

ISTH 2015 Abstract Submission

Topic: Blood coagulation tests

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EFFICACY AND MECHANISM OF CLOT CONTRACTION ARE DETERMINED BY BLOOD COMPOSITION

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Preferred Presentation Method: Oral or Poster

Travel Grant Application: Young Investigator Award

I confirm fulfilling the criteria for the Young Investigator Award: Yes

Background: The contraction of blood clots remains one of the least understood aspects of hemostasis and thrombosis, despite its potential clinical importance.

Aims: To investigate the kinetics of clot contraction and the mechanistic interplay between platelets, red blood cells (RBCs), fibrin(ogen), factor XIIIa, and thrombin.

Methods: A novel automated optical analyzer was used to follow the size of contracting clots.

Results: The rate and degree of clot contraction were critically affected by variation of platelet count, RBC volume fraction, fibrinogen concentration and fibrin crosslinking, thrombin activity, and platelet-fibrin interactions. Increasing platelet count above 250k/ul revealed a switch from monophasic to biphasic contraction kinetics, reflecting complex platelet contractile machinery. Modifying the fibrin structure through fibrinogen levels revealed that denser fibrin was more resistant to contraction as the ability of the network to propagate the platelet contractile force was impaired. Inhibition of Factor XIIIa-mediated crosslinking also made clots contract less. Decreasing thrombin concentration resulted in weaker contraction, which can be attributed to reduced myosin phosphorylation and cytoskeleton remodeling within platelets. Comparison of clot contraction in DVT patients untreated and treated with warfarin revealed that, in addition to thrombin added, endogenous thrombin generation is required for clots to contract in a normal manner. Lastly, increasing the volume fraction of RBCs resulted in changes in the initial phase of contraction and the final degree of contraction due to the deformable mechanical nature of RBCs and their influence on the overall force balance of the contracting system.

Conclusion: Collectively, these results reveal the complementary and antagonistic roles of varying blood components in the multifactorial mechanism of clot contraction, as well as providing a basis for understanding of the clinical significance of contraction.

Disclosure of Interest: None Declared

Keywords: Factor XIII, Fibrin, Platelet activation, Platelet reactivity, Thrombin