

**P030** A Strategy for Designing Inhibitors of  $\alpha$ -Synuclein Aggregation and Toxicity as a Novel Treatment for Parkinson's Disease  
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Parkinson's disease (PD) is characterised by the accumulation of fibrillar aggregates of  $\alpha$ -synuclein protein inside brain cells. It is likely that the formation of  $\alpha$ -synuclein aggregates plays a seminal role in the pathogenesis of PD, since three different mutations in the gene encoding  $\alpha$ -synuclein have been found in inherited forms of PD. It has been reported that lesions similar to those found in the PD brains can be created in transgenic animals over-express human  $\alpha$ -synuclein, and progressively develop a loss of dopaminergic cells together with motor abnormalities. Inhibiting and/or reversing  $\alpha$ -synuclein self-aggregation could, therefore, provide a novel approach to treating the underlying cause of these diseases. We synthesised a library of overlapping peptides spanning the entire  $\alpha$ -synuclein primary sequence, and identified the binding region responsible for its self-association. Modified short peptides containing  $\alpha$ -synuclein amino acid sequences from the binding region named  $\alpha$ -synuclein inhibitors (ASI), were found to interact with  $\alpha$ -synuclein and block its aggregation. We also developed a cell-permeable inhibitor of  $\alpha$ -synuclein aggregation (ASID). This ASID peptide was able to inhibit the DNA damage induced by Fe(II) in neuronal cells transfected with  $\alpha$ -synuclein. These short peptides could serve as lead compounds for the design of peptidomimetic drugs to treat PD.