**DETRIMENTAL IMPACT OF DIABETES ON EPHA2 KNOCKOUT MICE FOLLOWING MYOCARDIAL INFARCTION**

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We have previously shown that EphrinA1/EphA expression profile changes in response to myocardial infarction (MI) and exogenous EphrinA1-Fc administration following MI, positively influences wound healing. To determine whether EphrinA1-Fc would be of therapeutic value in the diabetic infarcted heart, it is critical to evaluate how the heart changes in response to diabetes with and without MI. We hypothesize that ephrinA1/EphA signaling is unfavorably influenced by ischemia, worsened in EphA2-KO mice, and further exacerbated by diabetes. Streptozotocin-induced diabetes in wild type (WT) and EphA2-KO mice was initiated 10 days before surgery. MI was induced by permanent left coronary artery ligation. At 4 days post-MI, we observed greater mortality in EphA2-KO mice compared to WT and this was worse in the EphA2-KO diabetic mice. Left ventricular mass and myocyte cross-sectional area were significantly decreased in EphA2-KO diabetic mice compared to diabetic WT. Therefore, it is expected that the hypertrophic response will be blunted and cardiac dysfunction worsened in diabetic EphA2-KO hearts post-MI. Interstitial fibrosis increased following onset of diabetes and is anticipated to be highest in infarcted diabetic EphA2-KO hearts. EphrinA1 and EphA6 gene expression did not change in response to either MI or diabetes but EphA6 increased 4-fold in infarcted diabetic EphA2-KO hearts. Concomitant alterations in protein expression, effects on cardiac function, histologic, and immunohistochemical parameters from diabetic WT and EphA2-KO mice hearts post-MI are under investigation and will be presented.