



MASTER'S DEGREE IN BIOMEDICAL RESEARCH

Research Project Proposal

Academic year 2023-2024

Project Nº 56 ASIGNADO

Title: TDP-43 pathology propagation in ALS and FTD cell based models

Department/ Laboratory

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Summary

ALS is a devastating, fatal and rare neurodegenerative disease without any effective cure. Although the ethiology is unknown, aggregates of the nuclear protein known as TDP-43 are present in more than 97% of ALS patients, both sporadic and familiar ones. Our group is working since the last ten years in recovering TDP-43 functional homeostasis with small molecules and have discovered some protein kinase inhibitors such as IGS2.7 and VNG1.47, CK1 and TTBK1 inhibitors respectively, with great therapeutic potential. They are able to decrease TDP-43 phosphorylation, recover its nuclear localization and restore intracellular transport mediated by TDP-43. Moreover, we have shown how TDP-43 pathology is propagated cell-to-cell by TNT cell structures and extravesicles present in the extracellular media. All of our studies are performed in a human-based cell model using immortalized lymphocytes from healthy controls and sporadic and familiar ALS.

The present work is planned to study TDP-43 propagation using myoblast from ALS patients. We first will characterize the TDP-43 pathology (f any) and in a second step we will look for tdp-43 propagation among similar cells (mioblasts) and dissimilar (lymphoblasts).

yes	
no	X

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