Biotechnologie et signalisation cellulaire

**Ph.D. Position (2019 – 2022)**

# Neuropsychiatric lupus and cerebral biodistribution of a therapeutic peptide

**University :** Université de Strasbourg, ED 414 « Sciences de la Vie et de la Santé » & ED 182 « Physique et Chimie-Physique »
**Teams :** « Neuroimmunologie et thérapie peptidique » & « Imagerie moléculaire »
**Research Units and addresses:**
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**Supervision :** Hélène Jeltsch-David & Patrice Laquerriere
**Key-words:** Neurolupus, murine model, brain, autophagy, behavior, peptide therapy, molecular imaging PET, autoradiography
**Project:** Combining life sciences and molecular imaging, this project focuses on the pathogenesis of neuropsychiatric systemic lupus erythematosus (NPSLE), a severe form of SLE with cerebral symptomatology, and the evaluation of a therapeutic strategy in a lupus-prone murine model.
The etiology of these dysfunctions remains largely unknown and complex factors, highly intertwined, participate in their genesis. Nowadays, there is no cure for NPSLE and current treatments rely on non-specific immunosuppression that generate unwanted side effects. Therefore, there is a crucial need to design and develop targeted therapeutics centered on molecular elements of the pathophysiological chain. Although a failure of proteolytic systems to eliminate aggregated/misfolded proteins is commonly described in inflammatory and neurodegenerative diseases, it has not been addressed whether this clearance system is affected in the brain of NPSLE patients and could be, at least in part, at the origin of the NP manifestations that are observed. The autophagy pathway being recently validated as relevant in the development of new therapeutic approaches to several inflammatory pathologies, a particular attention will be paid to cerebral autophagy dysfunctions and to the effects of a peptide targeting autophagy, the peptide P140, whose intracerebral biodistribution will be followed by an innovative technique of autoradiography. Requiring a high degree of interdisciplinarity, this project will combine a behavioral approach and molecular biology studies targeting whether, as suspected, certain autophagy pathways play a direct role at the cerebral level, or an indirect one at the systemic level, in the effectiveness of P140. Lastly, a new imaging technique associating the benefits of positon emission tomography (PET) and autoradiography. Thanks to the smart contribution of such imaging technique, we expect to be able to depict the cerebral biodistribution of P140 peptide. This might help to more precisely delineate the P140's mechanism of action and, therefore, leads to a better understanding of NPSLE pathogenesis. The future PhD student will integrate well-structured teams with CNRS researchers, Unistra professors, engineers, post-docs and other PhD students, which should offer him/her a favorable intellectual and technical environment.
**Funding :** The candidate will apply to the exam for a doctoral contract from the University of Strasbourg.
**Candidate profile :** Highly motivated candidates (Master degree with excellent academic records) with a background in molecular biology and immunology are strongly encouraged to apply. Previous laboratory experience in basic biochemistry, cellular biology and optical imaging would be valuable. Notions and interest in neurosciences, a good level in English, and the curiosity to acquire transversal competencies (chemistry, physics) will be undeniable assets. Please address CV, Master's grades, cover letter and contact data of two referees to hdavid@unistra.fr and patrice.laquerriere@iphc.cnrs.fr

**References linked to the project :**


Jeltsch-David, H. & Muller, S. (2014) *Nat Rev Neurol.* 10, 579-596
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