Particulate Matter (PM_{10}) alters Nucleotide Excision Repair pathway in lung epithelial cells

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Particulate matter with an aerodynamic diameter ≤10 μM (PM_{10}) is a major air pollutant and is classified as a carcinogen, primarily to the lung. PM_{10} is a heterogeneous mixture of metals, endotoxins and polycyclic aromatic hydrocarbons (PAH), which induces genotoxic damage, including PAH-DNA adducts formation; however, the mechanisms of carcinogenicity associated with exposure to PM_{10} need to be more precisely defined. The nucleotide excision repair pathway (NER) is responsible for repairing bulky DNA lesions, including adducts. This pathway includes more than 30 proteins, among which XPC, RAD23, XPD, XPA and ERCC1 act during the recognition, verification and repair of damage by binding to the DNA strand and forming protein complexes. Specifically, XPA requires posttranslational modifications for proper DNA repair. If DNA damaged is not correctly repaired, genomic instability and mutations might occur. DNA repair pathways can be inhibited by multiple compounds that are present in PM_{10}, nevertheless, the effect of PM_{10} exposure on the functionality of the NER pathway has not been described. In this study, it was evaluated whether PM_{10} (10 μg/cm^2) modified the levels, posttranslational marks and complex formation of the main NER proteins and whether these changes have an impact on repair function in A549 human lung cells. It was found that exposure to PM_{10} induce the formation and accumulation of benzo[a]pyrene diol epoxide-DNA adducts with an inhibition of NER pathway activity. PM_{10} exposure increased the levels of RAD23 and XPD, responsible for the recognition of damage and opening of the DNA strand, respectively and increased the levels of H4K20me2, that acts as a recruitment signal for XPA, the principal scaffold protein of this pathway. However, a decrease in the levels and phosphorylation of XPA at serine 196 was found (pXPA^{S196}) associated with the increase of phosphatase WIP1 levels, besides, the formation of the protein complex between XPA and RPA is inhibited. We conclude that PM_{10} deregulates the NER pathway and consequently induce the accumulation of DNA adducts in A549 human lung cells. These findings help to understand how PM_{10} exposure is a risk factor for lung carcinogenesis.