

P045 Alpha-synuclein is a high affinity copper binding protein
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α -Synuclein is implicated in the formation of abnormal protein deposits in the brain in a number of neurodegenerative disorders. The aggregation of α -synuclein is accelerated by metal ions, which can also promote the formation of hydrogen peroxide. We have developed a *de novo* expression and purification strategy for recombinant α -synuclein that avoids boiling or any other denaturing steps that may affect the physiological properties of the protein. This method produces α -synuclein in a completely monomeric form. Immobilised metal ion affinity chromatography was used to determine the relative binding of this protein to various metal ions, and it was found to selectively bind to Cu(II). Studies using isothermal calorimetry indicated the presence of multiple Cu(II) binding sites of very high affinity. Furthermore, the addition of Cu(II) to the protein resulted in a shift in its circular dichroism spectrum, indicative of a change from predominantly random coil to a more ordered structure. We conclude that the selective interaction between α -synuclein and Cu(II) is likely to play an important role in the pathogenesis of Parkinson's disease and related disorders, particularly with respect to the generation of reactive oxygen species in the early stages of protein aggregation.