T cells include helper and cytotoxic cells.

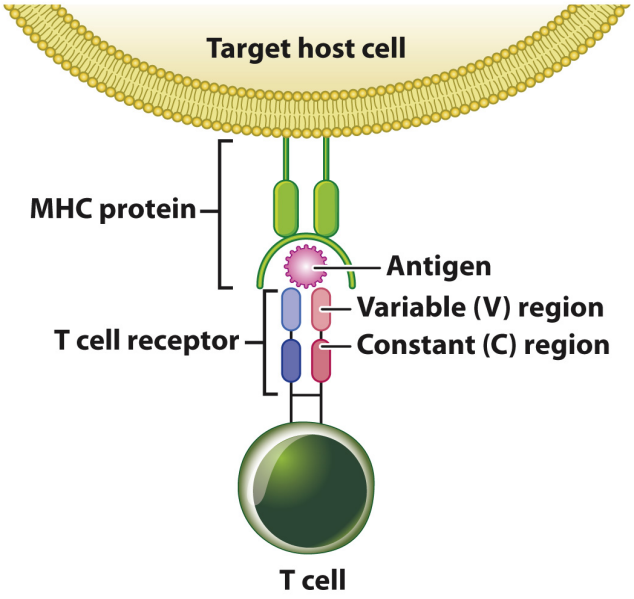
- **Helper T cells** help other cells of the immune system by secreting cytokines
    - Activates B cells to secrete antibodies
    - Activates macrophages, cytotoxic T cells, and other cells of the immune system
- **Cytotoxic T cells** kill other cells
    - Like B cells, they are activated by cytokines released by helper T cells
    - Effective against altered host cells, such as those infected with a virus
- There are different **glycoproteins** on helper and cytotoxic T cells
    - **CD4** is present on helper T cells
    - **CD8** is present on cytotoxic T cells
    - CD8 is higher and more powerful that CD4
- The CD4 : CD8 ratio is 2:1, so there are more CD4 on helper T cells compared to CD8 on cytotoxic T cells
- HIV infected individuals have fewer helper T cells and a lower CD4 : CD8 ratio

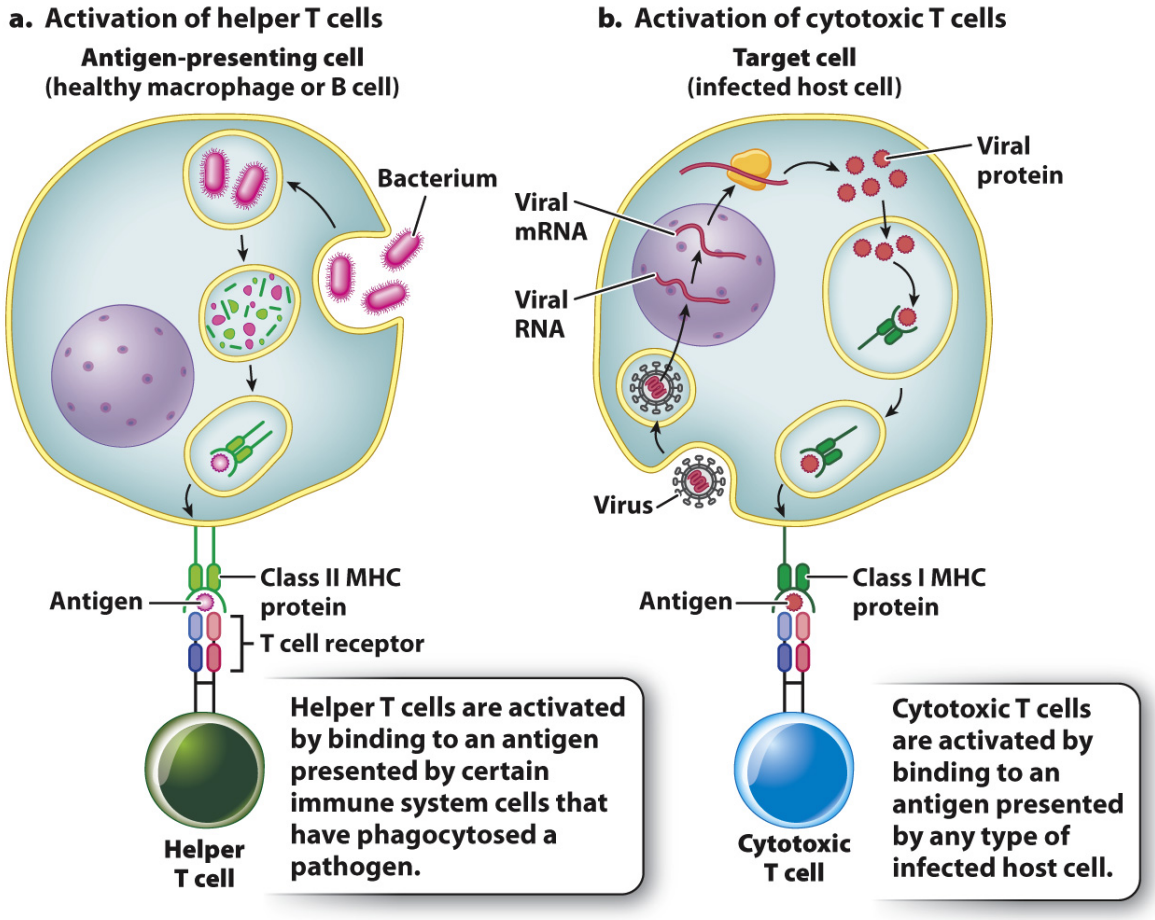
T cells have T cell receptors on their surface that recognize an antigen in association with MHC proteins.

