



Université de Bretagne Occidentale



PhD thesis in organic chemistry and applications for biology

Duration: 3 years

Title: Synthesis of amphiphilic compounds by using click chemistry

Laboratory: CEMCA, UMR CNRS 6521, équipe COSM, Université de Brest

PhD thesis supervision: Paul-Alain Jaffrès, pjaffres@univ-brest.fr, 02 98 01 61 53

Mathieu Berchel, Mathieu.berchel@univ-brest.fr, 02 98 01 62 86

Funding: Graduate contract from the University of Brest

Context: The group « Phosphorus, Lipid & Vectorization » (COSM research team from the CEMCA laboratory, UMR CNRS 6521) is involved in the design of amphiphilic compounds that are conceived for different applications. Accordingly, we have synthesized cationic amphiphiles that are used for nucleic acids delivery and applied for tendon healing, anti-tumor vaccination or for a therapeutic approach of cystic fibrosis. Some of our cationic amphiphiles were also identified for their outstanding bactericidal properties. Other type of amphiphilic compounds belonging to the glyco-glycerether lipids, were specially designed to modulate the activity on ionic channels that in a murine metastatic breast cancer model, abolished the occurrence of bone metastases. The use of click reaction for the construction of amphiphilic compound is an attractive strategy to design new molecular scaffold of amphiphilic compounds that will be tested for the applications mentioned above.

Objectives: On the basis of our preliminary results, we will synthesize amphiphilic compounds by engaging a lipid building block featuring a phosphorus and sulfur function in a click reaction involving either an amine or a Diels-Alder reaction. The first goal will be to set up a methodologic study in order to identify the best reaction conditions to observe the click reaction (rapidity, facility of purification of the product). We will assess the achievement of these click reactions under biphasic conditions (this condition should facilitate the purification of the product) and will also apply the methodology for the functionalization of nano-particles dispersed in water (liposomes). In a second step, we will apply our methodology to construct fluorescent amphiphiles, cationic amphiphiles for nucleic delivery or amphiphiles for the modulation of ion channels.

Missions: The recruited person will have to develop a methodologic part that will consist to evaluate the scope of the new click reactions. This work of organic chemist will include purification and the full characterization of the new products. Then, the recruited person will apply the methodology to prepare new amphiphilic compounds that will be tested for different application in biology.

Collaborations: The biologic test will be achieved with our current collaborators (Brest, Orléans). This PhD thesis will be also the occasion to set up collaboration with the group of Prof. S Sortino & Dr. A. Fraix (University of Catania -Italia) who are specialized in spectroscopy and photo-chemistry. We will apply our click reactions to design photo-reactive amphiphiles that can produce NO under irradiation. This collaboration will be also a part of the recent Erasmus agreement that was recently settled between the chemistry department (UBO) and the chemistry and Drug department from the University of Catania.

References : M. Berchel, T. Le Gall, O. Lozach, J.P. Haelters, T. Montier, P.A Jaffrès, *Org. Biomol. Chem.*, **2016**, *14*, 2846-53 ; D. Afonso, T. Le Gall, H. Couthon-Gourvès, A. Grélard, S. Prakash, M. Berchel, N. Kervarec, E.J. Dufourc, T. Montier, P.A. Jaffrès, *Soft Matter*, **2016**, *12*, 4516-20 ; W. Berthe, C.M. Sevrain, A. Chantôme, A.M. Bouchet, M. Gueguinou, Y. Fourbon, M. Potier-Cartereau, J.P. Haelters, H. Couthon-Gourvès, C. Vandier, P.A. Jaffrès, *ChemMedChem*, **2016**, *11*, 1531-1539 ; F. Herrera, C.M. Sevrain, P.A. Jaffrès, H. Couthon-Gourvès, A. Grélard, E.J. Dufourc, A. Chantôme, M. Potier-Cartereau, C. Vandier, A. Bouchet, *ACS Omega*, **2017**, *2*, 6361-6370 ; M. Berchel, S. Akhter, W. Berthe, C. Gonçalves, M. Dubuisson, C. Pichon, P.A. Jaffrès, P. Midoux, *J. Mater. Chem. B*, **2017**, *5*, 6869-6881 ; A. Mottais, M. Berchel, Y. Sibiril, V. Laurent, D. Gill, S. Hyde, P.A. Jaffrès, T. Montier, T. Le Gall, *Inter. J. Pharm.*, **2018**, *536*, 29-41.