MAbImprove 2-years post-doctoral position in Tours, France.

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Design, Synthesis and Analysis of Original Antibody-Drug Conjugates
Impact of chemical modifications on the MAb properties and applications in oncology.

Mission:
A 2-years post-doctoral funding in the **Labex MAbImprove** is available in our team of organic chemists and should start as soon as possible. The work will be carried out in the team directed by Prof. Marie-Claude Viaud-Massuard and will be supervised by Dr. Nicolas Joubert.

Keywords:
Organic chemistry, heterocyclic chemistry, peptide synthesis, bioconjugation, chemical biology, antibody-drug conjugates, cancer.

Project summary:
Following the visionary concept of the magic bullet introduced by Paul Ehrlich in 1906, the development of antibody-drug conjugates (ADC) is an expanding field of research. While optimizing the monoclonal antibody (MAb), ADC combines the specificity of a MAb with the cytotoxicity of a payload, which are linked together through a judiciously designed bifunctional linker. Heterogeneity and unoptimized linkages were the main drawbacks of first and second generation ADC implying difficulties in analysis, process of production and dosage when given to patients. Therefore, to generate homogeneous and blood stream stable ADC with a controlled drug-to-antibody ratio (DAR) of 4 on every native MAb of interest, we designed and patented original bioorthogonal technologies consisting in introducing the linker in the MAb (based on original heterocyclic bioconjugation heads) by replacement of interchain disulfide bridges after a reduction step. The choice of the linker that connects the drug to the antibody scaffold is a critical factor in determining the effectiveness of ADC therapy.

Therefore, the chemical design of the linker between the antibody and the drug molecule has been extensively studied since ADCs were invented. Indeed, several factors contribute to optimal linker function, including stability in vivo, hydrophobicity, propensity to aggregation and efficient drug release from ADC. In order to develop better ADC with optimized linkers, **this post-doctoral project aim to explore the chemical space** and study the impact of our linkers on ADC properties using trastuzumab as a model MAb. To tackle this challenge, we will construct a matrix of linkers (with multiple linkers of variable length and hydrophobicity, and release systems), payloads and bioconjugation technologies (our three patented heterocyclic heads) from various chemistries using our expertise in this field.

In summary, **this post-doctoral fellowship will design, synthesize and analyse original Antibody-Drug Conjugates for applications in oncology, and will tackle strong chemical challenges for the linker-drugs synthesis**. Moreover, **improvement of the bioconjugation process** will be a necessary complementary work he/she will have to do to complete this study.

Work environment:
The project is included in **Labex MAbImprove research grant** (mabimprove.univ-tours.fr) gathering teams from Tours and Montpellier and dedicated to the improvement of antibody-based therapeutics.

The scientific activity of the GICC (Genetics, Immunology, Chemistry and Cancer), is based on an interdisciplinary approach, combining biologists and chemists, and was evaluated A-ranked in the last AERES evaluation. It is in this context that our **team of organic chemists (GICC Team 4, Molecular and Therapeutic Innovation)**, also evaluated A-ranked in the last AERES evaluation, plays a unifying strategic role. Moreover, our team is part of the **Labex SynOrg** and also the **Labex MabImprove**.

The scientific strategy of our team of chemists is based on the studies of the interactions between small molecules and biological processes. Our work aims to design innovative heterocyclic structures to advance the methodological aspects of synthesis, and contribute to the understanding of the fundamental mechanisms of cell proliferation, in the context of the fight against cancer. Our research team activity has two main objectives: (1) The design, synthesis of small molecules with potential anticancer; (2) The bioconjugation of small molecules to macromolecules (biopharmaceuticals).

Candidates profile:
The candidate must have a good knowledge of organic chemistry, and hold a PhD in organic chemistry or bioorganic chemistry. An experience in medicinal chemistry will be much appreciated. Knowledges in biology, biochemistry and/or chemical biology will be welcome. The candidate must also be fully autonomous, demonstrate a high degree of motivation for working in an interdisciplinary project, and master both the techniques used in organic synthesis and the analytical techniques common in chemistry.

This post-doctoral fellowship will design, synthesize and analyse original Antibody-Drug Conjugates, and will tackle strong chemical challenges for the linker-drugs synthesis. Therefore, it will require an organic chemist with strong motivation, skills and experience to achieve this work. Moreover, improvement of the bioconjugation process will be a necessary complementary work he/she will have to do to complete this study: if not experienced in this field, the candidate should be eager to learn bioconjugation techniques.

Gross Salary: average 50 k€ per year.

Please send your cover letter and resume to both:
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