PhD position in organic chemistry (H/F)

Funding: ANR PRC 2022
Gross salary: ~2100€ /Mth
Starting date: November 2022
Group "Glycochemistry and Bioconjugates",
CEISAM laboratory, UMR6230, Nantes University.

Synthesis of multivalent sialidase inhibitors, as a therapeutic perspective against inflammatory bowel diseases

Research project:

Mucins are protective glycoproteins of the intestinal wall displaying on their surface sialic acids in important quantities such as N-acetylneuraminic acid (Neu5Ac). Neu5Ac serves as a metabolic substrate for the development of specific bacterial species in the microbiota. Several independent studies show that an excessive hydrolysis of Neu5Ac by bacterial sialidases (SAs) leads to an outburst of enterobacteria and in particular of adherent and invasive Escherichia coli strains (AIECs). These AIECs are overrepresented in the gut of patients with Crohn's disease, and play a fundamental role in the severity of the inflammation. The ANR project Sialobacter proposes to develop potent and selective multivalent inhibitors of SAs. The *in vitro* and *in vivo* evaluation of the compounds will be performed on biologically relevant targets and models. The multivalent inhibitors may constitute an innovative approach for the treatment of chronic inflammatory bowel diseases.

PhD work

The recruited PhD will perform the multi-step chemical synthesis of monovalent SA inhibitors. The compounds will be chemically appended to biocompatible scaffolds to form multivalent SA inhibitors. In a second step, the inhibitory activity of the compounds will be evaluated on biologically relevant targets.

Candidate profile

The PhD candidate should have a Master degree in organic chemistry and specific skills in the chemical synthesis and purification of organic molecules. A previous experience in carbohydrate chemistry is not mandatory but the candidate should have a strong motivation for developing chemical therapeutics and working at the chemistry-biology interface. The candidate will acquire a strong knowledge in carbohydrate and medicinal chemistry.

References

Polyvalent Transition-State Analogues of Sialyl Substrates Strongly Inhibit Bacterial Sialidases. Assailly, C. et *al. Chem. Eur. J.* **2021**, 27, 3142-3150.
Multivalent thiosialosides and their synergistic interaction with pathogenic sialidases. Brissonnet, Y. et *al*. *Chem. Eur. J.* **2019**, 25, 2358-2365.

Applicants should send their detailed CV and a letter of motivation to:
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