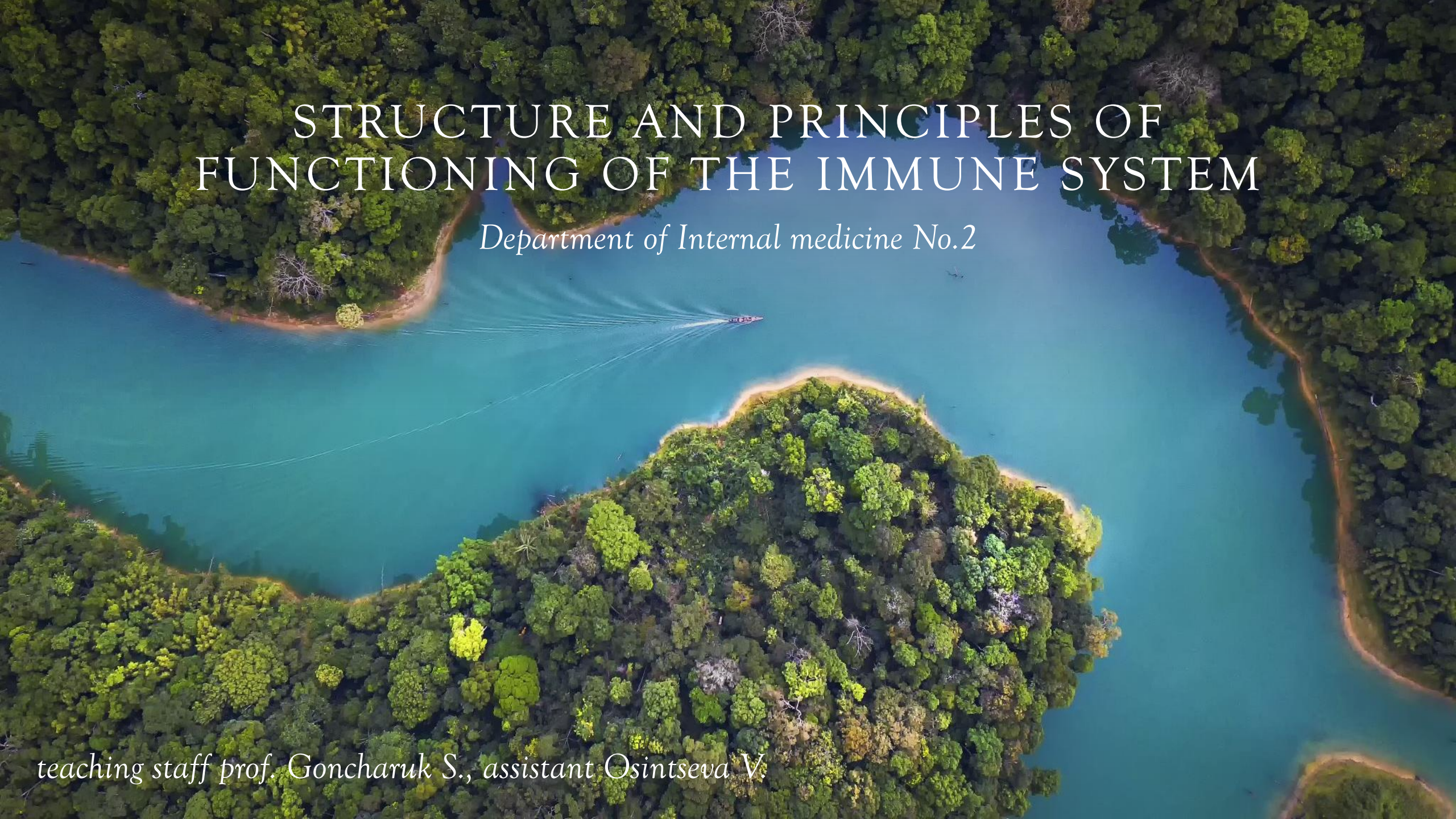


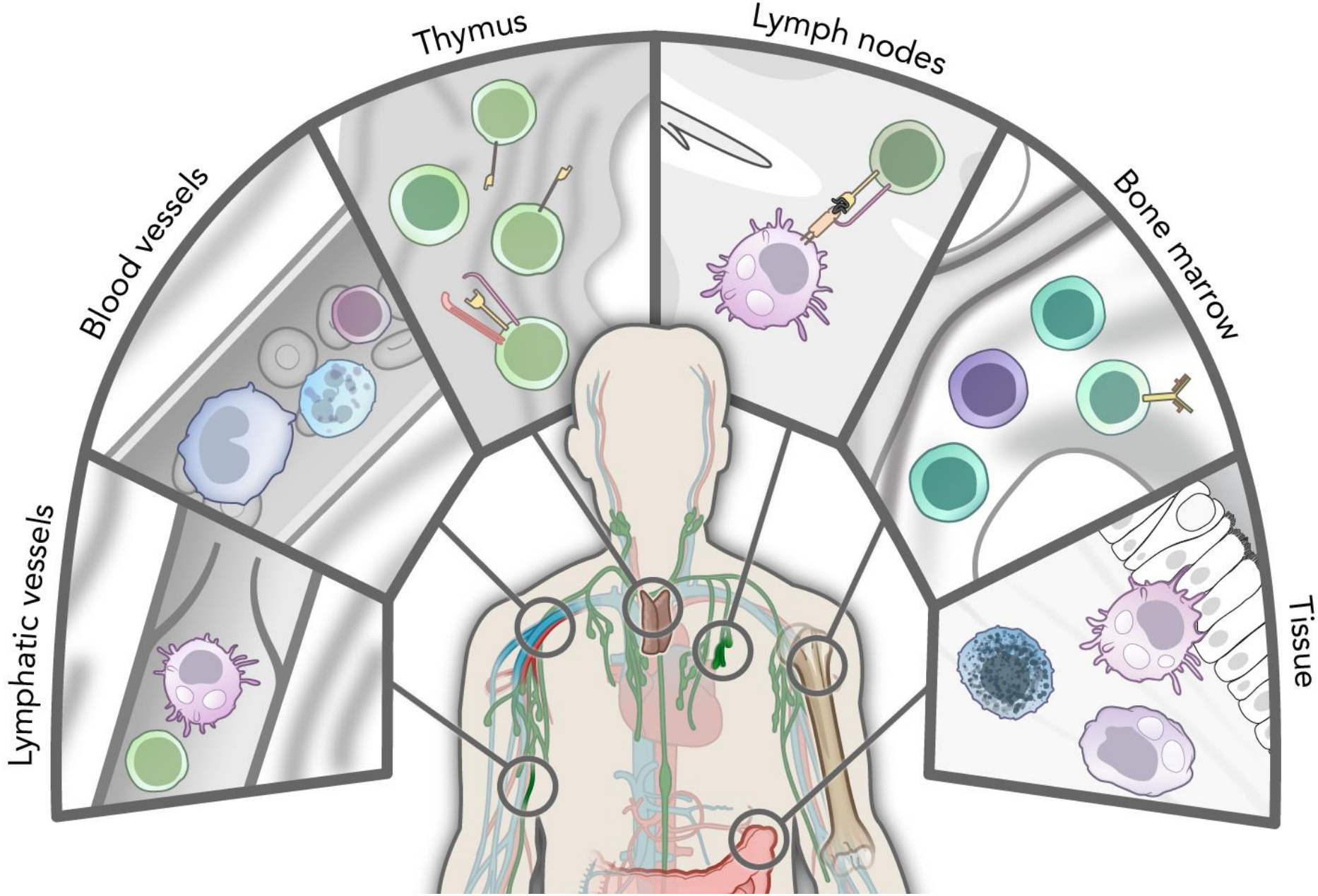
STRUCTURE AND PRINCIPLES OF FUNCTIONING OF THE IMMUNE SYSTEM

Department of Internal medicine No.2

teaching staff prof. Goncharuk S., assistant Osintseva V.

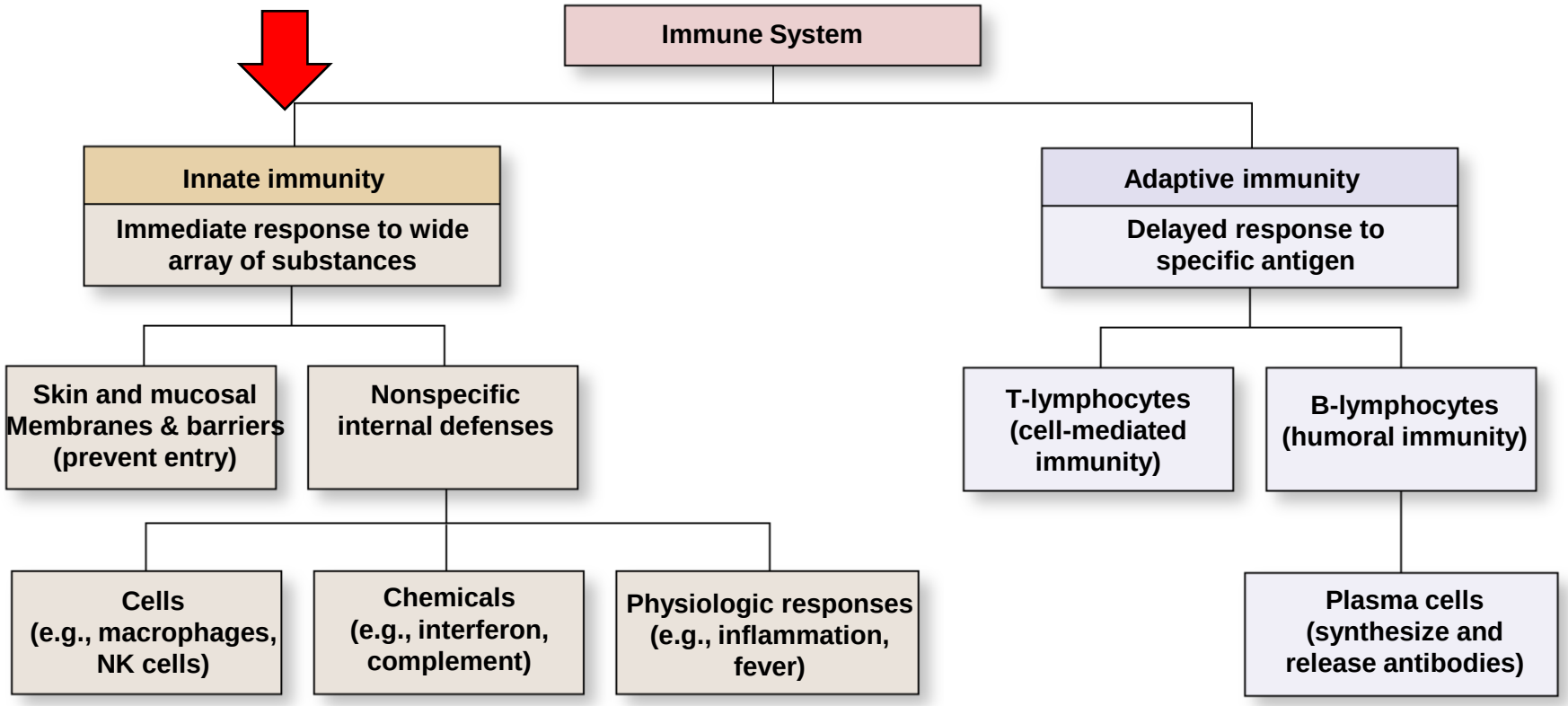
Immunity is defined as **resistance to disease**, specifically infectious disease

- The collection of cells, tissues, and molecules that mediate resistance to infections is called the **immune system**,
- and the coordinated reaction of these cells and molecules to infectious microbes comprises an **immune response**.
- **Immunology** is the study of the immune system, including its responses to microbial pathogens and damaged tissues and its role in disease

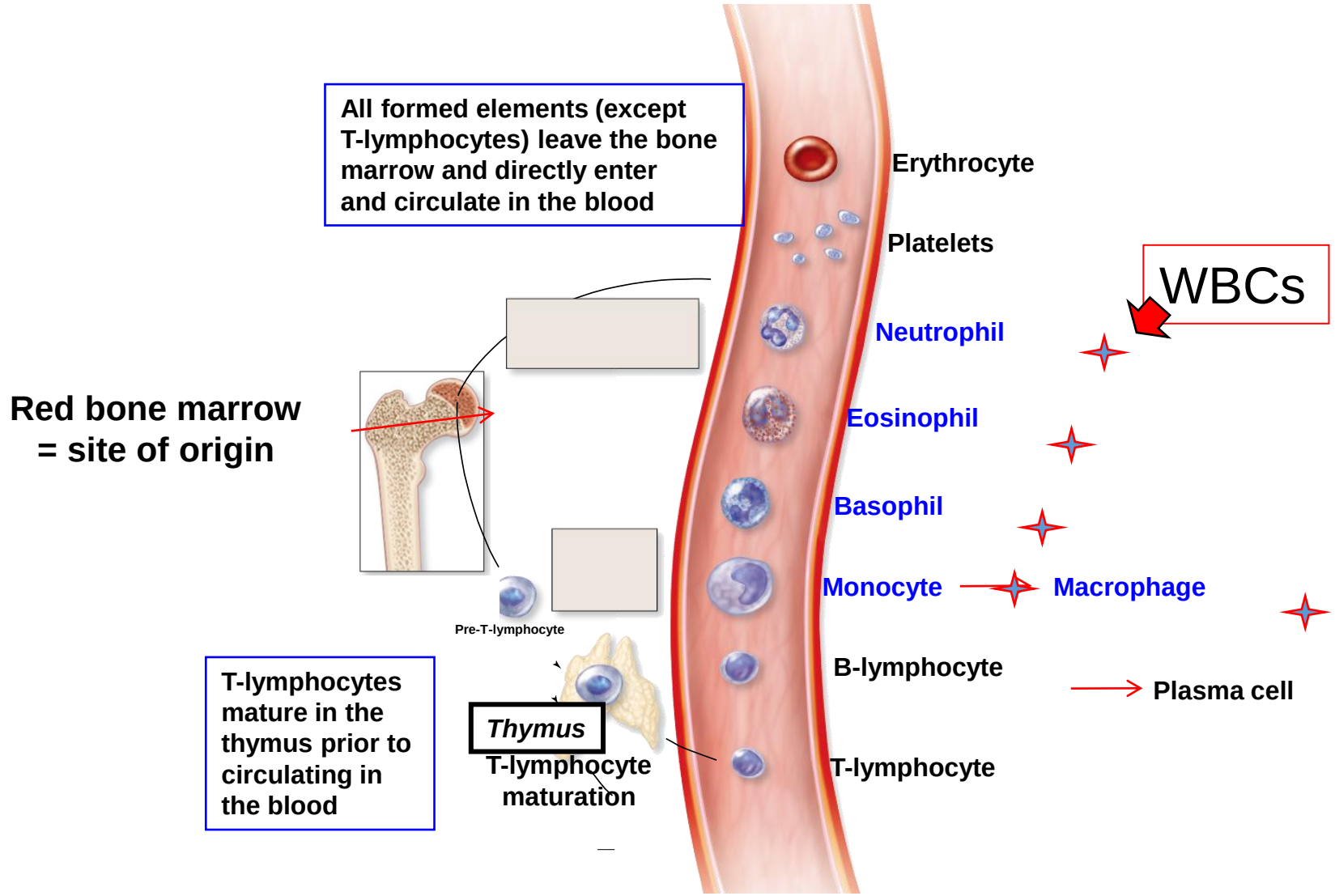

Thymus
Lymph nodes
Blood vessels
Bone marrow
Lymphatic vessels
Tissue

Basic definitions and concepts:

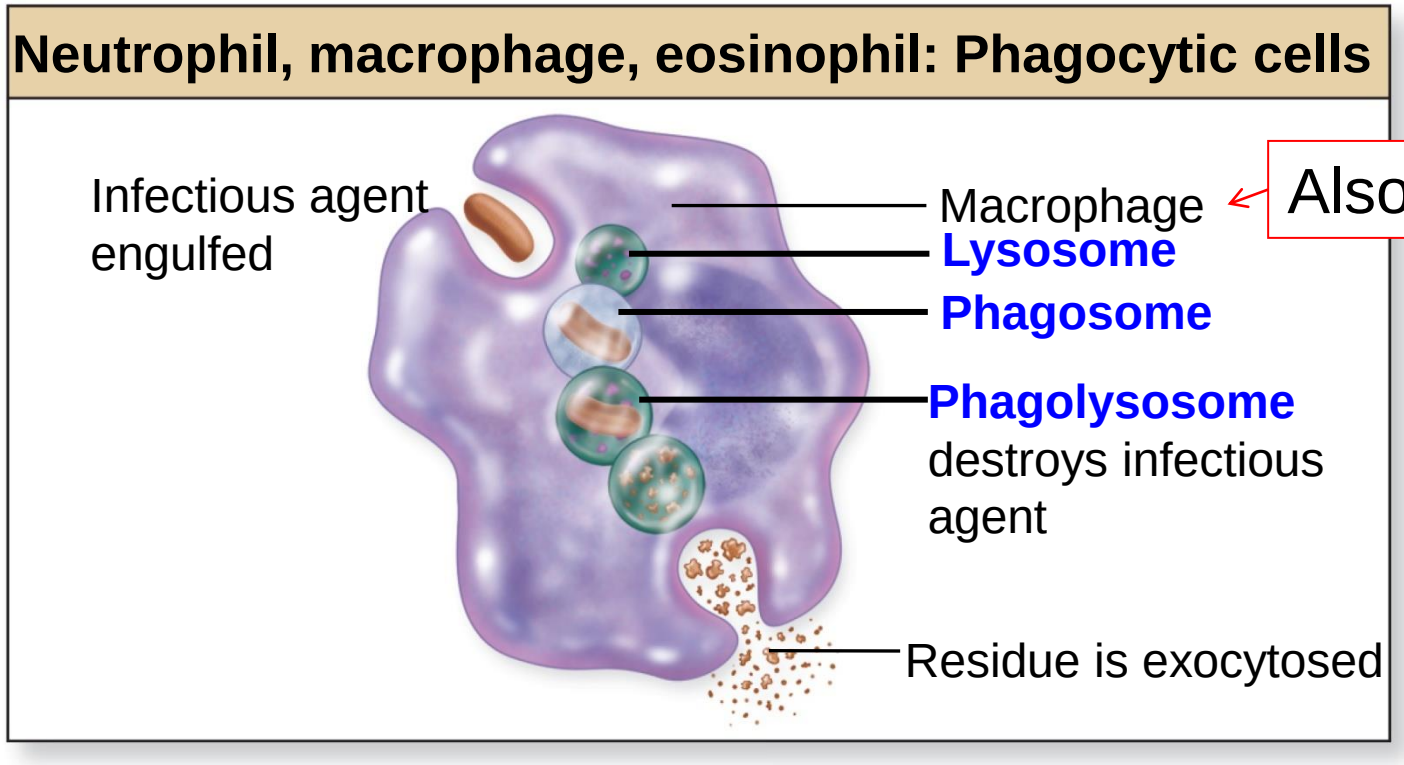
- The most important physiologic function of the immune system is to prevent or eradicate infections
- Non-infectious foreign substances and substances produced by self can sometimes cause immune responses; this can lead to disease
- Our understanding of immunology has led to many therapies for a wide variety of disorders


Immune System
Innate immunity
Immediate response to wide array of substances
Adaptive immunity
Delayed response to specific antigen
Skin and mucosal Membranes & barriers (prevent entry)
Nonspecific internal defenses
T-lymphocytes (cell-mediated immunity)
B-lymphocytes (humoral immunity)
Cells (e.g., macrophages, NK cells)
Chemicals (e.g., interferon, complement)
Physiologic responses (e.g., inflammation, fever)
Plasma cells (synthesize and release antibodies)

Major **cellular components** of the **Innate- Nonspecific System**



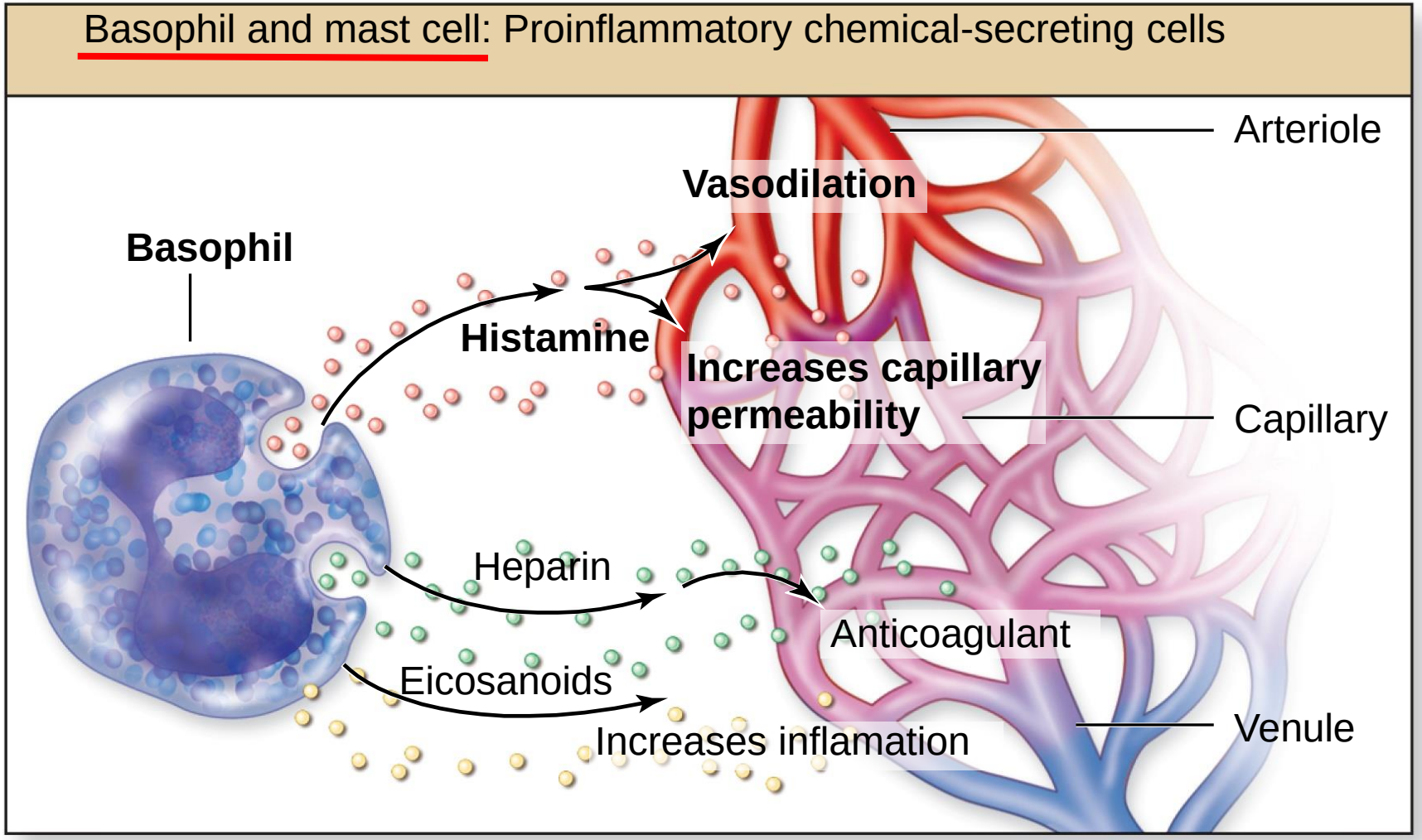
Phagocytes: engulf bacteria, release toxic chemicals, present antigens



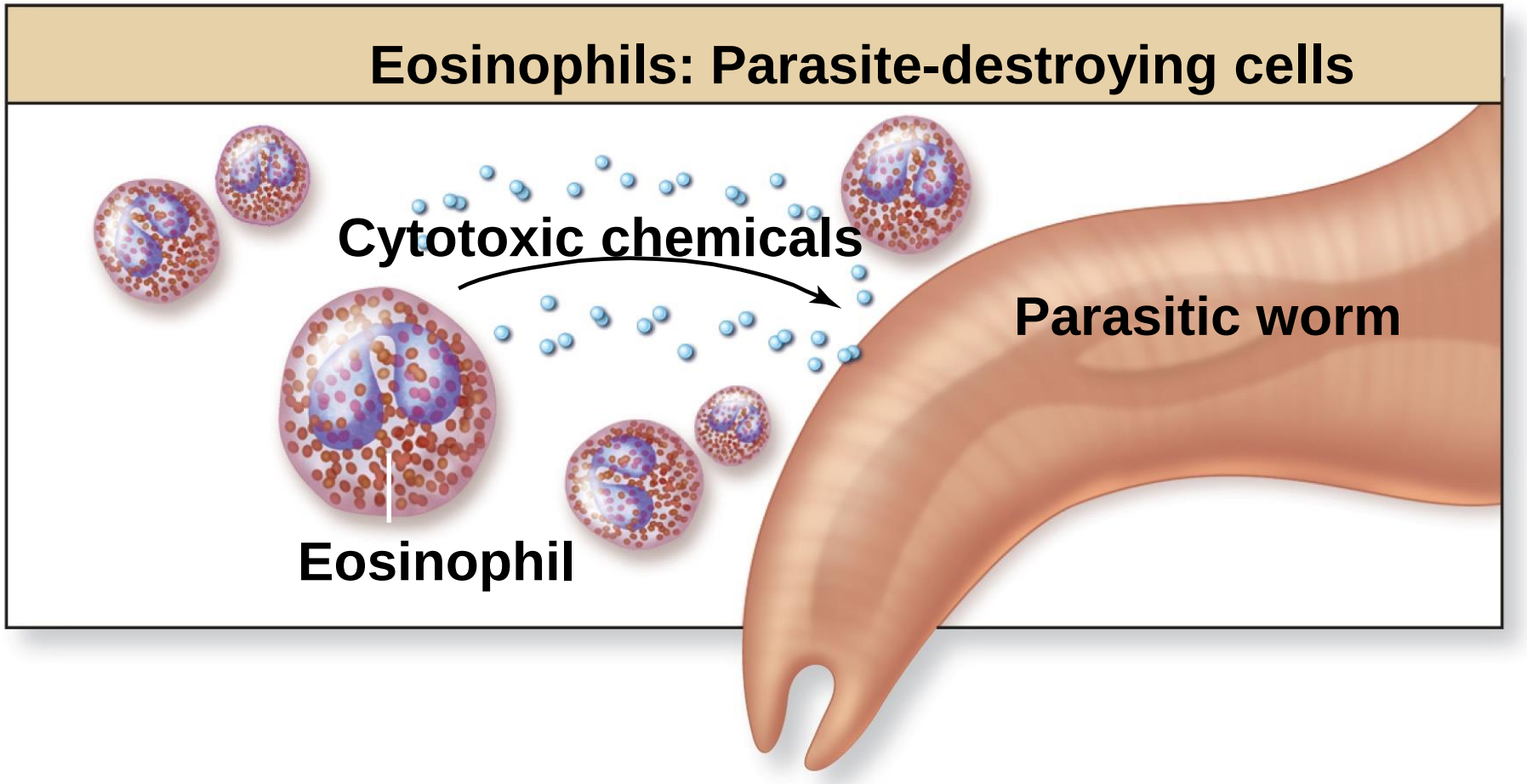
Also an APC

Originally WBCs – they migrate into connective tissue
The "clean-up crew": phagocytose debris and digest via lysosomes
Neutrophils enter first then macrophages (derived from monocytes)
Eosinophils involved with parasitic infections and antigen-antibody complexes

Basophils open up vessels & increase blood flow

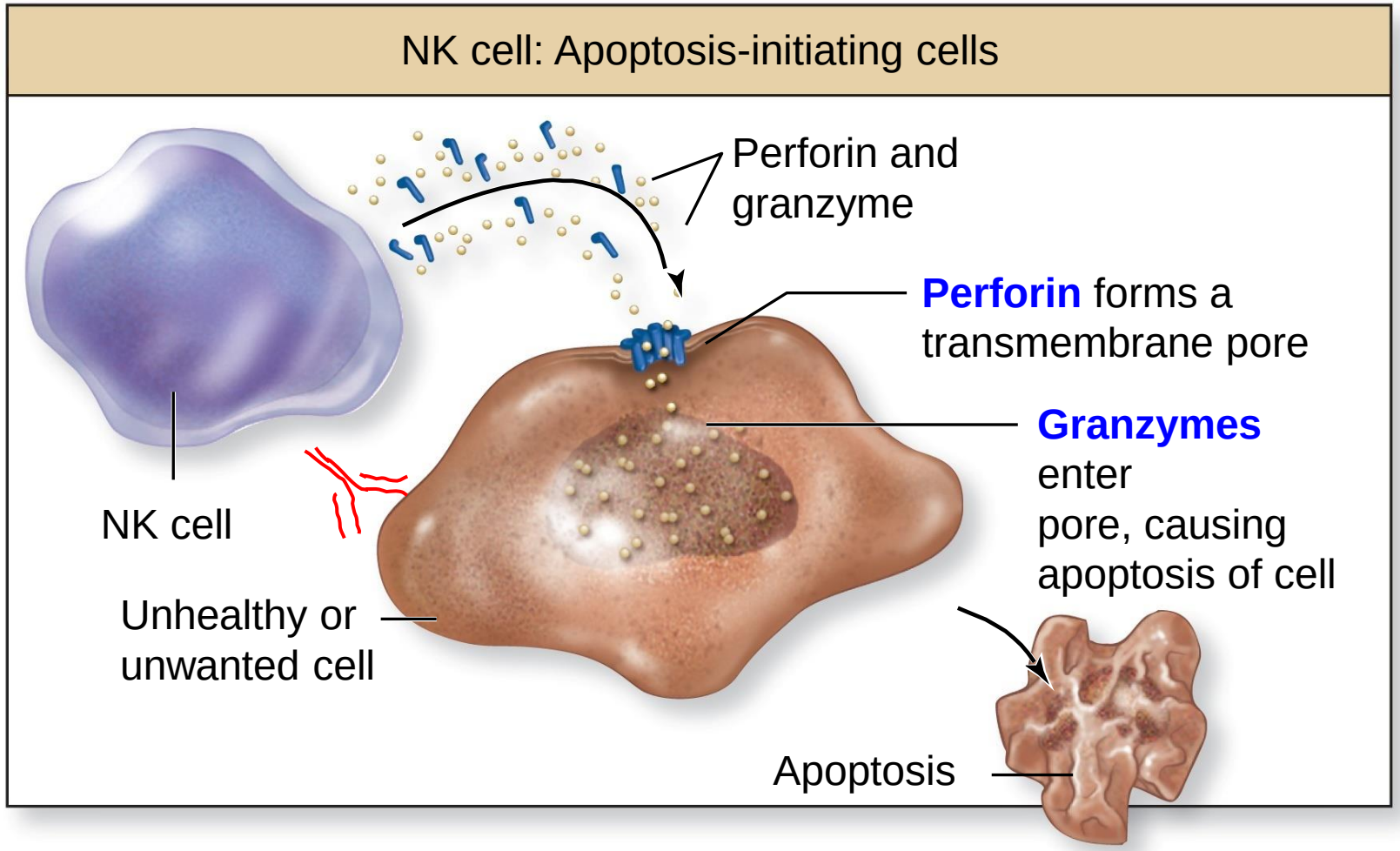


Eosinophils: Parasite-Destroying Cells



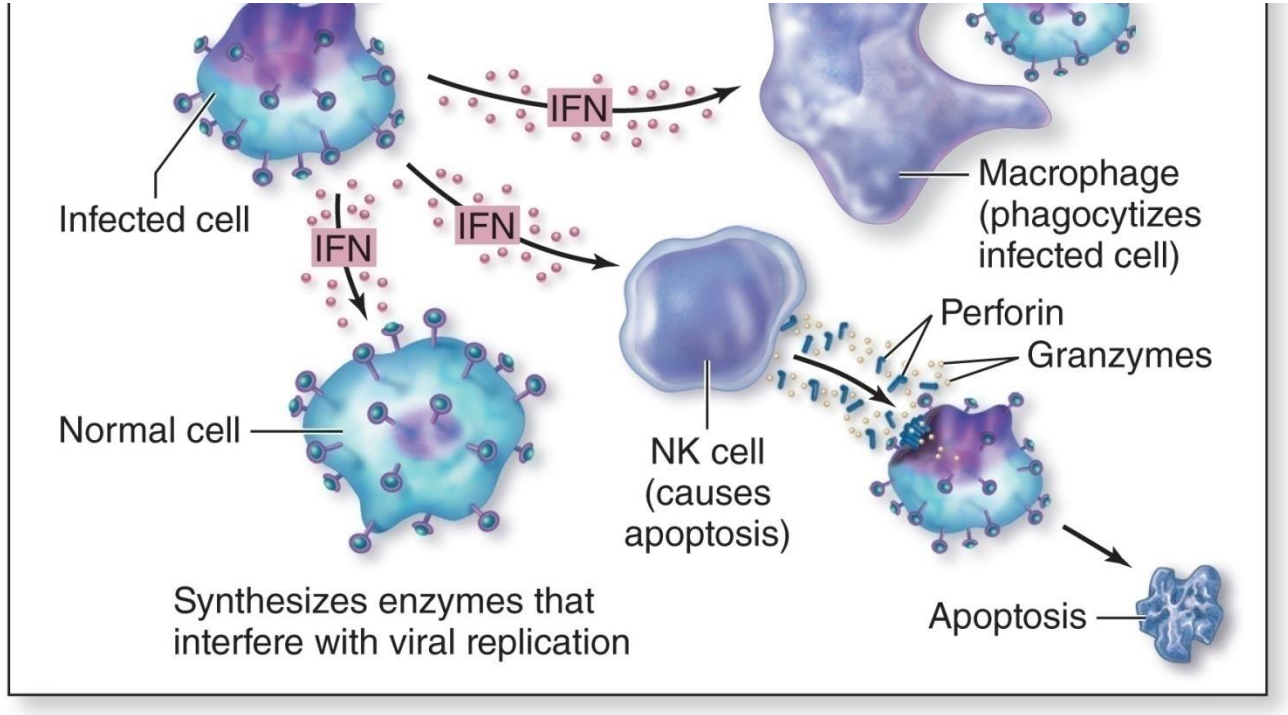
Eosinophils also phagocytose antigen-antibody complexes

Immunological surveillance: NK cells



Recognizes unhealthy cell (usually expressing abnormal proteins or viral proteins – uses perforins (make a hole in the membrane) and granzymes (initiate apoptosis – programmed cell death via gene expression

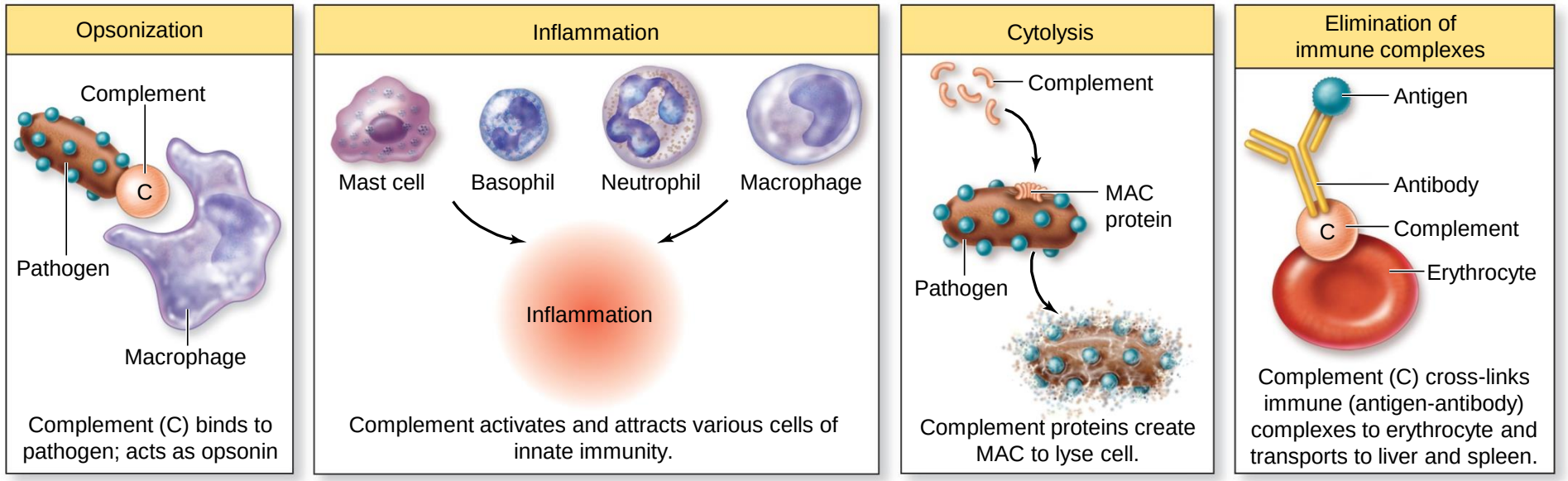
Interferons – signaling molecule (cytokine) released by viral-infected cells



- Binds receptors of neighboring cells:
  - promotes macrophage function and apoptosis of infected cell
  - triggers synthesis of enzymes destroying viral RNA or DNA
  - triggers synthesis of enzymes that inhibit synthesis of viral proteins

Complement Proteins (C1-C12)

~11 antimicrobial proteins in plasma – '*complements*' functions of antibodies
They have a number of functions (below) to defend against pathogens

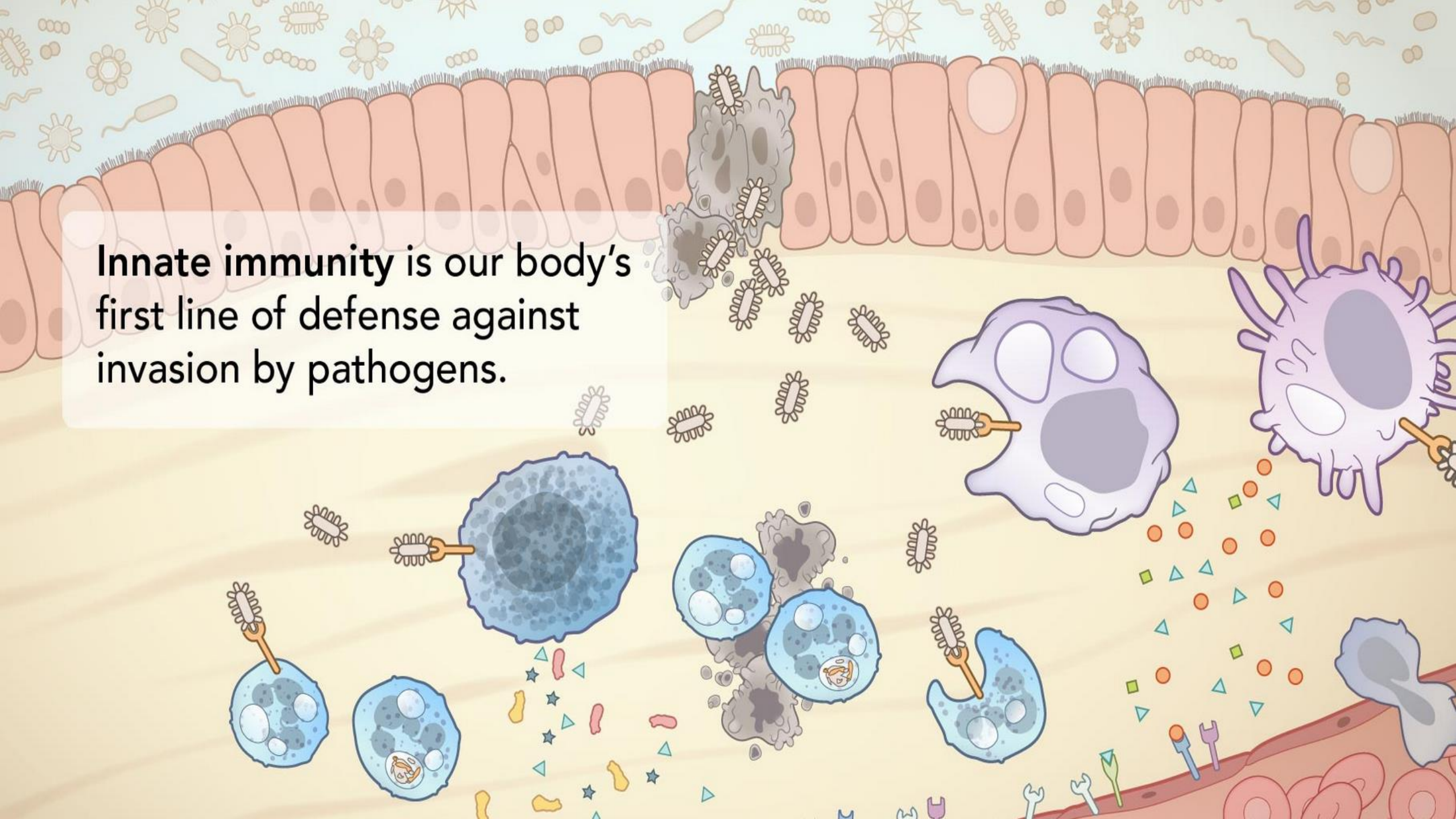


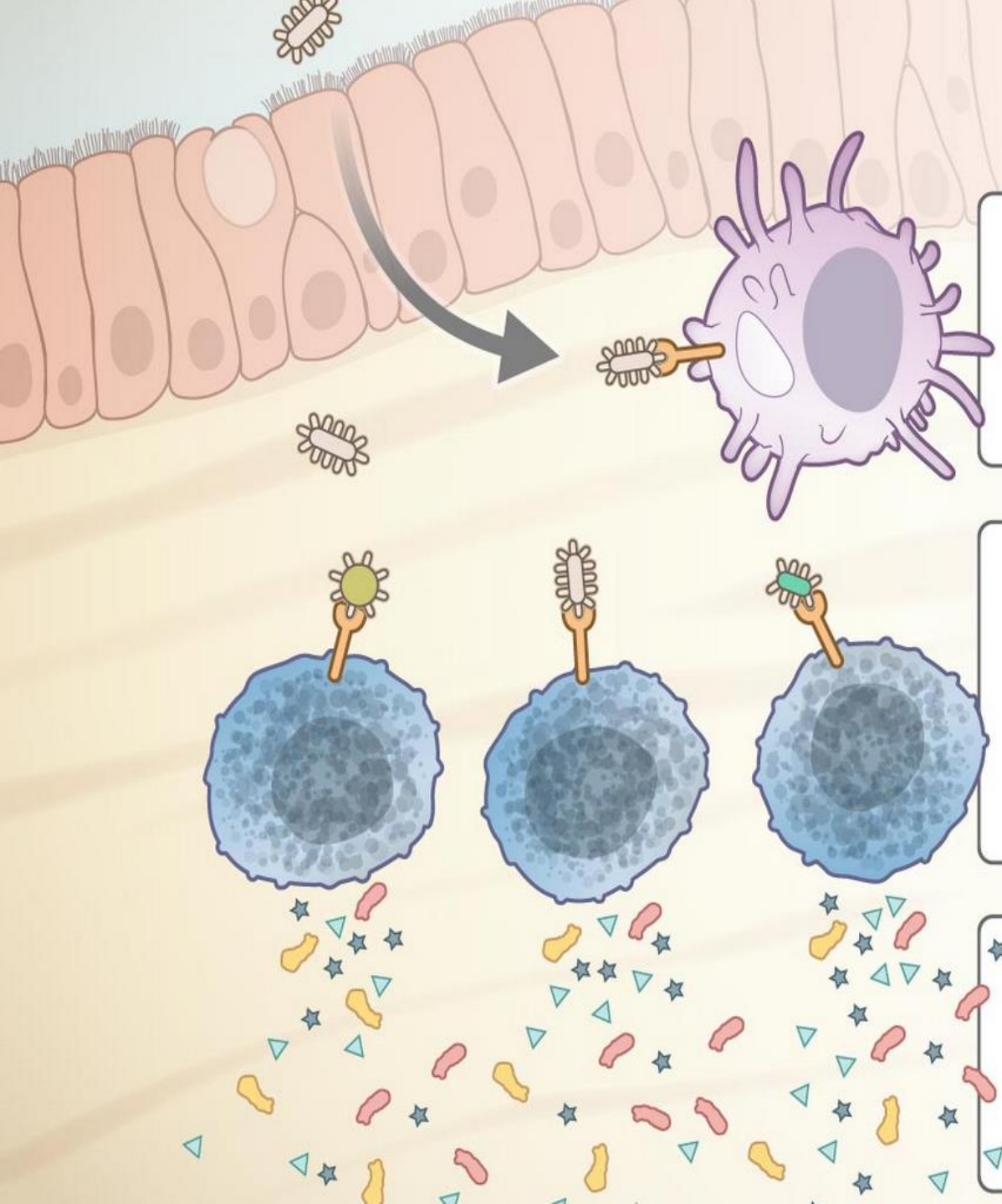
Opsonin – coats pathogen to make appear different and thus recognizable by macrophages
Inflammation - Activates mast cells, basophils, neutrophils, and macrophages to increase inflammatory response -
Cytolysis – causes cell lysis (Big MAC attack)
Eliminates Antigen-Antibody complexes on RBCs killed in spleen

Innate Immunity

—

Part 1


Innate immunity is our body's first line of defense against invasion by pathogens.



