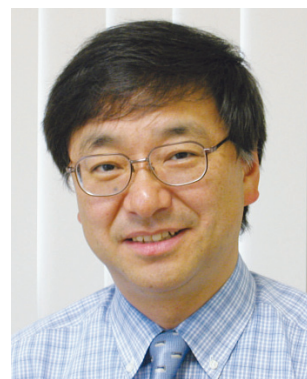


Biological Sciences

Discovery of Allergy-Causing Memory T Cells

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Background of Research

We are studying "immune memory." An influenza vaccine (vaccination) you get in every November or December and the DPT (diphtheria-pertussis-tetanus) vaccine given to small children are preventive methods against infectious disease using a function of "immune memory" in our body beneficially. That is a visible example of the contribution to medicine by Immunology. It was a major event in the history of medical science when the WHO declared the global eradication of smallpox in 1980 as a result of vaccination programs. More recently many people would remember the stories in the news about the production of a vaccine for the H1N1 swine flu virus, and public financial support for administering the human papillomavirus (HPV) vaccine to prevent cervical cancer. A vaccine is a prevention brought from the wisdom based on the experience. "Contracting a contagious (infectious) disease once, you won't contract it again, or if you do, it will only recur in a mild form. However the effect works specifically to the disease, but not for any other infectious diseases." Since it is as if the body remembers the disease previously contracted, the term "memory" came to be used to describe this effect. That is a symbolic phenomenon occurring in the acquired (or adaptive) immune system only vertebrates have, where T cells and B cells in lymphocytes play main roles. While immune memory is beneficial against infectious diseases caused by pathogenic microorganisms, there is also what could be described

as "bad" immune memory. Allergies and autoimmune diseases occur when the immune system does not work appropriately in its regulation. For example, people who suffer from Japanese cedar pollinosis have memory T cells specific to Japanese cedar pollen which non-sufferers do not, and with the cells these particular individuals experience symptoms with pollen allergy every year. Developing treatments for controlling immune memory has been eagerly awaited, whereby "good" immune memory would be boosted and "bad" immune memory would be suppressed.

Results from this research

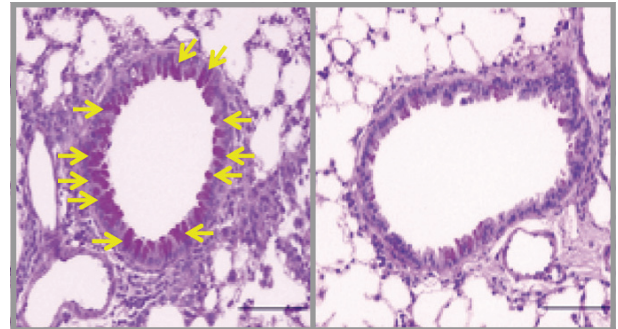
Our laboratory has been investigating memory T cells against allergens (antigens: foreign substances that cause allergies). Memory T cells are present in extremely small numbers, which led to impede the progress of the research. We therefore established a new experimental line that can produce large quantities of memory T cells to examine these cells thoroughly. We investigated their cell-surface molecules and found the fact that only one particular type of lymphocyte is capable of causing an allergic reaction. The lymphocyte produced large quantities of substance, a cytokine called IL-5 that is an inducer for biological reactions, resulting in attraction and activation of cells called eosinophils which trigger allergic response. We identified that this IL-5-producing cells selectively downregulated the expression of transcription factor Eome-

sodermine and also became harmful memory T cells. When we experimentally removed these cells from mice, they did not occur allergies (asthma). Furthermore we determined that the same cell populations are present in humans as well.

Prospective developments

Allergic diseases include asthma, atopic dermatitis, and allergic rhinitis. For chronic allergies that adults suffer in particular, steroid drugs have little or no effect, and even if symptoms can be controlled to some extent, the diseases are hard to cure. This discovery of allergy-causing memory T cells can be described as a major step forward the development for new treatments or even cures for intractable allergic disorders. We are now focusing on finding the target molecule that can stop the function of these cells.

“Immune memory” is a unique vital phenomenon that can be seen only in Immunology. We will continue to study, dreaming of the establishment of a new paradigm in the field of Immunology based on this study.



▲ **Fig.(A):**
A lung with asthma

▲ **Fig.(B):**
A lung with no allergy-causing memory T cells

In Figure (B) the lung has few cells causing mucus (sputum) overproduction (the cells in purple; marked with arrows).