

Genes-4U

Coagulation Factor XIII Val34Leu

Factor XIII (FXIII) is a zymogen that is converted into an active transglutaminase (FXIIIa) by the concerted action of thrombin and Ca^{2+} . Its main task is to crosslink α - and γ -chains of fibrin and α 2-plasmin inhibitor to fibrin. By this way FXIIIa strengthens fibrin and protects it from the prompt elimination by the fibrinolytic system. The common Leu34 allele associates with an increased FXIII-transglutaminase activity, which results in an increased and faster rate of fibrin stabilization. The **F XIII Val34Leu ToolSet™ for LightCycler™** allows detection of the **G163T** single nucleotide polymorphism in the F XIII gene which underlies the **Val**-to-**Leu** exchange in the catalytic A-subunit of Factor XIII.

Arterial and venous thromboembolism

There are contradictory results concerning the protective effect of Val34Leu polymorphism against arterial or venous thrombosis. The results suggest that the thrombo-protective effect of Leu34 allele prevails only in certain genetic and/or environmental constellations (1).

Chronic Venous Leg Ulcer (CVU)

In CVU, a significant trend toward a lower mean value of the ulcerated area was reported as the number of the polymorphic alleles (L34) increased (Val/Val = $11.9 \text{ cm}^2 \pm 23.6$; Val/Leu = $6.1 \text{ cm}^2 \pm 6.9$; Leu/Leu = $4.1 \text{ cm}^2 \pm 2.8$; $p = 0.01$). It was concluded that FXIII V34L polymorphism is significantly related to CVU progression and extension (2).

Myocardial infarction (MI)

In a study in 500 MI patients and 500 control subjects from the genetically isolated Newfoundland population the FII 20210A, FVL, and FXIII-A Leu34 variants and their association with MI were analysed. Especially, the prevalence of combined carriers of the FXIII-A L34 and FII 20210A alleles was 12-fold higher in MI patients than in control subjects ($P = .002$) and with 92% penetrance. It was concluded that interaction between the FII 20210A and FXIII-A Leu34 alleles forms a synergistic effect that strongly predisposes for MI, placing combined carriers at high risk for MI (3).

Further, in a large cohort of nonselected and consecutive acute MI patients from two different European populations, the presence of the Leu34 allele was shown to reduce the efficacy of fibrinolytic therapy. (4)

Coagulation Factor XIII Val34Leu

Early Pregnancy Loss

A successful outcome of pregnancy depends on proper placental formation. In the very beginning of this process, trophoblast invasion and fibrin deposition into the wall of the decidual veins play an important part. Two polymorphisms, coagulation factor XIII (FXIII) Val34Leu and plasminogen activator inhibitor 1 (PAI-1) 4G/5G, interfere with fibrin cross-linking and regulation of fibrinolysis. In a study of 49 unrelated Caucasian women with a history of early pregnancy losses and 48 unrelated parous healthy controls without a history of pregnancy loss, the isolated occurrence of PAI-1 4G/5G or FXIII Val34Leu was not statistically significant between cases and controls. However, for homozygosity of either or compound carrier status of both mutations, the overall relative risk for early pregnancy loss was reported as significantly increased (odds ratio = 2.4; 95% confidence interval, 1.1-5.5; P = 0.032, (5)).

Subconjunctival Haemorrhage(SCH)

One hundred seven white patients suffering from one or more episodes of idiopathic SCH and 107 healthy subjects were matched for age and gender, and genotyped for FXIII Val34Leu. Both homozygosity and heterozygosity for FXIII Val34Leu were found to predispose to idiopathic SCH, emphasizing the role of Leu34 allele as inherited risk factor for spontaneous, especially recurrent SCHs. (6)

References

- 1 **Bereczky Z.** et al. *Pathophysiol Haemost Thromb.* 2003/2004;33(5-6):430-7. PMID: 15692256
- 2 **Gemmati D.** et al. *Wound Repair Regen.* 2004;12(5):512-7. PMID: 15453833
- 3 **Butt C.** et al. *Blood.* 2003;101(8):3037-41. PMID: 12480694
- 4 **Marin F.** et al. *J Am Coll Cardiol.* 2005;45(1):25-9. PMID: 15629368
- 5 **Dossenbach-Glaninger A.** et al. *Clin Chem.* 2003;49(7):1081-6. PMID: 12816904
- 6 **Parmeggiani F.** et al. *Am J Ophthalmol.* 2004;138(3):481-4. PMID: 15364237