The assessment of neurotoxicity remains a major scientific challenge due to the complexity of the central nervous system. Current strategies to evaluate toxicity of chemicals and drug candidates are predominantly based on ex vivo or in vivo animal studies. These models have limited predictivity for neurotoxicity in humans and are not amenable to high-throughput testing.

Here, we show the development of an in vitro neurotoxicity model comprising iPSC-derived neurons and glial cells. The networks are grown in MIMETAS OrganoPlates®, microfluidic plates that enable culture of 96 parallel miniaturized organ models.

This 3D model of the human brain reduces the use of animal models and has the potential to better predict adverse effects in humans and hence improve clinical development success.

The OrganoPlate® is a high-throughput platform that combines the most recent advances in 3D cell culture and microfluidics. The OrganoPlate® contains 96 tissue chips and is compatible with standard laboratory equipment. Neurons and glia are seeded in extracellular matrix (ECM) in the gel channel (pink) and form networks. The adjacent medium channel (blue) supplies the cells with nutrients.

Three-dimensional networks in the OrganoPlate®

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3D networks of iPSC-derived neurons and glia for high-throughput neurotoxicity screening

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High-throughput evaluation of neurotoxic effects

Three different read-outs were employed for proof-of-concept of neurotoxicity detection

Neurite outgrowth

Neuronal activity by calcium imaging

Cell viability

Sponsored by AbbVie, BASF, GSK, and Sanofi under NC3R’s CRACK IT Challenge Neuratect