

Neuronal model systems and neurotoxicity

<https://neurodegenerationresearch.eu/survey/neuronal-model-systems-and-neurotoxicity/>

Principal Investigators

Dr L Panman

Institution

MRC Toxicology Unit

Contact information of lead PI

Country

United Kingdom

Title of project or programme

Neuronal model systems and neurotoxicity

Source of funding information

MRC

Total sum awarded (Euro)

€ 1,763,684

Start date of award

01/12/2012

Total duration of award in years

5.0

The project/programme is most relevant to:

Neurodegenerative disease in general

Keywords

Research Abstract

Neurodegenerative diseases are characterized by the differential vulnerability of specific neuronal cell populations to endogenous or environmental toxic insults. For example, in Parkinsons disease specifically the dopaminergic neurons of the substantia nigra degenerate, while the ventral tegmental area neurons remain relatively spared. The reasons for the selective degeneration of neuronal cell types are still largely unknown. The research in our group aims to identify the mechanism underlying the selective vulnerability of specific neuronal cell types to neurotoxic insult. We are developing an embryonic stem cell model system that can be used to

study these processes in vitro. Recently, we have shown that forced expression of neuronal lineage specific transcription factors can direct the differentiation of embryonic stem cells into several clinically relevant neuronal cell types including dopaminergic-, serotonergic- and noradrenergic neurons. Using a similar approach, we are planning to generate homogeneous populations of neuronal cell types that are affected in Parkinsons, Alzheimers and prion disease. We will compare the gene expression profile of affected neuronal cell types to neurons that are more resistant to stress. In addition, we will analyse the differential responsiveness of these cells to neurotoxicity by using chemicals or by introducing disease causing gene variants. Our second line of research is focussed on understanding the molecular mechanism underlying dopaminergic neuronal subtype specification. Dopaminergic neurons located in the midbrain are a very heterogeneous cell population and are implicated in several important neurological disorders including Parkinsons disease, Schizophrenia and anxiety. We will use embryonic stem cell derived dopaminergic neurons and mouse genetics to gain insight into processes controlling the diversification of dopaminergic neurons and the characterization of the distinct dopaminergic neuronal subtypes. Ultimately, our research may contribute to the understanding of the etiology of neurodegenerative diseases and may lead to the development of novel treatments.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

United Kingdom

Diseases:

Neurodegenerative disease in general

Years:

2016

Database Categories:

N/A

Database Tags:

N/A