Mechanism of multiwalled carbon nanotube- and asbestos-induced osteopontin/CD44 in Raw 264 macrophages

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Carbon nanotubes, including multi-walled (MWCNT) are new materials with a lot of technological applications. Because of their unique physicochemical characteristics, their toxicity is extensively studied and often compared to asbestos. Deposition of MW-CNT in mouse lung resulted in chronic inflammation and fibrosis. Recently we demonstrated that this response is associated with activation of osteopontin (OPN) in lung macrophages, which is similar to the effects of asbestos exposure. OPN through interaction with CD44 or several integrins is known to regulate multiple macrophage functions. Here, we investigated the mechanism of MWCNT- and asbestos-induced OPN/CD44 using *in vitro* model, Raw 264 cells. MWCNT as well as asbestos induced dose dependent OPN gene expression and protein release by 24 hrs. The protein release declined in 48 hrs post exposure. This response is preceded by CD44 gene expression at 6 hrs. Further, exposure of cells to high concentrations of MWCNT resulted in a mild reduction in colocalization between OPN and CD44 as early as 6 hrs. Both CD44 and OPN protein cellular levels were reduced by 96 hrs post-exposure as examined by confocal imaging. MWCNT and asbestos enhanced the ability of OPN and CD44 to associate extracellularly following 72hrs of exposure. In conclusion, exposure to MWCNT or asbestos induced gene expression of CD44 and OPN, protein release of OPN, and modifications of the interaction between CD44 and OPN at cellular and extracellular levels.

Key words: Cardiopulmonary system; Cardiopulmonary disorders; Cardiovascular disease; Cardiovascular system; Particulates; Leukocytes

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