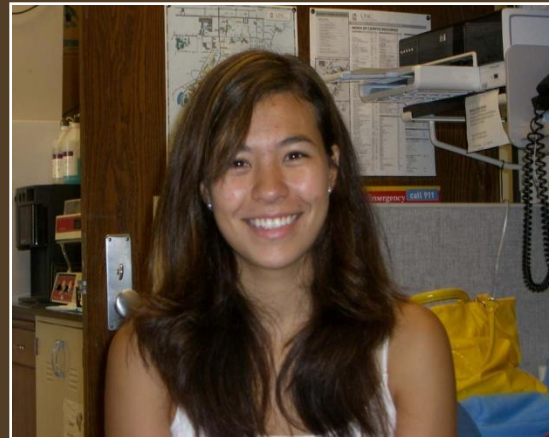


Fibrin Substitute using Recombinant Fibrinogen to Promote Hemostasis in Hemophilia

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Background & Goals

Hemostasis, the process of blood clotting, is induced by injury to the vessel wall. The cessation of blood loss via the formation of a clot requires a platelet plug and a network of stabilizing fibers. When a vessel wall is punctured, tissue factor comes into contact with platelets found in the plasma. This contact induces the bulk generation of an enzyme called thrombin. While thrombin interacts with other plasma proteins to form stable clots, it primarily converts fibrinogen to fibrin. Fibrinogen is protein present in plasma. Structurally, it contains 6 chains that all connect to form a central domain. Fibrinogen is cleaved by thrombin to form a mesh-like fibrin network necessary for the stability of a clot.

After the initial clot has formed, a clot retracts or “pulls in”. The clot retraction process is facilitated by Factor XIII. Factor XIII is a protein that crosslinks adjacent fibrin. The presence of factor XIII has been correlated with more stable clots and clot retraction. Hemophilia is the inability of blood to form stable fibrin networks in clots. I propose that the use of certain recombinant fibrinogen may provide a fibrin substitute that promotes hemostasis in hemophilia. The effects of recombinant fibrinogen upon platelet aggregation can be quantified by observing changes in turbidity of clots over time. By observing clot retractions in vitro, the effects of this recombinant fibrinogen can be determined. Furthermore, clot structure can be analyzed through the use of confocal laser microscopy.

Background

- Factor XIII is a transglutaminase responsible for crosslinking fibrin in a blood clot.
- Fibrinogen is a glycoprotein that gets converted to fibrin in a clot.

Goals

Study the effects of factor XIII in 3 ways:

- Clot Retraction
 - Generating clots and observing the rate of retraction *in vitro*
- Clot Formation
 - Monitoring change in turbidity of clots kinetically
- Clot Structure
 - Laser Scanning Confocal Microscopy

Results

In conducting preliminary research on clot retractions, observations led me to change my research interest from recombinant fibrinogen to the effects of factor XIII on fibrin clot formation.

Using a Factor XIII inhibitory antibody, here's what I learned:

- Factor XIII helps crosslink fibrin (in a clot) to fibrin (coating a plastic tube). Without Factor XIII, a clot will retract, or pull away from the plastic tube walls.
- FXIII = faster initial clot formation with **exogenous** thrombin
- FXIII = slower initial clot formation with **endogenous** thrombin