

Proposal of a new AOP for the neurotoxicity and developmental neurotoxicity assessment of glutamate receptor binding agonists that cause learning and memory impairment.

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Summary of Research:

The purpose of this study is to propose an adverse outcome pathway (AOP) in which the molecular initiating event (MIE) is the binding of a compound to the glutamate receptors, resulting in the adverse outcome (AO) defined as learning and memory impairment. First, we have established an algorithm for high content imaging to detect dendritic spines with drebrin immunoreactivity, and an image analysis method by machine learning. Then, morphological changes of dendritic spines were quantitatively evaluated using frozen hippocampal nerve cells from rat embryos and neurons derived from human iPS cells. We will validate the possibility as an alternative method for developmental neurotoxicity/neurotoxicity testing, using known compounds with learning and memory impairment.

Timeline:

March 1, 2020 –

Topics:

Presentation in LRI Research Report Meeting 2021 “Establishment of an in vitro test method for predicting the neurotoxicity and developmental neurotoxicity of glutamate receptor-binding compounds that cause learning and memory impairment.”

Publications:

Shogo Mase, Izuo Tsutsui, Toshinari Mitsuoka, Noriko Koganezawa, Hiroyuki Yamazaki, Yuuichi Kato, Hiroshi Kawabe, Tomoaki Shirao, Yuko Sekino, “Developmental neurotoxicity assessment of glutamate receptor binding agonists that cause learning and memory impairment : analysis of drebrin immunoreactivity in rat hippocampal cultured neuron” The 48th Annual Meeting of the Japanese Society of Toxicology, Kobe (Web), July 2021

Shogo Mase, Toshinari Mitsuoka, Noriko Koganezawa, Hiroyuki Yamazaki, Yuuichi Kato, Izuo Tsutsui, Tomoaki Shirao, Hiroshi Kawabe, Yuko Sekino “Upregulation of drebrin in dendritic spines and neuronal death induced by a synthetic cannabinoid, CP55940, in cultured rat hippocampal neurons” The 44th Annual Meeting of the Japan Neuroscience Society, Kobe (Web), July 2021.

Shogo Mase, Toshinari Mitsuoka, Noriko Koganezawa, Hiroyuki Yamazaki, Yuuichi Kato, Izuo Tsutsui, Tomoaki Shirao, Hiroshi Kawabe, Yuko Sekino “Effects of a synthetic cannabinoid, CP55940, on synaptogenesis of cultured hippocampal neurons: imaging analysis of drebrin immunocytochemistry” The 64th Annual Meeting of the Japanese Society for Neurochemistry, Nara (Web), September 2021