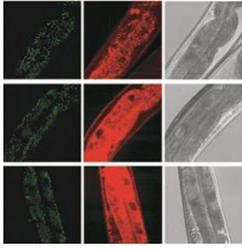


Mitochondrial crosstalk signalling in the regulation of ageing (MitoSigAge)



Resumen:

The project is funded by the European Research Council as a Starting Grant (StG).

Ageing is one of the most intriguing and fundamental biological processes, with clear implications for human health. Although mitochondria have been associated with ageing and age-related pathology, the underlying molecular mechanisms remain poorly understood. The most relevant genetic pathway regulating ageing is the insulin/IGF-1 signalling (IIS) pathway. Recently, we have shown that mitochondrial prohibitins (PHB) play a major role in cellular metabolism and mitochondrial biogenesis, affecting ageing in opposite ways in wild-type animals and IIS-defective *C. elegans* mutants.

Objetivos:

The aim of the research programme is to shed light on the intricate interaction between mitochondria and cell-signalling networks in the regulation of ageing.

Objetivos contribución:

The project, hosted by UPO, aims to:

- Elucidate the cellular signalling pathways involved in the metabolic responses to mitochondrial dysfunction upon PHB depletion in wild type animals and IIS-defective mutants, using genomewide RNAi screens,
- Conduct a comprehensive metabolic profiling of wild type and IIS mutants in the presence and absence of prohibitin.
- Identify genetic suppressors of prohibitins by performing forward genetic suppressor screens. Ultimately, the functional conservation of key genes discovered in *C. elegans* will be investigated in mammalian assays.

Entregables:

Given the complexity of biological systems and disease mechanisms, high-quality genome-scale analyses will help to accelerate basic and biomedical research by facilitating the formulation of more directed hypothesis to be experimentally tested. The completion of this project will certainly gather a considerable amount of data on the complex interaction networks influencing mitochondrial function, metabolism and ageing.

Impacto:

The project represents an integrative and innovative approach to identify cellular signalling pathways involved in mediating lifespan-extending metabolism adjustments and their consequences. The results stemming from this research will provide fundamental insights to understand the ageing process and to combat ageing-related diseases.

Presupuesto: 1,424,640.00

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