Aryl Hydrocarbon Receptor (AhR) Regulates Induction of Lung Inflammatory Mediators by Organic Dust

V. Meganathan, M. Stenhouse, S. Kusampudi, V. Boggaram; Cellular and Molecular Biology, Health Science Center University of Texas at Tyler, Tyler, TX, United States.

Corresponding author's email: velmurugan.meganathan@uthct.edu

Rationale: Agriculture and animal farming operations have been industrialized to increase efficiency and reduce costs. These operations produce high levels of indoor aerosolized dust referred to as organic dust. Inhalation of organic dust is a risk factor for the development of respiratory diseases such as occupational asthma, bronchitis, organic dust toxic syndrome, hypersensitivity pneumonitis, and chronic obstructive pulmonary disease (COPD). Aryl hydrocarbon receptor (AhR) is a transcription factor that is activated by environmental chemicals and endogenous metabolites and has been implicated in diseases driven by aberrant immune and inflammatory responses. Based on the important roles that AhR plays in the control of inflammation, we wished to determine its involvement in the regulation of organic dust induced lung inflammation. METHODS: The effects of aqueous extracts of poultry farm dust (dust extract) on AhR activation and expression in Beas2B airway epithelial cells were investigated by confocal immunofluorescence microscopy and western blotting, respectively. The involvement of AhR was investigated by determining the effects of AhR antagonist CH223191 and siRNA mediated knockdown of AhR on the induction of pro-interleukin (IL)-1β, ICAM-1, IL-6, and IL-8 levels by western blotting and enzyme linked immunosorbent assay (ELISA). The effects of CH223191 and AhR knockdown on ROS generation in cells was analyzed by 2',7'-dichlorofluorescein diacetate (DCFDA) labeling and effects on NFκB and STAT-3 activation were determined by western blotting. Results: We found that treatment of Beas2B cells with dust extract enhanced AhR nuclear translocation and AhR expression in a time-dependent manner. AhR antagonist CH223191 and siRNA knockdown of AhR reduced induction of pro-IL-1β, ICAM-1, IL-6, and IL-8 protein levels. Reductions of pro-IL-1β, ICAM-1, IL-6, and IL-8 protein levels were associated with inhibition of ROS generation and NFκB and STAT-3 activation. Conclusion: Our results indicated that AhR plays a positive role in dust extract induction of inflammatory mediators via control of ROS levels and NFκB and STAT-3 activation. (Supported by CDC/NIOSH Grant U54 OH007541)

This abstract is funded by: CDC/NIOSH Grant U54 OH007541

Am J Respir Crit Care Med 2022;205:A3584
Internet address: www.atsjournals.org **Online Abstracts Issue**