

Unfolding the role of UPR in Parkinson's Disease

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Country

Sweden

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Unfolding the role of UPR in Parkinson's Disease

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The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

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Research Abstract

Parkinson's Disease (PD) is the second most common neurodegenerative disease in the world, but there is still no medicine that can effectively stop disease progression. PD is characterized by accumulation of unfolded/misfolded proteins in neurons, which are sequestered into large cytoplasmic aggregates called Lewy-bodies. The protein alpha-synuclein (a-syn) constitutes the major protein component in Lewy bodies. Genetic evidence has shown that a-syn play a role in PD pathogenesis as gene duplication and triplication are linked to PD. Unfolded Protein Response is a signaling system that keeps the amount of unfolded proteins at low levels, by

regulating the protein folding capacity and protein synthesis of the cell. Analysis of post mortem tissue from PD patients show that UPR activity is upregulated in PD and mouse and cell culture models indicate that UPR activity might affect PD progression. Still, we now very little about the role of UPR in PD, as it has not been addressed thoroughly in appropriate animal and cell culture models. The role of UPR activity in PD progression will be explored in this application in a-syn and UPR modified mouse and cell culture models, and will answer if UPR should be a new focus area for PD drug targeting. Finally, this study will also answer if one clinically approved drug, Guanabenz, could be a novel candidate for PD treatment.

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