F2 (Prothrombin) 20210G>A Gene Mutation Associated with Inherited Predisposition to Thrombosis

The UNC Molecular Genetics Laboratory tests for *F2* (prothrombin) 20210G>A gene mutation which is responsible, in part, for inherited predisposition to venous thrombosis.

Biology of the disease: Heterozygous *F2* mutation is quite prevalent in the general population (about 2%) and is associated with a 3-fold increased risk of venous thrombosis. Affected individuals may be candidates for antithrombotic prophylaxis. Mutation in *F2* (G to A transition at nucleotide position 20210) results in slightly elevated prothrombin levels and an associated risk of venous thrombosis. However most patients with this *F2* 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 *F2* (prothrombin) 20210G>A gene 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 compound heterozygosity with *F5* Leiden gene mutation) favors long-term anticoagulation as compared to wild type or heterozygous *F2* mutation. (See references 2 & 3 below.)
   Note that the indication for ***F5* Leiden gene mutation** testing is identical to that of *F2* 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 2 & 3 below.

Laboratory Testing for prothrombin *F2* 20210G>A gene 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:

1. Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group. Recommendations from the EGAPP Working Group: routine testing for Factor V Leiden (R506Q) and prothrombin (20210G>A) mutations in adults with a history of idiopathic venous thromboembolism and their adult family members. Genet Med 13:67-76, 2011.
2. Moll S. Who should be tested for thrombophilia? Genet Med 13:19-20, 2011.
3. 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**
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