The innate immune system is...

Always ready to react

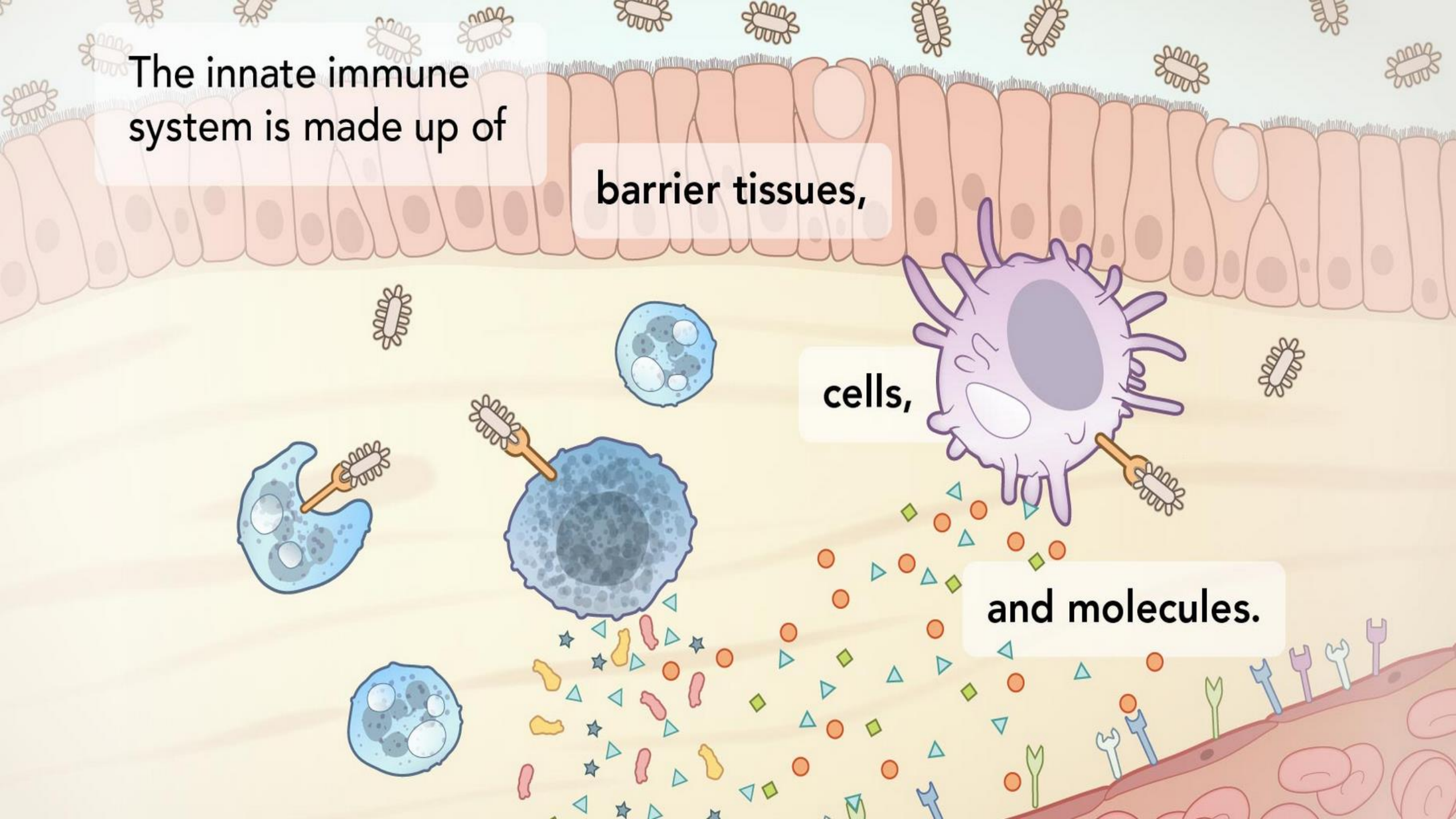
Provides the first response to injury and assault by pathogens.

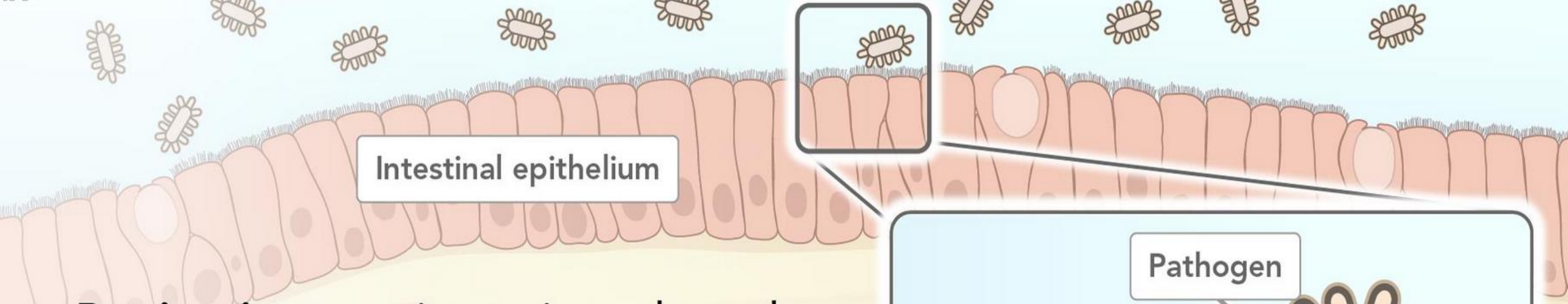
Broadly-specific

Recognizes common patterns associated with many pathogens or types of injury, rather than specific pathogens.

Consistent

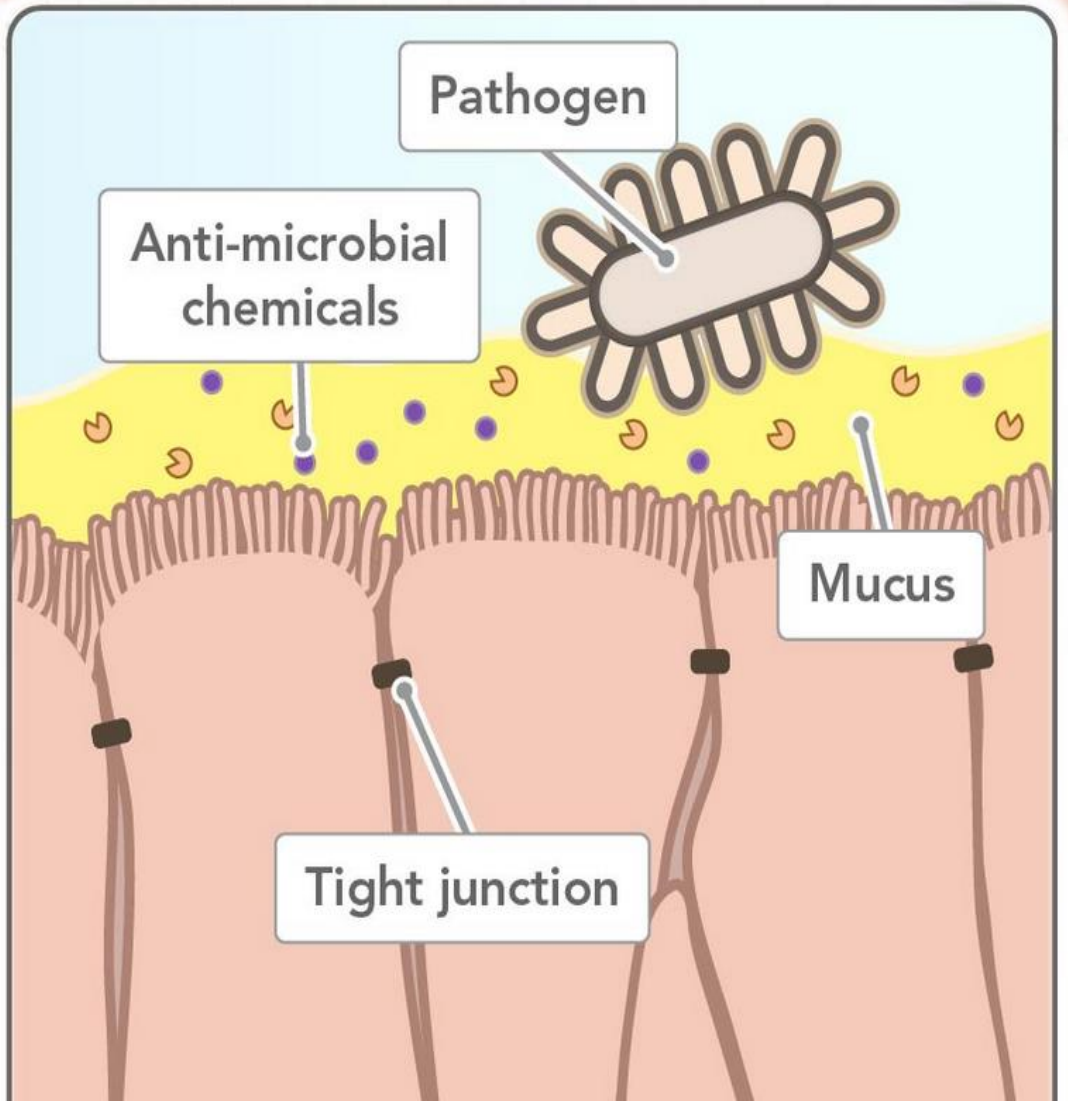
Reacts in the same way to repeated exposure to a particular threat.


The innate immune system is made up of
barrier tissues,
cells,
and molecules.

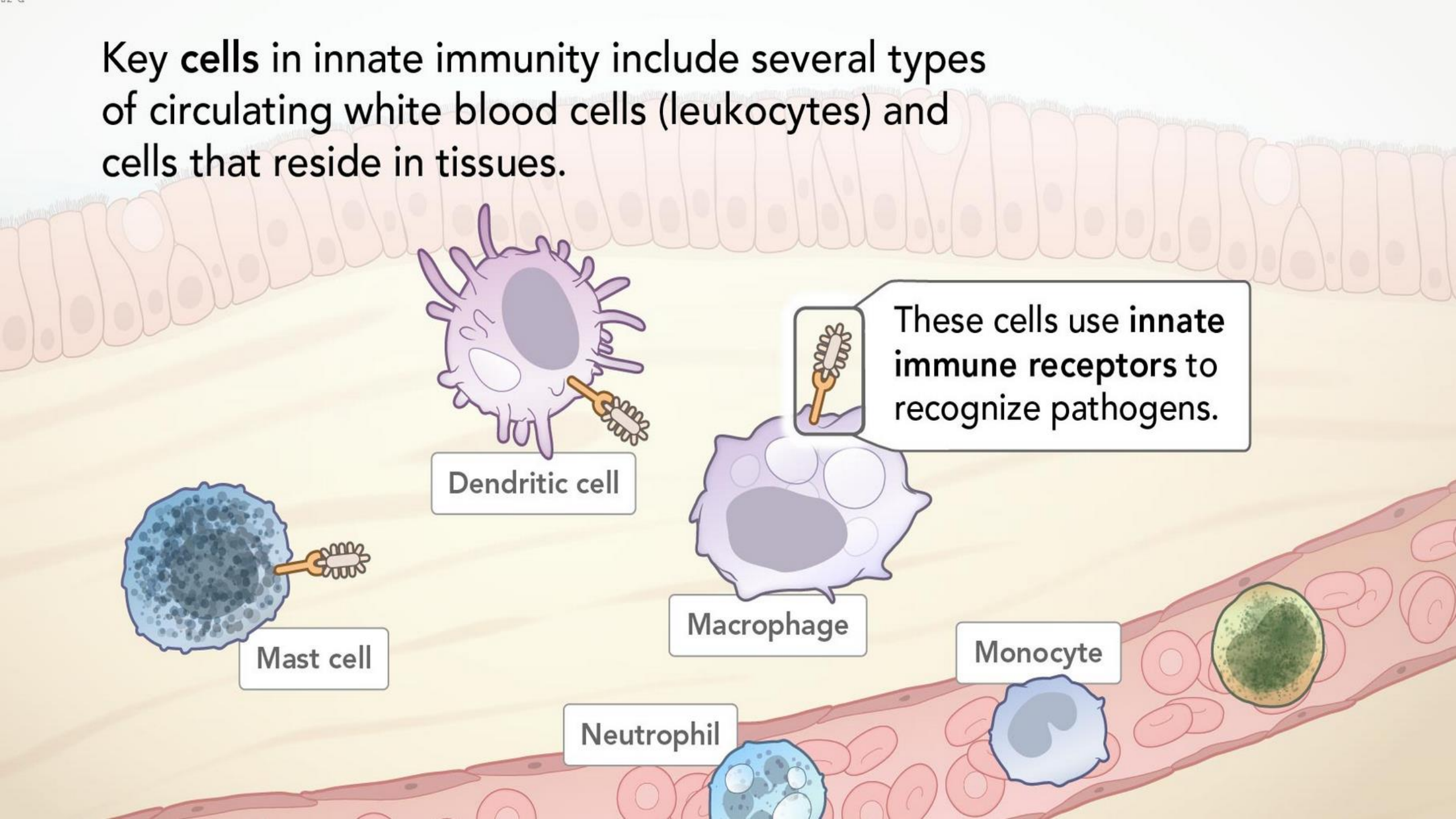


Barrier tissues exist at sites where the body interacts with the environment.

Mucus at mucosal barriers, keratin on the skin, tight junctions between epithelial cells, and anti-microbial chemicals made by epithelial cells are all barriers that physically and chemically prevent pathogens and commensal organisms from entering the body.

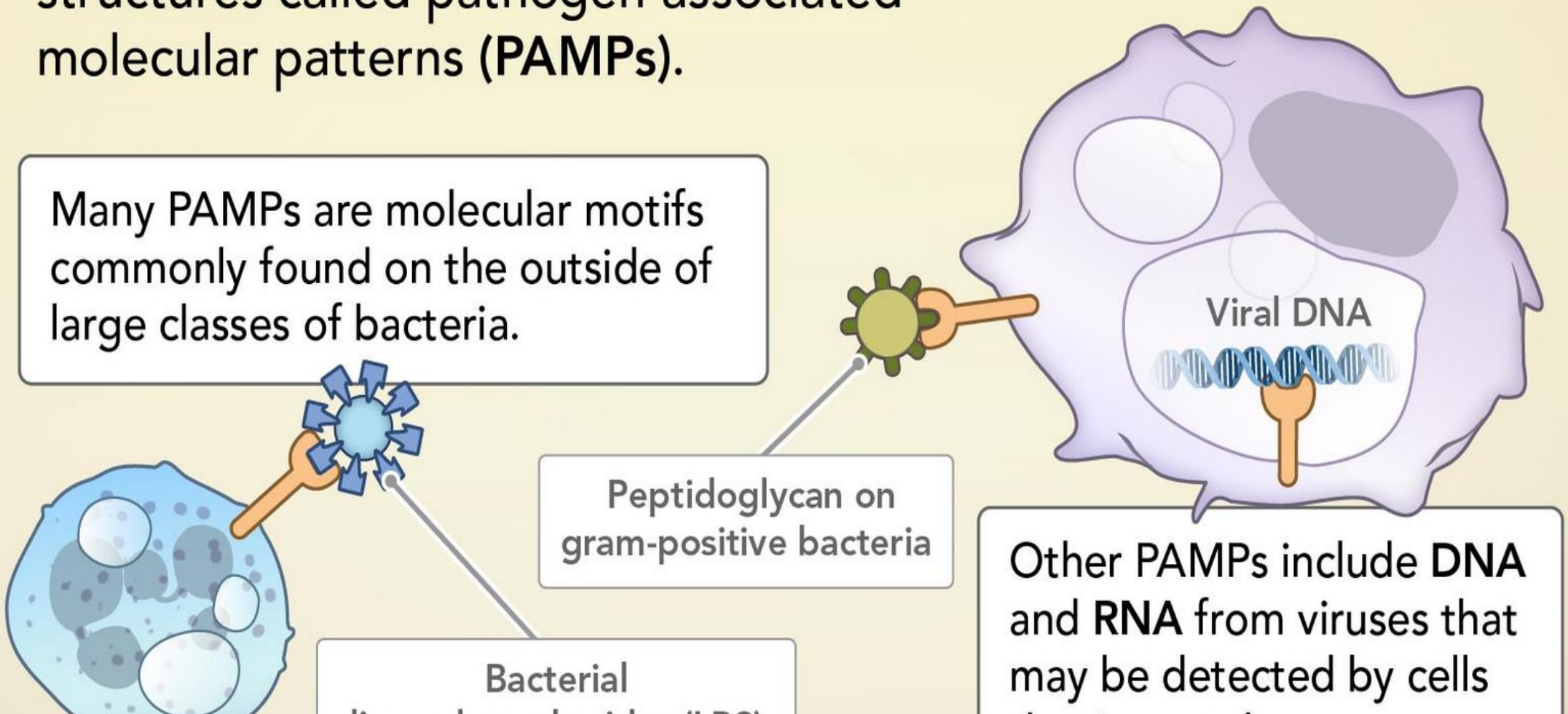


Key **cells** in innate immunity include several types of circulating white blood cells (leukocytes) and cells that reside in tissues.



The innate immune receptors on these cells are able to bind to a wide variety of threats by recognizing common structures called pathogen-associated molecular patterns (**PAMPs**).

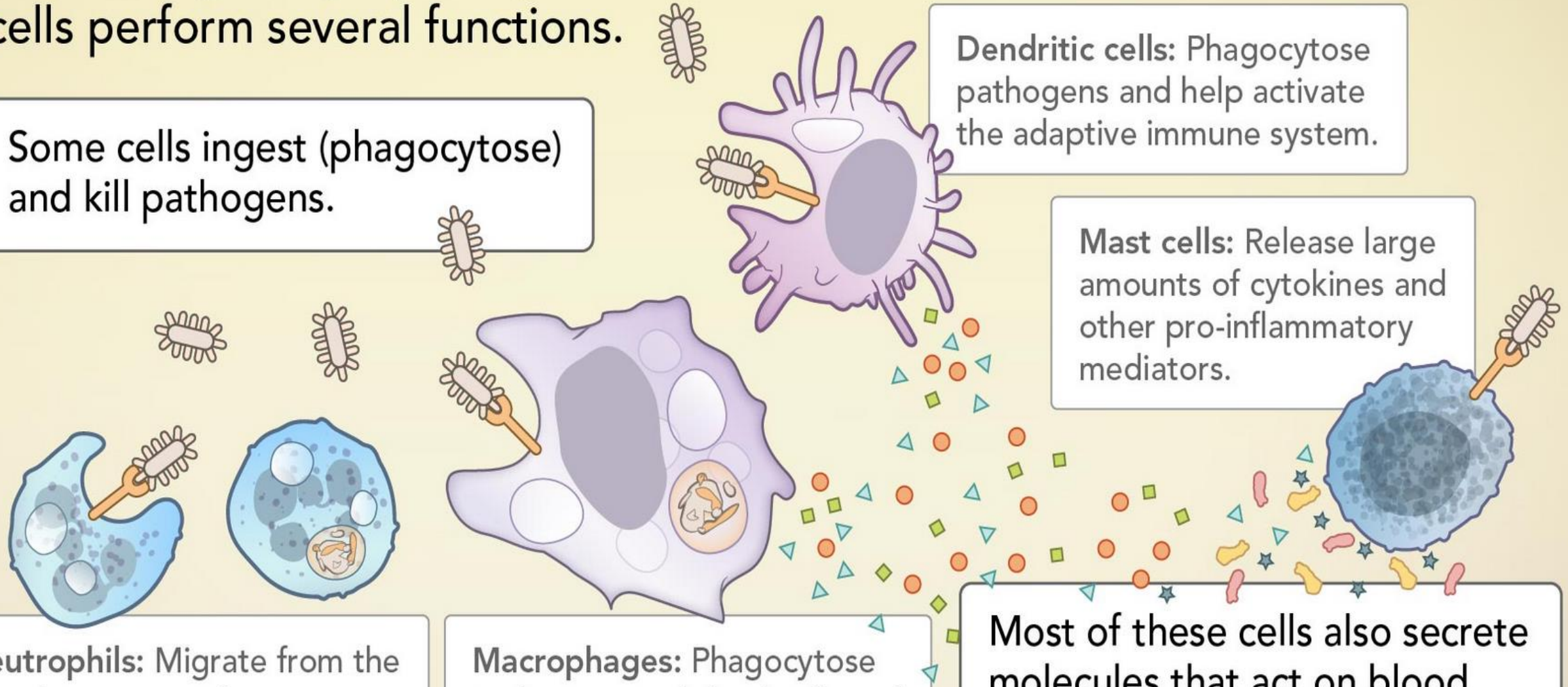
Many PAMPs are molecular motifs commonly found on the outside of large classes of bacteria.



Other PAMPs include **DNA** and **RNA** from viruses that may be detected by cells that ingest them.

After recognizing a pathogen, innate immune cells perform several functions.

Some cells ingest (phagocytose) and kill pathogens.



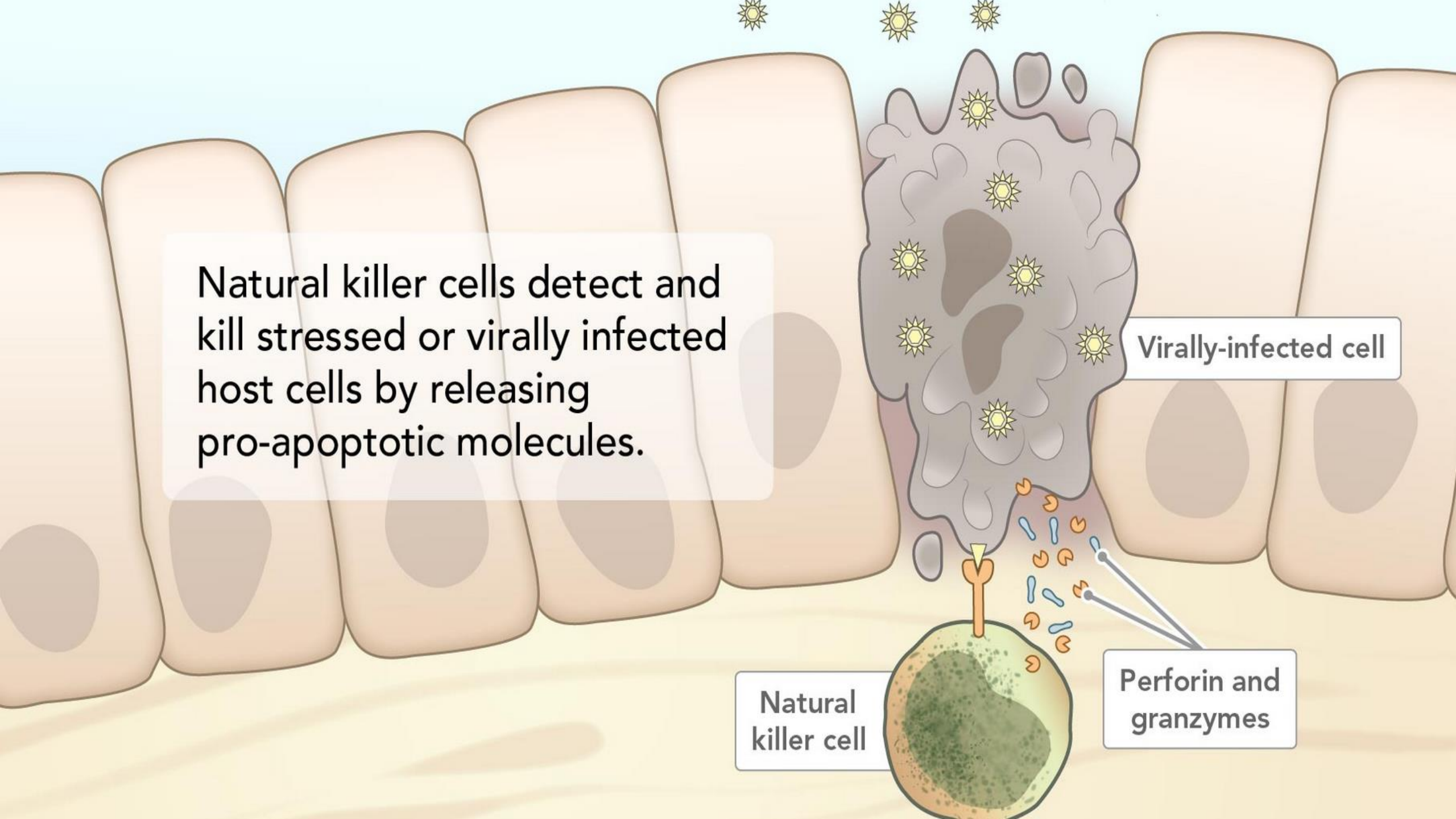
Dendritic cells: Phagocytose pathogens and help activate the adaptive immune system.

Mast cells: Release large amounts of cytokines and other pro-inflammatory mediators.

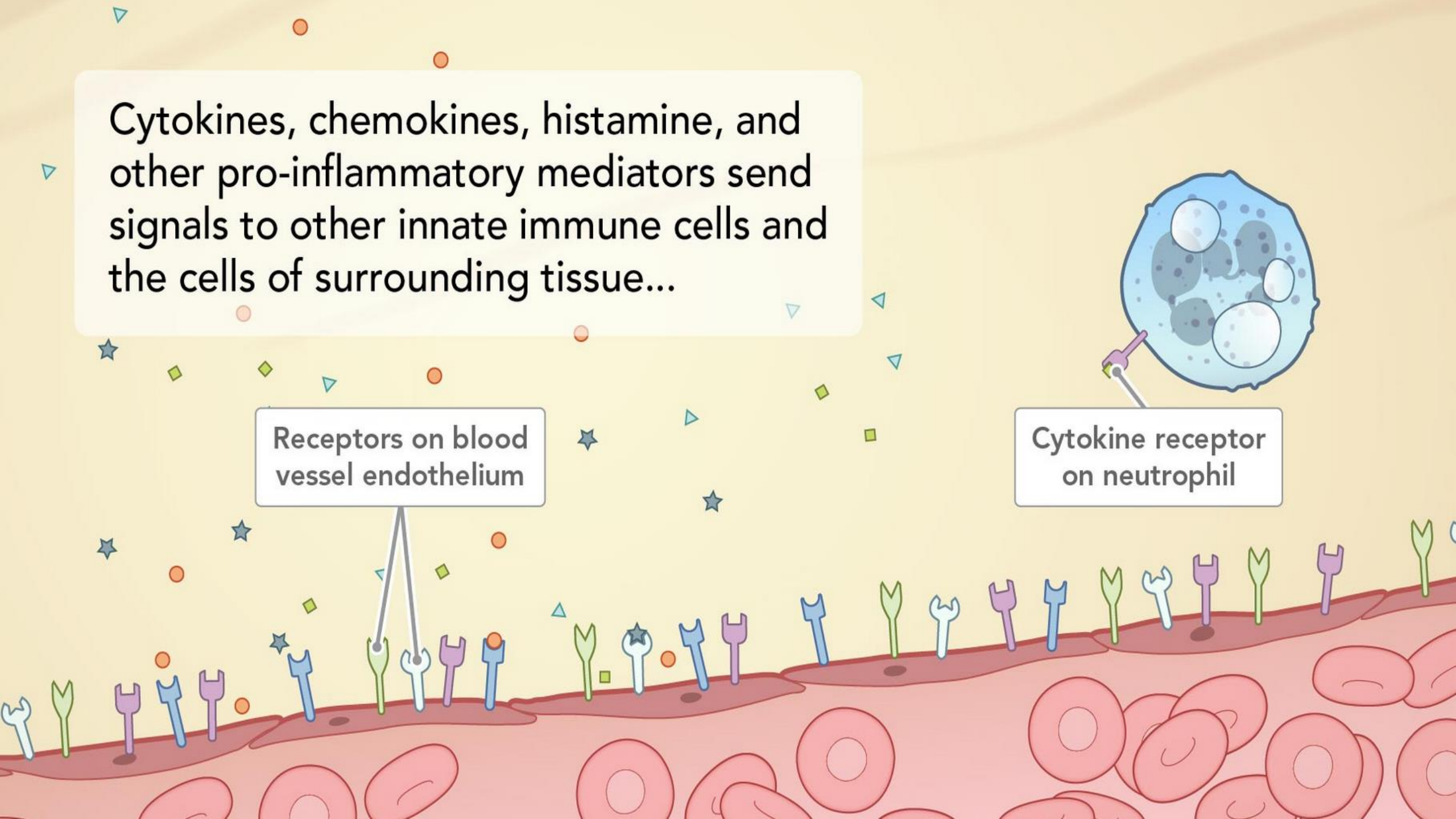
Neutrophils: Migrate from the blood stream to phacocytose and kill pathogens.

Macrophages: Phagocytose pathogens and dead cells and play a role in tissue repair.

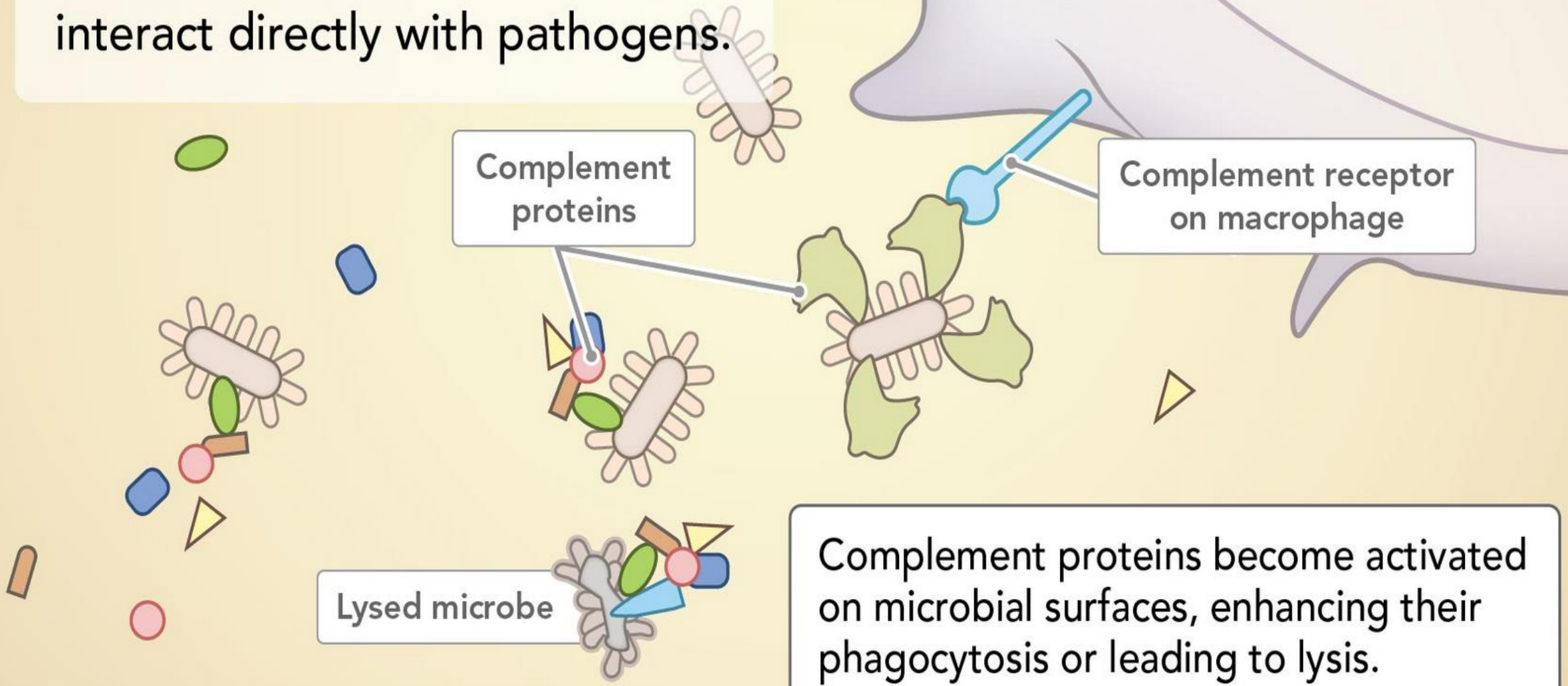
Most of these cells also secrete molecules that act on blood vessels to enhance recruitment of more inflammatory cells and molecules from the blood


Natural killer cells detect and kill stressed or virally infected host cells by releasing pro-apoptotic molecules.
Virally-infected cell
Natural killer cell
Perforin and granzymes

Cytokines, chemokines, histamine, and other pro-inflammatory mediators send signals to other innate immune cells and the cells of surrounding tissue...



... and allow proteins from the blood to enter the tissue and interact directly with pathogens.



Complement proteins become activated on microbial surfaces, enhancing their phagocytosis or leading to lysis.

