The Th2 adjuvant activity of indoor dust is dependent upon Dectin-1

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RATIONALE: Indoor dust (ID) contains environmental agents that promote T helper 2 (Th2) responses to inhaled allergens through a tumor necrosis factor (TNF)-dependent pathway. The main components of ID responsible for inducing Th2 responses are unknown. Here, we investigated if the Th2 adjuvant activity of ID is mediated by ligands for Dectin-1, a C-type lectin receptor that recognizes microbe-derived β-glucans.

METHODS: Using a cell reporter assay, we screened ID samples for bioactive Dectin-1 ligands. Using an ID-mediated asthma model, we compared allergic airway inflammation (airway eosinophilia, serum total IgE levels), TNF levels in bronchoalveolar lavage fluid (BALF), and airway hyperreactivity (AHR) in wild type (WT) and Dectin-1-deficient (Clec7a−/−) mice.

RESULTS: ID samples contained bioactive Dectin-1 ligands that activated nuclear factor kappa B signaling. In an ID-mediated asthma model, allergic airway inflammation was diminished in Clec7a−/− mice compared to WT mice, as demonstrated by decreased total airway cells, airway eosinophils and serum total IgE levels following allergen challenge. In contrast, allergen-induced AHR was similar in WT and Clec7a−/− mice. Following acute exposure to ID, Clec7a−/− mice had significantly decreased TNF levels in BALF compared to WT mice. In Clec7a−/− mice, addition of TNF during sensitization with ID and allergen restored airway eosinophilia upon allergen challenge.

CONCLUSIONS: Dectin-1 signaling is required for the Th2 adjuvant activity of ID, possibly by inducing TNF production during airway sensitization to inhaled allergens. Collectively, these findings suggest that Dectin-1 ligands within the indoor environment may contribute to asthma development by promoting allergic airway sensitization.