PhD thesis offer

CNRS Coordination Chemistry Laboratory – Director: ***Pre. Isabelle Malfant –*** https://www.lcc-toulouse.fr
Team ***F « Alzheimer, Amyloids and BioInorganic Chemistry »*** *headed by* ***Dr. C. Hureau***
Contact : Charlène Esmieu (charlene.esmieu@lcc-toulouse.fr, 05 61 33 31 20)
Thesis start date: 1st July 2026
36-month funding: Foundation « Vaincre Alzheimer »
Please attach to your application a brief CV summarising your career history, including two references, a cover letter and your most recent academic results.

Evaluation of new traceable copper ligands in cell lines as a therapeutic approach to Alzheimer's disease

Alzheimer's disease (AD) is the leading cause of dementia worldwide. To date, there is still no cure for this disease. Between 2003 and 2012, more than 200 molecules targeting the causes of the disease, rather than just its symptoms, failed at various stages of clinical trials. In this context, there is an urgent need to develop new research tools to aid in the design of effective drug candidates.

Although the mechanisms underlying this complex disease are not fully understood, there is a general consensus attributing the development of AD to the amyloid cascade. This process, shown in Figure 1 is based on the production of a peptide called β-amyloid (Aβ) and its accumulation, leading to the successive extracellular formation of oligomers, fibrils and amyloid plaques. Such aggregates are thought to trigger various pathological events associated with AD.

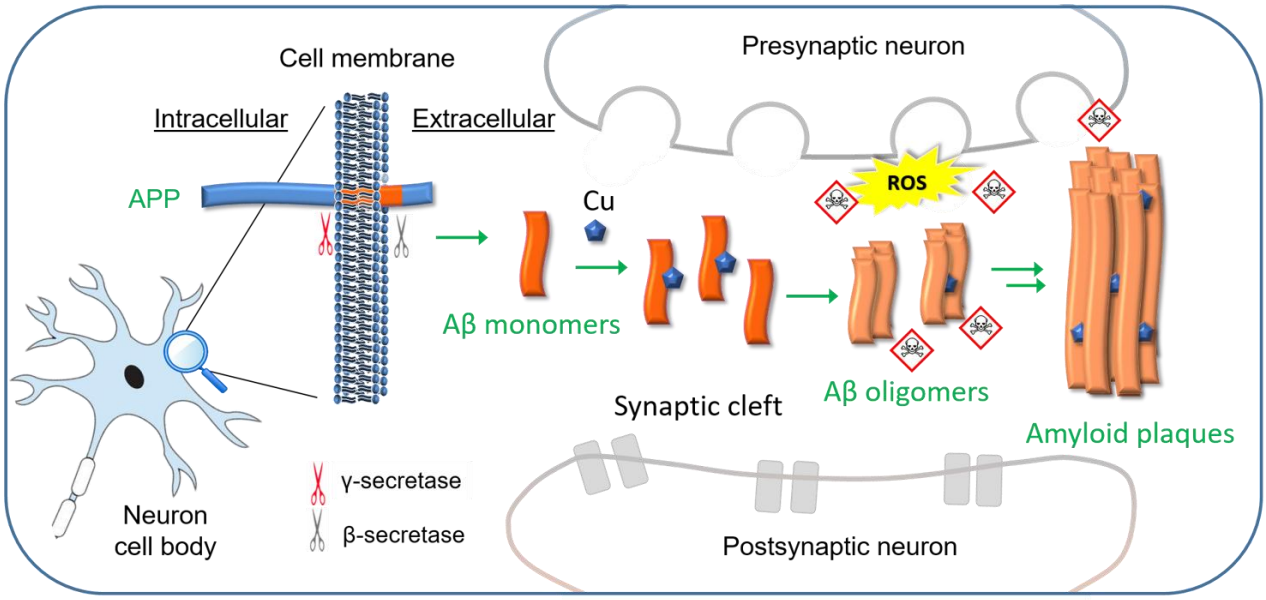

Figure 1: Schematic representation of the amyloid cascade hypothesis illustrating the involvement of copper ions.

