Protective Effects of Selenium on Cadmium Induced Cytotoxicity in PC12 Cells

(PC12 細胞におけるカドミウム誘導細胞毒性に及ぼすセレンの保護効果)

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Selenium (Se) is an essential oligo-element with certain biological functions in human body, protects cells from oxidative damages and can deliver anticancer effects. Cadmium (Cd), a highly toxic metal, can be accumulated in biological systems and contributes to several diseases like neurological disorders mostly *via* induction of reactive oxygen species (ROS). In this study, the cytotoxic effects of Se, as well as, the cytoprotective effects of Se on Cd-induced cytotoxicity were investigated using PC12 cells. The cell viability, DNA fragmentation increase, lactate dehydrogenase (LDH) release, glutathione (GSH) contents decrease showed that more than 5 μM of Se can induce cytotoxicity in PC12 cells through ROS generation. Western blotting analyses confirmed that Se (10-40 μM) promotes autophagy in PC12 cells via inhibition of mTOR activation and p62 accumulation. On the other hand, the cell viability assay and DNA fragmentation analyses showed that exposure to Cd (5 μM) for 48 h induced cell death *via* apoptosis in PC12 cells. LDH activity in cell culture medium exhibited cell wall damage due to Cd (5 μM) exposure in PC12 cells. Moreover, the reduction of GSH contents upon Cd (5 μM) exposure showed the increase of oxidative stress in PC12 cells. However, Se (5 μM) in co-exposure with Cd (5 μM) was found to increase GSH levels in PC12 cells and to decrease LDH activity in the cell medium. The western blot analyses of proteins related to apoptosis indicated the apoptotic cell death induced by Cd in PC12 cells. On the other hand, the co-exposure of Se (5 μM) with Cd (5 μM) significantly decreased the release of cytochrome c into cytosol from mitochondria, and upregulated ERK1 protein. The cell viability assay and DNA fragmentation assay upon simultaneous exposure also showed that Se can protect cells from Cd-induced cytotoxicity. These findings suggest that more than 5 μM of Se is cytotoxic of PC12 cells, and protection of Se (5 μM) on Cd-induced toxicity might be due to inhibition of Cd-induced ROS production and subsequently suppression of mitochondrial apoptosis pathway.