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## **New research sheds light on how allergic response changes with age**

*Study suggests how body 'learns' over time to tolerate certain allergens, as dendritic cells become hypersensitive with exposure*

RIKEN research reported this week suggests why some people develop new or different allergies and even adult-onset asthma as they grow older.

The findings by a group of researchers from RIKEN, Tokyo University and Musashino University are to be published soon in the peer-reviewed journal of the American Academy of Allergy, Asthma & Immunology. RIKEN is a leading Japanese research institute based in the city of Wako in Saitama Prefecture, near Tokyo.

Immature regulatory dendritic cells, the 'sentinels' of the body's immune system, can trigger violent responses to allergens when the cells are still developing, but may later act to suppress those responses as the cells mature. This gives clues as to the underlying mechanism of how the body 'learns' over time to tolerate certain allergens.

Allergens such as pollen, cat dander and house dust are increasingly the bane of allergy sufferers. Allergens can also bring on asthma attacks that affect up to one in four urban children in developed countries. In the worst attacks, the mucus membranes of the human body react violently when cued by the regulatory dendritic cells, severely restricting air passages and inflaming tissues in the lungs, nose and eyes. In essence, the body turns against itself in an effort to expel the offending airborne invaders through sneezing, coughing and upper respiratory tract congestion.

Medical science has largely been at a loss about the actual mechanism behind these attacks, though direct evidence of the malady itself is as close as the nearest cedar tree, ragweed plant or fuzzy pet. What Dr. Fujita and his RIKEN-supported team have seen, through cellular-level studies involving mice specially bred for sensitivity to specific allergen chemical compounds, is that there is more going on than was thought.

A main focus of the research was on the action of dendritic cells that exist in the

lymphatic system and peripheral tissues. These cells act as sentinels against bacteria and other alien invaders, including ragweed and other types of pollen. Activation of the immune system requires that an incipient invasion first be detected. This is carried out by tissue macrophages, which alert the body's innate immunity, and by dendritic cells, which alert the adaptive immune system. As part of the adaptive function, the body may not react to the first series of exposures but eventually becomes acutely sensitized to later exposures, thanks to those otherwise-helpful dendritic cells.

The researchers found through chemical indications at the cellular level that the anti-allergen response engages differently for immunized mice compared to non-immunized mice that had not previously been exposed to a specific allergen chemical compound. Controlling for the development stage of the dendritic cells, they recognized that the typical reaction of the cell was to send signals to fight off an allergen if the cell was immature, but could later tolerate the allergen after the dendritic cell had matured.

How this phenomenon might be manipulated to prevent the onset of certain types of asthma is one focus of subsequent research on what the authors say are promising 'novel approaches' on how to keep the body from turning on itself as part of an immune system gone awry.

**Original work:**

Fujita, S., Yamashita, N., Ishii, Y., Sato, Y., Sato, K., Eizumi, K., Fukaya, T., Nozawa, R., Takamoto, Y., Yamashita, N., Taniguchi, M. and Sato, K. Regulatory dendritic cells protect against allergic airway inflammation in a murine asthmatic model. *Journal of Allergy Clinical Immunology*, published online on Oct 17, 2007

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