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DELLE MARCHE

NAD Metabolism and Programmed Axon Death

Supervisor:
Prof. Giuseppe Orsomando

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

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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 lab team alongside colleagues from UNIVPM Departments D3A and SIMAU, all specializing in BIO/10-Biochemistry. They bring complementary skills and long-term experience in **NAD metabolism and enzymology**

DISCO (Medicine)

administration

Paolo Bonfigli

cell culturing

Francesca Mazzola

SIMAU (Engineering)

bioinformatics

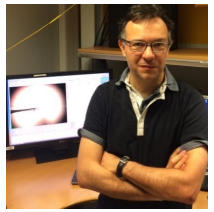
Leonardo Sorci
Weblink

D3A (Food Science)

enzymology

Nadia Raffaelli
Weblink

structural biology



Michele Cianci
Weblink

gene expression

Gasparrini Massimiliano
Weblink

Selected production

1 *eLife 2022* (cited by 5)
2 *J Bacteriol 2020* (cited by 9)
3 *PloS One 2014* (cited by 107)
4 *Front Biosci 2008* (cited by 87)
5 *Biochemistry 2007* (cited by 72)
6 *Cell Mol Life Sci 2004* (cited by 245)
7 *BBRC 2002* (cited by 111)

Lab skills/expertise

1 recombinant cloning & protein expression
2 protein purification & characterization
3 enzyme kinetics
4 cell culturing
5 quantitative analysis of metabolites in vivo
6 computational analyses of X-ray / Cryo-EM data

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Supervisor: Prof. Giuseppe Orsomando

International Collaboration

Prof. Michael P. Coleman

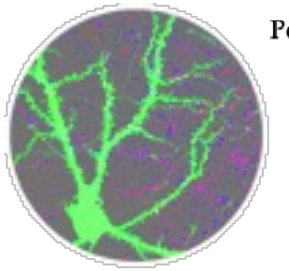
CAMBRIDGE NEUROSCIENCE

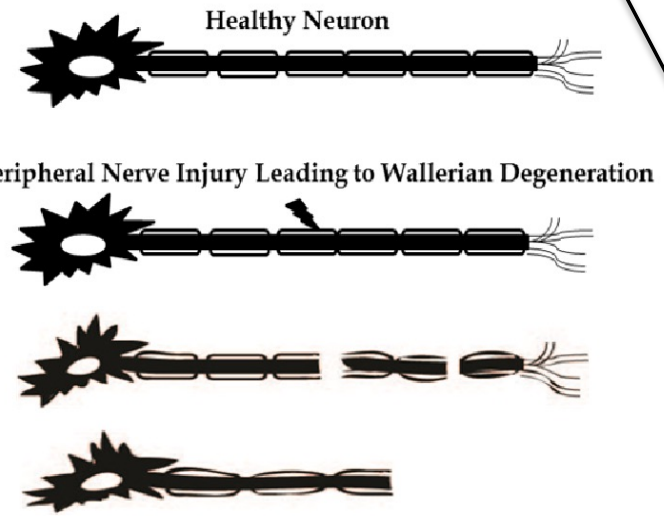
UNIVERSITY OF CAMBRIDGE

Michael P. Coleman

Weblink

The project also benefits from academic excellence in the field of **Programmed Axon Death** at the University of Cambridge, John van Geest Centre for Brain Repair (UK). A long-term collaboration between Prof. Michael P. Coleman and the Supervisor of this project is supported by **joint funding** & **publications** (14 total papers to date …)





Selected joint papers

(all relevant to the Project herein)

1 Molecules 2024 *(accepted for publication)*
2 iScience 2022 *(cited by 42)*
3 eLife 2021 *(cited by 16)*
4 Neurobiol Dis 2020 *(cited by 71)*
5 Exp Neurol 2019 *(cited by 41)*
6 Exp Neurol 2019 *(cited by 37)*
7 Cell Death Diff 2015 *(cited by 154)*
8 Cell Reports 2015 *(cited by 127)*

Collaboration Projects funded at UK

(with Supervisor as RU Leader & PI Coleman)

- Wellcome Trust Collaborative Award 220906/Z/20/Z. “Preventable axon degeneration in human disease” (2022/2025)
- BBSRC Industrial Partnership Award 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)

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The Department of Odontostomatologic and Specialized Clinical Sciences

Director: Prof. Andrea Giovagnoni

The **Department of Odontostomatologic and Specialized Clinical Sciences** is a scientific and educational organizational structure of the UNIVPM University, established in 2008. It is devoted to the promotion of scientific research, education, and the dissemination of research findings within 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, to provide cultural and educational activities and contribute to training and orientation activities based on the needs of students in cooperation with the Medical Association.

