

PhD Position in Synthetic Chemistry

Overview of the Post

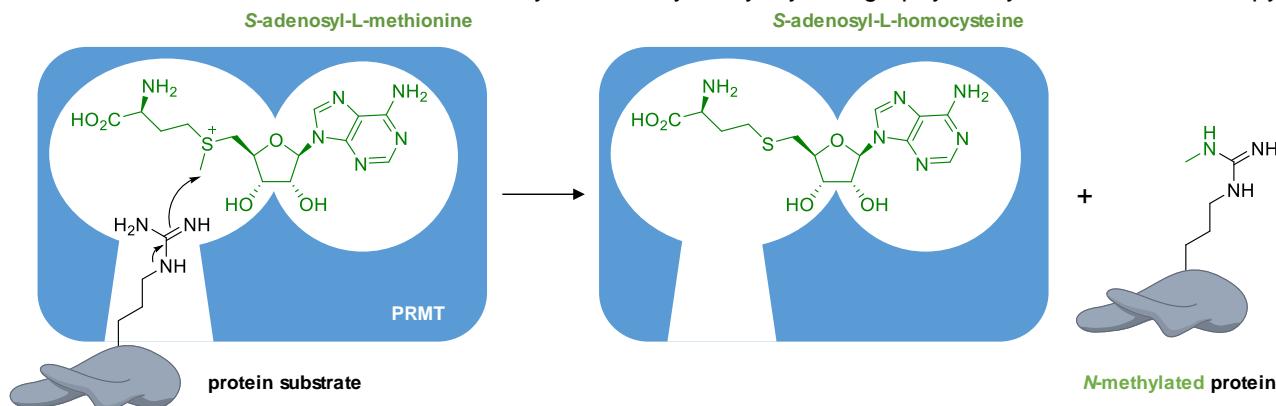
Research Group	BioFunctional Chemistry		
Location	UMR7199 – Faculty of Pharmacy – University of Strasbourg 74 route du Rhin, 67400 Illkirch		
Salary	Approximately 20 k€ per annum – teaching / demonstrating opportunities		
Hours	Full-time		
Contract type	36-month fixed term position funded by <i>Agence Nationale de la Recherche</i>		
Reporting to	Dr Guilhem Chaubet and Dr Alain Wagner		
Website	http://www.biofunctional.eu/		
Social networks	CAMB.UMR7199	BFC_UMR7199	BioFunctional Chemistry Lab

Job Description

The BioFunctional Chemistry group is looking for a competent and highly motivated organic chemist for a PhD project in the field of synthetic chemistry applied to structural biology, aiming at deciphering protein arginine methylation processes.

Protein arginine methylation is a widespread and prevalent post-translational modification (PTM) that has emerged as a major mechanism for regulating protein function in eukaryotic cells. This alkylation process is catalysed by protein arginine N-methyltransferases (PRMTs) via the transfer of methyl groups from the donor S-adenosyl-L-methionine (SAM) to the side chain of arginine residues (see Figure). Depending on the PRMT family, arginines can be either mono- or dimethylated, adding an extra degree of diversification to this group of PTM. Although once thought to be confined to histones and RNA binding proteins, a myriad of various proteins have since been shown to be arginine-methylated *in vivo*, impacting a plethora of biological processes such as RNA splicing, DNA repair, virus packaging and replication, tumour suppressor function or modulation of the immune response. It is therefore not surprising that dysfunction of arginine methylation is correlated with the development of many diseases. However, despite the large amount of biological and structural data on PRMTs, the dynamic biological process involving specific protein recognition prior to methylation remains to be elucidated. As part of a consortium with two other partners, one team of structural biologists (*Prof. Jean Cavarelli, Institut de Génétique et de Biologie Moléculaire et Cellulaire - CNRS UMR 7104 - Inserm U 1258, Strasbourg*) and one of mass spectrometry researchers (*Dr Sarah Cianferani, Laboratoire de Spectrométrie de Masse BioOrganique, CNRS UMR7178, Strasbourg*), this PhD project aims to understand how PRMTs recognise, bind and achieve specific arginine methylation of their substrates by characterising functional macromolecular PRMT complexes at the molecular level.

To achieve this, proteins incorporating unnatural arginine motifs will be utilized as a tethering tool to freeze a functional state of PRMT complexes prior to the methyl transfer. Several types of arginine mimics will be designed and synthesised; the resulting complexes between the PRMT and the protein substrates will then be generated and characterised by several biophysical methods, including native mass spectrometry. Three-dimensional structure determination will finally be done by X-ray crystallography or cryo-electron microscopy.



This PhD offers a unique opportunity for organic chemists to apply their knowledge to the synthesis of small molecules with high value and to the generation of unnatural peptide and proteins. Such an applied research project, at the interface of synthetic chemistry and biology, will permit the PhD student to become familiar with all cutting-edge techniques of a multidisciplinary environment.

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The responsibilities of the candidate will be as follow:

- Synthesize a new family of unnatural arginine residues
- Incorporate them into peptide and proteins
- Optimize and develop native chemical ligation procedures
- Work alongside mass spectrometry researchers and structural biologists
- Collaborate in the preparation of scientific reports and journal articles
- Take a share in the laboratory-based collective tasks
- Attend and participate actively in group meetings

The ideal candidate will have to demonstrate the following skills:

- Broad knowledge and experience in organic synthesis
- Experience in amino acid and peptide synthesis
- High degree of self-organization, discipline in documentation and reporting
- Be able to work effectively as part of a group, assume group responsibilities and supervise junior team members

In addition, good communication skills in both French and English will be sought after.

The BFC Group

The BioFunctional Chemistry group is currently run by Dr Alain Wagner and comprises 11 researchers – 2 permanent researchers, 3 engineers and technicians, 2 postdoctoral researchers, and 5 PhD students – possessing a strong knowledge in synthetic chemistry, bioconjugation techniques, cell culture, and protein expression and purification. This in-house multidisciplinary expertise allows the group to be competitive in the expanding field of bioconjugation, by being able to perform every step of the research in this area, from the synthesis of the molecules to their biological testing.

For representative and recent publications, please refer to:

- Ursuegui *et al.*, *Nature Commun.*, **2017**, 8, 15242
- Dovgan *et al.*, *Bioconjugate Chem.*, **2017**, 10.1021/acs.bioconjchem.7b00141
- Ripoll *et al.*, *ACS Appl Mater Interfaces*, **2016**, 8, 30665
- Ahmed Atto Al-Shuaeeb *et al.*, *Chem. Eur. J.*, **2016**, 22, 11365
- Liu *et al.*, *Angewandte Chemie Int. Ed.*, **2016**, 55, 12073

How to Apply

Applicants are invited to send a CV, transcripts of Master's studies (including grades) and a summary of their research achievement, as well as details of two referees, to Guilhem Chaubet (chaubet@unistra.fr) and Alain Wagner (alwag@unistra.fr).

