

P012 Alpha synuclein, metals and neurodegeneration
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Parkinson's disease (PD) is one of the most common neurodegenerative diseases, characterized by intracellular inclusions termed Lewy bodies (LBs) and Lewy neurites (LNs). Alpha-synuclein is the major component of these inclusions, and has been implicated in PD pathology. Mutations in alpha-synuclein gene are linked to cases of familial PD. Overexpression of the protein and its disease mutants in animal models leads to motor deficits similar to PD. There has been a suggested link between metals and the etiology of a number of neurodegenerative disorders including PD. Metals have been found to accelerate the aggregation of alpha-synuclein. However, the mechanism is not known. We aim to investigate the mechanism of alpha-synuclein aggregation and whether it is related to metal binding. We created mutant forms lacking potential metal binding sites such as one at the N-terminus. A thioflavin-T assay was used to monitor the aggregation of the protein. The effect of metals on accelerating the aggregation was assayed using low, physiologically relevant concentrations of alpha-synuclein and metals (Copper, Iron and Aluminium). Results showed that copper was the most effective at inducing the aggregation of WT alpha-synuclein at low concentrations, while less effect was observed with the mutant protein suggesting a role for this site in aggregation. In addition, aggregation experiments showed that the presence of His-tag on the N-terminus of the protein significantly increases its aggregation in the same conditions.