Exposure and harm to combustion-derived particles: searching for biomarkers

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The human lung is the portal of entry for ambient particulate matter (PM) from combustion-derived (CD) processes (e.g. diesel and shipping exhausts and wood burning). Over a 24 hour period a person will inhale 20m^3 of air resulting in deposition of particles on the epithelial surface of the lung. It has been well-established that exposure to CDPM (Figure 1) causes increased risk for cardiopulmonary diseases and exacerbation of pre-existing diseases.

The physicochemical properties of size, surface area and presence of transition metals have been implicated as drivers of the oxidative capacity of CDPM. However, the precise role of reactive organic compounds (ROC) in ambient aerosols, present either in the gas phase or the particle phase or in both phases, have not been fully-investigated for their relevance in the induction of the observed adverse health effects.

Oxidation of fatty acids linked to the cell membrane phospholipids leads to many metabolites that have been used as markers of the process. Such metabolites have long been considered to be involved in two possibly inter-related processes: cell/tissue damage and signalling. As one approach to resolve the role played by ROCs, their effects on fatty acid and lipid metabolism in human lung tissues will be studied in detail by using the standard biochemical techniques and lipidomics.

When addressing the toxicity of inhalation hazards such as CDPM, there is a need for a model system that resembles the human lung. In our *in vitro* exposure studies, normal human bronchial epithelial (NHBE) cells were grown at the air-liquid interface (ALI) using filter-well technology (Prytherch *et al* 2011), to create an *in vivo*-like 3-dimensional lung model (Figure 2). This model is a fully-differentiated, pseudo-stratified, muco-ciliary epithelium containing basal, serous, Clara, goblet and ciliated cells.

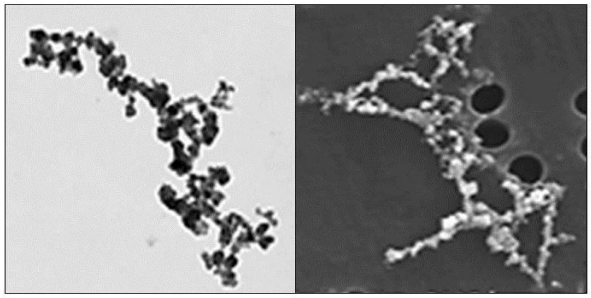

Figure 1. Transmission (left) and scanning (right) electron micrographs of CDPM.

NHBE cells were exposed to the following categories of CDPM at a dose of 152µg/cm^2: carbon black (CB; negative control; Monarch 120, Cabot UK; DQ12 quartz (positive control), shipping diesel engine PM (light fuel oil - LFO) and heavy fuel oil -HFO) collected during a HICE campaign for investigation of health effects of shipping diesel emissions at Rostock University. Following exposure (24 hours), tissue integrity (i.e. transepithelial electrical resistance (TEER); Figure 3) was measured to reveal CB and DQ12 reduced TEER by 19% and 56%, whereas both shipping diesel aerosols (H/LFO) induced about 74% disruption of tissue integrity (Figure 3).

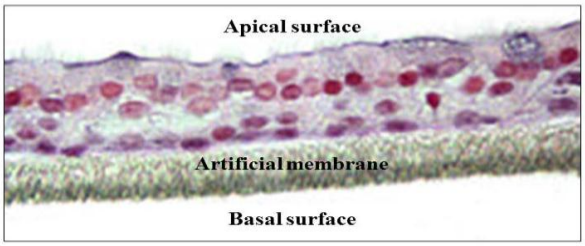

Figure 2. Light microscopy image of NHBE model (Haematoxylin & Eosin stained).

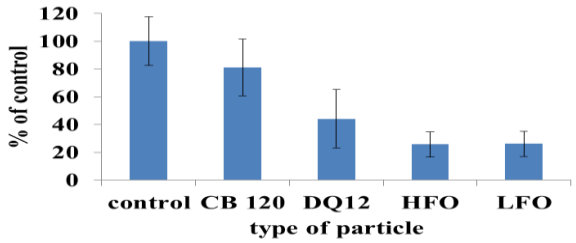

Figure 3. TEER readings for CDPM-exposed cells.

The fatty acid profiles were also affected post-exposure to CDPM. Data indicated that total fatty acid profiles demonstrated changes in ratios between saturated and unsaturated fatty acids. Levels of some polyunsaturated fatty acids, e.g. arachidonic acid (C20:4n-6), which is a precursor to production of pro-inflammatory mediators, slightly increased as a result of this exposure. Further work, applying both functional phospholipid and mediator lipidomics, will allow us to reveal mechanisms behind the changes observed, as well identifying biomarkers of cell damage by specific CDPM ROCs.

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