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Rationally designed peptide conjugates in Alzheimer Disease: implications for diagnosis and therapy

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Alzheimer Disease (AD) is a central neurodegenerative disorder characterized by behavioral disturbance and progressive cognitive impairment. It is the major cause of dementia affecting prevalently elderly individuals worldwide. The molecular pathways underlying AD onset implicates an abnormal turnover of the Aß monomer undergoing an aggregation process to generate oligomers and protofibrils. Aß oligomers are the most toxic substances for neurons, according to the amyloid cascade hypothesis. Unfortunately, there are challenges in diagnosing the early signs of the disease especially at the molecular level. Abnormal cognitive and behavioral clinical symptoms oIen indicate the accumulation of pathological markers in the brain. Therefore, early diagnosis and timely analysis of the condition are crucial for assessing the severity of the disease and providing appropriated treatment. Sensing molecules can be used to detect Aß biomarker and then assists early AD diagnosis. Among these, peptides may represent an opportunity for theragnostic intervention.
Peptide-based epitopes with covalently aNached other moieties able to explicate additional or complementary functions, including BBB permeation, metal chelation or aggregates disassembling, targeted imaging, and treatment, hold a promising potential for applications in AD.
In our laboratory, we have been synthesizing a variety of small peptides bio-conjugates differing by the peptide epitope or the conjugated scaffold. A range of molecular details, together with measured biological effects, have been listed with these systems, all of them accounting for the observed neuroprotection against the toxic insult induced by Aß oligomerization in primary cortical neurons. In this brief communication an overview of the design principles of the peptide conjugates, their neuroprotective activity, and their capability in detecting Aß peptide in solution are described in terms of potential use of these compounds as theragnostic agents and for the targeted drug delivery.

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