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Fine particle matters induce DNA damage and G2/M cell cycle arrest in human bronchial epithelial BEAS-2B cells.

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Abstract

There is compelling evidence that exposure to particulate matter (PM) is linked to lung tumorigenesis. However, there is not enough experimental evidence to support the specific mechanisms of $PM_{2.5}$-induced DNA damage and cell cycle arrest in lung tumorigenesis. In this study, we investigated the toxic effects and molecular mechanisms of $PM_{2.5}$ on bronchial epithelial (BEAS-2B) cells. $PM_{2.5}$ exposure reduced cell viability and enhanced LDH activity. The cell growth curves of BEAS-2B cells decreased gradually with the increase in $PM_{2.5}$dosage. A significant increase in MDA content and a decrease in GSH-Px activity were observed. The generation of ROS was enhanced obviously, while apoptosis increased in BEAS-2B cells exposed to $PM_{2.5}$ for 24 h. DNA damage was found to be more severe in the exposed groups compared with the control. For in-depth study, we have demonstrated that $PM_{2.5}$ stimulated the activation of HER2/ErbB2 while significantly upregulating the expression of Ras/GADPH, p-BRAF/BRAF, p-MEK/MEK, p-ERK/ERK, and c-Myc/GADPH in a dose-dependent manner. In summary, we suggested that exposure to $PM_{2.5}$ sustained the activation of HER2/ErbB2, which in turn promoted the activation of the Ras/Raf/MAPK pathway and the expression of the downstream target c-Myc. The overexpression of c-Myc may lead to G2/M arrest and aggravate the DNA damage and apoptosis in BEAS-2B after exposure to $PM_{2.5}$.

KEYWORDS:

BEAS-2B cells; Cell cycle arrest; Cytotoxicity; DNA damage; PM2.5; Ras/Raf/MAPK pathway