MuSkLE
PhD programme
Building, maintaining and repairing the functional locomotor system

Co-funded by the European Union

PhD Position 08 job vacancy

Reference:	**PP08**
Title:	**Deciphering mechanisms controlled by NuMA1 in the formation of functional skeletal muscle fibres**
Hiring institution:	**Lyon1**
Location:	University Claude Bernard Lyon 1, Villeurbanne, France.
Start date:	As from 1st September 2027
Duration:	36 months
Application deadline:	15th January 2027

Job description

Objective:	The recruited doctoral fellow (DF08**)** will develop *in vitro* and *in vivo* approaches to decipher the role of the protein NuMA1 for (a) the integrity of striated skeletal muscle fibres and for (b) the control of Muscle Stem Cell (MuSC) Activation. This project builds on available mouse models generated in the team and on the need to identify molecular pathways related to NuMA1 functions in either skeletal muscle progenitors or differentiated muscle cells. **State of the Art**: Skeletal muscle consists in bundle of thousands of post-mitotic multinucleated cells. We recently identified NuMA1 as a new factor controlling myoblast fusion and myonuclear positioning, which controls the nuclear-MicroTubule Organizing Center (n-MTOC) integrity and the microtubule network orientation. In order to address the role of NuMA1 *in vivo*, we developed two new mouse models allowing the conditional excision of *Numa1* specifically in (a) myofibers (Hsa^{CRE}; $Numa1^{f/f}$ mice), or (b) MuSCs after tamoxifen induction ($Pax7^{CRE\text{-}ERT2}$; $Numa1^{f/f}$). This approach shows failure in skeletal muscle development and adult muscle homeostasis. **Hypothesis and Originality**: We recently obtained single nuclei RNA-sequencing data from the Hsa^{CRE}; $Numa1^{f/f}$ muscles during aging. Various gene candidates are affected, downstream of NuMA1 in post-mitotic cells, and we hypothesize that some of them are controlling pathways related to skeletal myofibre integrity and functioning. We will conduct si/shRNA approaches, *in vitro* and *in vivo*, aiming to decipher their specific roles during muscle fibre maturation. The role of NuMA1 in MuSC quiescence-to-activation transition is completely unknown and alteration of NuMA1-related molecular pathways requires investigation. To do so, we will develop single cell RNA-sequencing, *ex vivo* skeletal muscle fibre analysis and *in vitro* modeling of skeletal muscle fibre. **Methodology and Work Plan**: The project is structured around two main objectives: 1- Analysing the single nuclei RNA-sequencing data associated with myonuclei activity in the Hsa^{CRE}; $Numa1^{f/f}$ muscle during aging and characterising the contribution of selected genes in the formation/maturation of skeletal muscle fibres using *in vitro* models of mature myofibre formation, combined with time-lapse video microscopy. 2- Characterization the behaviour of MuSC in the $Pax7^{CRE\text{-}ERT2}$; $Numa1^{f/f}$ mouse model, using single cell RNA-sequencing, *ex vivo* models of MuSC behaviour on mature myofibres, and validation of candidates downstream of NuMA1 using *in vitro* cell culture models combined with time-lapse video microscopy. *In vivo* challenging protocols of skeletal muscle will be developed with our INMG-PGNM partner (Dr. Gondin) to assess the fusing capacity of MuSCs within mature myofibres.
Collaborations and co-supervisions:	The PhD project will be implemented in collaboration with INMG-PGNM teams (Lyon).

Supervisors:	Vincent Gache – vincent.gache@inserm.fr
Place of work:	Institut NeuroMyogène (INMG-PGNM) Pathophysiology and genetics of neuron and muscle (PGNM) MNCA Team (Muscle Nuclear & Cytoskeleton Architecture) CNRS/UCBL1 UMR 5261 - INSERM U1315 - 8 avenue Rockefeller Lyon - France
Required degree	Master's degree or equivalent in Molecular and Cell Biology
Skills/Experience:	Essential: primary cell culture, experiments using mice models, microscopy (confocal/fluorescence), data analysis. Advantageous: transcriptomics analysis.
Keywords	Skeletal muscle fibres, skeletal muscle progenitors, cytoskeleton, time-lapse video microscopy, fusion, quiescence.

Mandatory requirements

Eligibility:	The doctoral fellow: - should not have resided or carried out his/her main activity (work, study) in the country where he/she is being recruited, i.e., France, **for more than 12 months in the 3 years before the application call deadline,** unless this time was part of a compulsory national service or a procedure for obtaining refugee status under the Geneva Convention. - **must be in possession of a master's degree** at the date of the call deadline. Applicants who have completed their cursus but not yet been awarded the formal master's degree by that date will not be considered eligible. - must be **a doctoral candidate** (not already in possession of a doctoral degree at the date of the application call deadline).
Languages:	Oral and written skills must meet the standards of academic English used in international research.

Job details

Type of contract:	Full time position
Gross salary:	The monthly **living allowance, including employer and employees' social charges, is €3,500.** This amount corresponds to a gross monthly salary estimated to €2,440 and to an estimated net monthly salary before income tax of approximately €1,976. On top of the monthly salary, the doctoral fellow will receive a **mobility allowance,** including employer and employees' social charges of €4,752 over the 36 months of the working contract. This amount corresponds to a gross monthly allowance estimated to €92 and to an estimated net monthly allowance before income tax of approximately €74.
Other benefits:	**Social Protection**: The fellow will benefit from **full social security coverage**, including health insurance, unemployment insurance, and pension contributions. He/she will also have access to occupational health services (*médecine du travail*), as required by French labour law. **Additional Insurance**: The fellow may choose to subscribe to complementary health insurance plans, at affordable rates (approximately €70 *per* month), of which 50% is paid by the employer. **Paid Leave**: The fellow is entitled to up to **33.5 days of paid leave annually** (for 35 hours worked per week), in accordance with national labour law, and will enjoy the same employment rights as other public-sector employees. **Transport**: The fellow benefits from significantly **reduced fares on public transport**, available in all partner cities. Additionally, the host institution will cover 50% of the monthly transportation costs. **Sports and culture:**The fellow will enjoy the cultural environment provided by the Lyon 1 campuses, where numerous exhibitions and activities open to the general public are organised throughout the year. The fellow may play his/her favourite sport in the largest University Sports Association in France, where over 30 activities are on offer year-round through the Sports & Physical Activity University Department. The fellow may also join one of the 70 student associations that unite the University.