The classical pathway begins with an antibody bound to a pathogen, the lectin binding pathway begins with mannose binding lectin protein binding mannose, and the alternative pathway is always active because there's always some C3 being cleaved into C3a and C3b.
All three pathways end with the creation of the MAC which will kill a pathogen, and along the way there's creation of C3a and C5a - both acting as chemotaxins and anaphylatoxins, and C3b acting as opsonins which will help phagocytes grab and destroy pathogens

Innate Immunity

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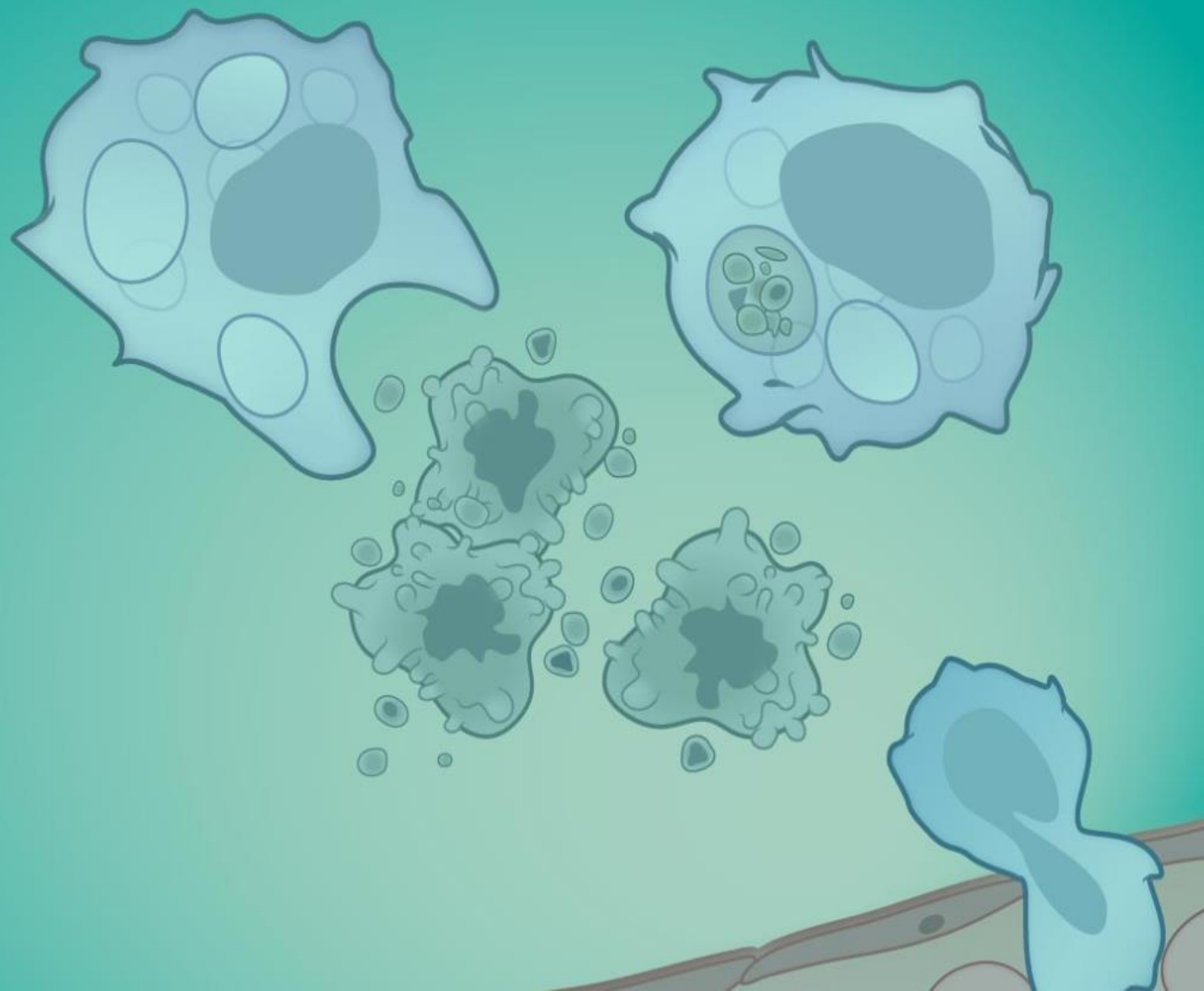
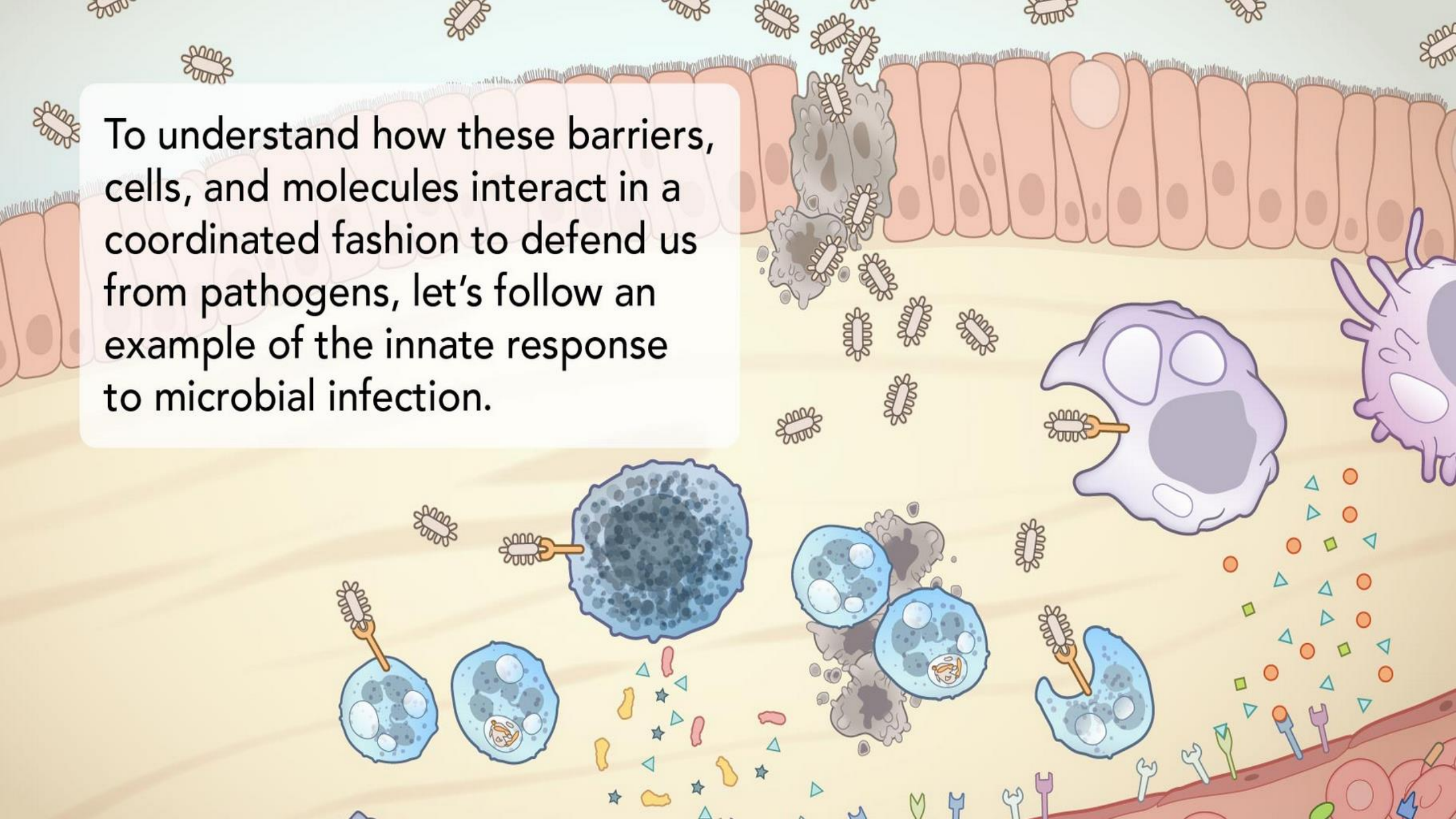
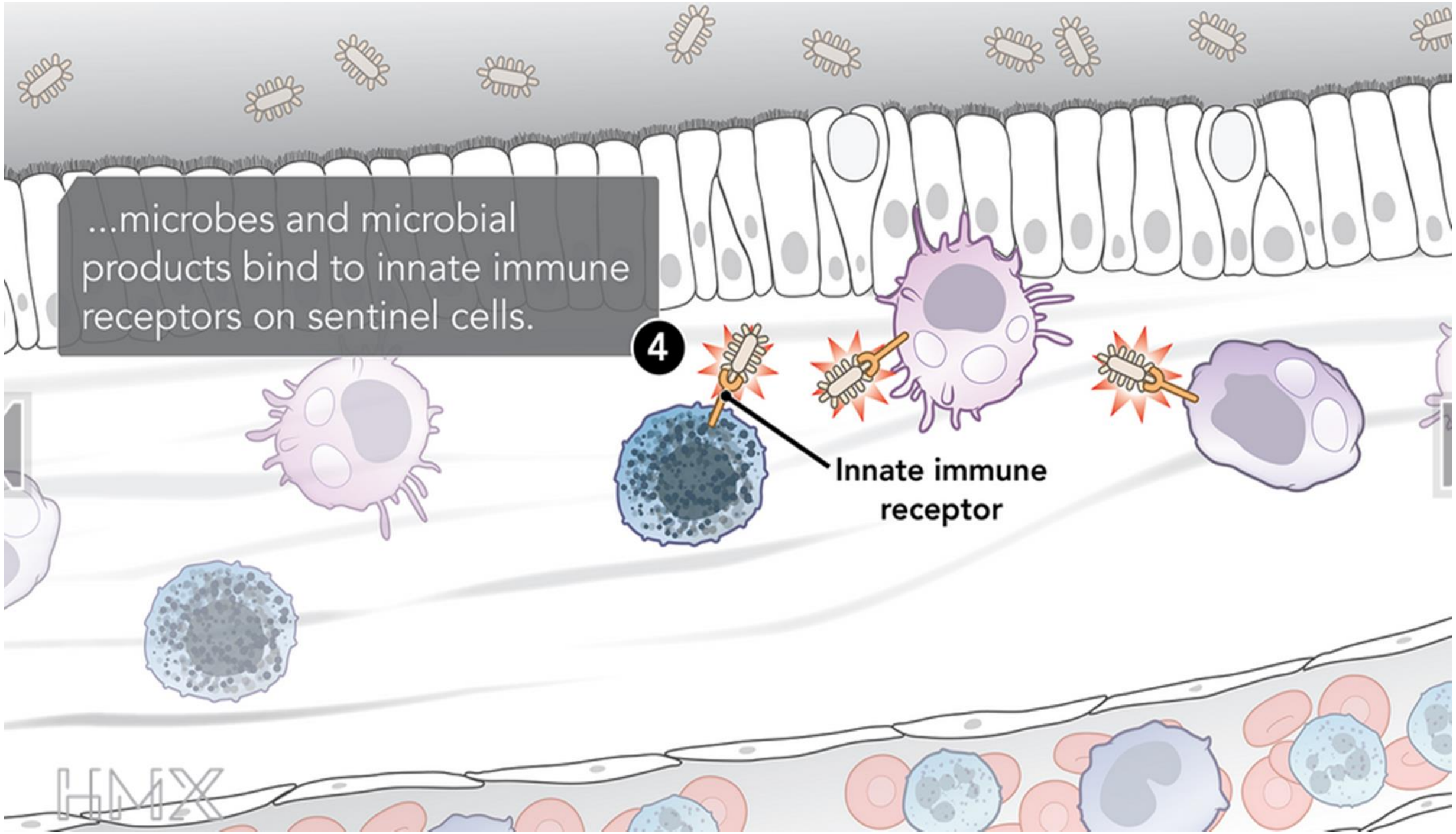
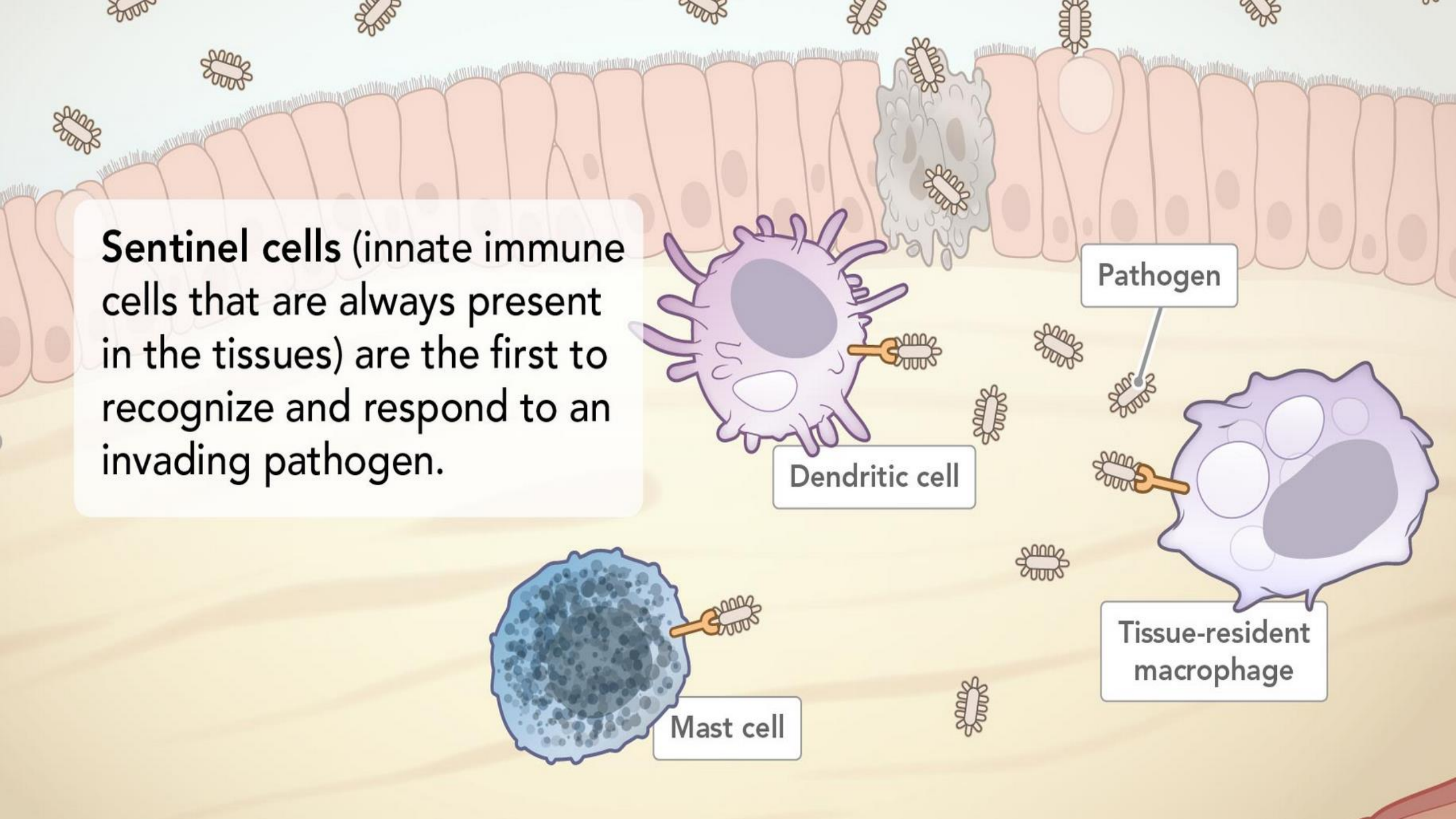
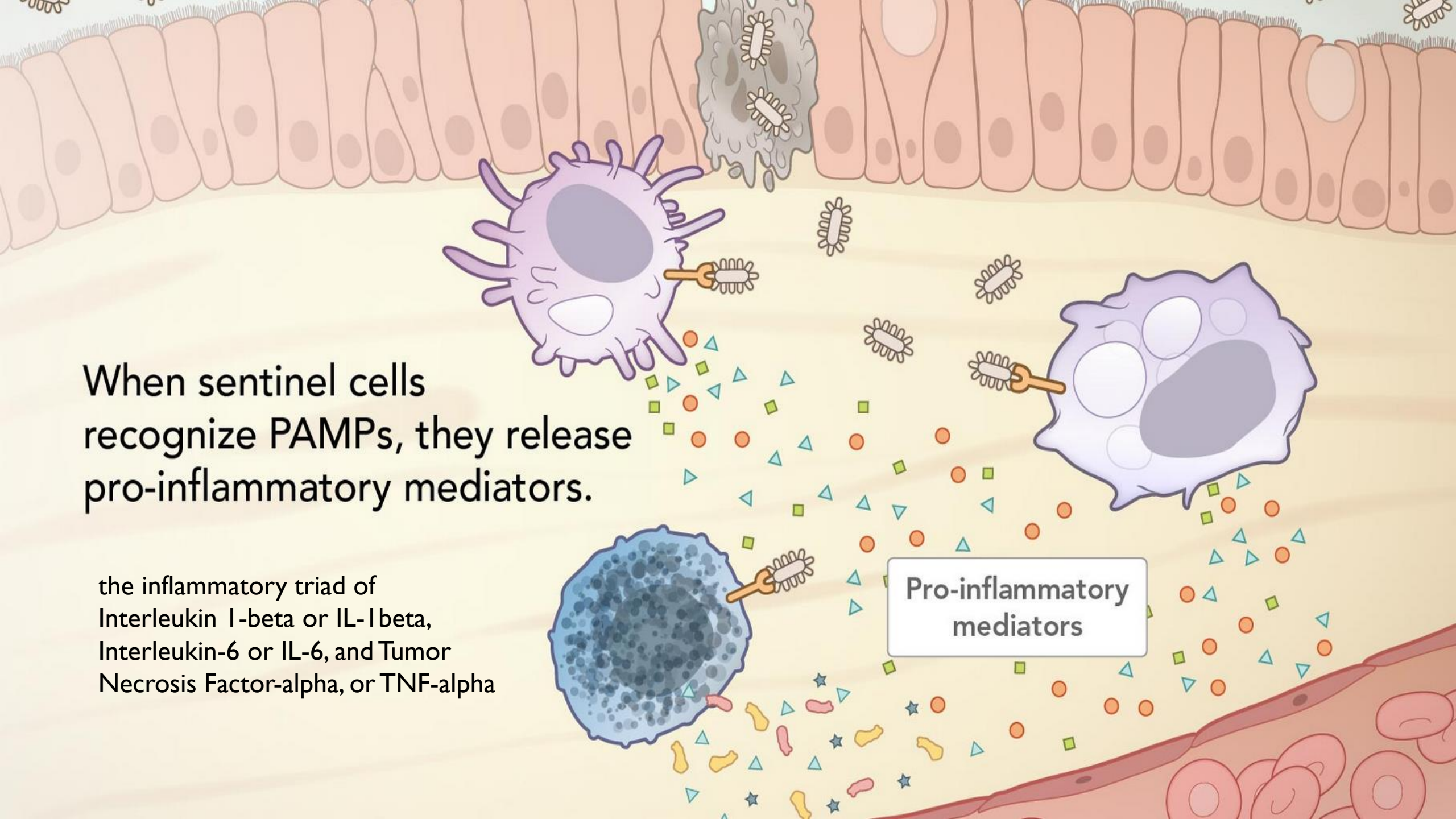
Part 2



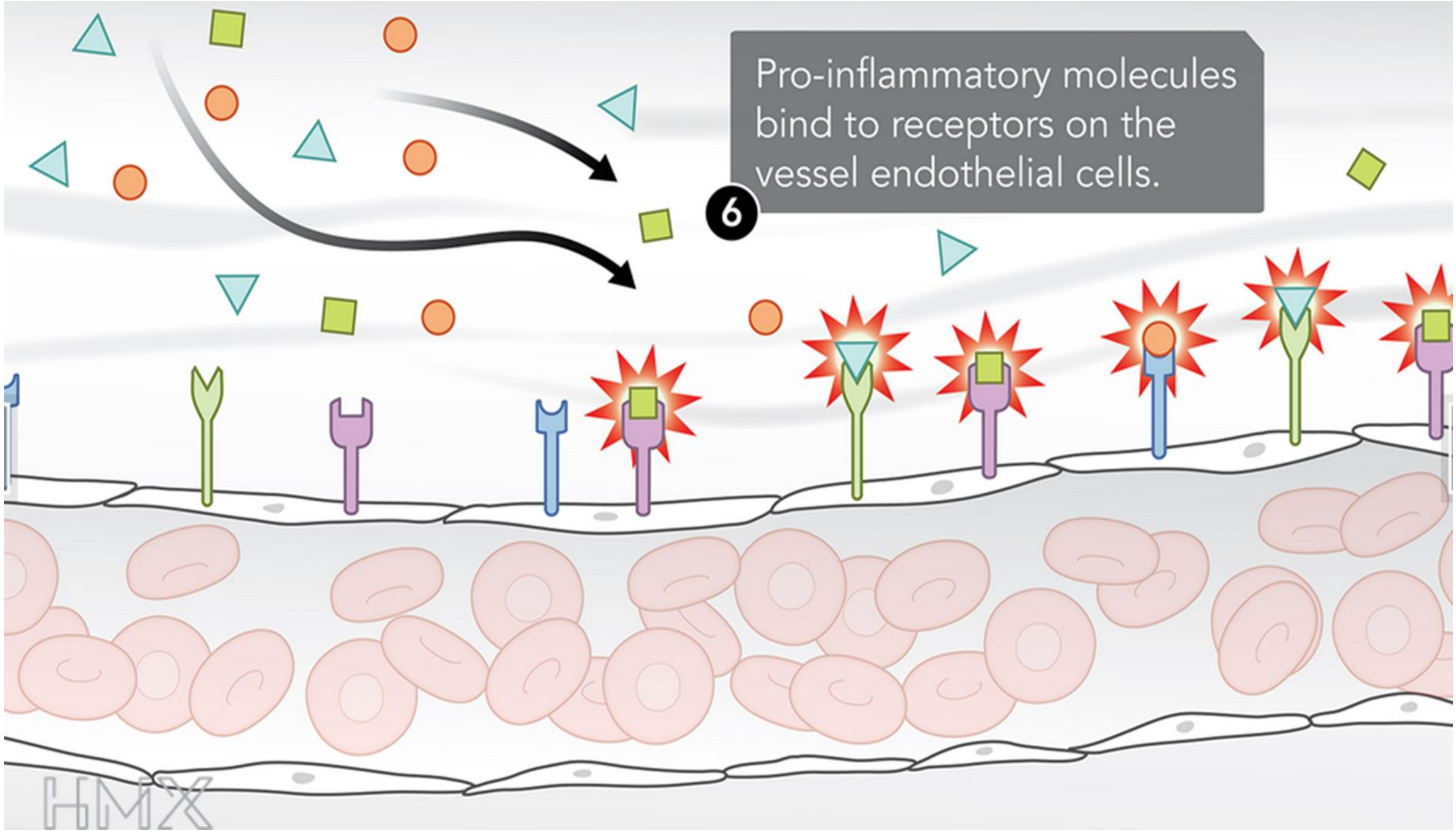

To understand how these barriers, cells, and molecules interact in a coordinated fashion to defend us from pathogens, let's follow an example of the innate response to microbial infection.

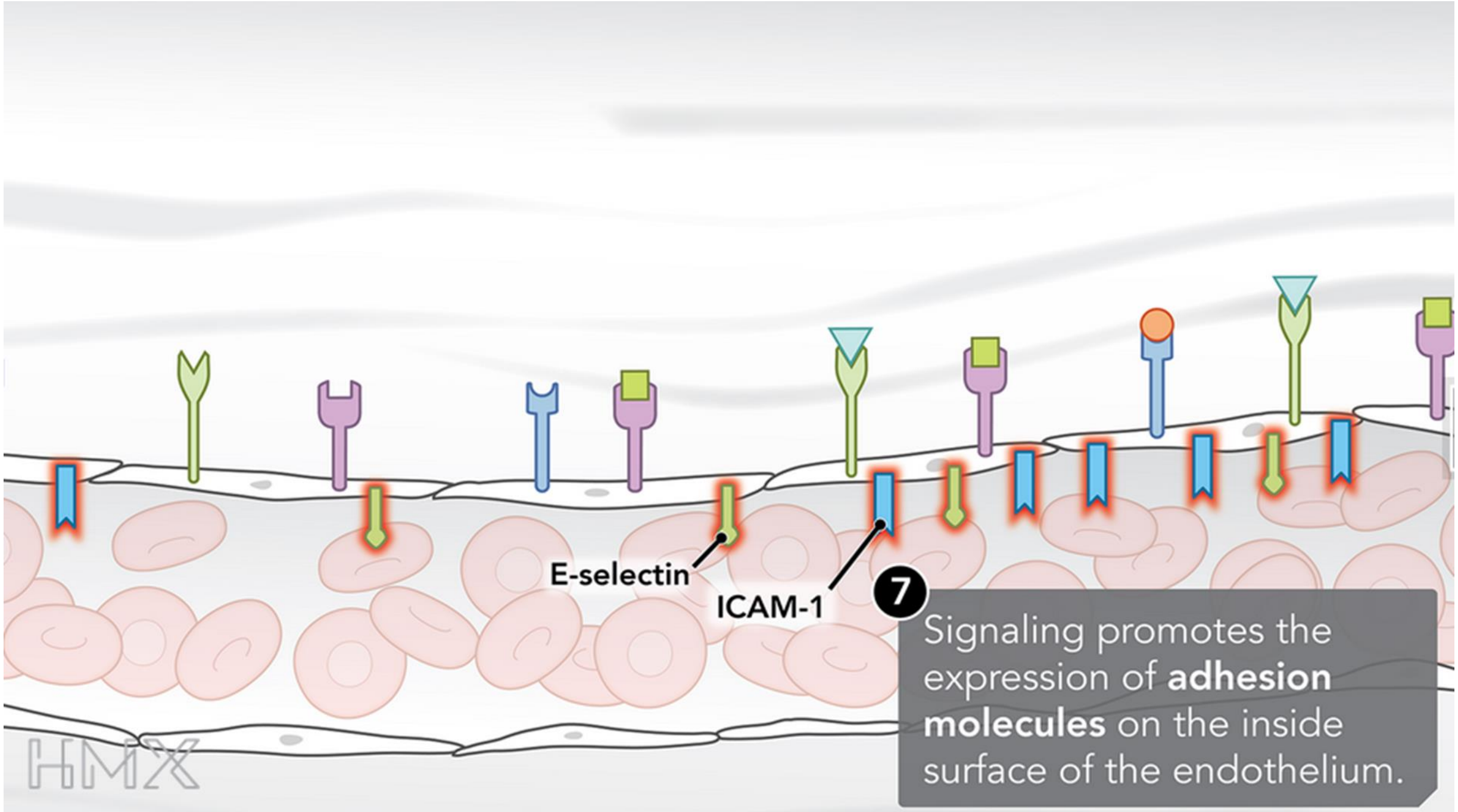

...microbes and microbial products bind to innate immune receptors on sentinel cells.
4
Innate immune receptor

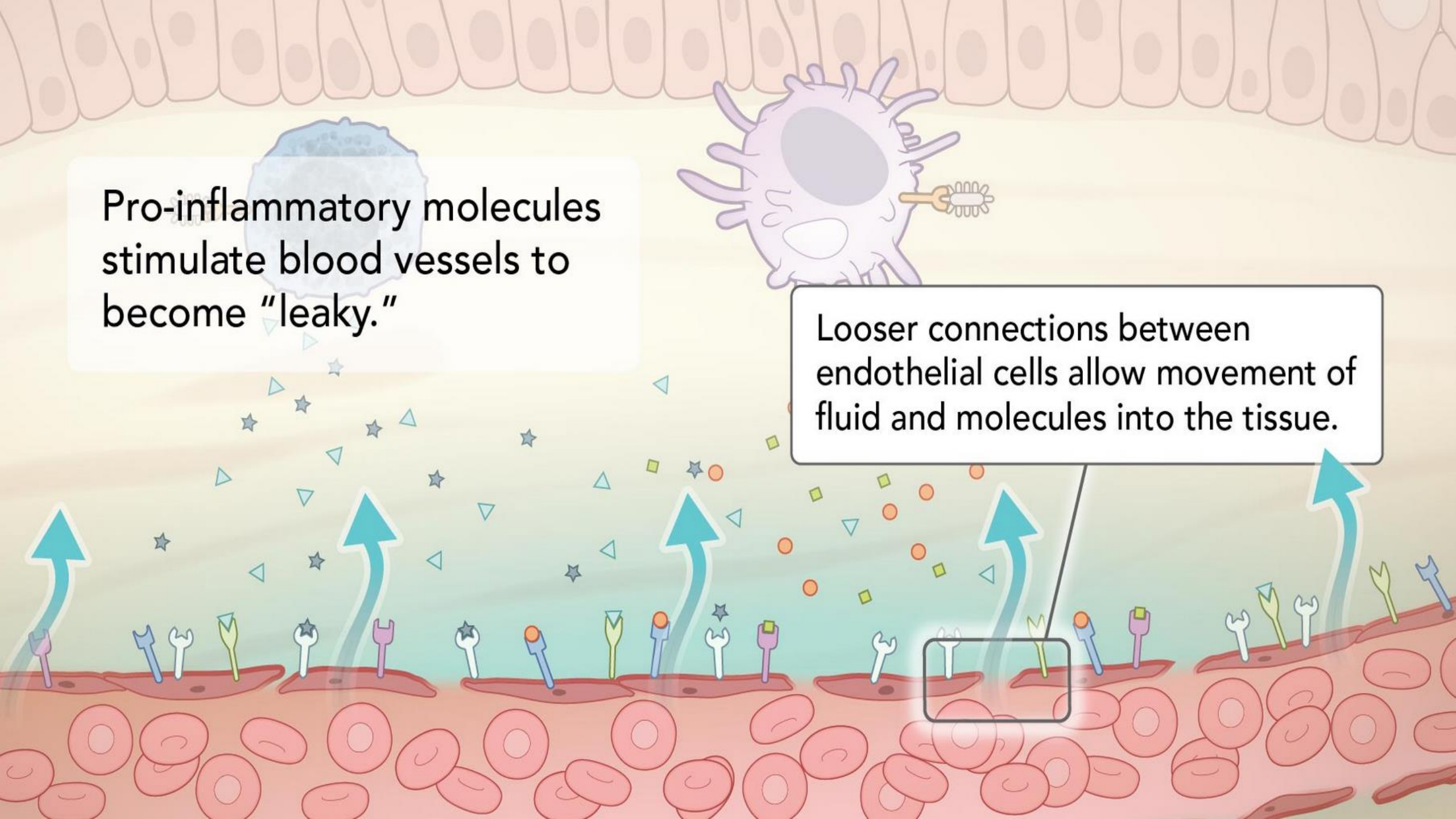

Sentinel cells (innate immune cells that are always present in the tissues) are the first to recognize and respond to an invading pathogen.
Pathogen
Dendritic cell
Tissue-resident macrophage
Mast cell



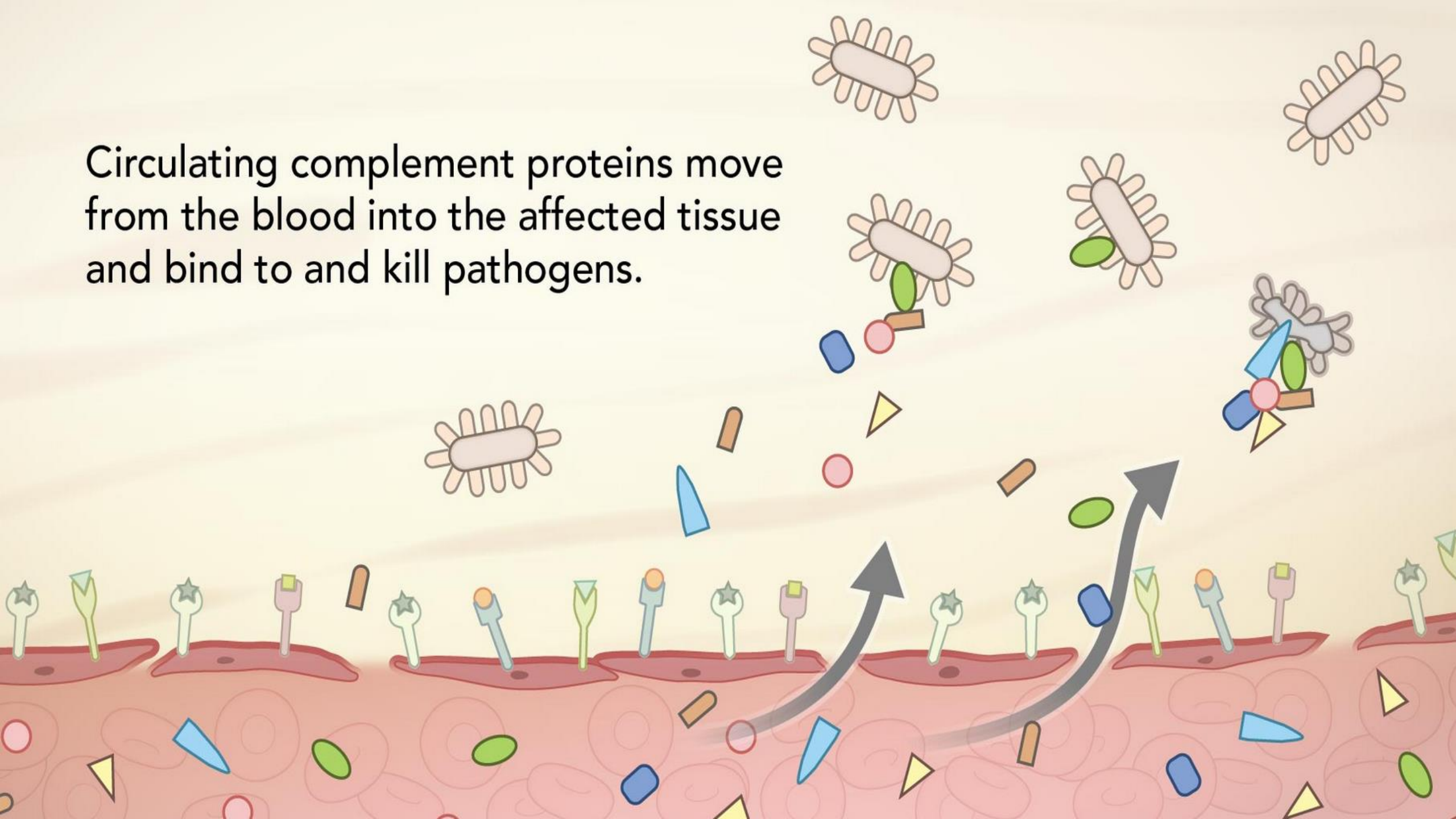
the inflammatory triad of Interleukin 1-beta or IL-1beta, Interleukin-6 or IL-6, and Tumor Necrosis Factor-alpha, or TNF-alpha


Pro-inflammatory molecules bind to receptors on the vessel endothelial cells.
6

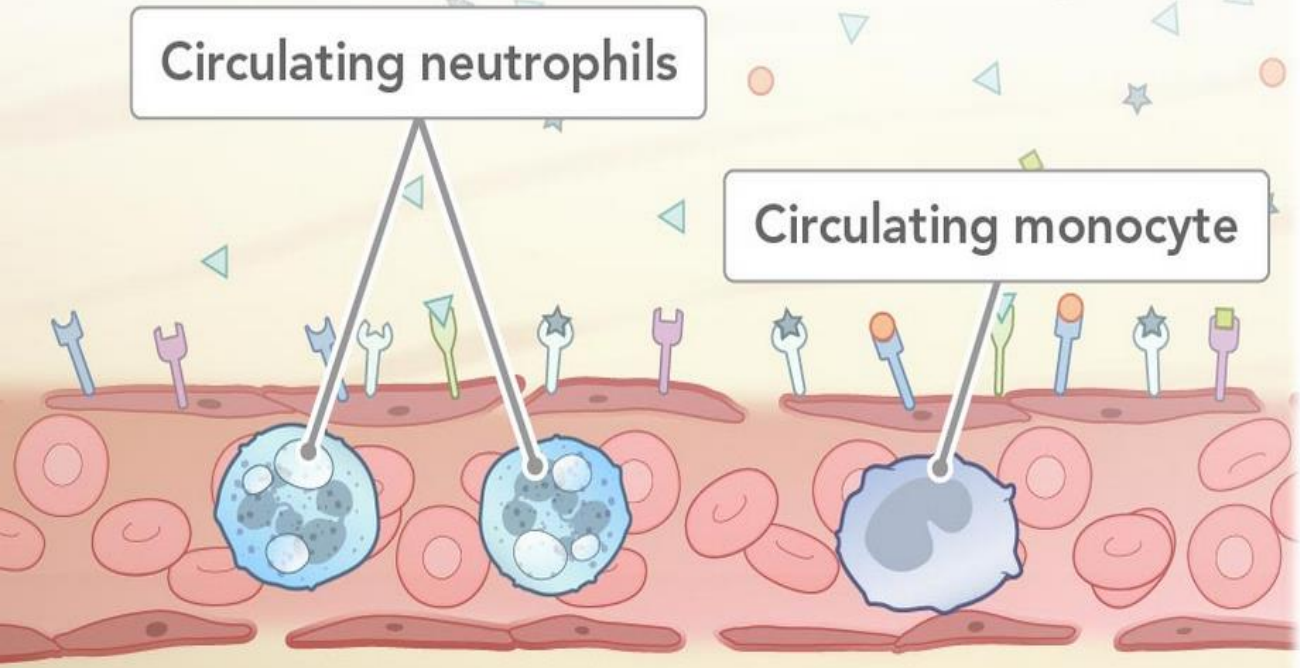

E-selectin
ICAM-1
7
Signaling promotes the expression of **adhesion molecules** on the inside surface of the endothelium.


Pro-inflammatory molecules stimulate blood vessels to become “leaky.”
Looser connections between endothelial cells allow movement of fluid and molecules into the tissue.

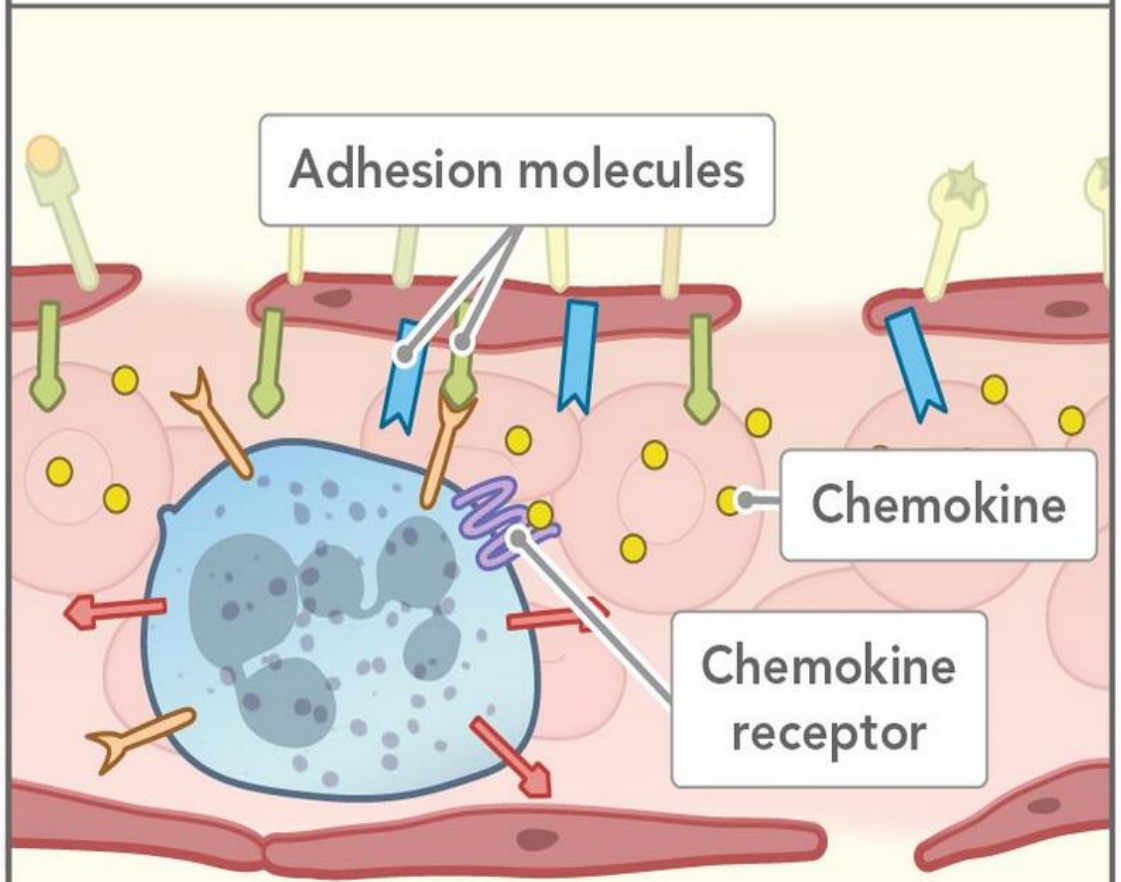
Circulating complement proteins move from the blood into the affected tissue and bind to and kill pathogens.

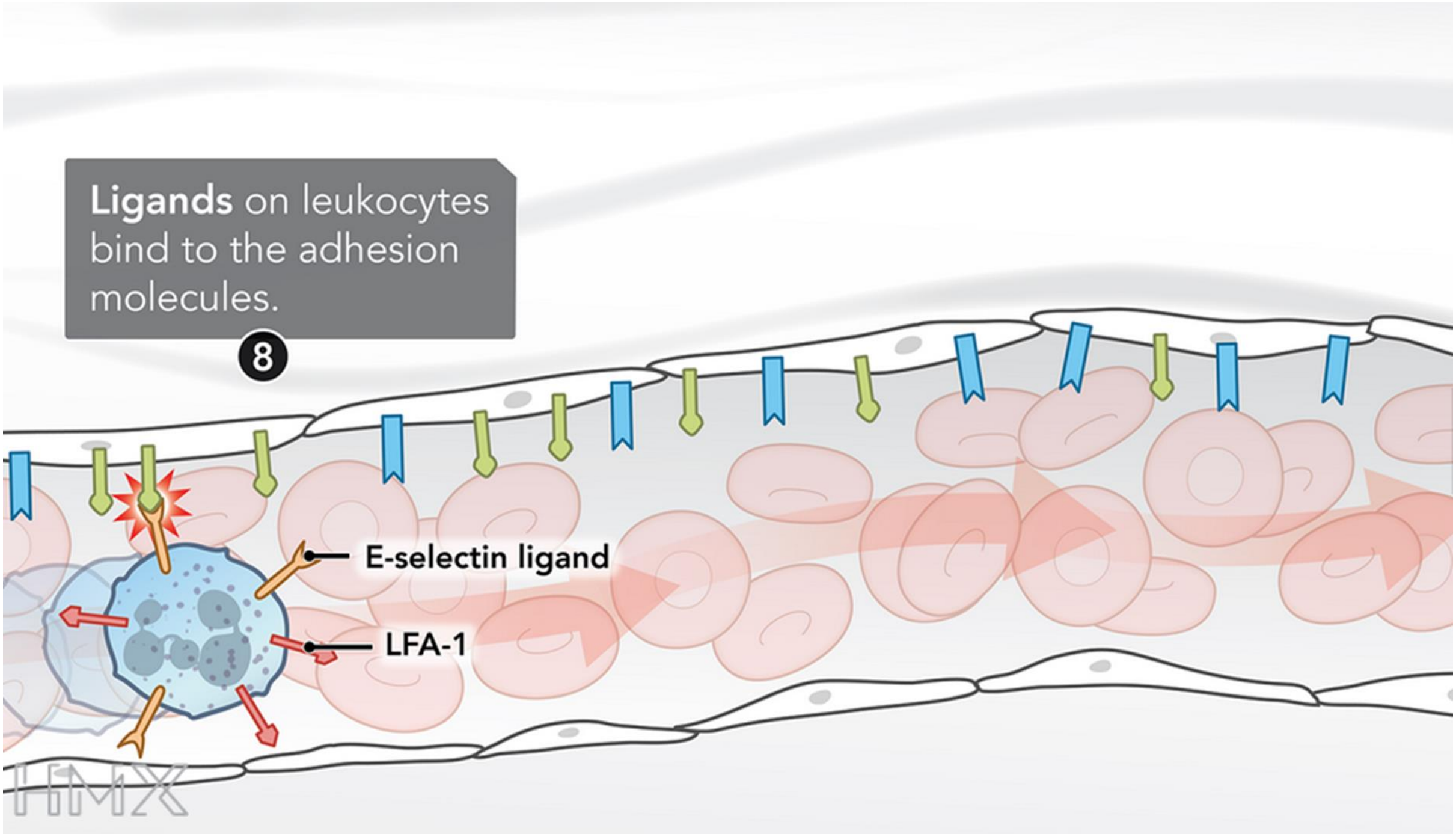


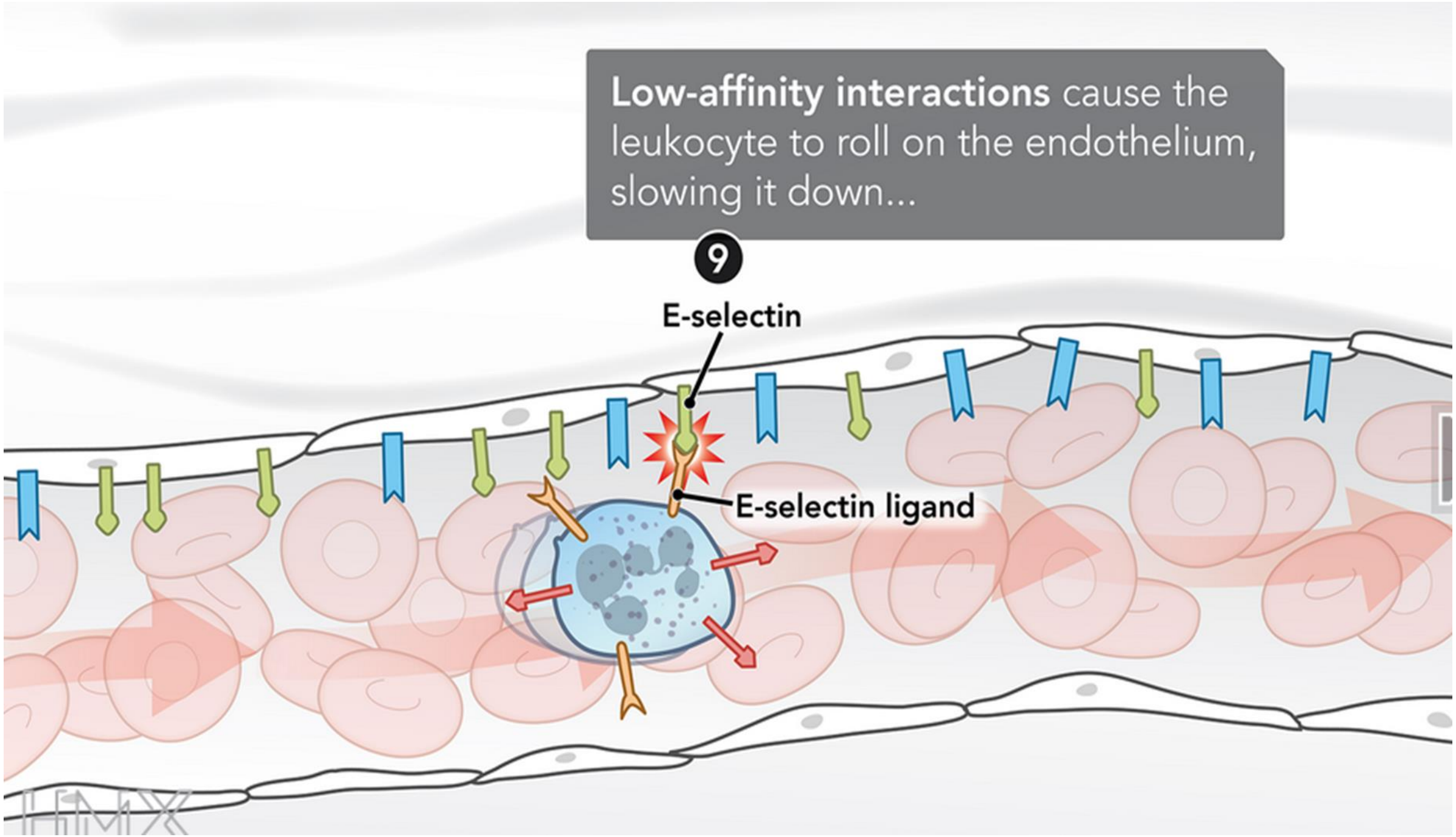
Cytokines also stimulate blood vessels to attract circulating immune cells.

