

Identifying therapeutic targets and causes of dopaminergic neuronal degeneration using *C. elegans* high-throughput genetic approaches

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Identifying therapeutic targets and causes of dopaminergic neuronal degeneration using *C. elegans* high-throughput genetic approaches

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The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

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Parkinson`s disease | C elegans | dopamin degeneration | molecular mechanisms

Research Abstract

Parkinson`s Disease, characterized by the progressive degeneration of dopaminergic neurons, afflicts millions of people. Yet, no effective therapeutic strategies are available.

This work uses *Caenorhabditis elegans* to study dopaminergic degeneration. *C. elegans* is a small nematode, highly amenable to genetics and high-throughput approaches, with a simple nervous system that is highly conserved at the level of gene expression and pathology with humans. This study also utilizes a mutant in a Transient Receptor Potential (TRP) channel, *trp-4(d)*, in which dopaminergic neurons properly develop but later on progressively degenerate.

OBJECTIVES:

1. Understand the molecular mechanisms of dopaminergic neurodegeneration
2. Identify potential therapeutic targets
3. Uncover novel causes of neuronal cell death

STRATEGIES:

1. We will use a candidate approach to investigate which of the known cell death pathways (apoptosis, autophagy, necrosis) mediate *trp-4(d)* dopaminergic degeneration.
2. We will use an unbiased 'forward genetic screening' approach, i.e. use *trp-4(d)* mutants and target the genomes with mutagens to identify genes that when mutated, stop dopaminergic cell death. High-throughput genetic technology (automated screening and Whole Genome Sequencing) will be employed for rapid mutant isolation and identification. Characterization of the retrieved genes will elucidate molecular mechanisms that block dopaminergic degeneration.
3. We will use similar high-throughput genetic screening approaches to find more genes like *trp-4(d)*, that when mutated have detrimental effect to the survival of DA neurons either in isolation or in the presence of known Parkinsonism genes.

IMPACT

The expected outcomes are of high medical significance and relevance to human neurodegenerative conditions. The proposed work, employing state of the art methodology, will not only enhance Norwegian competitiveness in disease related research but also contribute to Norwegian technological exc

Types:

Fellowships

Member States:

Norway

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Parkinson's disease & PD-related disorders

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