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A critical role of IL-18 in promoting pathogenesis of allergic diseases

Eosinophils are multifunctional leukocytes with diverse functions in health and disease. We first time demonstrate that IL-18 has a critical role in the development and maturation of eosinophils. Herein, we provide evidence that IL-18 differentiates eosinophils, even in the absence of endogenous IL-5, both *ex vivo* and under physiological conditions in vivo. IL-18 and IL-5 differentiated *ex vivo* eosinophils have differences in size, shape, granularity and differentially regulated *CD274 (PDL1)* transcript expression IL-18 activates B cells and subsets of specific T cells to produce IgE and eosinophil responsive cytokines including IL-5 and IL-13 to promote eosinophil influx into the tissues in experimental and human allergic diseases. IL-5 is an established factor for the rapid differentiation, expansion and survival of eosinophils. Eosinophils play a role in expelling gastrointestinal parasites in health and are involved in the pathogenesis of allergic states and allograft rejection. This distinct function of eosinophils is not yet not fully understood. The study provides a new understanding of eosinophil biology through the recognition of IL-18 differentiated *CD274 (PDL1)* expressing mature eosinophils that is detected even in blood of healthy individuals and allergic patients. Most importantly, it has been found that *PDL1* expressing eosinophils are increased in the blood of asthma patients and solely accumulated in the tissue under allergic conditions. Activated epithelial cells and antigen presenting cells are the major source of induced IL-18 in allergic diseases. Our *ex vivo* and *in vivo* data provide evidence that implicates IL-18 in the development and maturation of pathogenic *PDL1* expressing eosinophils. In brief, the analysis of mouse and human eosinophil in healthy and disease state indicates that IL-18 and IL-5 synergistically promote differentiation, maturation and proliferation of *PDL1* expressing pathogenic eosinophils in allergic disease states. Collectively, first time identified the role of IL-18 in transforming naive eosinophils to pathogenic *PDL1* expressing eosinophils and this finding may have broad implications regarding non-invasive diagnostic and therapeutic strategies for eosinophil-associated diseases.

Biography

Anil Mishra is the Chair of Edward G Schlieder Educational Foundation and Professor of Medicine. He is also the Director of Tulane Eosinophilic Disorder Center in the section of Pulmonary Diseases at Tulane University School of Medicine. He is an Elected Fellow of the American Academy of Allergy Asthma Immunology (FAAAAI) and the American Gastrointestinal Association (FAGA). He has published over 100 articles, book chapters and reviews on molecular mechanisms of pulmonary and gastrointestinal allergic responses in high impact factor journals.