[S8-1] [10/18/2002(Fri) 13:30-14:00/Hall B]

Cellular Factors Involved in Methylmercury Toxicity in Yeast

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Methylmercury causes severe central nervous system disorders. Despite the efforts of many researchers, the mechanisms involved in methylmercury toxicity and the defense against this toxicity remain unknown. We focused on the fact that drug resistance is sometimes involved in elevation of the concentration of the intracellular target of the drug. Screening for the genes conferring methylmercury resistance on cells transformed with individual genes would indicate the genes encoding the target molecules of methylmercury together with the genes for the defense against its toxicity. We investigated yeast genes obtained from a library, since yeast genes can be easily identified because the nucleotide sequences of the entire genome has been clarified. Plasmids carrying a chromosome fragment (usually containing 2-4 genes) were transfected into yeast cells, and genes contained in the chromosome fragments were expressed at high levels in the cells. Among such yeast cells, those that could grow on a medium containing methylmercury at a concentration that would not permit the growth of normal yeast cells were selected. Since these yeast cells acquired methylmercury resistance following the introduction of the gene fragments, genes conferring methylmercury resistance must be contained in the introduced gene fragments. Plasmids were isolated from the yeast cells that had acquired methylmercury resistance, and the chromosome fragments carried in the plasmids were investigated. We identified GFA1 (1) and CDC34 (2) as the genes involved in methylmercury resistance. GFA1 is the gene coding for L-glutamine•D-fructose-6-phosphate amidotransferase (GFAT), which is a catalytic enzyme involved in the production of glucosamine 6-phosphate from glutamine and fructose. CDC34 is the gene encoding ubiquitin transferase (Ubc3), which is involved in the ubiquitination of intracellular proteins.

(1) A. Naganuma et al.: FASEB J, **14**, 968 (2000).

(2) Gi-Wook Hwang, T. Furuchi and A. Naganuma: FASEB J, **16**, 709 (2002).