Furthermore, dysregulation of metal ion homeostasis, particularly for copper and zinc ions, is also linked to the amyloid cascade process. Numerous pieces of evidence have linked the high toxicity of Cu bound to Aβ to its ability to promote the oxidative stress observed in AD via the catalytic production of toxic reactive oxygen species (ROS) (Encyclopedia of Inorganic and Bioinorganic Chemistry, 2018, doi.org/10.1002/9781119951438.eibc2635). For these reasons, Cu is considered a

therapeutic target of interest. The removal of Cu from the Cu-Aβ complex by ligands (L) is a particularly promising approach because it combines the advantages of having an impact on (i) the production of ROS, (ii) the formation of toxic aggregates (Inorganic Chemistry, 2019, 58, 20, 13509-13527) and (iii) copper homeostasis.

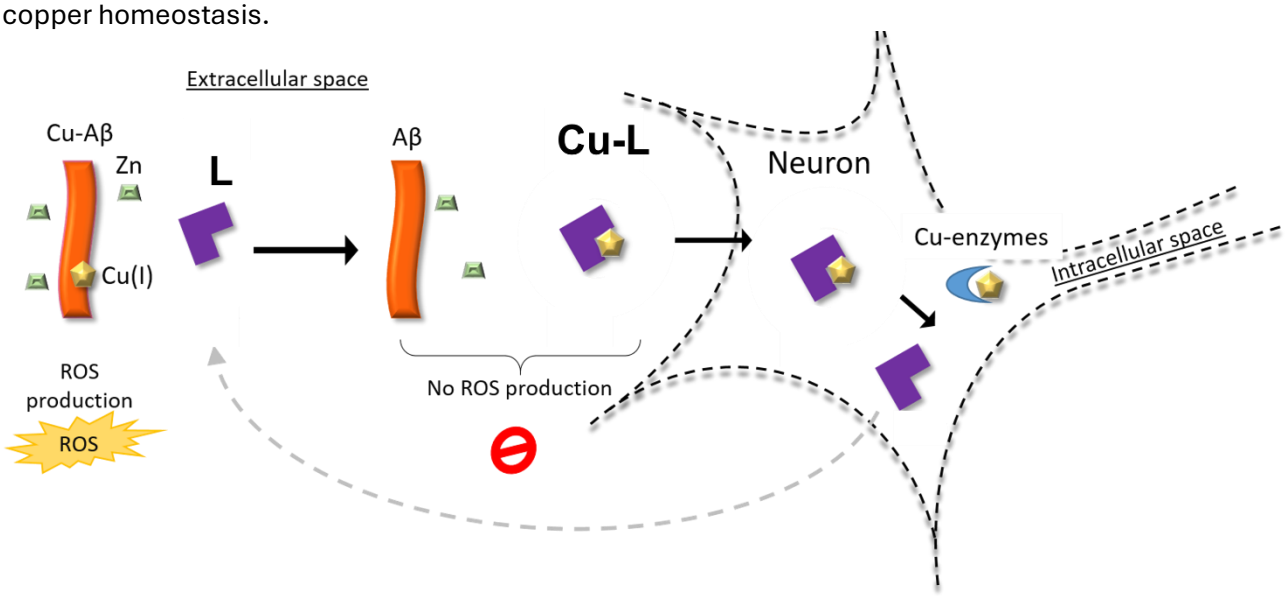

Figure 2: Schematic representation of the therapeutic effect of L

It is in this context that the proposed thesis topic fits. The work of the recruited person aims to test original ligands synthesised (L) at the LCC (Inorganic Chemistry, 2024, 63, 2340-2351), capable of removing copper from Cu-Aβ and stopping the associated ROS production (Figure 2). These studies will be conducted in vitro (in test tubes) and on model cell lines (in vivo). The experiments will focus on cultured cells to analyse how L penetrates cells, modifies Cu distribution, and influences cell viability and inflammation markers. The improvement in cell survival in the presence of L and Cu-Aβ will be studied using various techniques. L will be monitored in living cells using time-resolved confocal microscopy.

The candidate must be motivated, persevering and eager to work at the interface between chemistry and health in a multidisciplinary environment. The candidate must hold a Master's degree (or equivalent) in cellular/molecular biology, biochemistry, pharmacology or related disciplines. A keen interest in therapeutic chemistry and the chemistry-biology interface is essential.

The thesis work will be carried out between the Coordination Chemistry Laboratory (LCC) in Toulouse and the Institute of Cellular and Integrative Neurosciences in Strasbourg, within Dr Nicolas Vitale's team. In Toulouse, the thesis work will be supervised by Dr Charlène Esmieu, and Dr Christelle Hureau.