Masters Internship Offer

BioFunctional Chemistry Team (led by Alain Wagner)

University of Strasbourg

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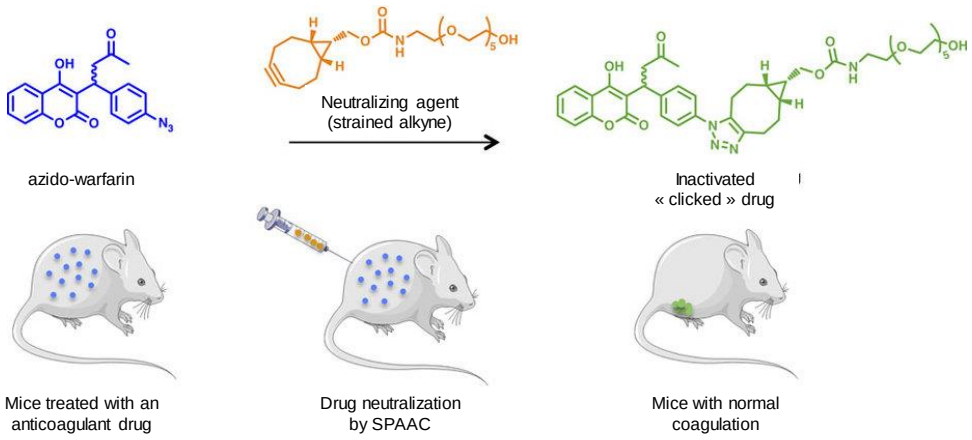
Topic	**Development of a new synthetic method to access novel strained alkynes**

Cyclooctynes are one of the smallest cyclic alkynes that can be isolated. Due to the strain imposed by the cyclic structure, bond angles in the alkyne motif drift away from the ideal 180°, making this triple bond far more reactive than in acyclic systems or in larger cyclic alkynes. This unusual reactivity led to the development of **strain-promoted alkyne-azide cycloaddition** (SPAAC), the non-catalyzed version of the classical Huisgen reaction. By suppressing the need for toxic Cu(I) catalytic species, SPAAC found major applications in bioorganic chemistry. For example, our group recently demonstrated that an appropriate cyclooctyne derivative could act as a neutralizing agent in vivo (see below). Mice were given azido-warfarin – the azido derivative of the anticoagulant drug warfarin, which can lead to detrimental side effects, such as hemorrhages. Addition of a neutralizing agent helped to inactivate the remaining circulating drug, and restored the coagulating activity in mice. Thanks to this **bioorthogonal reaction** – the azide moiety only reacts with the strained alkyne and vice versa – an azido drug could be neutralized after its desired therapeutic effect had been obtained, which could minimize potentially hazardous side effects.



Despite high-profile applications, strained alkynes are still suffering from various drawbacks, chief among which are their global hydrophobicity and length/cost in synthesis. This Master's project will be centered on **synthetic chemistry** and aims at **developing new synthetic methods towards novel cyclooctyne skeletons in a fast and efficient way**. Focus will be made on accessing compounds with low lipophilicity and high reactivity and most promising compounds could then be tested *in-vitro* for several applications (metabolomics approaches, cellular imaging, etc.).

The responsibilities of the candidate will be as follow:

- Synthesise new types of strained alkynes
- Evaluate their reactivity in SPAAC
- 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:

- Good knowledge of organic synthesis
- Understanding of the principles of analytical chemistry
- High degree of self-organisation, discipline in documentation and reporting
- Be able to work effectively as part of a group, assume group responsibilities

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

About the BFC Group

The BFC group is currently run by **Dr Alain Wagner** and comprises 13 researchers – 3 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 more details, please visit us at http://www.biofunctional.eu/ or follow us on Twitter @BFC_UMR7199

How to Apply

Applicants are invited to send a CV and transcripts of Master's studies (including grades) to Alain Wagner (alwag@unistra.fr) and Guilhem Chaubet (chaubet@unistra.fr).

References

Ursuegui *et al.*, *Nature Commun.*, **2017**, *8*, 15242 ; M. F. Debets *et al.*, *Acc. Chem. Res.*, **2011**, *44*, 805 ; C. J. Pickens *et al.*, *Bioconjugate Chem.*, **2018**, *29*, 686.

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