[S8-3] [10/18/2002(Fri) 14:30-14:50/Hall B]

Biomolecular Mechanism of Cadmium Toxicity

Jung-Duck Park

Department of Preventive Medicine, College of Medicine, Chung-Ang University

Cadmium (Cd) is an environmental pollutant and categorized as a human carcinogen, which has a tendency to accumulate in the human body. The level of Cd in renal cortex and liver are good indicators as an index of Cd exposure in general population. Geometric mean concentration of Cd is 27.4 and 3.1 /g wet weight in renal cortex and liver, respectively, in Korean. Cd is toxic to a number of tissues, notably the liver, kidney, testis, lung, lymphoid tissue and lung. In laboratory animals, acute exposure of Cd causes hepatotoxicity and testicular toxicity, while chronic exposure causes bone and renal damage. The testis is the most susceptible organ for acute Cd exposure in experimental animal, while the renal dysfunction due to proximal tubular damage is the first sign for chronic Cd exposure in general population.

Metallothionein (MT) is a low molecular weight, cystine-rich protein that binds with metals. The primary role of MT is transport and storage of essential metals, such as Zn and Cu, to maintain the homeostasis of metals. MT also binds with non-essential metals including Cd but its ability to protect against toxicity of toxic metals is much greater in Cd than other metals. Also MT plays a role of long biological half-life of Cd in body and transport Cd from liver to kidney as the Cd-MT complex. MT is also excreted in urine as the Cd-MT complex, so urinary MT could be use a valuable index with β2-microglobulin and NAG as screening test in epidemiologic study for Cd-exposed population.

Cd is not biodegradable and is taken up by plant from the soil, food is the main source of Cd in general population. Therefore, the mechanism of Cd absorption in the gastrointestinal tract is not understood well. Recently, a protein named divalent metal transporter 1 (DMT1), which is involved in transmembrane Fe transport, was cloned. DMT1 expression in intestine is upregulated by Fe deficiency states. However, the intestinal absorption of Cd increases when the body Fe stores are depleted. DMT1 has been shown to transport Fe and other divalent metal ions *in vitro*. However, it is not known whether DMT1 mediates the intestinal absorption of Cd. The DMT1 mRNA expression and Cd absorption in gastrointestinal tract were increased by the feeding of Fe-deficient diet (2-6 mg Fe/kg) for 4 weeks in rats and returned to the control levels of DMT1 and Cd absorption by following the Fe-supplemented diet (120 mg Fe/kg) for 4 weeks. These findings suggest that DMT1 might be play as an one of the mechanism of the intestinal Cd absorption in mammalian.