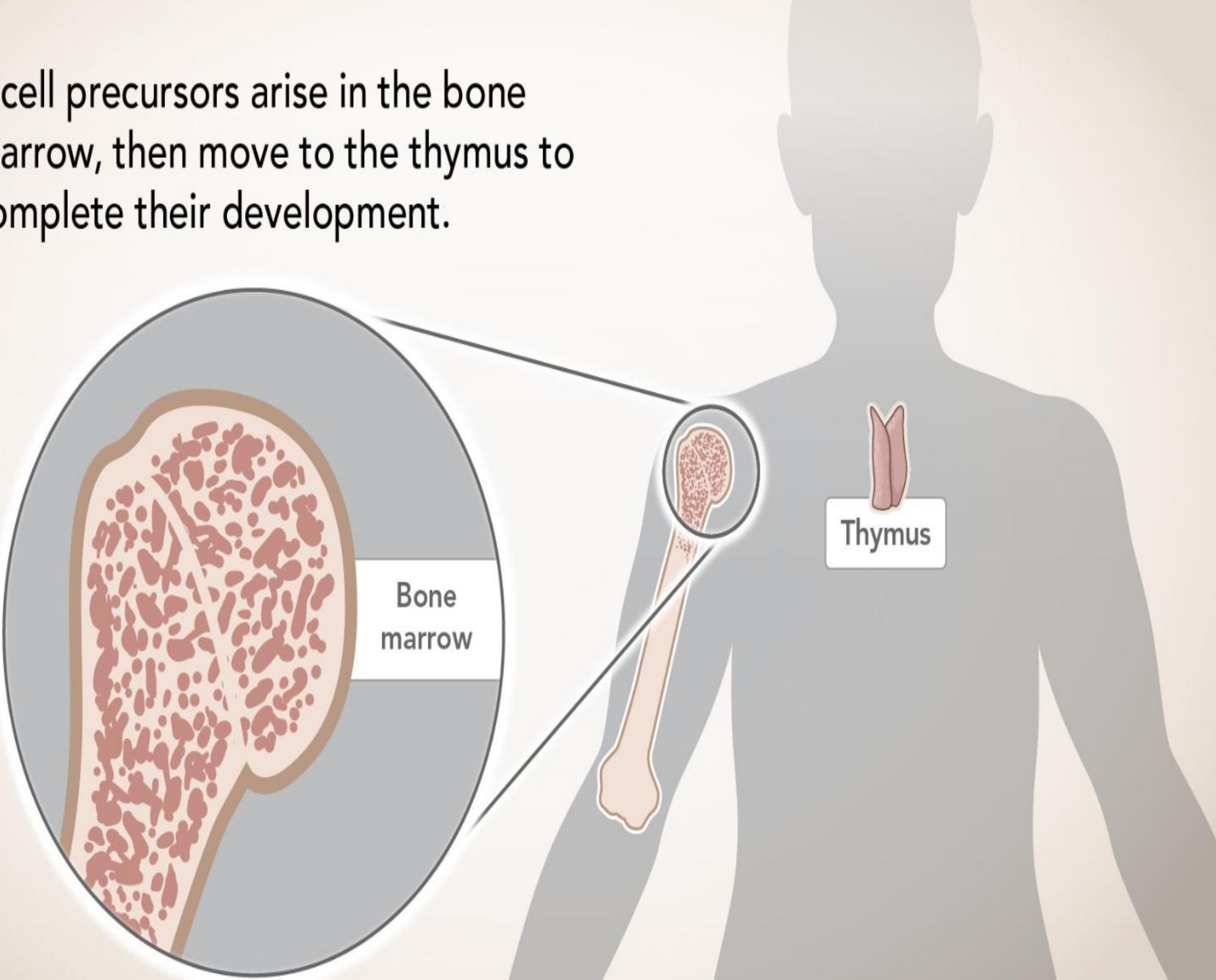
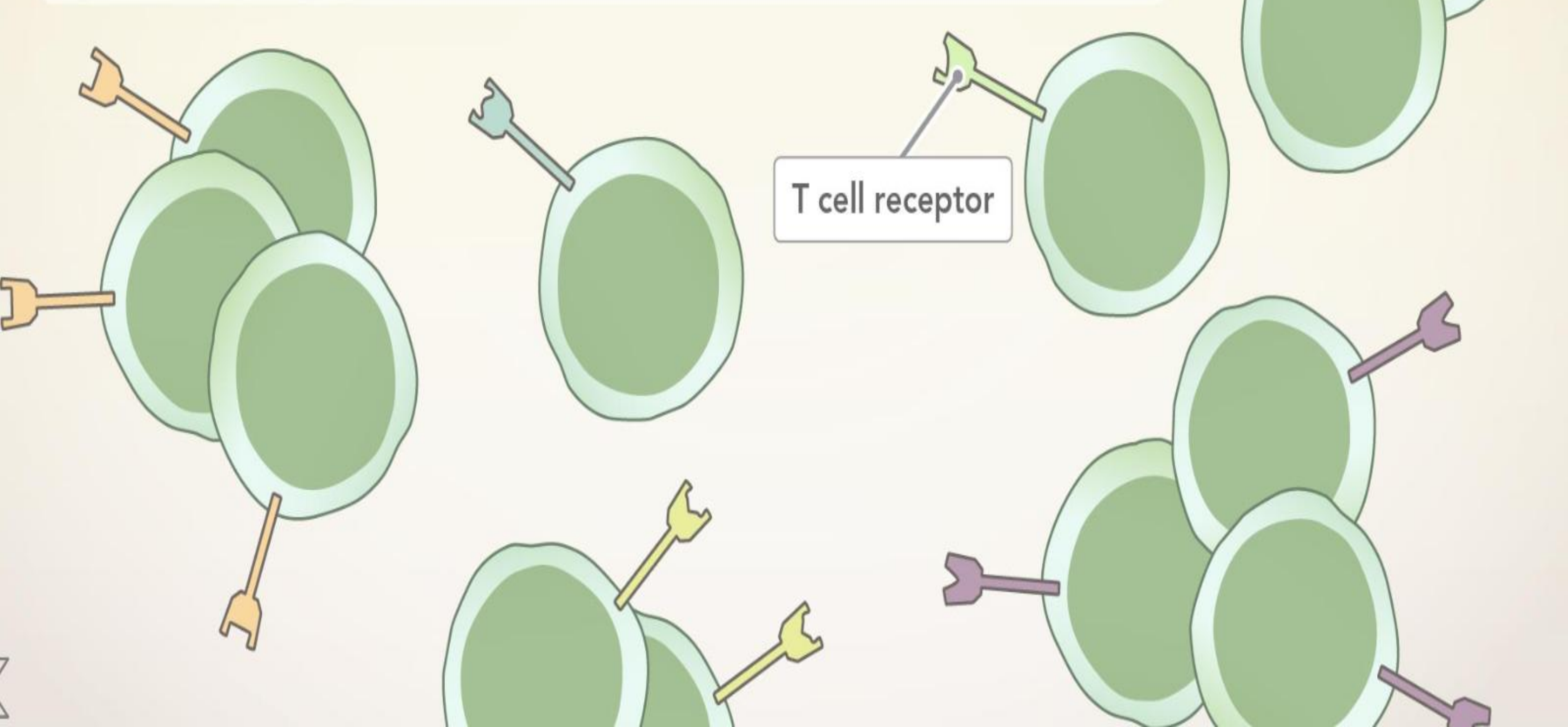
Adaptive immune system : T cells

T cell precursors arise in the bone marrow, then move to the thymus to complete their development.

