

Cu chelation with peptides as ligands in the context of Alzheimer's disease.

Alzheimer's disease (AD) is the most common neurodegenerative disease and the leading cause of dementia worldwide. Although extensive research has been conducted since its discovery in 1906, this disease remains incurable to this day. Since 2000, more than 200 drugs designed to address the causes of the disease—rather than just its symptoms—have failed at various stages of clinical trials. In light of this, there is an urgent need to develop strategies against new therapeutic targets.

Although the mechanisms underlying this complex disease are not fully understood, there is a consensus that the development of AD is attributable to the amyloid cascade. This process, shown in Figure 1, involves the production of a peptide called amyloid- β (A β) and the formation and extracellular accumulation of amyloid plaques through several stages. Such aggregates are thought to trigger various pathological events associated with AD.

Furthermore, dyshomeostasis of metal ions—particularly copper and zinc ions—is also linked to the amyloid cascade process. Amyloid plaques contain abnormally high concentrations of copper ions (mM). Extensive evidence has linked the high toxicity of A β -bound copper to its ability to promote the oxidative stress observed in AD through the catalytic production of reactive oxygen species (ROS). For these reasons, Cu is considered a therapeutic target of interest. The removal of Cu from the Cu-A β complex using peptide ligands is a particularly promising approach because it combines the advantages of affecting both ROS production and the formation of toxic aggregates.

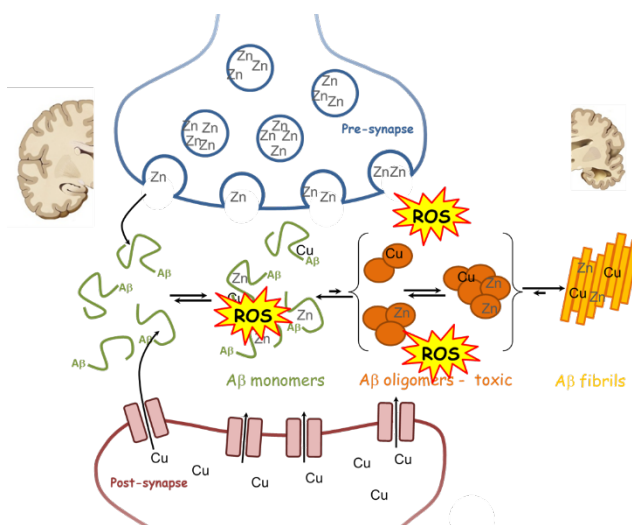


Figure 1. Amyloid cascade & the role of metal ions.

The proposed M2 thesis topic fits within this context. In particular, it aims (i) to study the impact of peptide ligands on Cu(A β)-induced ERO production and on the modulation of Cu-induced amyloid fiber formation, (ii) to characterize the coordination properties of Cu(II) and Cu(I) ions, as well as Zn(II) ions—which are also biologically relevant. These characterizations will be conducted using a wide range of physicochemical techniques (UV-vis, fluorescence, EPR, electrochemistry).

We are looking for a highly motivated student with a background in molecular chemistry and excellent grades. Candidates should have a keen interest in multidisciplinary projects in the field of bioinorganic chemistry. They should also be able to work autonomously and as part of a team.

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