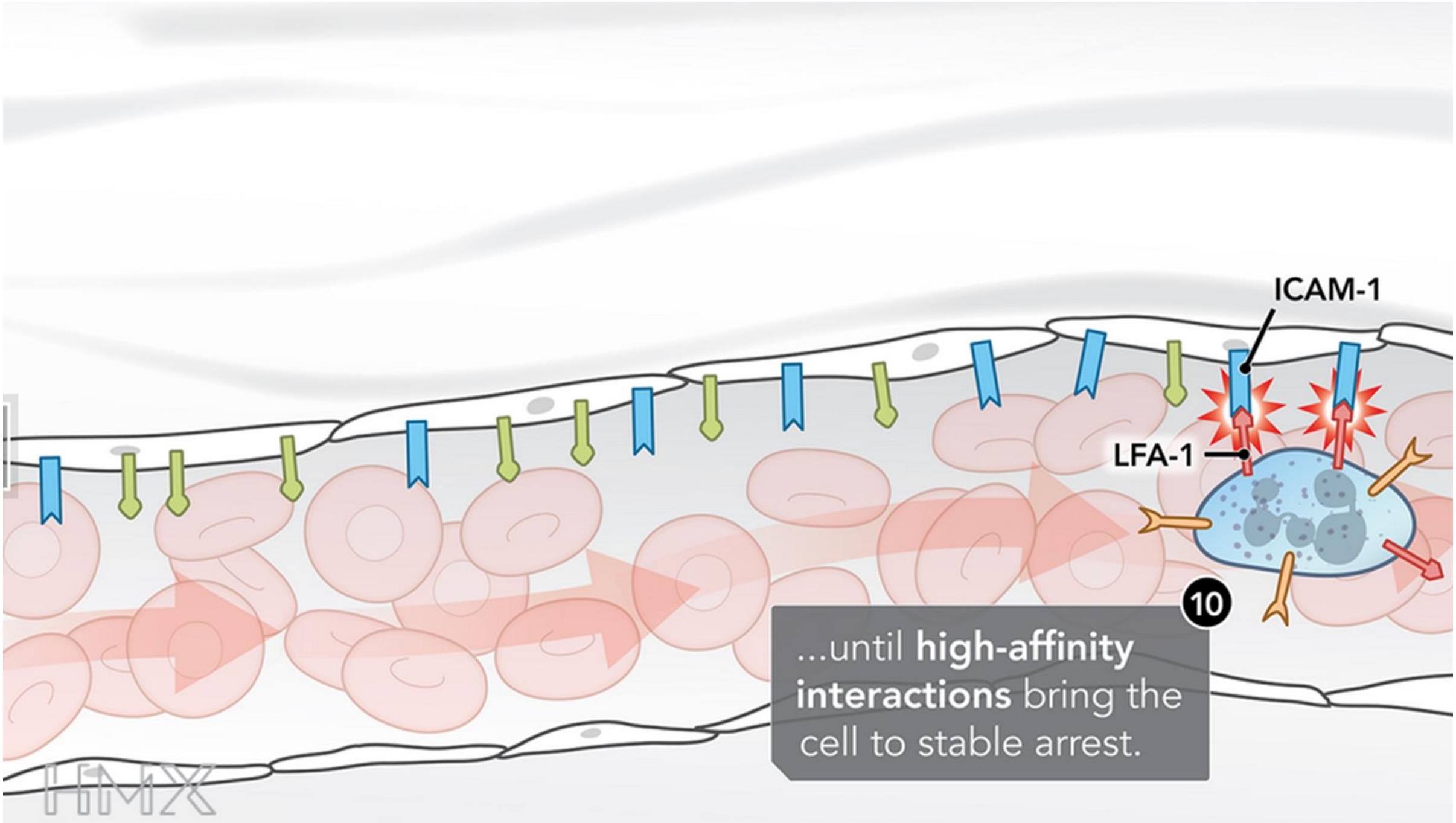


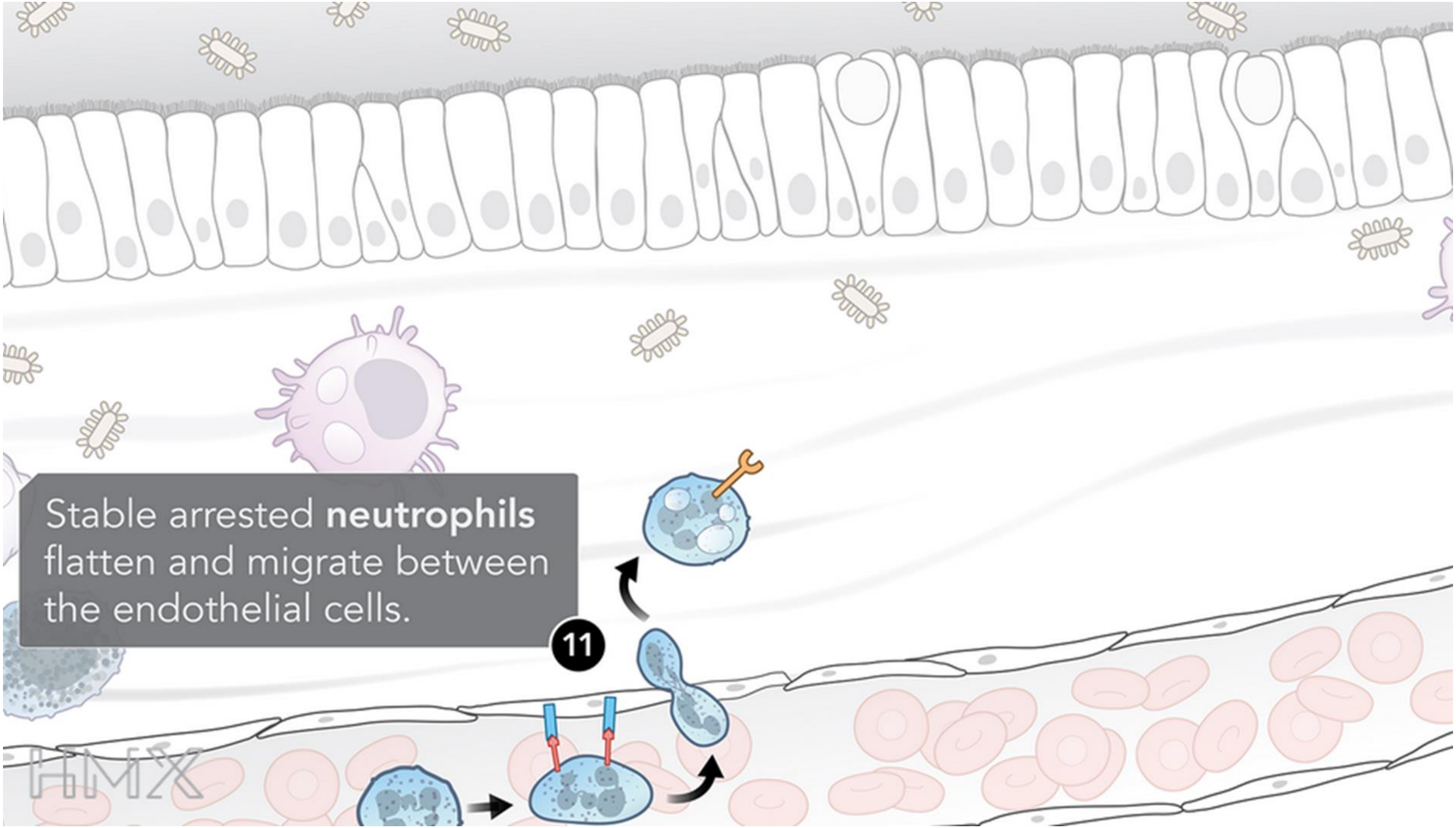
Adhesion molecules and chemokines on the surface of blood vessel endothelial cells allow cells to stick at the infection site.




Ligands on leukocytes bind to the adhesion molecules.
8
E-selectin ligand
LFA-1


Low-affinity interactions cause the leukocyte to roll on the endothelium, slowing it down...
9
E-selectin
E-selectin ligand

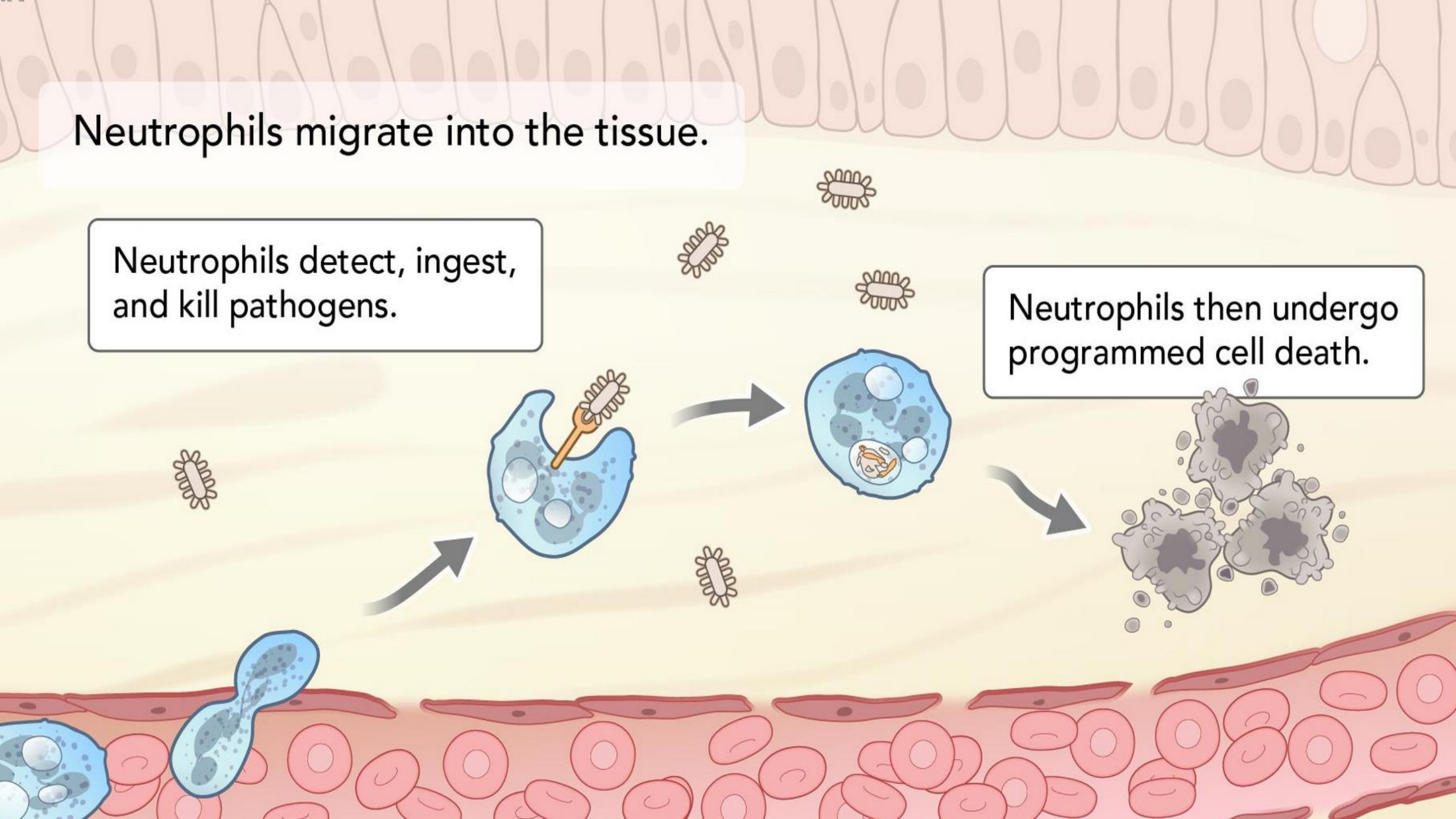

ICAM-1
LFA-1
10
...until **high-affinity interactions** bring the cell to stable arrest.

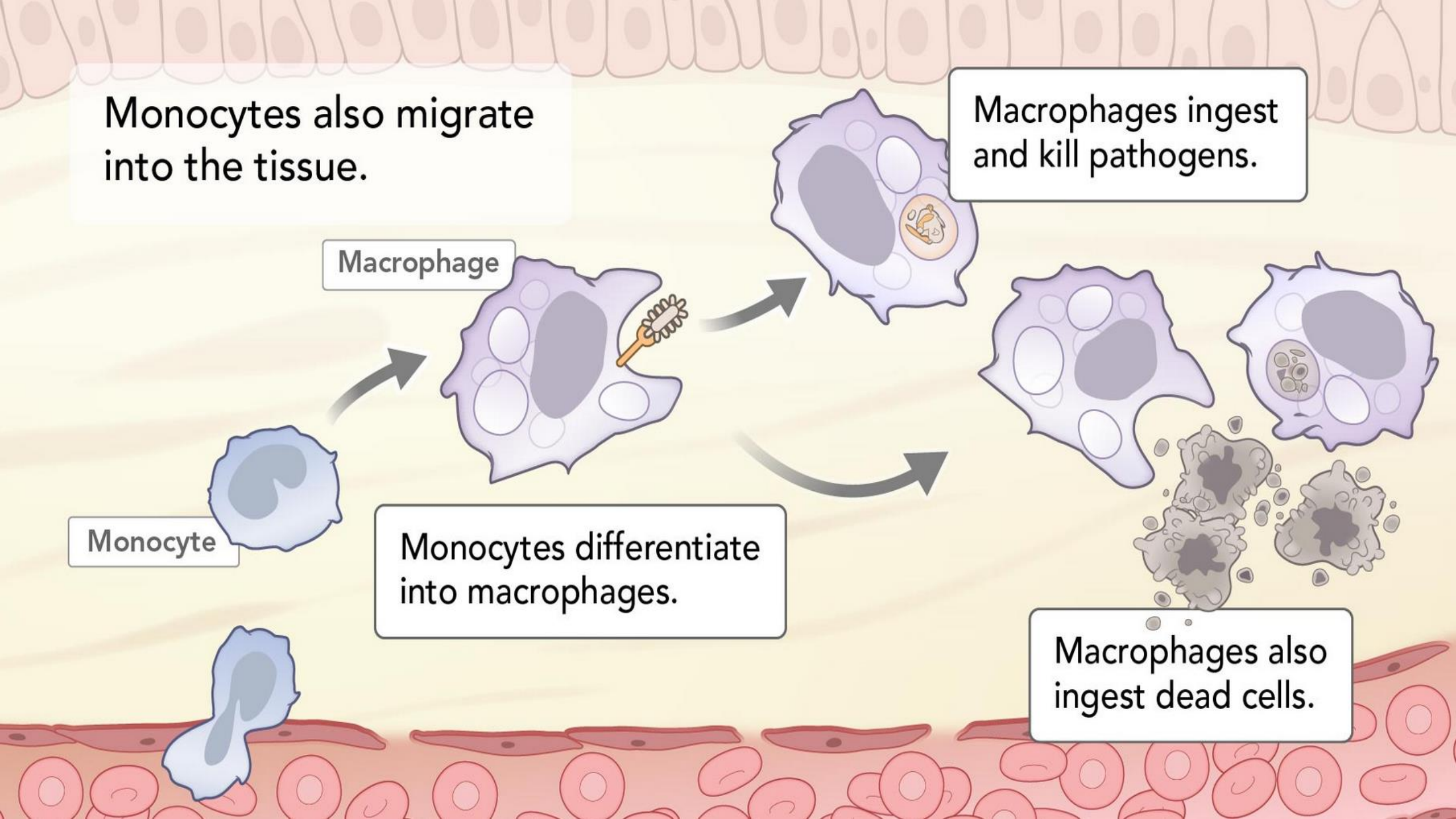

Stable arrested **neutrophils** flatten and migrate between the endothelial cells.
11

Neutrophils migrate into the tissue.

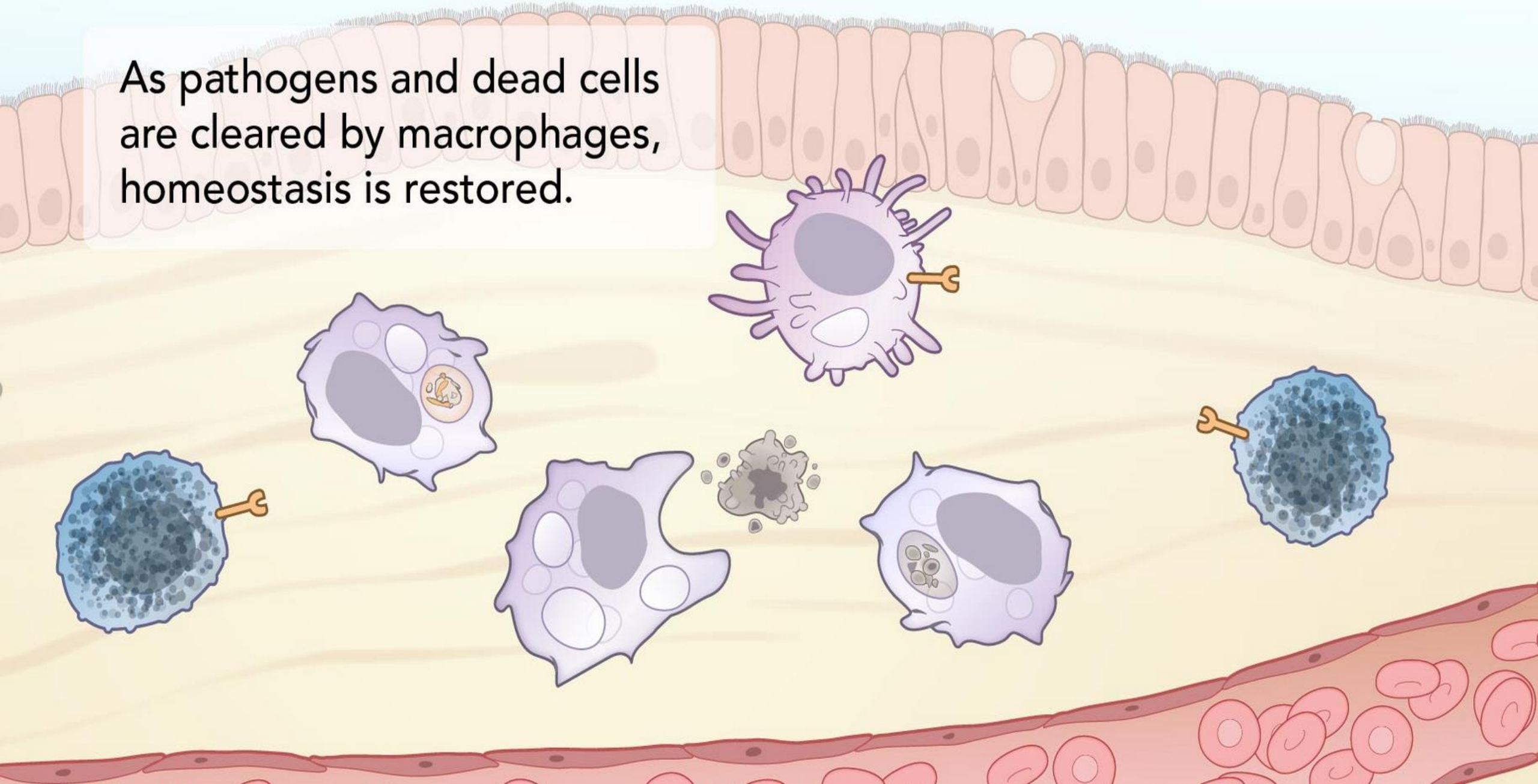
Neutrophils detect, ingest, and kill pathogens.

Neutrophils then undergo programmed cell death.

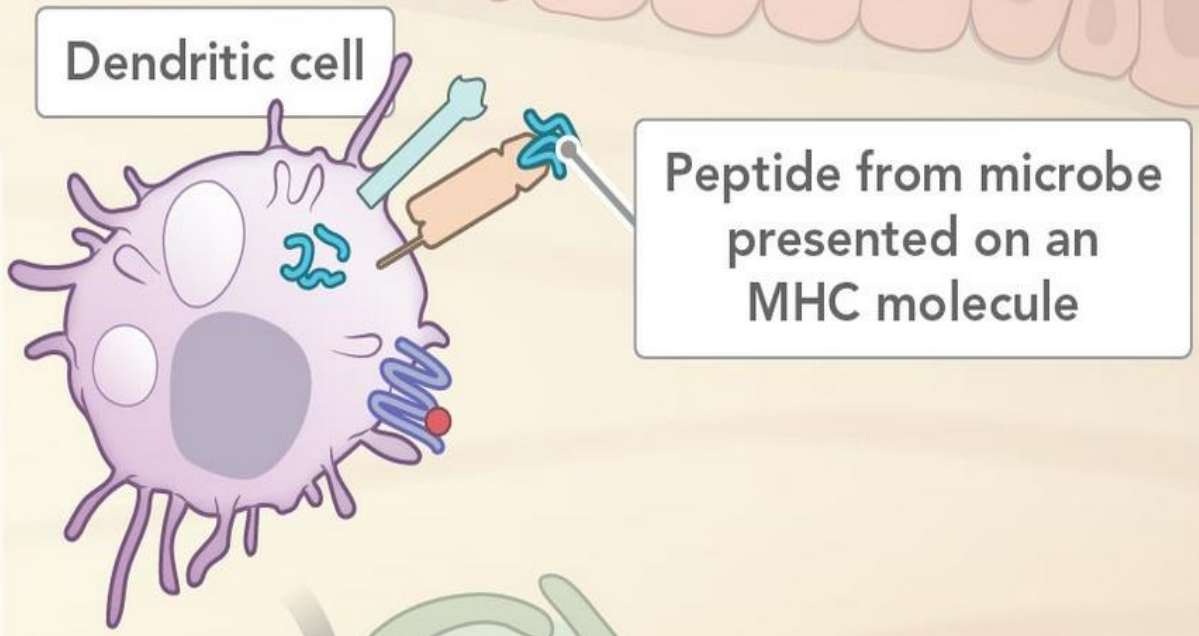



Monocytes also migrate into the tissue.
Macrophage
Macrophages ingest and kill pathogens.
Monocyte
Monocytes differentiate into macrophages.
Macrophages also ingest dead cells.

As pathogens and dead cells are cleared by macrophages, homeostasis is restored.

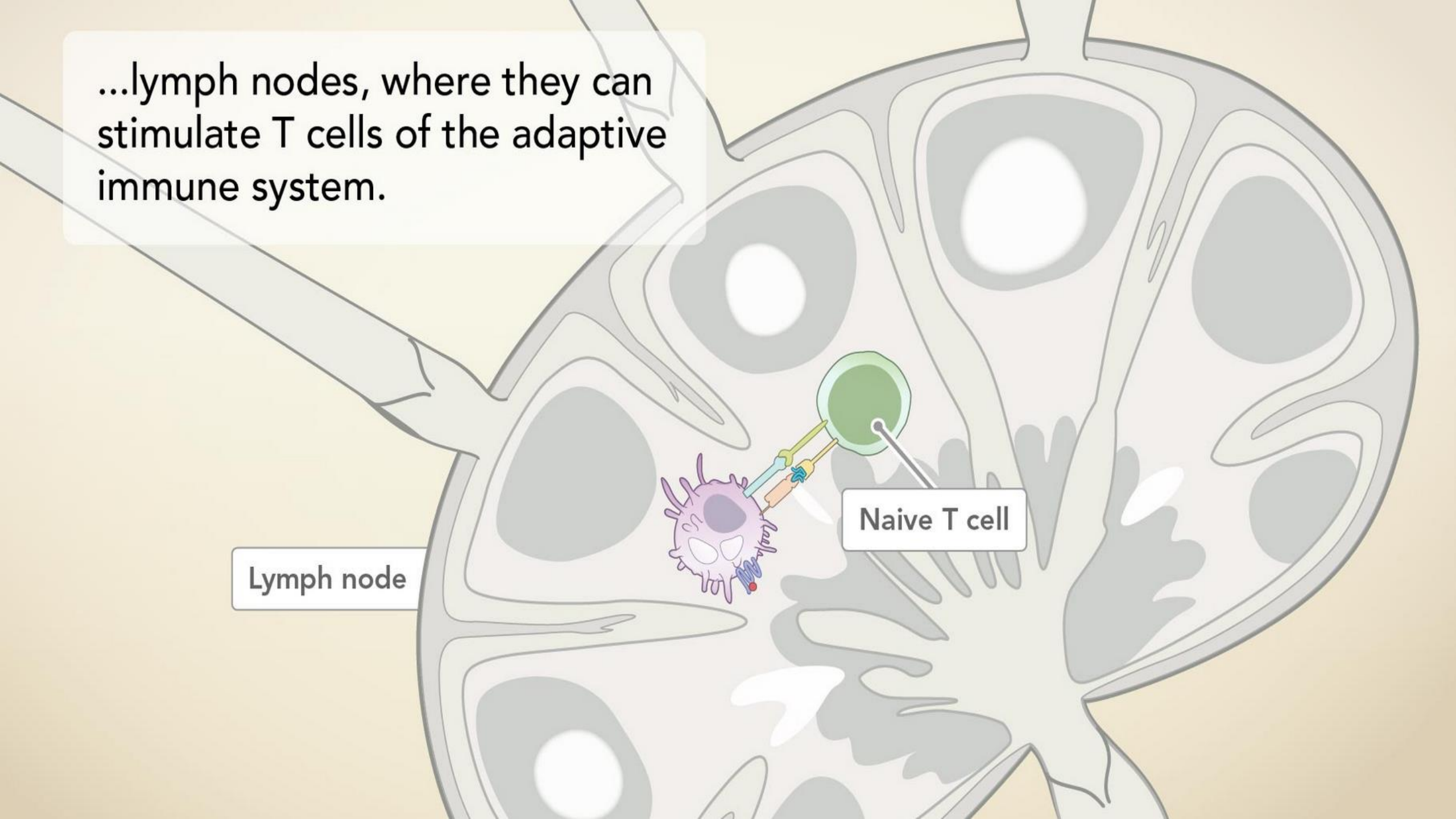


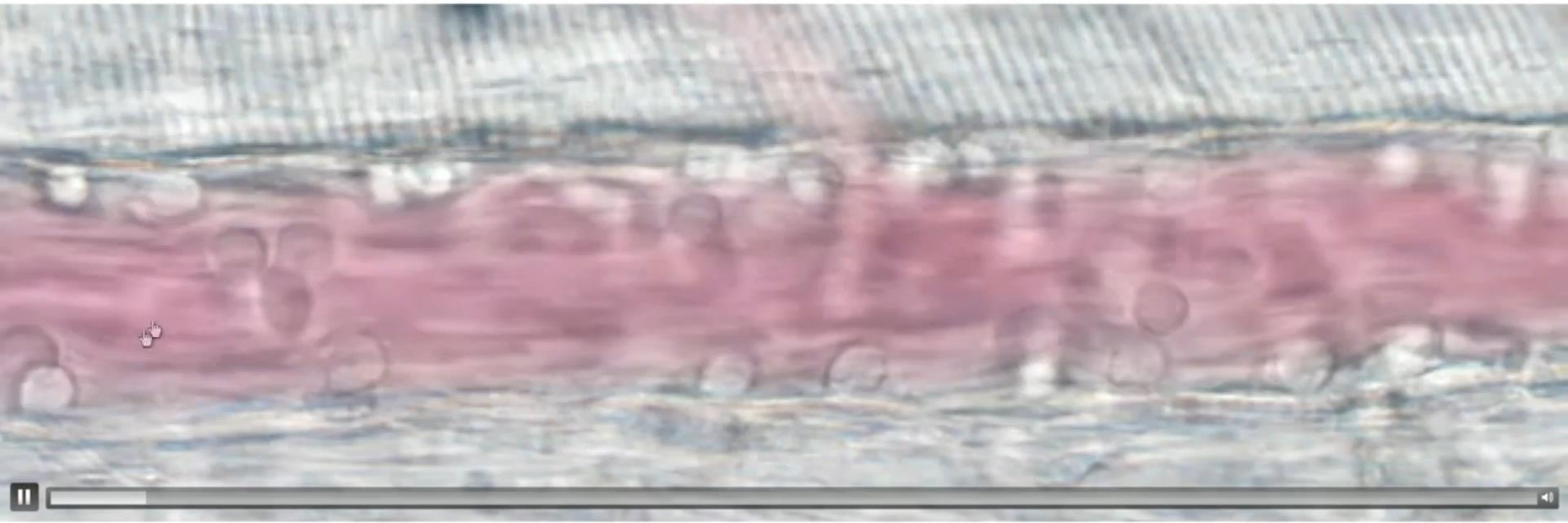
Additionally, dendritic cells ingest proteins made by pathogens at the site of infection and process them into peptides that are displayed on the dendritic cell surface.



These dendritic cells enter lymphatic vessels that drain into...

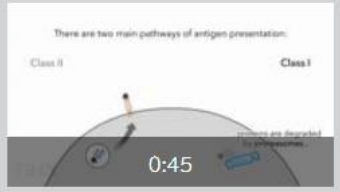
...lymph nodes, where they can stimulate T cells of the adaptive immune system.





ANTIGEN PRESENTATION

Class I Pathway



ANTIGEN PRESENTATION

Class II Pathway

Adaptive Immunity: B Cells

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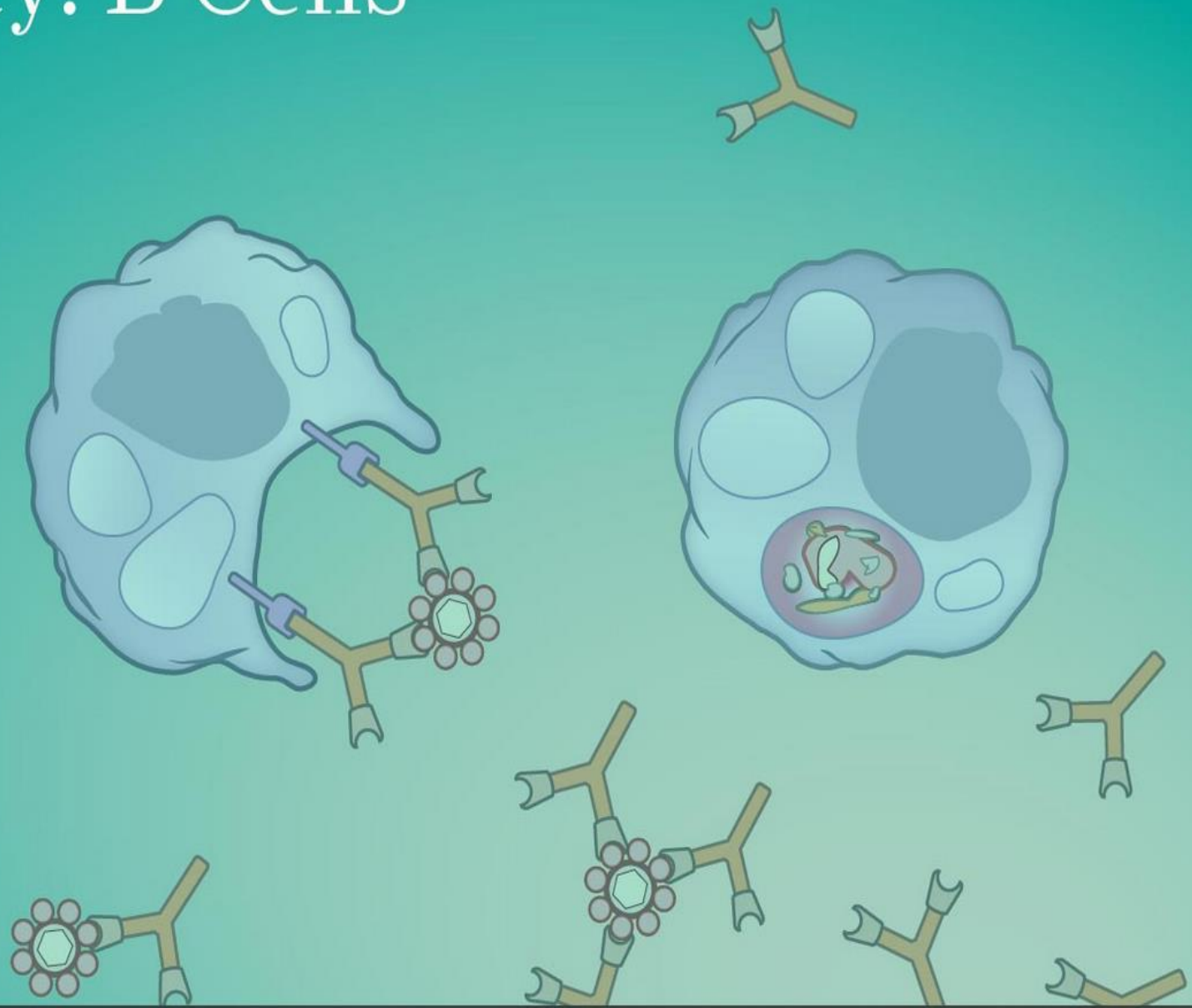
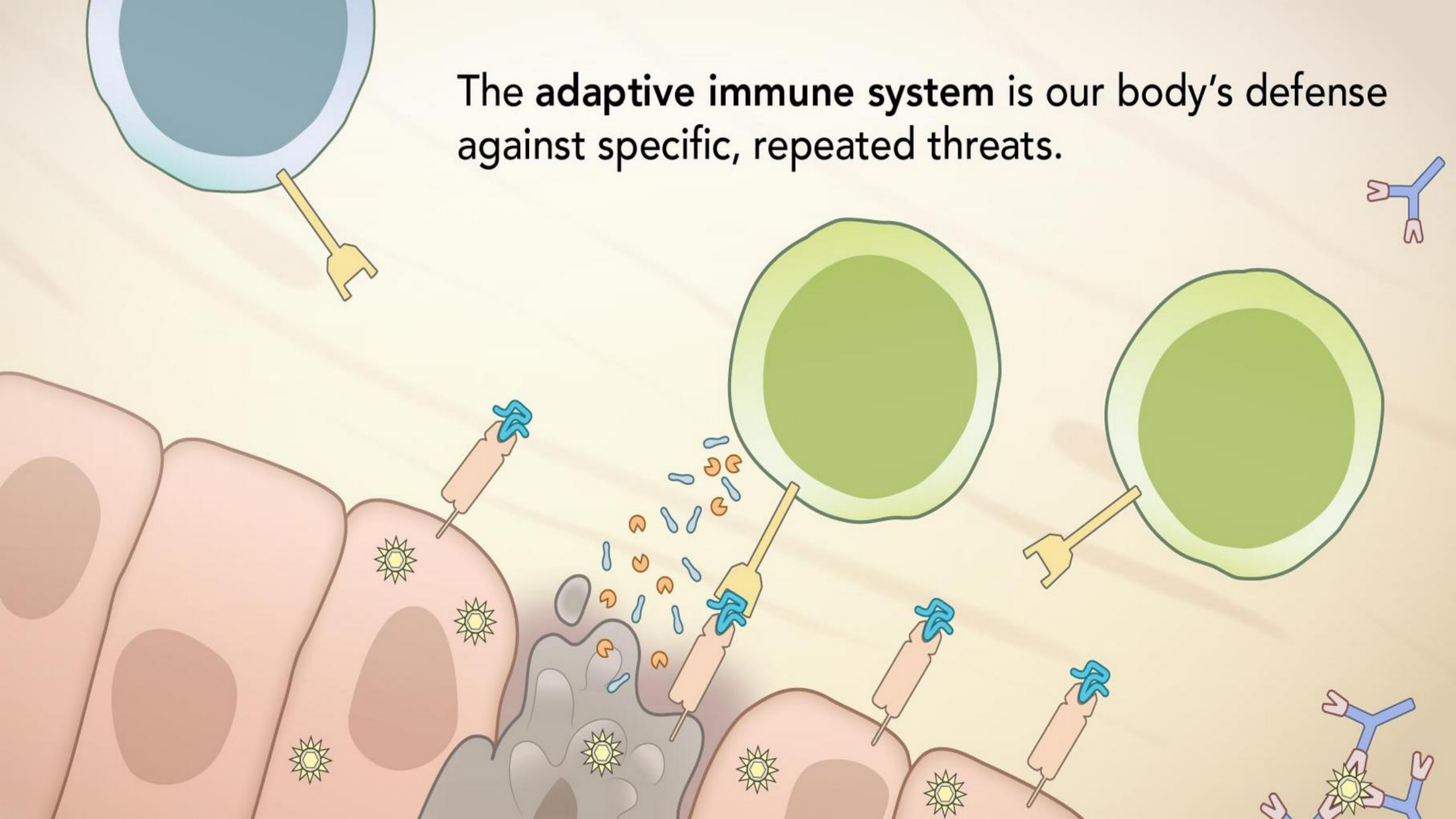
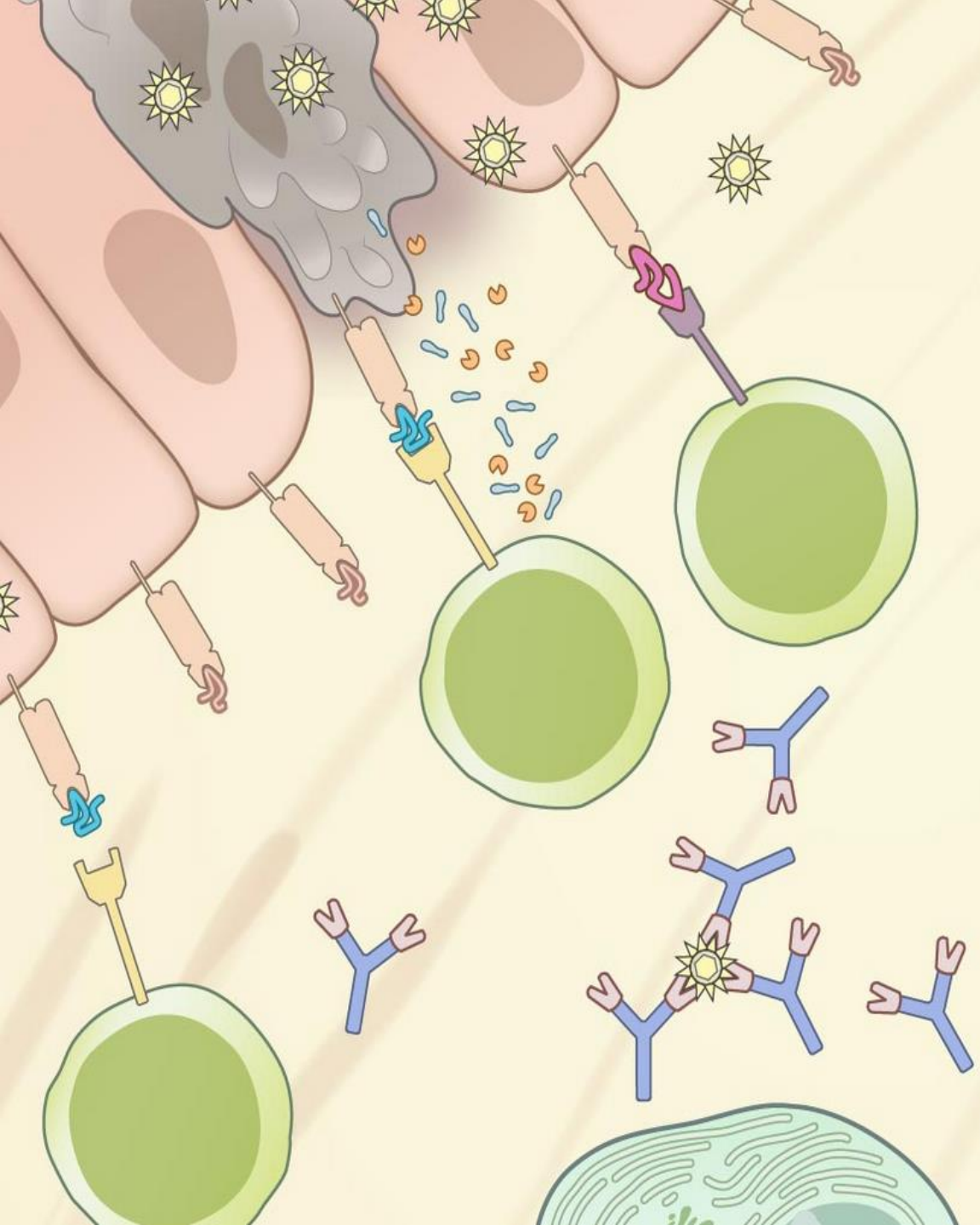
Part 1



The **adaptive immune system** is our body's defense against specific, repeated threats.





