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Toxicological Effects of Atmospheric Fine Particulate Matter on Human Bronchial Epithelial Cells: Metabolic Activation, Genotoxicity and Epigenetic Modifications

Authors : M. Borgie, Z. Dagher, F. Ledoux, A. Verdin, F. Cazier, H. Greige, P. Shirali, D. Courcot

Abstract : In October 2013, the International Agency for Research on Cancer (IARC) classified outdoor air pollution and fine particulate matter (PM2.5) as carcinogenic to humans. Despite the clearly relationship established by epidemiological studies between PM exposure and the onset of respiratory and cardiovascular diseases, uncertainties remain about the physiopathological mechanisms responsible for these diseases. The aim of this work was to evaluate the toxicological effects of two samples of atmospheric PM2.5 collected at urban and rural sites on human bronchial epithelial cells, BEAS-2B, especially to investigate the metabolic activation of organic compounds, the alteration of epigenetic mechanisms (i.e. microRNAs genes expression), the phosphorylation of H2AX and the telomerase activity. Our results showed a significant increase in CYP1A1, CYP1B1, and AhRR genes expression, miR-21 gene expression, H2AX phosphorylation and telomerase activity in BEAS-2B cells after their exposure to PM2.5, both in a dose and site-dependent manner. These results showed that PM2.5, especially urban PM, are able to induce the expression of metabolizing enzymes which can provide metabolic biotransformation of organic compounds into more toxic and carcinogenic metabolites, and to induce the expression of the oncomiR miR-21 which promotes cell growth and enhances tumor invasion and metastasis in lung cancer. In addition, our results have highlighted the role of PM2.5 in the activation of telomerase, which can maintain the telomeres length and subsequently preventing cell death, and have also demonstrated the ability of PM2.5 to induce DNA breaks and thus to increase the risk of mutations or chromosomal translocations that lead to genomic instability. All these factors may contribute to cell abnormalities, and thus the development of cancer.

Keywords : BEAS-2B cells, carcinogenesis, epigenetic alterations and genotoxicity, PM2.5
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