

PRO-INFLAMMATORY CYTOKINE RESPONSES TO EXPOSURE TO DIESEL SOOT

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Inhalation of particulate material (PM) of many types causes inflammation in the lung. The mechanisms by which PM activates the cellular and molecular processes resulting in recruitment of white blood cells (leukocytes) into the air spaces of the lung are not fully understood, but clearly involve stimulation of the production of small proteins called chemokines, which are chemoattractants for leukocytes.

This study was conducted to investigate the role of chemokines in the pro-inflammatory cascade following exposure to diesel soot (DS). Studies were conducted by intratracheal instillation of DS into rat lungs and exposure of a human alveolar epithelial cell line (A549 cells) in cell culture to the same material. In both systems, toxicity was assessed by measuring release of the intracellular enzyme, lactate dehydrogenase (LDH). Lung inflammation following instillation was measured by counting the numbers of leukocytes in the lung washes.

Doses of DS between 0.1 and 1 mg/rat increased the amount of the chemokine Macrophage Inflammatory Protein-2 (MIP-2) measured in the lung washes, but at higher doses, less MIP-2 was detected. In contrast, the number of inflammatory cells continued to increase throughout the dose range. Small increases in LDH were observed, reaching a plateau at doses above 1 mg/rat.

Similar results were observed in cultured A549 cells. Increased Interleukin-8 (IL-8: a human chemokine analogous to rat MIP-2) was measured in cells exposed to DS over the range of 0.03-1 $\mu\text{g}/\text{cm}^2$, but reduced levels of the chemokine were detected at higher doses. DS had little effect on the release of LDH. This indicates that DS was not acutely toxic to the cells and that the suppressed response at high doses in both systems was unlikely to be due to acute toxicity. Instead, DS may adsorb the chemokines, making them unavailable for assay.