

PHD POSITION (M/F/X) GENERATION OF HYBRID VECTORS TO REDUCE THE IMMUNOGENICITY OF AAVS BY PACKAGING THEM IN LNPS AND ALLOW LONGER TRANSGENE EXPRESSION USING AAVS.

AREA: HEALTHCARE/GENE THERAPY/VIRAL VECTORS/AAV NON-VIRAL VECTORS/NANOMEDICINE

START DATE: 09/15/2024

DEADLINE OF APPLICATION: 22/04/2024

The University of Liège is the biggest French-speaking public university in Belgium. It employs more than 5,700 staff members across four campuses, including 3,600 active teachers and researchers in all fields of the human and social sciences, science and technology, and health sciences. It hosts nearly 27,000 students of 123 different nationalities in one of the most multicultural and dynamic cities in Europe, less than an hour from Brussels and Cologne, two hours from Paris, and three hours from London and Amsterdam.

Actively involved in the social and environmental transition, ULiège supports students to fulfil their roles as responsible citizens (training in sustainable development, Green Office, etc.) and promotes ethical, multidisciplinary and open research. ULiège is committed to the region in which it operates and contributes towards local socio-economic development. It has developed numerous partnerships, notably with the university hospital. International and united, it participates in the [European University of Post-Industrial Cities, UNIC](#) initiative and has one of the most extensive collaborative networks in the world.

ULiège offers attractive career prospects [in a high-quality working environment](#), promoting well-being, diversity and equality of opportunity. Since 2011, ULiège has been proud to display the European [Human resources strategy for researchers](#) (HRS4R) label, which reflects its commitment to open, transparent and merit-based procedures. In addition, it recognises the quality and diversity of research in line with the recommendations of the [Coalition for Advancing Research Assessment](#) (CoARA). ULiège encourages its academic staff to travel internationally and welcomes international researchers through its EURAXESS centre.

ABOUT THE RESEARCH PROJECT

After injection, rAAVs will transduce cells with an efficacy that depends on the nature of the capsid (serotype). The possibility of modifying AAV capsids has opened a new avenue for more specific targeting of AAVs, as well as reducing their immunogenicity and inactivation by neutralising antibodies. Several approaches ("capsid engineering") have been developed to modify AAV capsids in order to overcome these problems. Among them, encapsulation (liposomes and micelles, hydrogels, exosomes, polymeric nanoparticles, etc.) allows non-viral vectors to be combined with viral vectors (AAV) and offers the advantage of optimising

therapeutic efficacy by combining the advantages of both types of vector and overcoming their respective limitations.

Encapsulating AAVs in liposomes not only abolishes their immunogenicity but also ensures long-term transgene expression. In addition, the transgene is better protected because AAVs are less susceptible to degradation than naked DNA or RNA.

Finally, another advantage of this approach is that AAV encapsulations can be coupled with other molecules such as oligonucleotides to have multiple (and temporal) effects on the targeted pathology. This could be very useful for the treatment of cancer and other complex diseases.

In this project, we plan to develop a method for combining lipid nanoparticles (LNPs) with AAV vectors.

We will then assess the potential for optimising the therapeutic efficacy of this approach in terms of:

- Reduction of AAV-related immunogenicity
- Improved transgene expression
- Better cell targeting
- Improved transgene protection.

These vectors could subsequently be improved in terms of targeting by inserting nanobodies on their surface, based on the methods developed by the project partners.

This project aims to **optimise Nanoparticles-AAV hybrid vectors for the treatment of cancer and other complex diseases, as well as their production and storage methods.**

The PhD will be conducted in the Laboratory of Pharmaceutical Technology and Biopharmacy (LTPB) (https://www.ltpb.uliege.be/cms/c_6516505/en/ltpb) and in GIGA Viral vectors platform at ULiège. This work will also be done in collaboration with the CER groupe (<https://cergroupe.be/>), UNamur GRPCT, ULB IMI, ULB UCDR and UCLouvain, partners of this project.

This project is part of the GT4health program, funded by the Walloon Region as part of its Win4Excellence program, which aims to develop various disruptive technologies as solutions to major challenges in the gene therapy sector. This multidisciplinary project involves ten partners from five French-speaking Belgian universities (ULiège, ULB, UCL, UNamur and UMONS), as well as the CER Group research centre.

JOB DESCRIPTION

LTPB and GIGA Viral vectors platform are searching for a motivated PhD student (Master in Pharmacy, Nanomedicine, Biomedical Sciences, Molecular Biology, Biochemistry or equivalent...) to contribute to this 4-year project.

The PhD candidate will play a pivotal role in the GT4health program by developing a method for combining lipid nanoparticles (LNPs) with AAV vectors and assess the potential for

optimising the therapeutic efficacy of this approach in terms of immunogenicity, transgene expression, cell targeting and transgene protection.

SPECIFIC DUTIES & ACTIVITIES

- ▶ Design and optimize combined LNP/AAV vectors formulations.
- ▶ Characterize formulations.
- ▶ Optimize the production method in order to guarantee scalability.
- ▶ Evaluate the efficacy (transgene expression, cell targeting, transgene protection...).
- ▶ Evaluate the toxicity (immunogenicity...)
- ▶ Collaborate closely with interdisciplinary teams to contribute to the overarching goals of the GT4health program.
- ▶ Present research findings at seminar, workshops and international conferences.
- ▶ Disseminate results through peer-reviewed publications.
- ▶ Assist in mentoring undergraduate students and junior lab members as needed.

