# DYNAMIC AUTOPHAGY IN THE INSULIN RESISTANT HEART

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Heart disease is the leading cause of death among people with diabetes. Cardiac failure morbidity rates nearly exceed morbidity rates of cancer. There are several mechanisms proposed to influence cardiac failure, such as altered cardiac autophagy. Autophagy is the catabolic pathway in which damaged organelles and proteins are degraded via lysosomic activity. Previous studies have shown that impaired autophagy resulted in cardiac failure in mice. The pathological role of autophagy in the insulin resistant heart is largely unknown, because of the limitations of measuring autophagic flux. Autophagic flux, or dynamic autophagy, reflects the process of the formation of the autophagosome, engulfment of damaged particles, and fusion of the lysosome for degradation. Our previous results via static imaging have shown a decrease in LC3I/LC3II lipidation, but this ratio could be a result of impaired lysosome fusion rather than impaired autophagy. By inhibiting lysosome fusion via Chloroquine, we were able to continue our research on dynamic autophagy in the insulin resistant heart. We hypothesized that reduced insulin resistance led to decreased autophagy. Our objective of this study was to measure the autophagic flux in the heart, as well as investigate the mechanisms involved in cardiac autophagy. We used a Total Insulin Receptor Knock-Out (TIRKO) mouse model to represent our diabetic group. We injected the mice with Chloroquine and harvested the heart tissue. Using Western Blot technology, we probed the membranes with 4 different antibodies: LC3B, ATG3, GAPDH, and Sequesterome/p62. Our results showed that there are increased levels of LC3I and P62 and decreased levels of ATG3 in the Chloroquine-treated mice, indicating that there is a lack of LC3I/LC3II lipidation occurring *via* downregulation of ATG3 and thus autophagosomes are not being formed. These results indicate that the autophagic pathway is impaired in the insulin resistant heart, which could influence cardiac health of diabetic patients.