Role of size and composition of traffic and wood burning aerosols in the molecular responses induced in airway epithelial and pulmonary artery endothelial cells.

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Introduction

Exposure to particulate pollution is suspected to be involved in cardio-respiratory and cardiovascular health effects. Urban populations living in megacities highly impacted by traffic are particularly vulnerable and more susceptible to develop diseases such as bronchopulmonary cancers, asthma and chronic obstructive pulmonary disease…). After inhalation, the finest particles could accumulate into the respiratory tract, cross the epithelial barrier and reach the systemic circulation where they could exert their deleterious effects on the cardiovascular system by direct interaction with the vascular endothelium. The respiratory tract is the first target of inhaled particles and endothelial cells, which line the inner surface of blood arteries, can have direct contact with the finest particles. Effects on endothelial cells can also be indirect resulting from secretions produced by epithelial cells in response to PM exposure and to different pollutants adsorbed on particles. Experimental studies have shown that lung inflammation seems to be the main short term effect to an acute particle exposure. However, the underlying biological mechanisms and the role of particle physico-chemical characteristics are still misunderstood.

The aim of this study is to evaluate (i) the direct toxicity of different urban PM size-fraction on human bronchial epithelial cells (16-HBE) and on pulmonary artery endothelial cells (HPAEC) (ii) the indirect activation of HPAEC after exposure to PM-induced 16-HBE epithelial secretions (iii) the relative sensitivity of these cells after exposure to the same PM size fraction.

Methods

Coarse, fine and ultrafine particles were sampled in Paris at specific periods of the day when they show high concentrations in combustion aerosols (traffic diesel emissions-TR and domestic heating with wood burning-WB). After recovery of particles from sampling filters, the two cellular models were directly exposed to the different size fractions from 1 to 10µg/cm², non cytotoxic concentrations Different endpoints were studied (i) production of reactive oxygen species by a fluorescent probe (H_2DCF-DA) (ii) pro-inflammatory response by measuring the release of various cytokines (IL-6, IL-8) by ELISA (iii) gene expression involved in these oxidative and inflammatory responses (Heme oxygenase-1-HO-1, IL-6, IL-8, GM-CSF, amphiregulin-AR), gene expression involved in xenobiotic metabolizing enzyme (CYP1A1, a predictive biomarker of polyaromatic hydrocarbon (PAH) bioavailability, NADPH quinone oxidoreductase NQO-1), by qPCR. In addition HPAEC were exposed for 24h to epithelial conditioned medium: culture medium from epithelial cells exposed or not for 24h to PM.

Results

Our results show similarities of response between the 2 target cells. Indeed a significant correlation was observed between 16-HBE and HPAEC cells for the CYP1A1 expression. It suggests that, in these cells, the PAH show a good bioavailability and induce the metabolism pathways of the organic compounds as also strengthened by a significant correlation for NQO-1 expression in both cell types. For the pro-inflammatory response, a significant correlation is observed between 16-HBE and HPAEC if we take into account the GM-CSF for the epithelial cells (a quite sensitive pro-inflammatory biomarker for these cells) and the IL-6 for endothelial cells (great sensitivity of IL-6 in these cells). Interestingly, endothelial cells were more sensitive to PM as compared to epithelial cells.

Whatever the cell type and the site of sampling, we observed a strongest reactivity of urban ultrafine and fine fractions as compared to the coarse fraction. No clear difference of toxicity was observed between traffic and wood burning aerosols suggesting that whatever the source of combustion the main short-term effect of an acute PM exposure is a pro-inflammatory response mediated through oxidative stress.

Moreover we provide evidence of an indirect pro-inflammatory response of HPAEC cells. When they are exposed to fine PM-induced epithelial secretions, they exhibited an increased IL-6 release. It suggests that epithelial mediators and/or soluble components of PM present in the conditioned medium were responsible for this pro-inflammatory effect.

Conclusion

Our results show that combustion (traffic and wood-burning) particles and especially the finest one can elicit a pro-inflammatory and oxidative response in both epithelial and endothelial cells and thus present a respiratory and cardiovascular disease risk.

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