# Immune cell plays dual role in allergic skin disease

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(Medical Xpress) -- An immune cell involved in initiating the symptoms of an allergic skin reaction may play an equally, or perhaps more important, role in suppressing the reaction once it becomes chronic. This finding in mice could have future implications for the treatment of atopic dermatitis, a chronic inflammatory skin disease that affects an estimated 10 to 20 percent of infants and young children. The research is by investigators at the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), part of the National Institutes of Health.

The study, published online in the journal *Immunity*, and led by Juan Rivera, Ph.D., NIAMS deputy scientific director and chief of the Laboratory of Molecular Immunogenetics, focused on a type of cell called a mast cell. Previous research has shown that early in the course of atopic dermatitis, mast cells produce irritating chemicals, including interleukin-4 (IL-4), interleukin-5 (IL-5) and interleukin-6 (IL-6), which attract inflammatory cells to the site of the allergic reaction.

To better understand mast cells' role, the researchers developed a mouse model. After initial exposure to a chemical allergen, mice are subsequently challenged by having their ears painted with the same allergen multiple times. This model is similar to atopic dermatitis in people. Some of the mice were also engineered to be deficient in mast cells.

When the scientists painted a chemical allergen one time on the ears of the mast cell-deficient mice, the reaction occurred more slowly,

demonstrating that mast cells contribute to the initiation of atopic dermatitis.

"When they applied the same allergen to these mice multiple times, the reaction was considerably worse than in mice with sufficient mast cells," said Rivera. "That tells us that although mast cells may participate early on in the development of the disease, it appears that they are suppressing the late stages of the disease or when the disease becomes chronic."

In fact, when the scientists replaced the mast cells in mast cell-deficient mice, they were able to reduce the severity of the disease. The researchers were surprised that the mast cells did not have to be at the site of inflammation to control inflammation, said Rivera. In fact, the greatest effect was seen with mast cell repopulation in the spleen, a key organ in immune response.

Further investigation showed that, in late stages of disease, the mast cells underwent a change that caused them to produce a different chemical called interleukin-2 (IL-2), needed by cells which are key to suppressing inflammation, known as regulatory T cells.

"What is unusual here is that the same type of cells that can be inflammatory, can also be regulatory," said Rivera.

While Rivera says it's too early to predict the therapeutic importance of these findings, he believes they do provide new information on the understanding of atopic dermatitis and a potential caution against the development of treatments that target mast cells.

"While blocking mast cells has been considered as a treatment for the disease, it may be counter-productive, particularly in the latter stages of the disease," he said.

The researchers' next step is to see if their findings hold true in people, comparing the products of mast cells from lesions in early– and late-stage atopic dermatitis. It's possible, for example, that individuals with very severe chronic disease may not have sufficient mast cells in the skin.

Currently, the most effective treatment for atopic dermatitis is topical corticosteroids, which can have significant side effects, including thinning of the skin, if used long-term.

"In general, we need a better understanding of the disease itself to develop better therapies for it," said Rivera. "The new study is an important step toward that end, providing researchers with a valuable new insight that could eventually lead to safer, more targeted treatments."

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