FOUNDATION LABORATORY

ANNOUNCEMENT

Date: May 18, 2012

Dear Valued Clients:

Foundation Laboratory is pleased to announce that effective May 17, 2012 Factor II (Prothrombin) 202110>A assay will be performed in-house. This FDA approved assay is performed using multiplex PCR with solid phase electrochemical methodology on GenMark Dx eSensor platform.

Thrombin is a "trypsin-like" serine protease protein that in humans is encoded by the *F2* gene. Prothrombin (coagulation factor II) is proteolytically cleaved to form thrombin in the coagulation cascade, which ultimately results in the stemming of blood loss. Thrombin in turn acts as a serine protease that converts soluble fibrinogen into insoluble strands of fibrin, as well as catalyzing many other coagulation-related reactions.

In the blood coagulation pathway, thrombin acts to convert factor XI to Xia, VIII to VIIIa, V to Va, and fibrinogen to fibrin. The Thrombin (Prothrombin) gene is located on the eleventh chromosome (11p11-q12). There has been an estimated 30 people in the world that have been diagnosed with the congenital form of Factor II deficiency, which should not be confused with mutation of prothrombin. The prothrombin gene mutation is called Factor II mutation. Factor II mutation is congenital. The factor II mutation is not usually accompanied by other factor mutations (i.e., the most common is factor V Leiden). The gene may be inherited heterozygous (1 pair), or much more rarely, homozygous (2 pairs), and is not related to gender or blood type. F2 G202110A is the second most common genetic defect influencing genetic risk for venous thromboembolism (VTE), with factor V Leiden being the most common. Homozygous mutations increase the risk of thrombosis more than heterozygous mutations, but the relative increased risk is not well documented. Other potential risk for thrombosis, such as oral contraceptives may be additive. The previously reported relationship of inflammatory bowel disease (i.e., Crohn's disease or Ulcerative Colitis) and prothrombin mutation or Factor V Leiden mutation has been contradicted by research.

Activation of prothrombin is crucial in physiological and pathological coagulation. Various rare diseases involving prothrombin have been described (i.e., hypoprothrombinemia). Anti-prothrombin antibodies in autoimmune disease may be a factor in the formation of lupus anticoagulant also known as antiphospholipid syndrome. Hyperprothrobinemia can be caused by the mutation at 20210A. Thrombin, a potent vasoconstrictor and mitogen, is implicated as a major factor in vasospasm following subarachnoid hemorrhage. This can induce an acute and prolonged narrowing of the blood vessel, potentially resulting in cerebral ischemia and infarction.

The American College of Medical Genetics (ACMG) recommends patients be tested for Factor II as diagnostic testing for venous thromboembolism (VTE) (specially before age 50) or an unprovoked VTE at any age, women

with VTE associated with pregnancy, use of oral contraceptive, or HRT, women with unexplained pregnancy loss after the first trimester.

Beyond its key role in the dynamic process of thrombus formation, thrombin has a pronounced pro-inflammatory character, which may influence the onset and progression of atherosclerosis. Acting via its specific cell membrane receptors (protease activated receptors: PAR-1, PAR-3 and PAR-4), which are abundantly expressed in all arterial vessel wall constituents, thrombin has the potential to exert pro-atherogenic actions such as inflammation, leukocyte recruitment into the atherosclerotic plaque, enhanced oxidative stress, migration and proliferation of vascular smooth muscle cells, apoptosis and angiogenesis.

Specimen Requirements:

- 5 ml whole blood in a lavender top tube, refrigerate.

Turn Around Time:

- 10 days

For supplies and other needs please contact your Foundation Laboratory representative.

Sincerely,

Reza M. Massoumi, Ph.D.
Director of Technical Operations