**Extracellular actin potentiates platelet aggregation through collagen activation pathway**

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Background: Tissue damage from severe trauma can lead to massive release of the cytoskeletal protein actin into the blood. Extracellular actin has complex effects on blood clotting, and excessive actin release is associated with platelet dysfunction after severe trauma. This implicates extracellular actin as a possible contributor to the changes in coagulation and microcirculation seen after trauma. However, actin’s specific effect on platelets and the pathways involved have not been directly tested and remain unknown. With these experiments, we sought to test and quantify this effect and begin to identify possible mechanistic pathways involved.

Methods: Healthy donor whole blood in 3.2% sodium citrate was incubated for 5 min with either a saline control or recombinant human skeletal muscle-derived actin (final concentration 200 nM). Samples were then activated with either 10 μM adenosine diphosphate (ADP) or 2 μg/mL collagen. The platelet aggregation response was then measured by impedance aggregometry. Each pair of control and actin conditions was run simultaneously. The impedance area under the curve (AUC) was compared between control and actin groups under each activation condition using a paired t-test with significance at p<0.05.

Results: The AUC in response to ADP was no different between the control and actin groups (mean 11.2 vs. 12.5, p=0.400, n=5). The AUC in response to collagen was significantly higher in the presence of actin compared to control (23.1 vs. 29.9, p=0.021, n=16). A dose-response relationship between exogenous actin concentration and aggregation response was also described.

Conclusion: The addition of exogenous muscle actin increases the platelet aggregation response, and this was noted through the collagen but not the ADP activation pathway. This suggests that actin release after injury could cause an overactivation response by platelets and contribute to derangement of microvascular blood flow. The mechanism by which actin potentiates this activation pathway requires further characterization.