Design of Cyclic Peptide Drugs for Parkinson's Disease through Molecular Simulations

Place of work/: BioISI Ed. C8 – piso 5 Workspace

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Protein aggregation is implicated in several human pathologies, ranging from sickle cell disease, a red blood cell disorder, to type 2 diabetes mellitus, and various neurodegenerative diseases, such as Alzheimer's, Huntington's, or Parkinson's disease (PD), commonly known as proteinopathies. A major challenge regarding drug design aiming at inhibiting or delaying protein aggregation for some of these diseases concerns the lack of specific protein binding regions. Over the past years several seemingly key regions governing the aggregation of α–synuclein, the most important protein involved in the formation of cytotoxic oligomers in PD, have been identified. Herein, we propose to design and probe, through computational chemistry methods, the binding affinity of cyclic peptides toward some of these regions. The project will involve the use of coarse-grained and all-atom molecular dynamics simulations of α–synuclein and several tailor-made cyclic peptides. Their affinity toward the aforementioned regions and potential implications to the structure of the monomer will be assessed and putative structural descriptors allowing to predict their influence on the protein's aggregation tendency will be investigated.

Students selected for this project, after thesis registration, are eligible to apply to the BioISI Junior Programme (supporting 8 students with a 6-month Scholarship BII), being the selection criterium the academic merit of the candidates.