PhD Program
in
TECHNOLOGY FOR HEALTH

ELECTRICAL FIELDS STIMULATION TO IMPROVE MATURATION OF HUMAN INDUCIBLE PLURIPOTENT STEM CELLS-DERIVED DOPAMINERGIC NEURONS

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Background

Human induced pluripotent stem cell (hiPSC) technology offers a modern and novel platform for modeling neurological and psychiatric disorders in vitro and provides access to patient-specific cells for drug discovery and personalized medicine. Several protocols have been developed over the last fifteen years with the goal of differentiating hiPSCs into various neural subpopulations, including dopaminergic (DA) neurons. DA neuron degeneration or dysfunction are a common feature of several neurological disorders, including Parkinson's disease, and psychiatric disorders such as depression and schizophrenia. The processes leading to the differentiation of DA neurons from hiPSC are mimicked in vitro by the addition or subtraction of growth factors and small molecules, providing the specification of neurons and their temporal differentiation. However, the time required to reach phenotypic maturity may be very long (2-3 months). Therefore, there is a need to identify and implement methodologies that accelerate this process. While exposure to growth factors and small molecules remains the predominant method, non-biochemical approaches have attracted the attention of researchers. In particular, electrical stimulation was tested to improve the efficiency of neural differentiation of stem cells in vitro. So far, no data are available in the literature about the use of electric fields to improve DA neuron differentiation and maturation from hiPSCs.

Objectives

My research aims to investigate the application of electric fields to accelerate the differentiation and maturation of DA neurons from hiPSCs, with the ultimate goal of improving the efficiency and accuracy of disease modelling and drug testing.

Methodologies

Human iPSCs will be differentiated into DA neurons using experimental protocols in which the outcome of exposure to electric fields of varying intensities and regimes will be compared with published standard protocols. The maturation of DA neurons employing these different approaches will be characterized using cellular, molecular and imaging techniques and time-to-maturation used as a primary endpoint. The cell biology experiments will be performed in the laboratory of Prof. L. Collo, Department of Molecular and Translational Medicine.

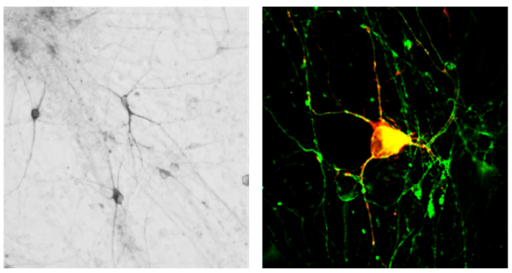

FIGURE 1. PHASE CONTRAST AND IMMUNOFLUORESCENCE IMAGES OF DA NEURONS

Expected Results and Impact

The proposed technological improvement, by accelerating the differentiation and maturation process of hiPSC-derived DA neurons, will have an impact on the efficiency of drug testing procedures relevant to industrial and academic drug discovery. In particular, the shortening of the maturation time of DA neurons, without losing the typical morphological and functional characteristics observed in standard protocols, will allow a faster production of DA neurons cultures, making the use of the hiPSC platform more aligned with the turnaround time of the other cellular platforms currently in use in drug discovery for neurodegenerative and psychiatric disorders.