**F5 (Factor V) Leiden Associated with Inherited Predisposition to Venous Thrombosis**

The UNC Molecular Genetics Laboratory performs a molecular test to detect *F5* (Factor V) gene mutation that is responsible, in part, for inherited predisposition to venous thrombosis.

**Biology of the disease:** Heterozygosity for the *F5* R506Q mutation is quite prevalent in the general population (about 5%) and is associated with a 4 to 7 fold increased risk of venous thrombosis, while homozygosity imparts a 9-80 fold increased risk. Affected individuals may be candidates for antithrombotic prophylaxis. The mutation results in resistance to activated protein C (APC-R) which promotes clot formation. However most patients with this *F5* mutation will not experience thrombotic events unless they also have coexisting risk factors for thrombosis such as: immobilization, surgery, hormone replacement therapy or oral contraceptives, pregnancy and perpeurium, obesity, other thrombophilias (e.g. anti-phospholipid antibody syndrome, *F5* Leiden gene mutation, or deficiency of selected coagulation factors such as protein S, protein C, or anti-thrombin).

**Clinical Indications for F5 Leiden mutation testing:**
1. Testing is recommended in patients with a symptomatic venous thrombotic event in whom it is uncertain, after evaluating other clinicopathologic risk factors, how long to continue anti-coagulation. Thrombophilia (homozygosity or heterozygosity for *F5* Leiden, or compound heterozygosity with *F2* 20210 gene mutation) favors long-term anticoagulation as compared to wild type. (See references 3 & 4 below.)
   **Note** that the indication for *F2* (prothrombin) 20210 gene mutation testing is identical to that of *F5* Leiden mutation testing, and thus it is recommended that the two mutation tests be performed as a panel; compound heterozygotes have a 20-fold increased risk of an initial thrombotic event and they likewise have an increased risk of clot recurrence compared to patients without either mutation.
2. Testing should be considered in some family members of a proband as summarized in references 3 & 4 below.

**Laboratory Testing for F5 Leiden mutation:** The preferred sample is EDTA anticoagulated blood (lavender-top tube, 3mL), which may be refrigerated up to 48 hours before analysis by real time PCR and allele-specific hybridization using analyte specific reagents (Roche) followed by melting curve analysis. Results are reported as heterozygous, homozygous, or normal genotype.

**References:**
4. www.clotconnect.org

Questions? **Call the Molecular Genetics Lab at** (919) 966-4408 or Dr. Weck at 966-4314. **E-mail kweck@unch.unc.edu**

Website= http://labs.unchealthcare.org/directory/molecular_pathology/index_html