ASSESMENT OF THE GENOTOXICITY OF TIO_2 NANOPARTICLES WITH GPT DELTA TRANSGENIC MICE

WANG Rui-Sheng, SUZUKI Tetsuya, MIURA Nobuhiko, HOJO Rieko, YANAGIBA Yukie, SUDA Megumi

Japan National Institute of Occupational Safety and Health, Kawasaki, Japan

Abstract

Titanium dioxide (TiO_2) nanoparticles (NPs) are increasingly utilized in many industrial applications. The genotoxicity of TiO_2 NPs has been investigated with in vitro assays, and some suggested that TiO_2 NPs have genotoxic effect. Several in vivo studies have also been reported recently, with inconsistent findings. In this study, the genotoxicity of dispersed TiO_2 suspensions was evaluated using several genotoxic endpoints after intravenous injections into mice. Male gpt Delta C57BL/6J mice were treated with TiO_2 NPs at doses of 2, 10 or 50 mg/kg of body weight once per week for 4 consecutive weeks, and sacrificed 9 and 90 days after the last administration. Observation with transmission electron microscope showed that most TiO_2 NPs in the liver were localized in the sinuses and inside Kupffer cells, although some were occasionally observed in parenchymal cells. The particles remains in the liver tissue even at 90 days. Ti content was dose-dependently increased in liver at 9 days as quantified with ICP-MS. The frequencies of the Pig-a mutant in erythrocytes and the micronuclei in reticulocytes were not increased by the administration of TiO_2 NPs. TiO_2 did not increase the level of DNA damage in the liver at 9 days. Neither the point mutation nor the deletion mutation frequency was increased in the liver at the two time points. These results indicate that TiO_2 NPs have no genotoxic effects on the liver and bone marrow in mice under the experimental conditions used.

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