MASTER'S DEGREE IN BIOMEDICAL RESEARCH
Research Project Proposal
Academic year 2023-2024

Project Nº 47

Title: Identification of the interactome of alpha-synuclein, a protein with a key role in Parkinson´s disease

Department/ Laboratory CIMA, Gene Therapy and Regulation of Gene Expression (Neurosciences)

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Summary

Parkinson´s disease (PD) is a neurodegenerative disease characterized by the selective death of dopaminergic neurons from the substantia nigra as well as the presence of intraneuronal structures called Lewy Bodies (pathological hallmarks of PD post-mortem brains). Lewy Bodies are mainly formed by the presynaptic protein alpha-synuclein (aSyn). Importantly, mutations in the gene encoding aSyn cause autosomal dominant cases of familial PD. Therefore, aSyn plays a key role in PD but the mechanisms by which aSyn causes dopaminergic neuronal death are not yet understood. Results from our laboratory strongly suggest that pathological protein-protein interactions of aSyn at early stages can be at the origin of the disease. Thus, the goal of this project is to identify the interactome (protein-protein interactions driven by aSyn) at early stages of neurodegeneration in animal models of PD that can provide new therapeutic targets for the disease.

To that, we have set up a methodological approach based on proximity biotinylation using the promiscuous biotinylase TurboID. When expressed as a fusion protein, TurboID biotinylates by proximity stable and transient interacting partners, allowing their identification by streptavidin affinity purification and mass spectrometry. We have generated AAVs that express aSynTurboID and injected them in the substantia nigra of mice. This approach enable us to identify the aSyn interactome at early stages of the neurodegeneration process before motor symptoms of the disease appear. Methodology: Automated microscopy and survival analysis, mouse model of PD, motor performance evaluation, immunohistochemistry analysis of brain tissue to address dopaminergic neuronal survival and expression of aSyn protein interactors.

yes	X
no	

Does the project include the possibility of supervised animal manipulation to complete the training for animal manipulator?