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Title: Genetic influence on inflammatory response in rats exposed to nanosized titanium dioxide particles

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Body: The emerging nanotechnologies have resulted in large productions of engineered nanomaterials (NM). Despite the increased production, health effects following inhalation of NM have not been fully assessed. This study aimed to investigate and monitor health effects following inhalation of TiO_2 nanoparticles (NP) in healthy rats and in rats with ongoing airway inflammation (asthmatic rats). We compared the responsiveness between two rat strains with differences in genetic susceptibility to develop inflammatory diseases; the Dark Agouty (DA) rat that is susceptible to develop chronic autoimmune diseases while the Brown Norwegian (BN) rat that is prone to develop allergic airway inflammation. Health effects of TiO_2 inhalation were studied in healthy rats and in rats with allergic airway inflammation induced by an experimental allergen (ovalbumin). We assessed respiratory function, inflammatory response in airways, activation of the immune system and effects on general health condition. Repeated exposure to TiO_2 NPs in healthy individuals resulted in an airway inflammation dominated by neutrophils in both strains. In DA rats there was also an increased hyperreactivity in airways and elevated levels of cytokines/chemokines in BAL. These changes were not seen in the BN strain. Both strains responded to challenge with the respiratory allergen by airway eosinophilia and bronchial hyperreactivity, but no significant strain differences was observed when rats with ongoing allergic airway inflammation were exposed to TiO_2 NPs. Our data implies that susceptibility to develop adverse effects in airways following NP exposure is influenced by genetic determinants.