Universidad de Navarra
Facultad de Ciencias

MÁSTER EN INVESTIGACIÓN BIOMÉDICA
Research Project Proposal
Academic year 2025-2026

Project Nº 34	
Title: *Evaluating PLA2G4E Gene Therapy as a Disease-Modifying Strategy in Parkinson's Disease*	
Department/ Laboratory *Therapeutic genes for neurodegenerative diseases Lab; Gene Therapy for Neurological Disease Program, Lab 2.06, CIMA.*	
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Summary

Parkinson´s disease (PD) is the most common movement disorder, affecting 1% of the population above the age of 65. Current therapies are symptomatic, underscoring the urgent need for neuroprotective or disease-modifying strategies. This gap likely stems from the complex neurobiology of neurodegeneration and the limited translational value of existing animal models. In the context of PD, recently it has been developed an advanced model of PD based in the progressive accumulation of neuromelanin in dopaminergic neurons of the *substantia nigra (SN)*. Using this model, we have recently identified PLA2G4E as a promising neuroprotective therapeutic candidate. Specifically, AAV9-mediated expression of PLA2G4E in the *SN* resulted in improved motor function, preservation of dopaminergic neurons and striatal terminals, and attenuation of neuroinflammatory markers. These findings highlight the potential of PLA2G4E gene therapy as a disease-modifying approach for PD. In the present project we propose to confirm this result using the PIGMO model—an innovative, progressive, and clinically relevant rodent model of PD. Unlike traditional toxin-based or fast-onset AAV9-hTyr models, PIGMO mimics the gradual accumulation of NM and associated pathology observed in human PD, affecting not only the SN but also other catecholaminergic nuclei such as the locus coeruleus (LC) and the dorsal nucleus of vagus nerve. This project will assess the therapeutic effects of PLA2G4E in PIGMO through behavioral, histological, and molecular analyses. Specifically, it will evaluate its ability to attenuate NM-associated neurodegeneration and inflammation, aiming to establish PLA2G4E as a robust disease-modifying therapy for PD. In addition, the project will also aim to characterize non-motor Parkinsonian alterations—such as mood, cognitive, and circadian disturbances—which are highly relevant to patient quality of life and often precede motor symptoms.

yes	x
no	

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