HYDROLYTIC CLEAVAGE OF PEPTIDE BOND BY METAL COMPLEXES IN ALZHEIMER'S DISEASE CONTEXT

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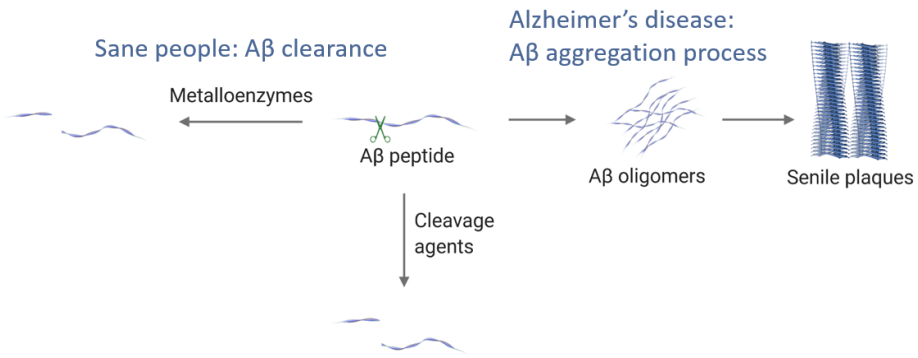
Alzheimer's disease is a neurodegenerative disease, characterized by the presence of aggregated β-amyloid peptide (Aβ), forming the amyloid plaques, in the synaptic cleft. In healthy brain, Aβ peptide is naturally cleared by metallopeptidases, particularly neprilysin. It is thus hypothesized that the accumulation of this peptide in Alzheimer's disease brain could come from a dysfunction of these enzymes [1].

The project presented here aims at studying complexes able to hydrolyse peptide bonds in model molecules, and to use them afterwards to cleave Aβ. Some complexes with azamacrocyclic ligands have indeed already been reported for their ability to cleave Aβ [2,3]. For the present study, a colorimetric test has been set up, which makes possible to screen the ability of several metal ions (Co, Cu, Zn) and families of ligands to cleave an amide bond. The screening results, as well as the most promising complexes will be presented during the talk.

To test these complexes on Aβ, another assay based on fluorescence anisotropy has been developed. It allows to monitor the kinetics of Aβ cleavage and to evaluate the approximate size of the obtained fragments. A proof of concept has been performed with proteases known to cleave Aβ, and the most promising metal complexes have been tested as well.



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