ORAL COMMUNICATIONS

A SELF-FOLDING HUMAN NEURAL TUBE MODEL USING 4D SMART SCAFFOLDS

C. Dell'Amico[1], I. Chiesa[2], A. Toffano[1], A. Esposito[2], P. Mancini[2], C. Magliaro[2], A. Louvi[3], C. De Maria[2], M. Onorati[1]

[1]Department of Biology, Unit of Cell, Molecular, and Developmental Biology, University of Pisa, Italy; [2]Department of Information Engineering and Research Center Enrico Piaggio, University of Pisa, Italy; [3]Departments of Neurosurgery and Neuroscience, Yale School of Medicine, New Haven, USA

The human brain originates from the neural tube that detaches from the ectodermal layer and gradually develops into a mature structure through highly regulated molecular and cellular processes. Here, stem cell technology is combined with 4D bioprinting, a fabrication process that utilizes additive manufacturing, to generate a 4D-neural tube (4D-NT). This consists of a scaffold that can self-fold over time, which is then populated with iPSC-derived neuroprogenitors, mimicking neural tube cellular architecture. The scaffold's "smart" self-folding behavior is driven by the differential swelling properties of bilayer films, which create a deformation gradient upon hydration. Cellular analyses reveal a highly efficient induction of neuroprogenitors on 4D-NTs, demonstrating the ability of this model to mimic the spatial and structural complexity of the developing human neural tube. Furthermore, 4D-NTs seeded with iPSCs with a mutation in WDR62, associated with autosomal recessive primary microcephaly (MCPH), recapitulate the earlier observations obtained in 2D/3D neural cultures, thereby validating the newly developed 4D-NT platform and suggesting it represents a tool that can facilitate understanding of human neural development and disease.