Peroxisome Proliferator-Activated Receptor Gamma (PPAR-γ) Activator 15d-PGJ2 Suppresses Organic Dust Induction of Lung Inflammatory Mediators Independently of PPAR-γ

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

Background: Long-term exposure to organic dust is associated with chronic lung inflammation and development of respiratory diseases. Peroxisome proliferator-activated receptor gamma (PPAR-γ), a transcription factor belonging to the nuclear hormone receptor family has been reported to modulate inflammatory responses in several organs including lung. In this study, we hypothesized that activation of PPAR-γ modulates organic dust induced lung inflammation. Methods: Settled poultry farm dust was extracted with D-PBS to prepare dust extract. The effects of PPAR-γ agonists, 15-Deoxy-Delta-12,14-prostaglandin J2 (15d-PGJ2), Rosiglitazone, and GW1929 on inflammatory gene expression in Beas2B bronchial epithelial cells and THP-1 macrophages were analyzed by real time qRT-PCR, ELISA, and western blotting. Effects on cell toxicity were determined by MTS assay. Cellular reactive oxygen species (ROS) levels were measured by 2',7'-dichlorofluorescein diacetate (DCFDA) labeling. NF-κB and STAT-3 activation was analyzed by western blotting. Results: Among the PPAR-γ agonists tested, 15d-PGJ2 potently inhibited dust extract induction of pro-IL1β, ICAM-1, IL-6 and IL-8 proteins, whereas Rosiglitazone and GW1929 did not. Inhibitions of IL-1β, ICAM-1, IL-6 and IL-8 proteins were found to be due to reduced mRNA expression. 15d-PGJ2 inhibited ROS production and NF-κB and STAT-3 activation. MTS assay showed that 15d-PGJ2 did not cause cell toxicity. PPAR-γ antagonists and siRNA knock down of PPAR-γ had no effect on dust extract induction of inflammatory mediators. Conclusion: Our data has indicated that 15d-PGJ2 suppresses organic dust induced lung inflammatory mediators independentenly of PPAR-γ activation. 15d-PGJ2 suppression of inflammatory mediators may be due to inhibition of ROS production and NF-κB and STAT-3 activation. Acknowledgement: Supported by Centers for Disease Control and the National Institute of Occupational Safety and Health Grant U54 OH007541.

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