Description of Funded Research Projects
1st Call for H.F.R.I. Research Projects to support Post-Doctoral Researchers

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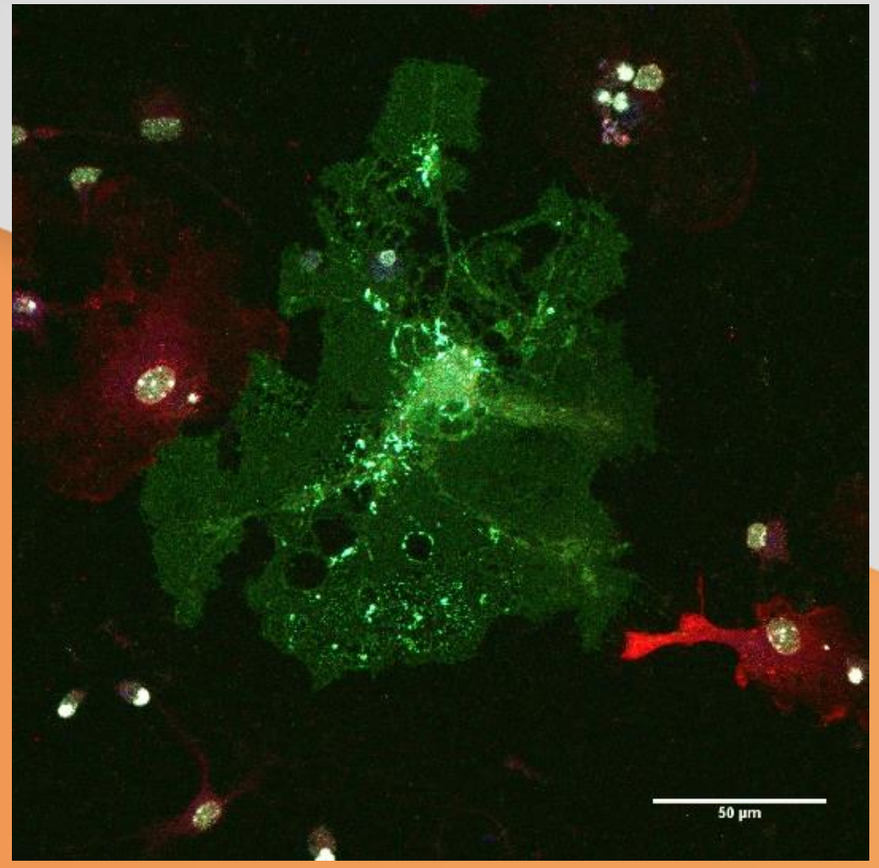
Research Project Title:

The role of Autophagy in the development and maintenance of Myelin

Principal Investigator:
Maria Savvaki



Popular Title:
Regulating the levels of myelin, the substance that surrounds and protects nerves

Scientific Field:
Life Sciences

Host Institution:
IMBB, FORTH

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Research Project Summary

The proposed study aims to investigate the significance of autophagy in the CNS, focusing on myelin-producing glia. Myelin provides mammals with an evolutionary privilege that insulates the axon and ensures the rapid and efficient propagation of action potentials along its length. Its disruption is a common feature of demyelinating neurodegenerative diseases as well as aging and age-related disorders in humans. In all cases, myelin decline is associated with disrupted neuronal conduction and motor/cognitive impairment. Recent studies implicate defective regulation of autophagy in demyelinating disorders in humans and rodent models, but little is known about the underlying mechanism. Since CNS demyelinating pathologies comprise a major cause of disability worldwide and remain untreatable, it is vital to investigate the underlying mechanisms.

Autophagy comprises a major degradation mechanism which engulfs, removes, and recycles unwanted cytoplasmic material including damaged organelles and toxic protein aggregates. Through its role in energy production and in maintaining cellular homeostasis, autophagy is crucial during development, and its dysregulation has been linked to aging and several disorders, including certain cancers, cardiomyopathies, and neurodegenerative diseases. One important feature of autophagy is that it is a process easily targeted by caloric restriction (CR), thus rendering its regulation druggable. There are several CR mimetics (CRMs) that are natural non-toxic compounds, widely used in traditional medicine and which have been shown to effectively activate the autophagic mechanism.

Our hypothesis is that autophagy is essential for maintaining the homeostasis of CNS myelinating glia, thus we anticipate that manipulations regulating autophagy could provide a novel and effective therapeutic approach for demyelinating pathologies. Our ultimate goal is to uncover a novel molecular mechanism mediating central myelin homeostasis and to provide insights into the aging effects of autophagy on myelin and the use of natural FDA-approved autophagy activators as therapeutic agents for the cure of myelin pathologies.

Project Impact on Society

Myelin pathologies refer to conditions where intrinsically normal myelin is destroyed either due to immune system-mediated responses (demyelination) or to genetic defects (dysmyelination). The most common demyelinating disorder, affecting young adults between 15 and 55 years of age, is multiple sclerosis (MS). MS is a devastating neurodegenerative disease of the CNS, characterized by myelin loss, varying degrees of axonal pathology and progressive neurological dysfunction. MS has a severe impact on patients' quality of life with social and economic implications and prevalence that varies markedly geographically.

The available treatments can only ameliorate or prevent specific aspects of MS, while they fail to promote myelin restoration and effective neuroprotection. Our research is oriented towards this direction, since we propose to investigate a novel mechanism interfering with myelin formation/maintenance as well as myelin disruption, aiming to reveal new therapeutic targets and unravel the beneficial effect of commercially available, FDA- approved, natural agents (CRMs).

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To me, H.F.R.I. funding would mean...

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At a time when the financial crisis in our country has left a serious impact on many aspects of society, including the field of scientific research, the existence of a national funding body is timelier and more necessary than ever.
This is the first time that postdoctoral researchers are funded in Greece as primary investigators, and it is the first of a series of important steps to enable young scientists to excel. Funding for research performed by postdoctoral researchers will give a significant impetus to the country's scientific progress. In addition, H.F.R.I. funding promotes the re-establishment of gifted Greek researchers from abroad thus limiting the destructive consequences of “brain drain”.

The Principal Investigator,
Maria Savvaki

Funding

Amount: **175,000 €**

Duration: **36 months**

Foundation: **H.F.R.I.**

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Hellenic Foundation for Research & Innovation

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