Surface modifications of silica nanoparticles are crucial for their inert versus proinflammatory and immunomodulatory properties.

Abstract: Silica (SiO_2) nanoparticles (NPs) are widely used in diverse industrial and biomedical applications. Their applicability depends on surface modifications, which can limit potential health problems. To assess the potential impact of SiO_2 NP exposure and NPs chemical modifications in allergic airway inflammation. Mice were sensitized by five repetitive intraperitoneal injections of ovalbumin/aluminum hydroxide (1 ?g) over 42 days, then intratracheally instilled with plain or modified SiO_2 NPs (50 ?g/mouse), and subsequently aerosol challenged for 20 minutes with ovalbumin. One or 5 days later, allergic inflammation was evaluated by cell differentiation of bronchoalveolar lavage fluid, lung function and gene expression and histopathology, as well as electron and confocal microscopy of pulmonary tissue. Plain SiO_2 NPs induced proinflammatory and immunomodulatory effects in vivo, highlighted by enhanced infiltration of inflammatory cells in the bronchoalveolar lavage fluid, induction of a pulmonary T helper type 2 (Th2) cytokine pattern, differentiation of type 2 macrophages, and by morphological changes in the lung of sensitized mice. These effects were dramatically attenuated using...
surface-functionalized NPs with amino and phosphate groups, but not with polyethylene glycol. The role of macrophages in taking up SiO$_2$ NPs was confirmed by flow cytometry, confocal microscopy, and gene expression analysis. Our data suggest that amino and phosphate surface modifications, but not polyethylene glycol (PEG), mitigate the proinflammatory and immunomodulatory effect of SiO$_2$ NPs in allergic airway inflammation, paving the way for new strategies in the production of nanomaterials with lower health impact for humans.

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