MiRNAs have been shown to participate in a variety of physiological and pathological processes in the CNS, and recent studies have linked miRNA deregulation to neurodegenerative diseases, including Parkinson's disease (PD). Neuropathological changes associated to PD progress in a topological predictable manner, leading to the degeneration of the nigrostriatal dopaminergic pathway. Deregulation of the transcriptome in brain samples from PD patients has been widely reported and whether this altered transcriptome is associated to miRNA deregulation needs to be addressed. Here we have analyzed miRNA expression profiles in several brain areas of PD patients at different neuropathological stages of the disease to discover gene expression networks modulated by miRNAs relevant to PD neuropathology. Our results show a strong and significant down-regulation of the miR-34b/c cluster in brain areas that are severely affected; whereas less drastic but still significant down-regulation was observed in areas slightly affected.

In vitro functional assays show that depletion of either miR-34b or miR-34c compromise neuronal viability by inducing oxidative stress and altering mitochondrial function. The present results suggest that miR-34b/c deregulation could be an indicator of PD progression, since the extent of down-regulation correlates with the degree of neuropathological affection. Furthermore, changes in the expression of this miRNA cluster may contribute to the initial transcriptome deregulation associated to PD, involving oxidative stress and mitochondrial integrity pathways.