Center for Infection & Immunity of Lille

CIIL

NEWSLETTER

#6 | April 2022

We are relieved that COVID-19 does not disturb anymore our scientific activities, and we are now back to a quasi-normal life. After the presentation of the different research themes developed within the CIIL in the previous Newsletters, we propose today to present the projects of the young researchers recently recruited at the CNRS and Inserm. We were lucky to recruit 5 young researchers during the past 4 years. These new researchers reinforce the scientific project of the CIIL and they contribute to its dynamism. In this Newsletter, 4 of them present their scientific profile, their project and the motivations that let them to work at the CIIL.

Jean Dubuisson

The profiles of our young recruits

Vincent DIEMER

Recruited at CNRS in 2018, Chemical Biology of Flatworms team led by Oleg MELNYK

What is your academic and scientific background before your recruitment at CNRS ?

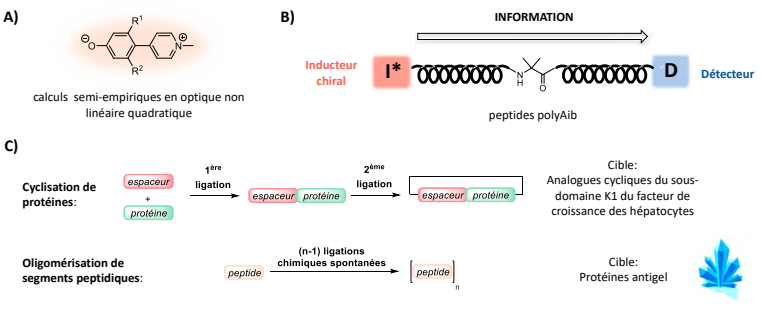
As a chemical engineer, I did a thesis at the interface of organic chemistry and physics. I synthesized polyaromatic anionic structures to validate optical properties predicted by calculation (Fig. A). In order to deepen and diversify my chemistry skills, I then completed four postdoctoral fellowships (2008-2018). After additional experience in aromatic chemistry (2008-2010), I directed my research activities towards the design, synthesis and study of peptide and peptidomimetic structures capable of transmitting chiral information along their helical structure (Fig. B). In 2016, I finally joined the CBF team led by Dr. O. Melnyk and specialized in total protein synthesis. Initially a post-doctoral fellow in the laboratory, I became a research fellow, following my appointment to the CNRS (Section 16: Chemistry of Life) in October 2018.

On which research project were you recruited ?

I was recruited by the CNRS to develop new chemical tools to prepare functional proteins or protein mimetics. The strategy classically used to access such objects consists in assembling peptide fragments via chemical ligation reactions (Fig. C). In this field, I have developed a new method to cyclize the protein backbone. Based on two successive redox-controlled ligations, this approach has been exploited to prepare cyclic analogues of proteins. In this way, I was able to study the impact of cyclization and thus structure rigidification on the agonistic properties of a protein ligand of the MET receptor.[1] More recently, I have developed a new technique of oligomerization of peptide segments that I plan to use to prepare repetitive sequences of amino acids mimicking the structure and properties of natural antifreeze proteins. Produced by some organisms to protect themselves from the cold, such proteins are able to control the growth of ice crystals. Supported by the ANR in 2021, this project opens the way to new additives that would notably improve cryopreservation techniques for certain stages of the Schistosoma mansoni parasite and thus facilitate the study and exchange of this parasite with its complex life cycle.

What does the CIIL environment offer you to develop your project ?

The CBF team and more generally the CIIL is an ideal multidisciplinary environment to carry out these projects developed at the interface between chemistry and biology. I benefit from the experience of my chemist colleagues in total protein synthesis, from all the instrumentation necessary to prepare targets as complex as proteins as well as from the support of many biologists with whom I can collaborate to characterize the properties of the synthesized objects.