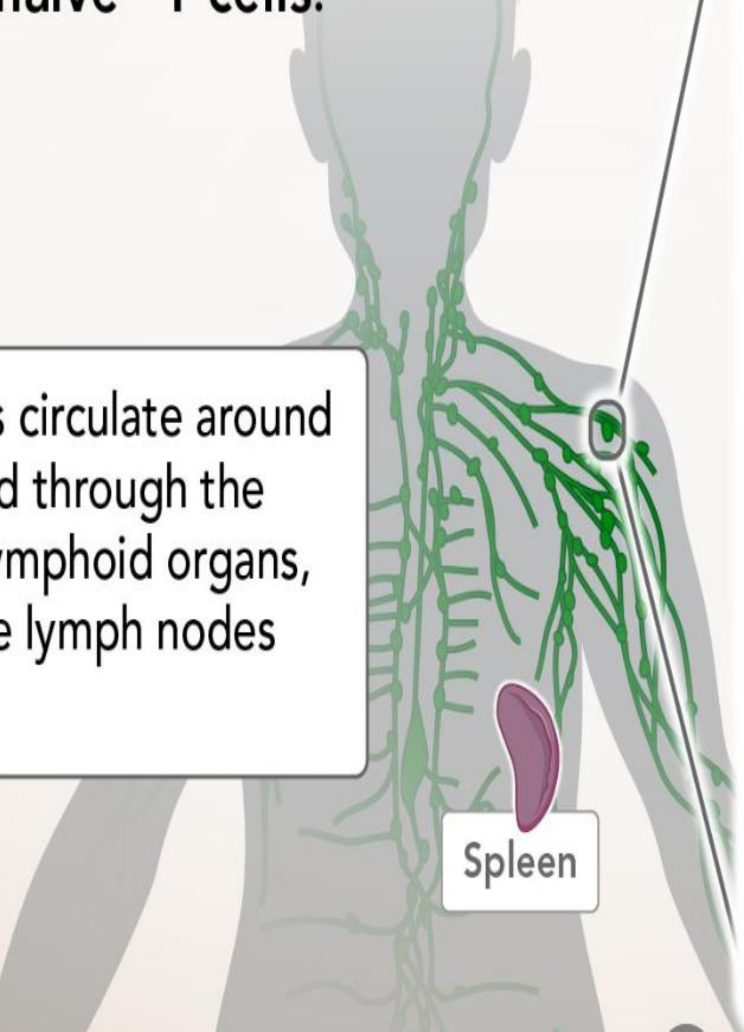


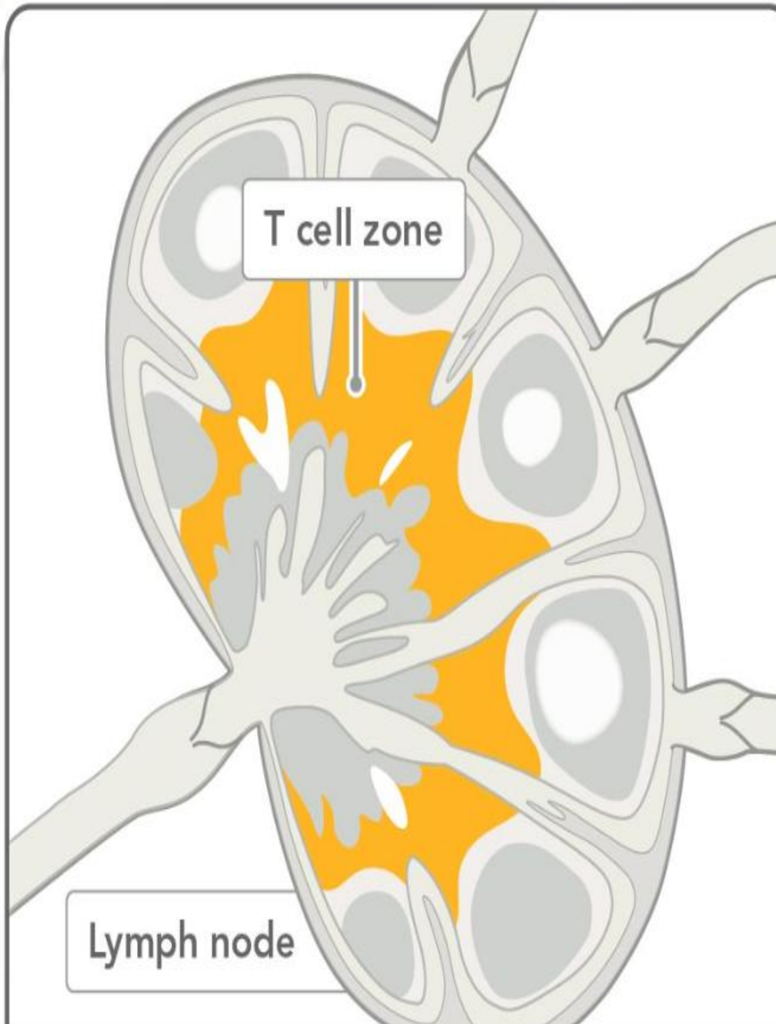
As T cell precursors mature, a series of steps leads to expression of a T cell receptor (TCR) specific for a single antigen. Each developing T cell clone expresses a unique TCR, with a unique antigen specificity.



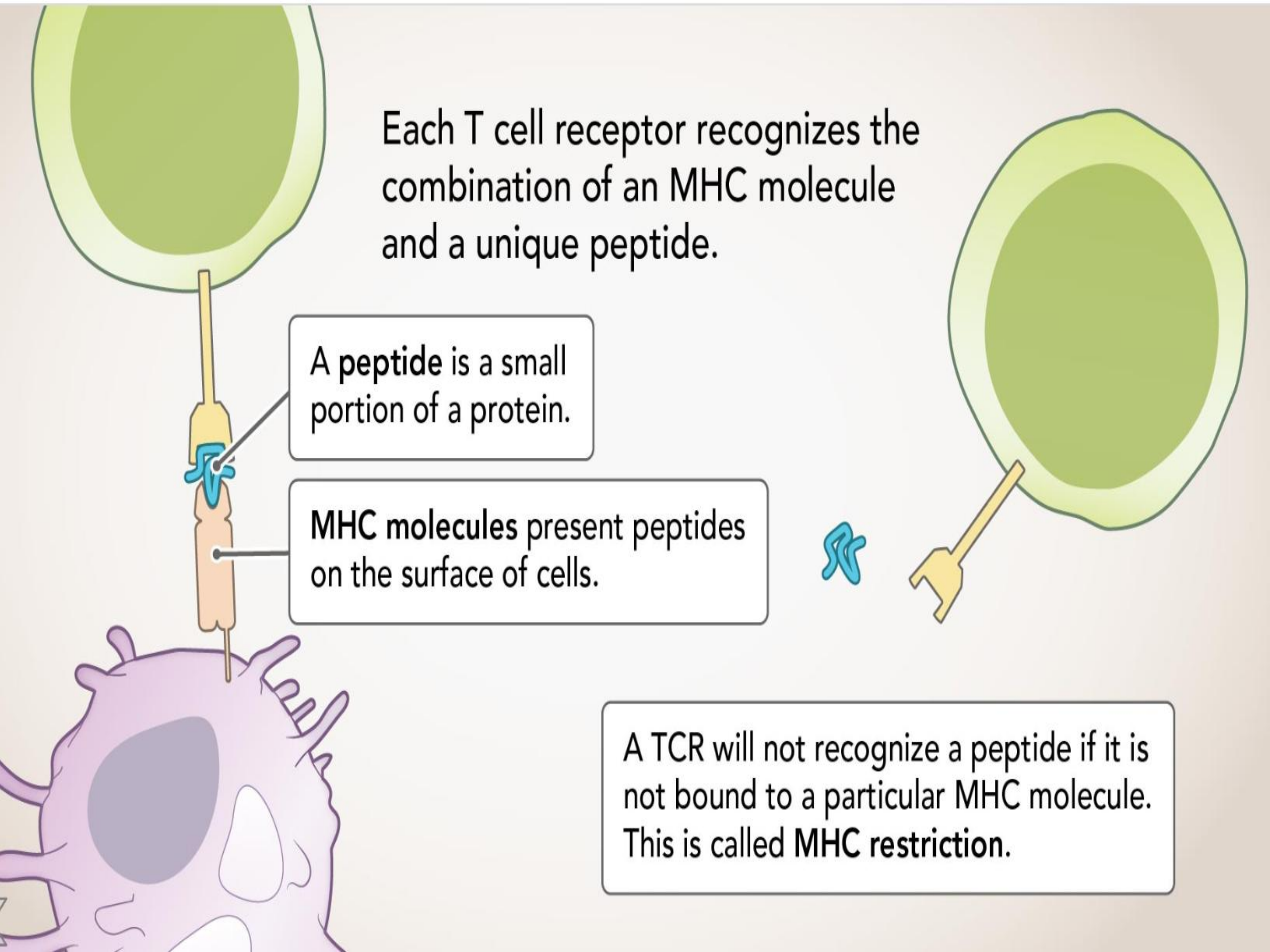
Mature T cells that leave the thymus but have not been activated by antigen yet are called "**naive**" **T cells**.

Naive T cells circulate around the body and through the secondary lymphoid organs, including the lymph nodes and spleen.



