P23. Design, synthesis and testing of a novel and efficient fluorescent compound for the staining of amyloid beta fibrillar aggregates.

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More than 46 million people are affected by Alzheimer’s disease (AD), a neurodegenerative disorder that, since it was discovered in 1906, has become the major cause of dementia in humans. AD is characterized, in its early phase, by an inability to create new memories and a failure to retrieve ancient ones and, in more advanced stages, by the loss of important human skills such as reasoning, abstraction and language. Histologically, the two classic lesions that characterize AD are senile plaques, made of extracellular fibrillar deposits of amyloid beta peptide (Aβ) aggregates, and intraneuronal neurofibrillary tangles composed of hyperphosphorylated tau protein [1]. According to the amyloid cascade hypothesis, aggregation of Aβ triggers the development of AD. In a previous study, we reported the discovery of four chemical compounds that inhibit the aggregation of Aβ17-40 and Aβ1-42 in vitro and in fungi models [2]. As these compounds interact with Aβ aggregating species, suitable fluorescent derivatives could be used to stain and detect Aβ fibrils by means of fluorescence microscopy. Therefore, we have design and synthesized four fluorescent compounds derived from one of the previously identified inhibitors. All of them interfere with Aβ17-40 aggregation (as it has been demonstrated by turbidimetry, dynamic light scattering and transmission electron microscopy) and one of them is an efficient marker for Aβ1-42 fibrils via fluorescence microscopy and exhibits a greatest sensitivity than thioflavin T (ThT) staining.

References