The adaptive immune system has...

Specificity

The adaptive immune system responds in a targeted way to specific antigens rather than general categories of pathogens.

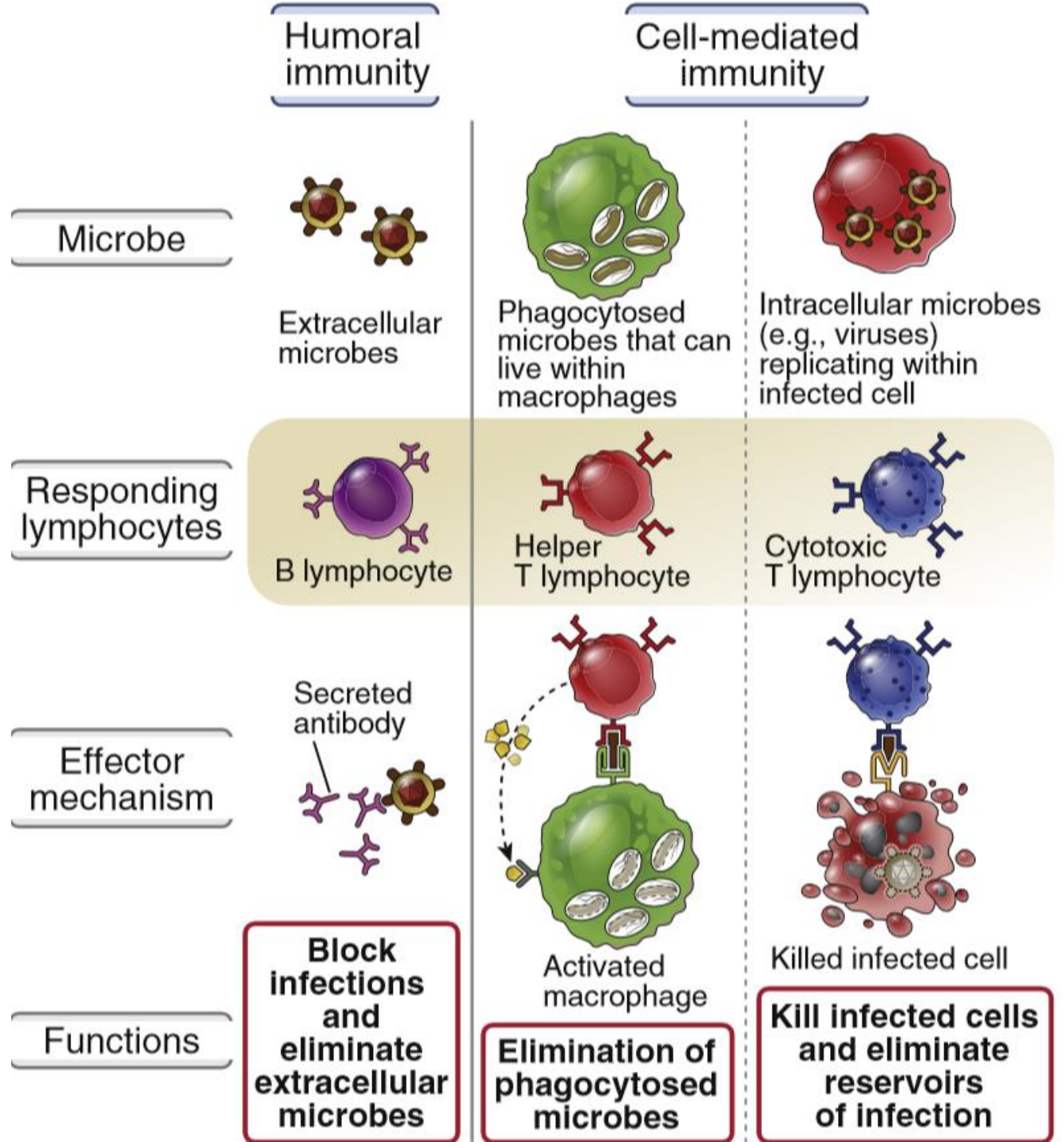
Recognition of self

The adaptive immune system can identify and respond to dangerous foreign molecules while ignoring harmless foreign molecules and molecules produced by our own body.

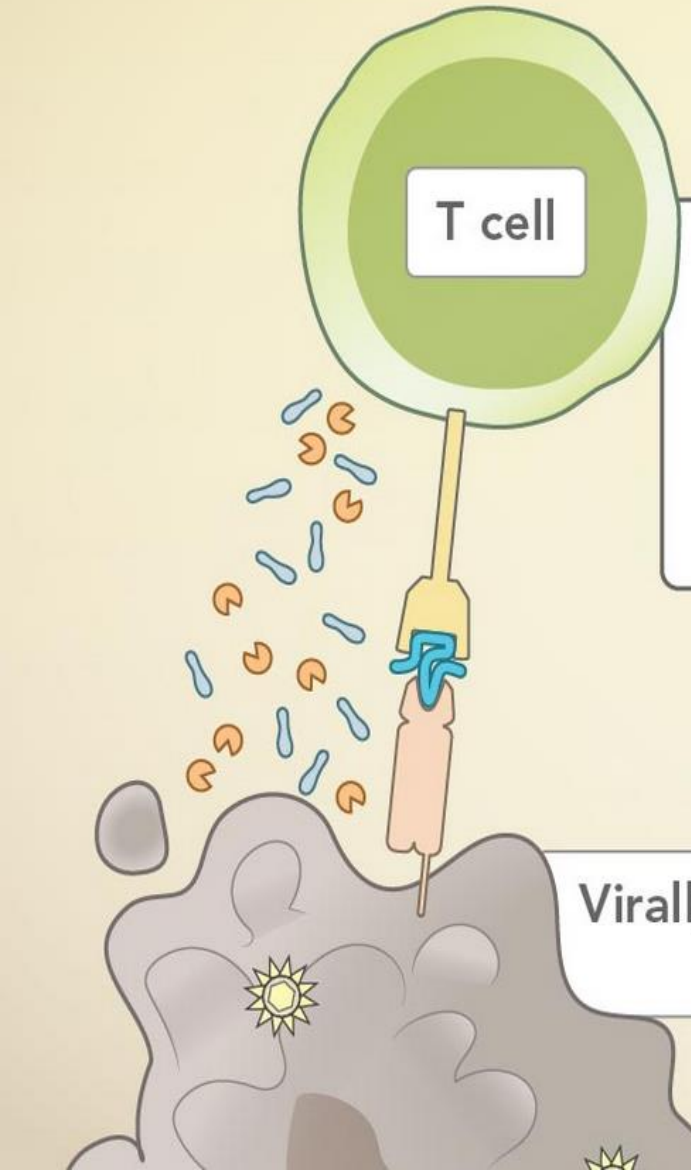
Memory

After the adaptive immune system has responded to a threat, it will be able to do so more quickly and robustly in the future

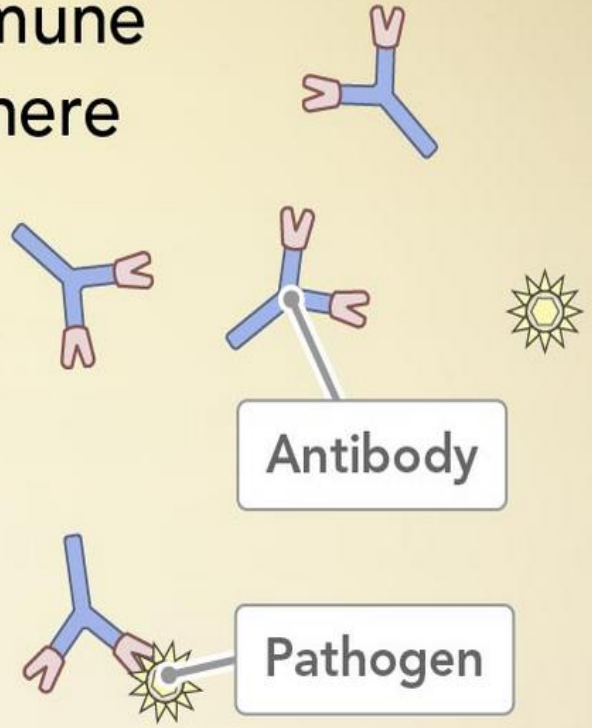
Feature	Functional significance
Specificity	Ensures that distinct antigens elicit specific responses
Diversity	Enables immune system to respond to a large variety of antigens
Memory	Leads to enhanced responses to repeated exposures to the same antigens
Clonal expansion	Increases number of antigen-specific lymphocytes from a small number of naive lymphocytes
Specialization	Generates responses that are optimal for defense against different types of microbes
Contraction and homeostasis	Allows immune system to respond to newly encountered antigens
Nonreactivity to self	Prevents injury to the host during responses to foreign antigens



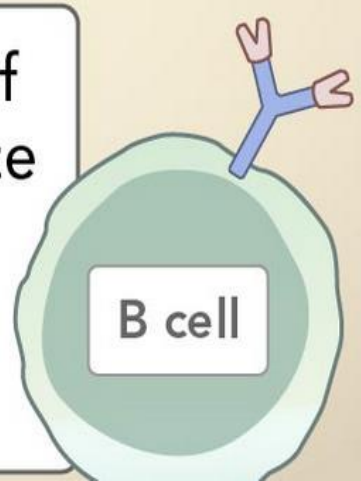
The unique cells of the adaptive immune system are called "lymphocytes." There are two types of lymphocytes.



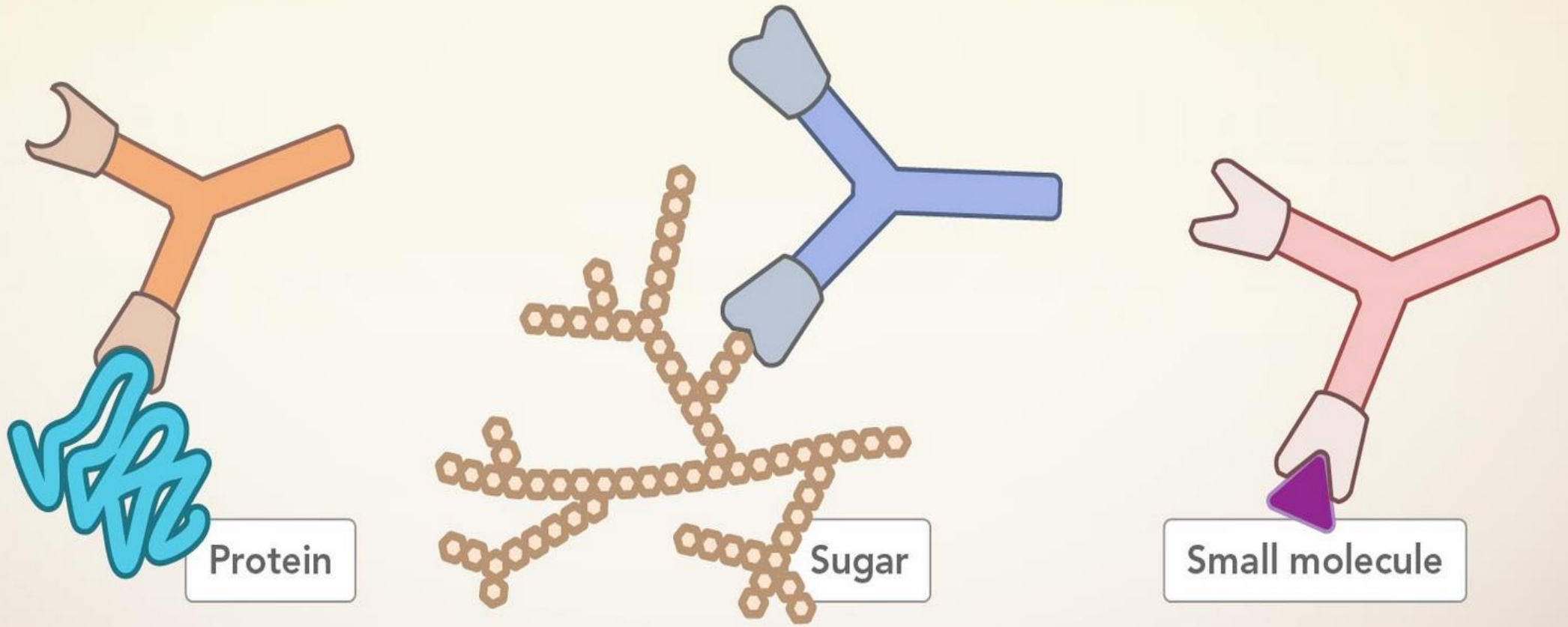
T cells recognize protein fragments (peptides) presented on specific surface proteins and either kill pathogens or help other immune cells.



B cells lead to the production of antibodies. Antibodies recognize many types of molecules and assist in the removal of pathogens in a variety of ways.



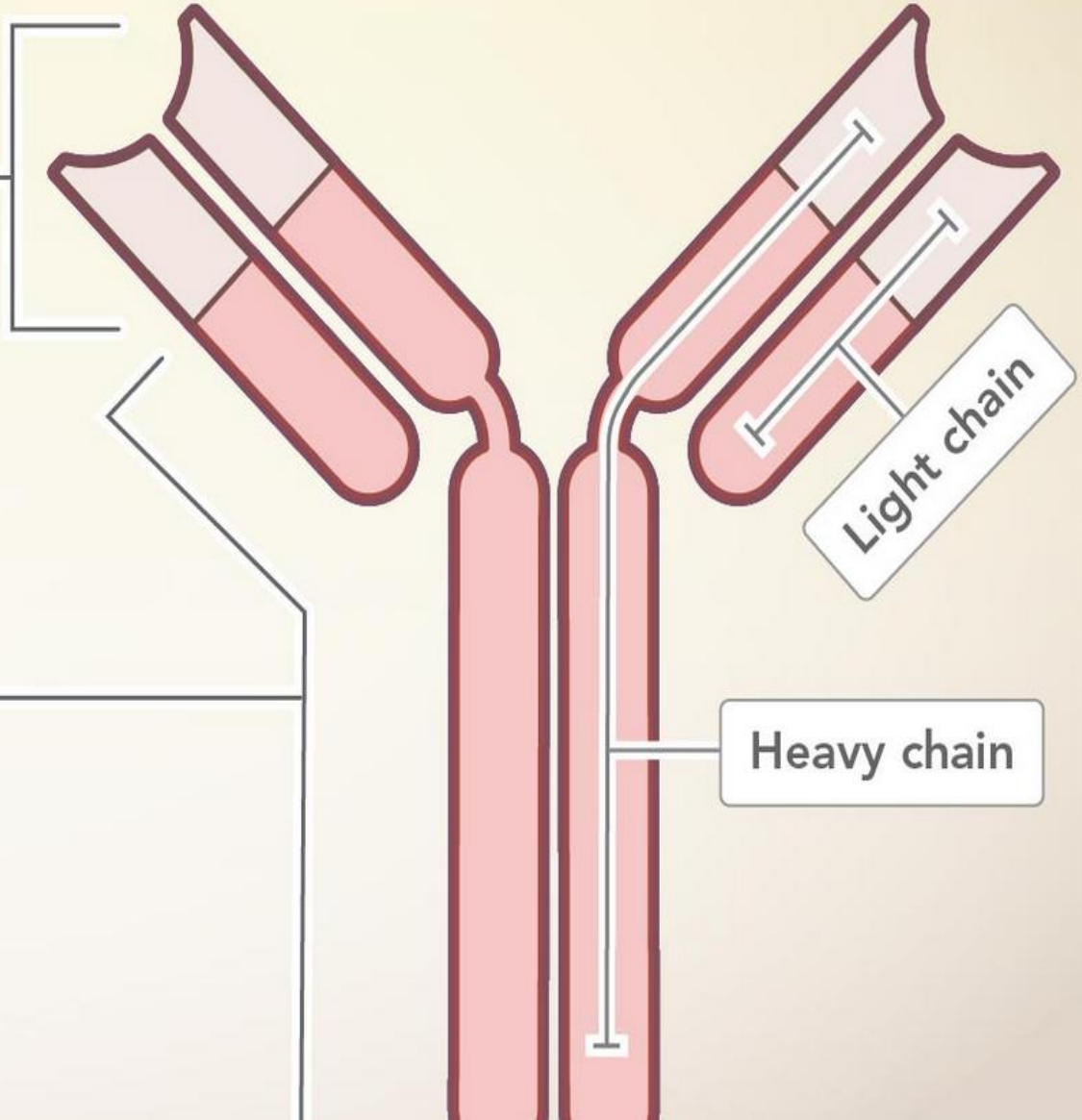
The main function of B cells is to produce **antibodies**, specialized proteins that can bind to many different kinds of antigens.



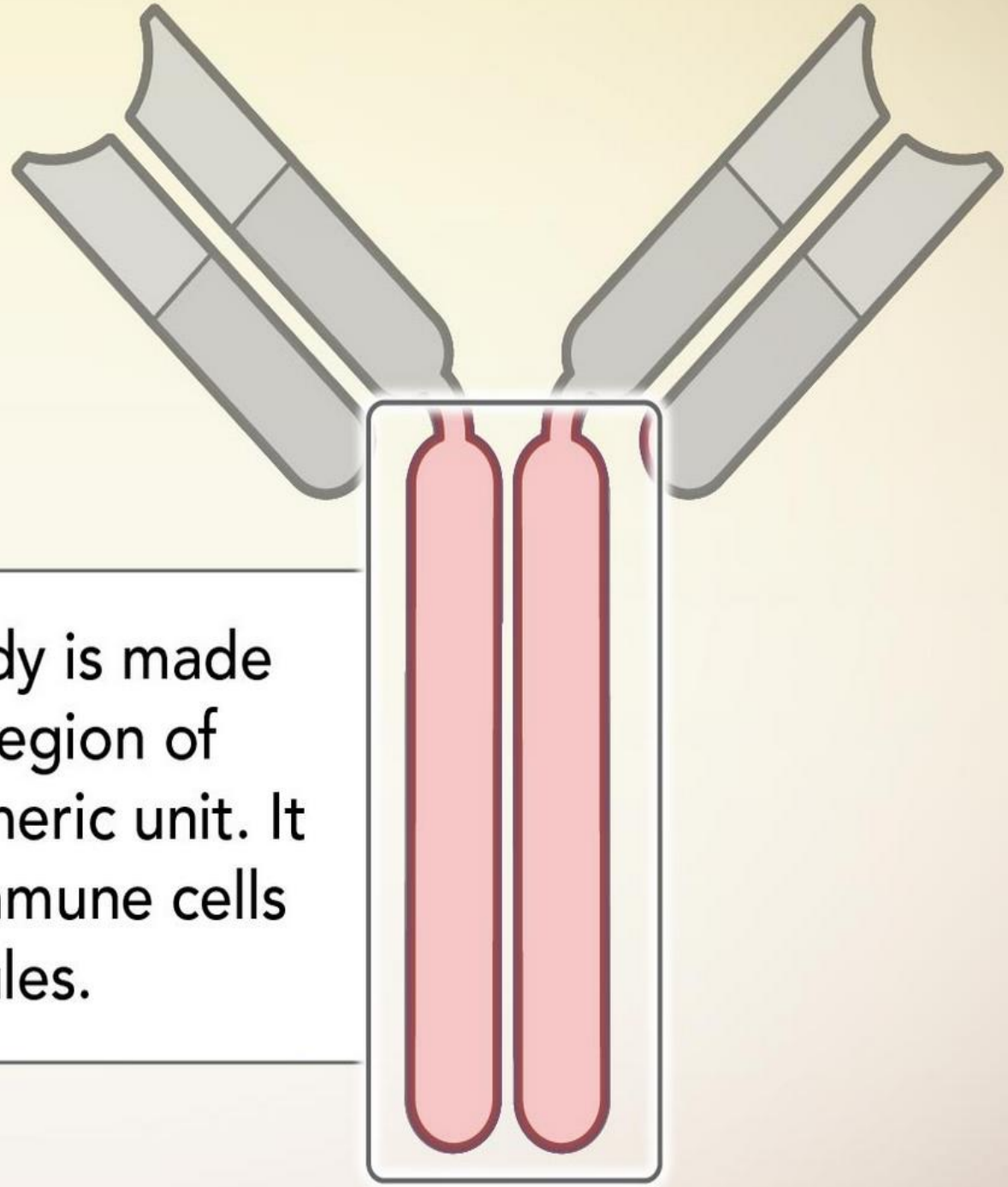
All antibodies have the same basic structural components.

The **antigen recognition site** is highly variable from one B cell clone to another, and binds to antigens.

The **constant region** of an antibody is different for each of the different isotypes (including IgG, IgA, IgM, IgD, or IgE).

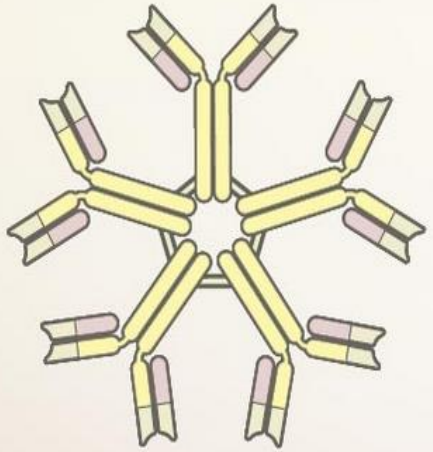


The **Fc region** of an antibody is made up of part of the constant region of each Ig heavy chain in a dimeric unit. It binds to Fc receptors on immune cells and to complement molecules.

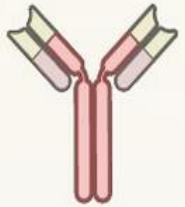


There are 5 major types of heavy chain constant regions which determine the isotype of the antibody. Antibodies perform several different functions which vary between isotypes.

IgM

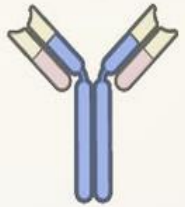


IgG

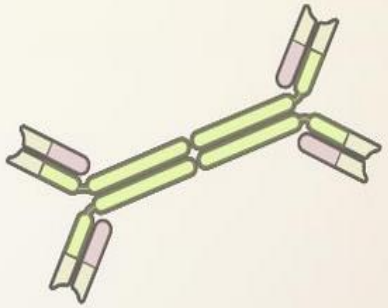


IgD

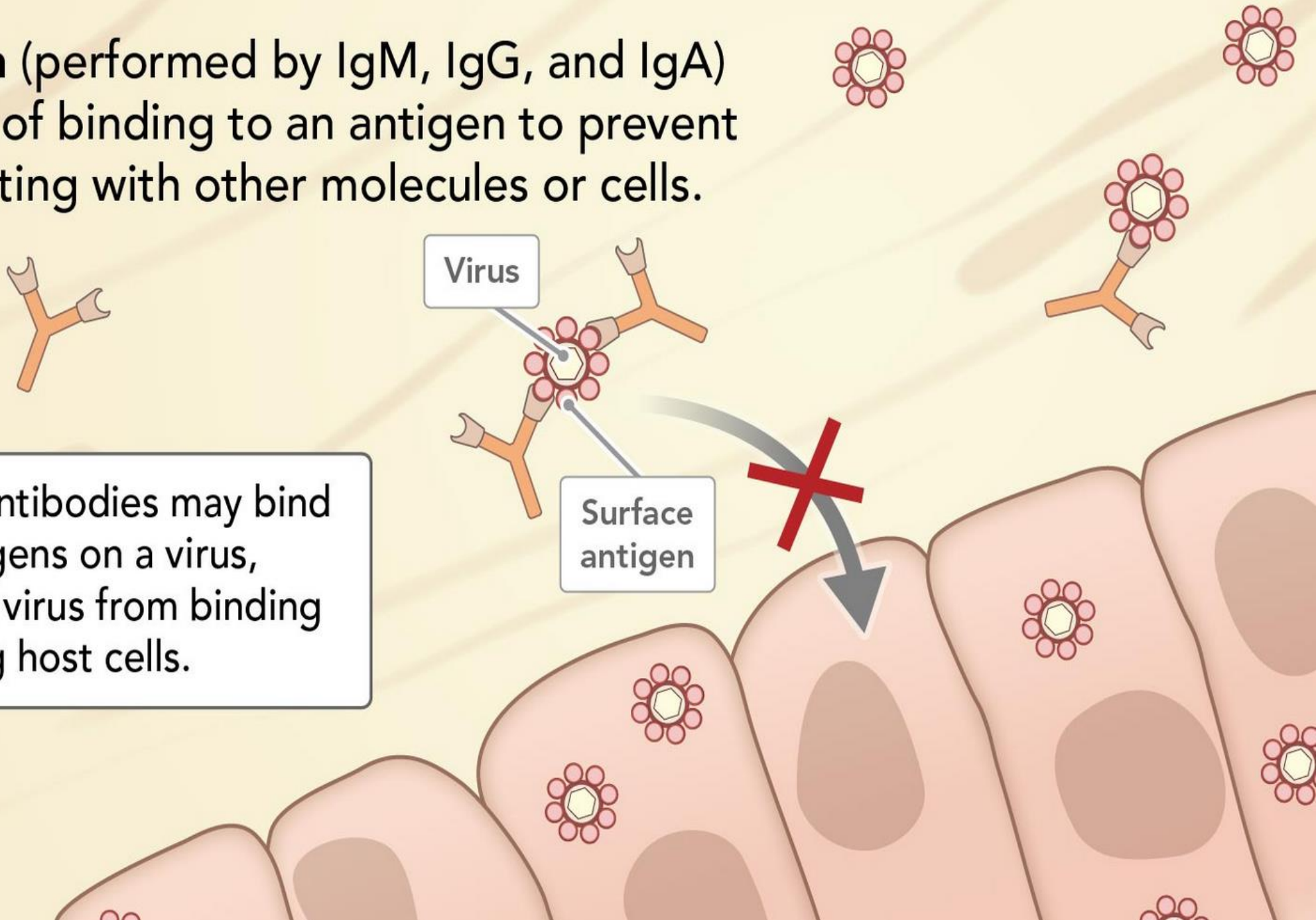
IgE



IgA



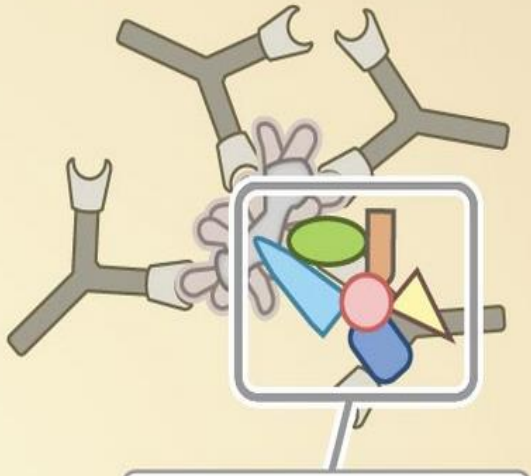
Neutralization (performed by IgM, IgG, and IgA) is the process of binding to an antigen to prevent it from interacting with other molecules or cells.



For example, antibodies may bind to surface antigens on a virus, preventing the virus from binding to and invading host cells.

Complement fixation (performed by IgG and IgM) refers to the ability of antibodies to activate the complement system.

Antibodies help initiate binding of complement proteins to the surface of a pathogen. This can help with opsonization by complement receptors.

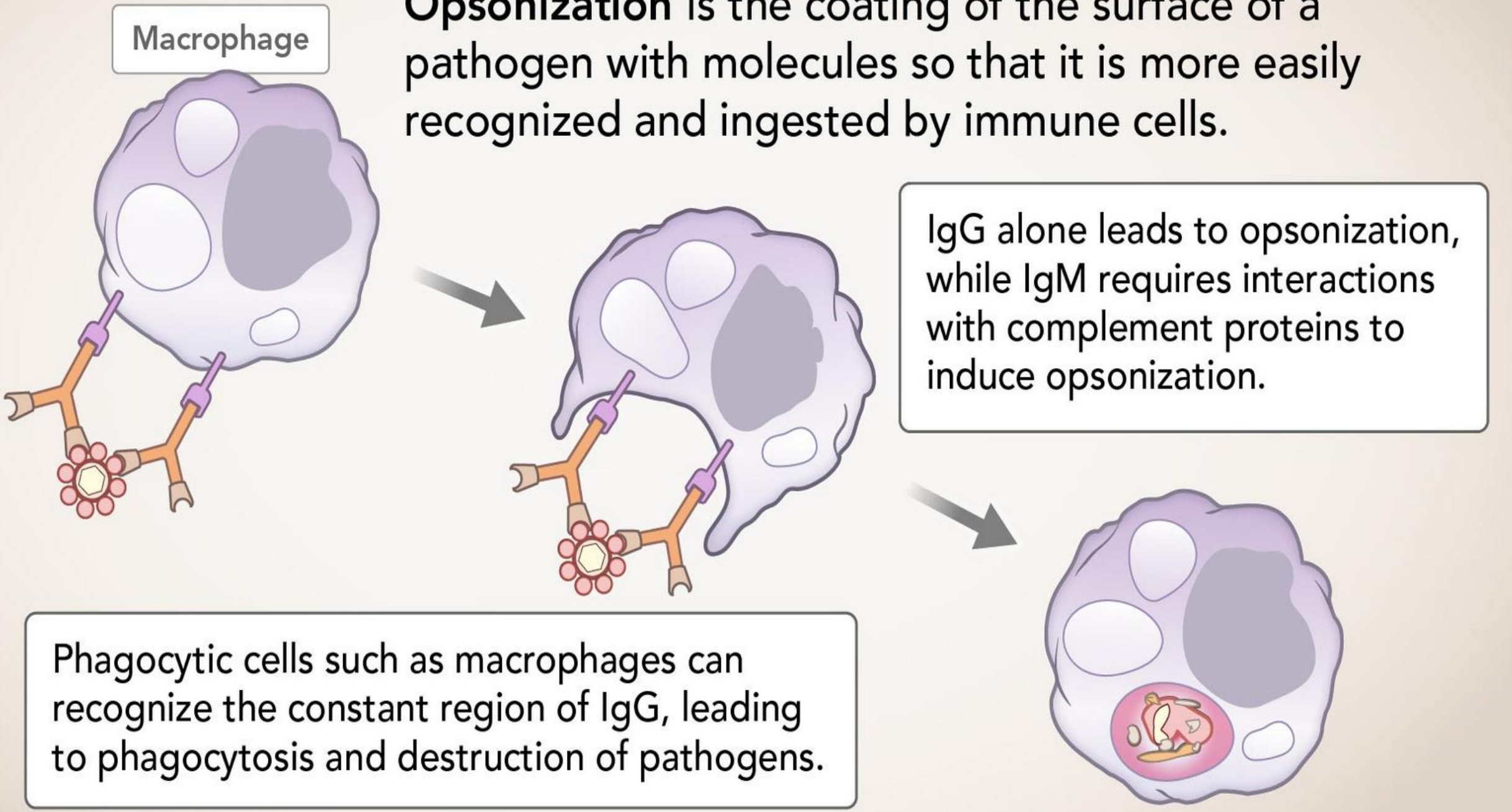


Membrane attack complex

Complement proteins

The complement cascade also leads to the formation of the membrane attack complex, which leads to cell lysis.

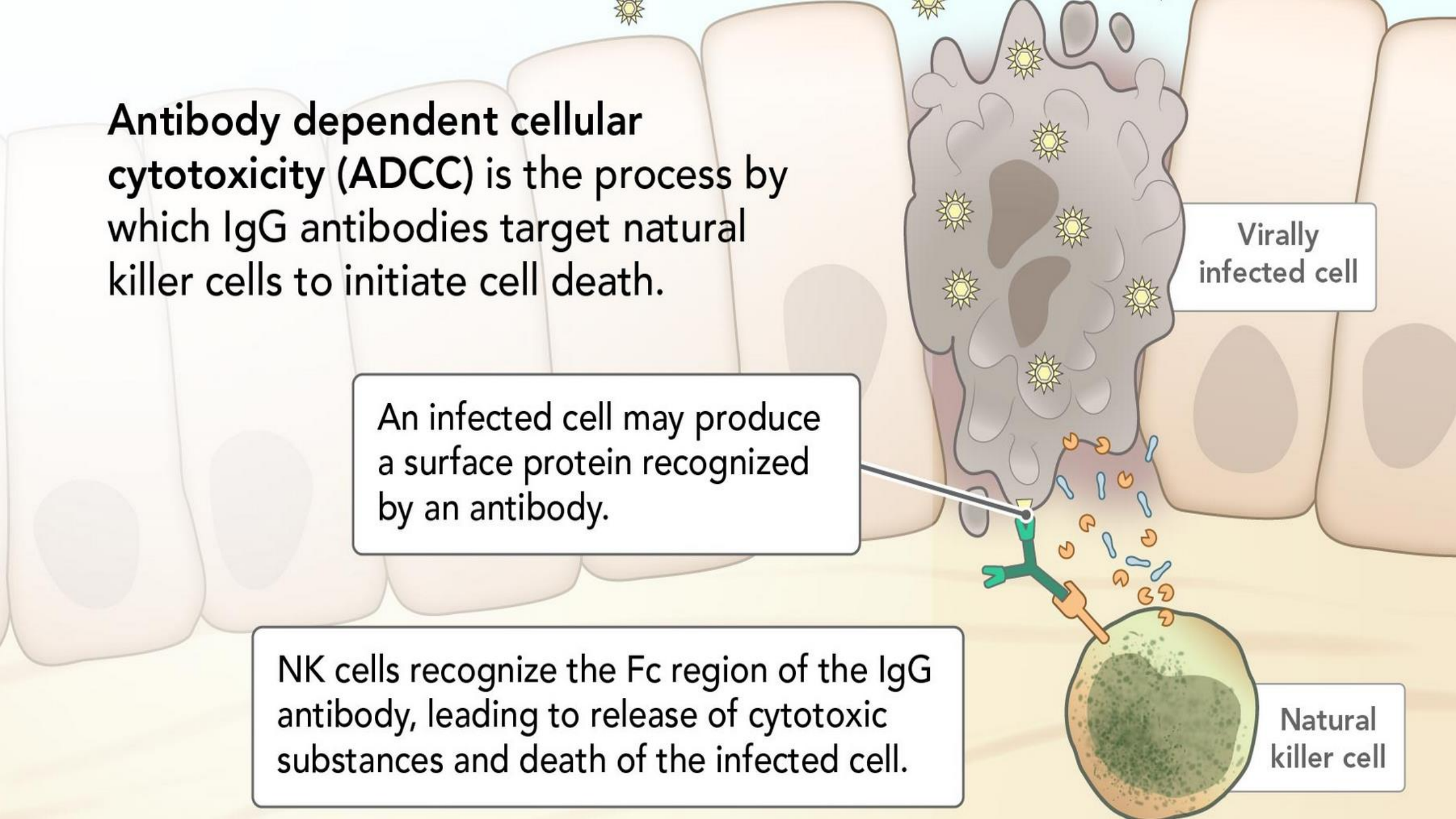
Opsonization is the coating of the surface of a pathogen with molecules so that it is more easily recognized and ingested by immune cells.



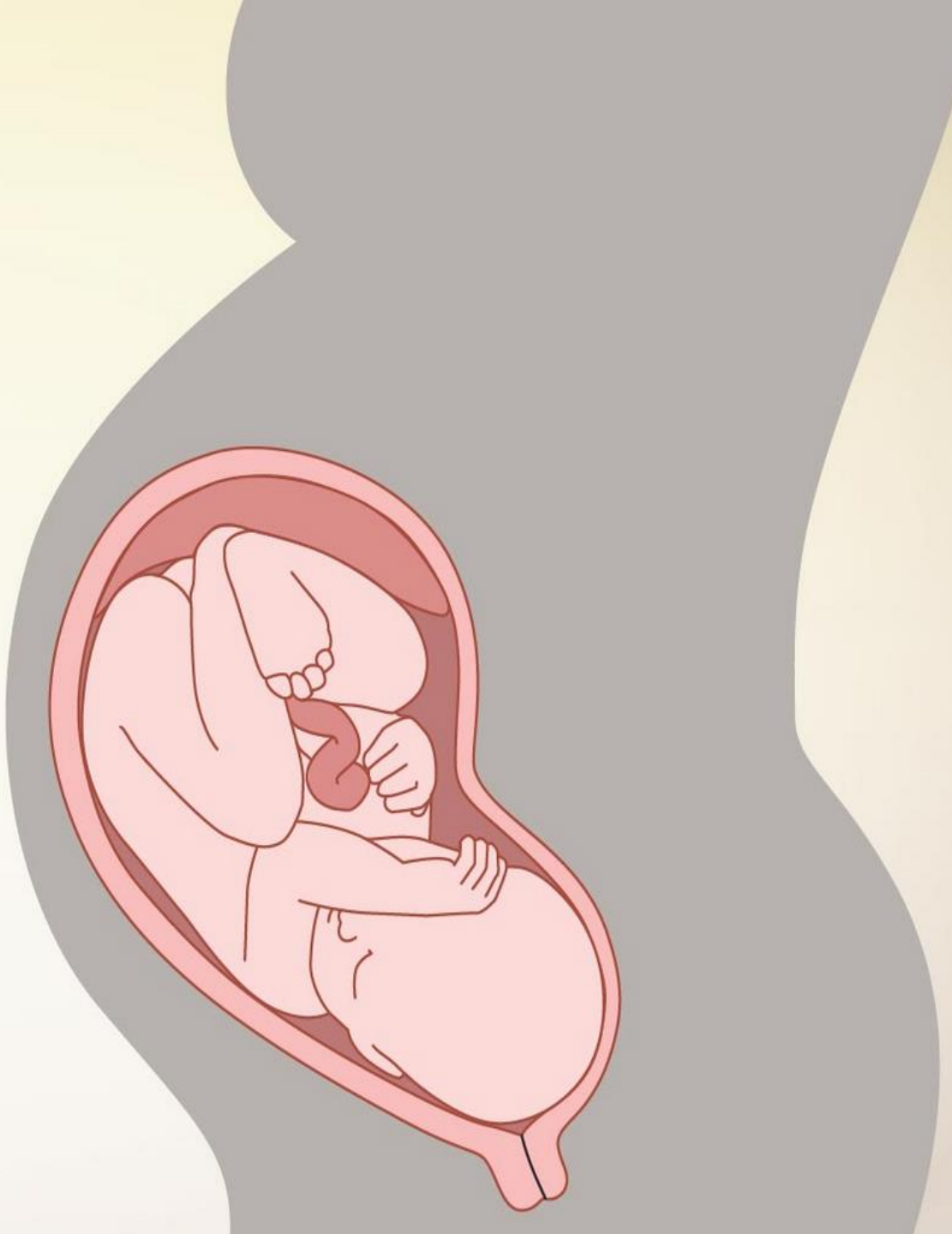
IgG alone leads to opsonization, while IgM requires interactions with complement proteins to induce opsonization.

Phagocytic cells such as macrophages can recognize the constant region of IgG, leading to phagocytosis and destruction of pathogens.

Antibody dependent cellular cytotoxicity (ADCC) is the process by which IgG antibodies target natural killer cells to initiate cell death.



Antibodies also mediate **neonatal immunity.** Maternal IgG transported through the placenta to the fetus protects babies from infections for about 6 months after birth.