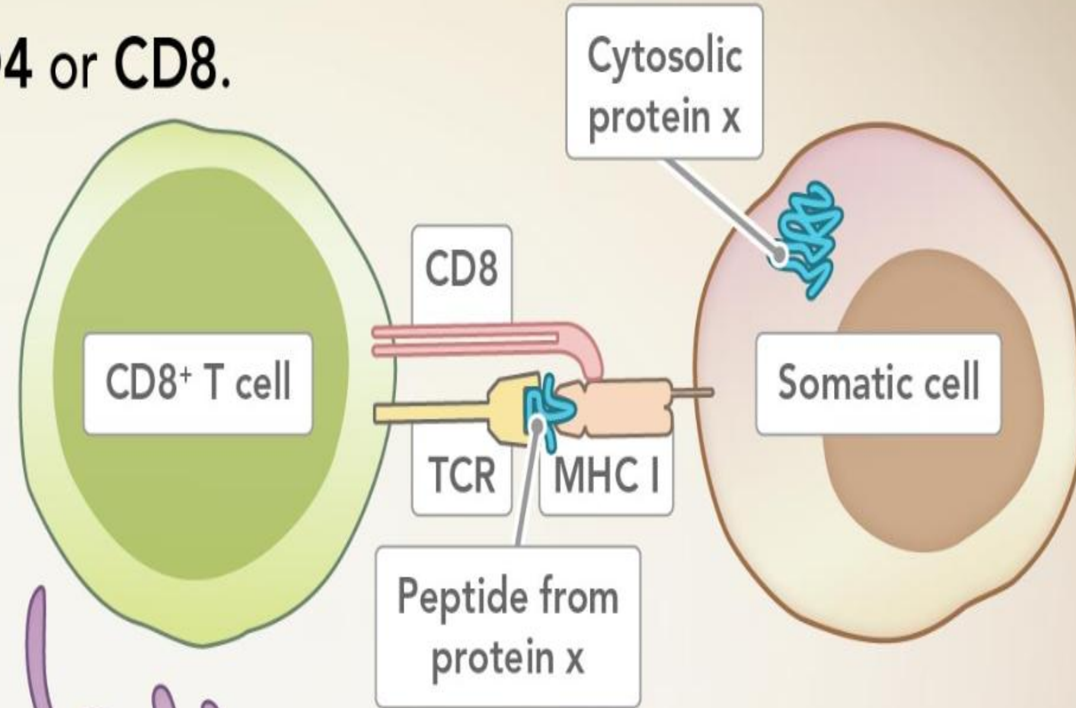


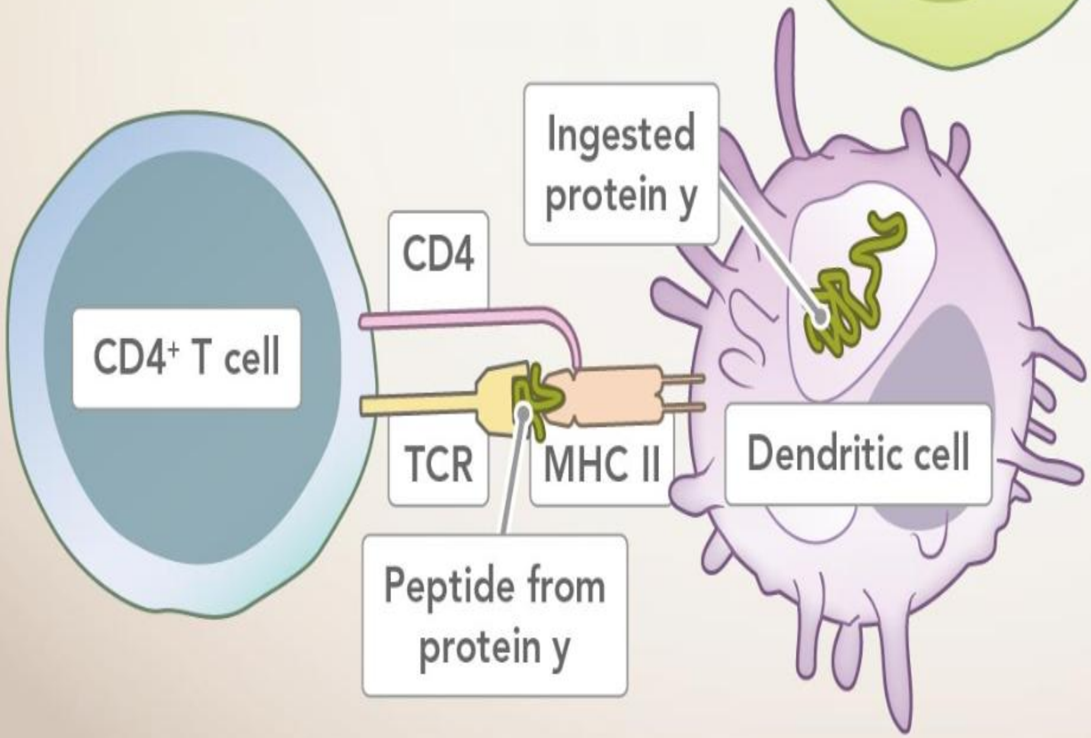
The area of the lymph node where naive T cells gather is called the **T cell zone.**


Each T cell receptor recognizes the combination of an MHC molecule and a unique peptide.
A **peptide** is a small portion of a protein.
MHC molecules present peptides on the surface of cells.
A TCR will not recognize a peptide if it is not bound to a particular MHC molecule. This is called **MHC restriction**.

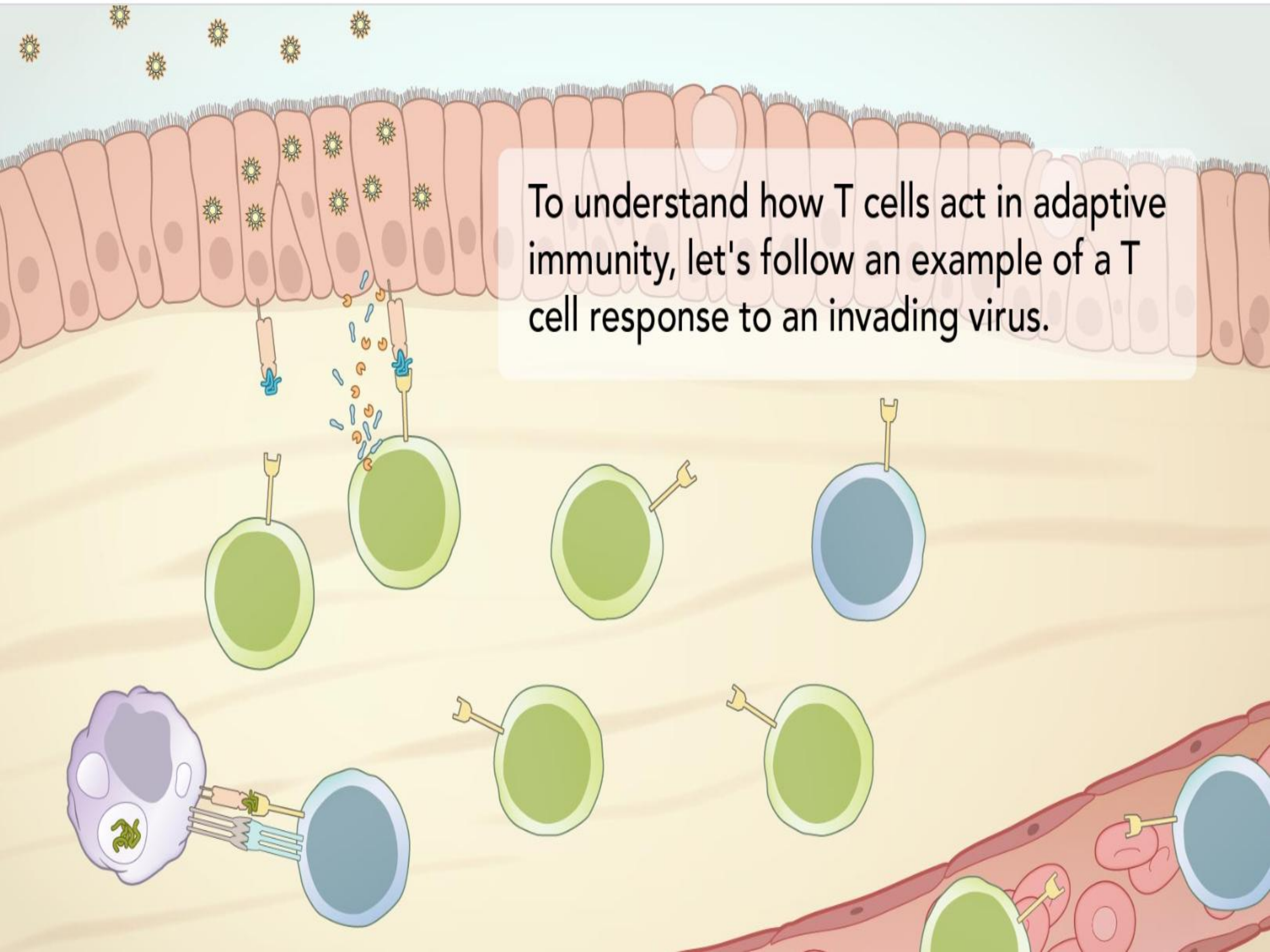
T cells can express either **CD4** or **CD8**.

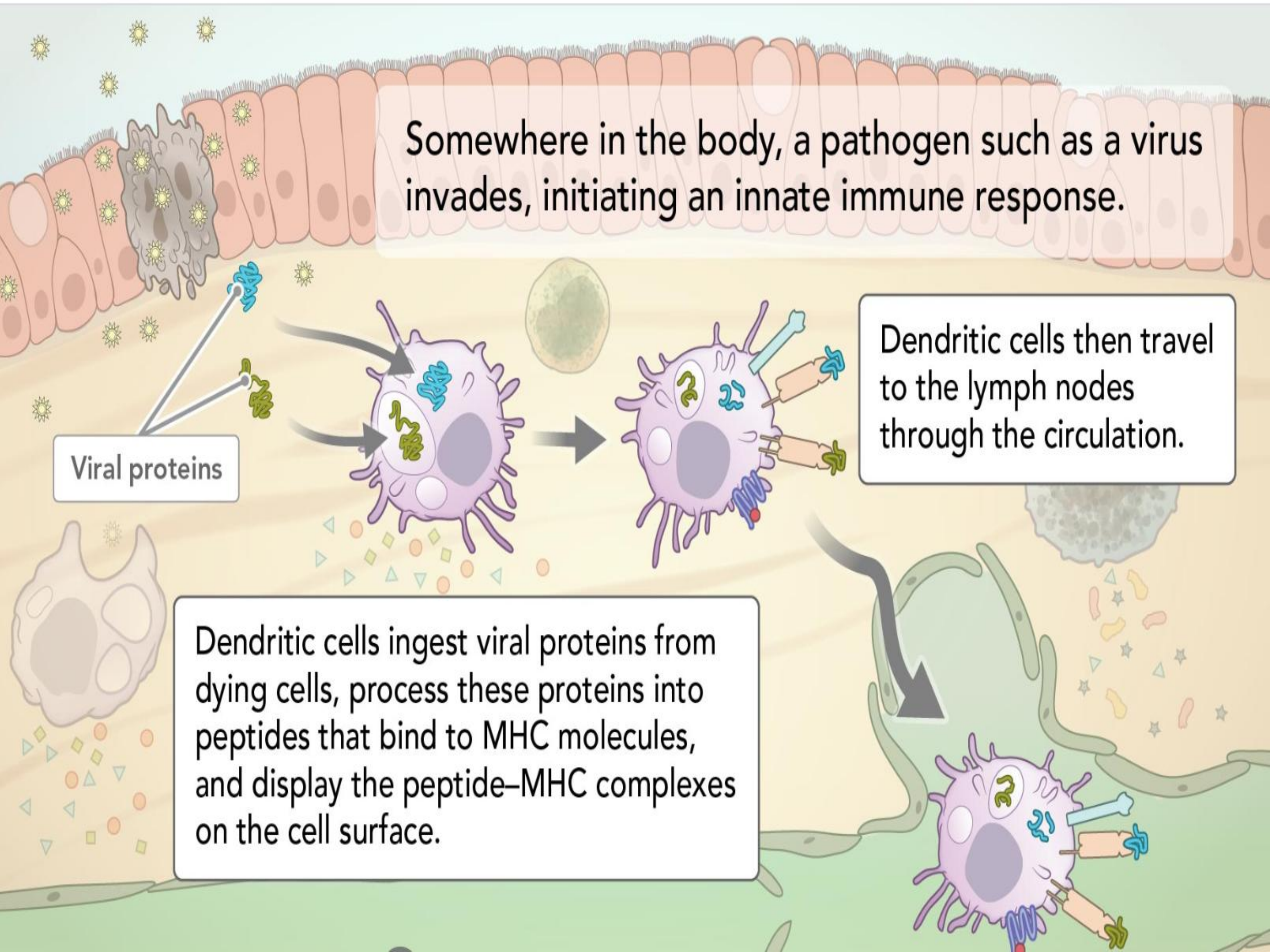
CD8⁺ T cells recognize peptides bound to **MHC I molecules**, which are present on most nucleated cells.



