**Project Title:** Development of highly effective treatment on mitochondrial dysfunction in Parkinson's disease

**Host School/ Institute**: Northern Clinical School

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**Project Type:** Laboratory Based

**Project Category:** Molecular biology, Chronic Diseases/Illness, Neuroscience, Cell Biology

**Project Keywords:**
1. Parkinson’s disease
2. Mitochondria
3. Autophagy
4. Bioenergetics

**Project Description:**

Parkinson’s disease (PD) is the most common neurodegenerative movement disorder. Patients with PD have a specific loss of dopaminergic neurons in the substantia nigra. The cause of this neurodegeneration is still unknown, but both genetic and environmental factors are known to play key roles. Mutations in Parkin are the most frequent genetic cause of autosomal recessive early-onset PD. The Parkin gene encodes an E3 ubiquitin ligase which mediates protein degradation through the ubiquitin-proteasomal system. Recently, there has been a link between PD and mitophagy, a removal of mitochondria by autophagic degradation, through the PINK1/Parkin pathway. Parkin mutations are strongly associated with impaired mitophagy and mitochondrial dysfunction in cellular models of PD.

Previously, we identified the first case of a homozygous Parkin mutation carrier who had no Parkin protein, but did not develop PD. In further investigation, we discovered that a Parkin-independent mitophagic pathway compensated for the loss of Parkin in the mutation carrier, suggesting its therapeutic potential for mitochondrial dysfunction. Meanwhile, several proteins have been shown to be involved in the pathway, but their roles in mediating mitophagy remain unclear.

In this project, we will investigate the ability of several proteins associated with the Parkin-independent mitophagic pathway in enhancing the beneficial effect of the pathway on rectifying dysfunctional mitochondria in cell lines derived from Parkin/PINK1-related PD patients using various techniques such as cDNA synthesis, quantitative real-time RT-PCR, manipulation of gene expression by siRNA and lentivirus, Western blotting and confocal microscope-assisted live cell imaging. Positive outcomes may serve the basis of developing a highly effective therapeutic avenue to treat mitochondrial dysfunction in PD.