

## JOB DESCRIPTION

Job Title :  
PhD Position

Job Summary :  
PhD Position at interface biology-chemistry in Strasbourg on the design of copper-selective peptidic transporters to prevent amyloid- $\beta$  toxicity

(English, max 1000 characters)

Job Description :  
(English, detailed information – max 3000 characters)

### **PhD Position at interface biology-chemistry in Strasbourg**

#### **Design of copper-selective peptidic transporters to prevent amyloid- $\beta$ 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- $\beta$  peptide (A $\beta$ ).

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 of 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 A $\beta$  (collaboration C. Hureau LCC, Toulouse) and if, as such, they can protect neuronal model cells from toxicity of Cu-A $\beta$ .

Competences that will be developed for the candidate during the PhD:

Scientific competences:

- Design of potential peptide candidates, solid-state peptide synthesis and peptide purification
- Bioconjugation of fluorophores to peptides
- Spectroscopic techniques to study metal-peptide interactions and their reactivity in the test tube (EPR, collaboration with B. Vileno; CD, NMR, electronic absorption, fluorescence, etc)
- Cell culture (PC12 cells & primary neurons), immunofluorescence, and cell imaging
- Memory testing in a mouse models

Other competences:

- Presentation of scientific results in written and oral form, in French and English
- Working in a group and between two labs, and acquire and integrate two different scientific cultures (chemistry and biology)
- Working in an autonomous fashion under the supervision of experienced researchers
- Leading a PhD project and supervision of internship students (Licence or Master)

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.

Starting date: September/October 2019

Gross salary: ca 1700 Euros/month

Main research field : Neurosciences & Chemistry

Agricultural sciences / Anthropology / Architecture / Arts / Astronomy / Biological sciences / Chemistry / Communication sciences / Computer science / Criminology / Cultural studies / Demography / Economics / Educational sciences / Engineering / Geosciences / Environmental science / Ethics in health sciences / Ethics in natural sciences / Geography / History / Information science / Juridical sciences / Language sciences / literature / Mathematics / Medical sciences / Neurosciences / Pharmacological sciences / Philosophy / Physics / Political sciences / Religious sciences / Sociology / Technology / Other / All

Offer Requirements :

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 chemistry would be welcome, but are not a prerequisite.

Speaking French is not mandatory, English is enough.

Eligibility criteria:

Master 2 diploma

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**JOB DETAIL**

Type of contract : temporary
Status : full-time
Company / Institute : Institute of Chemistry and INCI
Country : France
City : Strasbourg
Postal Code : 67000
Street : 4 rue B. Pascal

**APPLICATION DETAILS (mandatory)**

Provisional start date : 01/10/2019
Application deadline : 31/05/2019
Application e-mail : : <a href="mailto:pfaller@unistra.fr">pfaller@unistra.fr</a> and <a href="mailto:vitalen@inci-cnrs.unistra.fr">vitalen@inci-cnrs.unistra.fr</a>