MOVEMeNt: Decoding alpha motor neurons diversity and selective vulnerability to disease

Alpha motor neurons (aMN) are a clinically relevant neuronal population that selectively degenerates in neuromuscular diseases, including amyotrophic lateral sclerosis (ALS) and spinal bulbar muscular atrophy (SBMA). Distinct classes of aMNs (SFR, FFR and FF) degenerate at different rate in these diseases, with the fast fatigable (FF) MNs degenerating first.
The molecular mechanisms underlying this selective vulnerability are only partially known. Understanding the molecular logics that shape the identity and function of aMN subtypes in vivo is directly relevant to the development of novel therapeutic strategies. Here I propose to harmonically integrate my solid background in dissecting the molecular fingerprints of distinct neuronal subtypes in adult mice by undertaking new technologies I pioneered at Harvard University, with new skills and knowledge I will build at the Host Institution, which will be critical for the successful achievement of my goal. The overreaching goal of MOVEMeNt is to identify the molecular substrate of disease vulnerability in aMNs. I will (Aim 1) isolate and FACS-purify aMN-nuclei from adult mouse spinal cords, based on the specific expression of aMN markers. Single cell transcriptomic analysis will reveal class-specific molecular fingerprints, including factors playing key roles in suptype-specific development, function, and disease vulnerability. I will also (Aim2) analyze the transcriptional changes of differentially vulnerable aMN classes upon retrograde labeling and functional denervation by neurotoxin intoxication. This work will return candidate genes directly controlling terminal sprouting and remodeling, critical steps that disease-resistant aMN subtypes normally undertake for neuronal loss compensation upon insult. More broadly, I aim to contribute in filling an important knowledge gap by generating the first transcriptomic roadmap of aMN subtypes, and pinpointing at new candidates for therapy development.

UNIPD Team Leader: Maria Pennuto

MSCA Fellow: Emanuela Zuccaro

Department: Department of Biomedical Science

Coordinator: Università degli Studi di Padova (Italy)

Other Participants:

Total EU Contribution: Euro 183.473,28

Call ID: H2020-MSCA-IF-2018

Project Duration in months: 24

Start Date: 01/02/2020

End Date: 31/01/2022

Find out more: