

P023 Studies on the aggregation of an amyloidogenic alpha-synuclein peptide fragment

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The aggregation of α -synuclein to form insoluble fibrillar inclusions is the probable key event in the onset of many neurodegenerative diseases. Previous studies have identified key regions within the α -synuclein sequence that are necessary for the aggregation of the protein, including a central hydrophobic region (encompassing residues 71-82). A peptide corresponding to this region (α -syn(71-82)) has been synthesised and used to study the structural characteristics of fibrils formed and to assess which residues form the critical self-recognition element. Solid-state nuclear magnetic resonance (NMR) structural studies on fibrils formed have revealed structural heterogeneity across the backbone of the peptide, with distinct ordered and disordered regions. One therapeutic strategy for prevention of amyloid diseases is to inhibit or reduce the rate of formation of amyloid fibrils. Our NMR results have been used to guide the synthesis of a range of unnatural peptides as inhibitors of α -synuclein aggregation. Preliminary screening has identified potential lead compounds for the treatment of neurodegenerative diseases such as Parkinson's.