

Resolvin D2 Promotes the Resolution of Allergen-Induced Lung Inflammation

Hong Yong Peh^{1,2,3,4,5,6,7}Thayse R Bruggemann^{1,2,3,4}Wanxing Eugene Ho^{5,6,7}Chang Cheng^{5,6,7}WS Daniel Tan^{5,6,7}WS Fred Wong^{5,6,7}Bruce D Levy^{1,2,3,4}

¹Division of Pulmonary and Critical Care Medicine, ²Department of Internal Medicine, ³Brigham and Women's Hospital, ⁴Harvard Medical School, ⁵Department of Pharmacology, ⁶Yong Loo Lin School of Medicine, ⁷National University of Singapore

Background: Asthma is a chronic inflammatory disease without complete resolution. The production of specialized pro-resolving mediators (SPMs) is defective in asthma, so they represent a potential therapeutic opportunity. We hypothesize that docosahexaenoic acid derived resolvin D2 (RvD2) can promote the resolution of asthma.

Methods: BALB/c mice were challenged intra-tracheally with house dust mite (HDM). Bronchoalveolar lavage (BAL) fluid was collected at predefined protocol endpoints for peak inflammation and during resolution. To determine impact on resolution, some mice were given RvD2 (100 ng, intra-nasally) for 2 days after the last HDM challenge, and the resolution index for eosinophils and other markers were calculated.

Results: Airway HDM challenge led to marked increases in BAL eosinophils and BAL fluid pro-inflammatory cytokine and chemokine levels. Histology demonstrated changes in airway inflammation and mucous cell metaplasia in HDM-challenged lungs. NF- κ B and Nrf2 expression were increased the lungs of HDM allergic mice. Compared to vehicle, treatment with RvD2 significantly decreased BAL inflammatory macrophage and eosinophil counts, and accelerated the resolution of HDM-evoked inflammation with a marked decrease in the resolution index for BAL eosinophils from 5 days to 1 day. Interestingly, RvD2 attenuation of eosinophils specifically targeted the inflammatory eosinophil population, but not the resident eosinophils. The impact of RvD2 on cytokine expression and NF- κ B and Nrf2 activity is under current investigation to determine mechanisms for RvD2's pro-resolving actions.

Conclusion: RvD2 promotes resolution of allergen-induced inflammation in a murine model of allergic asthma.