[1] *V. Diemer, N. Ollivier, B. Leclercq, H. Drobecq, J. Vicogne, V. Agouridas, O. Melnyk, A cysteine selenosulfide redox switch for protein chemical synthesis, Nat. Commun. 2020, 11, 2558.*

Sébastien BONTEMPS-GALLO
Recruited at CNRS in 2019, Plague and Yersinia pestis team directed by Florent SEBBANE

What is your academic and scientific background before your recruitment at the CNRS ?

Since 2008 and my first steps in a research laboratory, I have been working on one question: How do bacteria adapt to their environment to establish an infection? I have tackled this question through different animal pathogens (Borrelia burgdorferi - Lyme disease, Yersinia pestis - plague) or plants (Dickeya dadantii - soft rot disease).

During my PhD research from 2010 to 2013 under the supervision of Pr Jean-Marie Lacroix at the University of Lille (UMR8576 CNRS), I was able to highlight the complex role of osmoregulated periplasmic glucans in the physiology and virulence of D. dadantii. In parallel, I studied the cell signaling mechanisms that allow this plant pathogen to detect and adapt to osmotic stress. I also studied the role of the bacterial envelope stress perception system CpxAR in virulence during an ATER position for 9 months. Then, I continued my journey with a post-doctoral fellowship from 2014 to 2018 at the National Institutes of Health (NIH - Rocky Mountain labs, Montana, USA) in the laboratory of Dr. Frank Gherardini. My work describing the role of osmotic stress on gene regulation during the infectious cycle of Borrelia burgdorferi demonstrated that this spirochete uses osmolarity as an important signal to adapt and regulate genes required for survival in the tick (through Hk1/Rrp1) and transmission to a new host (through Rrp2-RpoN-RpoS). I also highlighted the effect of protein acetylation on the metabolism of B. burgdorferi. In 2018, I joined the Center of Infection and Immunity of Lille, more specifically the Plague and Yersinia pestis team of Dr Florent Sebbane. In 2019, I obtained a tenured position of Chargé de Recherche at the CNRS and in 2021, I defended my Habilitation to Supervise Research.

On which research project were you recruited ?

Plague is a deadly zoonosis caused by the bacterium Yersinia pestis and transmitted by fleas. This re-emerging disease is a global public health problem. The emergence of multi-drug resistant strains used against the disease and the absence of a vaccine, urges us to think about new control strategies. However, our knowledge on the environment of the digestive tract of the insect in which the bacterium evolves and multiplies in order to be able to disseminate is limited and hinders our understanding of the molecular mechanisms of propagation of Y. pestis. My project is therefore to (1) characterize the environment in which Y. pestis evolves, as well as (2) understand the cell signaling mechanisms essential for the bacterium to adapt to its vector. Finally, I will screen for new antibacterial molecules targeting Y. pestis and enterobacteria.

The work is supported by an I-site University Lille North-Europe Young researchers grant in 2020 and an ANR JCJC grant in 2021.

What does the CIIL environment offer you to develop your project ?

The CIIL is home to the only team in Europe capable of studying the complete infectious cycle of the plague. The infrastructures developed by Dr. Florent Sebbane for plague bacillus investigation associated with the equipment and technical platforms of the center allow me to develop my project.

Arnaud MACHELART

Recruited at Inserm in 2020, Chemogenomics of Intracellular Mycobacteria team led by Priscille BRODIN

What is your academic and scientific background before your recruitment at the Inserm ?