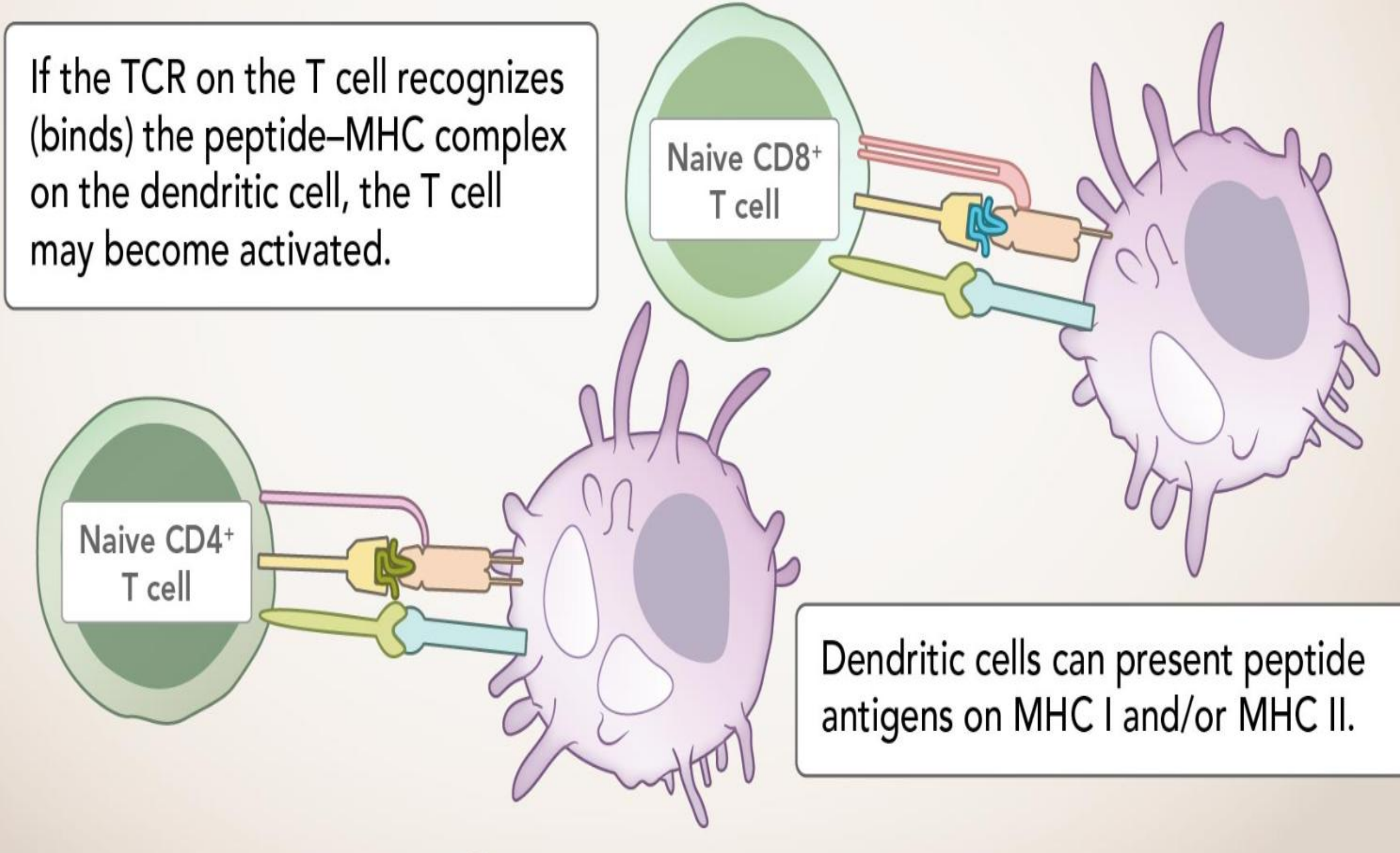


CD4⁺ T cells recognize peptides bound to **MHC II molecules**, which are only present on specialized antigen-presenting cells.

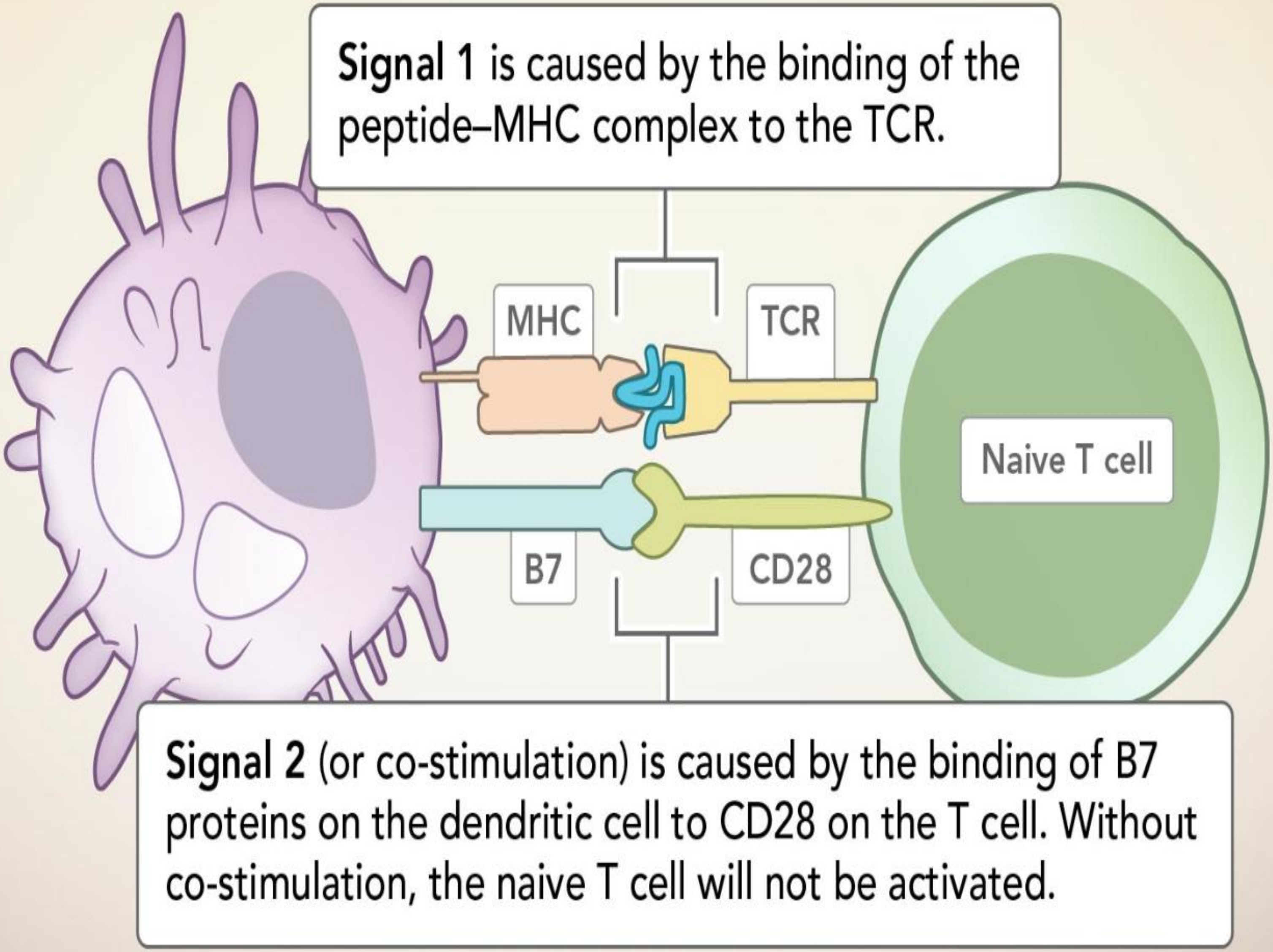

To understand how T cells act in adaptive immunity, let's follow an example of a T cell response to an invading virus.


Somewhere in the body, a pathogen such as a virus invades, initiating an innate immune response.
Viral proteins
Dendritic cells then travel to the lymph nodes through the circulation.
Dendritic cells ingest viral proteins from dying cells, process these proteins into peptides that bind to MHC molecules, and display the peptide–MHC complexes on the cell surface.

