Factor XIII Val34Leu polymorphism is associated with the formation of smaller whole blood clots at high fibrinogen levels

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Background: The factor XIII-A polymorphism, Val34Leu, results in 2.5-fold faster FXIII activation, but paradoxically, protection against venous thrombosis (VT). This effect is hypothesized to result from fibrinogen concentration-dependent clot structure changes. During VT, FXIII mediates red blood cell (RBC) retention in contracted clots and consequently, clot weight. The effect of the Val34Leu polymorphism on whole blood clot weight and structure has not been investigated.

Aim: Determine the effect of the FXIII-A Val34Leu polymorphism on whole blood clot weight and composition.

Methods: Platelet-poor plasmas from 86 human donors (40 FXIII-A Val/Val, 28 FXIII-A Val/Leu, and 18 FXIII-A Leu/Leu) were reconstituted with freshly-isolated platelets and O-negative RBCs. Contracted clots were analyzed by scanning electron microscopy. Multiple regression analyses were used to assess the contribution of donor sex, age, clotting times, thrombin generation, FXIII activity, and fibrinogen level to clot weight.

Results: Univariate analysis showed clot weight did not differ between reconstituted whole blood clots generated from FXIII Val/Val, FXIII Val/Leu, or FXIII Leu/Leu plasmas. In a multiple linear regression analysis adjusting for fibrinogen level, compared to FXIII Val/Val, presence of the Leu allele (FXIII Val/Leu, FXIII Leu/Leu) was significantly associated with reduced clot weight. Sex, FXIII activity, clotting times, and thrombin generation did not correlate with clot weight for any genotype. Fibrin diameter and density did not differ between FXIII Val/Val and FXIII Leu/Leu clots at any fibrinogen concentration.

Conclusion: In plasmas with high fibrinogen levels, presence of the Leu allele is associated with formation of smaller whole blood clots. The Val34Leu polymorphism may protect against VT by decreasing clot RBC retention and consequently, reducing clot size.

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I am a graduate student and would like to apply for the Outstanding Abstract Award.