

# UNIVERSITÀ Politecnica Delle Marche

NAD metabolism and programmed axon death

## Supervisor: Prof. Giuseppe Orsomando

Department of Odontostomatologic and Specialized Clinical Sciences (DISCO) (<u>https://www.disco.univpm.it/</u>)





# Supervisor: Prof. Giuseppe Orsomando Research Group Description

**Giuseppe Orsomando**, PhD in Protein Biology, Associate Professor of Biochemistry (*ORCID*, *CV link*, *publications*, H-index 30), is joining a team at UNIVPM which includes colleagues from Departments D3A and SIMAU, all specializing in **BIO/10-Biochemistry**; they bring complementary skills and long-term experience in **NAD metabolism and enzymology** 







# Supervisor: Prof. Giuseppe Orsomando

International Collaboration

# Prof. Michael P. Coleman







Michael P. Coleman Weblink



The project also benefits from a long-term collaboration with an academic excellence in the field of **Programmed Axon Death** at the **University of Cambridge**, John van Geest Centre for Brain Repair (UK). **Prof. Michael P. Coleman** and the Supervisor, in the last 13 years, have shared **publications & fundings** 

### selected joint papers

1 <u>iScience 2022</u> (cited by 57) 2 <u>eLife 2021</u> (cited by 24) 3 <u>Neurobiol Dis 2020</u> (cited by 89) 4 <u>Exp Neurol 2019</u> (cited by 46) 5 <u>Exp Neurol 2019</u> (cited by 42) 6 <u>Cell Death Diff 2015</u> (cited by 193) 7 <u>Cell Reports 2015</u> (cited by 144)



Peripheral Nerve Injury Leading to Wallerian Degeneration





## joint fundings

- Wellcome Trust Collaborative Award 220906/Z/20/Z. "Preventable axon degeneration in human disease" (2022/2025)
- <u>BBSRC Industrial Partnership Award</u> BB/S009582/1. "The regulation of axon degeneration by SARM1" (2019/2021)
- Medical Research Council MR/N004582/1. "Variability in Human Axon Survival" (2016/2019)





# The Department of Odontostomatologic and Specialized Clinical Sciences Director: Prof. Andrea Giovagnoni

The **Department of Odontostomatologic and Specialized Clinical Sciences** is the scientific and educational organizational structure of the UNIVPM University established in 2008, devoted to the promotion of scientific research, education and the dissemination of scientific research results in the community.

Its main objectives are to plan, organize and regularly evaluate the quality of research activity carried out in the scientific fields and disciplines under its competence; to plan, organize and manage the first-level and master's courses of the Faculty of Medicine; and, finally, provide to cultural and educational activities and contribute to training and orientation activities based on the needs of students in cooperation with the Medical Association.

https://www.disco.univpm.it/



Nutrition in patological condition





# **Supervisor: Prof. Giuseppe Orsomando** Project Idea: NAD Metabolism and Programmed Axon Death

**Background**: many neuropathologies in humans share a preventable, non-apoptotic cell death mechanism termed **Programmed Axon Death** or **Wallerian Degeneration** (WD) that our team contributed recently to unveil. Its key molecular players are all NAD-metabolism related enzymes, i.e. **NMNAT2** that crucially synthesizes NAD within axoplasm alongside with downstream NAMPT, and **SARM1** which is a tightly regulated multidomain protein endowed with a multicatalytic NAD-consuming activity. So, NMNAT2 crucially regulates NAD levels in axons, as well as NMN levels, the key NAD precursor, while SARM1 senses these fluctuations *in vivo*, ultimately determining axon survival or death. Events downstream of SARM1 activation are unknown at present and represent one main object of this project



### **Project OBJECTIVES**

- 1) identifying molecular events in axon degeneration occurring downstream of SARM1 activation
- 2) exploring further on balancing of the NAD pathway intermediates regulating axon survival or death
- 3) exploring further on neurodegenerative diseases that are linked to NMNAT2 or SARM1
- focusing on drug targeting of SARM1 or NMNAT2, aimed at one-shot therapies for many different kind of neurological disorders in humans

#### 👄 🔿 Axon degeneration

Programmed Axon Death is a widespread mechanism driven by the activation of SARM1 and prevented in healthy axons by its negative regulator NMNAT2. Any insult disrupting or damaging NMNAT2 causes SARM1-dependent axon death.