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A journey to medical science: Critical role of T cell-specific cilia protein

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After graduating from medical school, I worked as an internal medicine resident for 4 years. Although my internal medicine residency was difficult, I felt happy when the patients were recovered after the initiation of my treatment and were discharged. Furthermore, writing a research paper by collecting discharged patient data was a pleasure to share my knowledge with many doctors. My thesis of master's degree was about the development of early diagnostic methods between severe drug allergy and lymphoma. I could identify the difference between the two diseases while conducting this research, but I could not explain why these differences have occurred and I had to make predictions based on previously published papers. As a result, I wanted to explore the mechanism that can cause the difference between the patient and normal groups. Therefore, I decided to enter the graduate school of medical science to find out the precise mechanism of asthma by conducting research in immunology.

Asthma is a chronic respiratory disease caused by allergens such as house dust mites, pollen and animal dander. When exposed to these allergens, asthma patients experience coughing, wheezing and dyspnea. Even though some patients can be treated with commercially available drugs, there are patients with severe refractory asthma who do not respond to these existing therapeutics. Severe refractory asthma is typically caused by smoking, fine dust, and ozone, rather than by allergens. This non-allergic asthma shows different pathogenesis such as elevation of epithelial-derived cytokine by protease and infiltration of neutrophils in their sputum. These patients with severe refractory asthma are difficult to treat, and their quality of life is poor due to frequent exacerbation. Therefore, it is necessary to develop asthma medication with a novel mechanism that is different from the previously developed drugs.

CD4+ T cell is a maestro in the adaptive immune system. CD4+ T cell orchestrates target cells like cytotoxic T cell, eosinophil, and phagocytes by releasing various cytokines after it recognizes peptide binding to MHC II of antigen-presenting cell (APC). Depending on which type of CD4+ T cell differentiates, diverse diseases can occur such as asthma and autoimmune disease. Recent researches have suggested the importance of immunological

synapse, known as supramolecular activation cluster (SMAC). SMAC is the process of CD4+ T cell activation by recognizing the appropriate APC stimulus, which is similar to a neural synapse. Malformation of SMAC can reduce T cell activation. However, proteins participating in the process of SMAC formation are poorly understood.

Interestingly, we identified that the protein associated with cilia formation promotes CD4+ T cell activation, proliferation, and differentiation in a mouse model of allergic inflammation. In addition, this protein acts as a critical regulator of SMAC formation by binding to endosome-forming protein. Without this cilia-related protein, SMAC did not form and the activation and differentiation of CD4+ T cells were reduced. In addition, we generated this cilia-related protein knockout mice specifically in T cells using Cre-Lox recombination. As a result, the depletion of cilia-related protein attenuated protease allergen-induced inflammation. Thus, cilia-related protein may represent a novel therapeutic target for the treatment of patients with respiratory disease who do not respond to current standard therapies.