YOUR PROFILE

○ REQUIRED SKILLS :

- ▶ The candidate must hold or is about to complete (before 1th July 2024) a Master's degree Pharmacy, Nanomedicine, Biomedical Sciences, Molecular Biology, Biochemistry or equivalent ...).
- ▶ Strong motivation to contribute to nanomedicine formulation at the service of cutting-edge developments in gene therapy.
- ▶ Excellent communication skills.
- ▶ Excellent level of spoken and written English (ability to communicate effectively with colleagues and present research findings with clarity).
- ▶ Ability to write scientific reports and publications in English.

○ DESIRABLE SKILLS :

- ▶ Experience and knowledge in nanotechnologies, nanoparticles, nanomedicine, virology, biochemistry, biosafety are highly welcome.

○ SOFT SKILLS :

- ▶ Excellent organizational skills.
- ▶ Ability to work independently and collaboratively in a multidisciplinary team environment.

○ LANGUAGES :

- ▶ Excellent level of spoken and written English is necessary. Ability to communicate effectively and fluently with colleagues and present research findings with clarity.
- ▶ French knowledge is a plus but is not mandatory.

TERMS OF EMPLOYMENT

- ▶ Type of contract : PhD position
- ▶ Work schedule : 5days/week, 38h/week
- ▶ Contract duration : 48 months
- ▶ Start date : 15st September 2024

OUR OFFER

With your career path and personal details, ULiège Human Resources Department can assess the gross monthly salary. Employment benefits such as reimbursement of public transportation fees and access to a [variety of training](#) opportunities are also included.

▶ WORK ENVIRONMENT

The PhD thesis will take place in the Laboratory of Pharmaceutical Technology and Biopharmacy (LTPB) and in the CER Groupe.

The LTPB takes part of the Center for Interdisciplinary Research on Medicines (CIRM) and is renowned for its expertise in the non-viral nanoparticle's development and evaluation. LTPB is composed of about 15 members.

LTPB's main objective is to design new pharmaceutical systems for controlled drug delivery and administration of drugs. LTPB is made up of researchers from different disciplines (pharmacists, chemists, biologists, biomedical sciences graduates), which allows it to consider not only the formulation but also the physicochemical characterization and biological evaluation of medicines. With its multidisciplinary approach, the LTPB has considerable assets to address different research themes around drug formulation. LTPB offers a collaborative, stimulating and supportive research environment with ample opportunities for networking (participation to local, regional, national and international research networks).

CER Groupe is a non-profit organization active in several life sciences sectors in a regulated environment (ISO, GLP). CER Groupe is also providing preclinical in vivo testings in different topics (oncology, bone remodeling, immunisation,...) and could be supported by its bioluminescence/fluorescence imagery equipment to track labelled products. The in vivo team involved in the thesis granted by GT4Health Win4Excellence program is composed of 5 technicians/preclinical assistants, 3 project managers, one referent DVM and one preclinical manager.

The PhD thesis will be carried out under the supervision of Prof. Geraldine PIEL (LRPB) and Gaëtan Thirion (CER Groupe). The PhD thesis will be performed in close collaboration with Dr. Antoine Debuigne (CERM, ULiège), Prof. J. Douxflis (UNamur), and Prof. V. Flamand (ULB).

HOW TO APPLY

Please send the following documents in pdf to Geraldine Piel Geraldine.piel@uliege.be (and a copy to Emmanuel Di Valentin edivalentin@uliege.be) by April 22th 2024 :

- a cover letter outlining research interests and career goals,
- a detailed CV,
- contact information for professional references.

Please ensure that all documents are submitted in English.

SELECTION PROCEDURE

- ▶ Application submission: Geraldine.piel@uliege.be and edivalentin@uliege.be by April 22nd 2024.
- ▶ Initial Screening: to assess candidate qualifications, research experience, and alignment with the position requirements.
- ▶ Interview Stage: face to face or by Teams by Géraldine Piel and Emmanuel Di Valentin
- ▶ Final Selection: selected candidate will be notified of its acceptance in May-June.

CONTACT DETAILS AND FURTHER INFORMATION

Informal inquiries about the project are welcome. Please feel free to contact Prof. Geraldine Piel: Geraldine.piel@uliege.be and Emmanuel Di Valentin edivalentin@uliege.be

Release date: 02/04/2024

Privacy policy

Personal data collected following your application will be processed by Dr. Antoine Debuigne of the University of Liege for the sole purpose of recruitment.

The data will be processed within the framework of pre-contractual measures (art. 6-1, b. of the General Data Protection Regulation) and kept for up to 9 months after the publication of the vacancy. Your personal data will not be passed on to any third parties.

In accordance with the provisions of the GDPR (EU 2016/679), you may exercise your data protection rights (right of access, rectification, erasure, restriction, and portability) by contacting ULiège Data Protection Officer (dpo@uliege.be - Mr. Data Protection Officer, Bât. B9 Cellule "GDPR", Quartier Village 3, Boulevard de Colonster 2, 4000 Liège, Belgium). You may also lodge a complaint with the Data Protection Authority (<https://www.autoriteprotectiondonnees.be> , contact@apd-gba.be).