Doctoral scholarship offer
Musculo-Skeletal system, Locomotion, Exercise (MuSkLE)

Title of the Internship: Characterization of new secreted biomarkers in spinal muscular atrophy

Laboratory (name, n°, website): Institut NeuroMyoGène, Laboratoire Physiopathologie et Génétique du Neurone et du Muscle ; https://pgnm.inmg.fr/

Research team (name, website): Schaeffer team, then Vuillerot / Jacquier team in January 2027

Supervisor to contact (name, email address): Arnaud JACQUIER (arnaud.jacquier@univ-lyon1.fr)

Project description

Context: Spinal muscular atrophy (SMA) is a prototypical neuromuscular disorder caused by recessive mutations in the *SMN1* gene, leading to spinal motor neuron degeneration and progressive muscle atrophy. At the Hospices Civils de Lyon, Prof. Vuillerot has followed a cohort of 45 SMA patients and established a biobank hosted in Prof. Schaeffer's department, including patient-derived cells and liquid biopsies collected before and during treatment over more than one-year period. Using proteomic approach, our group identified panels of 191 and 66 plasma protein biomarkers correlating with disease severity (Motor Function Measure) or therapeutic response. Among these, 71 and 77 are linked to muscle or neuronal functions, and 28 and 26 correspond to actively secreted proteins (patent pending). Our group aims to better identify and characterize novel biomarkers in neuromuscular disorders, which is critical to improve early diagnosis, monitor disease progression, and accurately assess therapeutic responses in an evolving treatment landscape.

Objective: The aim of this doctoral project is to elucidate the role of these secreted biomarkers in SMA pathophysiology and to identify novel signaling pathways affecting motor neurons or muscle. With the help of a statistician (assistant professor), bioinformatic analyses will be used to infer cellular sources and associated pathways, and SMA biomarkers will be cross-referenced with known secreted cues to distinguish neuronal and muscle components. The most promising candidates will then be investigated *in vitro* for their secretion profiles and functional effects on human motor neurons and myoblasts derived from SMA patients and controls. Finally, these biomarkers will be investigated in other neuromuscular diseases (biobanks constitution in progress). Overall, this integrated strategy seeks to uncover novel molecular mechanisms in neuromuscular disorders and to identify specific protein biomarkers with therapeutic potential to improve patient outcomes.

Methodologies:

- Culture of human iPSCs and their derivatives
- Cellular differentiation techniques and coculture (motor neurons, myoblasts)
- Cell biology analyses (immunofluorescence, confocal imaging, viability assays, morphometric analysis)
- Biochemistry (Western blot, Elisa, protein analyses)
- Molecular biology (RT-qPCR, transfection, sequencing)
- Bioinformatic and biostatistics

Skills required:

- Master's student in Cell Biology, Molecular Biology, Neuroscience, or a related field
- Strong interest in biomedical research and biomarkers
- Prior experience in cell culture, proteomic analysis, or lab techniques is not mandatory but desirable
- Motivation, rigor, teamwork, and scientific curiosity are essential

Supervision and Environment:

The student will be supervised by the PI and will work closely with an assistant professor (Thomas Chetot) within a multidisciplinary team, in a stimulating and collaborative scientific environment. This project will lead to collaboration with multiple teams at PGNM on physiological and metabolic aspects. Results will be patented with the help of the SATT Pulsalys (already two patents filed in the team) and published.