Identification & characterisation of novel genes that regulate neurodegeneration and aging using Caenorhabditis elegans

https://neurodegenerationresearch.eu/survey/identification-characterisation-of-novel-genes-that-regulate-neurodegeneration-and-aging-using-caenorhabditis-elegans/

Title of project or programme

Identification & characterisation of novel genes that regulate neurodegeneration and aging using Caenorhabditis elegans

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
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- United Kingdom

Source of funding information

Medical Research Council

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755981.86

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Total duration of award in months

24

The project/programme is most relevant to

- Neurodegenerative disease in general

Keywords

Research abstract in English

“Neurodegenerative diseases result from progressive deterioration and loss of cells in the central nervous system. This leads to a decline in the quality of life and often involves disturbances in controlling movements, cognitive impairment and dementia. As result of an ageing population, the incidence of degenerative diseases will dramatically increase in the future. Without new preventing measures and without the development of new treatments, it will not be possible to sustain financially the major public health systems. Thus, as most of human neurodegenerative pathologies are poorly understood and untreatable, uncovering novel modulators of the mechanisms involved in neurodegeneration represents one of the critical aims of the medical research today. Therefore, genetic dissection of neuronal responses to neurotoxins and ageing in simple models such as Caenorhabditis elegans is likely to shed light on significant genes which enhance or suppress neurodegenerative processes. Due to thorough genetic characterization, short lifespan and well characterized anatomy, C.elegans is a powerful model system to investigate regulation of the molecular processes associated with neuronal demise. Despite its great simplicity as multicellular animal, C.elegans has been widely used for rapid and inexpensive evaluation of therapeutic drugs and characterization of molecular candidates that confer altered susceptibility to a certain treatment. The principle is to screen for mutants that are either resistant or hypersensitive to a compound and/or present a clear behavioural phenotype and then genetically characterize the pathways involved. The study is complemented by the use of mammalian model systems, such as animals and primary neuronal cultures.

The central theme of my Programme has two major aims: 1) to determine the cascade of events occurring during calcium mediated cell death triggered by neurotoxins; 2) to identify genes involved in aging and aging-related neuronal degeneration.

My recent work has shown the importance of calcium-activated proteases, calpains, in the deregulation of calcium homeostasis and in the increase of leakiness of the nuclear pore complex. In addition, we are in process to characterize the role of new genes, which were identified by RNAi screening in worms, in aging and neuronal degeneration. We are trying to identify genetically and biochemically the mechanism by which the loss of these genes can alter the normal lifespan of the animal and can modulate cell death.

These findings might shed lights on the mechanisms underlying cell death and aging and might have important translational applications.

My programme has strong collaborative interactions with the intramural programmes of the Toxicology Unit, especially with Prof Gerry Melino and Prof Martin Dyer.”

Lay Summary