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Importance of IL-23 to the development of emphysema

Pulmonary emphysema is characterized by alveolar destruction and persistent inflammation of the airways. We have recently reported that IL-17A and Th17 cells play a critical role to the development of porcine pancreatic elastase (PPE)-induced emphysema. Differentiation of Th17 cells is shown to be induced by IL-23. To determine the contribution of IL-23 to the development of pulmonary emphysema a mouse model of PPE-induced emphysema was used in which responses of IL-23p19-deficient (IL-23^{-/-}) and wild type (WT) mice were compared. Intra-tracheal instillation of PPE induced emphysematous changes in the lungs was associated with increased levels of IL-23 in lung homogenates. Compared to WT mice, IL-23^{-/-} mice developed significantly lower static compliance values and markedly reduced emphysematous changes on histological analyses following PPE-instillation. These changes were associated with lower levels of IL-17A and fewer Th17 cells in the lung. The neutrophilia seen in bronchoalveolar lavage (BAL) fluid of WT mice was attenuated in IL-23^{-/-} mice, and the reduction was associated with decreased levels of KC and MIP-2 in BAL fluid. Treatment with anti-IL-23p40 monoclonal antibody significantly attenuated PPE-induced emphysematous changes in the lungs of WT mice. These data identify the important contributions of IL-23 to the development of elastase-induced pulmonary inflammation and emphysema, mediated through an IL-23-IL-17 pathway. Targeting IL-23 in emphysema may be a potential therapeutic strategy for delaying disease progression.

Biography

Nobuaki Miyahara is a Professor at the Okayama University, Japan. He is graduated from Hiroshima University School of Medicine in 1988. He has completed his PhD in Department of Medicine II, Okayama University School of Medicine in 1994. He had done research on allergic airway inflammation at the National Jewish Health in Denver, CO, USA (Dr. Erwin Gelfand's Lab) from 2001 to 2008. Currently, he works at Department of Medical Technology, Okayama University Graduate School of Health Sciences, and Department of Allergy and Respiratory Medicine, Okayama University Hospital. His research interest is pathogenesis of COPD and asthma.

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