MuSkLE

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PhD Position 01 job vacancy

Reference:	**PP01**
Title:	**Muscle pathophysiology in AGO1 and AGO2 genetic disorders**
Hiring institution:	**UCBL1**
Location:	University Claude Bernard Lyon 1, Villeurbanne, France.
Start date:	01st January 2027
Duration:	36 months
Application deadline:	30th April 2026

Job description

Objective:	**The recruited doctoral fellow (DF01)** will investigate the molecular and cellular mechanisms by which pathogenic variants in AGO1 and AGO2 disrupt skeletal muscle development and function. Argonaute proteins are core components of the RNA-induced silencing complex (RISC) and essential mediators of microRNA (miRNA)-dependent gene regulation. Beyond their canonical role in post-transcriptional gene silencing, AGO proteins participate in transcriptional regulation, mRNA stability control, and alternative splicing, contributing broadly to the fine-tuning of developmental gene expression programs. Heterozygous pathogenic variants in AGO1 and AGO2 have been identified in individuals presenting neurological manifestations co-occurring with hypotonia and early muscle anomalies, suggesting that AGO dysfunction directly affects the muscular system. The high sequence identity between AGO proteins, their partial functional redundancy, and the substantial overlap in clinical phenotypes support the hypothesis that shared molecular mechanisms underlie AGO-related disorders. The project aims to disentangle muscle-intrinsic versus systemic effects of AGO dysfunction, assess redundancy between AGO1 and AGO2, and identify dysregulated gene regulatory networks resulting from impaired miRNA-mediated control. Four objectives will be pursued: 1) Refine the clinical and phenotypic spectrum associated with pathogenic AGO variants in collaboration with clinical partners; 2) Generate and characterize muscle-specific AGO1 and AGO2 conditional knockout mouse models, including single and double knockouts; 3) Characterize membrane excitability, Ca^{2+} signaling, and EC coupling using electrophysiology and Ca^{2+} imaging in isolated muscle fibers from the mouse models; 4) Complement these functional analyses with molecular approaches and detailed structural characterization of muscle fiber subcompartments using confocal and

	super-resolution microscopy; These analyses will integrate whole-organism phenotyping, tissue-level characterization, and cellular and transcriptomic investigations. Overall, the project will clarify how AGO dysfunction impairs muscle development and leads to hypotonia, potentially identifying shared therapeutic targets.
Collaborations and co-supervisions:	The PhD project will be co-supervised by Dr Vincent Jacquemond (muscle physiology specialist) and Dr Binnaz Yalcin (expert in genetics). The doctoral fellow will collaborate with the team of Dr Jean-Christophe Antoine, a neurologist specialised in AGO-related neuropathies at the University Hospital of Saint Etienne.
Supervisors:	Vincent Jacquemond (vincent.jacquemond@univ-lyon1.fr) Binnaz Yalcin (binnaz.yalcin@inserm.fr)
Place of work:	INMG/PGNM
Required degree	Master's degree or equivalent in Neuroscience, Physiology, Genetics or Biomedical Sciences
Skills/Experience:	- Strong background in molecular and cellular biology, neurobiology, or physiology - Knowledge of RNA biology and gene regulation mechanisms - Experience with molecular biology techniques - Basic skills in transcriptomic data analysis and statistics - Ability to work independently and in a multidisciplinary team - Excellent written and oral communication skills in English - Experience with mouse models and developmental biology (desirable) - Experience in imaging, electrophysiology, or functional phenotyping (a plus)
Keywords	Argonaute proteins; AGO1; AGO2; neurological disorders; mouse models; hypotonia; skeletal muscle; microRNA; gene regulation; genotype–phenotype correlation

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 **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 €€, and to an estimated net monthly salary before income tax of €€. On top of the monthly salary, the doctoral fellow will [receive a **mobility allowance,** including employer and employees' social charges of €4752] Or [have access to a budget of 4752 €] to cover relocation expenses.
Other benefits:	**Social Protection**: The doctoral 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 doctoral fellow may choose to subscribe to complementary health insurance plans, such as LMDE or SMERRA, at affordable rates (approximately €42 *per* month). Host institutions will provide 15 euros per month. **Paid Leave**: The doctoral fellow is entitled to up to **45 days of paid leave annually**, in accordance with national labour law, and will enjoy the same employment rights as other public-sector employees, including student union membership. **Transport**: The doctoral 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.