- Like B cells, all T cells originate in the mammalian bone marrow
    - However, T cells mature in the thymus
- A mature T cell is characterized by the presence on the plasma membrane of a **T cell receptor (TCR)**, a protein receptor that recognizes and binds to the antigen
    - Similar to antibodies on B cells
    - Recognize antigens with a specific structure
    - There is diversity between T cells, but one T cell has only one type of TCR

- Binding of TCR to an antigen triggers the T cell to divide into clones
    - Results in a pool of T cells that are each specific for a given antigen
- Diversity is a result of **genomic rearrangement** of V, D, J, and C gene segments

- TCRs are different from antibodies in three ways
    - They are composed of **two polypeptide chains** rather than four
    - They are **not secreted** like antibodies, but are always membrane-bound on the T cell surface
    - Does not recognize an antigen by itself; it recognizes an antigen in association with proteins that appear on the surface of cells that are encoded by the **major histocompatibility complex (MHC)**
- The MHC is a cluster of genes in all mammals that encode for proteins on the surface of the cell
    - High rate of **polymorphism**, meaning there is a lot of variation in the protein sequence among different individuals
        - **Class I genes** are expressed on the surface of all nucleated cells
        - **Class II genes** are expressed on the surface of macrophages, dendritic cells, and B cells
        - **Class III genes** encode several proteins of the complement system and proteins involved in inflammation
- When an antigen enters the body, it may be recognized by an antibody directly or be taken up by **antigen-presenting cells**, which include macrophages, dendritic cells, and B cells
    - These cells take up the antigen and return portions of it to the cell surface bound to MHC Class II proteins
    - Helper T cells recognize processed antigen and **MHC class II proteins by their T cell receptor**
    - When TCR binds to antigens and MHC class II proteins, the **helper T cells release cytokines** that activate other parts of the immune system, such as macrophages, B cells, and cytotoxic T cells





- **Cytotoxic T cells** also recognize antigens displayed by host cells but **only for class I MHC**

TABLE 43.2 Comparison of Helper and Cytotoxic T Cells

	HELPER T CELL	CYTOTOXIC T CELL
Functions	Activation of macrophages Activation of B cells Activation of cytotoxic T cells Secretion of cytokines	Cell killing
Surface molecule	CD4	CD8
MHC protein recognized by the T cell	Class II	Class I

- Once activated, T cells divide and form clones of helper or cytotoxic T cells
    - Some cells are memory cells
    - T cells can sometimes be activated too strongly

- The counterpart in T cells is called **delayed hypersensitivity reaction**, which means the immune reaction does not begin right away

    - Delayed hypersensitivity reactions are initiated by helper T cells that release cytokines

The ability to distinguish between self and nonself is acquired during T cell maturation.