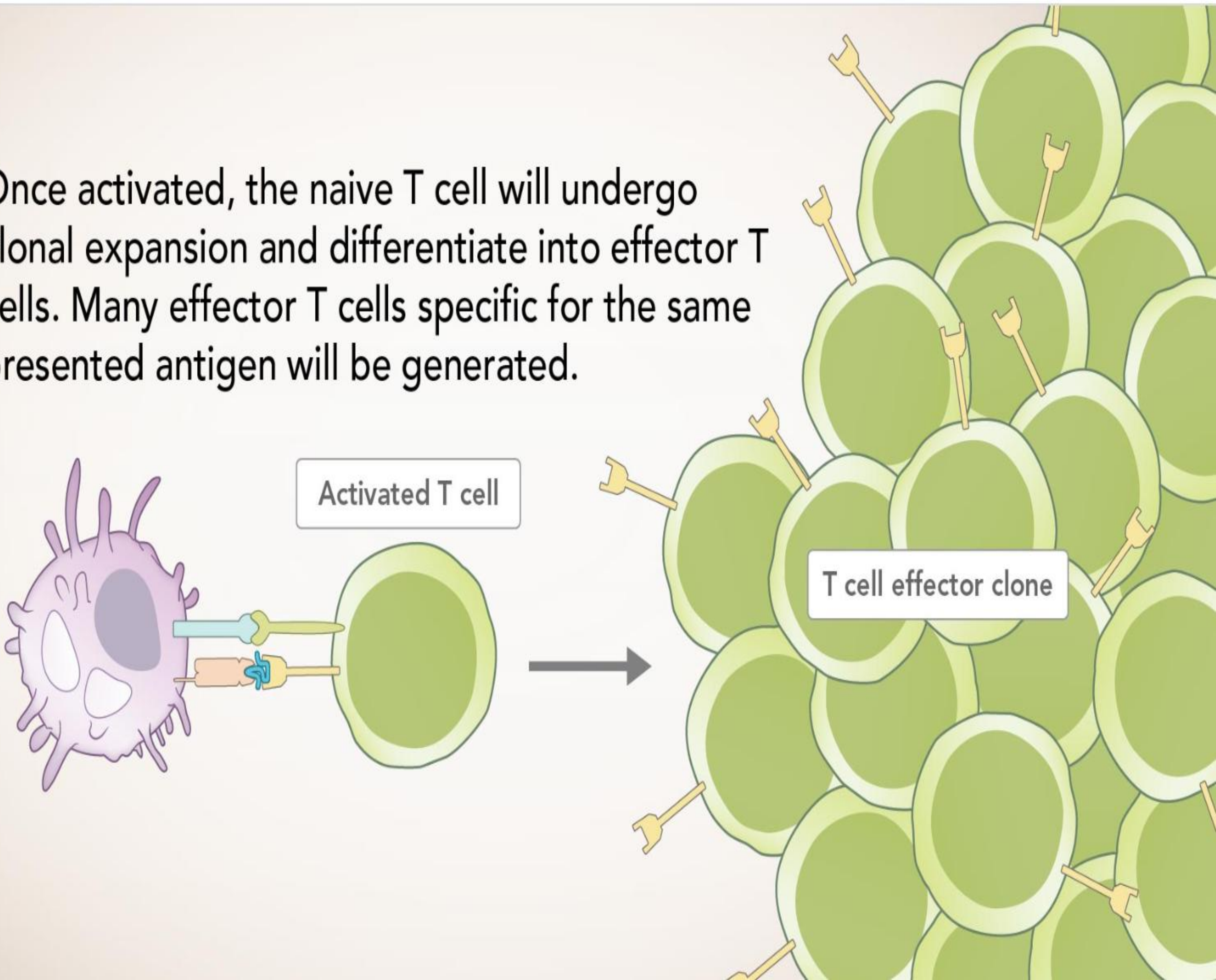
In the lymph nodes, naive T cells encounter these dendritic cells presenting viral peptides on an MHC molecule.



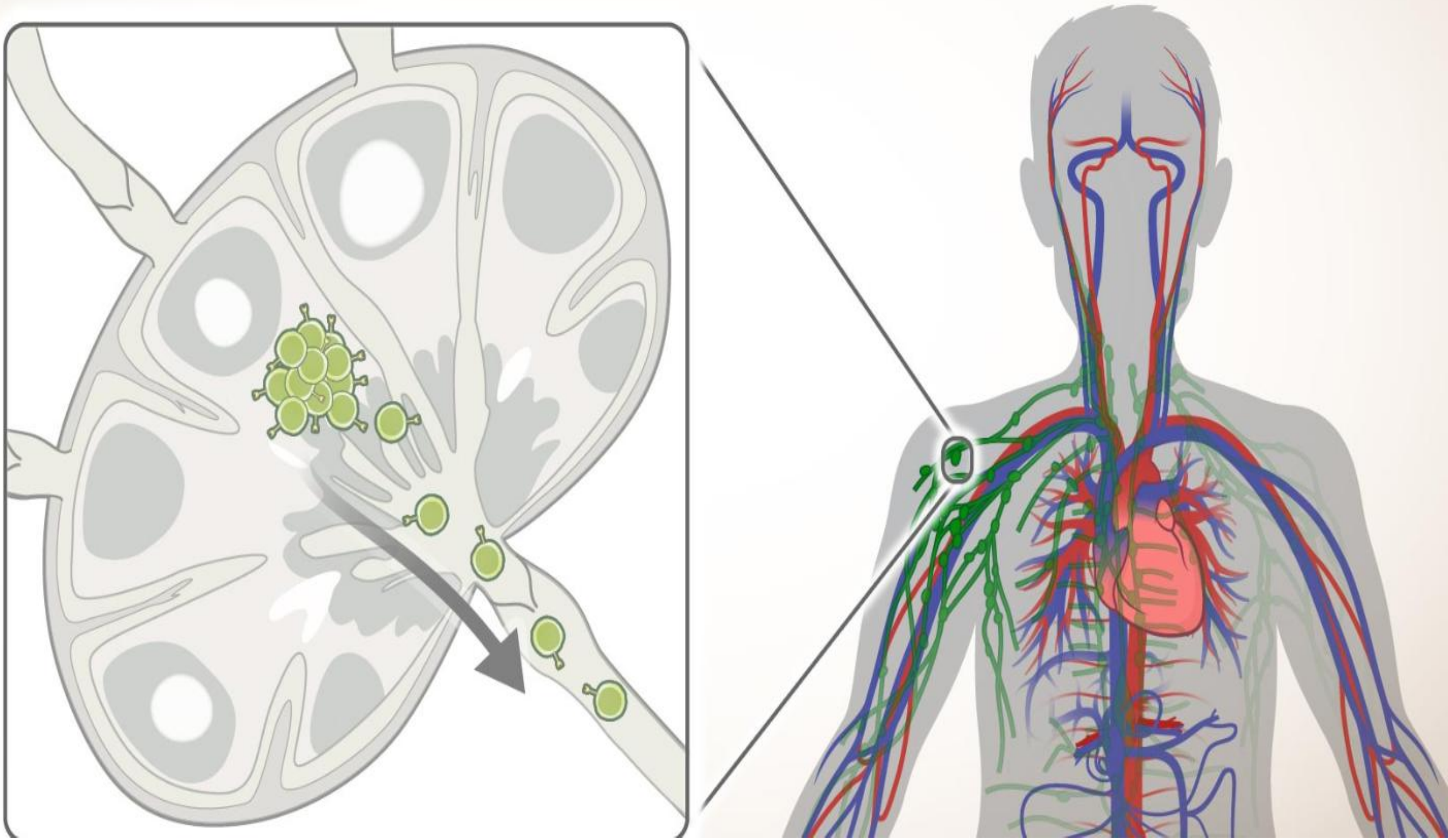
To become activated, the naive T cell must receive two signals:



Once activated, the naive T cell will undergo clonal expansion and differentiate into effector T cells. Many effector T cells specific for the same presented antigen will be generated.

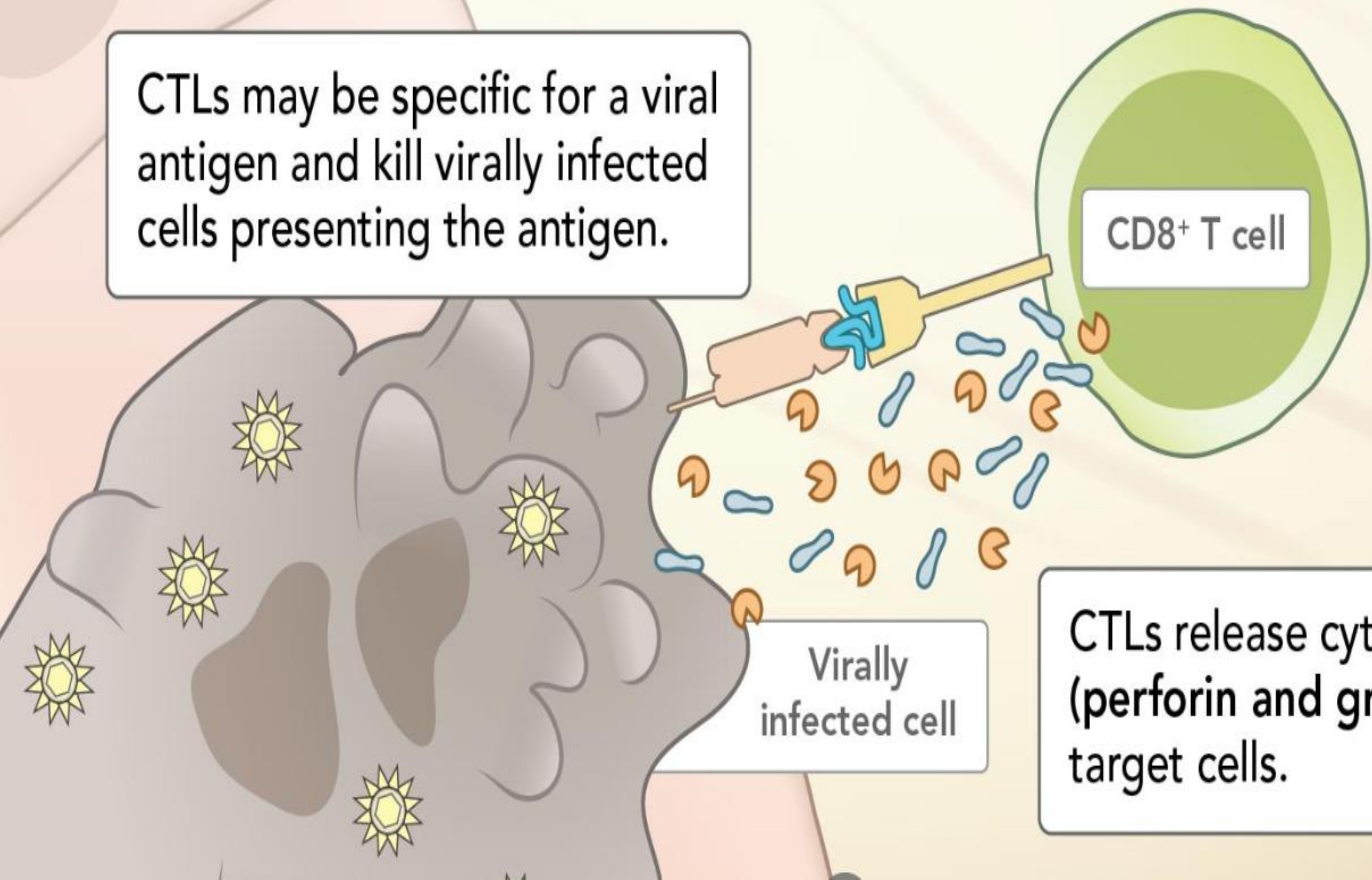


Effector cells can then leave the lymph node and travel through the circulation to carry out immune functions.