Adaptive Immunity: B Cells

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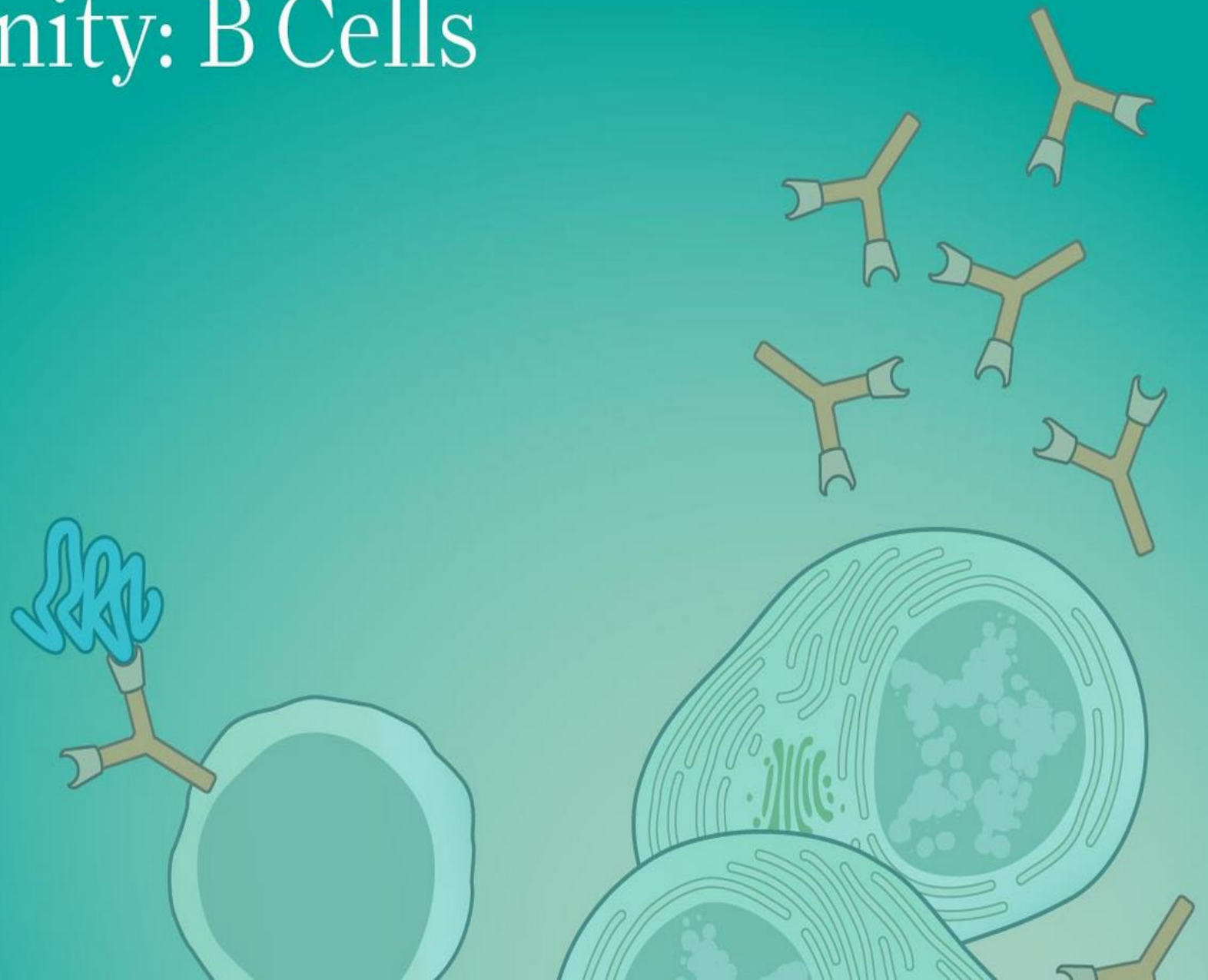
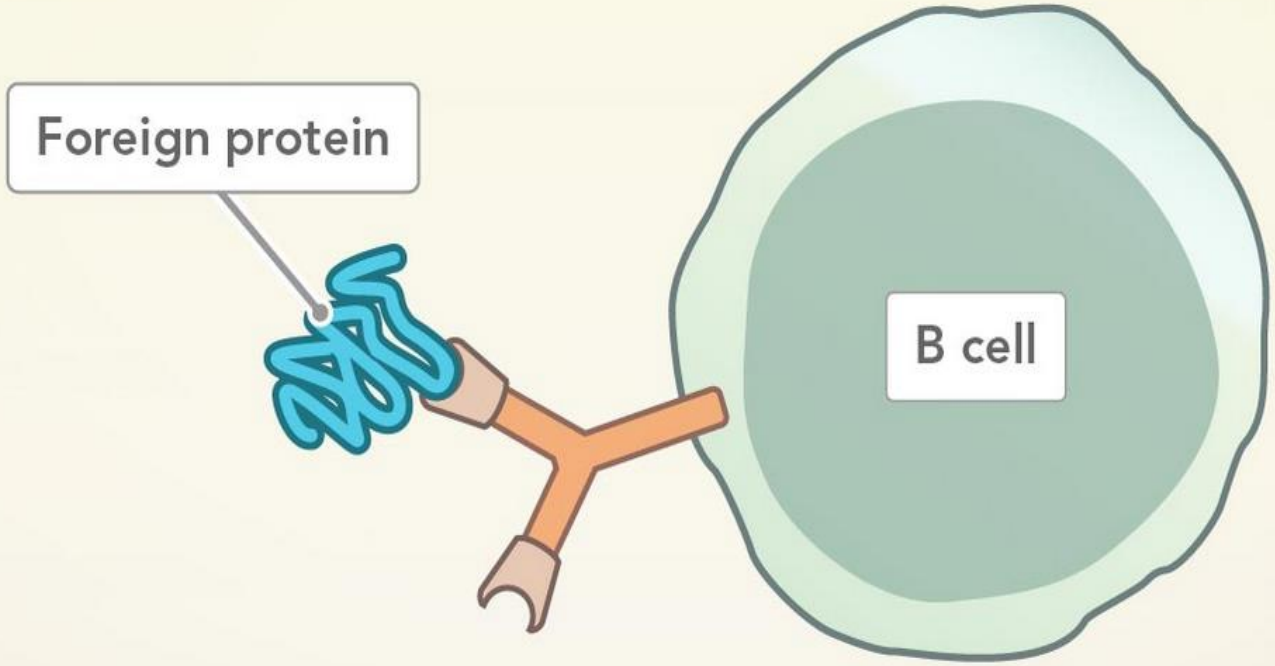
Part 2

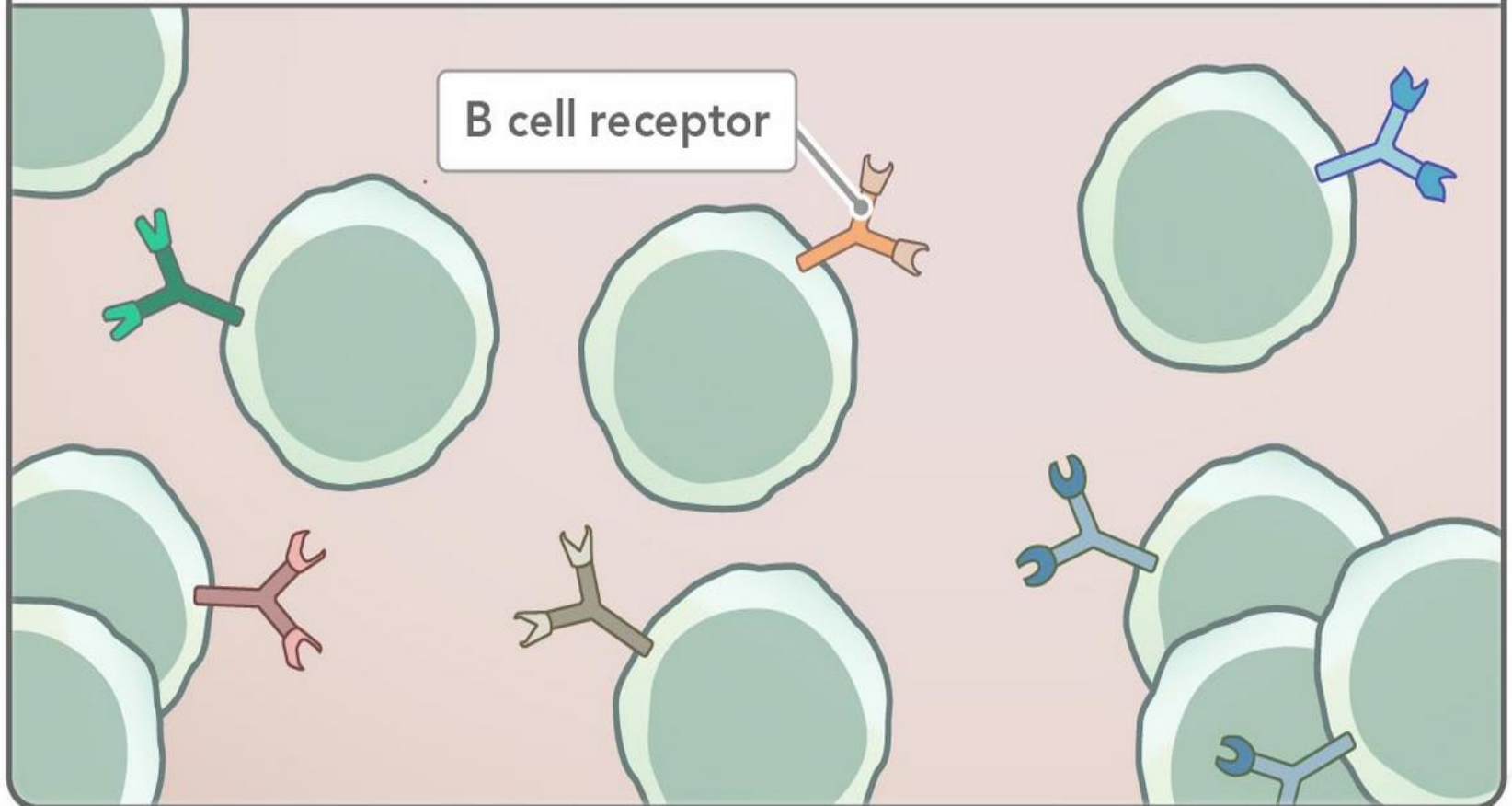


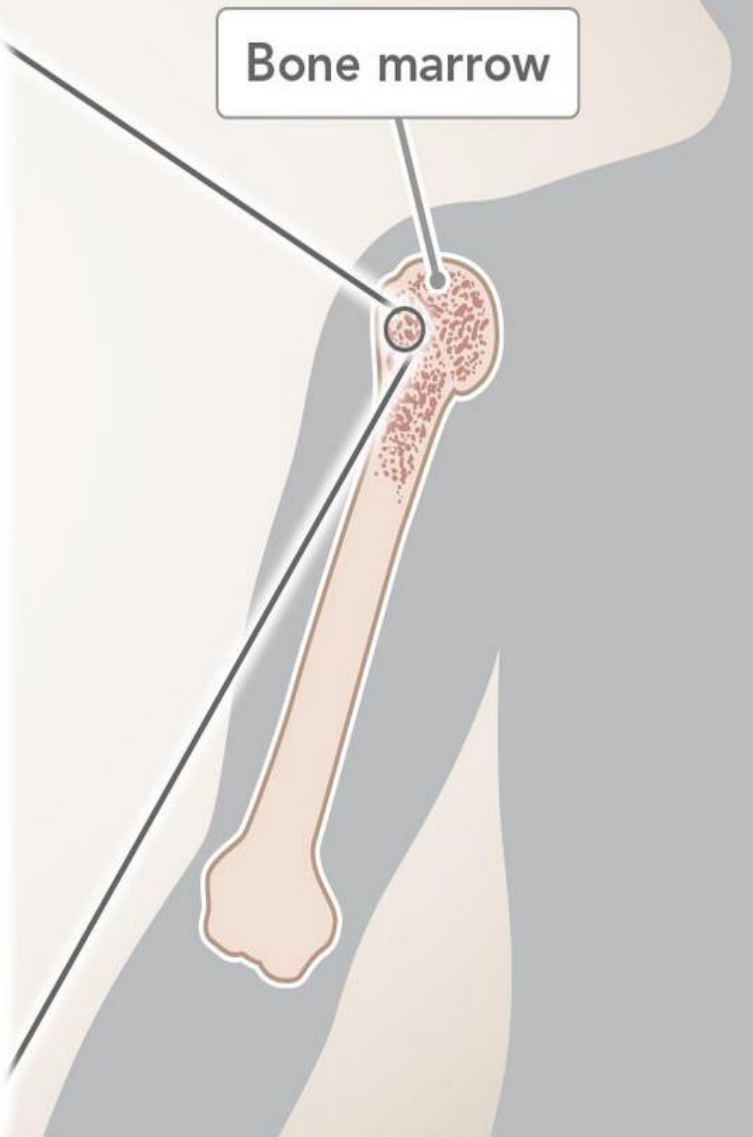
To understand how B cells produce antibodies for specific antigens, let's follow an example of antibodies being produced in response to a foreign protein.



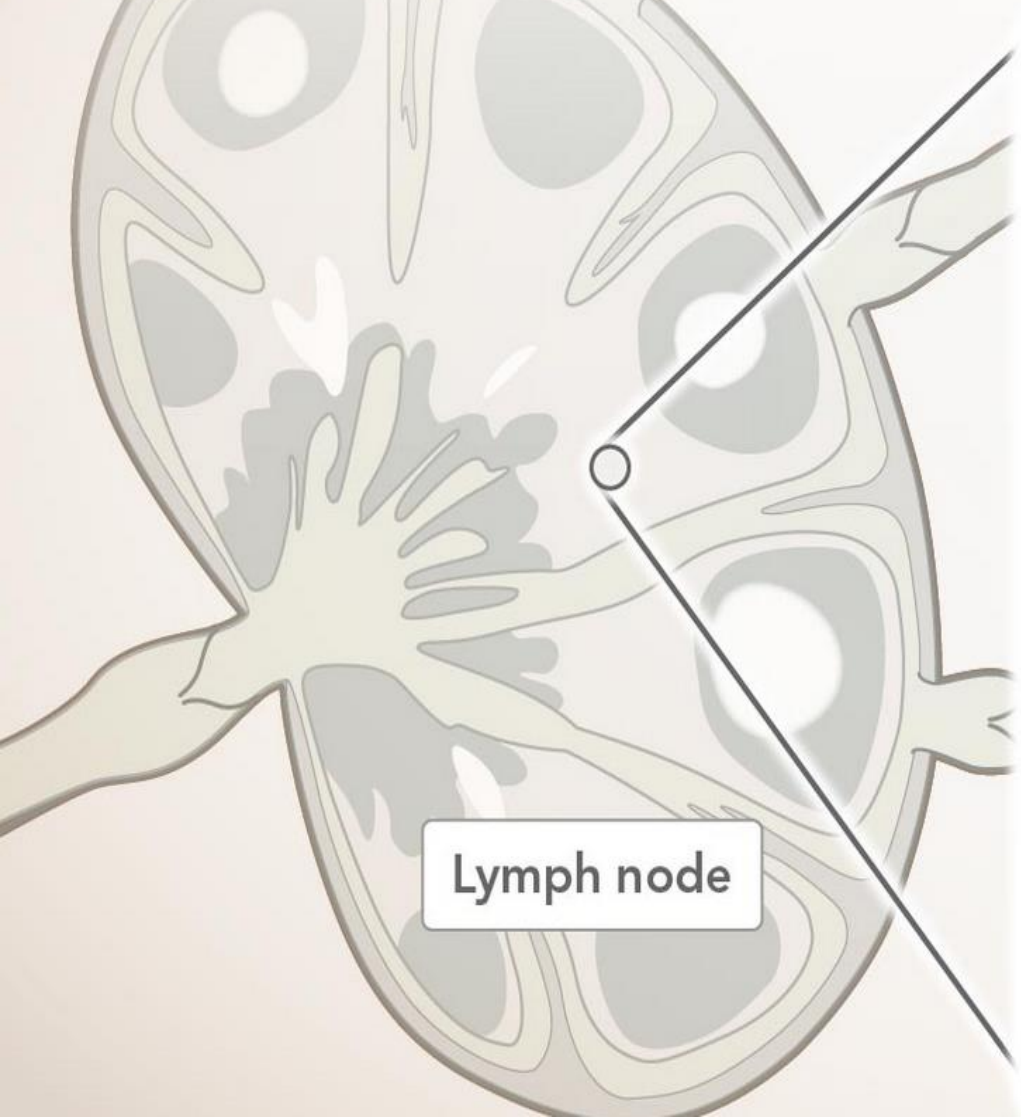
B cells develop in the bone marrow. Each immature B cell expresses a B cell receptor with a random, unique specificity.

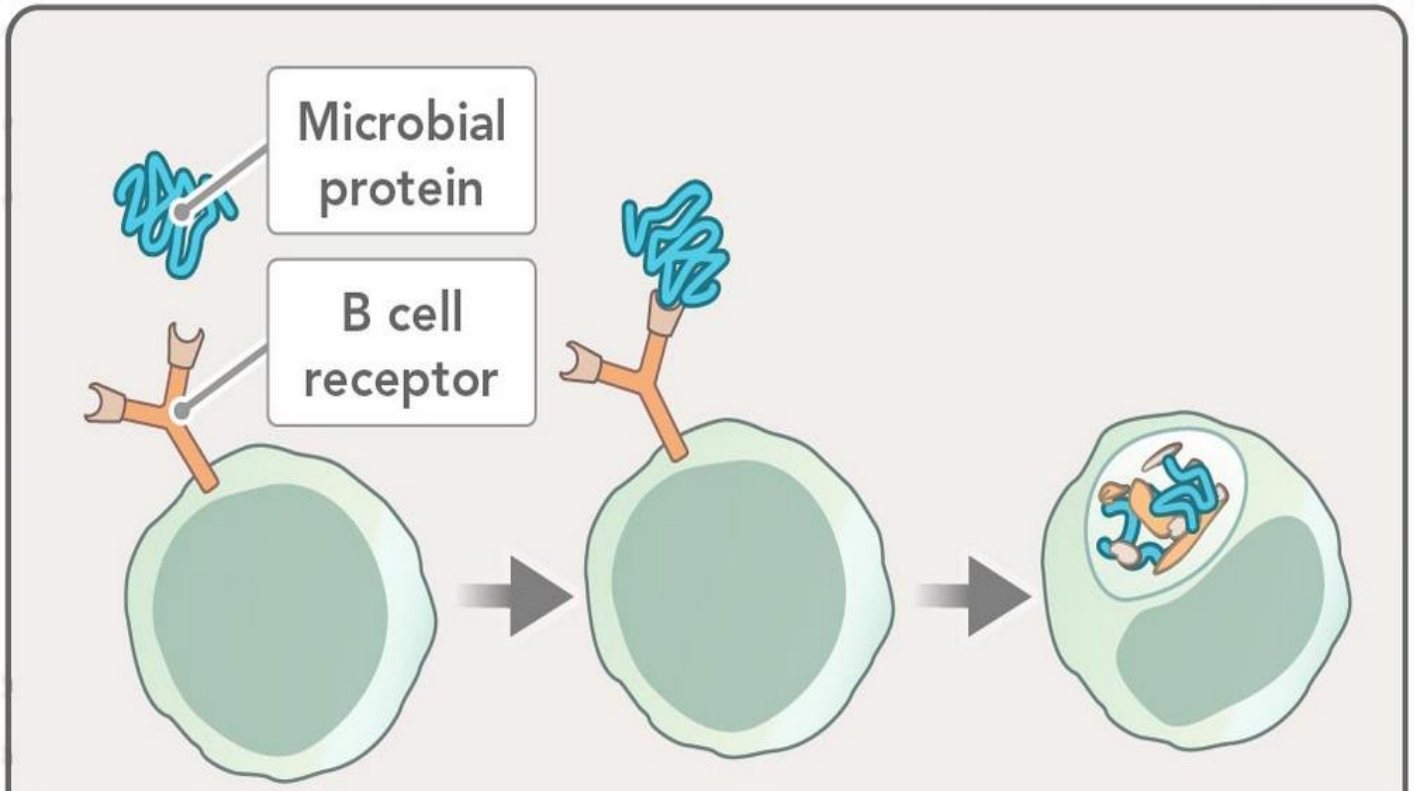
The B cell receptor on each cell is a membrane bound form of antibody and will recognize a specific antigen.





These cells circulate through secondary lymphoid organs, where they might encounter specific microbial molecules or antigens.

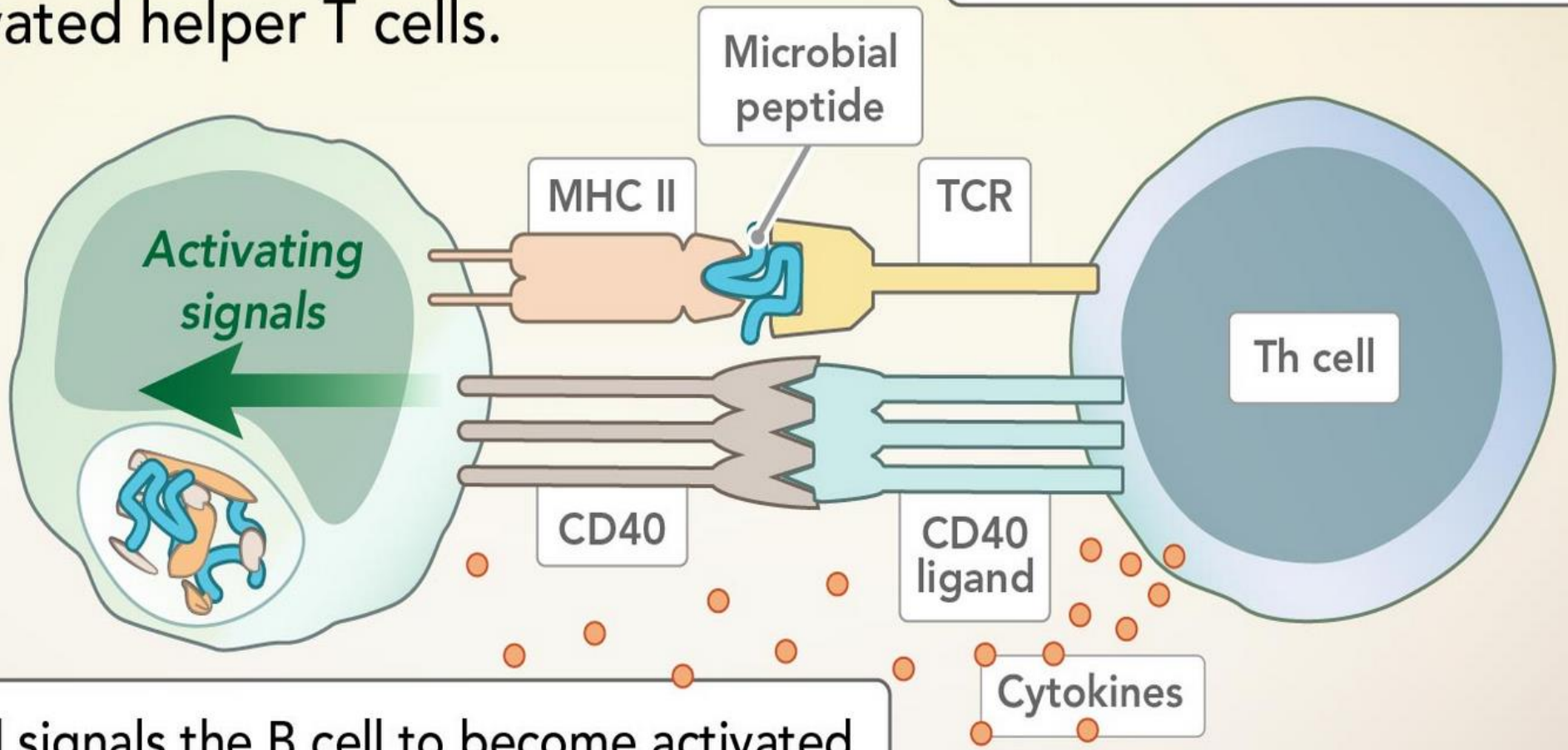




If the B cell receptor on a B cell recognizes a protein antigen, the B cell is partly activated and internalizes the protein.

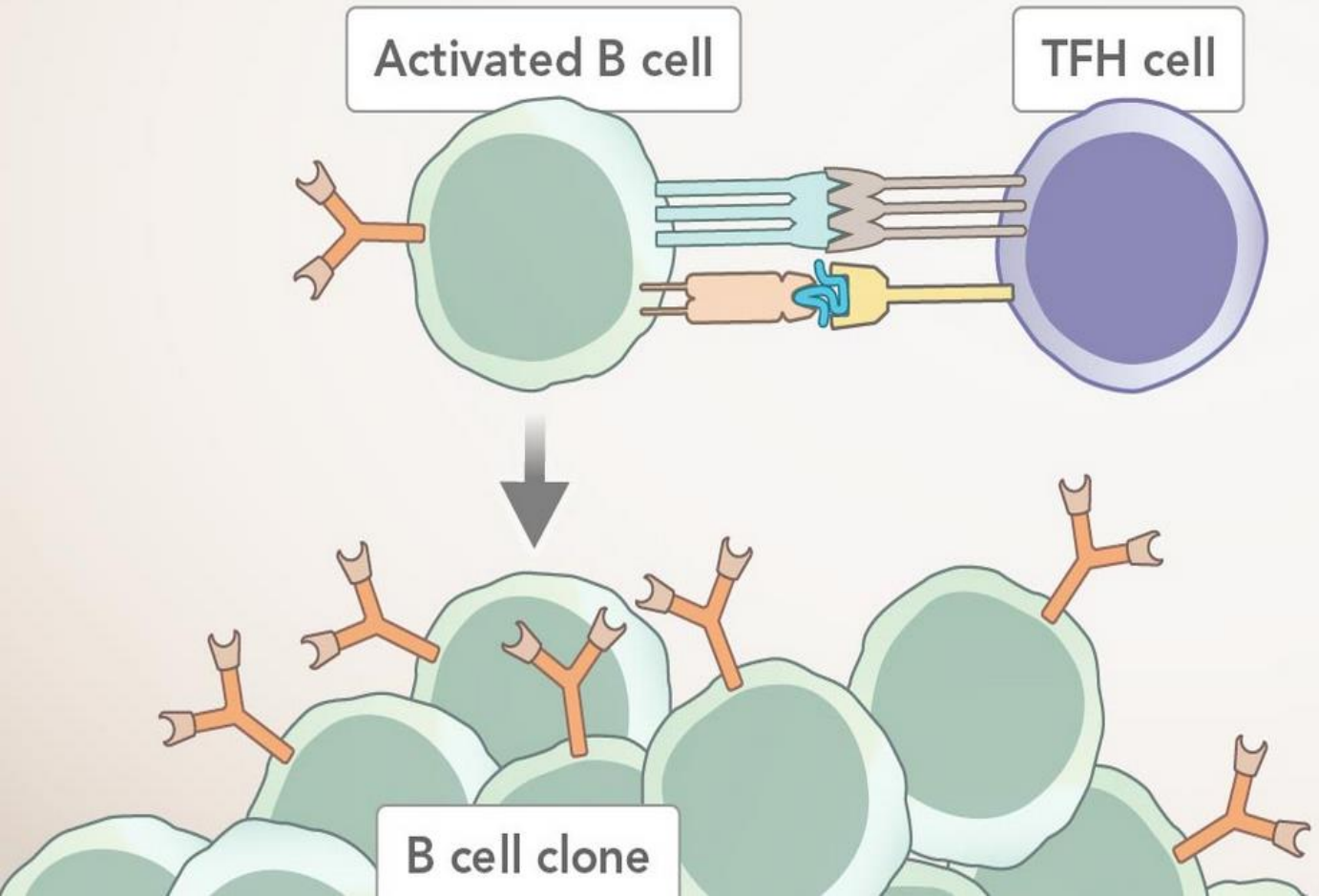
The B cell presents processed peptides from the protein antigen on MHC II, allowing interaction with activated helper T cells.

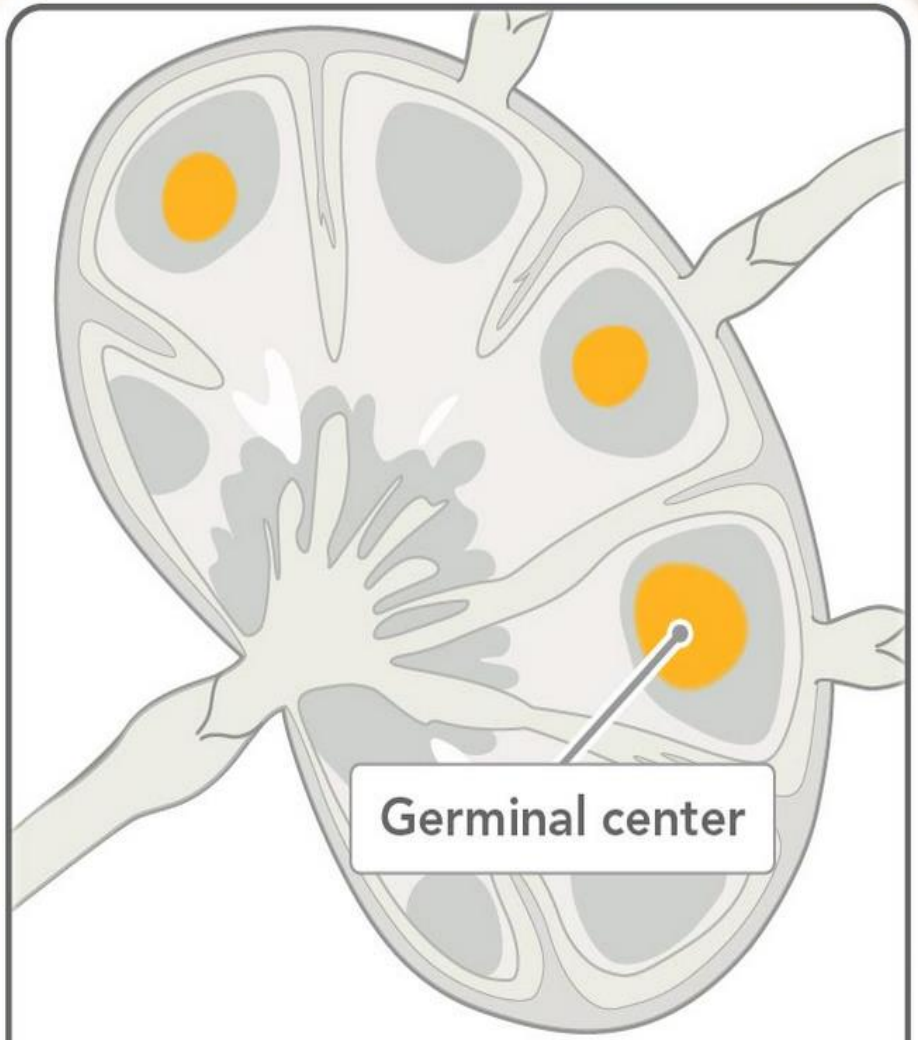
Helper T cells that recognize the peptide bind to the peptide/MHC II complex.



The T cell signals the B cell to become activated using CD40 ligand and secreted cytokines.

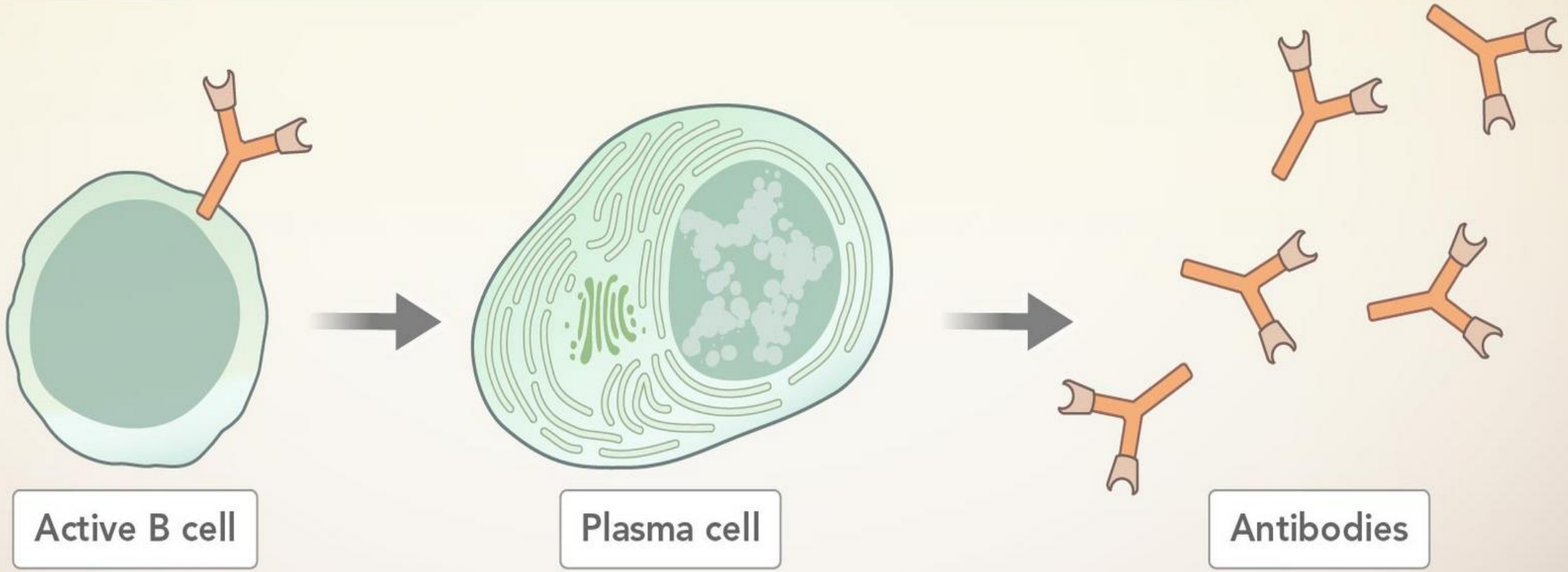
With help from follicular helper T cells, the activated B cell undergoes **clonal expansion,** creating many B cells with B cell receptors specific for the protein.



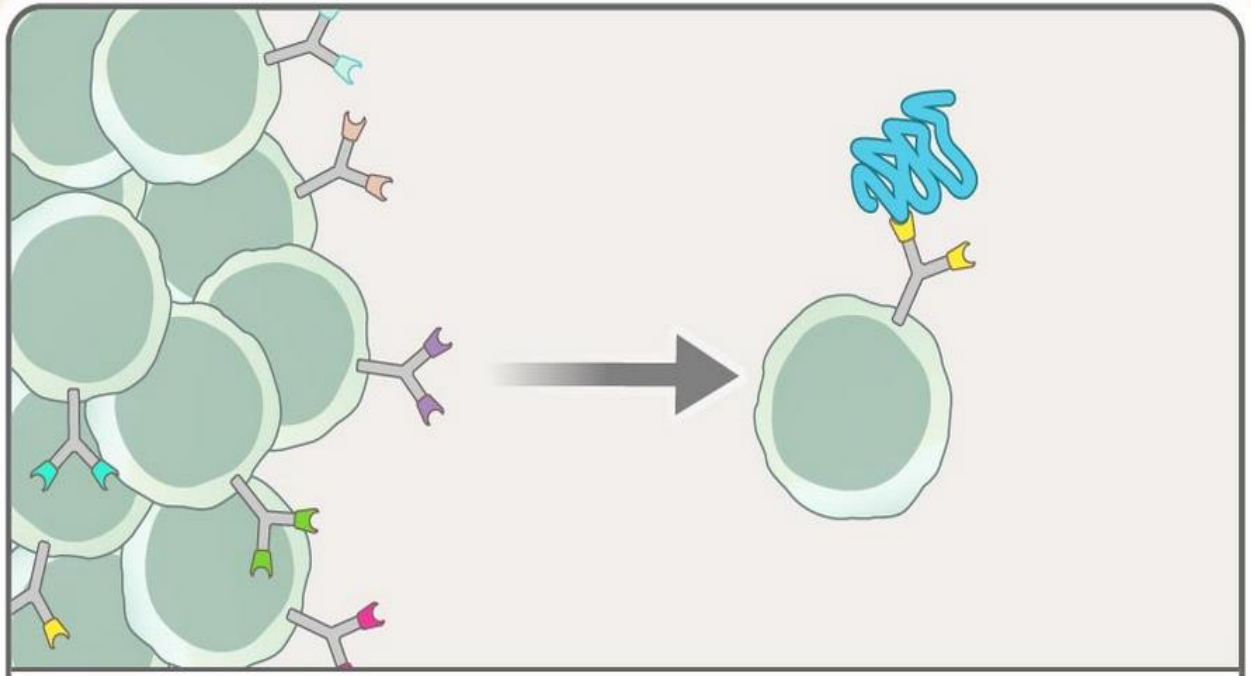


The area of the lymph node where the B cells expand becomes a **germinal center.**

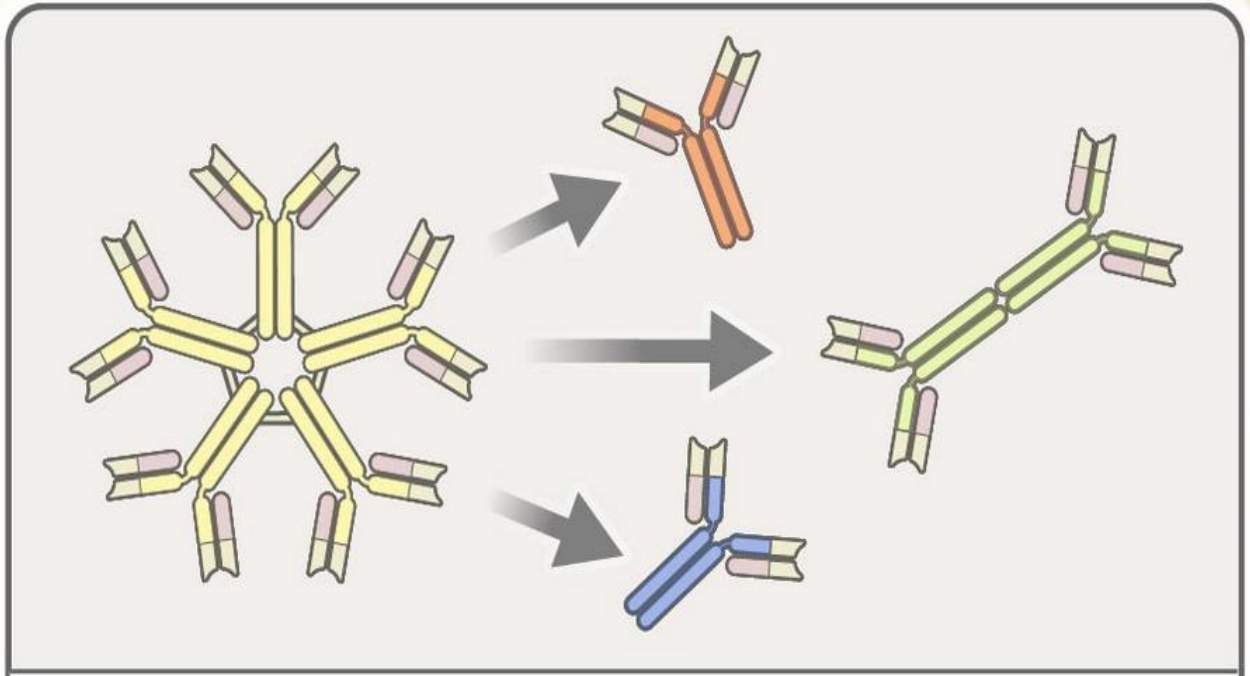
These activated B cells can then differentiate into **plasma cells**, which produce antibodies with the same antigen-binding site as the original B cell receptor.



Germinal centers are sites at which dividing B cells undergo affinity maturation and isotype switching.



