ETUDES DES INTERACTIONS ENTRE OXYSTÉROLS ET TRANSPORTEURS ABC AU NIVEAU DE LA BARRIÈRE HÉMATO-ENCÉPHALIQUE : IMPLICATION DANS LES MALADIES NEURODÉGÉNÉRATIVES

OXYSTEROLS AND ABC TRANSPORTERS AT THE BLOOD-BRAIN BARRIER : ROLE IN NEURODEGENERATIVE DISEASES.

We are look ing for a highly motivated student with a major in cell biology who has a strong interest in multi-disciplinary research. The PhD position is available at the Blood-brain barrier laboratory UR2465 (LBHE: Laboratoire de la barrière hémato-encéphalique) located in Artois University, in Lens, France.

The research project

The research project, under the supervision of Pr. Fabien Gosselet, aims at studying the effects of oxysterols, that are cholesterol metabolites, on the blood-brain barrier physiology.
Pr. Fabien Gosselet previously supervised 8 PhD students and published more than 90 manuscripts in peer-reviewed journals.

Aim

The recruited PhD student will be embedded in the LBHE lab which has a recognized expertise in the modelling of the BBB, from animal (bovine, rat and mouse) and human cells, and evaluation/regulation of BBB properties under physiological and pathological conditions (acute or chronical drug exposure, Alzheimer disease, Stroke, Cancer).
The blood-brain barrier (BBB) isolates the brain from the whole body. This barrier is very important for the brain homeostasis and neuron functioning. ABC transporters are expressed at the BBB level and are key molecular players of molecules/lipids exchanges between the central nervous system and the bloodstream. Our previous works showed that some of these oxysterols can modify the expression of ABC transporters, thus resulting in modifications of the transport of amyloid peptides across the BBB, highlighting their importance in Alzheimer's disease.
In this current project, we will study other oxysterols in the frame of another neurodegenerative disease, the multiple sclerosis (MS). This latter disease is characterized by a permanent inflammatory process resulting in the degradation of the myelin sheat surrounding the neurons. The BBB physiology in this disease is still debated and the exact contribution of the BBB in MS needs further investigation. On the other side, recent studies demonstrated that oxysterol levels are altered in MS patients. Therefore, the objective of the PhD student at LBHE is to study the impact of these new oxysterols on BBB permeability and physiology.

Your profile

- Master degree in cell biology with experience in cell culture and molecular biology.
- Ability and motivation to work independently as well as collaboratively in an interdisciplinary team.
- Exceptional communicative and intercultural skills.
- English writing and presenting skills.

The main responsibilities of the candidate will be:
- To manage and carry out an independent, cell biology based, research project.
- To contribute to writing articles for scientific journals.
- To disseminate research results in the scientific community (via international conferences) and in the non-scientific community (via outreach and public engagement).

Conditions

The candidate applies to take part of the competition to Artois university PhD research program for a 3 year PhD scholarship. The selected candidate will have to apply to the doctoral school selection process consisting to an oral evaluation of the candidate. Attribution of the PhD scholarship will be given according to the ranking of the candidate in the selection process

How to Apply

Only complete applications will be considered.
Submission deadline is September 1st, 2022.
Please submit a complete application as a single PDF FILE (<10MB) named
"surname_name_.pdf" and containing the required following documents:
- A meaningfull letter of motivation allowing understanding the motivation for the application and the choice of the research project
- A complete and detailed CV.
- Copies of the university Master Certificates for the respective University degrees or alternatively a certified copy confirming the enrolment and the date of finalization of the master program of the candidate.
- Names and full contact details of two referees.

You can send these documents in pdf format to Pr. Fabien Gosselet : fabien.gosselet@univ-artois.fr mentioning "BBB & Oxysterols" in the subject. For inquiries you can send a message to this same address. The deadline for application is September 1st, 2022. Interviews by zoom will then take place. The starting date of this position is October 2022.

To read for more information.

1: Saint-Pol J, Gosselet F. Oxysterols and the NeuroVascular Unit (NVU): A far true love with bright and dark sides. J Steroid Biochem Mol Biol. 2019 Jul;191:105368. doi: 10.1016/j.jsbmb.2019.04.017. Epub 2019 Apr 23. PMID: 31026511.

2: Gosselet F, Saint-Pol J, Fenart L. Effects of oxysterols on the blood-brain barrier: implications for Alzheimer's disease. Biochem Biophys Res Commun. 2014 Apr 11;446(3):687-91. doi: 10.1016/j.bbrc.2013.11.059. Epub 2013 Nov 22. PMID: 24275140.

3: Saint-Pol J, Candela P, Boucau MC, Fenart L, Gosselet F. Oxysterols decrease apical-to-basolateral transport of Aß peptides via an ABCB1-mediated process in an in vitro Blood-brain barrier model constituted of bovine brain capillary endothelial cells. Brain Res. 2013 Jun 23;1517:1-15. doi: 10.1016/j.brainres.2013.04.008. Epub 2013 Apr 17. PMID: 23603412.

4: Saint-Pol J, Vandenhaute E, Boucau MC, Candela P, Dehouck L, Cecchelli R, Dehouck MP, Fenart L, Gosselet F. Brain pericytes ABCA1 expression mediates cholesterol efflux but not cellular amyloid-β peptide accumulation. J Alzheimers Dis. 2012;30(3):4 89-503. doi: 10.3233/JAD-2012-112090. PMID: 22433669.

5: Menaceur C, Gosselet F, Fenart L, Saint-Pol J. The Blood-Brain Barrier, an Evolving Concept Based on Technological Advances and Cell-Cell Communications. Cells. 2021 Dec 31;11(1):133. doi: 10.3390/cells11010133. PMID: 35011695; PMCID: PMC8750298.

6: Lamartinière Y, Boucau MC, Dehouck L, Krohn M, Pahnke J, Candela P, Gosselet F, Fenart L. ABCA7 Downregulation Modifies Cellular Cholesterol Homeostasis and Decreases Amyloid-β Peptide Efflux in an in vitro Model of the Blood-Brain Barrier. J Alzheimers Dis. 2018;64(4):1195-1211. doi: 10.3233/JAD-170883. PMID: 30010117.

7: Gosselet F. Modélisation in vitro de la barrière hémato-encéphalique [Modelling of the blood-brain barrier]. Med Sci (Paris). 2017 Apr;33(4):423-431. French. doi: 10.1051/medsci/20173304013. Epub 2017 May 12. PMID: 28497739.