Jie Dong et al., J Clin Toxicol 2015 2015, 5:3
http://dx.doi.org/10.4172/2161-0495.S1.015

OMICS International
conferenceseries.com
4th Global Summit on
Toxicology
August 24-26, 2015 Philadelphia, USA

Multi-walled carbon nanotube-induced lung inflammation and fibrosis

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Occupational and environmental exposure to respirable fibers and particles potentially causes lung fibrosis that is often progressive and non-curable in humans. The production of multi-walled carbon nanotubes (MWCNT) has been dramatically increased in recent years due to their widespread applications, which has raised a concern regarding their health impacts on humans. Considering the similarities of MWCNT and asbestos fibers, lung inflammation and fibrosis have been associated with the major pathologic effects of MWCNT. However, the features and molecular mechanisms of MWCNT-induced lung pathology are still largely unknown. We systematically studied the effects of pulmonary exposure to MWCNT on the initiation and progression of inflammation and fibrosis in mouse lungs. We found that MWCNT functioned as a potent fibrotic agent that induced rapid-onset and progressive fibrosis upon a single exposure to low doses; moreover, the fibrotic response was accompanied by significant inflammatory infiltration and cytokine expression that peaked before the appearance of marked fibrosis. To understand the underlying mechanism, we analyzed the effects of MWCNT on the expression of a variety of pro-inflammatory, pro-fibrotic, and fibrosis marker genes at both mRNA and protein levels. Significantly induced expression of these genes was observed in MWCNT-exposed mouse lungs and in particular, in the fibrotic foci where MWCNT were deposited, supporting that MWCNT trigger both inflammatory and fibrotic responses in the lungs. Furthermore, we found that Nrf2, a critical regulator of the body's defense to oxidative stress, played an important role in suppressing MWCNT-induced lung inflammation and fibrosis, evidenced by induced oxidative stress and activation of Nrf2 by MWCNT in wild-type lungs, and remarkably enhanced levels of induced oxidative stress, inflammation and fibrosis observed in Nrf2 deficient lungs upon MWCNT exposure. These findings reveal that MWCNT potently induce lung fibrosis that is preceded by an acute inflammatory response, and oxidative stress plays a role in this process. Our study provides a detailed evaluation on MWCNT-induced pathologic effects in the lungs, offers evidence on the utilization of MWCNT-treated mice as a new animal model to study lung fibrosis, and contributes to both the general concept on fibrogenesis and the mechanism identification specific to MWCNT-initiated fibrosis.

Biography

Jie Dong completed the PhD degree at Duke University, and performed Postdoctoral studies at Yale University School of Medicine, and now works at CDC/NIOSH with a research focus on the molecular mechanisms of lung inflammation and fibrosis induced by occupational exposure, more specifically, by multi-walled carbon nanotubes.

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