Title: Protective effect of curcumin on pulmonary and cardiovascular effects induced by repeated exposure to diesel exhaust particles

Body: Particulate air pollution has been linked to increased risk of cardiopulmonary diseases. However, the underlying mechanisms are not fully understood. We have previously demonstrated that single dose exposure to diesel exhaust particle (DEP) causes lung inflammation and peripheral thrombotic events. Here, we evaluated several cardiopulmonary endpoints two days after repeated doses of DEP (15 µg/mouse) every other day for 6 days, and the potential protective effect of curcumin (the yellow pigment isolated from turmeric) thereon. DEP exposure increased macrophage and neutrophil numbers, tumor necrosis factor α (TNF α) [but not interleukin-6 (IL-6)] in the bronchoalveolar lavage (BAL) fluid, and enhanced airway resistance to methacoline measured invasively using Flexivent. DEP also significantly increased Plasma C-reactive protein and TNFα concentrations, systolic blood pressure (SBP), as well as the pial arteriolar thrombosis. It also significantly enhanced the plasma D-dimer and plasminogen activator inhibitor-1. Pretreatment with curcumin 1h before exposure to DEP significantly prevented the influx of inflammatory cells and the increase of TNF α in BAL, and the increased airway resistance caused by DEP. Likewise, curcumin prevented the increase of SBP, CRP, TNF α, D-dimer and PAI. The thrombosis was partially but significantly mitigated. Our findings suggest that repeated exposure to DEP induces increases in airway and systemic inflammation, TNF α production in both in BAL and plasma, airway resistance, SBP, and coagulation. In conclusion, pretreatment with curcumin prevented the cardiopulmonary effect and inhibited the release of TNF α induced by DEP.