PhD Position

at interface biology-chemistry in Strasbourg

Design of copper-selective peptidic transporters to prevent amyloid-β toxicity

PhD Project between two research groups financed by IDEX interdisciplinary program. The two groups are located in adjacent buildings:
Partner Chemistry: Team Peter Faller: IC UMR-7177 CNRS/Université de Strasbourg
Partner Biology: Team Nicolas Vitale: INCI UPR-3212 CNRS/Université de Strasbourg

Project background: Despite intensive efforts to understand the causes and progress of neurodegenerative diseases, such as Alzheimer's disease (AD), there has been very little therapeutic progress for the patient. Interestingly, copper (Cu) homeostasis is known to be critical to many cellular functions and dis-regulation in Cu levels has been reported in several neurodegenerative diseases, like AD. However, there are no tools available yet to correct this potentially important contributing factor to the onset and/or development of these diseases. Indeed, loosely bound Cu is a very efficient catalyst in reactive-oxygen-species production and it contributes to the oxidative stress observed in several neurodegenerative diseases. Furthermore Cu accumulates in AD brains in the extracellular amyloid plaques, where Cu is bound to the main constituents of these plaques, the amyloid-β peptide (Aβ).
In this context, small molecules having a so-called Cu-*ionophore* activity, *i.e.* that bind this loosely bound, extracellularly Cu and transport it back into the cell, showed very promising therapeutic results.
Aim: The aim of the present project is to design and study compounds that are able to re-equilibrate the Cu-homeostasis in the context of AD.
Working program:
i) Design peptides with Cu-*ionophore* activity: Synthesis and characterization of Cu-*ionophores* (solid-phase peptide synthesis)
ii) Test of peptidic Cu-*ionophores* for their Cu transport efficiency and specificity (vs other metals) on cultured PC12 cells and cortical or hippocampal neurons.
iii) Synthesis of a fluorescent version the best Cu-*ionophores* to monitor Cu-release from the transporter within cells by fluorescence microscopy.
iv) Test if Cu-*ionophore* is able to remove Cu from Aβ (collaboration C. Hureau LCC, Toulouse) and if, as such, they can protect neuronal model cells from toxicity of Cu-Aβ.

Profile searched: The student to enter this PhD project should have a Master in chemistry or biology, with preference for a chemist with biological knowledge or a biologist with a (bio)-chemical background. Further experience in cell biology, biochemistry or biological inorganic chemistry would be welcome, but are not a prerequisite.

Application dead-line: 31 May
Starting date: September/October 2019
Gross salary: ca 1700 Euros/month

For application or inquiry, contact the supervisors:
Peter Faller: pfaller@unistra.fr and Nicolas Vitale: vitalen@inci-cnrs.unistra.fr