Plano de trabalhos para tese de Mestrado 2016/2017

Exploring stem cell-derived 3D models to unravel the role of microenvironment remodelling in neurological disorders

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Duração: 1 ano lectivo

Sumário:

Brain microenvironment plays an important role in neurological development, function and degeneration. Extracellular matrix (ECM) components modulate neural cell survival, migration, proliferation and neuronal function. Few studies have demonstrated a mechanistic correlation between changes in ECM and neurodegeneration. The major challenge in studying these mechanisms is the lack of human cell models in which the molecular crosstalk between different cell types are represented so that and consequent microenvironment remodelling during disease progression can be recapitulated *in vitro.*

At the Advanced Cell Models Lab of the Animal Cell Technology Unit our research is focused on assessing the role of tissue microenvironment in disease progression and biopharmaceutical response, developing and employing advanced cell-based disease models. We have implemented a methodology based on perfusion bioreactors for three-dimensional (3D) neural differentiation of neural stem cells derived from induced pluripotent stem cells (hiPSC-NSC). This generates tissue-like 3D structures containing neuronal, astroglial and oligodendroglial cells than can be maintained in culture for long periods of time. Importantly, we've demonstrated *in vitro* recapitulation of neural cellular and extracellular developmental features along this culture time.

We are now working with iPSC derived from neurodegenerative disease patients (Alzheimer's and Parkinson's disease) and lysosomal storage disorders patients (Mucopolysaccharidosis VII). These disease models are currently being developed and validated in terms of recapitulation of cellular and molecular hallmarks of the diseases.

The specific objective of this research project is to characterize the dynamic remodelling of extracellular protein signatures in these neural disease models during long-term cultures, and compare them between each other and with models derived from healthy donors. Ultimately this will contribute to identify molecular players involved in early stage events of disease progression.

Methodologies: Neural differentiation of human stem cells (hiPSC and hNSC), 3D cell culture, bioreactor culture, luminescence-based assays, immunodetection (microscopy, Western blot, ELISA), confocal microscopy, proteomics analysis.