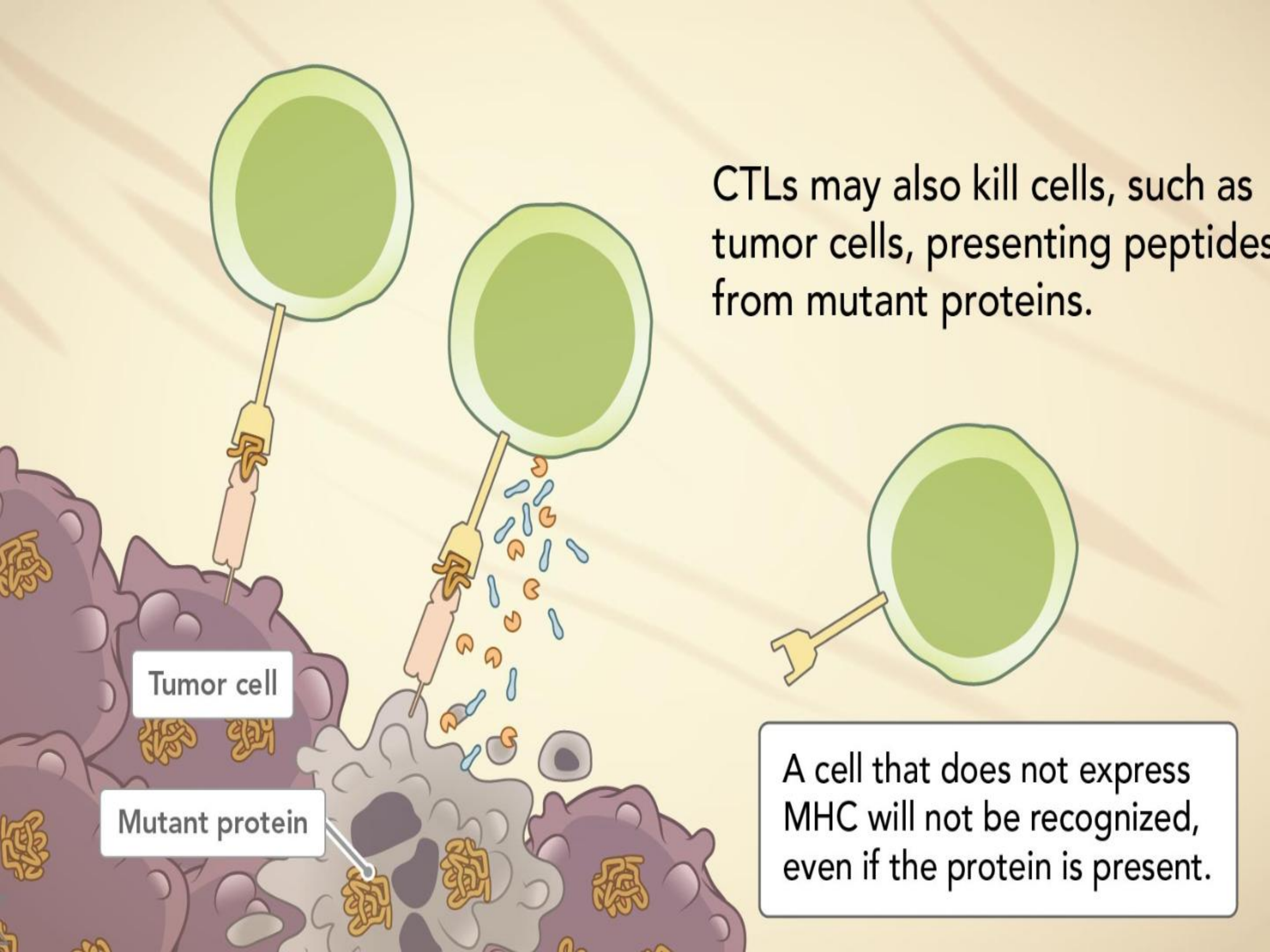


Effector $CD8^+$ cells are also called **cytotoxic T lymphocytes** (CTLs). These cells travel through the body and kill cells presenting the peptide–MHC I complex they recognize.

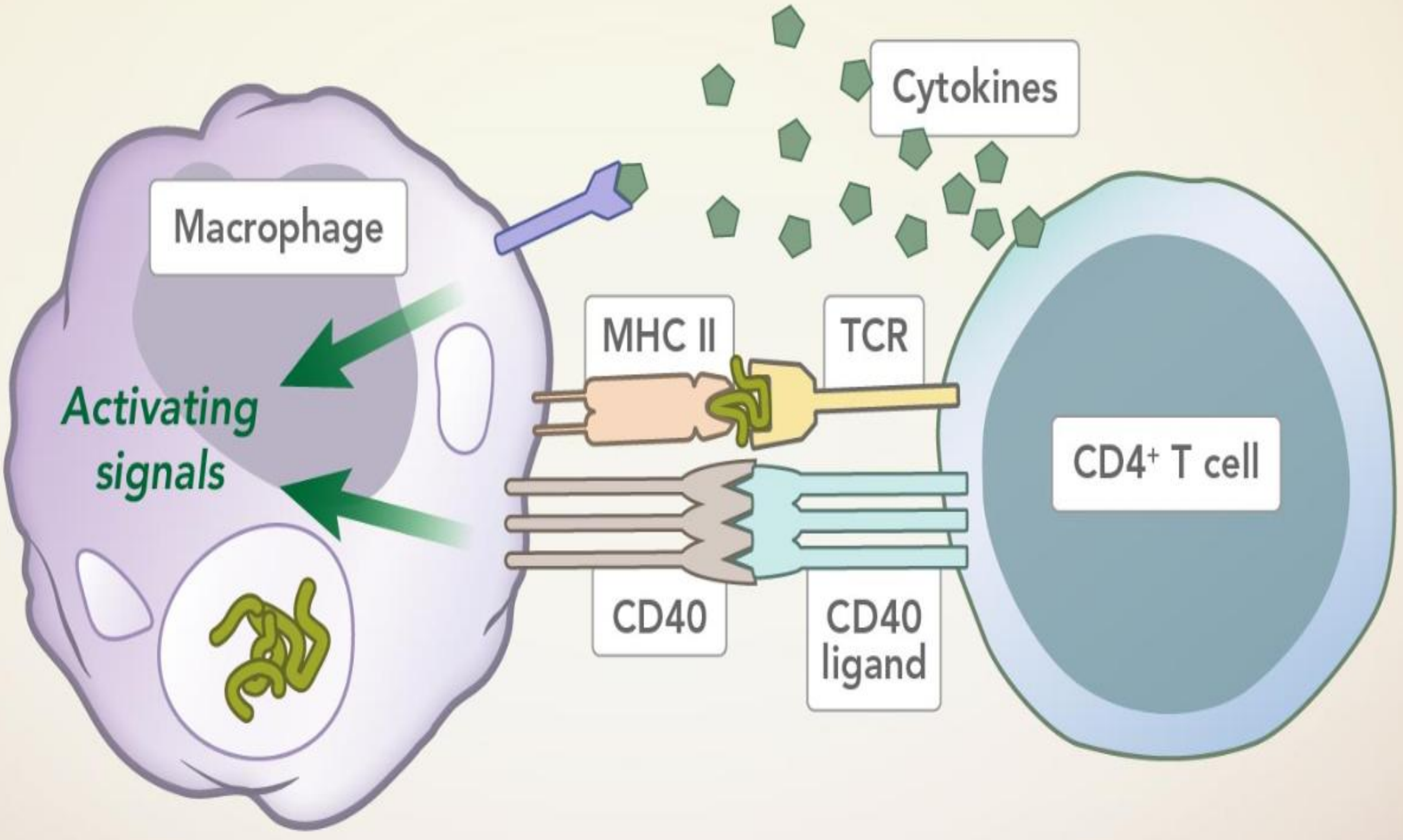
CTLs may be specific for a viral antigen and kill virally infected cells presenting the antigen.



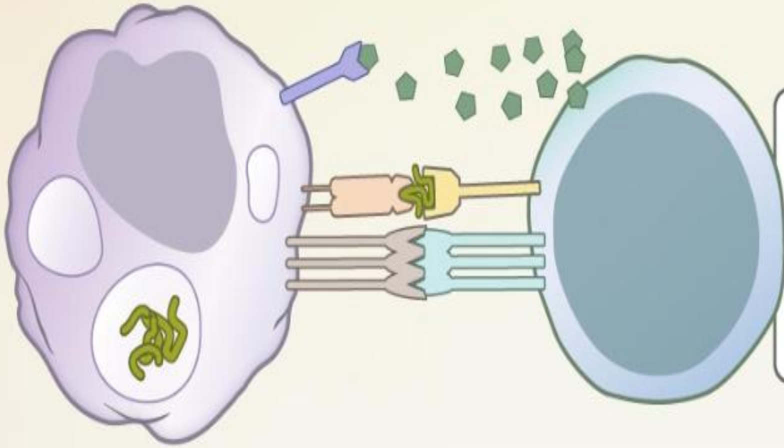
CTLs release cytotoxic molecules (**perforin and granzymes**) to kill target cells.


CTLs may also kill cells, such as tumor cells, presenting peptides from mutant proteins.
Tumor cell
Mutant protein
A cell that does not express MHC will not be recognized, even if the protein is present.

