A FRET pair for Illuminating Amyloid Fibril Formation

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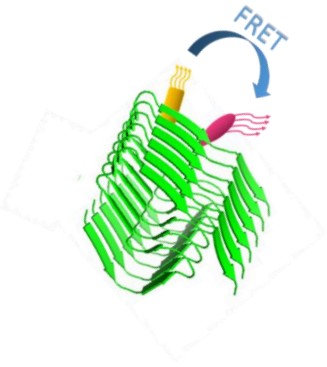
The presence of proteinaceous plaques and amyloid fibers resulting from the aberrant aggregation of certain proteins is the main molecular hallmark of neurodegenerative diseases such as Alzheimer's and Parkinson's. The conformational change from early, nontoxic aggregates to pre-fibrillar aggregates, followed by a subsequent cooperative growth is a critical step in the amyloid fibrillation process.[1] One of the most widely used methodologies to detect and monitor processes of biological importance, such as the aggregation of misfolded proteins, is the use of fluorescent probes in fluorescence microscopy, due to its high specificity and sensitivity.[2] The use of environment-sensitive fluorophores, which vary significantly their photophysical properties depending on the immediate environment, is a powerful tool used in the study of protein-protein interactions and amyloid aggregation.[3] Herein, we envisaged that using simultaneously two different fluorophores, capable of interacting with and reporting on the formation of pre-amyloid aggregates, would be an efficient methodology to maximize the contrast in the detection of such aggregates increasing the ratio image values obtained using multi-dimensional fluorescence lifetime imaging microscopy (FLIM), especially if fluorescence resonance energy transfer (FRET) is feasible between the pair of dyes. In this work we applied this concept in the study of amyloid fibrillization of the protein apoferritin.



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