

Title	Photo-flexible molecules to target neurodegenerative diseases [FlexMol]
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Project description:

As we age, our same metabolism together with some external factors conspire against us, resulting in the misfolding of proteins which are associated to degenerative diseases like Alzheimer's and Parkinson's. At the moment there is no treatment for any of the known degenerative diseases. However, there is hope. The increasing knowledge of the causes of incorrect proteins accumulation is beginning to pay off with possible pharmacological treatments. As the number of known incorrect proteins structures grows, scientists have more options to find common structures for the design of specific chemical inhibitors of aggregation. Although we are at risk of accumulating misfolded proteins every day we age, to function properly our cells must continually make proteins. Thus understanding misfolding will ultimately help protecting us from serious diseases. To do this, within this project we plan to develop a set of dynamical adapting foldamers, which are created chemically by following bio-inspired concepts, and aimed at powerfully interact with proteins thus to providing us new information on the very early stages of these incurable diseases. The first outcome of the FlexMol project will be the production of a large number of intrinsically photo-controllable foldamers which are to be considered as very innovative supra-molecules. Their rational studies will end up in a selection of a certain number of candidates to be applied on binding-interaction with alpha-synuclein (protein associated to Parkinson). The second outcome of the FlexMol project will be the studies of aggregation prone proteins associated to Parkinson disease in cells, in presence of the selected foldamers, prior and after photo-irradiation. Of course, cytotoxicity, cell-internalization and related distribution of foldamers will also be studied. The PhD student will acquire: (i) organic synthetic protocols, (ii) peptide synthesis, (iii) a varieties of characterization methodologies, (iii) bases of biochemical experiments.

Publications:

1. *J. Am. Chem. Soc.*, **138**, 8007-8018 (2016). **2.** *Soft Matter*, **12**, 238-245 (2016). **3.** *RSC Adv.*, **6**, 73650–73659 (2016). *ACS Nano*, **9**, 4156-4164 (2015). *Macromolecules*, **47**, 7272–7283 (2014).

Collaborations/Network:

Biochemistry: Luigi Bubacco (Italy). Supramolecular Chemistry: Jonathan Clayden (UK).

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