

## PhD position in organic chemistry

**Title:** Synthesis of glycoconjugates based on *C*-glycoside analogues of T<sub>N</sub> antigen for anticancer immunotherapy

**Supervisor:** Dr Stéphane Guillaume ([stephane.guillaume@univ-lemans.fr](mailto:stephane.guillaume@univ-lemans.fr)).

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**Laboratory:** Equipe MSO – Institut des Molécules et Matériaux du Mans (IMMM) – UMR CNRS 6283, – Le Mans Université (<http://immm.univ-lemans.fr>).

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A strategy of anticancer immunotherapy is based on the administration of a vaccine containing a tumor-associated antigen in order to activate immune cells and to produce specific antibodies directed to these antigens. Tumor-associated carbohydrate antigens (TACAs) are specific of some cancer cells as they are highly expressed on surface membrane of numerous human cancer cells. In opposite, they are quite not detectable on normal cells. So, these antigens represent an interesting and potential therapeutic target in immunotherapy strategy. However, the main problem of TACAs is their low immunogenicity which not allows to induce a strong immune response. To reach such immune response, it is necessary to obtain a T-cell dependent immune response and, for that, TACAs are conjugated to a carrier protein or a peptide, which are T epitope.<sup>1</sup> Nevertheless, the main drawback of such carbohydrate-derived molecules is their low metabolic or chemical stability due to the hydrolytic lability of the glycosidic bond limiting their use as potential drug candidates.

In that context, we propose to prepare more stable mimics such as *C*-glycoside analogues of T<sub>N</sub> antigen. The first goal of this PhD project is the synthesis of constrained or not *C*-glycosides of T<sub>N</sub> antigen following a recent reported methodology of the team.<sup>2</sup> In addition, a complementary study about the preferred conformation of the new analogues will be implemented using NMR analysis or molecular modeling. Finally, the new analogues will be conjugated to some glycolipids which have the ability to activate a sub-population of T cells. Antigenicity and immunogenicity of the new glycoconjugates will be evaluated.

**Profile of the candidate:** Strongly motivated candidate displaying a Master degree in molecular organic chemistry field and interested in an organic synthesis project at the biology/chemistry interface. The candidate will have the ability to work in team, a scientific curiosity and an experience in multi-step synthesis. Knowledge of glycochemistry would be appreciated.

**Application:** applicants should send a cover letter and a CV with the names of at least two referent persons to the two supervisors (see above).

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<sup>1</sup> O. Ouerfelli, J. D. Warren, R. M. Wilson, S. J. Danishefsky, *Expert Rev. Vaccines* **2005**, *4*, 677-685.

<sup>2</sup> a) F. Rouzier, R. Sillé, O. Montiége, A. Tessier, M. Pipelier, G. Dujardin, A. Martel, A. Nourry, S. Guillaume *Eur. J. Org. Chem.* **2020**, 6749–6757.