

2013 Report for the project: **“Discovery of neuroprotective mechanisms using a DJ-1 Celegans model and a unique in Norway technology”**

Despite the many neurodegenerative diseases that afflict the aging population, the triggers of neuronal cell death as well as the underlying molecular mechanisms are largely unknown. This lack of understanding hinders the development of therapeutic strategies. The objective of this study was to understand the molecular mechanisms of dopaminergic neurodegeneration using a *C. elegans* model in combination with advanced genetic methodologies. As a result of this project we elucidated some aspects of neuronal degeneration.

In particular, we characterized a new animal model of dopaminergic neurodegeneration in terms of timing and cell-type specificity of neuronal death. Our results revealed that in our model, classic apoptosis is not involved in dopaminergic cell death but the neurons die instead through a different mechanism (necrosis). Furthermore, we implicate intracellular calcium homeostasis as contributing factor to dopaminergic degeneration. Our findings are included in a manuscript under revision for Journal of Neuroscience.

Furthermore, we set out to discover novel causes of dopaminergic degeneration. For this, we performed forward genetic screens on ‘sensitized’ *C. elegans* that carry human alpha-synuclein or mutations in orthologs of human Parkinsonism (PARK) genes, e.g. DJ1, Parkin, and PINK1. We retrieved a mutant collection, which we are currently analysing. We expect this analysis to reveal potential interacting partners of human PARK proteins and new insights into molecular mechanisms of Parkinson’s disease.

The funds from the Norwegian Parkinson’s Association greatly facilitated this project, and were allocated for consumables and running costs as explained in the original application.

Maria Doitsidou  
Senior Researcher/Group Leader  
Stavanger University Hospital

Associate Professor  
University of Stavanger

[maria.doitsidou@uis.no](mailto:maria.doitsidou@uis.no)  
<http://core.uis.no/category.php?categoryID=7338>