

Title of Project : Microscopic analysis based on the quantitative behavioral tests in rodents for identification of the molecular target of developmental neurotoxicity.

Masaki Kakeyama

(The University of Tokyo, Graduate School of Medicine, Assistant Professor)

Research Area : Environmental Sciences

Keyword : Toxicology

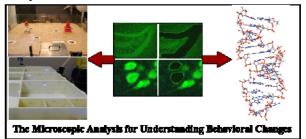
[Purpose and Background of the Research]

The aim of this study is to develop the microscopic analysis methodology, and identify the molecular marker for developmental neurotoxicity of environmental chemicals. Maternal exposure to environmental chemicals has been reported to affect the brain development in offspring, even when mothers are exposed to low levels that do not affect themselves. It is the emergent and important problem to elucidate the causal relationship between the chemical exposure and the mental health of children, and to scientifically evaluate its degree. In this study, we start from the animal behavioral study, and assess new microscopic approach to explain the scientific meaning of behavioral changes, and find the biomarker of neurotoxicity.

[Research Methods]

Cognitive and emotional behavioral tests will be assessed in rats and mice which were maternally exposed to low doses of environmental chemicals. We develop the microscopic analysis and apply it to neurotoxicology by using brain samples from animals subjected to behavioral tests after chemical exposure.

In the microscopic analyses, the brain areas and neurons that were activated by the behavior, and that were affected by the chemical exposure, will be identified histologically. Gene expression study by using immuno-laser microdissection methodology for mRNA quantification will be performed to examine the molecular events which reflect behavioral tests and chemical exposure. Microstructural and developmental analyses of the brain will also be assessed.



[Expected Research Achievements and Scientific Significance]

The analyses of molecular event which is accompanied with behavioral changes will provide the scientific basis for understanding the result of behavioral tests. Our microscopic analyses placed the emphasis in the neurons and timing in which the adversity appears will enable us to detect the adversity conventionally and sensitively. The causal relationship of exposure and its effect will be clarified after the analysis through the time series of the development.

[Publications Relevant to the Project]

- Kakeyama M, Sone H and Tohyama C. Perinatal Exposure of Female Rats to 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin induces central precocious puberty in the offspring. J Endocrinol. 197: 351-358, 2008.
- Tse D, Langston RF, Kakeyama M, Bethus I, Spooner PA, Wood E, Morris RGM. Schemas and memory consolidation. Science, 316:76-82, 2007.

Term of ProjectFY2009-2013

[Budget Allocation] 79,200

79,200 Thousand Yen

[Homepage Address and Other Contact Information]

http://env-health.m.u-tokyo.ac.jp/member/k ake.html/research