# Dendritic cells ensure immune tolerance

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Dendritic cells are essential to the body's immune defenses. Now, Ludwig-Maximilians-Universitaet Muenchen (Germany) researchers show that they also have to protect the body from itself: They help to identify any immune cells that attack the body's own tissue and need to be destroyed or pacified.

One of the most important tasks of the immune system is to identify what is foreign and what is self. If this distinction fails, then the body's own structures will be attacked, the result of which could be an autoimmune disease such as diabetes mellitus type 1 or multiple sclerosis. The only way to protect against these afflictions is to destroy all immune factors that turn against the body's own tissue - in other words: immune tolerance.

A team working with LMU researcher Dr. David Vöhringer has now investigated exactly what role dendritic cells play in this process. There has long been suspicion that these cells, which are important for the body's defenses, are also essential for the establishment and maintenance of immune tolerance. "We investigated mice that lacked this cell type from birth," reports Vöhringer. "It turned out that immune cells that attack the body's own tissue survive in these animals, and thereby trigger an autoimmune response. It follows that dendritic cells play a major part in protecting against autoimmune disease."

T cells are a type of white blood cell that are key actors in the body's immune defenses. Each T cell has a receptor on its surface for recognizing just one single antigen. Antigens are molecular structures,

mostly fragments of proteins. T cells do not dock onto free antigens, however: they rely on other cells which can present antigens to them. It is the dendritic cells that are primarily responsible for this job. They present the T cells with various antigens, and if an antigen matches a receptor, then that T cell will trigger an immune response from the body.

This is how the body defends itself against pathogens and other intruders. But behind this tactic lies an element of danger to the organism: what happens if the antigen is not foreign, but originates from the body's own tissue instead? A wrongly induced immune response can lead to a severe autoimmune disease that, if left untreated, could lead to destruction of organs or even death. So-called autoreactive T cells, which recognize the body's own structures, must be eradicated or pacified to avoid that they can cause harm. A T cell screening process therefore takes place in the thymus, the bilobular organ in the upper thorax, to distinguish the good from the bad of these dangerous lone mavericks. Each individual T cell is tested, and the autoreactive ones destroyed.

The remaining T cells are checked a second time in the peripheral lymphatic organs of the body. This constant quality control goes on mostly in the lymph nodes and the spleen. As has been known for a while now, dendritic cells can induce peripheral tolerance although it remained unclear whether they are essential for this process. Dendritic cells migrate continuously out of tissues and organs into the lymph nodes, bringing tissue material with them and present it to T cells. Any T cell that reacts to the body's own proteins is then deactivated or killed off.

Most recent findings have shown that dendritic cells are essential to generate and maintain immunological tolerance. "Our work on mice has proven that without dendritic cells, even the first, central screening of autoreactive T cells in the thymus runs only at reduced efficiency," reports Vöhringer. "In these animals, the thymus releases T cells that

react to the body's own material. These are then activated in the peripheral organs - and trigger autoimmunity."

In light of the crucial role these cells play, it is a logical question as to how autoimmunity can be triggered at all without dendritic cells. After all, it is the dendritic cells that undertake certain critical tasks during an immune response. "Among other things, they are specialized in presenting antigens to T cells, which is what makes an immune response at all possible in the first place," says Vöhringer. "So we are left with the question as to what type of cell activates the autoreactive T cells if the supposedly most important antigen-presenting cells - the dendritic cells - are missing. We already have a few candidates for this, and are studying their function more closely now."

Source: Ludwig-Maximilians-Universität München