COLLABORATIVE IBEC INTERNATIONAL PhD PROGRAMME

Position

1. Project Title:
   Refining iPSC-Based Spinal Cord Model Systems by Fabricating Developmentally Programmed Extracellular Matrix Cues

2. Research project/ Research Group description

The goal of this research project is to refine induced pluripotent stem cell (iPSC) neuronal models by providing developmentally appropriate extracellular matrix (ECM) cues. iPSC technologies have provided unprecedented access to the human CNS and have enabled the construction of models to study neurodevelopment and neurological disease mechanisms. However, cultures of iPSC-derived neurons have limitations such as insufficient morphological maturation, synaptic connectivity and electrophysiological activity. Indeed, transcriptional analyses suggest that they resemble neurons of late embryonic to early postnatal stages, which hinders the study of adult-onset neurodegenerative diseases. We hypothesize that the lack of appropriate spatiotemporal ECM signals is a major contributor to these limitations. The ECM is an intricately organized intercellular scaffold of secreted proteins and complex sugars that configures spatiotemporal microenvironments throughout the CNS. It provides critical structural support for neurons, serves as a reservoir for soluble factors, and mediates cellular signaling that modulates neuronal development, maturation, and aging. However, the temporal diversity and functional effects of the matrisome, defined as the ensemble of ECM and ECM-associated proteins, in the CNS are poorly characterized. As a result, the design of in vitro platforms for culturing iPSC-derived neurons that truly recapitulate the physiological ECM is impossible. Here, we will first use biochemical purification and quantitative mass spectrometry (MS)-based proteomics to define the composition and nature of remodeling of the human CNS matrisome in vivo. We will then leverage our combined expertise in iPSC technologies and biomaterials to establish ECM-mimetic matrices that can recapitulate the architecture and modulatory activity of the physiological matrisome to facilitate the maturation and aging of 2D and 3D stem cell-derived neural models *in vitro*.

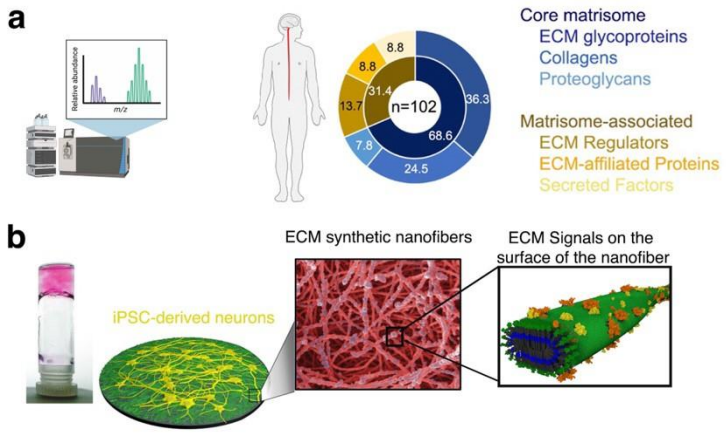

Figure 1. Work Flow. **(a)** LC-MS/MS profiling and Pie chart of core matrisome components in adult spinal cord ECM. **(b)** Synthetic ECM mimetic peptide hydrogel schematics to model iPSCs derived neurons.

3. Job position description

The applicant will actively engage in all facets of the proposed research alongside collaborators with diverse expertise, receiving multidisciplinary training during their laboratory tenure. The student will design and implement ECM mimetic matrices that replicate the architecture and functionality of the physiological CNS matrisome.

Under the supervision of principal investigators, the applicant will employ various cell culture techniques, including primary neuronal and glial cultures, cell lines, and stem cell differentiation protocols to create human iPSC-derived neural models. They will utilize advanced methods such as subcellular fractionation, protein immunoprecipitation, Western blotting, immunocytochemistry, and immunohistochemistry to characterize the extracellular matrix (ECM) and its role in neuronal maturation. Furthermore, the applicant will design and characterize synthetic platforms using rheological analysis for mechanical properties, scanning electron microscopy (SEM) for surface topography, and spectroscopic techniques like Fourier-transform infrared (FTIR) and nuclear magnetic resonance (NMR) to verify material composition. Bioprinting and microfluidic platforms will also be employed during the course the project. High-throughput techniques, including quantitative mass spectrometry for matrisome profiling and single-cell RNA sequencing (scRNAseq), will be used to delineate the composition and remodeling of the human CNS ECM.

The applicant will collaborate with interdisciplinary teams of experts in biomaterials, tissue engineering, neurobiology, and stem cell technologies at IDIBELL and IBEC. A strong background in neurobiology, materials science and/or stem cell research is requested. The applicant should demonstrate proactivity and adaptability to thrive in multidisciplinary and international teams. Proficient written and oral English skills are required to effectively communicate with collaborators, present research findings, and prepare manuscripts.

Group Leader IBEC

1. Title: Dr.
2. Full name: Zaida Alvarez Pinto
3. Email: zalvarez@ibecbarcelona.eu
4. Research Group: Biomaterials for Neural Regeneration

Collaborator in the other institution

1. Title: Dr.
2. Full name: Juan Alberto Ortega Cano
3. Email: jalabertoortega@ub.edu
4. Institute: IDIBELL
5. Research group: Neurodevelopmental Disorders