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Dendritic Cells Initiate the Immune Response

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Dendritic cells are professional antigen processing cells. They have a number of receptors that enhance the uptake of antigens, and they are specialized to convert these antigens into MHC-peptide complexes that can be recognized by lymphocytes. However, the dendritic cells need to do more than present antigens to T cells. They are also potent accessory cells that directly trigger and control responses by T cells and by all other types of lymphocytes.

Some early studies showed that dendritic cells carry on their surface high levels of major histocompatibility complex (MHC) products, which are critically recognized by T-lymphocytes. The high levels of MHC led Steinman to test these cells in the mixed leukocyte reaction (MLR), a well-known clinical assay for identifying the compatibility of tissue transplants between donors and recipients. At the time, this assay was known as mixed "lymphocyte" reaction, because it presumed that the B lymphocytes were presenting MHC products from the organ transplant donor to the recipient's T cells.

Instead, Steinman found that dendritic cells were the major stimulators and were unusually potent. In fact, a dendritic cell to T cell ratio of 1 to 100 sufficed to initiate vigorous and optimal responses. Moreover, the dendritic cells directly activated both the subset of helper T cells as well as the killer T cells. Once activated by dendritic cells, the T cells could also interact vigorously with other antigen presenting B cells and macrophages to produce additional immune responses from these cells.

The term "accessory" has since been replaced by the terms "professional" and "co-stimulatory," but the basic concept is unchanged. Dendritic cells provide the T cells with needed accessory or co-stimulatory substances, in addition to giving them a signal to begin to grow and function. For

example, two of these specialized activities include the production of cytokines, like interleukin-12 and interferons, and the expression of a number of needed membrane molecules like CD40, CD70, and CD86.

Dendritic cells also influence the type or quality of the response. A T cell, for example, has to know whether the enemy is a virus that needs to be resisted with its own interferons and cytolytic molecules, or whether the pathogen is a parasite that requires a different set of protective cells to respond with antibodies. Therefore, when dendritic cells migrate to the body's pool of T cells areas in the lymph nodes, they need to orchestrate two fundamental components from the repertoire of lymphocyte functions. First the dendritic cells select the rare specific T cells from the assembled repertoire that recognize the specific peptide information the dendritic cells are carrying. Amazingly, only one in 10,000-100,000 of the T cells in that repertoire are able to respond to this information. Second, the rare T cells that are selected for expansion then differentiate into helper and killer T cells that have the appropriate functions to eliminate the infection or disease causing stimulus. After these two decisions have been made, the newly activated T cells leave the lymph node to return to the body surface or peripheral organ to eliminate the antigens. For orchestrating these various processes efficiently and precisely, the dendritic cells are considered to be "conductors of the immune orchestra."