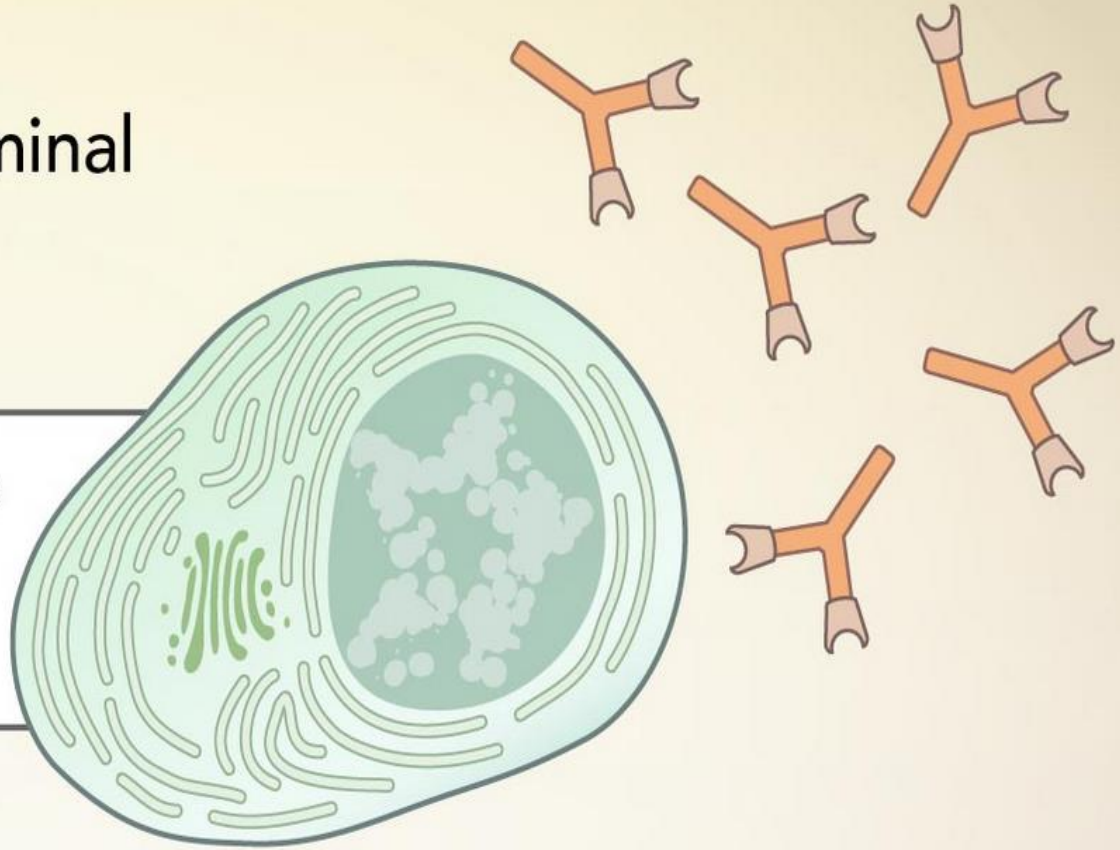
Affinity maturation: B cell receptors are mutated in the germinal center (somatic hypermutation) and the highest affinity B cells are selected to become memory B cells and long lived plasma cells.

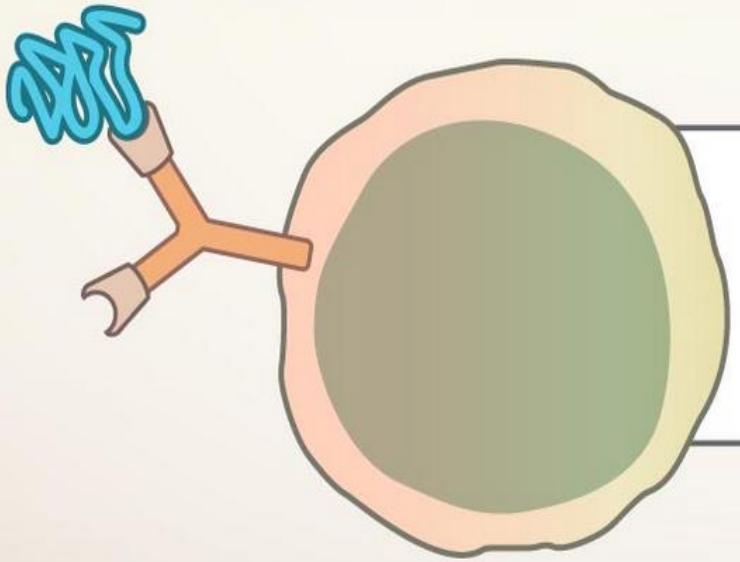


Isotype switching: The heavy chains of B cell receptors are changed so that different antibody isotypes can be produced, creating a more robust immune response.

High affinity B cells selected in the germinal center give rise to...

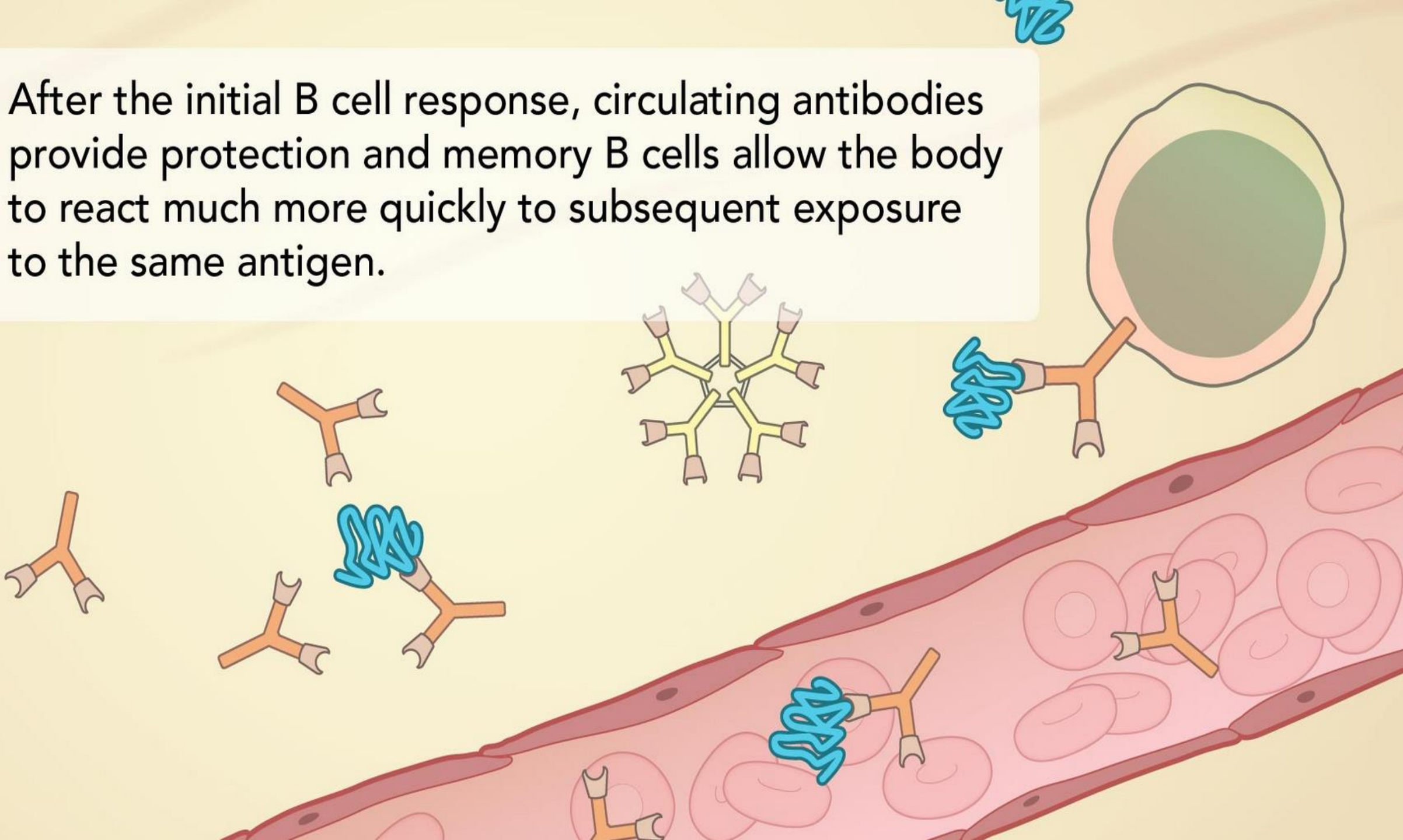
Long-lived plasma cells. These cells produce high affinity antibodies that will circulate in the body even after the infection is cleared.





Memory B cells. These will become re-activated and produce more plasma cells if re-exposed to the antigen in the future.

After the initial B cell response, circulating antibodies provide protection and memory B cells allow the body to react much more quickly to subsequent exposure to the same antigen.



Adaptive Immunity: T Cells

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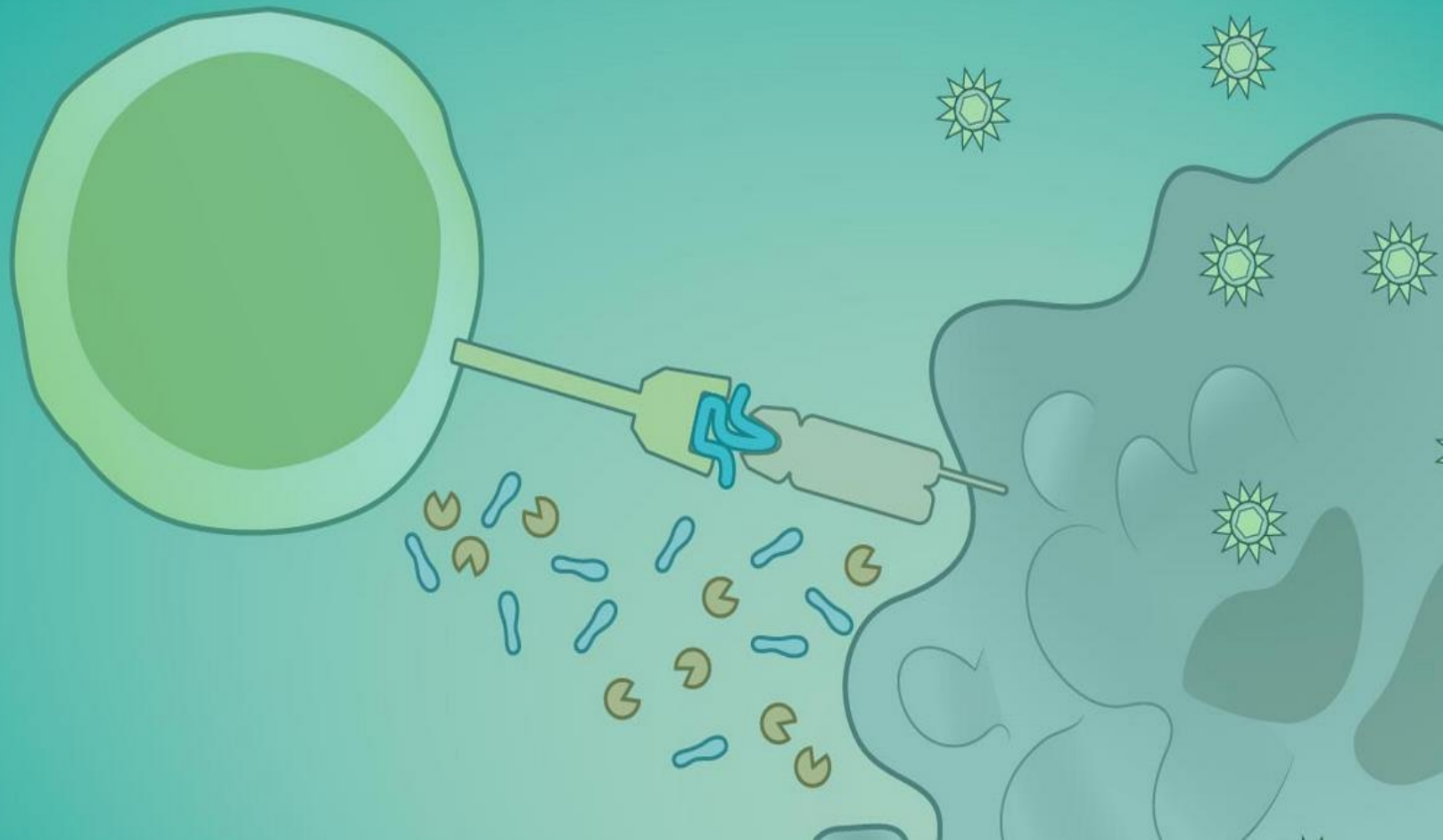
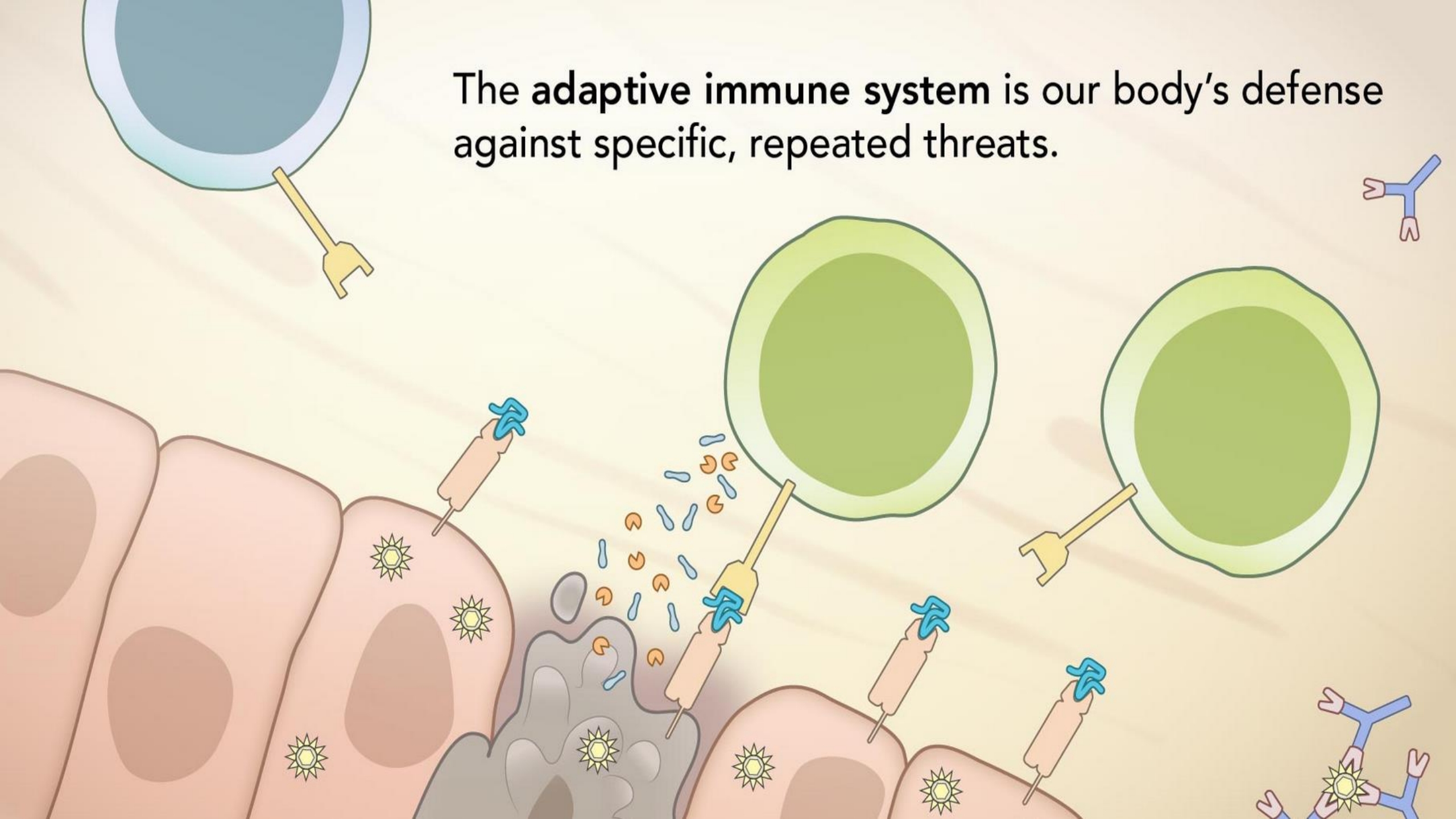
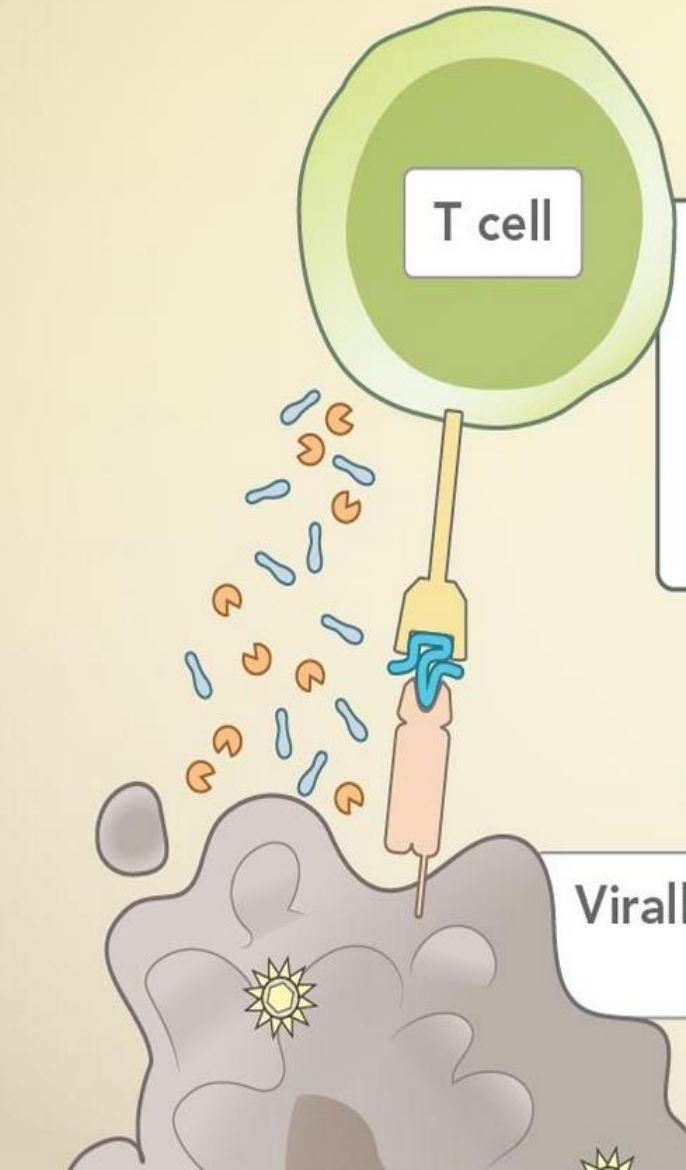
Part 1



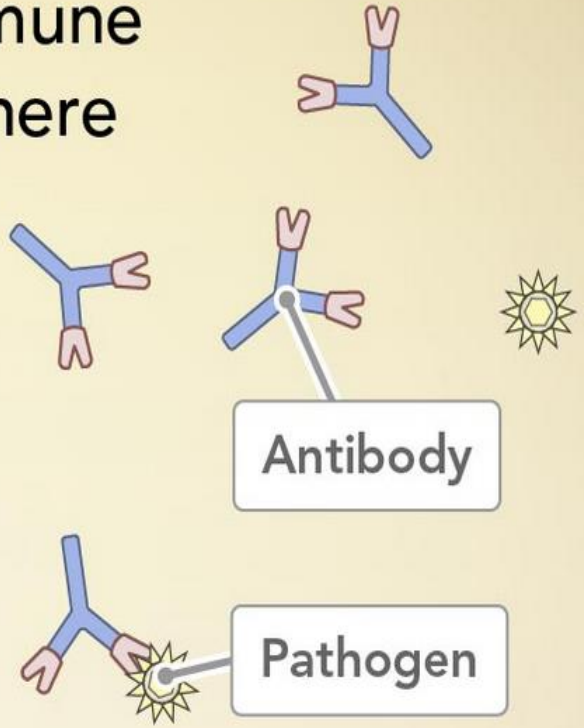
The **adaptive immune system** is our body's defense against specific, repeated threats.



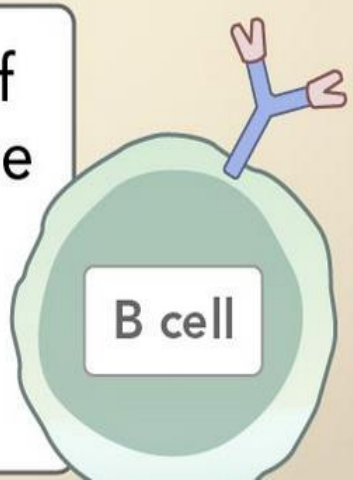
The unique cells of the adaptive immune system are called "lymphocytes." There are two types of lymphocytes.



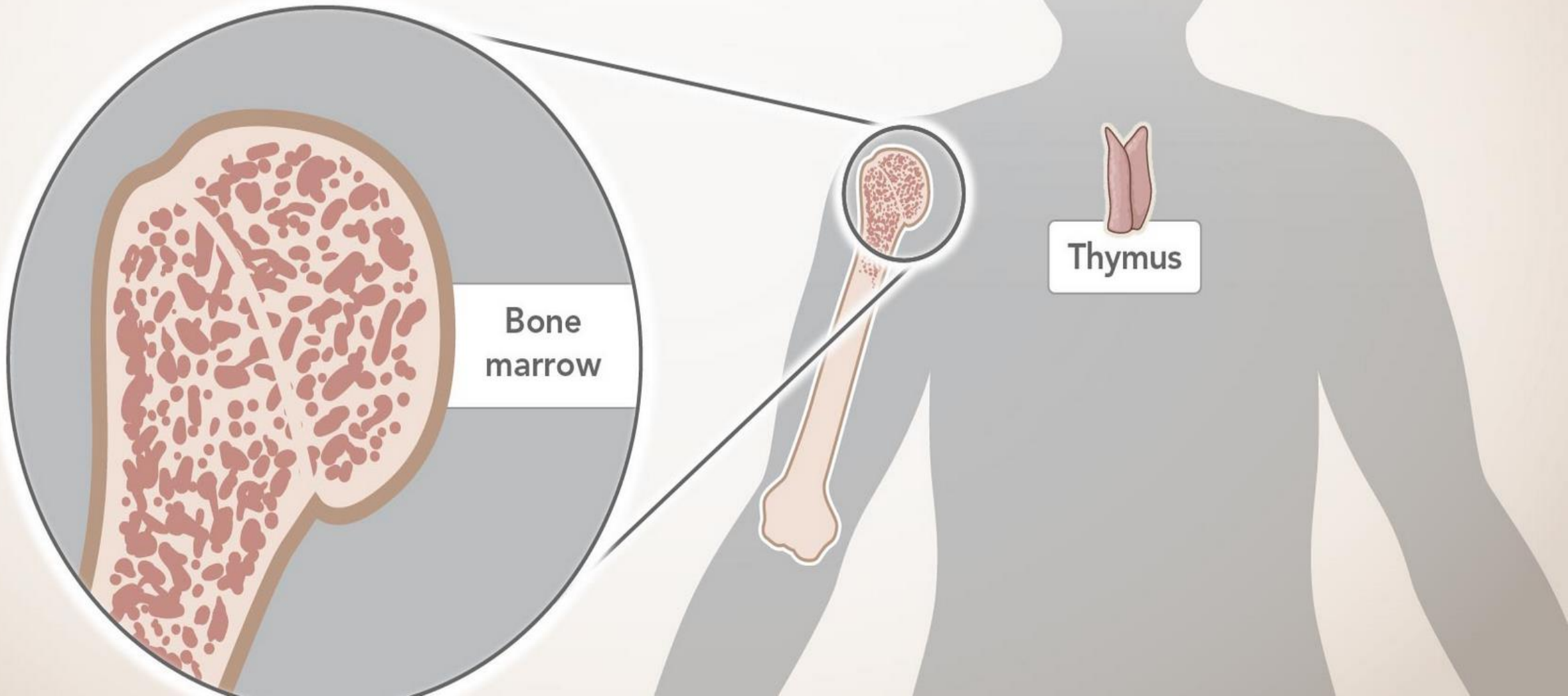
T cells recognize protein fragments (peptides) presented on specific surface proteins and either kill pathogens or help other immune cells.



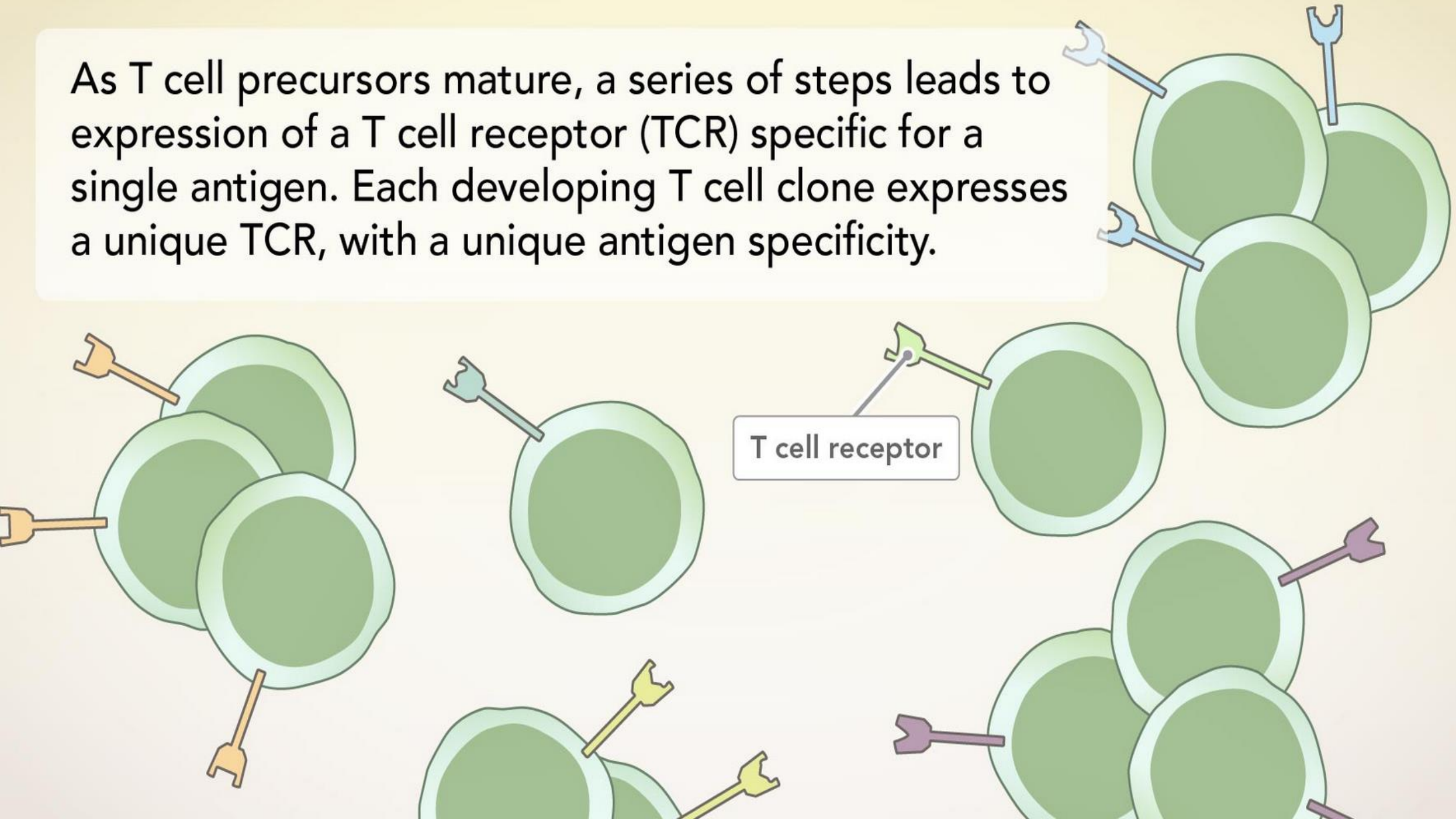
B cells lead to the production of antibodies. Antibodies recognize many types of molecules and assist in the removal of pathogens in a variety of ways.



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

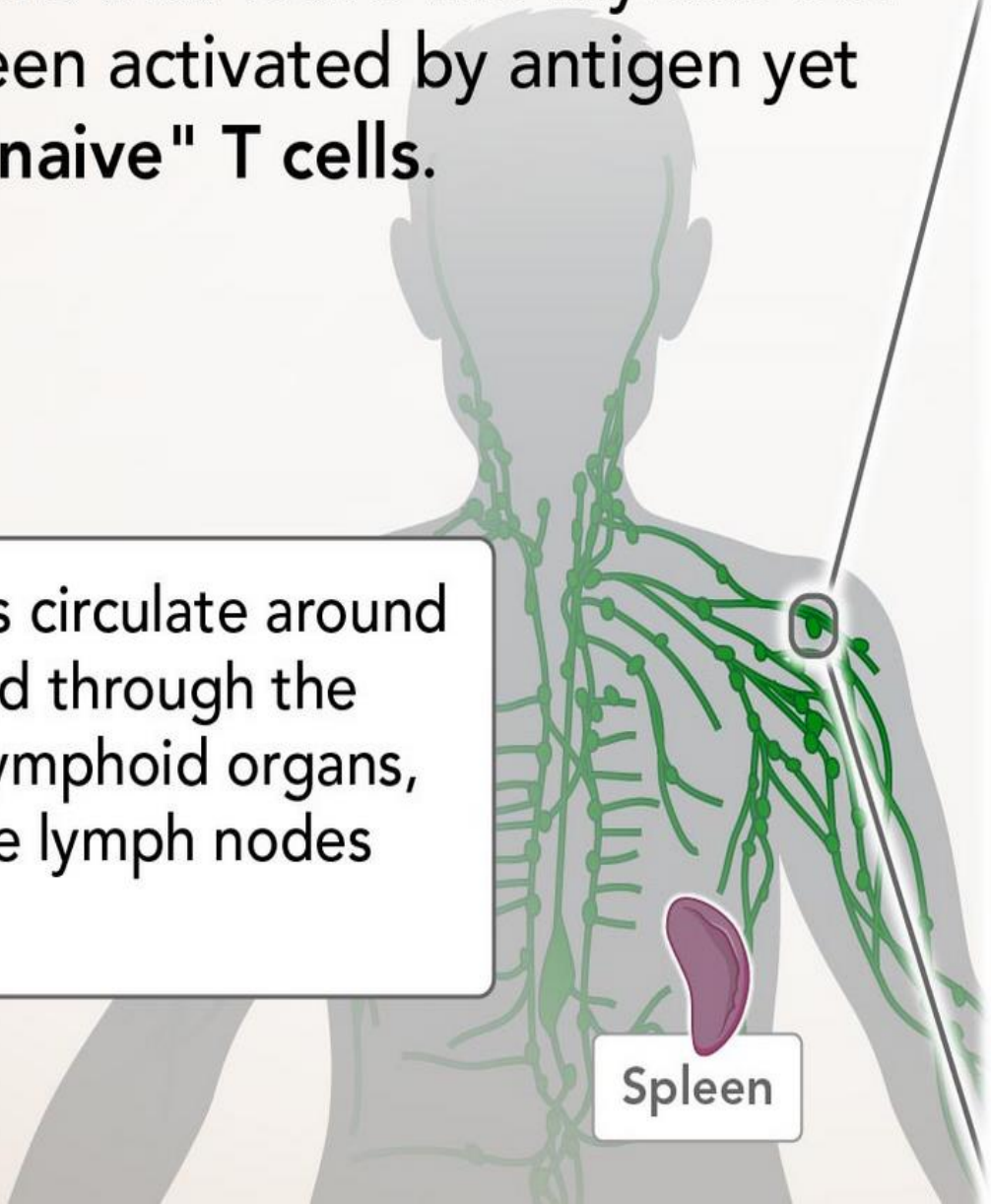


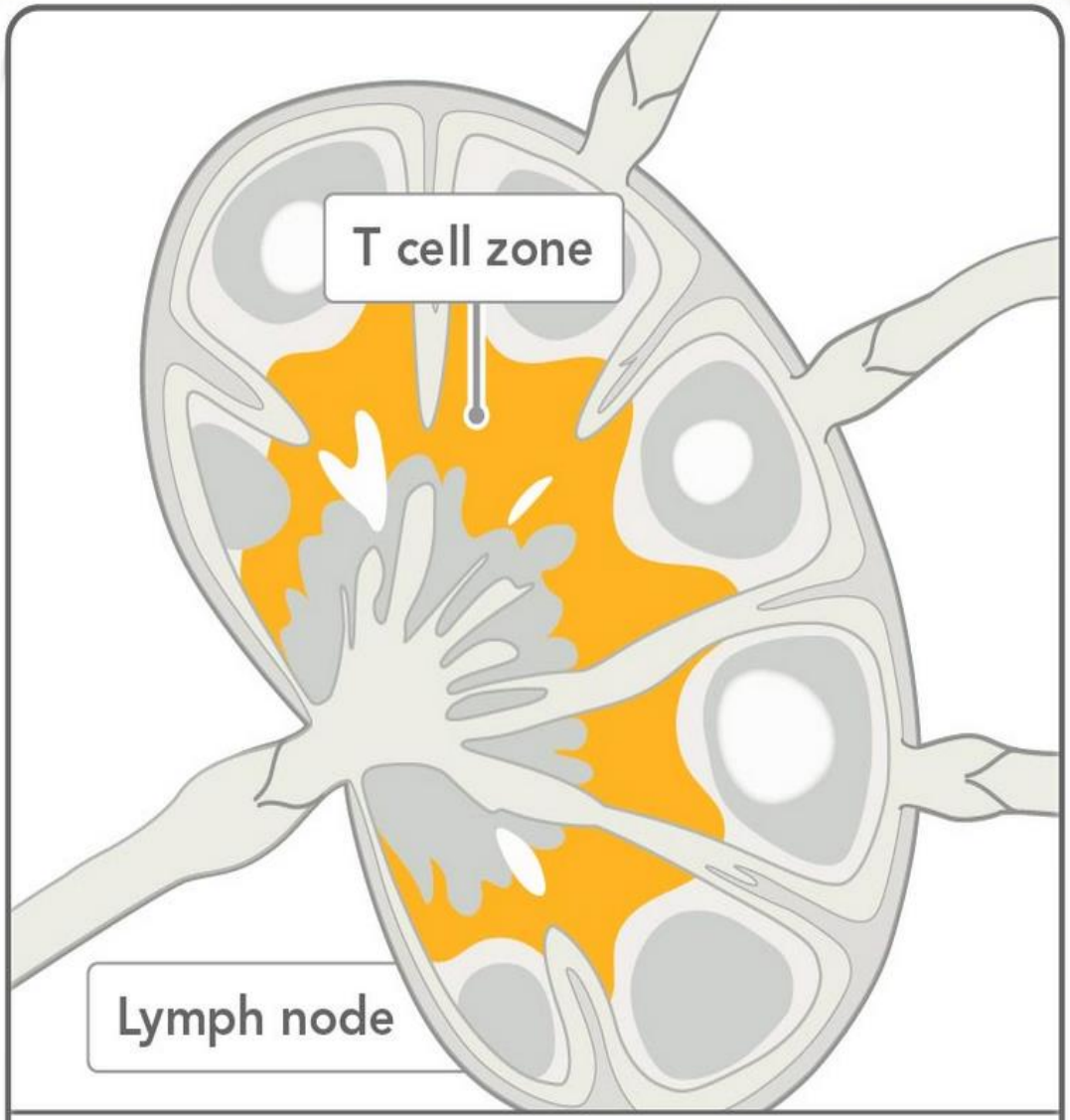
As T cell precursors mature, a series of steps leads to expression of a T cell receptor (TCR) specific for a single antigen. Each developing T cell clone expresses a unique TCR, with a unique antigen specificity.



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.



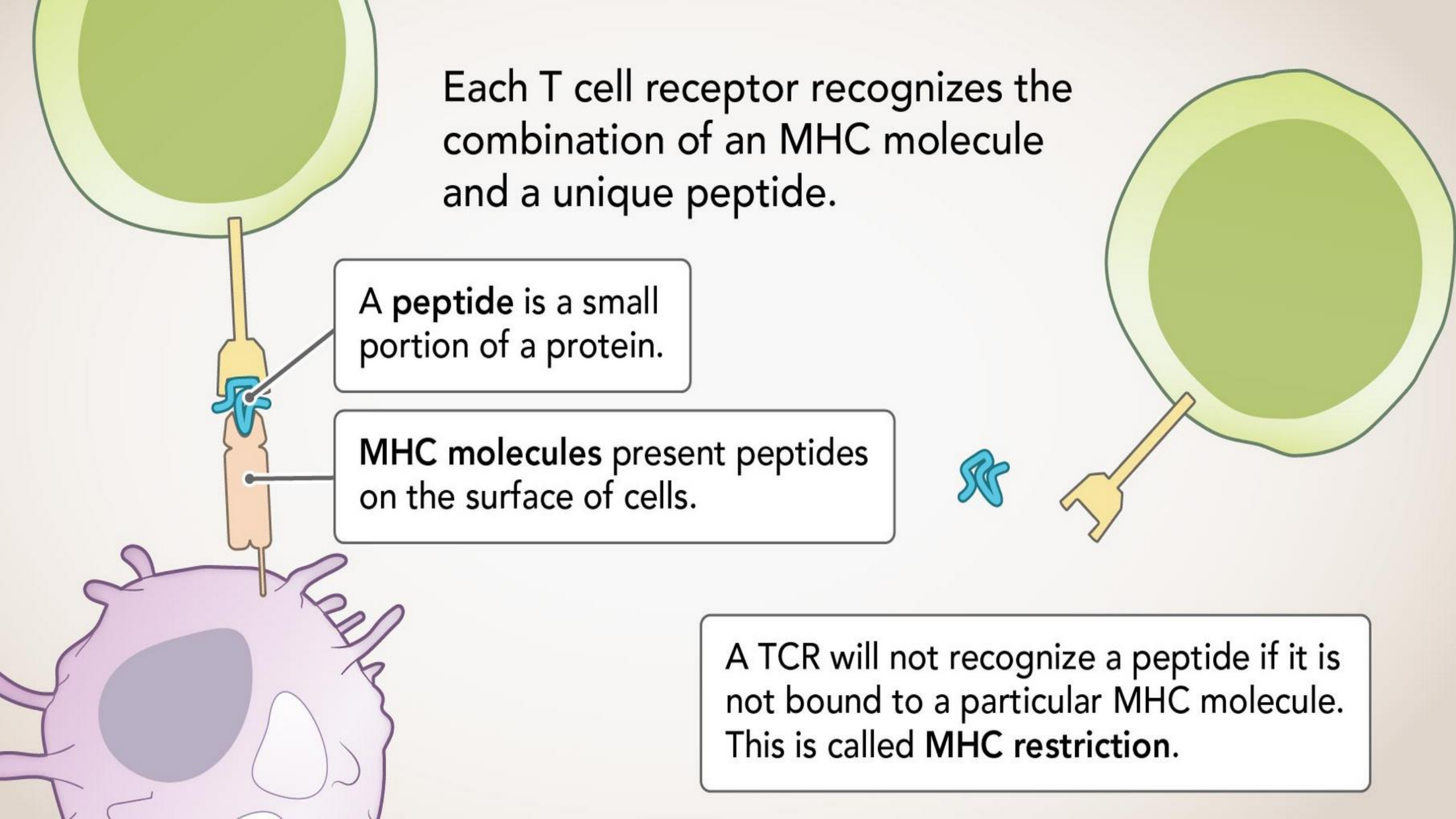


The area of the lymph node where naive T cells gather is called the **T cell zone**.

Each T cell receptor recognizes the combination of an MHC molecule and a unique peptide.

A **peptide** is a small portion of a protein.

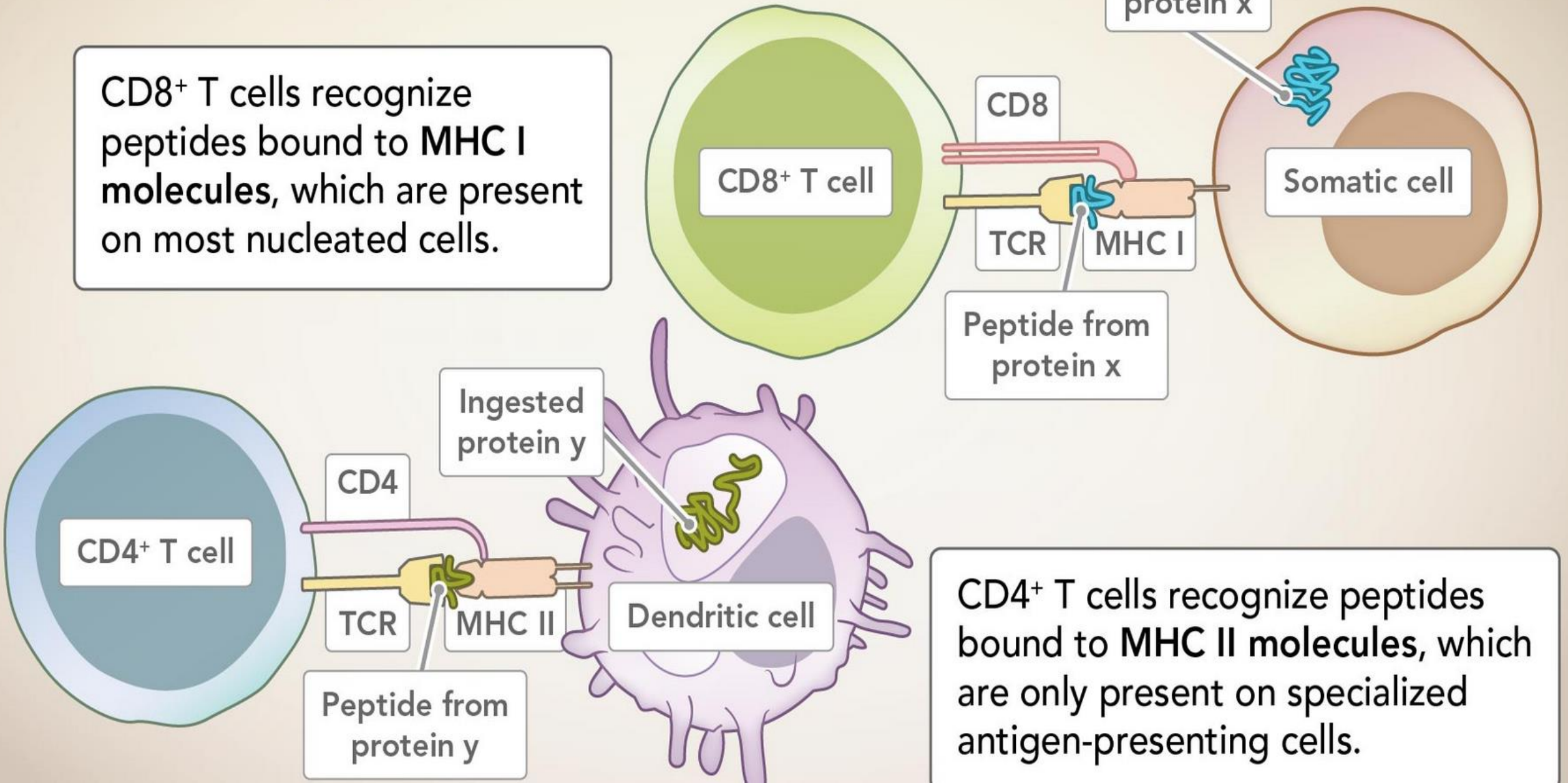
MHC molecules present peptides on the surface of cells.



