

AUTHORS: Mitchell LA, Lauer FT, Burchiel SW, McDonald JD

TITLE: MECHANISMS FOR HOW INHALED MULTIWALLED CARBON NANOTUBES SUPPRESS SYSTEMIC IMMUNE FUNCTION IN MICE

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**ABSTRACT:** The potential health effects of inhaling carbon nanotubes are important because of possible exposures in occupational settings. Previously, we have shown mice that have inhaled multiwalled carbon nanotubes have suppressed systemic immune function. Here, we show the mechanisms for this immune suppression. Mice were exposed to 0, 0.3 or 1 mg m<sup>-3</sup> multiwalled carbon nanotubes for 6 h per day for 14 consecutive days in whole-body inhalation chambers. Only those exposed to a dose of 1 mg m<sup>-3</sup> presented suppressed immune function; this involved activation of cyclooxygenase enzymes in the spleen in response to a signal from the lungs. Spleen cells from exposed animals partially recovered their immune function when treated with ibuprofen, a drug that blocks the formation of cyclooxygenase enzymes. Knockout mice without cyclooxygenase enzymes were not affected when exposed to multiwalled carbon nanotubes, further confirming the importance of this enzyme in suppression. Proteins from the lungs of exposed mice suppressed the immune function of spleen cells from normal mice, but not those from knockout mice. Our findings suggest that signals from the lung can activate signals in the spleen to suppress the immune function of exposed mice.