P34 MEASURING PROTEIN AGGREGATION IN LYMPHOBLASTS FROM ALS PATIENTS WITH A TURBIDOMETRIC ASSAY

C. Pérez de la Lastra[1], C. Tosat-Bitrián[1], V. Nozal[1], A. Martínez[1], A. Martín Requero[1], V. Palomo[1].

[1] Centro de Investigaciones Biológicas-CSIC, C/ Ramiro de Maeztu 9, Madrid, carmpe13@ucm.es

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Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease characterized by the degeneration of upper motor neurons in the brain and lower motor neurons in the spinal cord, which are responsible for voluntary muscle movement. Due to the heterogeneity of the disease and the lack of biomarkers the diagnosis of the patients and pharmacological response is intricate. [1, 2]

Current experimental models do not reflect on this diversity, therefore a model consisting of samples extracted from patients is essential to characterize the pathology. Considering the degeneration in ALS is multisystem, an analysis of lymphoblasts from blood samples is proposed. [3, 4]

Here we have studied protein aggregation in healthy controls, sporadic and familiar patients, characterizing the pathological aggregation. We are observing that the proteinopathy aspect of sporadic ALS is manifested in this model. By turbidimetry measurements of protein extracts, a difference in the total amount of protein aggregation comparing patients with healthy controls is shown. Moreover, this methodology enables a rapid evaluation of promising drug candidates, and we show here how some of them are able to rescue the pathologic aggregation of the patients.

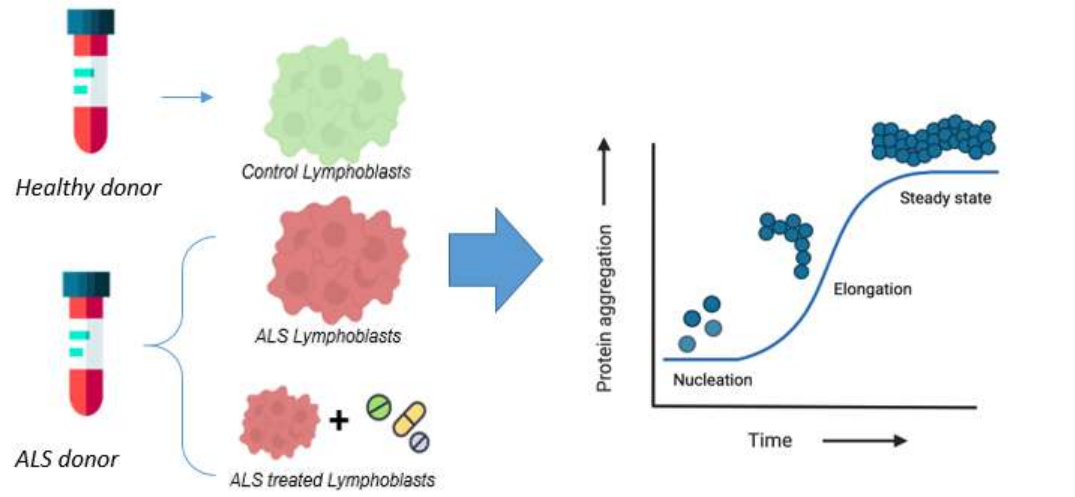

Figure 1. Scheme representing our project methodology and the process of protein aggregation over time with our lymphoblastic lines

References

[1] Hardiman, O., Al-Chalabi, A., Chio, A., Corr, E. M., Logroscino, G., Robberecht, W., van den Berg, L. H. Nature Reviews Disease Primers. 2017, 3, 17071.

[2] Robberecht, W., Philips, T. Nat Rev Neurosci. 2013, 14, 248-264.

[3] Posa, D., Martínez-González, L., Bartolomé, F., Nagaraj, S., Porras, G., Martínez, A., & Martín-Requero, Á. Molecular Neurobiology. 2018, 56(4), 2424-2432.

[4] Luotti S., Pasetto L., Porcu L. Neurobiology of Disease. 2020, 139, 104815.