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Introduction to Dendritic Cells

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## Dendritic Cell and Immune Tolerance

Steinman Laboratory

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## **Dendritic Cells and Immune Tolerance**

Most studies have focused on the dendritic cells' role in activating T cells to resist foreign antigens, especially infections. Recent research in Steinman's laboratory, in close collaboration with other laboratories at Rockefeller, is showing that dendritic cells can also make the immune system tolerate harmless antigens, including those from the body's own tissues, cells, and proteins. This is necessary to keep the body from making an immune attack on itself.

The dendritic cell system appears to play a pivotal role in two kinds of immune tolerance. Usually, when young T cells are launched from the thymus, the dendritic cells participate in eliminating those cells bearing "self-reactive antigens" before they can harm the body's own tissues, a mechanism known as central tolerance.

Since some T cells may slip through this process, or other self-antigens do not access the thymus, or still others arise later in life, the dendritic cells also participate in the mechanism known as peripheral tolerance that restrains their activity. In the absence of infection or inflammation, the dendritic cells are in an immature state, but they are not quiescent. Like perpetual custodians, they clean house and collect trash. Sweeping non-stop through tissues and into lymphoid organs, the dendritic cells capture all kinds of antigens—the harmless self-antigens, those from dying cells, and the many nonpathogenic antigens encountered from the environment.

Two mechanisms have been identified that allow dendritic cells to induce tolerance. The antigen-loaded immature dendritic cells silence T cells by either deleting them or by inducing regulatory T cells that suppress the reactions of other immune cells. When the dendritic cells subsequently mature in response to infection, the preexisting tolerance nullifies any reaction to innocuous antigens and allows the dendritic cells to focus the immune response on the pathogen.

Other current research is providing clues about the dendritic cells' occasional failures to maintain tolerance. Failure to silence the immune system can lead to autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis. If dendritic cells are too tolerant, this can create a permissive environment for chronic infectious agents, such as HIV. Infections and tumors can exploit the tolerogenic function of dendritic cells, shut down the normal immune defenses, and perpetuate disease.