# Supervisor Project Idea

## Supervisor GIUSEPPE ORSOMANDO

*Insert a brief CV and/or external link, the total number of publications, the ORCID link, 5 of the most significant/recent publications, and a list of funded projects and awards.* max 300 words

CV link:
https://www.univpm.it/Entra/Docenti_1/Medicina_e_chirurgia_1/docname/idsel/449/docname/GIUSEPPE%20ORSOMANDO
Publications number: 50 peer-reviewed papers & 7 preprints; H-index 30; SCOPUS citations ~2400
ORCID link: https://orcid.org/0000-0001-6640-097X

Publications related to the project:

1 Cirilli et al. (2024) **Molecules** (doi 10.3390/molecules29040847) https://www.mdpi.com/1420-3049/29/4/847
2 Angeletti et al. (2022) **iScience** (doi 10.1016/j.isci.2022.103812) https://pubmed.ncbi.nlm.nih.gov/35198877/
3 Loreto et al. (2021) **eLife** (doi 10.7554/eLife.72823) https://elifesciences.org/articles/72823
4 Huppke et al. (2019) **Experimental Neurology** (doi 10.1016/j.expneurol.2019.112958) https://www.sciencedirect.com/science/article/pii/S0014488619301049
5 Di Stefano et al. (2015) **Cell Death and Differentiation** (doi 10.1038/cdd.2014.164) https://www.nature.com/articles/cdd2014164

Projects funded (all joint by the supervisor as local coordinator of research unit):

2022/25 UK grant Wellcome Trust Collaborative Award 220906/Z/20/Z. Title: "Preventable axon degeneration in human disease" (PI Prof. M. P. Coleman, University of Cambridge)
2019/21 UK grant BBSRC Industrial Partnership Award BB/S009582/1. Title: "The regulation of axon degeneration by SARM1" (PI Prof. Micheal P. Coleman, University of Cambridge)
2016/19 UK grant Medical Research Council MR/N004582/1. Title: "Variability in Human Axon Survival" (PI Prof. Micheal P. Coleman, University of Cambridge)

## Research Group Description

*Provide the name the reference department and a brief description of the research group, including external links, and available instrumentations and infrastructures.* max 300 words

Department of Clinical Sciences (DISCO), Section of Biochemistry (https://www.disco.univpm.it/presentazione) in the laboratory led by the supervisor Prof. Giuseppe Orsomando (https://www.disco.univpm.it/content/bio10-amici-adolfo). The team is further strengthened by colleagues from UNIVPM Departments D3A and SIMAU, who possess expertise in the same field and can provide valuable support.
This research group boasts extensive experience in NAD metabolism and enzymology. The laboratory is equipped for various tasks including cloning, expression, purification, and structural analysis of recombinant proteins. Additionally, the team conducts enzyme kinetics and quantitative analysis of metabolites *in vivo*. The available equipment includes a cold room, a laminar-flow hood plus CO2 incubator, several FPLC/HPLC machines, spectrophotometers, a multifunctional plate reader, a French press, a sonicator, an ultracentrifuge, a lyophilizer, and all necessary resources for computational analyses of X-ray / Cryo-EM data.
The project also benefits from the support of Prof. Michael P. Coleman and his research group in Cambridge (https://www.neuroscience.cam.ac.uk/directory/profile.php?mcoleman), an academic excellence in the study of programmed axon death, who will provide strategic support for neuronal cell culturing, manipulation, and analysis. Their collaboration with the supervisor is long-term, as evidenced by joint funding and publications.

## Title and goals

*Provide the title of the topic and a short summary of the project idea.* max 200 words

**NAD METABOLISM AND PROGRAMMED AXON DEATH**

We focus on human neurodegeneration and neuropathologies characterized by a preventable, non-apoptotic mechanism of cell death termed Programmed Axon Death or Wallerian degeneration (WD), that our team has contributed to unveiling in recent years. Key molecular players in this process include NMNAT2, a vital enzyme leading to NAD synthesis within axoplasm, and SARM1, a recently discovered tightly regulated multidomain protein with multicatalytic NAD-consuming activity. These are both crucial for NAD metabolism in neurons by regulating levels of NAD intermediates or sensing their fluctuations, ultimately determining the fate of axons, either survival or death. However, the mechanism downstream of SARM1 activation is presently unknown.
In this view, we propose an experimental plan outlined as follows: 1) further exploration of the role of NAD pathway in regulating axon survival or death; 2) deeper investigation into neurodegenerative diseases associated with NMNAT2 or SARM1; 3) development of novel drugs targeting SARM1 or NMNAT2 to treat neurological disorders.

**Contact details** (*including email address of the supervisor*)

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