BH3- Only Proteins and Cellular Bioenergetic in the Control of Neuronal Survival and Cell Death: Role in Ischaemic Injury and Neurodegeneration

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Title of project or programme

Title of PI	BH3- Only Proteins and Cellular Bioenergetic in the Control of Neuronal Survival and Cell Death: Role in Ischaemic Injury and Neurodegeneration

Principal Investigators of project/programme grant

Title	Forname	Surname	Institution	Country
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Source of funding information

Science Foundation Ireland

Total sum awarded (Euro)

3471112.00

Start date of award

01-01-2009

Total duration of award in months

60

The project/programme is most relevant to

- Neurodegenerative disease in general

Keywords

Neuronal Apoptosis, Excitotoxicity, Ca2+ Mediated Cell Death, ER Stress, Proteasomal Stress, Ischemic Stroke, Neurodegeneration, BH3 Only Proteins, BIM, PUMA, Mitochondria, Bioenergetics, Computational Biology, Systems Biology

Research abstract in English

The proposed programme will investigate key mechanisms underlying neuronal survival and cell death in response to ischemic brain injury and during chronic neurodegeneration. Based on previous research, we will investigate the role of pro-apoptotic BH3 Only Proteins and cellular and mitochondrial bioenergetics in cell death and cell survival decisions in response to neuronal Ca2+ overloading, endoplasmic reticulum stress, proteasomal inhibition, and oxygen/glucose deprivation. These studies will be conducted using established neuronal cell culture and organotypic slice culture systems, and key findings will be translated into appropriate animal models. Building on our expertise and previous investments in single-cell analysis, quantitative microscopy, and computational biology, we aim to identify key decision and intervention points using both hypothesis-driven and systems-driven research approaches. These investigations will generate novel therapeutic targets and prognostic tools for drug discovery, which could ultimately benefit the treatment of ischemic brain injury, chronic neurodegeneration, and potentially other disorders of inappropriate cell death signalling.

Lay summary

Stroke and age-related brain disorders are leading causes of death and disability which, with increasing life expectancy in Ireland, impose a growing economic and societal burden. Current treatment regimes are limited in their effectiveness, partially due to a lack of understanding of why nerve cells die or survive during brain injury. This research programme tackles this important question by investigating a family of genes that mediate stress-induced cell death, and by addressing the role of reduced energy supply during brain injury. The programme involves an established collaboration with SIEMENS engineers who will bring essential computational approaches into this research programme that facilitate the analysis of biological networks, and accelerate the identification of new targets for future therapy. The research programme also allows for the development and dissemination of new, Irish born, technology by integrating the activities of LUXCEL Biosciences, a pioneer in oxygen sensing technologies, into the research programme.

In which category does this research fall?

- Basic research