Pathogenic Th2 (Tpath2) cells in airway inflammation

Toshinori Nakayama, MD, PhD

Department of Immunology, Graduate School of Medicine, Chiba University, and CREST-AMED, AMED, 1-8-1 Inohana Chuo-ku, Chiba 260-8670, Japan

To develop more effective vaccines and strategies to regulate chronic inflammatory diseases, it is important to understand the mechanisms underlying the generation and maintenance of immunological memory. In 2011, we identified a highly pathogenic IL-5-producing memory Th2 cell subset in allergic airway inflammation (Endo et al. Immunity, 2011). Based on these data, we propose a new model called "Pathogenic Th population disease induction model" in the pathogenesis of Th1/Th2/Th17 diseases (Endo et al. Trends in Immunology, 2014). We have extended our research, and found that the pathogenic Th2 cells (Tpath2 cells) are a distinct cell population generated in vivo, and express high levels of IL-33 receptor component, ST2. The IL-33-ST2-p38MAPK pathway plays crucial roles and selectively licenses memory Th2 cells to induce allergic airway inflammation. In addition, we found that IL-33 induced upregulation of IL-5 by human memory $CD4^+$ T cells isolated from nasal polyps of eosinophilic chronic rhinosinusitis patients. Therefore, IL-33-ST2-p38 signaling appears to directly instruct memory Th2 cells to become Tpath2 cells that produce huge amount of IL-5 and induce eosinophilic inflammation in the airway (Endo et al. Immunity, 2015). These newly identified memory type Tpath2 cells are CD44+ CD62Llo CXCR3lo CCR4+ CCR8+ IL-7Rα+ ST2+ CD4 T cells.