Novel Treatment Strategies for Disease Modification and Neuroprotection in Parkinson´s Disease

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Country

Sweden

Title of project or programme

Novel Treatment Strategies for Disease Modification and Neuroprotection in Parkinson´s Disease

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Swedish Research Council

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€ 326,442

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01/01/2016

Total duration of award in years

3

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Research Abstract
The goal of the project is to explore two novel approaches to neuroprotection and disease modification in Parkinson´s disease, focusing on the ability of the affected neurons to defend themselves against the disease-causing protein ?-synuclein. In these studies we will make use of an animal model of Parkinson´s disease (PD) developed in our lab. This model, which is based on AAV-mediated overexpression of the disease-causing protein ?-synuclein in midbrain

dopamine (DA) neurons, reproduces the progressive degenerative changes seen in human PD. This model provides an attractive tool for studies of neuroprotective and disease-modifying therapeutic interventions. The project is designed to explore (i) the role of autophagy as a defense mechanism against ?-synuclein induced toxicity, (ii) the role of ?-synuclein fibrils as a trigger of PD-like pathology and spread across synapses in the brain, and the therapeutic potential of a new class of drugs designed to promote the selective degradation of ?-synuclein oligomeres, and (iii) the therapeutic potential of a recently developed orally active agonist/activator of the nuclear receptor Nurr1 to block ?-synuclein-induced toxicity. The research will be performed in my lab at the Wallenberg Neuroscience Center in Lund in collaboration with Prof. Thomas Perlmann´s lab in Stockholm. The ?-synuclein toxicity and degradation studies will be carried out in collaboration with Prof Virginia Lee in Philadelphia, using therapeutic peptide constructs provided by Prof. Yu Tian Wang in Vancouver. The project will be completed within the 3-year grant period. The two therapeutic strategies explored here – elimination of toxic ?-synuclein oligomeres and activation of Nurr1 function – will provide new interesting research tools and may also open up new ways to treat PD using either degradation-targeting peptides or activators of Nurr1 function. The Nurr1 activating drug explored here, IVA3132, is in pre-clinical development by the Inventiva company with the goal to move the drug toward a clinical trial.

Further information available at:

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Investments < €500k

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