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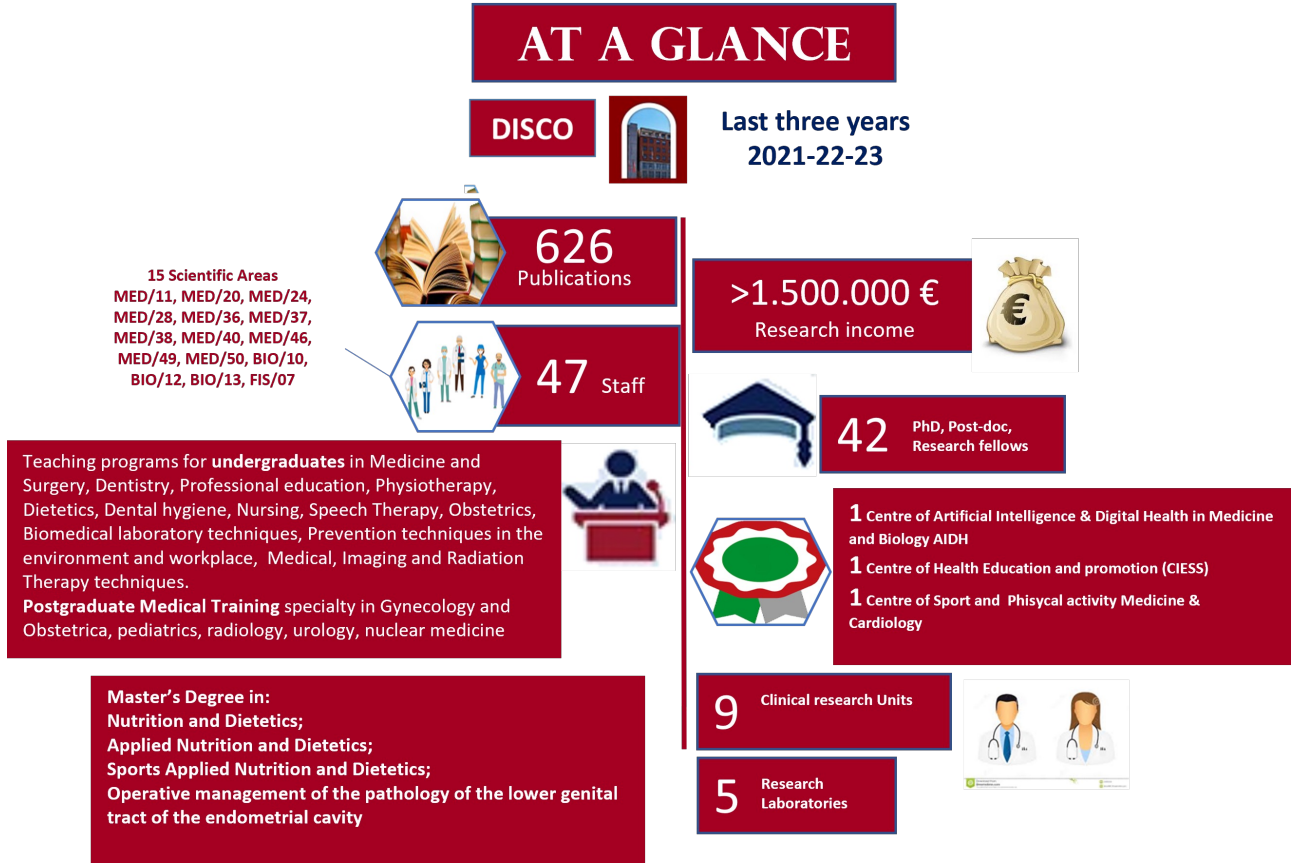

