

## Oral Presentation Finalist

### Inhibition of Type 2 Sodium-Glucose Transporters and Na<sup>+</sup>/H<sup>+</sup> Exchanger-1 Produces Similar Cardioprotective Effects in Response to Ischemia-Reperfusion Injury

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**Background:** Recent studies indicate that inhibition of Type 2 Sodium-Glucose Transporters (SGLT2i) augments diastolic filling volume and mitigates myocardial ischemic injury. During the course of a summer research experience, our group initiated a study testing the hypothesis that inhibition of the Na<sup>+</sup>/H<sup>+</sup> Exchanger-1 (NHE-1) mimics the cardioprotective effects of SGLT2i in response to ischemia-reperfusion injury.

**Methods:** Lean swine (~50 kg) were anesthetized, a thoracotomy performed, and perivascular flow transducers placed around the left anterior descending (LAD) and circumflex coronary (LCX) arteries. A pressure-volume (PV) catheter was then inserted into the left ventricle. Swine received a 15 min infusion of vehicle (DMSO; n = 3), the SGLT2i Canagliflozin (30 μM; n = 3), or the NHE-1 inhibitor Cariporide (1 μM; n = 3) prior to a 60 min total occlusion of the LCX and 2-hour reperfusion period. Following reperfusion, the LCX was re-occluded and a 2.5% Patent Blue 5 solution was administered to identify area at risk. The heart was excised, sectioned, and incubated in a 2,3,5-triphenyltetrazolium chloride (TTC) solution. Images were collected and analyzed for area at risk and infarct size.

**Results:** In the vehicle treated group, 2 of the 3 swine studied died prematurely before the completion of the protocol; one at baseline and one during ischemia. Our preliminary findings showed that left ventricular end diastolic volume increases in response to regional myocardial ischemia in the swine that received either Canagliflozin or Cariporide. This increase in diastolic volume was associated with an increase in stroke volume (i.e. Frank-Starling effect) and a reduction in myocardial infarct size in both treatment groups. Blood pressure tended to decrease to a similar extent in all groups.

**Conclusion:** These preliminary studies demonstrated that inhibition of SGLT2 and NHE-1 produce similar functional and protective effects in response to regional ischemia-reperfusion injury. Further experiments are necessary to verify these findings and examine the extent, if any, to which SGLT2i directly modulates NHE-1 activity.



*Bianca Blaettner is a third year medical student who is currently interested in general surgery. "I love being in the operating room and hope to work with Doctor's Without Borders to provide medical care to developing countries." While she entered the summer without any expectations of pursuing research after medical school, Blaettner said, "I had such a great time with the Tune lab doing pig surgeries, learning how to suture, and how to analyze data. The summer I spent with them opened my eyes to the different aspects of research and I hope to continue doing research for my last years of medical school and into my professional career." She also adds a shout out to the Tune Lab for a great summer (even with the 6 AM start time). If you don't like research, a great lab will change your mind!*