Mapping the late-life health promoting mechanisms in worms and mammals

https://neurodegenerationresearch.eu/survey/mapping-the-late-life-health-promoting-mechanisms-in-worms-and-mammals/

Principal Investigators
Institution
Contact information of lead PI
Country

European Commission

Title of project or programme

Mapping the late-life health promoting mechanisms in worms and mammals

Source of funding information

European Commission FP7-Seventh Framework Programme

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€ 1,438,899

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6.0

The project/programme is most relevant to:

Neurodegenerative disease in general

Keywords
Research Abstract
Aberrant protein aggregation (proteotoxicity) is an underlying mechanistic event common to numerous late-onset human neurodegenerative maladies including Alzheimer's (AD) disease. Recent studies indicated that the ageing process plays key roles in enabling protein aggregation to become toxic late in life. The insulin/IGF signaling pathway (IIS) is a major ageing, stress resistance and lifespan regulator in worms and mice. We found that IIS reduction protects worms and mice from toxicity associated with the AD linked peptide, A?. These findings point to the alteration of ageing by IIS reduction as a promising research avenue towards the development of neurodegeneration therapies. In the nematode C. elegans, both effects of IIS reduction; longevity and protection from proteotoxicity are dependent on the activity of the FOXO transcription factor DAF-16. However, these functions of DAF-16/FOXO differ temporally;

in worms the mediation of longevity by DAF-16 is restricted to reproductive adulthood while protection from proteotoxicity extends also to late adulthood. This differential temporal activity pattern suggests that different DAF-16 co-factors and target genes play roles in the mediation of longevity and in protection from proteotoxicity. Thus, a careful characterization of the late life DAF-16 regulated protective mechanism is required to evaluate the therapeutic potential of IIS reduction as a future treatment for neurodegenerative disorders. Here I propose to use nematodes and mice to explore the DAF-16/FOXO co-factors and target genes that mediate stress resistance and protection from proteotoxicity in the aged organism. Dual experimental approach will be utilized to achieve this goal; a directed genetic screen for the identification of co-factors and temporally differential set of DNA microarrays for the recognition of late life DAF-16/FOX target genes. This project is expected to yield new insight and to serve as a platform for future studies.

Lay Summary
Further information available at:

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Investments > €500k

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European Commission

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Neurodegenerative disease in general

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