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

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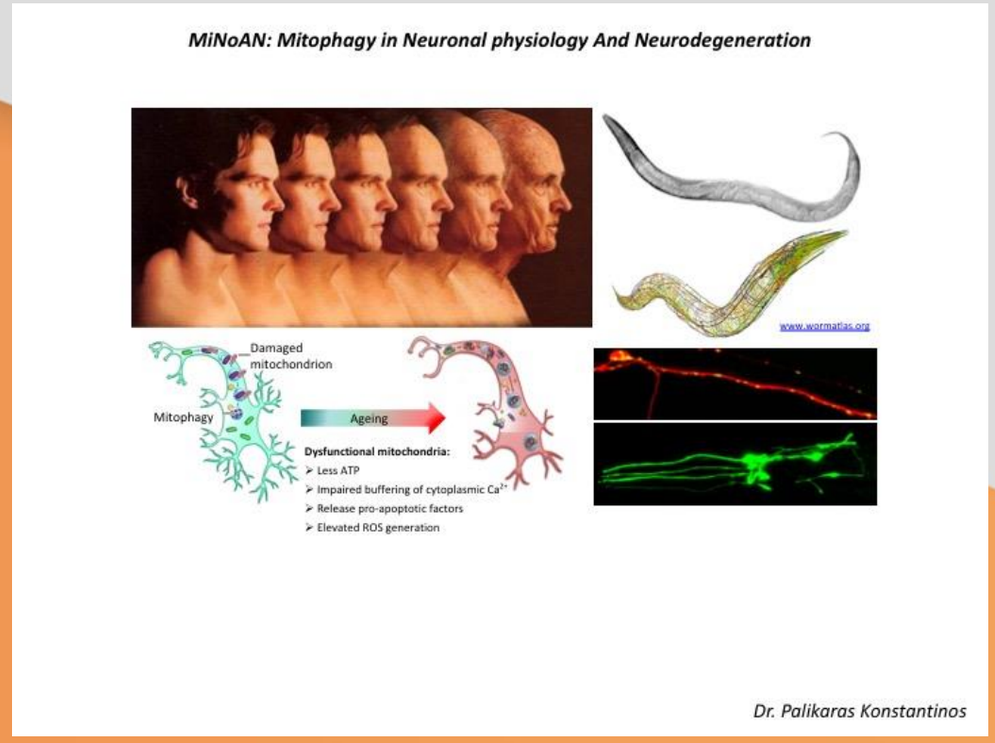
Research Project Title:

Mitophagy in Neuronal physiology and Neurodegeneration

Principal Investigator:
Konstantinos Palikaras



Popular Title:
The role of mitophagy in neuronal physiology

Scientific Field:
Life Sciences

Host Institution:
Foundation for Research & Technology Hellas (FORTH) – Institute of Molecular Biology & Biotechnology (IMBB), Hellas

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Research Project Summary

Recent findings implicate mitochondrial abnormalities in the pathogenesis of neurodegenerative diseases, highlighting that mitochondrial DNA mutations, autophagy and oxidative stress are factors contributing to neurodegeneration. Autophagic dysfunction and oxidative stress occur early in all major neurodegenerative diseases, suggesting that these abnormalities have a causal role in disease pathogenesis.

Elimination of impaired mitochondria is essential in long-lived and constantly highly metabolic active cells, including neurons, among others. Neuronal cells rely on proper mitochondrial function. Therefore, it is not surprising that several mitochondrial diseases are accompanied by neurological abnormalities. The cytosolic E3 ubiquitin ligase Parkin and the mitochondrial phosphatase and tensin homolog (PTEN)-induced kinase 1 (PINK1), mutations of which are associated with the autosomal recessive form of parkinsonism have been implicated in the mitophagy process. The PINK1/Parkin pathway is the best-studied molecular pathway mediating selective autophagy of impaired and/or aged mitochondria. Although, the primary targets of the disease are neuronal cells, our knowledge on the PINK1/Parkin pathway is mainly based on in vitro studies using established cell lines.

Analysis/monitoring of mitophagy in Caenorhabditis elegans neurons and further exploring the role of PINK1/Parkin pathway in regulating neuronal processes will provide critical insights on mechanisms most relevant to development and progression of neurodegenerative disorders. Additionally, the identification and characterization of novel genes or chemical modulators of neuronal mitophagy will lead to new therapeutic approaches for the prevention and amelioration of neurodegenerative diseases. An essential future challenge is to devise model organism systems to better understand the common pathways and relative contribution of mitochondrial dysfunction to the pathogenesis of neurodegenerative disorders, as well as to develop therapeutic approaches that target mitophagy and its consequences.

Together, the results of this research proposal will lead to an unprecedented understanding of age-related breakdown of neuronal function and will provide critical insights with broad relevance to human health and quality of life.

Project Impact on Society

With the world's population ageing, degenerative diseases have become a high priority topic for our society. Understanding the mechanisms of neuronal ageing is absolutely crucial to envision new and innovative strategies to improve end-of-life care and find novel therapeutic approaches for degenerative diseases. In this sense, Dr. Palikaras' project will significantly contribute to unravelling the cellular and molecular basis of age-related neurodegenerative diseases.

Dr. Palikaras’ funded research aims to investigate the molecular pathways orchestrating mitochondrial dynamics and mitophagy in neuronal function and metabolism during ageing. To conduct his research, Dr. Palikaras will use a highly malleable genetic model organism, the nematode Caenorhabditis elegans. Combining this powerful model organism with state of the art imaging technologies, Dr. Palikaras will be able to monitor mitochondrial biogenesis and mitophagy in vivo and decipher the molecular mechanisms mediating neuronal degeneration during ageing.

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

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The HFRI grant will give me the opportunity to build an entirely new research team and perform forefront research using state of the art techniques in Greece. Furthermore, I will develop and acquire skills and tools that will promote my career as an independent scientist.

The Principal Investigator,
Konstantinos Palikaras

Funding

Amount: **180,000 €**

Duration: **24 months**

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

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