Mitochondrial transplantation - a novel therapy for cardiac disease

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Introduction: Heart disease is the leading cause of death for both men and women in the United States. About 5.7 million adults suffer from heart failure due to underlying causes such as ischemia/reperfusion injury or hypertrophy both of which are a direct result of impaired mitochondrial function. We hypothesize that augmentation and replacement of damaged mitochondria would allow for myocardial cell rescue.

Materials and Methods: Methods and procedures have already been established to allow for the isolation of viable, structurally intact, respiration competent, autologous mitochondria, isolated from remote skeletal tissue in a short time-frame of less than 30 minutes. First, internalization of mitochondria was determined in isolated neonatal cardiomyoctes. Secondly, pre-clinical large animal studies in anticipation of use in humans were performed to ascertain safety, efficacy and lack of immunogenic response of mitochondrial transplantation.

Results: In vitro studies showed that mitochondria are internalized and augment ATP levels. Local injection and intracoronary injection of mitochondria showed specific distribution throughout the LV, validated by PET/microCT imaging, with no effect on rhythm, heart rate of pressures. The use of human mitochondria in animals allowed for the differentiation between native animal mitochondria and transplanted human mitochondria based on immune reactivity to a monoclonal anti-human mitochondria antibody on post-mortem histological tissue analysis. Injected mitochondria are taken up by myocardial cells and are present in the myocardium for at least 4 weeks following injection. Furthermore, injected mitochondria did not elicit any immune or inflammatory response.

Conclusion: Mitochondria are therapeutic targets to prevent the development of ventricular failure in response to pathological stimuli. Injection of viable mitochondria provides a safe and robust therapeutic intervention of enhancing mitochondrial function to meet energy needs. At the same time, maintaining mitochondrial function prevents cardiomyocyte loss to apoptosis.