**DECIPHERING THE ROLE OF MITOPHAGY-LYSOSOME DYSFUNCTION IN THE DIABETIC HEART**

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Mitochondrial dysfunction plays an important role in diabetic heart damage. A healthy pool of mitochondria is maintained through a number of quality control mechanisms including mitophagy that degrades dysfunctional mitochondria through the lysosome. In the present study, we investigated the function of mitophagy-lysosome system in the diabetic heart. Diabetes was induced in mice by streptozotocin. We showed that mitophagy flux was reduced in the diabetic heart as indicated by a novel mitophagy reporter, which was accompanied by oxidative stress, apoptosis and impaired cardiac function. Overexpression of the E3 ligase Parkin enhanced mitophagy and reduced diabetic cardiac injury. In contrast, inactivation of Parkin gene had the opposite effects. These results suggest that mitophagy is essential for maintaining mitochondrial quality and cardiac homeostasis in diabetes. In addition, using a novel dual fluorescent lysosome reporter, we showed that diabetes triggered lysosomal injury but reduced lysophagy flux, leading to the accumulation of injured lysosomes and the release of lysosomal enzymes such as cathepsin D, which may partly account for the reduced mitophagy flux and diabetic heart damage. Studies are underway to determine if enhancing lysophagy can reduce diabetic cardiac injury by removing injured lysosomes and accelerating mitophagy flux.