

Title *

Nanomaterial-induced Pulmonary Acute Phase Response Constitutes a Causal Link between Inhalation of Nanomaterials and Risk of Cardiovascular Disease

Abstract *

Inhalation of particles is associated with increased risk of cardiovascular disease in epidemiological studies. Inhalation of nanomaterials induces pulmonary inflammation that is proportional to the total surface area of the inhaled and deposited nanomaterials.

We have recently shown that pulmonary exposure to nanomaterials including carbon black, titanium dioxide particles, carbon nanotubes and diesel exhaust particles induces a time and dose-dependent acute phase response both at mRNA and protein levels. The acute phase response is a systemic alarm response, and the blood levels of acute phase proteins CRP and SAA are associated with risk of cardiovascular disease in prospective epidemiological studies.

Pulmonary acute phase response measured as *Saa3* mRNA levels correlates closely with neutrophil influx and with the total surface area of deposited nanomaterials. This implies that inhalation of nanosized particles induces a much stronger acute phase response per mass unit than inhalation of larger particles and that the accompanying risk of cardiovascular disease should be proportional to the total deposited surface area. This is especially relevant in relation to the consideration of nanoparticle-specific occupational exposure levels, and underscores the importance of occupational exposure as risk factor for cardiovascular disease.

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