

OPEN PhD Position at the Coordination Chemistry – Lab in Toulouse – FRANCE

In the ALZOID (Alzheimer and amyloid) group

A PhD position is immediately available in the ALZOID group, headed by Dr. Christelle Hureau to work on new chelating agents within the context of Alzheimer's disease.

Summary: Alzheimer's disease (AD) is one of the most serious diseases mankind is now facing as its social and economic impacts are increasing rapidly. AD is very complex and the amyloid- β ($A\beta$) peptide as well as metallic ions (mainly copper and zinc) have been linked to its aetiology. While the deleterious impact of Cu is widely acknowledged, intervention of Zn is certain but still needs to be figured out.

The main objective of the present proposal, which is strongly anchored in the bio-inorganic chemistry field at interface with spectroscopy and biochemistry, is to design, synthesize and study new drug candidates capable of (i) targeting Cu(II) bound to $A\beta$ within the synaptic cleft, where Zn is co-localized and (ii) disrupting the aberrant Cu(II)- $A\beta$ interactions involved in ROS production and $A\beta$ aggregation, two deleterious events in AD. The drug candidates should thus have high Cu(II) over Zn selectively to preserve the crucial physiological role of Zn in the neurotransmission process. Zn contribution is always underestimated (if not completely neglected) in current therapeutic approaches targeting Cu(II) despite the known interference of Zn with Cu(II) binding.

To reach this objective, it is absolutely necessary to first understand the metal ions trafficking issues in presence of $A\beta$ alone at a molecular level (i.e. without the drug candidates). This includes: (i) determination of Zn binding site to $A\beta$, impact on $A\beta$ aggregation and cell toxicity, (ii) determination of the mutual influence of Zn and Cu to their coordination to $A\beta$, impact on $A\beta$ aggregation, ROS production and cell toxicity.

Methods used will span from organic synthesis to studies of neuronal model cells, with a major contribution of a wide panel of spectroscopic techniques including NMR, EPR, mass spectrometry, fluorescence, UV-Vis, circular-dichroism, X-ray absorption spectroscopy...

Profile searched: Creative, self-motivated candidates with an interest in developing an independent research program at the interface between chemistry and biochemistry, with a strong interest for physico-chemical methods and coordination chemistry.

This 3-years PhD project is funded by an ERC grant – Gross salary: 1750 Euros/month.

Please send your CV and contact details of previous supervisors to christelle.hureau@lcc-toulouse.fr ;

Dead-line for application: end of December 2016.