- Only some TCRs are useful

- Useful TCRs must be able to react with the host's own MHC proteins, and cannot react with other molecules that are normally present on cells of the host

    - In other words, **T cells must respond only to self MHC proteins in association with nonself antigens**

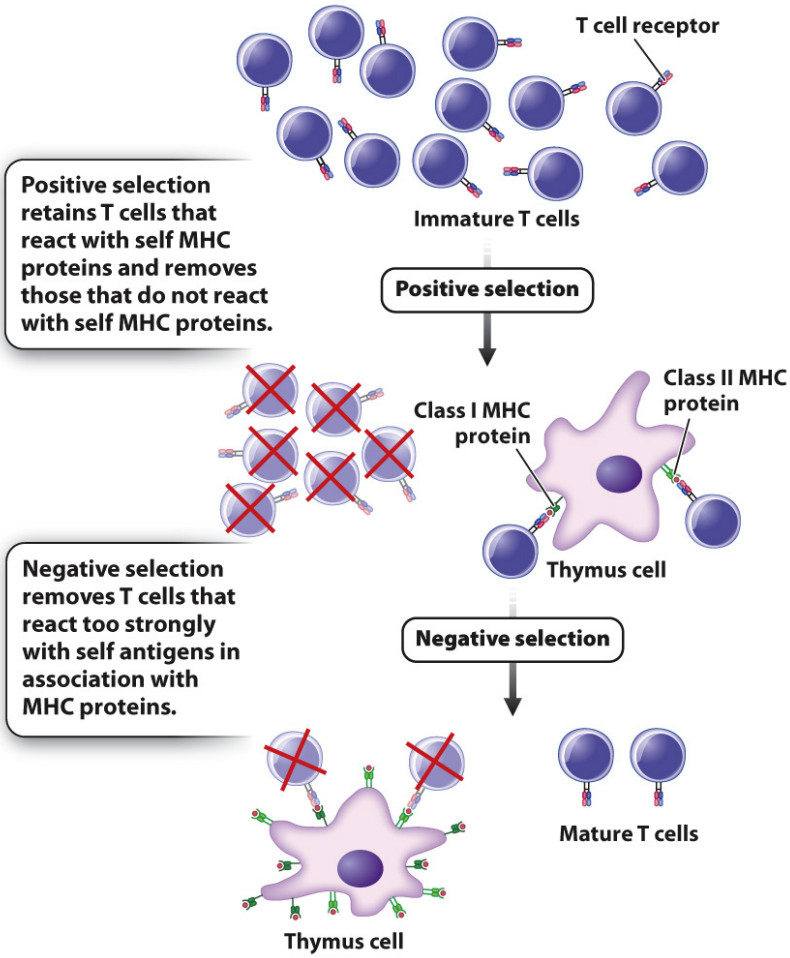
    - It **cannot respond to other self molecules of an organism's own cells**

- A sorting process eliminates T cells that are not useful

- As T cells mature in the thymus, they interact with the cells of the epithelium

    - The T cells that recognize self MHC proteins on epithelial cells are **positively selected**

- The T cells that react too strongly to self antigens in association with MHS are **negatively selected** and eliminated through cell death



- First, T cells become **MHC restricted** and must interact with **antigens associated with MHC** proteins
- Second, T cells exhibit **tolerance** and do not respond to **self** antigens
- B cells also exhibit **tolerance** to self antigens because they go through a similar negative selection process
- This mechanism is not perfect, and there are some unfit cells that escape this check and proceed to circulation
- Failure of the ability to distinguish self from nonself can lead to **autoimmune disease**