

## Effects induced by particles derived from two anthropogenic sources on respiratory, cardiovascular and central nervous systems

Paola Marmiroli<sup>1,2</sup>, Chiara Milani<sup>2</sup>, Elisa Ballarini<sup>1,2</sup>, Elisabetta Donzelli<sup>1,2</sup>, Luca Crippa<sup>1,2</sup>, Guido Cavaletti<sup>1,2</sup>, Paola Palestini<sup>2,3</sup>, Francesca Farina<sup>2,3</sup>.

<sup>1</sup> Experimental Neurology Unit, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy

<sup>2</sup> Milan Center for Neuroscience, School of Medicine and Surgery, University of Milano-Bicocca, Milano, Italy

<sup>3</sup> Milan Polaris Research Center, University of Milano-Bicocca, Monza, Italy

Air pollution represents a well-known environmental problem related to public health. Particulate matter (PM) is a heterogeneous mixture of chemicals, metals and soils. Its adverse effects have been correlated with particles size, being smaller particles more likely to cause a worst damage, so their study deserves more attention. Ultrafine particles (UFPs,  $d_{ae} < 100$  nm) are short-lived particles dispersed in the environment. In Lombardy, diesel combustion and solid biomass burning are the most relevant contributors to primary UFPs emissions (15-30 nm in diameter). Toxicological studies, mainly *in vitro*, indicate specific effects for particles of different origin but comparative *in vivo* studies are scarce. PM exposure has been primarily associated to pulmonary and cardiovascular diseases through oxidative stress and inflammatory response, but recently it has been postulated that PM exposure could also be an important risk factor for neurotoxicity and could have a role in neurodegenerative diseases.

In this study we analysed in BALB/c mice the effect of single and repeated intratracheal instillation of diesel (DEP) and biomass (BC) particles on respiratory, cardiovascular and central nervous systems, comparing the two different UFPs sources. The study was performed at biochemical and histopathological level. Different pro-inflammatory, cytotoxic, pro-coagulant and oxidative stress markers were measured. For the histopathological evaluation, sections of lung, heart and different parts of the central nervous system (CNS) were examined at light microscope, using standard staining techniques and immunohistochemical methods. Inflammation was also monitored in living mice following BC or DEP intratracheal repeated administration using the FMT 1500 fluorescence tomography imaging system and the MMPsense 750 Fast probe.

Our results indicate that even a single instillation of both the sources of UFPs induces a wide range of biochemical changes in the respiratory and cardiovascular systems, then confirmed by repeated instillation. In the CNS similar modifications were observed, although these were much more evident after repeated instillations. Histological examination demonstrated the presence of macrophages containing particles in the lungs after UFPs single and, more abundantly, repeated administration. However, significant changes were not observed in sections of heart and CNS.

DEP was more effective in inducing oxidative stress and inflammation compared to BC.

### Keywords

Air pollution, particulate matter, imaging, inflammation, oxidative stress