

Proteomics of Acute Limb Ischemia

Introduction: Acute Limb Ischemia (ALI) is a sudden decrease in limb perfusion due to occlusion of a peripheral artery by thrombosis or embolism. ALI puts patients at risk of severe limb damage or amputation if not treated urgently with revascularization. This study aims to analyze the proteomic composition and structure of ALI clots and compare them to in vitro clots. We hope to better understand the roles of target proteins in coagulation, fibrinolysis, red blood cell (RBC) degradation, and complement activation.

Methods: Arterial thromboemboli were collected after revascularization procedures and stored following an IRB approved protocol. Samples were processed following previously published methods¹. Liquid chromatography mass spectrometry (LC-MS/MS) was used to determine protein composition and abundance 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: We found that 141 proteins had a significantly increased abundance and 38 had a significantly decreased abundance in the ALI clots compared to in vitro clots (p-value < 0.05). 59 proteins played roles coagulation, 8 in regulation of fibrinolysis, 6 were related to RBC degradation, and 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. Upregulation of proteins that both inhibit and promote fibrinolysis demonstrates the highly dynamic process of thrombosis and the importance of regulating fibrin deposition and degradation. We also found a significant increase in hemopexin and haptoglobin which are released from RBC degradation. We found an increase in 7 complement proteins which play various roles in regulating coagulation, fibrinolysis, and platelet activation. Characterization of proteins that regulate fibrin deposition/degradation and coagulation will help to better understand the etiology of thrombosis and guide surgical and medical management of ALI.

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. <https://doi.org/10.1074/jbc.AC119.007981>