Research options available for topic A

Research topics a) and b) offered by every Doctoral Course involved in UNIPhD are frameworks within which every applicant has to present an original research project in collaboration with a Supervisor at the University of Padua.

Potential Supervisors at Unipd have proposed the following detailed research options, which are related to the research topic. They are offered as a guideline and should facilitate your contact with potential Supervisors. Supervisors' e-mail is specified in every research option table. You are welcome to contact them directly.

Note that this research option list is not at all exhaustive and, within the topic you have chosen, you are free to propose a different research project.

Doctoral Course	**BIOMEDICAL SCIENCES**
Macro-area	Medical and Biomedical Sciences
Department name	Department of Biomedical Sciences
Webpage	*http://doctorate.biomed.unipd.it/*
Research topic A	**Effects of exercise and inactivity in controlling the mitochondrial network and neuromuscular junction** Mitochondrial function and dynamics are greatly affected by exercise or inactivity in skeletal muscles of rodents and humans. Furthermore, mitochondrial alterations result in secretion of hormones and metabolites that affect physiology of distal organs in processes that are likely to involve the neuromuscular junction. Information should be obtained to differentiate between adaptive mitochondrial changes induced by exercise and maladaptive modifications associated with inactivity and aging.
Link to the UNIPhD Call (Academic Year 2022/2023)	*https://www.unipd.it/en/uniphd*
Latest Update	*11.01.2022*
#Number of available Research Options	*2* *Scroll down to see all the Research Options*

1 Research Option Description

Doctoral Course	**PhD in Biomedical Sciences**
Department name	Department of Biomedical Sciences - DSB
Research topic A	Effects of Exercise and Inactivity in Controlling the Mitochondrial Network and Neuromuscular Junction
Research option	IMPACT OF EXERCISE AND INACTIVITY ON NEUROMUSCULAR JUNCTION INTEGRITY, MITOCHONDRIAL FUNCTION AND MUSCLE PERFORMANCE IN AGING HUMANS
Supervisor	Supervisor: Marco NARICI marco.narici@unipd.it Supervisory Team: Giuseppe De VITO, Ornella ROSSETTO, Michela RIGONI, Marco PIRAZZINI, Russell HEPPLE (University of Florida, USA)
Webpage	http://doctorate.biomed.unipd.it/ https://www.biomed.unipd.it/research-areas/muscle-physiology-in-health-and-disease/muscle-contractility-and-neuromuscular-plasticity/overview/ https://www.biomed.unipd.it/research-areas/neuroscience/neuroparalysis-and-neuroregeneration-lab/overview/ https://www.personalgenomics.it/
Context of the research activity and objectives	The project will focus on the effects of exercise and inactivity on neuromuscular junction integrity and mitochondrial function in maintaining neuromuscular health across the lifespan. Both human and animal models shall be used to investigate the fundamental mechanisms regulating adaptations and maladaptations to exercise and inactivity. Human-based studies will involve young and older participants in which NMJ function and muscle contractility will be correlated to NMJ morphology, gene expression, and mitochondrial function, assessed in vivo and in vitro with muscle biopsies and blood samples, NMJ histology and motor unit (MU) behaviour from high-density EMG and MU potential recordings, via surface and intramuscular EMG. Mitochondrial function (respiration, ROS, sensitivity to mitochondrial permeability transition) shall be assessed both in human and animal muscle samples. Appropriate murine models shall also be used to illuminate the molecular and cellular mechanisms underlying the remodelling of the neuromuscular system with aging, exercise and inactivity.
Infrastructures	**Academic:** i) Neuromuscular Physiology Laboratory, DSB, University of Padova, ii) Neuroparalysis and Neuroregeneration Laboratory, DSB, University of Padova, iii) Department of Physical Therapy, Department of Physiology & Functional Genomics, University of Florida, Gainesville, FL, United States. **Non-academic:** Personal Genomics Company, Verona, Italy
Skills and competencies for the development of the activity	Human MU characterisation in vivo, muscle contraction, RNA sequencing, NMJ imaging and electrophysiology. Mitochondrial function/dysfunction: In permeabilized muscle fiber bundles, mitochondrial respiratory function by high resolution respirometry, and mitochondrial ROS production and sensitivity to Ca^{2+}-induced mitochondrial permeability transition by spectrophotometric methods. Next Generation Sequencing (NGS): RNAseq analyses on muscle and blood samples,
Training offer	PhD courses: 1) Neuromuscular plasticity with use, disuse and ageing, 2) Pathophysiology of mitochondria: From energy conservation to disease pathogenesis and therapy
Possible Secondments	Academic secondment (8-12 months): Prof. Russell Hepple's Laboratory Department of Physical Therapy, Department of Physiology & Functional Genomics, University of Florida, Gainesville, FL, United States.

