The 1691 point mutation of the Factor V gene causes an arginine to glutamine substitution at position 506 in the Factor V protein and renders it partially resistant to inactivation by Activated protein C (APC). APC resistance is regarded as the most prevalent coagulation abnormality associated with venous thrombosis.

How are the results reported?

The results for Factor V Leiden testing are reported as one of three possible results:

NORMAL: A **normal** result means that the Factor V Leiden allele (or mutation) was not detected on either version/copy of the Factor V gene.

HETEROZY: This result (**Heterozygous**) indicates that one copy of the Factor V allele has been identified with theLeiden mutation.

HOMOZYGO: This result (**Homozygous**) indicates that both copies of the Factor V allele have been identified with theLeiden mutation.

Important Additional Notes:

- This assay is a germline genetic assay and should only be ordered once on any particular patient. The Factor V Leiden genotype is constitutional and does not change.
- The Factor V Leiden assay is typically ordered in conjunction with the Prothrombin 20210A mutational assay and other markers of hypercoagulability, in patients with thrombosis.

References:

1. Burick, A., Wisotzkey, J.D., Najarian, M.P., Monk, J.S., Rhoads, J.E., *The Role of Preoperative Factor V Leiden Screening in Different Geographic Populations.* **The American Surgeon**. 63:547-550, 1997.
2. Ridker, PM, et al. (1997) Ethnic Distribution of Factor V Leiden in 4047 Men and Women: Implications for Venous Thromboembolism screening. *JAMA*, 277, 1305-1307.
3. Grody, WW, et al. (2001) AmericanCollegeof Medical Genetics Consensus Statement of Factor V LeidenMutation Testing. *Genetics in Medicine*, 3, Vol.2, 139-148.
4. Press, RD, et al. (2003) Clinical Utility of Factor V Leiden(R506Q) Testing for the Diagnosis and Management of Thromboembolic Disorders. CAP Consensus Conference XXXVI: *Diagnostic Issues in Thrombophilia*.
5. Wisotzkey, J.D., P. Bayliss, E. Rutherford and T. Bell. *Placental Genotyping of the Factor V Leiden, Prothrombin 20210A and the Methylenetetrahydrofolate Reductase (MTHFR) C677T Alleles in IUGR Pregnancies (Letter)*. **Thrombosis and Haemostasis,** 81:844-845, 1999
6. Wisotzkey, J.D., Bell, T. and Monk, J.S. *Simultaneous Polymerase Chain Reaction Restriction Fragment Length Polymorphism (PCR-RFLP) Identification of the Factor V Leiden Allele and the Prothrombin 20210A Mutation.* **Diagnostic Molecular Pathology**, 7:180-183, 1998.
7. Spector et al. Technical standards and guidelines: Venous thromboembolism (Factor V Leiden and prothrombin 20210G>A testing): A disease-specific supplement to the standards and guidelines for clinical genetics laboratories. **Genet Med**, 7:444-453, 2005.

Information compiled by Jeffrey Wisotzkey, Ph.D