

PhD Position in Synthetic and *In-Vivo* Chemistry

Overview of the Post

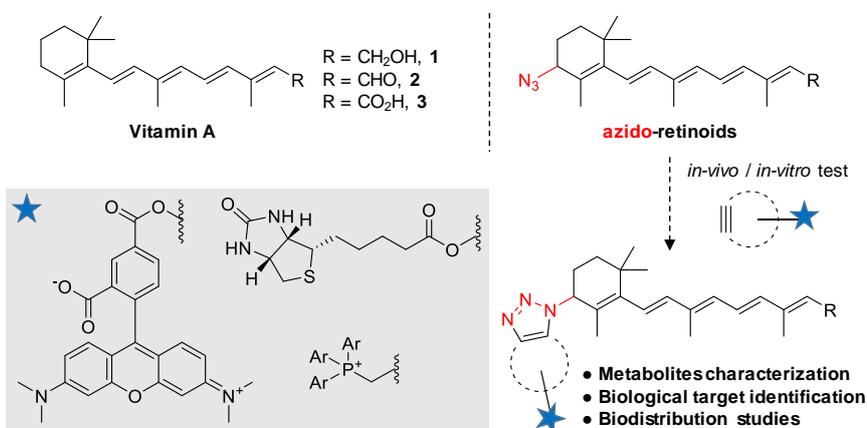
Research Group	BioFunctional Chemistry
Location	UMR7199 – Faculty of Pharmacy – University of Strasbourg 74 route du Rhin, 67400 Illkirch
Salary	Approximately 20 220 € per annum
Hours	Full-time
Contract type	36-month fixed term position funded by <i>Agence Nationale de la Recherche</i>
Reporting to	Dr Alain Wagner and Dr Guilhem Chaubet
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 *in-vivo* bioorthogonal reactions. This project will be conducted in close collaboration with biologists (Dr Wojciech Krezel, *Institut de Génétique et de Biologie Moléculaire et Cellulaire - CNRS UMR 7104 - Inserm U 1258, Strasbourg*) and mass spectrometry experts (Dr François Fenaille, *Laboratoire d'Études du Métabolisme des Médicaments, CEA, Saclay*), and aims at discovering the *in-vivo* active form of vitamin A.

Vitamin A is a micronutrient critical for normal development and physiology in vertebrates, which corresponds to a collection of structurally related polyene compounds, including retinol **1**, retinal **2** and all-*trans*-retinoic acid **3**. While the latter is currently considered as the major active form of vitamin A, results obtained in Dr Krezel's team indicate otherwise and suggest the existence of other bioactive forms of vitamin A. This project thus aims at identifying the structures of such species thanks to a combination of *in-vivo* bioorthogonal chemistry and mass spectrometry analyses.

Bioorthogonal chemistry is the ability to perform synthetic transformations in living organisms and complex media (in plasma, cells, tissues, etc.) without interfering with any natural chemical process. Azide groups are classically employed in this regard as they are naturally absent from biomolecules and can thus be easily functionalised with alkynes via Huisgen 1,3-dipolar cycloaddition with little or no side reactions. By designing



unnatural azido-analogues of retinol, retinal and all-*trans*-retinoic acid, we would be able to functionalise them on demand with various alkyne probes that will also be developed in the frame of this project. These probes will be equipped with different functional group (e.g. fluorophore, mass spectrometry tag, biotin), which will allow us to capture, identify and characterize all metabolites produced *in-vivo* from the unnatural azido-retinoids.

Thus this PhD offers a unique opportunity for organic chemists to use their knowledge in an applied research project at the interface of synthetic chemistry and biology, by developing new conjugation tools and familiarise themselves with all cutting-edge techniques of a multidisciplinary environment.



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The responsibilities of the candidate will be as follow:

- Synthesise a new family of unnatural retinoids
- Synthesise several alkyne probes for various applications
- Optimise and develop bioconjugation procedures
- Work alongside mass spectrometry researchers and 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
- Understanding of the principles of bioconjugation methodology
- High degree of self-organisation, 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 Alain Wagner (alwag@unistra.fr) and Guilhem Chaubet (chaubet@unistra.fr).

