Environ Toxicol. 2017 Oct;32(10):2234-2243. doi: 10.1002/tox.22439. Epub 2017 Jun 24.

Immunotoxic effects of thymus in mice following exposure to nanoparticulate TiO $_2$

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PMID: 28646487 DOI: 10.1002/tox.22439

Abstract

Titanium dioxide nanoparticles (TiO_2 NPs) have been extensively used in industry, medicine, and daily life, and have shown potential toxic effects for animals or humans. We noted that the effects of TiO_2 NPs on the immune system and its mechanism of action in animals or humans have not been elucidated. Thus, mice were exposed to the TiO_2 NPs (0, 1.25, 2.5, or 5 mg kg^{-1} body weight) for 9 consecutive months. Exposure to TiO_2 NPs was accumulated in the thymus, leading to a decrease in body weight and increases in the weight of the thymus or thymus indices. In the blood, exposure to TiO_2 NPs significantly decreased white blood cell, red blood cell, reticulocyte, haemoglobin, and mean corpuscular haemoglobin concentration; and increased mean corpuscular volume, mean corpuscular haemoglobin, platelets, and mean platelet volume. The reductions of lymphocyte subsets, including CD3+, CD4+, CD8+, B cell, and natural killer cell, were observed in the TiO_2 NP-treated mouse thymus. Appearance of starry-sky aspect of the cortex that is given by the body of macrophages, bleeding, severe hemolysis or congestion, fatty degeneration, and cell apoptosis or necrosis were observed in the thymus following TiO_2 NPs exposure. Importantly, TiO_2 NPs increased expression of nucleic factor-κB(NF-κB), IκB kinase1/2, interleukin-1β, interleukin -4, regulated upon activation normal T-cell expressed and secreted, cyclooxygenase 2, neutrophil gelatinase-associated lipocalin, purinergic receptors-7, interferon-inducible protein 10, hypoxia inducible factor 1-α, p-c-Jun N-terminal kinase, p-p38, and p-extracellular signal-regulated kinase 1/2 protein, respectively; whereas suppressed expression of IκB, peroxisome proliferater-activated receptor-γ, trefoil factor 1, peroxisome proliferator activated receptor gamma coactivator-1α, and prostaglandin E2 proteins in the thymus, respectively. Taken together, these results suggest that TiO_2 NPs exerts toxic effects on lymphoid organs and T cell and innate immune cell homeostasis in mice and that these immunotoxic potential effects may result from the activation of NF-κB-mediated mitogen-activated protein kinases (MAPKs) pathway.

Keywords: NF-κB-mediated MAPKs pathway; immune/inflammatory factors; immunotoxicity; thymus; titanium dioxide nanoparticles.

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