Three years PhD position available at the Institut NeuroMyoGene, Lyon France

Project title:
Propagation and toxicity of pathogenic determinants of Amyotrophic Lateral Sclerosis

Amyotrophic Lateral Sclerosis (ALS) is a fatal and incurable paralytic neurodegenerative disorder caused by the loss of motor neurons in the brain and spinal cord. ALS is the third most frequently diagnosed neurological disorder after Alzheimer’s and Parkinson’s disease. In France, ALS is responsible for 1,000 death/year. ALS initiates in mid-life by focal muscle weakness, evolving rapidly into a generalized muscle wasting that leads irrevocably to death within 2-3 years of clinical onset.

Key pathological hallmarks of ALS are the deposition of misfolded proteins (TDP-43; SOD1 or FUS) or peptides (i.e. dipeptide repeats in the familial C9orf72 mutation context) into cytoplasmic inclusions in motor neurons and/or glia in the spinal cord/brainstem and motor cortex and the progressive spreading of pathological aggregated through the nervous system. In the last past years, TDP-43, SOD1 or FUS were found to display many similarities with prion proteins especially in their capacity to form aggregates that propagate in a seed-dependent and self-templating manner. In addition, a wealth of studies also demonstrated that ALS has its initial roots in motoneuron, which are then followed by activation of neighboring glial cells, whose perpetuate a regional and temporal progression along the spinal cord. Identifying and targeting this mechanism of glial propagation remain the pivotal clue to efficiently intervene on disease course. Oligodendroglial pathology is a key feature of ALS, despite their contribution in the propagation of motoneuronal damage remain elusive.

In this context, the proposed PhD project aims at investigating:
(1) the molecular and cellular mechanisms by which the ALS pathological aggregates can spread during the course of the disease.
(2) the contribution of oligodendrocyte in ALS pathological aggregates dissemination motoneuron degeneration and oligodendroglial propagation in the pathology.

This study will be carried out in human cellular models through the use of classical tools of biology (transfection, transduction with retroviral vectors, silencing with interfering RNAs, Western blotting, immunofluorescence confocal microscopy, etc...).

The PhD position is fully funded for 3 years through the national agency for research (ANR) at the Institut Neuromyogène (http://www.inmg.fr/) with Dr Pascal Leblanc (L. Schaeffer’s team).

We seek a very motivated student candidate with solid technical skill in molecular and cellular biology. CV, motivation and recommendation letters, Master 1&2 grades and e-mails of the candidate internship supervisors should be sent by e-mail to pascal.leblanc@univ-lyon1.fr.

The position will be available starting from January 2020.