What is the ExposUM Doctoral Nexus?

The Doctoral Nexus proposed by the ExposUM Institute are networks of 3 to 4 PhD students from different disciplines and affiliated to at least two different research units.

Compared with a traditional PhD, taking part in a Doctoral Nexus will encourage the ability to work in a team and to design projects in a transdisciplinary way while deepening one's own field of expertise.

A specific teaching programme will be offered and the doctoral students concerned will also have the opportunity to organise a seminar within the Nexus network.

Theses are funded from the outset for 4 years, including the PhD student's salary and an environmental allowance

Title of thesis subject: **Gut microbiota and amyloidosis in Alzheimer's disease**

Planned start date of thesis: **01/10/2025**

Thesis supervisor: **CLAEYSEN Sylvie, Institute of Functional Genomics (IGF), UMR 5203**

Background

Alzheimer's disease (AD), the most common form of dementia, is based on progressive and irreversible neuronal degeneration, accompanied by memory and cognitive deficits leading to total loss of autonomy. This neuropathology is characterized post-mortem by the presence of 1/intraneuronal neurofibrillary degeneration containing hyper-phosphorylated tau proteins, and 2/extracellular amyloid plaques consisting mainly of aggregated ß-amyloid (Aß) peptides. The causality of amyloid pathology in Alzheimer's disease has recently been confirmed by the marketing of antibodies directed against these amyloid aggregates, aducanumab (ADULHEM®) and lecanemab (LEQEMBI®), which, by significantly reducing the cerebral amyloid load, achieve a modest cognitive benefit in treated patients.

The gut microbiota, the community of commensal microorganisms that colonize our intestines, appears to be linked to brain amyloid production. Animal models of AD, raised in the absence of germs or treated with a cocktail of antibiotics, showed a marked reduction in cerebral amyloid load. Conversely, intracerebral injection of pathogens (bacteria, viruses, or fungi) into these transgenic AD mouse models induces accumulation of amyloid peptides in the vicinity of the infectious agents. In humans, infectious agents such as herpes virus (HSV1, *Helicobacter pylori*, *Chlamydophila pneumoniae* or *Porphyromonas gingivalis* represent an increased risk for the development of AD.

Microbial exposure throughout life, reflected in part by the composition of the intestinal microbiota, is therefore a significant risk factor for AD, a complex and heterogeneous disease whose aetiology remains to be determined.

Objectives and methods

The aim of this thesis will be to study the ability of microorganisms selected by the **AMYLOPATH** Nexus to promote amyloidosis in mouse models of AD and to induce behavioural deficits. The selected microorganisms and proteins will be injected or administered by gavage to murine model (5XFAD transgenic mice and/or mice humanized by faecal microbiota transfer). The animals' cognitive performance will be measured using a series of behavioural tests. Neuropathology will also be evaluated (amyloidosis, neuronal inflammation) using ELISA and immunofluorescence. Similar team achievements: PMID: 31881553, PMID: 26774030, PMID: 28844596, PMID: 24399967, hal-04853031.

Expected results

This thesis will demonstrate that commensal or pathogenic microorganisms and proteins derived from them can induce amyloid pathology and associated cognitive deficits. By identifying certain causal agents, this project will suggest ways of stratifying AD patients according to the presence or absence of these causal agents, thereby refining personalized patient management.

Application procedure

The application must include the following

- a CV
- a letter of motivation
- a copy of the degree required for registration
- any additional specific information requested by the doctoral school CBS2 https://edcbs2.umontpellier.fr/

If you would like to apply for this position, please send an e-mail to sylvie.claeysen@inserm.fr with a CC to andrey.kajava@crbm.cnrs.fr and exposum-aap@umontpellier.fr to inform them of your interest.

Before Monday 31 May, 2:00 PM CET

The University of Montpellier

KEY FIGURES

RESEARCH CENTERS

From space exploration and robotics to ecological engineering and chronic diseases, UM researchers are inventing tomorrow's solutions for mankind and the environment.
Dynamic research, conducted in close collaboration with research organizations and benefiting from high-level technological platforms to meet the needs of 21st century society.
The UM is committed to promoting its cutting-edge research by forging close links with local industry, particularly in the biomedical and new technologies sectors.
More Information: https://www.umontpellier.fr/en/recherche/unites-de-recherche

SCIENTIFIC APPEAL

Open to the world, the University of Montpellier contributes to the structuring of the European higher education area, and strengthens its international positioning and attractiveness, in close collaboration with its partners in the I-SITE Program of Excellence, through programs adapted to the major scientific challenges it faces.
More Information: https://www.umontpellier.fr/en/international/attractivite-scientifique