

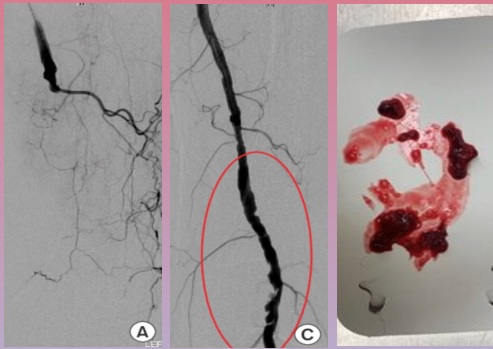
# Proteomics of Acute Limb Ischemia

Robert Stegman<sup>1</sup> Max V Wohlaer<sup>2</sup>

<sup>1</sup>University of Colorado School of Medicine, Aurora, CO, <sup>2</sup>UCHealth Heart and Vascular Center – Anschutz Medical Campus, Aurora, CO

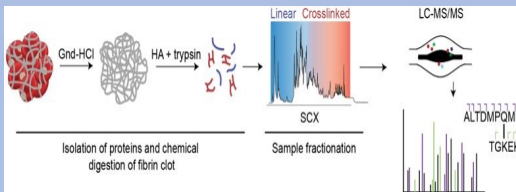
**Introduction:** Acute Limb Ischemia (ALI) is a sudden decrease in limb perfusion due to occlusion of a peripheral artery by thrombosis or embolism. This study aims to compare the proteomic composition of ALI clots to in vitro clots and understand the roles of target proteins in coagulation, fibrinolysis, red blood cell (RBC) degradation, and complement activation.

**Methods:** Arterial thromboemboli were collected after revascularization and stored following an IRB approved protocol and processed following published methods<sup>1</sup>.



Angiogram imaging of ALI clot before (A) and after (C) revascularization<sup>2</sup>.

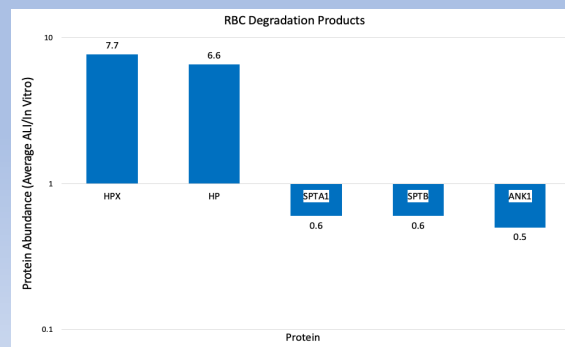
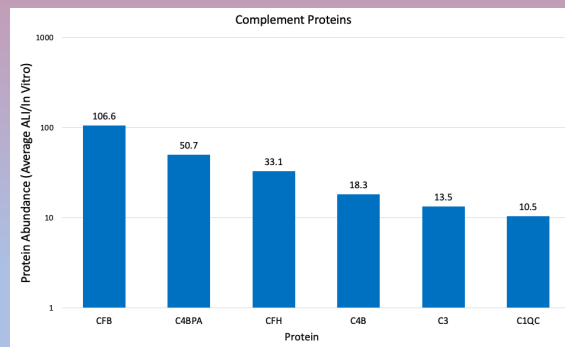
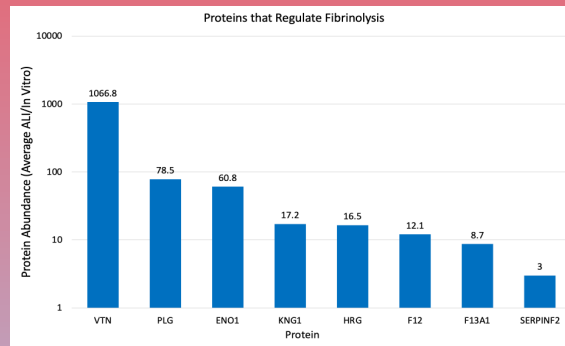
Liquid chromatography mass spectrometry (LC-MS/MS) was used to determine protein composition in samples of ALI clots and in vitro clots from healthy donors.



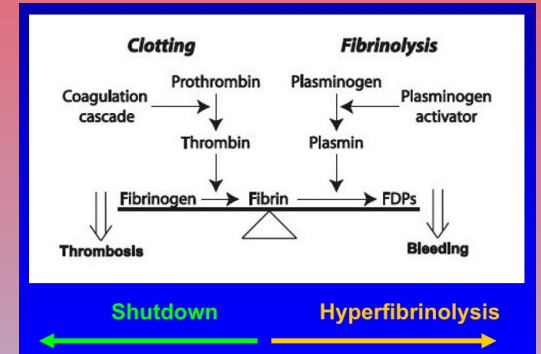
We performed a literature review of proteins with significantly increased or decreased abundance in ALI clots and categorized them based on their roles in coagulation, fibrinolysis, RBC degradation and complement.

## Results:

- 141 proteins had a significantly increased abundance
- 38 proteins had a significantly decreased abundance
- 59 proteins played roles coagulation
- 8 in regulation of fibrinolysis
- 6 were related to RBC degradation
- 7 were involved in the complement system



**Conclusion:** We found increased abundance of 3 pro-fibrinolytic proteins, 4 anti-fibrinolytic proteins, and 1 protein with both pro-fibrinolytic and pro-coagulation roles. Increased abundance of proteins that both inhibit and promote fibrinolysis demonstrates the highly dynamic process of thrombosis and the importance of regulating fibrin deposition/degradation.



We also found a significant increase in hemopexin and haptoglobin which are released from RBC degradation and act as free hemoglobin and free heme binders respectively.

There was also an increased abundance of 7 complement proteins which play various roles in regulating coagulation, fibrinolysis, and platelet activation.

**Discussion:** Coagulation is a complex process involving the coagulation cascade, fibrin deposition/crosslinking, and stabilization/degradation. Characterization of proteins that regulate coagulation and fibrin deposition/degradation will help to better understand the etiology of thrombosis and guide ALI management.

## References:

1. Schmitt, L. R., Henderson, R., Barrett, A., Darula, Z., Issaian, A., D'Alessandro, A., Clendenen, N., & Hansen, K. C. (2019). Mass spectrometry-based molecular mapping of native FXIIIa cross-links in insoluble fibrin clots. *The Journal of biological chemistry*, 294(22), 8773–8778.
2. Endovascular Strategies in the Management of Acute Limb Ischemia - Scientific Figure on ResearchGate. Available from: [https://www.researchgate.net/figure/Angiographic-images-of-a-patient-presenting-with-left-lower-extremity-acute-limb\\_fig1\\_332191325](https://www.researchgate.net/figure/Angiographic-images-of-a-patient-presenting-with-left-lower-extremity-acute-limb_fig1_332191325) [accessed 9 Nov, 2023]