

Commentary

Immunological function of the thymus

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DESCRIPTION

The thymus is a specialized primary lymphoid organ of the immune system. Lymphocytes or thymus T-cells mature in the thymus gland. T cells are critical to the adaptive immune system, where the body specifically adapts to foreign invaders. The thymus is located in the upper front of the chest, in the anterior superior mediastinum, behind the sternum and in front of the heart. It consists of two lobes, each consisting of a central medulla and an outer cortex surrounded by a capsule.

The thymus is made up of immature T cells called thymocytes, as well as lining cells called epithelial cells that help thymocytes develop. T cells that develop successfully react appropriately with the body's MHC immune receptors (so-called positive selection) and not against the body's proteins (so-called negative selection). The thymus gland is the largest and most active in the neonatal and preadolescent periods. During adolescence, the thymus begins to decrease in size and activity, and thymus tissue is gradually replaced by adipose tissue. However, some T-cell development continues throughout adulthood.

Abnormalities of the thymus can lead to decreased T-cell counts and autoimmune diseases such as autoimmune polyendocrine syndrome type 1 and myasthenia gravis. They are often associated with cancer of thymus tissue, called a thymoma, or tissue that arises from immature lymphocytes, such as T cells, called lymphoma. Removal of the thymus gland is called a thymectomy. Although the thymus has been identified as a part of the body since the time of the ancient Greeks, it has only been since the 1960s that the function of the thymus in the immune system has become better understood.

Function

T cell maturation: The thymus facilitates the maturation of T cells, an important part of the immune system that provides cellular immunity. T cells begin as hematopoietic progenitors in the bone marrow and migrate to the thymus, where they are called thymocytes. In the thymus, they undergo a maturation process that

involves the cells reacting against antigens ("positive selection"), but not against antigens found in the body's tissues ("negative selection"). After maturation, T cells emigrate from the thymus to provide vital functions in the immune system.

Each T cell has a specific T cell receptor that is specific to a specific substance called an antigen. Most T-cell receptors bind to the major histocompatibility complex on body cells. MHC presents an antigen to a T-cell receptor that becomes active when it matches a specific T-cell receptor. To function properly, a mature T cell must be able to bind to an MHC molecule ("positive selection") and not respond to antigens that come from body tissues ("negative selection"). Positive selection occurs in the cortex, and negative - in the medulla of the thymus gland. After this process, the surviving T cells leave the thymus, which is regulated by sphingosine-1-phosphate. Further maturation occurs in the peripheral circulation. Part of this is due to hormones and cytokines released by thymus cells, including thymulin, thymopoetin, and thymosins.

Positive selection: T cells have different T cell receptors. These different receptors are formed by *V(D)J* gene recombination, stimulated by the *RAG1* and *RAG2* genes. This process is error-prone, and some thymocytes fail to make functional T-cell receptors, while other thymocytes make T-cell receptors that are autoreactive. When a functional T-cell receptor is formed, the thymocyte will begin to simultaneously express CD4 and CD8 cell surface proteins.

The survival and nature of the T cell depends on its interaction with the surrounding thymic epithelial cells. Here, the T-cell receptor interacts with MHC molecules on the surface of the epithelial cells. A T cell with a receptor that is unresponsive or weakly responsive will die by apoptosis. A responding T cell will survive and reproduce. Mature T cells express only CD4 or CD8, but not both. This depends on the strength of binding between the TCR and MHC class 1 or class 2. A T cell receptor that binds primarily to MHC class I tends to produce mature "cytotoxic" CD8 positive T cells; The T-cell receptor, which binds mainly to MHC class II, tends to generate CD4-positive T cells.

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Negative selection: T cells that attack the body's own proteins are eliminated in the thymus, a process called "negative selection." Epithelial cells in the medulla and dendritic cells in the thymus gland express basic proteins from other parts of the body. The gene

that drives this is *AIRE*. Thymocytes, which strongly react to their own antigens, do not survive and die by apoptosis. Some CD4-positive T cells exposed to self-antigens persist as T-regulatory cells.