PhD student position

"Synthesis of original nucleoside analogs as a therapeutic solution to fight (re)emerging RNA viruses"

To be filled in October 2021

Laboratory: CEISAM-UMR CNRS 6230 (https://ceisam.univ-nantes.fr/), SYMBIOSE team

Subject : Synthesis of original nucleoside analogs as a therapeutic solution to fight (re)emerging RNA viruses
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Context and objectives of the thesis:
The Covid-19 pandemic reminds us of our vulnerability to viruses, and especially to emerging RNA viruses (SARS-CoV-2, Zika virus, Dengue virus, Chikungunya virus, Ebola virus, ...). Along with a prophylactic approach (vaccines), the development of antivirals targeting viral RNA polymerase, which plays a central role in the viral replication cycle, constitutes a complementary therapeutic approach. Inhibition of RNA polymerase with small chemical molecules is an essential strategy beside vaccination, providing an effective curative treatment of severe forms of the disease. As such, nucleoside analogs, known for their potential in antiviral chemotherapy for decades, could provide an effective therapeutic solution [1].
The project of this thesis is based on the expertise of the team in the synthesis of nucleoside and nucleotide analogues [2, 3]. The synthesis of new nucleoside analogs will be developed, with relevant structural modifications at the 1', 2', 3'or 4' positions of the furanose part of the molecule. Some synthetic strategies developed in the laboratory can give access to pertinent key precursors, and so open the way to libraries of nucleoside analogs, which could be tested as potential antivirals. Moreover, modelization study with the biological target (RNA polymerase) and the most relevant molecules could give rational informations for the optimization of the structures in order to enhance antiviral activity. The antiviral evaluation of the new molecules will be carried out by a dedicated platform on a large panel of viruses.

Environment et collaborations
CEISAM laboratory is the molecular chemistry laboratory of the University of Nantes with 5 research teams recognized in organic synthesis, theoretical chemistry, and physical and analytical chemistry. It has analysis platforms with a park of equipments for NMR (NMR platform), spectrometric analyzes (AMaCC platform) and other specific analytical equipments.

The Symbiose team with 7 researchers and teachers, is involved in projects including total synthesis and programs at the interface of chemistry-biology. The projects are developed by PhD students (around 5) and masters/contract agents (around 10). The team maintains a dynamic and conviviality through regular seminars to discuss about the scientific programs, and offers so a wide scientific culture.

The PhD student will integrate the GAVO program (Generation d' Anti-Viraux Originaux ; Supervised by J. Lebreton), a national research consortium including three laboratories of organic chemistry with expertise in the synthesis of nucleosides and nucleic acids, along with a molecular modeling team. Two members of our team will supervised the PhD student (Monique Mathé-Allainmat and D. Dubreuil)
The funding will allow comfortable support to the candidate for the development of its research work and participation to conferences. The antiviral evaluation of the new molecules on a large panel of viruses will be carried out by a biological platform associated to the program. As such, participation to regular meetings of the consortium, with chemists in organic chemistry and modelisation as well as biologists, will give to the candidate a good expertise at the chemistry-biology interface.

Required profile :
The applicant must have a master's degree in organic chemistry and so good knowledge of organic synthesis and analytical chemistry (HPLC, mass spectrometry, NMR, ...). Experience in nucleoside and / or nucleic acid chemistry would be appreciated. As part of this project, the candidat will have to promote his (her) research work in consortium meetings, but also in participation to conferences.

Application deadline : july 10, 2021

Références :

[1]. A. Ami, H. Ohrui, *ACS Med. Chem. Lett.* **2021**, *12*, 510−517
[2]. J. Lebreton, J.-M. Escudier, L. Arzel, C. Len. *Chem. Rev.* **2010,** *110,* 3371–3418.
[3] L. Arzel, D. Dubreuil, F. Dénès, V. Silvestre, M. Mathé-Allainmat, J. Lebreton, *J. Org. Chem*. **2016**, *81*, 10742−10758.