CO-CULTURES BETWEEN NEURONS AND ASTROCYTES TO ADDRESS ALZHEIMER´S DISEASE PATHOLOGY (D15)

Topic
AS03 Stem Cells, Organoids, Neural Injury Neurotoxicity and Repair

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Abstract Body
Background: Alzheimer's disease (AD) is characterized by presenting a complex pathology, not fully resolved yet. This fact, together with the lack of reliable models, has impeded the development of effective therapies. Recently, several studies have shown that functional glial cell defects have a key role in the pathology of AD. However, this glial dysfunction, currently, cannot be correctly modeled using the available animal models, so we hypothesized that cells derived from Alzheimer's patients can serve as a better platform for studying the disease. In this sense, human pluripotent stem cells (hPSC) allow the generation of different types of neural cells, which can be used for disease modeling, identification of new targets and drugs development. Methods: We have a collection of hiPSCs derived from patients with sporadic forms of AD stratified based on APOE genotype. We have differentiated these cells towards neural cells and mature them to neurons or astrocytes using a serum-free approach, to assess intrinsic differences between those derived from AD patients or healthy controls. Results: We have implemented a serum-free approach and generated neural precursors and astrocytes from all the lines tested. We observe differences at the phenotypic level and a reduced capacity to differentiate towards neural lineage in those lines derived from APOE4 carriers. Conclusions: Our preliminary data suggest intrinsic differences in the neural differentiation capacity between cell lines derived from APOE4 or APOE3 carrier subjects. Further experiments would contribute to elucidate novel pathogenic pathways associated with neurodegeneration and susceptible of therapeutic modulation, likely contributing to the development of new effective drugs against AD. This study was supported by ISCiii (Spain), co-financed by FEDER funds, through grants PI21/00915 (AG) and PI21/00914 (JV); by Junta de Andalucia through Consejería de Economía and Conocimiento grants UMA20-FEDERJA-048 (JAGL), PY18-RT-2233 (to AG) and US-1262734 (JV), co-financed by Programa Operativo FEDER 2014-2020, and SNGJ4-11 (LCP).