Assessing the direct and indirect effects of diesel exhaust particles on human intestine tissue

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Traffic-borne pollutants represent a notable proportion of ambient air pollution that can contribute to adverse effects in humans. During inhalation, fractions of traffic-borne aerosols can translocate from the alveoli to the bloodstream and accumulate within secondary organs beyond the lungs, such as the brain, liver, kidney, and intestine. However, understanding the specific impact of traffic-borne aerosols on those secondary organs remains an ongoing challenge. In this study, we aim to evaluate the direct and indirect effects of standard diesel exhaust particles (DEPs) on human intestine tissue *in-vitro*. The direct exposure of combustion-derived aerosols simulates aerosols that are swallowed after being cleared by the airway mucociliary activity. In contrast, indirect exposure simulates the translocation of the particles and/or release of lung-derived mediators through the blood circulation to the secondary tissues. The human intestinal Caco-2 / HT-29 and THP-1 monocyte-derived macrophage cell lines were co-cultured for 21 days in cell culture media and then exposed directly to 20 and 80 $\mu g.mL^{-1}$ DEPs for 24 hours. To mimic indirect exposure, the same DEP concentrations were given to lung cells, and the collected supernatants were added to the intestine tissues. Subsequently, tissue integrity and cell viability of the intestinal tissue, as well as the release of mediators such as pro-inflammatory IL-8 chemokine and IL-6, IL-1β cytokines in the media were assessed to understand the adverse effects of DEPs on the intestinal tissue. Our data suggested that the adverse effects of DEPs on the intestine tissue were induced upon indirect exposure to lung cell supernatants with an increase of IL-8 release from the intestinal cells, suggesting that translocated DEPs or lung-derived mediators could be the main contributors to adverse effects on the secondary tissues. We will expand the time of intestine exposure to DEPs and include additional key events to highlight the importance of lung-derived mediators and fractions of combustion-derived particles in traffic-borne pollutants toxicity on the secondary tissues.

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