Endothelial glycocalyx damage is induced by elevated plasma succinate

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Supplemental Video

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Background
Hypoxia-inducing events such as hemorrhagic shock have been shown to cause sloughing of a carbohydrate-protein matrix found on the luminal surface of endothelial cells. Shedding of this luminal coating, called the glycocalyx, has become a known hallmark for coagulopathies in trauma. Plasma succinate levels have also been shown to be elevated in critically ill and trauma patients. Furthermore, succinate buildup has been implicated in a variety of ischemia-reperfusion injuries, through eliciting an increase in mitochondrial reactive oxygen species. Our lab has previously reported that glycocalyx shedding in a cell culture model of hypoxia-reoxygenation is dependent on mitochondrial reactive oxygen species.

Methods
This study attempts to further elucidate the relationship between glycocalyx shedding and coagulopathy in trauma by exploring a possible causative mechanism between succinate buildup and glycocalyx damage. We hypothesized that succinate administration alone could cause glycocalyx degradation in otherwise healthy rats. We injected 1000 mg of succinate in 1.5 ml of lactated Ringer's solution through the external jugular vein. Control animals were injected with lactated Ringer's alone. After 60 minutes, intestinal tissues were harvested and the rats euthanized. Tissue was flash frozen and sectioned, followed by methanol fixation. Glycocalyx damage was measured via fluorescent-labelled wheat germ agglutinin.

Results
Glycocalyx damage was found to be significantly elevated in the intestinal vasculature of rats exposed to plasma succinate.

Conclusions
We conclude that succinate buildup alone is sufficient to damage the glycocalyx, and thus may be the primary means of glycocalyx damage in trauma patients. Future experiments aim to explore specific mechanisms by which succinate buildup and glycocalyx damage may be causally linked.

Learning Objectives
Describe how the human endothelial glycocalyx is implicated in complications in trauma
Discuss how increased succinate levels can negatively affect glycocalyx structure
Identify how future therapies may improve trauma patient outcomes by inhibiting glycocalyx degradation