

CRISPR-Cas9 genetic screens for genes conferring survival to oxidative stress in dopamine neurons

<https://neurodegenerationresearch.eu/survey/crispr-cas9-genetic-screens-for-genes-conferring-survival-to-oxidative-stress-in-dopamine-neurons/>

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Contact information of lead PI Country

United Kingdom

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CRISPR-Cas9 genetic screens for genes conferring survival to oxidative stress in dopamine neurons

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Parkinson's UK

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€ 294,293

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01/11/2015

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3

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Research Abstract

There are currently no disease halting treatments for Parkinson's disease (PD). With the recent failure of numerous neuroprotective therapies for PD at the clinical testing stage (Phytopharm's Cogane, Ceregene's AAV-Neurturin, etc), there is a critical need for identifying novel neuroprotective pathways. Large scale whole-genome, random mutation analysis (using the CRISPR-Cas9 system) represents one of the most efficient methods by which unidentified

molecular mechanisms can be discovered. Working in Prof Allen Bradley's lab at the Wellcome Trust Sanger Institute, I have utilised this approach to identify interesting new targets in specific cancers – highlighting novel protective functions in specific genes. I would now like to apply this technology to midbrain dopamine (DA) neurons with the goal of determining novel neuroprotective genes. By stressing cultured DA neurons with hydrogen-peroxide and rotenone, and then sequencing DNA extracted from the surviving cells, I hope to identify the mutations that infer either vulnerability or strength in the cells. Upon validating all of the newly identified targets, I will generate mutant mice for behavioural analysis and PD modelling in collaboration with Prof Roger Barker's lab at the University of Cambridge. In parallel with the behavioural testing, I will replicate the oxidative stress screens in human ES cell-derived DA neuron, allowing me to identify conserved neuroprotective mechanisms. The goal of this work will be to identify a range novel pathways which can be further investigated and hopefully lead to neuroprotective therapies.

Further information available at:

Types:

Investments < €500k

Member States:

United Kingdom

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