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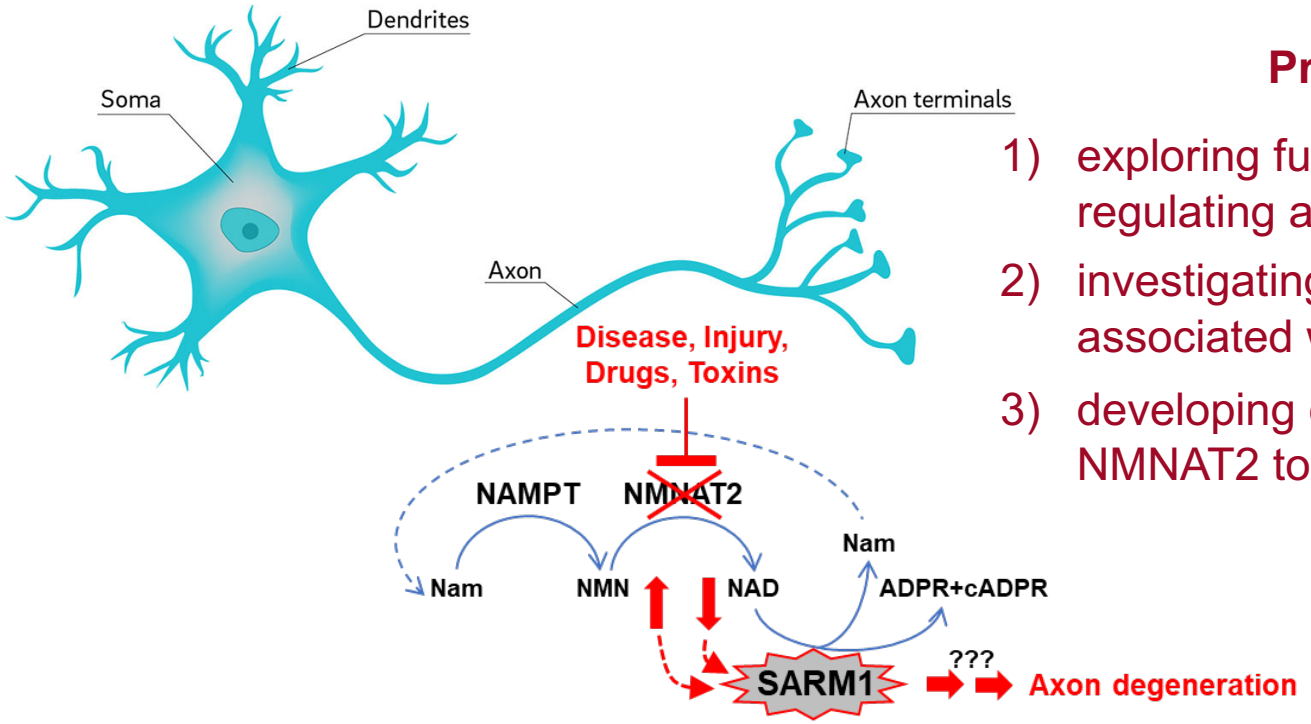
Supervisor: Prof. Giuseppe Orsomando

Project Title :

NAD Metabolism and Programmed Axon Death

Background: Human neurodegeneration and neuropathologies are characterized by a preventable, non-apoptotic cell death type termed **Programmed Axon Death** or **Wallerian Degeneration** (WD). Our team has contributed to unveiling its mechanism in recent years. Key molecular players in this process include **NMNAT2**, a key enzyme for NAD synthesis within axoplasm, along with the downstream enzyme NAMPT, and **SARM1**, a recently discovered tightly regulated multidomain protein with multicatalytic NAD-consuming activity. NMNAT2 in axons crucially regulates levels of NAD and those of the NAD intermediate NMN; SARM1 senses their fluctuations *in vivo,* ultimately determining the fate of axons, either survival or death. However, the mechanism downstream of SARM1 activation is presently unknown.



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.

Project OBJECTIVES

1) exploring further the role of NAD pathway in regulating axon survival or death
2) investigating neurodegenerative diseases associated with NMNAT2 or SARM1
3) developing drugs targeting SARM1 or NMNAT2 to treat neurological disorders