Biochemical and functional analysis of F-box only protein 7 (FBXO7) in neurons

The second most common of the neurodegenerative diseases, Parkinson’s disease (AD), is caused by loss of dopaminergic neurons in the striatum leading to impaired motor control. Genetic analyses have revealed several recessively and dominantly inherited mutations in genes causing symptoms reminiscent of those of PD. Mutations in the FBXO7 gene have been linked to three families presenting with Parkinsonian-pyramidal syndrome, but its role in neurons remains unknown. I will here show a characterization of FBXO7 localization pattern and a functional analysis focusing on FBXO7 as a player in mitochondrial morphology.

In this study I characterized the expression and localization of FBXO7. I found FBXO7 in different brain regions and cytoplasmic localization at subcellular level. FBXO7 is a subunit of the SCF E3 ubiquitin ligase and my data indicate that at least one mutation identified in affected parkinsonism individuals fails to form a proper FBXO7-SCF ligase complex. In addition, loss-of-function analyses support the notion that FBXO7 is implicated in mitochondrial fusion and fission dynamics. Taken together, the FBXO7-SCF ligase appears to be required for the proper function of neurons. To examine FBXO7 function in vivo I have also initiated the establishment of a conditional knockout mouse designed to obliterate FBXO7 expression specifically in dopaminergic neurons, which are the neurons degenerating in parkinsonism.