	Non-academic secondment (5 months): Personal Genomics Company, Verona, Italy

2 Research Option Description

Doctoral Course	**PhD in Biomedical Sciences**
Department name	Department of Biomedical Sciences - DSB
Research topic A	Effects of Exercise and Inactivity in Controlling the Mitochondrial Network and Neuromuscular Junction
Research option	IMPACT OF MITOCHONDRIAL DYNAMICS ON THE EXPRESSION AND SECRETION OF NEUROTROPHIC FACTORS
Supervisor	Supervisor: Marco SANDRI marco.sandri@unipd.it Team: Vanina ROMANELLO, Co-supervisor: Marcus KRUGER (CECAD, Institute for Genetics , University of Cologne, GERMANY)
Webpage	http://doctorate.biomed.unipd.it/ https://www.biomed.unipd.it/research-areas/muscle-physiology-in-health-and-disease/signaling-pathways-that-control-protein-homeostasis-in-muscles/overview/ https://www.cecad.uni-koeln.de/research/principal-investigators/prof-dr-marcus-krueger/ https://www.fondbiomed.it/
Context of the research activity and objectives	We have recently shown that mitochondrial dynamics, e.g. fusion and fission, are greatly affected by exercise or inactivity in skeletal muscles of rodents and humans (Tezze et al Cell Metabolism 2017). Moreover, we have also found that alterations of the mitochondrial shaping machinery in muscles affect physiology of distal organs via secretion of hormones and metabolites. The project will aim to dissect the nuclear gene expression changes that are controlled by mitochondrial network and promote the secretion of cytokines/hormones that affect motor neuron-muscle synapse. We will use inducible muscle specific knockout and transgenic mice for the fusion and fission proteins as well as physical inactive mice. To determine gene expression and chromatin landscape changes we will perform single nucleus RNA and ATAC seq on muscles. To determine how mitochondrial shape and exercise affect the secretion of neurotrophic factors we will use transgenic mice that allow the metabolic labelling of newly synthesized proteins specifically in muscles. The metabolically labelled proteins will be identified in muscle and blood by proteomic approach. Gain and loss of function of the identified neurotrophic factors will be performed by gene delivery. Super resolution confocal microscopy will be employed to monitor the morphology of muscle-motor neuron synapse, named neuromuscular junction (NMJ), while electromyography will be used to check the function of NMJ. Mitochondrial respiration, ROS production and membrane potential in muscles of transgenic and inactive mice will be assessed.
Infrastructures	**Academic:** i) Genomic laboratory, DSB, University of Padova, ii) Mitochondrial signalling Laboratory, DSB, University of Padova, iii) CECAD, Institute for Genetics, Faculty of Math. Nat. Sciences, University of Cologne, Germany. **Non-academic:** Fondazione per la Ricerca Biomedica Avanzata, Padova, Italy
Skills and competencies for the development of the activity	Molecular biology, mitochondrial respiration, mitochondrial membrane potential, mitochondrial ROS production, Super-resolution confocal imaging, RNA sequencing, promoter studies, Chromatin Immunoprecipitation, cloning in mammalian expression vectors, AAV-mediated gene delivery, protein purification and proteomics.

Training offer	PhD courses: 1) The single cell analyses in genomics and proteomics, 2) Pathophysiology of mitochondria: From energy conservation to disease pathogenesis and therapy
Possible Secondments	(6 months): Prof. Marcus Kruger's Laboratory CECAD, Institute for Genetics, Faculty of Math. Nat. Sciences, University of Cologne, Germany. (12 months): Fondazione per la ricerca Biomedica Avanzata, Padova, Italy.