



*University of Utah*

UNDERGRADUATE RESEARCH JOURNAL

**MPC1 CARDIAC SPECIFIC DEFICIENCY CAUSES HEART FAILURE AND EXACERBATES REPERFUSION INJURY IN ISCHEMIA-REPERFUSION**

**Timothy Hui (Stavros G. Drakos)**

**Nora Eccles Harrison Cardiovascular Research & Training Institute, University of Utah School of Medicine**

Coronary artery disease and its role in myocardial infarction (MI) has become the leading cause of death and disability globally. Treatment of MI has improved with advances in reperfusion. However, up to 50% of the damage that occurs after acute myocardial infarction (AMI) is due to reperfusion injury. Unfortunately, there has been little success in reducing reperfusion injury. Our study utilized an Impella, a percutaneous ventricular assist device, to unload the left ventricle (LV) of a porcine heart while simultaneously reperfusing the ischemia, resulting in more salvaged myocardium. Furthermore, a recent study of a porcine ischemia reperfusion (I/R) injury model has implicated a transporter protein, mitochondrial pyruvate carrier (MPC), as being cardio-protective during I/R. The study, which utilized isolated mouse hearts subjected to I/R, indicated that inhibition of MPC using an inhibitor exacerbated myocardial infarction. While the exact mechanism of MPC in I/R injury is not well understood, we hypothesize that the reduced level of MPC in cardiac muscle will exacerbate the impact of IR injury in adult mice. To test this, cardiac specific and inducible MPC1 knockout mice were generated through cre-loxP-mediated-Recombination which allows the gene to be deleted when the mouse is 8 weeks old upon tamoxifen injection. The MPC1<sup>-/-</sup> mouse revealed signs of heart failure 10-12 weeks post-induction such as, increased left ventricular end diastolic diameter, decreased ejection fraction, decreased fractional shortening, and increased LV mass as compared to the wild type littermates. Preliminary data of I/R injury on these mice before development of heart failure symptoms indicated that the MPC1 deficiency exacerbated the MI in comparison to the control group. The MPC1 deficient mice appeared to be more susceptible to mortality during the reperfusion compared to the wild type mice. This observation hints at a possible role of MPC1 in myocardial salvage during I/R. In the future, more ischemia reperfusion experiments will be carried out in order to increase our sample size and confirm the preliminary data. Additionally, we will examine the metabolic profile and gene expression in these mice during I/R.