Regulatory protein:protein interactions between Huntingtin and aggregation modulators

Place of work: Protein Misfolding and Amyloids in Biomedicine Laboratory, BioISI – Biosystems & Integrative Sciences Institute, Faculdade de Ciências da Universidade de Lisboa, Lisboa

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Huntingtin (HTT) is self-propagating amyloidogenic protein implicated in Huntington's disease (HD) whose pathological deposition causes neuronal death. Age-dependent loss of proteostasis is primarily responsible for the formation of aggregates observed in HD patients and understanding the underlying mechanisms accounting for the protective activity of molecular chaperones is critical not only to establish how is protein aggregation regulated in in the brain but also to develop pharmacological modulation capable to enhance chaperone functions such as those involving S100 proteins. S100 proteins are calcium-binding proteins produced by astrocytes that are increased from early stages of neurodegeneration. The Gomes lab recently identified one of these proteins, S100B, as having novel chaperone activities capable to inhibit amyloid aggregation and toxicity, making them novel players in brain proteostasis in neurodegenerative diseases. Also, the Wanker lab has found interactions in yeast two-hybrid screens. In this collaborative project that comprises a training period in Berlin, the selected trainee will carry out experiments to investigate regulatory interactions using different structural, biochemical, and cellular methods. In particular, the student will express and purify the target proteins, will carry out protein aggregation assays using kinetic methods and will investigate protein interactions using biophysical spectroscopies and fluorescence spectroscopy.