Biochemical Analysis of Post Translation Modification to the Parkinson's Disease Protein Alpha-Synuclein

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Parkinson’s disease (PD) is caused by the unknown death of dopamine-generating cells in the substantia nigra. The pathology of PD is determined by neurodegeneration of dopaminergic neuron and the appearance of Lewy Bodies (LB) in the surviving neurons. LB are composed of lipids and aggregation of hyperphosphorylated alpha-synuclein (a-syn). Alpha Synuclein is a small protein composed of 140 amino acids whose function is currently unknown. In vitro biochemical assays have demonstrated a-syn has a propensity to form fibril structures. We hypothesize that phosphorylation of a-syn, which is the primary form found in LB’s, will affect the rate of fibril formation along with the morphology of the fibrils. Recombinant wild type and S129E (mimics phosphorylation at ser129) a-syn were expressed in E-Coli and purified using anion exchange chromatography. The rate of fibril formation for both samples, which was determined using ThioFlavin fluorescence, demonstrate that the S129E a-syn had a much shorter lag phase (~3 fold) prior to fibril formation. However both wild type and S129E reached identical fluorescence intensity. These results demonstrate that phosphorylation of a-syn does not affect the morphology of the fibrils but rather decrease the energy barrier of association that promotes fibril formation.

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