THE CAUSAL ROLE OF AIRBORNE NANOPARTICLE ACTIVATED ONCOGENE EXPRESSION IN THE PROGRESSION OF LUNG ADENOCARCINOMA

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Background and aims: Studies have suggested that exposure to nanoparticles is associated with the increased respiratory morbidity and mortality. Our epidemiological study has shown that exposure to traffic air pollution is associated with the risk of lung cancer. Oncogene activation and enhanced cell proliferation plays an important role in tumor initiation and progression. In the study, we aimed to explore whether c-Met oncogene activation is involved in the cell proliferation of lung adenocarcinoma following nanoparticle exposure.

Methods: Ultrafine carbon black (ufCB; 14 nm in diameter) was applied as a representative airborne nanoparticle. Cell proliferation assay with the use of pharmacological inhibitors were used to delineate the pathways involved in nanoparticle-induced tumor cell proliferation. Western blotting for c-Met oncogene phosphorylation, Met kinase activity assay and immunofluorescence staining were carried out to provide the mechanistic evidence for the involvement of c-Met signaling in ufCB-induced lung adenocarcinoma cell proliferation.

Results: The results demonstrate that ufCB at 50 • g/mL and 100 • g/mL induced dose- and time-dependent increases in the proliferation of lung adenocarcinoma cells. Met kinase inhibitor SU11274 and ERK1/2 inhibitor PD98059 significantly reduced cell proliferation incurred by ufCB exposure. Western blotting demonstrated that ufCB exposure triggered the phosphorylation of c-Met and ERK1/2. In accordance, ufCB significantly increased Met kinase activity. Moreover, SU11274 successfully suppressed ufCB-induced ERK1/2 phosphorylation, indicating that c-Met oncogene activation is responsible for the phosphorylation of ERK1/2 and cell proliferation.

Conclusion: The present results demonstrate that c-Met oncogene signaling plays an important role in nanoparticle-induced proliferation of lung adenocarcinoma cells. This has great implication on the role of airborne nanoparticle exposure in promoting tumor progression.