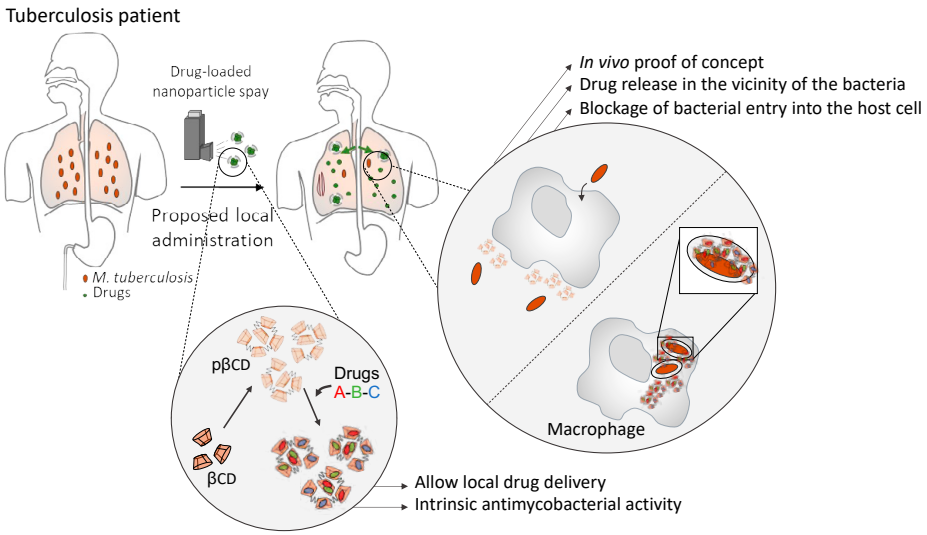
I completed a master's degree in molecular and cellular biology at the University of Namur in Belgium, the country in which I grew up. During these years, I was able to acquire different skills in immunology and infectiology, in particular by doing an internship in the laboratories of Jean-Jacques Letesson (University of Namur) and Eric Muraille (Université Libre de Bruxelles) in order to study the impact of Brucella melitensis infection on the splenic microarchitecture. I also did an internship at the Institut Pasteur de Cayenne, French Guiana, to demonstrate the presence of regulatory cells in skin lesions of leishmaniasis patients (Eliane Bourreau's laboratory). In 2012, I obtained a regional grant (FRIA-FNRS) to complete a PhD at the University of Namur during which I investigated the host response during B. melitensis infection and its deregulation during co-pathology (allergic asthma or trypanosomiasis). In 2016, I joined Priscille Brodin's team at the CIIL for a post-doc. Thanks to the help of the team members, the expertise of many collaborators and the financial support (FRM, JPI-AMR, ITN-Cyclonhit), I developed a multidisciplinary expertise that allowed me to set up an innovative research project for which I was recruited at Inserm in 2020.

On which research project were you recruited ?

Through my research project, I want to develop a method that will improve the treatment of tuberculosis, a pulmonary bacterial infection that kills 1.5 million people every year. The current treatment to cure the disease is an oral multi-antibiotic therapy that can last up to 2 years and is associated with various problems of bioavailability, toxicity and effectiveness. In view of the difficulties encountered in bringing new antibacterial molecules to the market, I propose to use nanotechnologies to locally administer an optimal combination of antibiotics using a spray (see figure). In close collaboration with the laboratory of Ruxandra Gref (Institut des Sciences Moléculaires d'Orsay), I use sugar-based nanoparticles, made of a polymeric beta-cyclodextrins (pβCD), which has the particularities of being non-toxic and of spontaneously co-incorporating several drugs. The administration of antibiotic-loaded nanoparticles via the pulmonary route in infected animals will significantly reduce the bacterial load by reducing the treatment time, the amount of drug administered and the systemic toxicity. These nanoparticles deliver the encapsulated compounds closer to the bacteria inside the infected macrophages. Remarkably, we also observed that administration of the nanoparticles in the absence of antibiotics modulated the lung environment to make it unfavourable to bacterial replication. In particular, we observed that pβCDs inhibited the pathogen's ability to infect macrophages. Over the next few years, we will study in detail how the nanoparticles exert an antimycobacterial effect and optimize the combination of incorporated antibiotics to develop a powerful tool to fight tuberculosis.

What does the CIIL environment offer you to develop your project ?

