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3D in vitro cell culture models for the assessment of neurotoxicity

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We talk about neurotoxicity when exposure to natural or manmade toxic substances interferes with normal nervous system activity and function. Neurotoxicity might disrupt or even kill neurons or the surrounding glia cells by interfering with neural function. Special attention must be given to susceptible subgroups, the very young (developmental neurotoxicity, DNT) and the aging population. So far, neurotoxicity has been evaluated by using animals. Currently, there is an international consensus that new approach methods (NAMs), e.g. based on stem cells, are needed that inform on neurotoxicity in a faster, cheaper and more human-relevant way than current animal experiments. Only the use of such methods allows gain of information on the neurotoxic hazard of the approx. 30,000 chemicals that are currently in use within our every-day life.
In recent years, we have been developing human stem cell-based cell systems that aim at serving as test methods for life stage-specific neurotoxicity. Therefore, we use human primary neural progenitor cells (hNPC) or human induced pluripotent stem cells (hiPSC) as our cellular templates. One focus of this work lies on the study of human relevance of the in vitro models. These are then further used for toxicity studies. Here, some of the models will be presented. For analysing DTN, we apply the test methods NPC1-6 using high content imaging. Here, we recently investigated the toxicity of flame retardants for brain development. In addition, we set up hiPSC-derived neural cultures for analysing neuronal network formation on microelectrode arrays.
In summary, this talk should give an overview over the cellular work we perform to study neurotoxicity. Such data is currently feeding into novel hazard and risk assessment paradigms at a regulatory level. Here we collaborate with the European Food Safety Authority and the US-Environmental Protection Agency on how to implement such NAMs for regulatory decision-making.

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