ReprOids - Reprogramming of somatic cells into organOids: patient-centred neurodevelopmental disease modelling from nascent induced pluripotency

Understanding the neurodevelopmental causes and mechanisms of the brain disease is challenging due to the limited access to the human brain tissues, the complexity of brain anatomy and the lack of accurate models to recapitulate human brain development. The convergence between induced pluripotent stem cell and organoid technology enable to recapitulate key features of early human neurodevelopment disease in vitro. However, the low efficiency, high cost and technical variability of generating induced pluripotent stem cells (hiPSC) and organoids make an impossible challenge to design a powered study for associating patient genotype to organoids' in vitro phenotypes. I will generate technology to produce human brain organoids from a selected patient in a robust, timely and seamless process and to capture - so far undetected - neurodevelopmental phenotypes. This will be obtained by combining reprogramming to nascent states of pluripotency with neurodevelopmental morphogenesis in three-dimension. Starting from a single nascent naive hiPSC, we will develop a process to form an epiblast cyst, then neuroepithelial cyst and forebrain organoid in continuous three-dimension process. I will use this technology to investigate genetic and epigenetic modifications in the early phase of neural development of Fragile X Syndrome (FXS). We will generate brain organoids from large cohorts of FXS patients for: i) profiling the whole spectrum of in vitro phonotypes associated with the variety of patient' genetic and epigenetic modifications; ii) revealing unexplored developmentally regulated mechanisms; iii) design a powered study to assess targeted therapeutic options in FXS. ReprOids will allow the generation of human brain organoids from large cohorts of patients capturing in vitro the whole spectrum of disease manifestations. This will have huge impact in patient clinical management at the diagnostic, prognostic or therapeutic level.

ERC Grantee: Nicola Elvassore

Department: Industrial Engineering

Coordinator: Università degli Studi di Padova

Total EU Contribution: Euro 2.500.000,00

Call ID: ERC-2021-AdG

Project Duration in months: 60

Find out more: https://cordis.europa.eu/en