Cellular Systems Involved in Development and Regulation of Toxicity of Methylmercury

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【Outline of survey】

Methylmercury is a toxic compound producing severe disorders in the human central nervous system. However, the mechanism underlying the toxicity of methylmercury is not fully understood. We demonstrated that overexpression of Cdc34, an ubiquitin-conjugating enzyme, induces a resistance to methylmercury toxicity. Cdc34 is a component of the ubiquitin-proteasome system (UP system) that is involved in the intracellular degradation of proteins. We have analyzed the mechanism of acquisition of resistance to methylmercury that involves the overexpression of Cdc34 and we have found that enhancement of cellular proteolysis by the UP system helps to protect cells against the toxic effects of methylmercury. In this study, therefore, we will search and identify the methylmercury toxicity-regulating proteins whose degradation is enhanced by the UP system. Moreover, we will examine the mechanism of action of these proteins against toxicity of methylmercury.

【Expected results】

This study will provide novel information on the molecular mechanism of toxicity of methylmercury and its cellular regulation system. The obtained information will contribute further progress of research on prevention of methylmercury intoxication, identification of hypersensitive people to methylmercury, and establishment of accurate maximum permissible level of methylmercury. Toxicological significance of UP system will also be demonstrated by this study, and the information will bring about significant further development of studies on role of UP system in cellular response to toxic substances.

【References by the principal investigator】

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・Hwang, G. W., Furuchi, T. and Naganuma, A., A ubiquitin-proteasome system is responsible for the protection of yeast and human cells against methylmercury. FASEB J., 16: 709-711 (2002).

【Term of project】 FY2007− 2011

【Budget allocation】 18,000,000 yen

(2007 direct cost)

【Homepage address】 http://www.pharm.tohoku.ac.jp/~seitai/seitai-index.html