PhD Student in Organic and Medicinal Chemistry

Description

3-year PhD fellowship available in team COrInt (UMR CNRS 6226 ISCR) at Université de Rennes to work on the synthesis and development of protein-protein interaction disruptors involving CD95.

Project

In women, breast cancer is the most common type of cancer and the second leading cause of cancer death. Among breast cancers, the triple-negative molecular subtype (TNBC) is characterized by its aggressiveness, its rapid evolution, in particular with numerous metastases, and by the lack of targeted therapies compared to the other forms of breast cancer. In this context, the involvement of the CD95 receptor and its ligand (CD95L) has been clearly demonstrated. Thus, the goal of this project is to inhibit CD95 pathways as new therapeutic options for TNBC patients. Two key CD95-protein interactions are targeted and disruptors will be design and synthesize according to the sequences of specific CD95-domains involved in these interactions. As a medicinal chemistry program, the project will be running in collaboration with biologists as well as molecular modelers.

See for our recent publications on this topic:

• Disrupting the CD95-PLCγ1 interaction prevents Th17-driven inflammation. *Nat Chem Biol*, **2018**, *14*, 1079. https://doi.org/10.1038/s41589-018-0162-9

• Synthesis of peptidomimetics and chemo-biological tools for CD95/PLCγ1 interaction analysis. *Bioorg Med Chem Lett*, **2019**, *29*, 2094. https://doi.org/10.1016/j.bmcl.2019.07.006

• Probing the side chain tolerance for inhibitors of the CD95/PLCγ1 interaction. *Bioorg Med Chem Lett*, **2019**, *29*, 126669. https://doi.org/10.1016/j.bmcl.2019.126669

Job description

The successful applicants will join the team COrInt (UMR CNRS 6226 ISCR) to work under the supervision of Dr Mickael Jean at Université de Rennes (Campus Villejean). Two kinds of CD95-protein interaction disruptors are considered in this project:

1. Design and synthesis of (cyclic)pseudopeptides, incorporating proline analogues, and peptidomimetics based on sequences of interest.
2. Synthesis of labelled compounds for biological investigations.
3. Structure optimizations according to structure-activity relationship, *in silico* predictions…

The successful applicants will work closely with international collaborators involved in the project (biologists, molecular modelers). All results will be disseminated in English (presentations, written reports, and articles) and participation in international conferences will be encouraged.

Skills/Qualifications

• Excellent past achievements

• Strong background in Synthetic Organic Chemistry. Familiar to medicinal chemistry, peptide chemistry, multistep synthesis and molecular modeling. Knowledge in antibody functionalization will be appreciated.

• Able to synthesize novel compounds and develop robust synthetic routes and protocols

• Experienced in the structural characterization of organic compounds, especially by NMR spectroscopy (also LC, LCMS, HRMS)
• Team worker
• Creativity and problem-solving skills
• Strongly developed logic and critical thinking skills
• Skills in English and in communication

Eligibility criteria

Applicants of any nationality are eligible.
PhD: Eligible applicants hold a Master degree (or will receive a Master degree no later than summer 2023) in Chemistry or a related field.

Selection process

Applications should be sent by email to mickael.jean@univ-rennes1.fr and should include:

- a cover letter to Dr. Mickael Jean, motivating the application for this position and considering the listed requirements
- a CV, including publications or communications (if applicable)
- recommendation letters or contact details of two persons that can provide a reference