Technician position available (4 months) in the blood-brain barrier laboratory, Artois University, Lens, France.

The candidate will work at the Blood-brain barrier (BBB) laboratory, UR2465 for 4 months (September-December 2023).

The BBB-Lab is recognized as world expert in the modeling of the BBB. This team has carried out pioneering works in establishing animal models of the BBB which has been used to investigate BBB physiology and distribution of compounds for pharmaceutical industries. New BBB models have also been used to better characterize the BBB physiology in stroke (FP7 Eustroke and EU Joint programs (MAGBBRIS, iMATRIX, etc). In 2013, the team set up a human in vitro model of the BBB which is now widely used for mechanistic studies and for permeability screenings, and consisting to cultivate $CD34^{+}$-hematopoietic stem cells with brain pericytes.

Applications are invited for a 4 months technician position under the supervision of Pr Fabien Gosselet. The ideal start date would be around September 2023, for 4 months.

The successful candidate will test toxicity and passage of molecules across in vitro models of blood-brain barrier.

Please send CV and motivation letter to fabien.gosselet@univ-artois.fr (http://lbhe.univ-artois.fr/membres-lbhe/fabien-gosselet).

Project (English version): Most of neurodegenerative diseases are associated with the cerebral deposition of peptides and proteins able to form amyloid fibers by a process called amyloidogenesis. Interestingly, the proteins involved in this phenomenon share important similarities with antimicrobial peptides, suggesting a role for these microorganisms in the occurrence of these neurological diseases. The majority of current therapeutic strategies against these diseases consist in inhibiting these aggregation processes by developing various approaches (antibodies, small molecules, etc.) which unfortunately do not always cross the blood-brain barrier (BBB) that isolates the brain from the rest of the body.
The synthetic peptide QBP1 is a promising molecule against amyloidogenesis because it is able to block the aggregation of these proteins without showing in-vivo toxicity. It shows a strong sequence similarity with several antimicrobial peptides suggesting an antibacterial activity which has however never been studied. However, this peptide poorly crosses the BBB, thus limiting its use in human therapy. This collaborative project between three research teams (AGIR, GEC, LBHE) from Amiens and Artois Universities aims to select analogues of QBP1, with improved and optimized antimicrobial activity, but also capable of crossing the human blood-brain barrier effectively in order to inhibit the formation of cerebral amyloid aggregates. Ultimately, our project will make it possible to propose new molecules which can then be evaluated for their effectiveness in combating the onset and progression of neurodegenerative diseases.

Projet (en français): La plupart des maladies neurodégénératives est associée au dépôt cérébral de peptides et protéines, capables de former des fibres amyloïdes par un processus appelé amyloïdogenèse. Il est intéressant de noter que les protéines impliquées dans ce phénomène partagent d'importantes similitudes avec les peptides antimicrobiens, suggérant ainsi un rôle de ces microorganismes dans la survenue de ces maladies. Quoiqu'il en soit, la majorité des stratégies thérapeutiques actuelles consiste à inhiber ces phénomènes d'agrégation en développant diverses approches (anticorps, petites molécules, etc) qui ne parviennent pas toujours à franchir la barrière hémato-encéphalique (BHE) isolant le cerveau du reste de l'organisme. Le peptide synthétique QBP1 est une molécule prometteuse contre l'amyloïdogenèse car il est capable de bloquer l'agrégation de ces protéines sans montrer de toxicité in-vivo. Il montre une forte similarité de séquence avec plusieurs peptides antimicrobiens suggérant une activité antibactérienne qui n'a pourtant jamais été étudiée. Cependant, il passe peu la BHE, limitant ainsi son utilisation dans le cadre de la thérapie humaine. Ce projet collaboratif entre trois équipes de recherche (AGIR, GEC, LBHE) de l'A2U vise à sélectionner des analogues de QBP1, avec une activité antimicrobienne améliorée et optimisée, mais aussi capables de franchir la barrière hématoencéphalique humaine effcicacement afin d'inhiber la formation des agrégats amyloïdes cérébraux. A termes, notre projet permettra de proposer de nouvelles molécules qui pourront par la suite être évaluées pour leur efficacité à lutter contre la survenue et la progression des maladies neurodégénératives.

Your responsibilities:

• Passage of molecules across the human blood-brain barrier.

• Toxicity assessment of the molecules by permeability studies, qPCR, immunoblot and immunofluorescence technics.

• Preparation of scientific publications, contribution to grant applications

Your qualifications:

• Undergraduate or master diploma or equivalent in cell or molecular biology or related fields

• A knowledge of a wide range of methods in biochemistry and molecular biology

• High motivation to do research

• Fluency in English or French