

RESEARCH REPORT - No. 1001 FY 2010-2012

Title of research project	Development of novel method monitoring the effect of exposure of agricultural chemicals on developmental brain using gene-expression monitoring mice.
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【Abstract】

Objectives: Some agricultural chemicals (insecticides and herbicides) disrupt functions of the brain through their effects on gene expression. To monitor the effects of exposure to agricultural chemicals on gene expression and functions of developmental brain, it is useful to develop the novel method using mice to monitor gene-expression

Methods: To monitor the neuronal activity-dependent gene expression in the mouse brain, we used the immediate-early genes and generated the activity-regulated cytoskeleton-associated protein (Arc) –luciferase (Luc) transgenic (Tg) and brain-derived neurotrophic factor (BDNF)-Luc Tg mouse strains. By using these novel mouse strains, we have monitored the gene expressions of Arc and BDNF with the changes in bioluminescence signals after the acute and chronic treatments with agricultural chemicals. We also used primary neuronal cultures to reveal the molecular mechanisms of the effects of treatment with some agricultural chemicals on gene expression.

Results: We have succeeded to generate the Arc-Luc and BDNF-Luc Tg mouse strains. By using Arc-Luc Tg mouse strain, we detected significant increases in bioluminescence signals after the treatment with deltamethrin and glufosinate ammonium (GLA). After the low-dose and chronic treatment with GLA at juvenile stages, we detected significant decrease in bioluminescence signals in adult Arc-Luc Tg mice. We also detected increase in bioluminescence signals in BDNF-Luc Tg mice after the treatment with an excitotoxin kainate. Furthermore, we revealed the molecular mechanisms involved in the signaling pathway which induce BDNF gene expression after the treatment with deltamethorin in primary neuronal cultures.

Consideration/Conclusion: Our approaches using novel Tg mouse strains and primary neuronal culture will be valuable to monitor the effects of exposure of agricultural chemicals on gene expression and the brain functions .