

The Impact of Ambient Ultrafine Particles on Atherosclerosis and Asthma Exacerbation: The Role of Oxidative Stress?

Our principle hypothesis is that most of the pro-inflammatory potential of PM in atherosclerosis and asthma exacerbation resides in the ultrafine particles (aerodynamic diameter < 0.15 μm, UFP) that are highly enriched for redox cycling organic chemicals. We have shown that exposure of apoE null mice to ambient UFP developed significantly larger early aortic atherosclerotic lesions, increased systemic oxidative stress and upregulation of antioxidant enzyme genes than those exposed to PM2.5 (aerodynamic diameter < 0.15 μm). Gene cluster analysis of human microvascular endothelial Araujo, JA et al. 2008 cells shows that diesel exhaust particle (DEP) chemicals and oxidized lipids synergistically regulated a large number of genes involved in protective, inflammatory and immune responses.

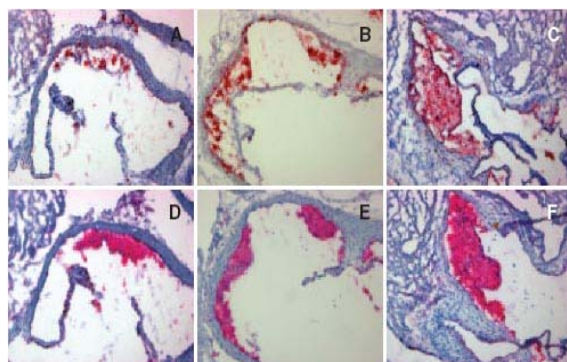
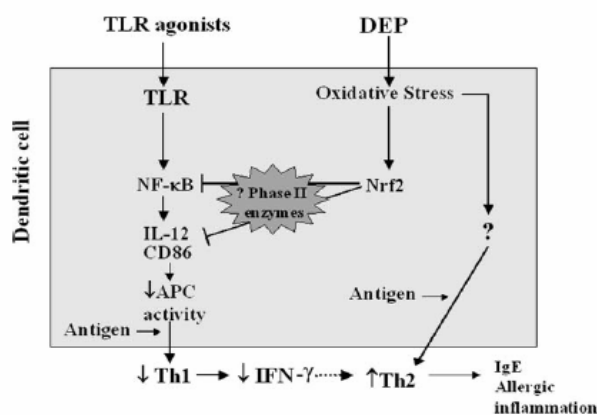


Figure 4. Representative histological photomicrographs. A through C, Oil red O staining for neutral lipids in representative aortic root sections of FA (A), FP (B), and UFP (C) mice. D through F, MOMA-2 immunohistochemical staining in adjacent aortic root sections to those shown in the top row, corresponding to the same FA (D), FP (E), and UFP (F) mice. Both oil red O and MOMA-2 staining yielded red-stained areas. UFP mice exhibited more extensive atherosclerotic plaques (C and F) than FP (B and E) or FA animals (A and D), all consisting primarily of foam cells and macrophages (fatty streaks). Original magnification, ×100.

A close association between the adjuvant effects of UFP on allergic sensitization and its pro-oxidative organic chemicals have also been identified using a highly sensitive mouse model. Intranasal exposure of 0.5 mg UFP, but not PM2.5, strongly promoted ovalbumin-induced allergic inflammation in the nose and lung. One of the potential mechanisms by which UFP enhance allergic inflammation is the interference of antigen presenting cell (APC) function through the generation of oxidative stress by PM chemicals. Pro-oxidative organic DEP chemicals are able to induce oxidative stress in dendritic cells, a major type of APC, leading to T-help 2 immune response, which is the basis of allergic inflammation.



In summary, our studies suggest that due to their extremely small size, large surface area and significantly greater amount pro-oxidative organic chemicals, UFP are far more dangerous in inducing adverse cardiovascular and pulmonary effect.

References/Publications

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