Master Studies position at the Institute of Biochemistry and Molecular Biology I
Heinrich Heine Universität Düsseldorf

The Research Group on **mtDNA, Quality Control, and Aging** is seeking highly motivated master students to pursue their theses. Join our recently established vibrant and dynamic team,

Tittle: Modulation of VPS35 to counteract mitochondrial damage. A novel approach to fight mitochondrial diseases

Mitochondrial dysfunction has emerged as a critical determinant in the pathogenesis of numerous human diseases e.g. Leigh syndrome (LG) and Friedreich's ataxia (FA). In most cases, these are progressive, rare and uncurable neurological disorder that typically begins in early childhood and lead to premature dead ascribed to heart or lung failure. Clinical presentation of mitochondriopathies is subjected to a typical "threshold effect", meaning that symptoms appear when mitochondrial damage and consequent downstream neuromuscular deficit surpass a critical threshold.

Modulating mitochondrial quality control mechanisms has emerged as a promising therapeutic strategy to ameliorate disease progression. Enhancing mitochondrial biogenesis, promoting mitophagy, and restoring mitochondrial dynamics through pharmacological agents has shown potential in restoring mitochondrial function and mitigating disease-associated pathology. However, uncontrolled and non-selective mitophagy could lead to pleiotropic effect produced by removal of the mitochondrial pool. Similarly, enhancing the biogenesis or dynamics of compromised mitochondria may not solve the problem at the root. Instead, a more effective therapeutic strategy should specifically target defective mitochondria or mitochondrial parts.

Recently, we found that the retromer orchestrate a quality control mechanism that specifically removes damaged mitochondrial pieces. Here, VPS35, the main component of this complex involved in endosomal trafficking, participates in the generation of mitochondrial derived vesicles which facilitate mitochondrial clearance. This pathway represents a novel mitochondrial checkpoint with potential benefits to counteract mitochondrial dysfunction and diseases.

The aim of this proposal is to understand the involvement of a newly identified drug in the activation of the retromer. For this project, we will use cellular models for LS and FA and analyze if modulation of the retromer is sufficient to counteract the cellular deficits associated to this devastating disease. The completion of this project can provide understanding about mitochondrial quality control, offering potential insights for treatment in the long term.

REQUISITS: Degree on Biology or similar. Besides a basic knowledge of molecular biology, no particular skills are required. Experience in any of the fields involved in the development of the project (e.g, microscopy, cell biology and biochemistry) will be valued. Fluency in English is mandatory. This project is a collaborative project between Dr. Natascia Ventura (Ventura's Lab) from the Institute of Clinical Chemistry and Laboratory Medicine and the IUF- Leibniz Research Institute for Environmental Medicine and Prof. David Pla Martín (Pla Martin Lab). Experimental work will be performed mainly at the Institute of Biochemistry and Molecular Biology I, located at the HHU campus but with active collaboration between both groups.

CONTACT: If you are interested, send an email to plamartin@hhu.de including CV and a brief motivation letter.