The CIIL allows me to interact with expert teams in the fields of infection (especially tuberculosis), immunity, antibiotic therapy and pulmonary administration. The ease of interaction with the different members of the center has already allowed me to collaborate on different topics in order to advance my research project. The CIIL also encourages interactions between teams by supporting new intra-CIIL projects (Sars-Coinf-TB - F. Trottein). The outreach of the center also facilitates local, national and international interactions that allow us to advance our research ambitions and give them visibility. As an example, I can count on the long-standing collaboration set up by Priscille Brodin with Ruxandra Gref. The CIIL and the campus of the Institut Pasteur de Lille offer valuable opportunities for interaction with various cutting-edge technological platforms. The CIIL also relies on the support of many people who are essential to the progress of our research projects. I am thinking in particular of the staff of the administrative and management services, the NSB3 laboratory, the animal facility, the dish washing and the maintenance of the building.



Laurye VAN MAELE

Recruited at Inserm in 2021, Bacteria, Antibiotics and Immunity team, directed by Jean-Claude SIRARD

What is your academic and scientific background before your recruitment at the CNRS ?

I studied at the universities of Lille:

- University of Lille I: DEUG in Science and Technology, License in Cellular Biology and Physiology, Master 1 in Biology and Biotechnology.
- University of Lille II: Master 2 Biology and Health, Doctorate in Molecular and Cellular Aspect of Biology.

I did my master 2, my PhD and a first post-doctorate (5 years) under the supervision of Dr Jean-Claude Sirard. My work consisted in dissecting the immune responses of the lung mucosa induced by TLR5 signaling after administration of flagellin, structural protein of the bacterial flagellum, in the airways or the pulmonary parenchyma. I had the honor of presenting these results at the inauguration of the Center for Infection and Immunity of Lille on February 22, 2010.

I then carried out a second 4-year post-doctorate in the team of Dr Stanislas Goriely at the Institute of Medical Immunology (ULB - Gosselies campus) where I coordinated a project on tristetraproline, a mRNA decay protein in psoriasis.

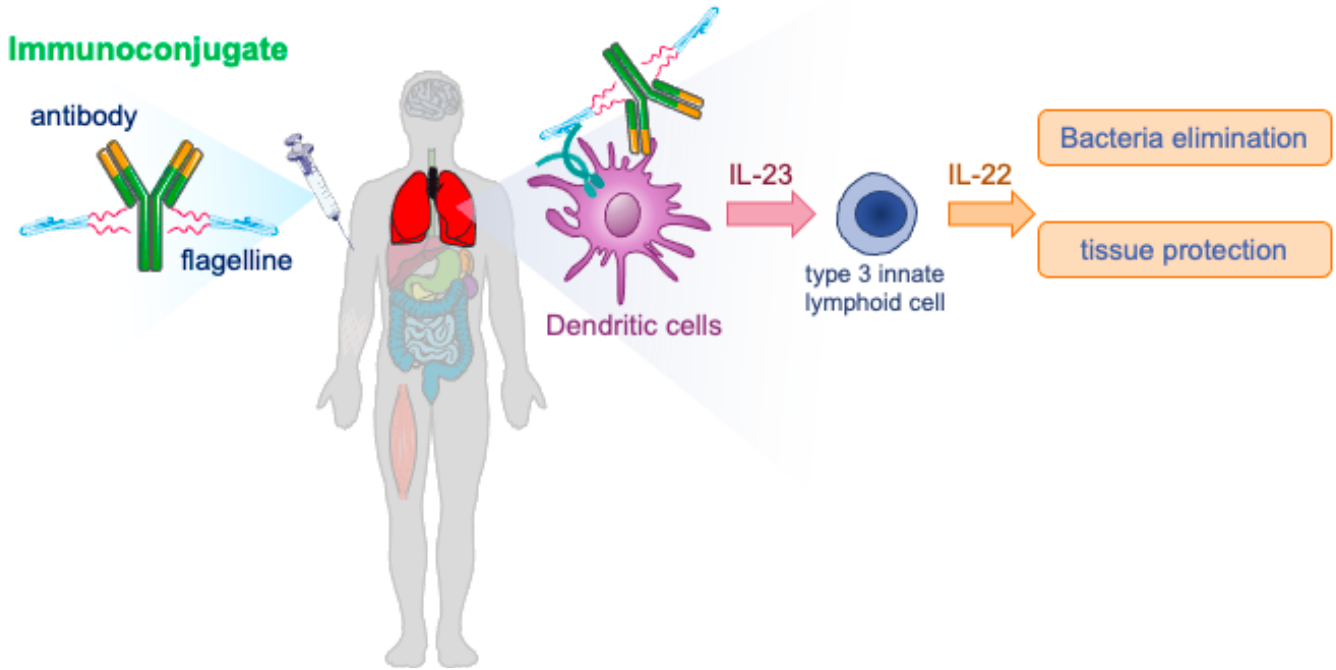
Since 2017, I came back to the CIIL, in the team of Dr Jean-Claude Sirard, where I am developing a project on immunotherapies for antibiotic-resistant bacterial pneumonia caused by Klebsiella pneumoniae.