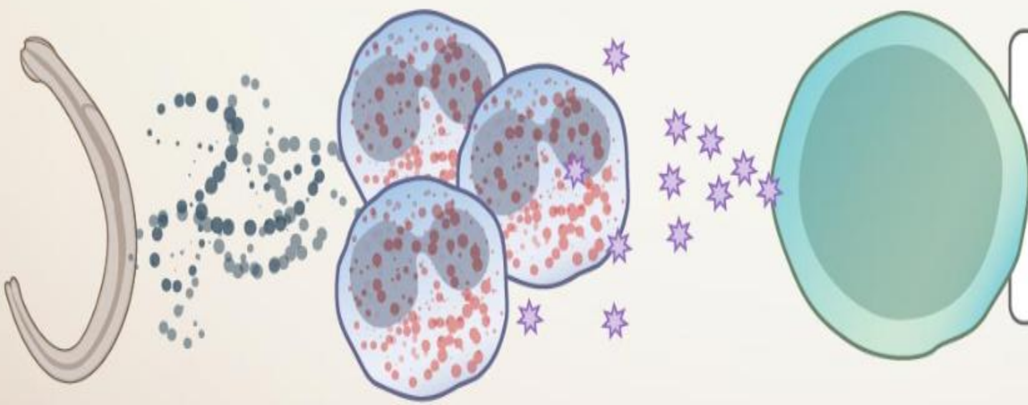
CD4$^+$ effector cells are also called **helper T cells**. These cells help other immune cells execute their functions.



Different subtypes of CD4⁺ T cells have different functions.

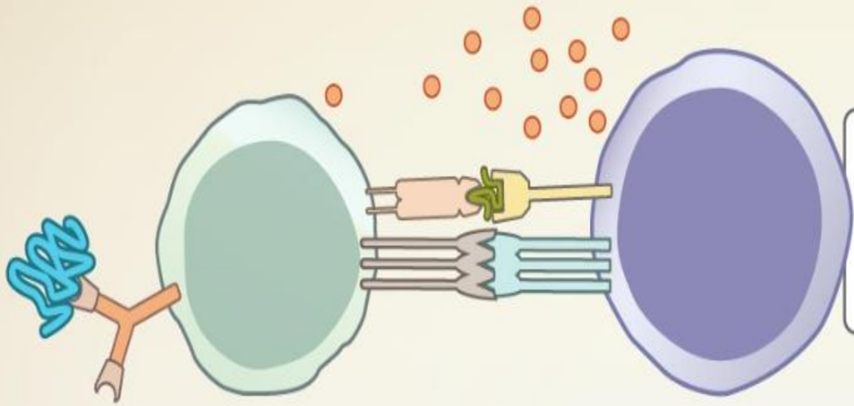


Th1 cells activate macrophages to enhance their ability to kill intracellular microbes.

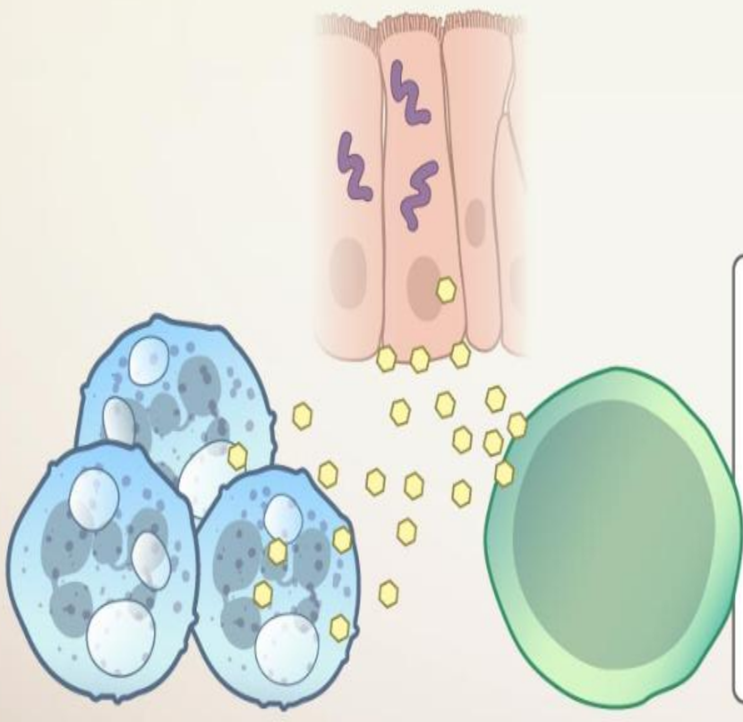


Th2 cells activate eosinophils that kill parasites and macrophages to promote tissue repair and fibrosis.

Different subtypes of $CD4^{+}$ T cells have different functions.

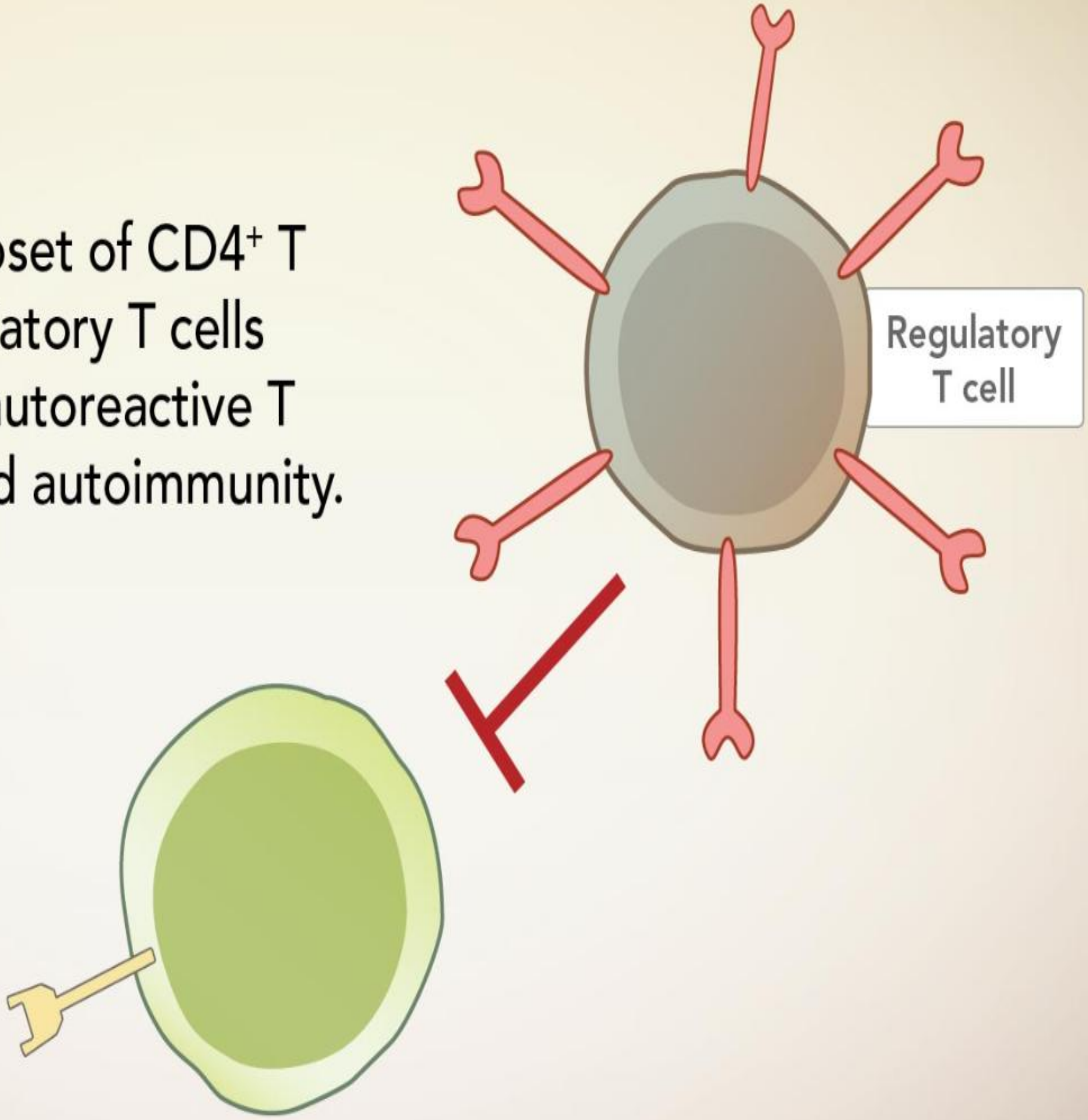


T follicular helper (Tfh) cells help B cells generate effective antibody responses.

