PARTICULATE MATTER INDUCES INTRINSIC AND EXTRINSIC APOPTOTIC PATHWAYS IN HUMAN ALVEOLAR TYPE II CELLS IN A P53-INDEPENDENT WAY

Castro L.P.; Menck C.F.M.; Carvalho H

1Departamento de Microbiologia, Instituto de Ciências Biomédicas, Universidade de São Paulo (USP), São Paulo, SP, Brazil; 2Departamento de Biofísica e Radiobiologia, Centro de Ciências Biológicas, Universidade Federal de Pernambuco (UFPE), Recife, PE, Brazil.

Despite the advances in emissions reduction through motor and fuel new technologies, the increasing number of cars in large cities, notably in developing countries, poses a serious risk for exposed population due to increased levels of air pollution. Air pollution is associated to the worsening of respiratory, allergic and cardiovascular diseases, besides being associated to lung cancer. Among the air pollutants, particulate matter (PM) is of particular interest due to its major contribution to the health effects attributed to air pollution. The objective of this study was to evaluate the effects of PM from diesel exhausts on apoptosis in immortalized human alveolar type II cells (A549 line). For this purpose, we used western blot, Real-Time PCR assays and Flow Citometry. PM induced dose and time-dependent apoptosis, measured by quantification of sub-diploid nuclei using FACS. Apoptosis was confirmed by activation of caspase-3, as detected by western blot. Cells treated with PM also showed decreased cell survival accessed by MTT assay. Treatment with diesel-derived PM did not result in phosphorylation or activation of p53, as evaluated by Western Blot. Despite the absence of p53 activation, increased expression of pro-apoptotic Bcl-2 family members Noxa and Puma was observed on cells treated with diesel-derived PM, as assessed by Real-Time PCR. We also found increased expression of Fas, determined by Real-Time PCR and western-blot. Despite the absence of p53 activation, the effect of diesel-derived PM on the expression of Noxa, Puma and Fas was partially reduced in cells treated with p53 inhibitor pifithrin-α. We suggest that another p53 family member may control expression of Noxa, Puma and Fas in A549 cells treated with diesel-derived MP. These results may help to understand the process of cell death in the lung of individuals exposed to air pollution.

Keywords: Apoptosis, Air pollution, p53
Supported by: FAPESP