On which research project were you recruited ?

I was recruited at Inserm in CCS6 in 2021 on a project proposing to develop immunoconjugates composed of an antibody specific for lung IL-23 producing dendritic cells and flagellin. This strategy will make it possible to direct the immunostimulatory activity of flagellin in the lung, on the dendritic cells which produce IL 23 and activate IL 22 dependent anti-infectious defenses. My aim is to develop an anti-infective therapy against antibiotic-resistant pneumonia while reducing side effects.

What does the CIIL environment offer you to develop your project ?

The CIIL is a recognized research center on infectious diseases with themes such as microbiology, biology of infection and the research for new vaccines and therapies. It allows excellent interactions and scientific emulation that will contribute to the development of my project. In addition, the CIIL and the campus of the Pasteur Institute of Lille host platforms of excellence, essential to my research project, such as the BioImaging Center Lille for microscopy and cytometry, TAG and LIGAN for high throughput transcriptomics and genomics, Billille for bioinformatics and biostatistics analyses, as well as laboratories and an animal facility adapted to the use of pathogenic and genetically modified organisms.



The news in brief ...

Welcome to our new support teams:

Following the closure of UMS 3702 on January 1st 2022, the direction of the Institut de Biologie de Lille (IBL) has been transferred to the CIIL. The personnel of the technical service (Jonathan Carlier, Nicolas Ampen-Guffroy et Marc Messemanne) and the account manager of the building (Régine Blanchet) are now under the direction of our unit. Furthermore, 30% of the activity of the personnel of the informatic service (Karl Oulmi, Geoffrey Bercker et Jérémy Maton) of the unit PLBS is dedicated to support the CIIL teams hosted in the IBL. At the end of this year, the IBL building will only be occupied by teams of the CIIL as well as several platforms of the unit PLBS. Several teams located in the Emile Roux building will move to the 3rd floor of the IBL after the departure of the teams working on cancer (CANTHER et ONCOTHAI).

Technical service:


Jonathan Carlier


Nicolas Ampen-Guffroy


Marc Messemanne

Informatic service:


Karl Oulmi


Geoffrey Bercker


Jérémy Maton

Account manager of IBL:


Régine Blanchet

Since January, our center has been equipped with an intranet allowing you to find all the information related to the scientific, administrative and social life on campus. You can access it with the following link : https://intranet.ciil.fr

Recently published in the journal Nature:
A «where I work» profile of a talented postdoc in Ruben Hartkoorn's team, Juan Carlos JIMENEZ CASTELLANOS, and his passion for bacterial efflux pumps : https://lnkd.in/esTjdybP


Lucas Barioulet pour Nature

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