Title of Research:

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Evaluation methods for toxicity using indices of developing neurons

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Summary of Research:

In recent years, basic research in the field of neuroscience has revealed many molecules involved in neurite outgrowth and neuronal reorganization, but there have been few attempts to evaluate the toxicity of chemical substances using these molecules as indicators. The purpose of this study was to identify better indicators of developmental neurotoxicity of chemicals from key molecules in neurodevelopment and to clarify their usefulness in assessing developmental neurotoxicity of chemicals.

First, we established culture conditions for primary cultured neurons of the rat cerebral cortex and examined changes in mRNA expression of 12 key molecules which play an important role in neurodevelopment until days in vitro 21. The results showed three major patterns: genes whose expression was low in early culture and increased with culture, genes whose expression was maximum in mid-culture, and genes whose expression was maximum in early culture and decreased with culture. Next, we used methylmercury, a known developmental neurotoxin, to investigate the effects of these molecules on gene expression. We found that methylmercury suppressed the expression of three genes, *Dlg4*, *Syp* and *Bdnf*. In the next year, we will investigate whether these gene expression changes are also observed with other developmental neurotoxicants and whether these phenomena are reproduced in human iPS neurons, which will provide clues for the development of evaluation indices for developmental neurotoxicity.

Timeline:

March 1, 2020 - February 28, 2021

Topics:

Oral presentation at JCIA LRI Annual Workshop 2020 “Evaluation methods for toxicity using indices of developing neurons” (On-line, August 21st, 2020)