Toxicogenomic Solution (II) on Neurotoxicity of Methylmercury : Identification of Genes associated with Early and Late response of Methylmercury in Human Neuroblastoma Cell Line

Youn-Jung Kim[1], Hye-Jung Yun[1], Eun-Young Kim[1], Hee-Kyung Jeon[1], Young-Gyu Chai[2] and Jae-Chun Ryu[1]

[1]*Toxicology Laboratory, Korea Institute of Science & Technology P.O. Box 131, Chengryang, Seoul, 130-650, Korea*

[2]*Department of biochemistry, University of Hanyang, Ansan, Kyunggido, Korea*

Methylmercury is known to have devastating effects on the mammalian nervous system. In order to characterize the mechanism of methylmercury-induced neurotoxicity, we investigated the analysis of transcriptional profiles on human 8k cDNA microarray by treatment of 1.4 uM methylmercury at 3, 12, 24 and 48hr in human neuroblastoma SH-SY5Y cell line. The methylmercury response of some of the identified genes was significant at early time points (3hr), that of others was at late time points (48hr). The early response genes that may represent those involved directly in the methylmercury response included pantothenate kinase 3, A kinase (PRKA) anchor protein (yotiao) 9, neurotrophic tyrosine kinase, receptor, type 2 gene, associated with NMDA receptor activity regulation or perturbations of central nervous system homeostasis. Also, when SH-SY5Y cells were subjected to a longer exposure (48h), a relative increase was noted in a gene, glutamine-fructose -6-phosphate transaminase 1, reported that overexpression of this gene may lead to the increased resistance to MeHg. To confirm the alteration of these genes in cultured neurons, we then applied real time-RT PCR with SYBR green. Thus, this results suggest that a neurotoxic effect of the methylmercury might be ascribed that in the early phase, methylmercury alters NMDA receptor regulation or homeostasis of neuronal cells but in the late phase, it protects cells from effects of methylmercury.