# Generation of "mini-brains" from pluripotent stem cells to study developmental neurotoxicity

**A. Bernabeu-Zornoza*, C. Palmer, R. Coronel, A. Zambrano and I. Liste***

*Unidad Funcional de Investigación de Enfermedades Crónicas (UFIEC). Instituto de Salud Carlos III (ISCIII), Majadahonda, Madrid, Spain*
*E-mail: adela.bernabeu@gmail.com, iliste@isciii.es*

Due to the complexity of the human brain, it is difficult to study many brain disorders in model organisms. The results that we can obtain *in vitro* nowadays are all made in monolayer cell cultures (2D), and, although highly valuable, those methods are devoid of a tridimensional component necessary for normal organ development. Therefore, the ability to model human brain development in vitro represents an important step in our study of developmental processes and neurological disorders.

It has recently been described that pluripotent stem cells (PSCs) in a suitable environment are capable of generating three-dimensional (3D) structures called "cerebral organoids" or "mini-brains". They recapitulate different stages of human cortical development, generating a variety of regional identities organized in discrete domains able to connect with each other. Organoids can be further engineered to mimic disease-relevant genetic and epigenetic states of a patient. Human PSC-based *in vitro* models that reflect human physiology have the potential to reduce the number of drug failures in clinical trials and offer a cost-effective approach for assessing chemical safety.

We are setting up human and mouse PSCs three dimensional organoids culture systems. The differentiation in organoids (3D) is being carried out according to the protocol recently published by Lancaster and Knoblich (2014) *Nature Protocols* 9(10):2329-40. The characterization of cultures and identification of different neural structures and phenotypes are being performed by immunocytochemistry and qRT-PCR.

Together, these studies would indicate that 3D organoids can recapitulate human and mouse neurodevelopment and it can be useful to study the pathogenesis of neurological diseases and toxicity. This combined strategy demonstrates the value of human cell-based assays for predictive toxicology and should be useful for both drug and chemical safety assessment.



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