

Differentiated Human Neuroprogenitor Cells for Neurotoxicity Testing

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The current protocol for neurotoxicity testing is based on animal experiments. Furthermore, mechanistic insights of neurotoxicants are assessed mainly *in vitro* employing tumor cell lines. Because there are species differences between rodents and man and cell biological differences between tumor and normal cells, this study aims to investigate if neurotoxicity can also be studied in primary human cells which have differentiated from human neural progenitor cells (hNPCs). hNPCs form the three neural celltypes of the brain: neurons, astrocytes and oligodendrocytes and are thus a promising model to assess toxicity in this co-culture system.

Differentiated hNPCs express marker genes for gabaergic, cholinergic, dopaminergic and serotonergic neurons as well as NMDA receptor subtypes. Moreover, they react to glutamate and acetylcholine with an intercellular Ca^{2+} increase. First results with model compounds show that treatment of differentiated cells with subcytotoxic methylmercury concentrations reduces beta(III)tubulin expression in Western blot analyses. Furthermore, MPP⁺ (1-Methyl-4-phenyl-pyridin) which is selectively toxic to dopaminergic neurons reduces protein levels of dopamin decarboxylase.

More compounds are needed to evaluate if these cells are capable of predicting neurotoxicity and thus serve as an alternative to animal models in these human-derived cells