Platinum nanoparticles induce endogenous antioxidative defense mechanisms in rat skeletal muscle cells

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論 文 名　：Platinum nanoparticles induce endogenous antioxidative defense mechanisms in rat skeletal muscle cells.(白金ナノ粒子処理はラット筋管細胞株において内在的な抗酸化防御機構を示す)

区　　分　：甲

論　文　内　容　の　要　旨

Prolonged exposure to excessive reactive oxygen species (ROS) increases risk factors for many diseases. Therefore, elimination of ROS as well as prevention of its production becomes critically important. In the present study, we evaluated the levels of cytotoxicity and ROS scavenging activity induced by synthetic platinum nanoparticles (Pt NPs). Pt NPs were synthesized, and their average size were 1.7, 2.2, 3.4 nm. Synthetic Pt NPs of 2.2 nm were found to scavenge endogenous H_2O_2 most in L6 rat skeletal muscle cells. Moreover, Pt NPs of 2.2 nm could scavenge both induced and endogenous H_2O_2 significantly at a very low concentration (10^{-2} mg/l). To investigate the mechanism, we used the hierarchical oxidative stress model, lower amount of oxidative stress induces antioxidant enzymes by the antioxidant responsive element (ARE) activated by nuclear factor erythroid-2-related factor-2 (Nrf2), as an experimental model. To evaluate this possibility, we assessed glutathione concentration and gene levels of several antioxidant enzymes in Pt NP-treated (10^{-3}-10 mg/l) L6 cells. Reduced glutathione (GSH), one of the non-enzymatic defense molecules, was increased in the range of 10^{-3}–1 mg/l, but not in the 10 mg/l Pt NP-treated cells. Most of the gene transcripts for oxidative stress inducible heme oxygenase-1 (HO-1), glutathione reductase (GR), Copper-Zinc Superoxide Dismutase (CuZn-SOD), Manganese Superoxide Dismutase (Mn-SOD), glutathione peroxidase (GPx), and catalase (Cat) were increased significantly by Pt NPs at 10^{-1}–10 mg/l. Such upregulatory effects induced by synthetic Pt NPs in the range of 10^{-2}–10 mg/l can be explained by the hierarchical oxidative stress model. To investigate whether antioxidative proteins such as GR, Cat, Mn-SOD, HO-1, Nrf2 are upregulated by Pt NPs, we assessed Western Blotting. These protein expressions were significantly increased by Pt NPs at 1–10 mg/l and nuclear fraction of Nrf2, especially, is accumulated by Pt NPs at 1–10 mg/l. Present results together with previously published data indicate that Pt NPs could exert a critical role in maintaining intercellular redox homeostasis and are expected to be a new type of endogenous antioxidant, controlling the activity of Nrf2 and the expression of HO-1, distinctively different from existing exogenous antioxidants, and thus would be useful to be developed as an efficient agent targeting various inflammatory diseases.