# Assessment of developmental neurotoxicity using human iPS cells

Tsunemoto Kazunobu[1], Shigeru Yamada[1,2], Yasunari Kanda[1]

*[1]NIHS, [2]PEIJ*

Evaluation of developmental toxicology has been an integral part of safety assessment issue for new compounds. One of the basic ideas behind developmental toxicity tests is that children differ significantly from adults in some aspects of their basic biology and responses to compound exposures.

Because current developmental neurotoxicity (DNT) guideline (OECD TG426) requires a lot of animals and costs, it is necessary to establish more predictable approach using human iPS cells (hiPSCs). Here, we tried to search suitable structural and functional endpoints by evaluating antifouling agent, such as tributyltin (TBT), as a positive compound using hiPSCs, which was expected to provide novel human cell-based applications for alternative in vitro testing approaches.

We focused on neural differentiation process (Structure) using hiPSCs. TBT reduced the expression of several genes, including *OTX2*, a marker of neurogenesis. We further focused on electrophysiological properties (Function) using hiPSC-derived neurons. TBT reduced the number of spikes and network burst neurons using microelectrode array (MEA) recordings. These data suggest that TBT inhibited neural differentiation from iPSCs and spontaneous firing of neurons. Our data indicate that integrated analyses using iPSCs and iPSC-derived neurons are useful for DNT assessment.