Human Neurospheres Can Identify Neurotoxicants In vitro

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Current developmental neurotoxicity (DNT) testing guidelines propose investigations in rodents, which require huge amount of animals. With regards to the 3Rs and the European Regulation of Chemicals (REACH), alternative testing strategies are needed, which refine and reduce animal experiments by allowing faster and cheaper screening.

We have established a 3D test system for DNT screening based on primary human fetal neural progenitor cells which is now embedded in the BMBF joint project “Development of predictive in vitro test for developmental neurotoxicity testing“. Within this project, different cell models are compared with regard to their DNT predictability employing a battery of test compounds.

In our system first results indicate that the well known developmental neurotoxicant methlymercury effects proliferation, migration and differentiation of neurospheres in a nanomolar range, while a negative test substance, the liver toxicant paracetamol, showed interference with these processes in millimolar concentrations. Furthermore, the DNT compounds MAM, valproic acid and lead also affect these endpoints, while glutamate, which is not developmentally neurotoxic, is well distinguishable. At the shorter timepoints, specific effects on those DNT endpoints are observed at concentrations which do not cause cytotoxicity.
Taken together, we have established the human neurosphere model as a system-based in vitro test method for elucidating the potential of chemicals to disturb human brain development. Testing more chemicals will give us an answer on the predictability of our test system.