

Nanoparticles Activated Inflammasome Lead to Airway Hyperresponsiveness and Inflammation in a Mouse Model of Asthma

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Abstract : Background: Nanoparticles may pose adverse health effects due to particulate matter inhalation. Nanoparticle exposure induces cell and tissue damage, causing local and systemic inflammatory responses. The inflammasome is a major regulator of inflammation through its activation of pro-caspase-1, which cleaves pro-interleukin-1 β (IL-1 β) into its mature form and may signal acute and chronic immune responses to nanoparticles. Objective: The aim of the study was to identify whether nanoparticles exaggerates inflammasome pathway leading to airway inflammation and hyperresponsiveness in an allergic mice model of asthma. Methods: Mice were treated with saline (sham), OVA-sensitized and challenged (OVA), or titanium dioxide nanoparticles. Lung interleukin 1 beta (IL-1 β), interleukin 18 (IL-18), NACHT, LRR and PYD domains-containing protein 3 (NLRP3) and caspase-1 levels were assessed with Western Blot. Caspase-1 was checked by immunohistochemical staining. Reactive oxygen species were measured for the marker 8-isoprostane and carbonyl by ELISA. Results: Airway inflammation and hyperresponsiveness increased in OVA-sensitized/challenged mice and these responses were exaggerated by TiO₂ nanoparticles exposure. TiO₂ nanoparticles treatment increased IL-1 β and IL-18 protein expression in OVA-sensitized/challenged mice. TiO₂ nanoparticles augmented the expression of NLRP3 and caspase-1 leading to the formation of an active caspase-1 in the lung. Lung caspase-1 expression was increased in OVA-sensitized/challenged mice and these responses were exaggerated by TiO₂ nanoparticles exposure. Reactive oxygen species was increased in OVA-sensitized/challenged mice and in OVA-sensitized/challenged plus TiO₂ exposed mice. Conclusion: Our data demonstrate that inflammasome pathway activates in asthmatic lungs following nanoparticles exposure, suggesting that targeting the inflammasome may help control nanoparticles-induced airway inflammation and responsiveness.

Keywords : bronchial asthma, inflammation, inflammasome, nanoparticles

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