IL-6 Stimulates Autophagy in Wild Type and NRF2 Knock Out Mice β-cells

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Background and Hypothesis:
Pancreatic β-cells exhibit high levels of metabolic activity which generates reactive oxygen species (ROS). ROS can lead to β-cell damage and death, which could contribute to diabetes development. Therefore, pathways reducing ROS are of interest as potential therapeutic targets. We have demonstrated that IL-6 stimulates autophagy and protects β-cells from ROS and apoptosis. IL-6 also stimulates the translocation of NRF2 to the mitochondria, which is accompanied by several markers of mitophagy, the autophagic degradation of mitochondria. In this study, we ask where NRF2 fits in the pathway downstream of IL-6 by asking if NRF2 is required for IL-6 stimulation of autophagy and/or mitophagy.

Experimental Design or Project Methods:
Wild type and NRF2 knockout mice were intraperitoneally injected with saline or IL-6 for thirty minutes, and the pancreata were cryopreserved, and cryosectioned. Immunofluorescence staining was carried out for LAMP-1 (a component of lysosomes) and LC3 (a component of autophagosomes). Slides were imaged with a LSM 700 confocal microscope.

Results:
IL-6 stimulated autophagy in wild type and NRF2 knockout mice, whereas saline injection did not.

Conclusion:
We have confirmed that IL-6 stimulates autophagy in pancreatic islets and shown that NRF2 is not required for this process. Ongoing experiments are investigating if NRF2 is required for IL-6 stimulation of mitophagy. These results help us understand how NRF2 functions downstream of IL-6 in the protection of β-cells