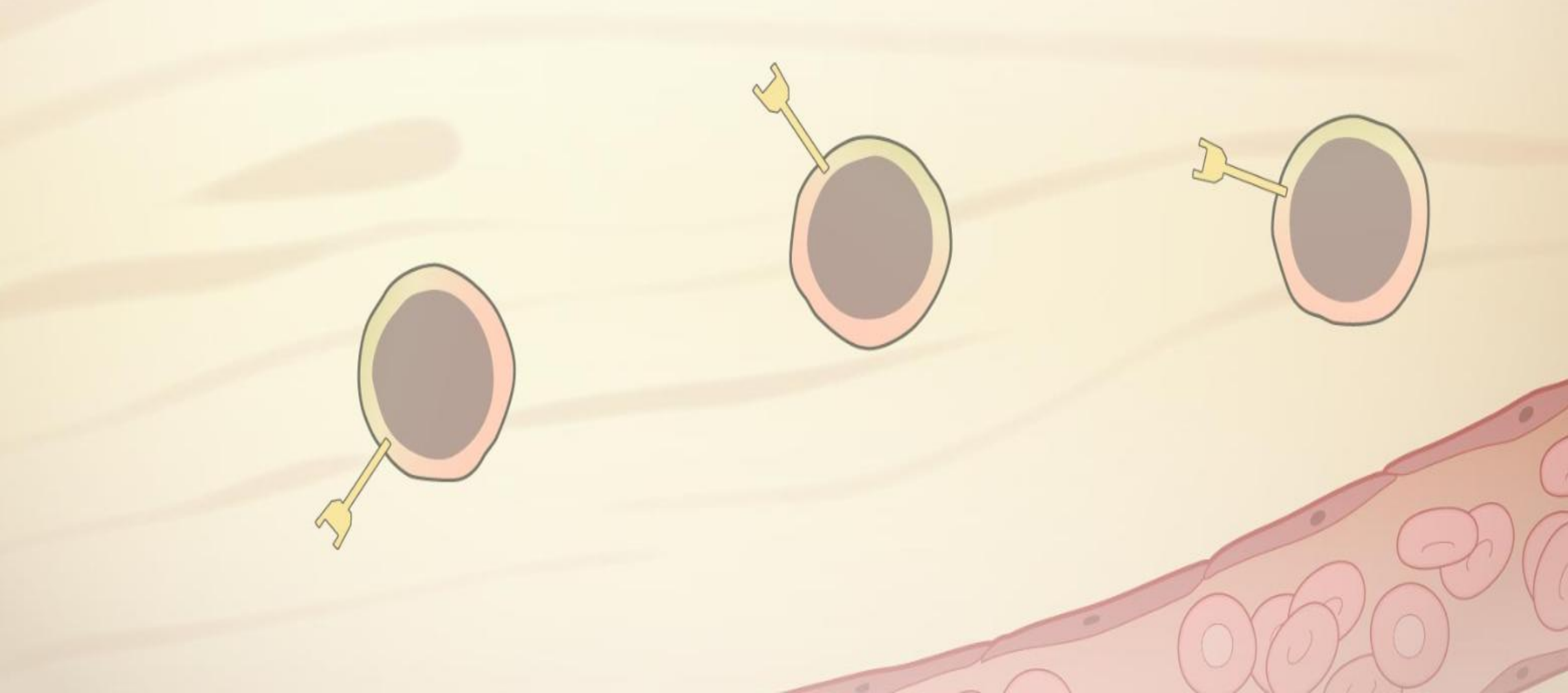


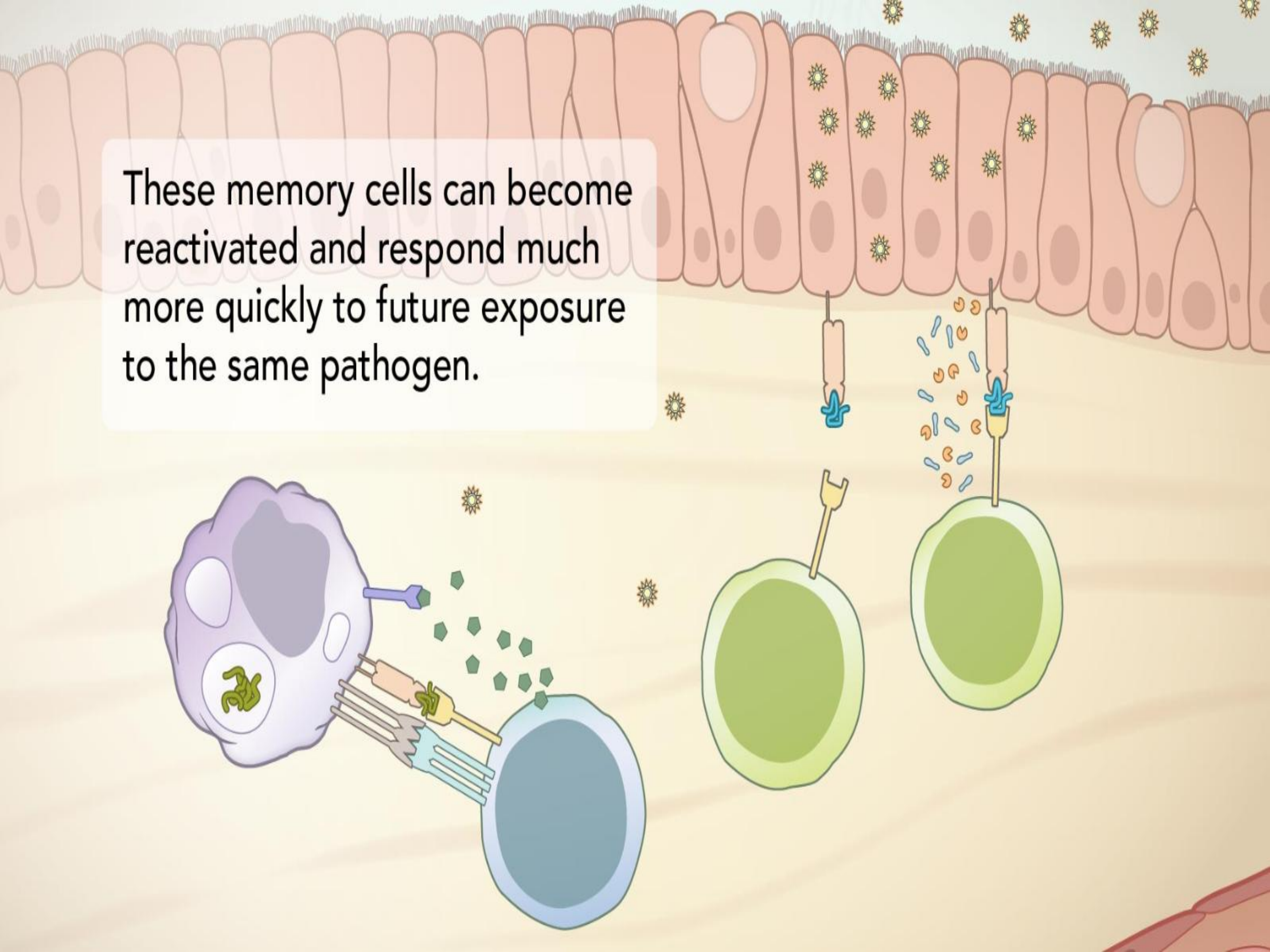
Th17 cells promote inflammatory responses, including recruitment of neutrophils, to kill extracellular microbes and stimulate epithelial cells to express antimicrobial molecules at barrier tissues.

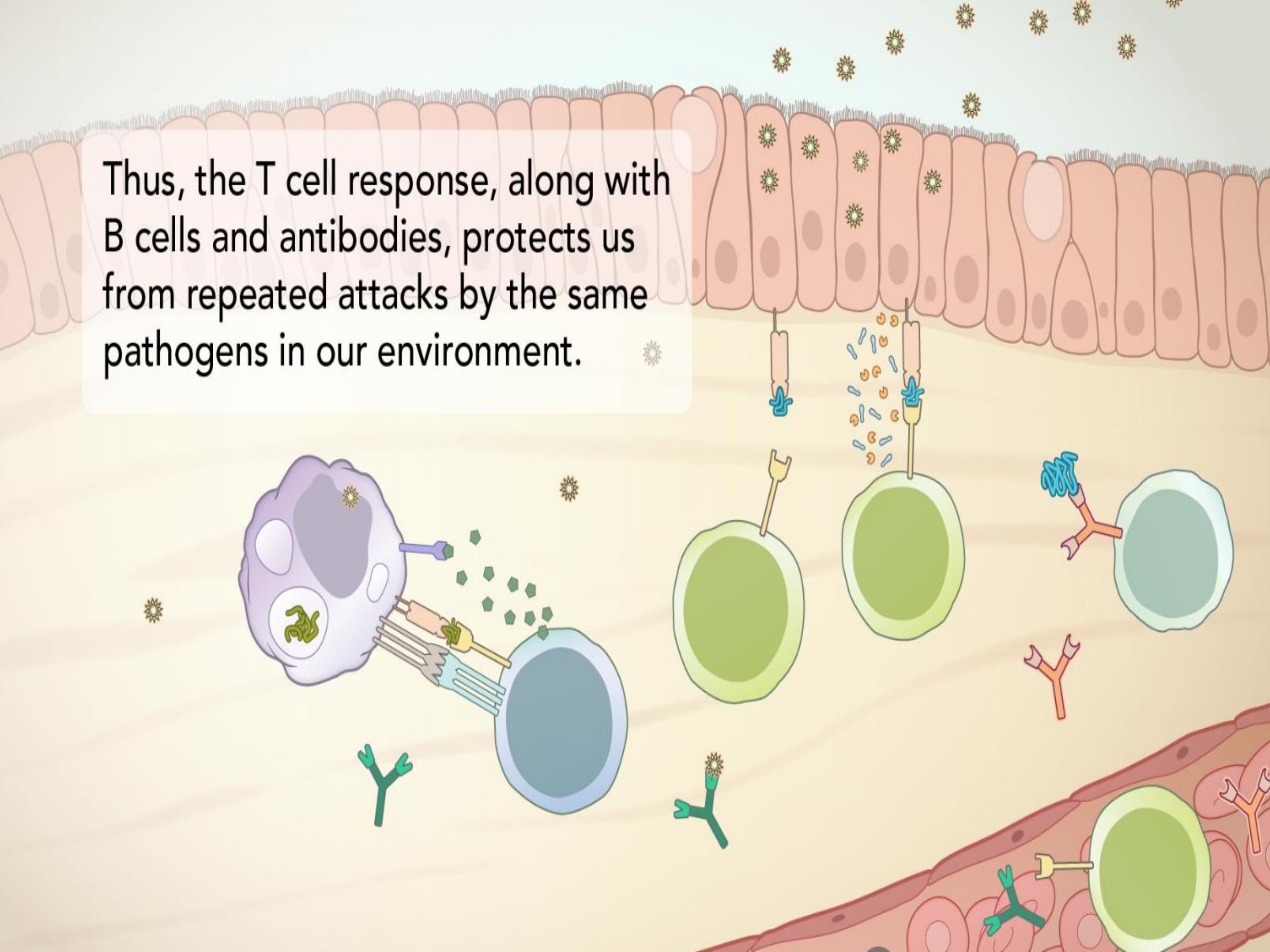
An additional subset of $CD4^+$ T cells, called regulatory T cells (Tregs), prevent autoreactive T cell activation and autoimmunity.



After a T cell response has eliminated an infection, some long-lived **memory T cells** specific for the microbe will remain in the body.




These memory cells can become reactivated and respond much more quickly to future exposure to the same pathogen.


Thus, the T cell response, along with B cells and antibodies, protects us from repeated attacks by the same pathogens in our environment.