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A Lecture Series Focused on Induced Pluripotent Stem Cells



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BRAIN SPHERES: APPLICATIONS AND FUTURE

The lessons learned in cancer research, where drug development has shown an extremely high failure rate (more than 90%), and human disease studies, have shown us that the current models used are not optimal to predict human toxicity. The cost per drug is estimated at \$1.2–1.3 billion dollars, and it takes approximately 8 years to complete the whole process. In addition, with the implementation of REACH and the need to test the large number of substances produced and used in the European Union, scientists and regulators agree on the fact that the current test guidelines are too expensive and time-consuming to allow the evaluation and classification of all these compounds. Current guidelines for neurotoxicity and developmental neurotoxicity are under OECD/EFSA revision, with the objective of developing faster and cheaper methods that allow to evaluate and prioritize the big amount of chemicals on the market. Thus, it is crucial to develop models that better mimic human physiology. We have developed a 3D human iPSC-derived brain model (also called BrainSpheres). This model has shown to recapitulate key events of neurodevelopment. BrainSpheres are very reproducible in terms of size and cellular composition, with no necrotic centers. They not only contain neurons and astrocytes but also functional oligodendrocytes with axonal myelination between 40 and 50 %, which is rarely observed *in vitro*. In the last years, we have used BrainSpheres model to study the effects of neurotoxicants on different brain development processes, being able to assess the sensitivity of pesticides in brain development, evaluate nanomaterials neurotoxicity, develop several assays for DNT evaluation and evaluate drug efficacy on glioblastoma tumors. Here, we summarize the main advances of this model and its applications.



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