

Molecular Mechanism Involved in Toxicity of Methylmercury

Gi-Wook Hwang (Grad. Sch. Pharm. Sci., Tohoku Univ.)

Methylmercury is a toxic environmental pollutant, causing serious neurological and developmental effects in humans. However, the mechanism underlying the methylmercury toxicity is not fully understood. To elucidate the mechanisms of methylmercury toxicity and of defense against methylmercury, we searched for factors that determine the sensitivity of yeast cells to methylmercury, and found that ubiquitin-proteasome system (UPS), one of protein-degradation system, is involved in protection of yeast against methylmercury toxicity. It is possible to conclude that yeast cells have some proteins that enhance methylmercury toxicity and this toxicity might reduced by degradation of such proteins mediated via UPS. Therefore, we next screened for proteins that enhance methylmercury toxicity, and found that Eno2 and Dld2 involved in synthesis of intracellular pyruvate. As a result of functional analysis, the both proteins might enhance methylmercury toxicity by promotion of the pyruvate inflow into the mitochondrial matrix. The accumulated pyruvate in the mitochondrial matrix enhances methylmercury toxicity before its metabolic changes to acetyl CoA. These findings provide important key for the elucidation of the molecular mechanism of methylmercury toxicity.