Ferritin cage engineering to isolate a defined number of Alpha-synuclein peptide fragments

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Alpha-Synuclein(α-Syn) is an intrinsically disordered protein associated with Parkinson's disease. Aggregation to form oligomers and fibrils are the common pathway of their deposition in Lewy body.[1] Oligomers were found to be toxic and play crucial role in the disease.[1] Therefore, it is important to know the detail of structure, dynamics, and properties etc. of an oligomer to understand its role in the disease and to develop oligomer specific drugs. However, little is known about a defined oligomer due to difficulty in precise isolation and structural characterization.[2,3,4] In this work, we aimed to encapsulate a defined number of alpha-synuclein peptide fragments into the ferritin cage to isolate and characterize the oligomers (Figure 1). We choose various lengths of the alpha-synuclein peptides which are known as the toxic core and to play crucial role in oligomerization as well as fibrillization.[5] Those fragments were genetically fused to the C-terminal of ferritin monomer which is located inside the cage. During in vivo expression of the fused protein monomer and self-assembly, alpha-synuclein is expected to be encapsulated into the cage and form oligomers. This presentation will describe the method of encapsulation of α-Syn peptide fragments into the ferritin cage with detailed characterization of the oligomer, studies on stability, structural dynamics and various biophysical properties like ThT (Thioflavin T) assay, inhibition of oligomerization etc.

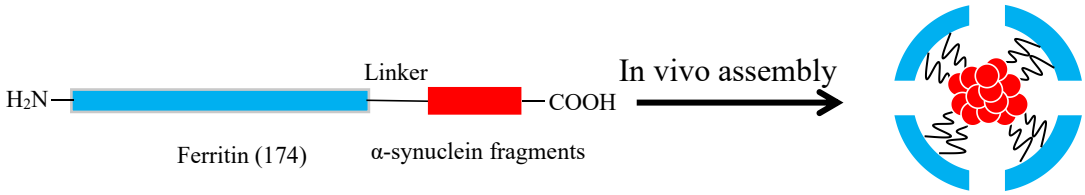

Figure 1: Schematic representation of the encapsulation of α-Syn oligomer into ferritin cage.

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