Project Title: Identification of biomarkers to identify ALS subjects among patients affected by motor neuron disorders

Background to the project:

Amyotrophic Lateral Sclerosis (ALS) is a lethal neurodegenerative disease affecting adults (40-70 years old) characterized by a degeneration of motor neurons causing a progressive muscular atrophy[1,2]. Its progression is marked by major disability followed by death 3-5 years after the onset. The disease is mostly sporadic with an incidence of 2-3/100,000 inhabitants[3]. Diagnosis of ALS is difficult and exclusively based on clinical examination, electromyography studies, and on the exclusion of disorders mimicking ALS (e.g. adult-onset spinal muscular atrophy (SMA-IV) and SBMA)[4-6]. It is thus crucial to find biomarker(s) specific for ALS to improve the diagnosis and to allow neuroprotective drug treatment starting at earlier stages.

To date, ALS pathogenesis remains unknown. Studies in animal models and ALS patients show that motor neuron degeneration starts at the neuromuscular junction and that post-synaptic muscle changes may play an active role. We have already confirmed that ALS muscle secretome is affected, and that this secretome is toxic as once added to the culture medium of healthy muscle cells or of healthy motor neurons, it induces cellular stress and cell death.

Working with an established international collaborative network - S Knoblach (Genetic Medicine, CNMC, Washington, US), H Blasco (Universite de Tours, Tours, France) and PF Pradat (Paris Motor Neuron Disease (MND) Center, Pitie Salpetriere, Paris, France) - the student will pursue the following aims: (1) identify secreted biomarkers that distinguish ALS from other motor neuron disorders; (2) validate that the secretion of these biomarkers is specific to ALS muscle stem cells; and (3) validate secreted biomarker candidates in a moderate-sized patient cohort.

Skills required of applicant The project requires good skills in cell culture, as well as rigorous and methodical approach to lab work. The candidates should be familiar with RNA and protein extraction. Experience in PCR, RT-PCR, ELISA test and western blot would be a plus. Knowledge of specific bioinformatics tools to analyse OMICS data and statistical analysis would be beneficial, but can be learned during the project. Good written/oral communication skills are encouraged as well as attention to detail.

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References:

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2- Brown RH, Jr., Meininger V, Swash M. Amyotrophic lateral sclerosis. London: Martin Dunitz, 2000
3- Kunst CB. Complex genetics of amyotrophic lateral sclerosis. Am J Hum Genet. 2004; 75:933-94