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Abstract

There are three mineral forms of natrual titanium dioxide partilces: rutile, anatase and brookite. Two types of nanosized titanium dioxide, anatase ($anTiO_2$) and rutile ($rnTiO_2$), are being manufactured in large quantities worldwide and widely used in industry, commercial products and biosystems. Large quantity production and widespread application of $nTiO_2$ have given rise to concern about its health and environmental effects. Previous reports indicated that under ultraviolet irradiation, $anTiO_2$ is more toxic than $rnTiO_2$ *in vitro* because of the difference in their crystal structures. In the present study, we compared the *in vivo* and *in vitro* toxic effects caused by $anTiO_2$ and $rnTiO_2$. Female SD rats were treated with 500 μg/ml of $anTiO_2$ or $rnTiO_2$ suspensions by intra-pulmonary spraying 8 times over a two week period. In the lung, treatment with $anTiO_2$ or $rnTiO_2$ increased alveolar macrophage numbers and levels of 8-hydroxydeoxyguanosine (8-OHdG). These increases tended to be lower in the $anTiO_2$ treated group compared to the $rnTiO_2$ treated group. MIP1α mRNA and protein expression in the lung tissues treated with $anTiO_2$ and $rnTiO_2$ was also significantly up-regulated. Higher mRNA and protein expression of MIP1α were seen in the $rnTiO_2$ group than in the $anTiO_2$. In cell culture of primary alveolar macrophages (PAM) treated with $anTiO_2$ and $rnTiO_2$, expression of MIP1α mRNA in the PAM and protein in the culture media was

significantly higher than in control cultures. Similarly to the *in vivo* results, MIP1α mRNA and protein expression was significantly lower in the anTiO_2 treated cultures compared to the rnTiO_2 treated cultures. Furthermore, conditioned cell culture media from PAM cultures treated with anTiO_2 had less effect on A549 cell proliferation compared to conditioned media from cultures treated with rnTiO_2. However, no significant difference was found in the toxicological effects on cell viability of ultra violet irradiated anTiO_2 and rnTiO_2. Conclusively, our results indicate that anTiO_2 is less potent in induction of alveolar macrophage infiltration, 8-OHdG and MIP1α expression in the lung, and growth stimulation of A549 cells *in vitro* than rnTiO_2.