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.

Adaptive Immunity: T Cells

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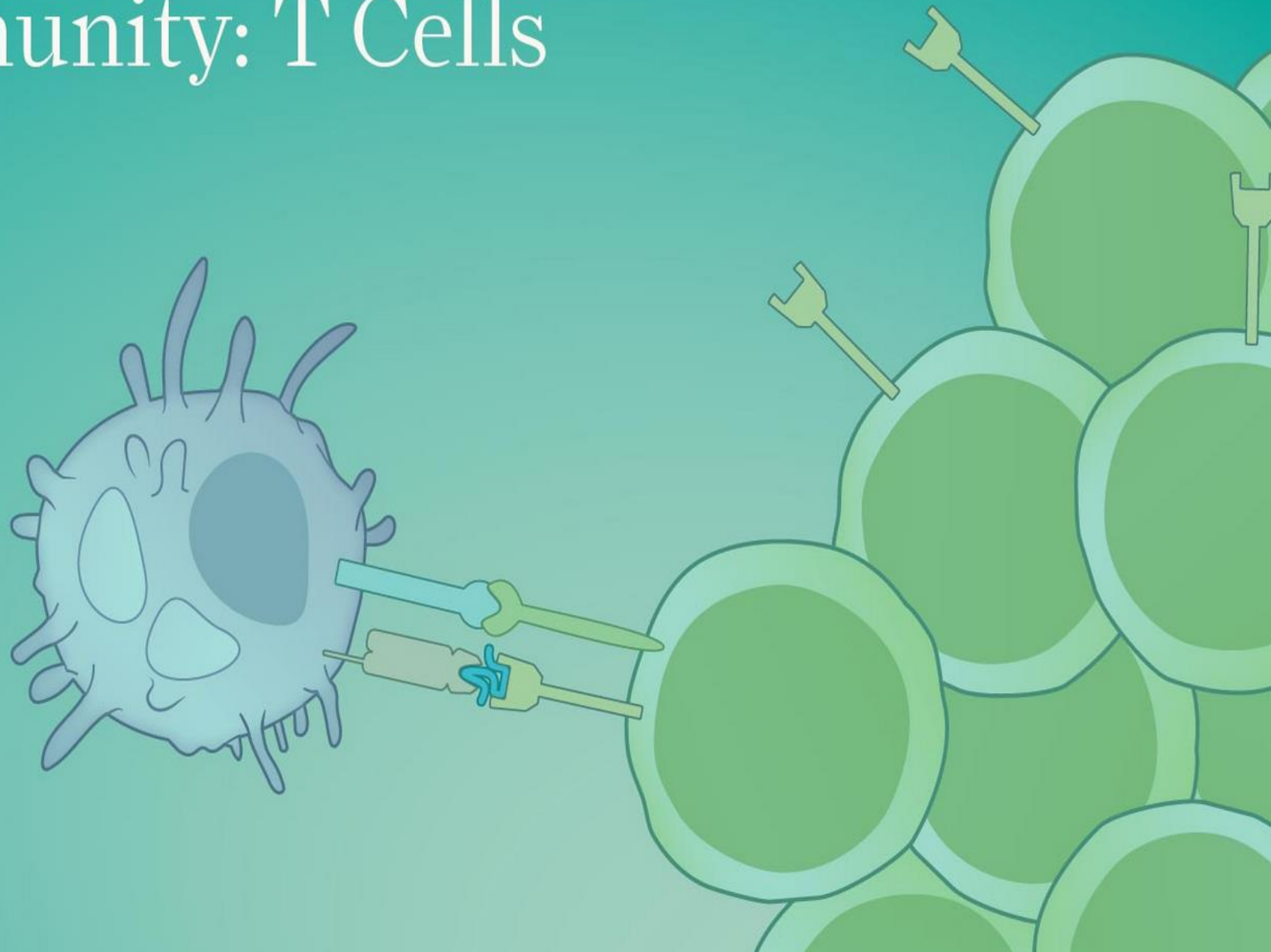
Part 2



In addition to the well-established Th1 and Th2 subsets recently so-called Th17 cells were described.
Which cytokines are being released in high amounts by these subsets?
(A) Th1: Interferon-alpha, Th2: IL-15, Th17: IL-17
(B) Th1: IL-1, Th2: IL-2, Th17: IL-17
(C) Th1: Interferon-gamma, Th2: IL-4, Th17: IL-22
(D) Th1: IL-12, Th2: IL-4, Th17: IL-17
(E) Th1: TNF-alpha, Th2: IL-6, Th17: IL-22

Immuncompetent T lymphocytes are selected in the thymus. What is the fate of theT cells that have a high affinity for self-MHC?
(A) Clonal expansion and migration to the peripheral lymph nodes
(B) Clonal anergy
(C) Migration to the peripheral lymphoid organs where they go into apoptosis
(D) Deletion in the thymus via induction of apoptosis
(E) Homing to the bone marrow as part of a feed back loop

Recognition by T cells is a very important tool for any response to a certain antigen.
How does the T cell recognize antigen?
(A) The T cell recognizes antigen via pattern recognition receptors.
(B) The T cell recognizes antigen via the T cell receptor for antigen (TCR), whereby
for every antigen there is already a specific receptor coded at the level of DNA.
(C) The T cell recognizes antigen via the T cell receptor for antigen (TCR), which has
a high diversity generated at the level of DNA.
(D) The T cell receptor recognizes antigens via binding to membrane-bound IgD antibodies.
(E) The T cell receptor recognizes antigens via the CD3 structure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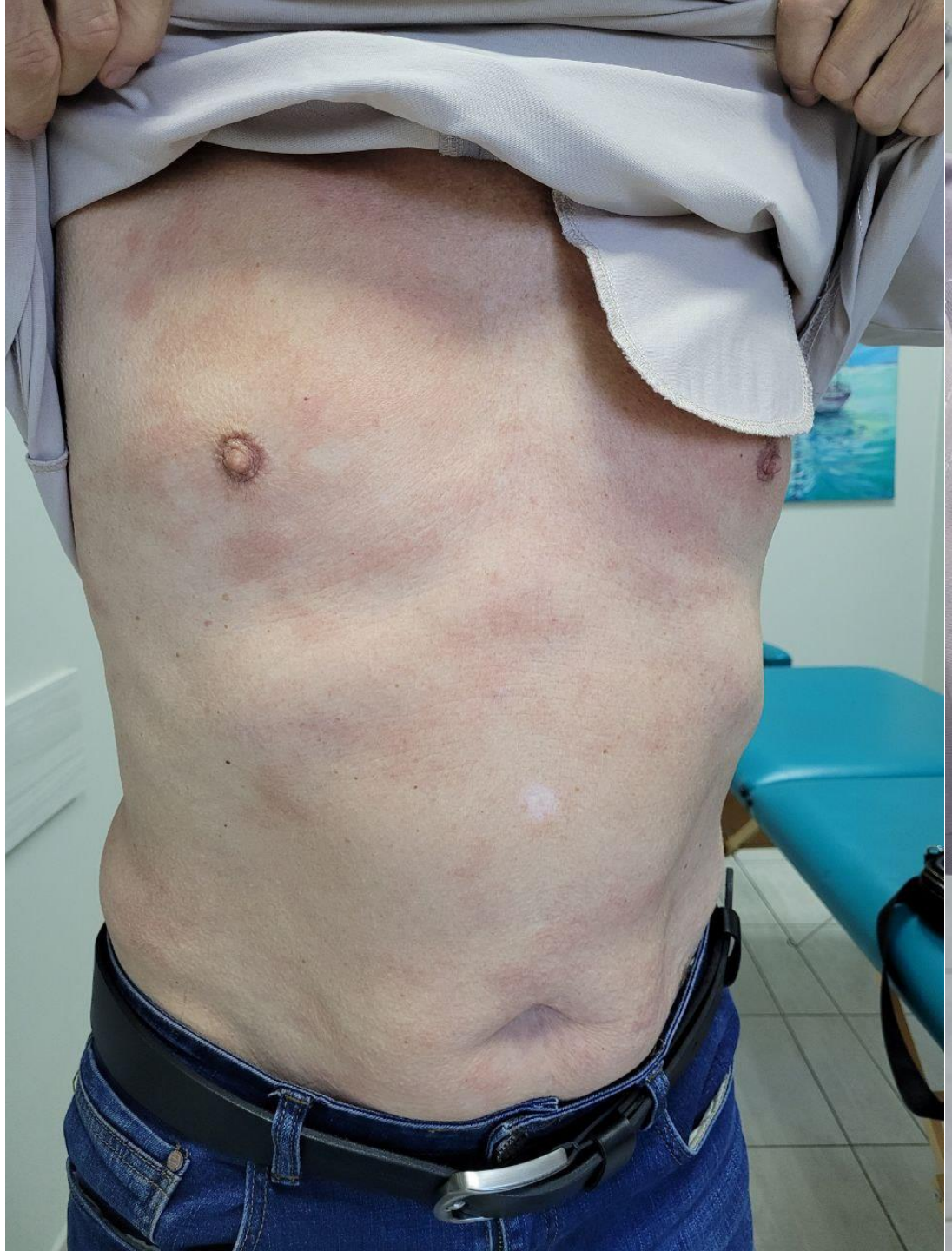
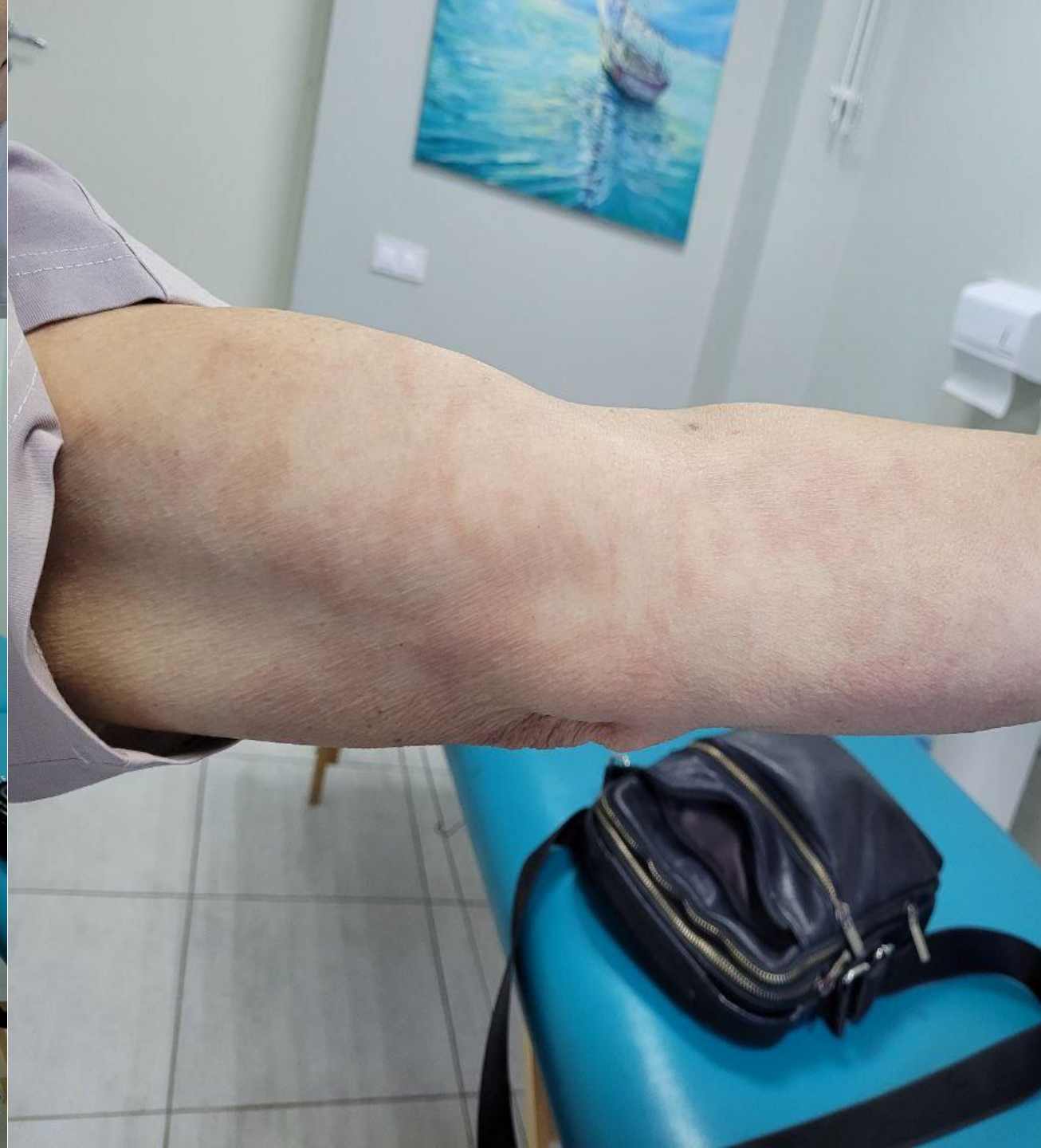
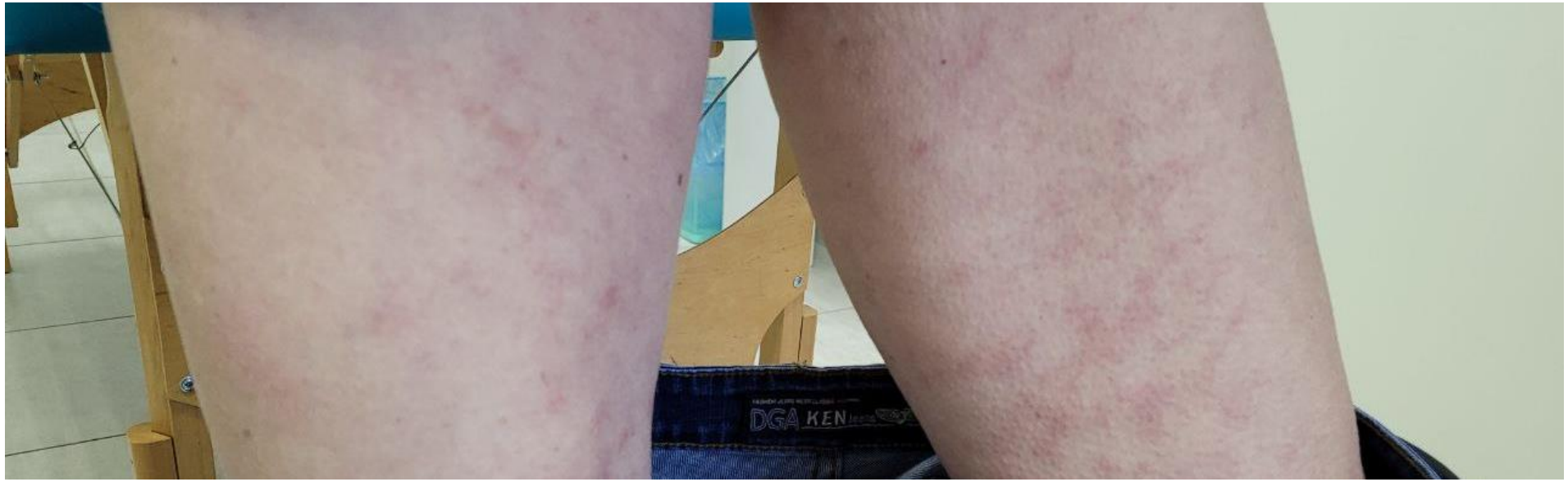
ПІБ. Емцов Николай Андраниович
Дата народження: 27.11.54
Адреса
Телефон: 0966143050, 0936383749 Viber



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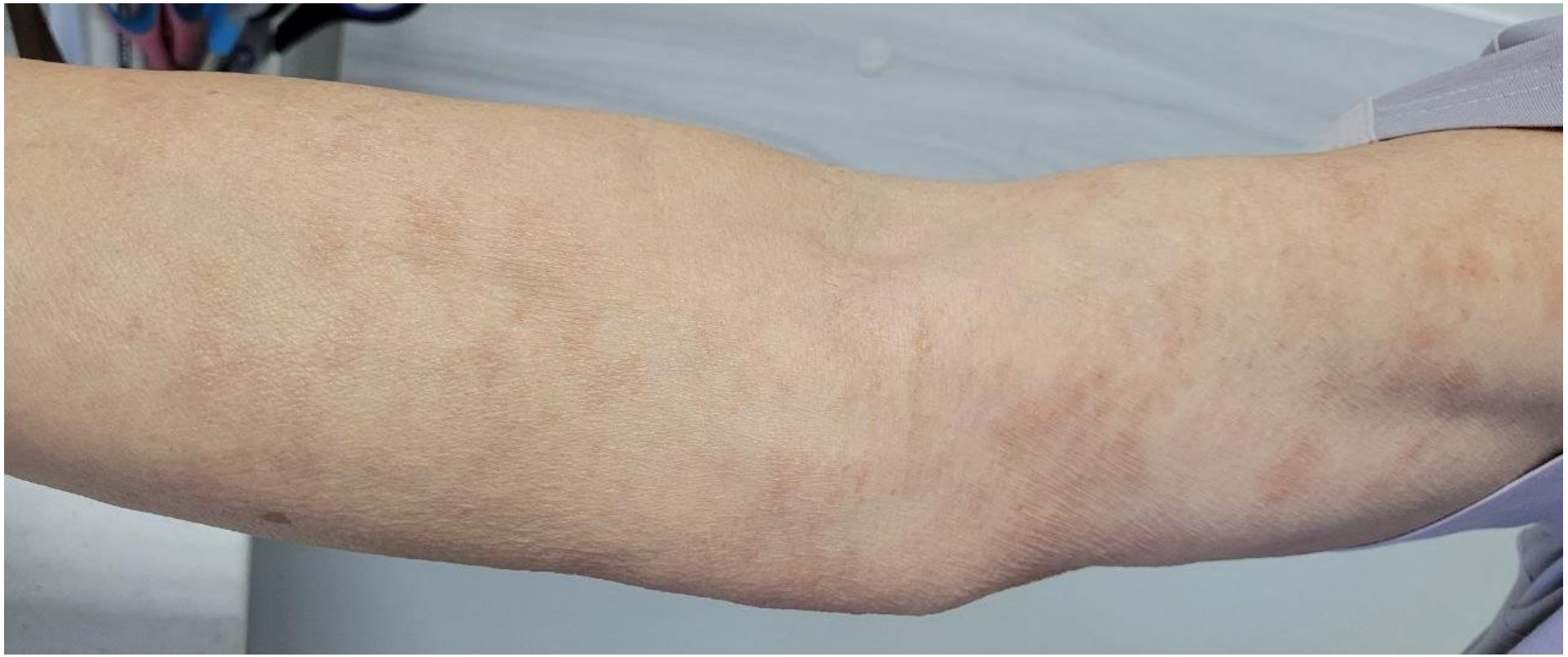


ФИО: Елізов М.А 1954 ХМ - 387 с. Мостиська 17

Время: 14-03-2022 09:16 Код: 1 Отд.: Пол Возраст:

Режим: Цельн. Тест: Гемограма крові, ч, р

Парам	Рез.	Номин.диапаз	Парам	Рез.	Номин.диапаз
WBC	8.7 x 10⁹/L	4.0 - 10.0	MCV	L 75.8 fL	82.0 - 95.0
Lymph#	3.2 x 10⁹/L	0.8 - 4.0	MCH	30.7 pg	27.0 - 31.0
Mid#	0.9 x 10⁹/L	0.1 - 0.9	MCHC	H 406 g/L	320 - 360
Gran#	4.6 x 10⁹/L	2.0 - 7.0	RDW-CV	13.5 %	11.5 - 14.5
-ymph%	36.8 %	20.0 - 40.0	RDW-SD	37.1 fL	35.0 - 56.0
Mid%	H 9.8 %	3.0 - 9.0	PLT	165 x 10⁹/L	100 - 300
Gran%	53.4 %	50.0 - 70.0	MPV	9.6 fL	7.0 - 11.0
GB	156 g/L	110 - 160	PDW	15.9	15.0 - 17.0
BC	5.07 x 10¹²/L	3.50 - 5.50	PCT	0.158 %	0.108 - 0.282
CT	38.4 %	37.0 - 50.0			

DATA Male, 67 y.o

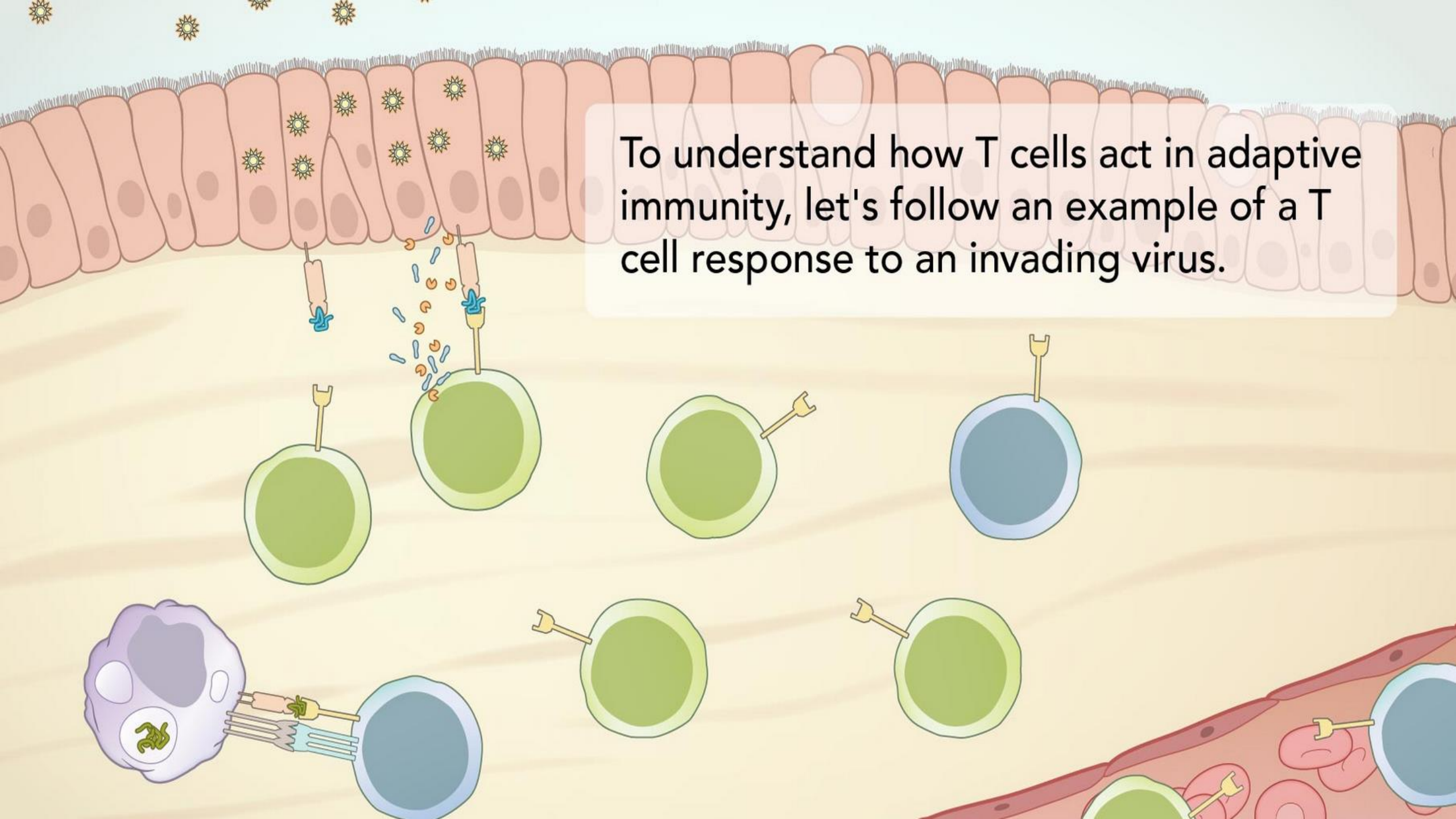
Complaints on
- skin not-itching rash appeared in 1 month after covid-19 infection in February 2022,
- persisted nasal mild congestion worsening at spring and late summer-early fall

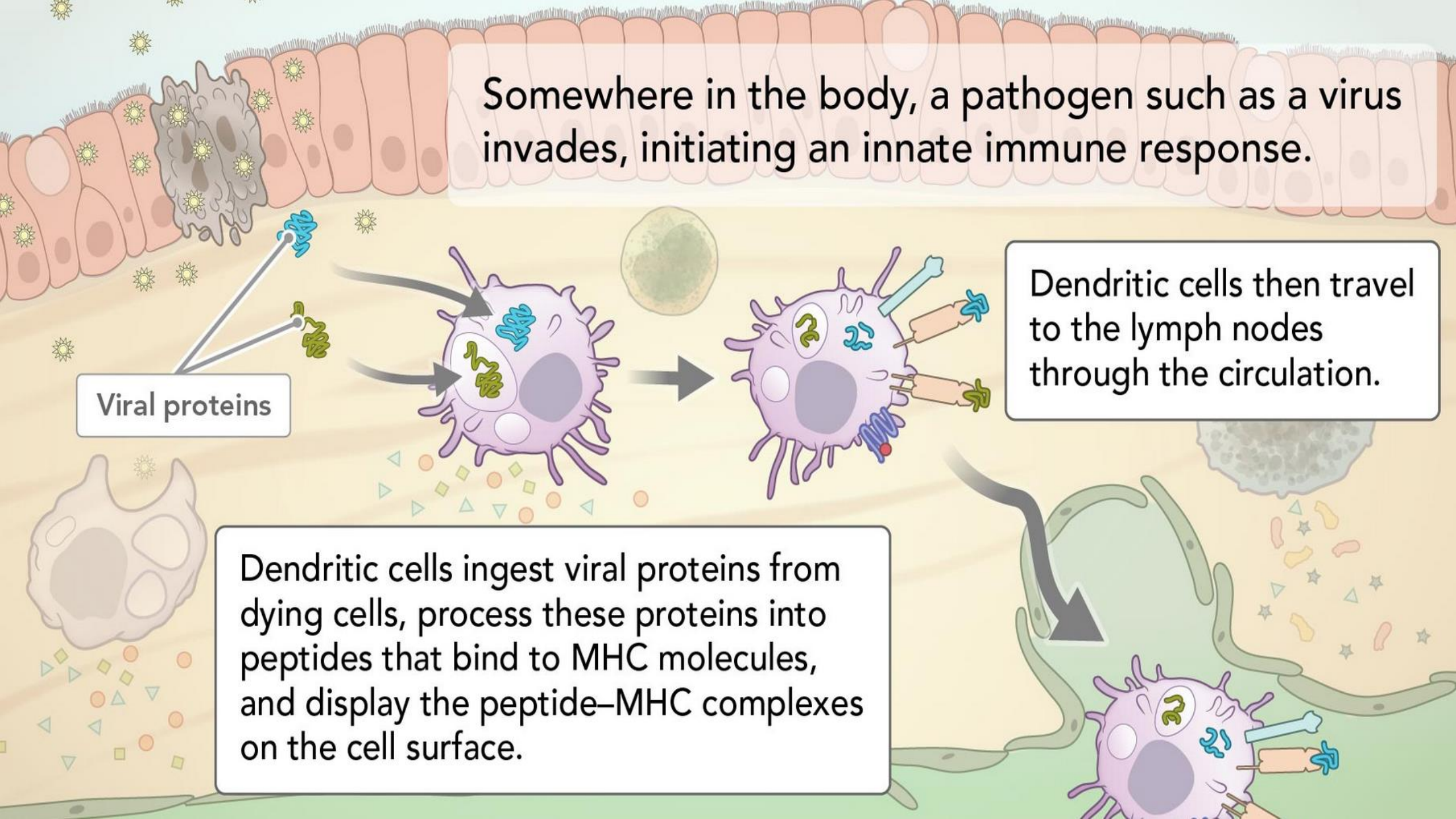
06/06/22
eosinophil cationic protein (ECP) – 7,66 ng/mL (0,2-24)
Total IgE – 8,81 IU/ml (1-87)
Prostate-Specific Antigen (PSA) – 7,10 ng/mL (0-4,1)
Thyroid Stimulating Hormone (TSH) – 0,795 IU/l (0,4-4,0)
T3 – 2,63 ng/dL (0,69-1,7)
T4 – 1,06 pg/mL

CBC:
WBC – 6,02x10^9/L
Eos – 6% (1-5%)

18/07/22 Prostate-Specific Antigen (PSA) – 8,25 ng/mL (0-4,1)

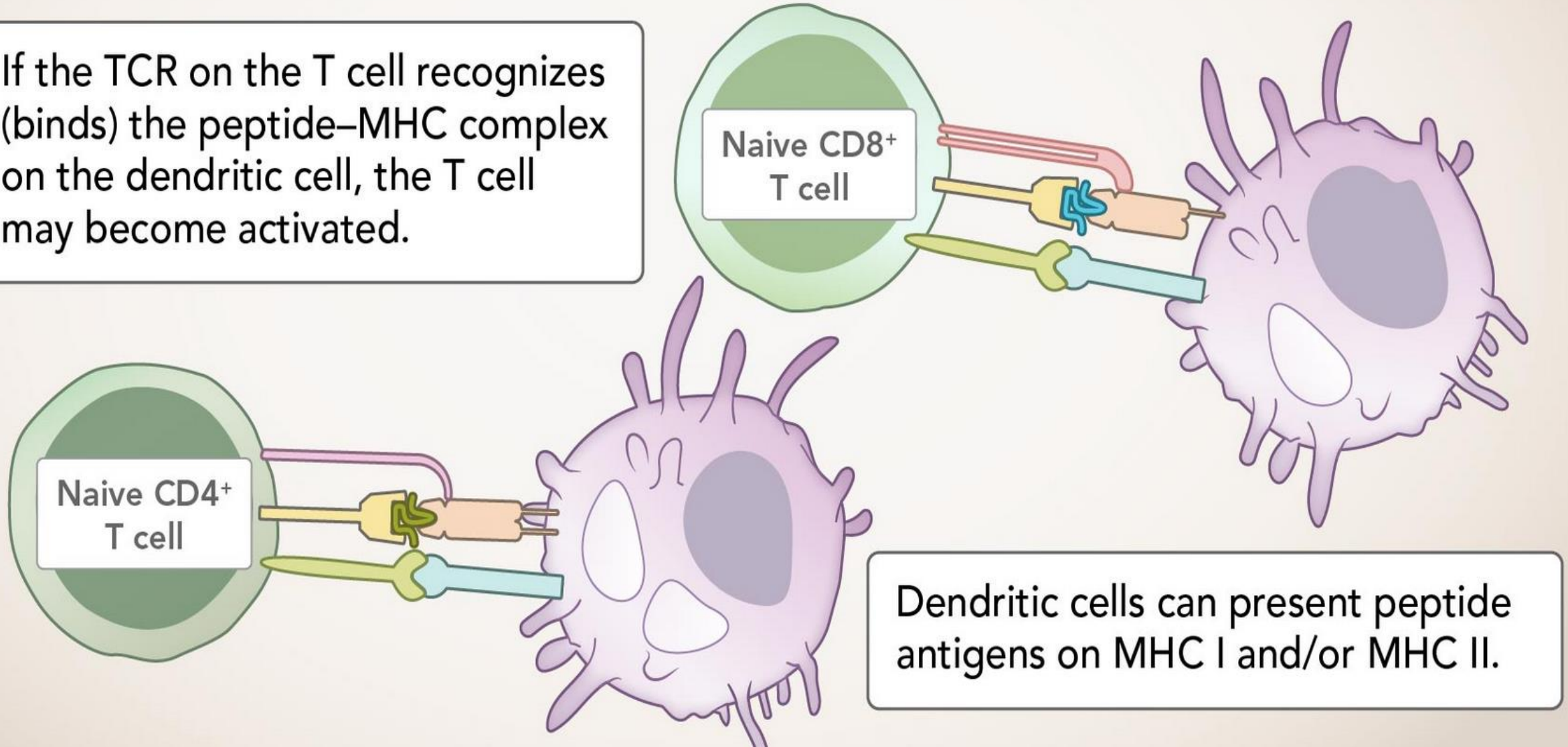
Qs: can patient has booster dose of the coronavirus (COVID-19) vaccine,
Can patient be treated with androgen suppression therapy and chemotherapy?


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 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.
Dendritic cells then travel to the lymph nodes through the circulation.

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

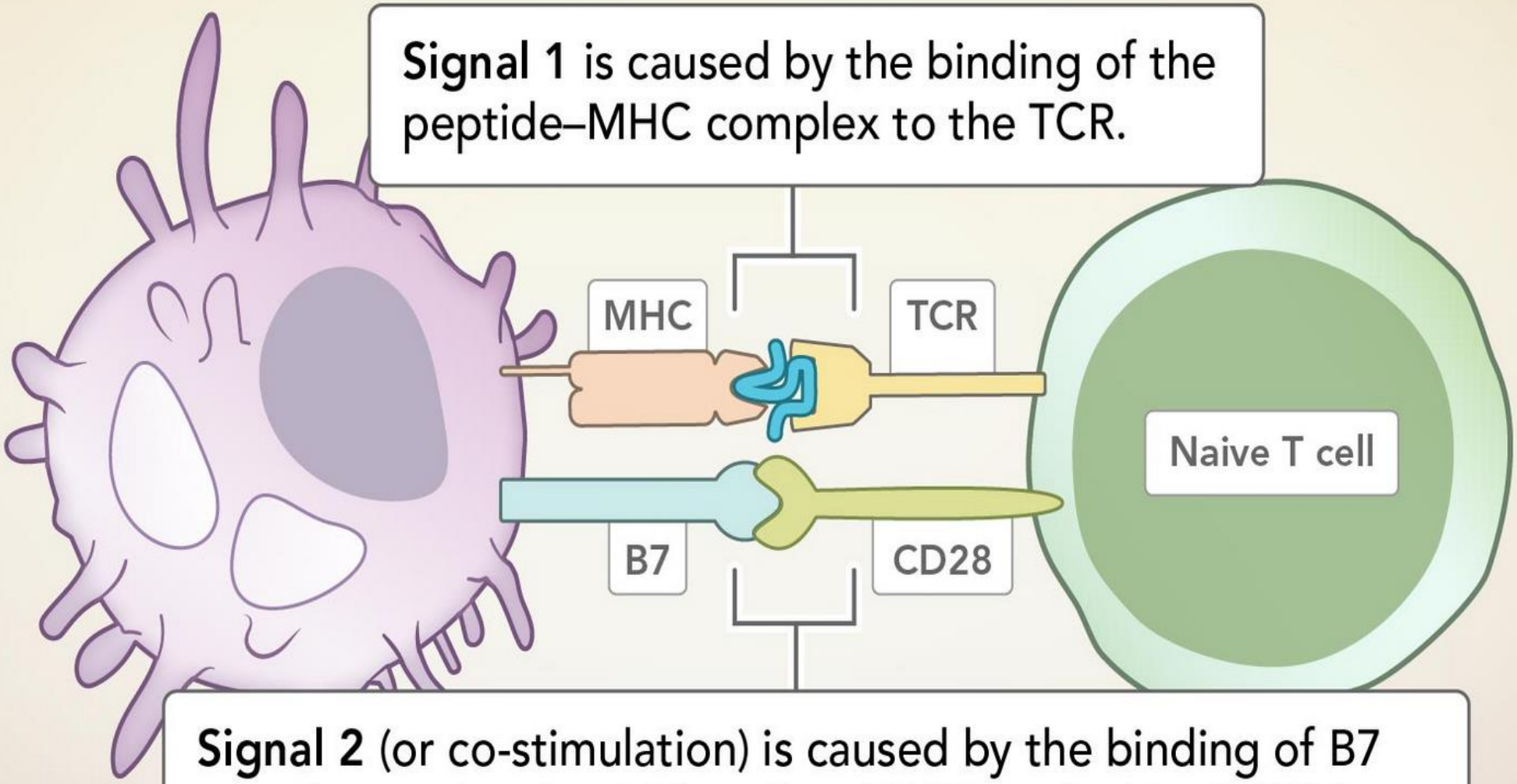
If the TCR on the T cell recognizes (binds) the peptide–MHC complex on the dendritic cell, the T cell may become activated.



Dendritic cells can present peptide antigens on MHC I and/or MHC II.

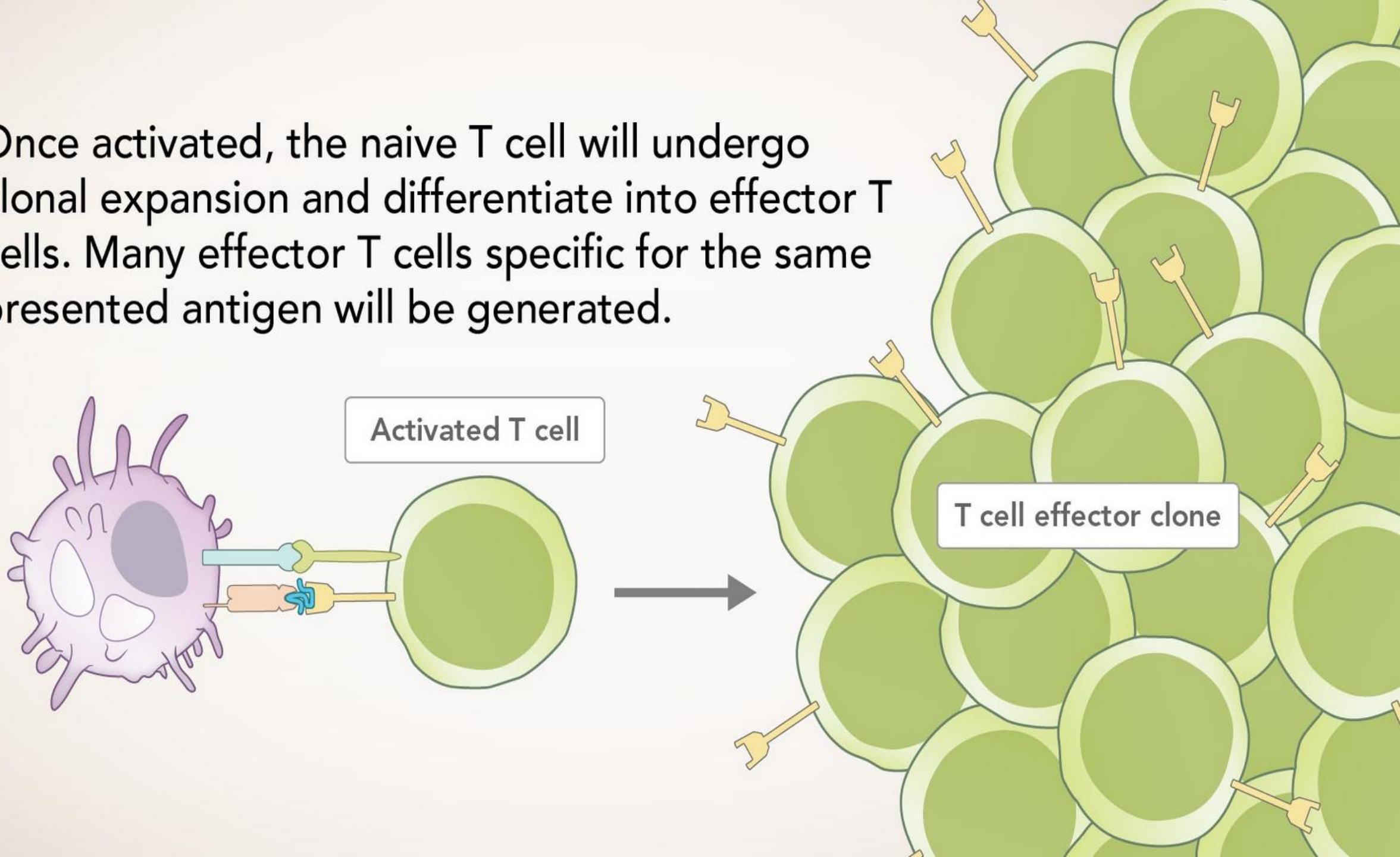
To become activated, the naive T cell must receive two signals:

Signal 1 is caused by the binding of the peptide–MHC complex to the TCR.

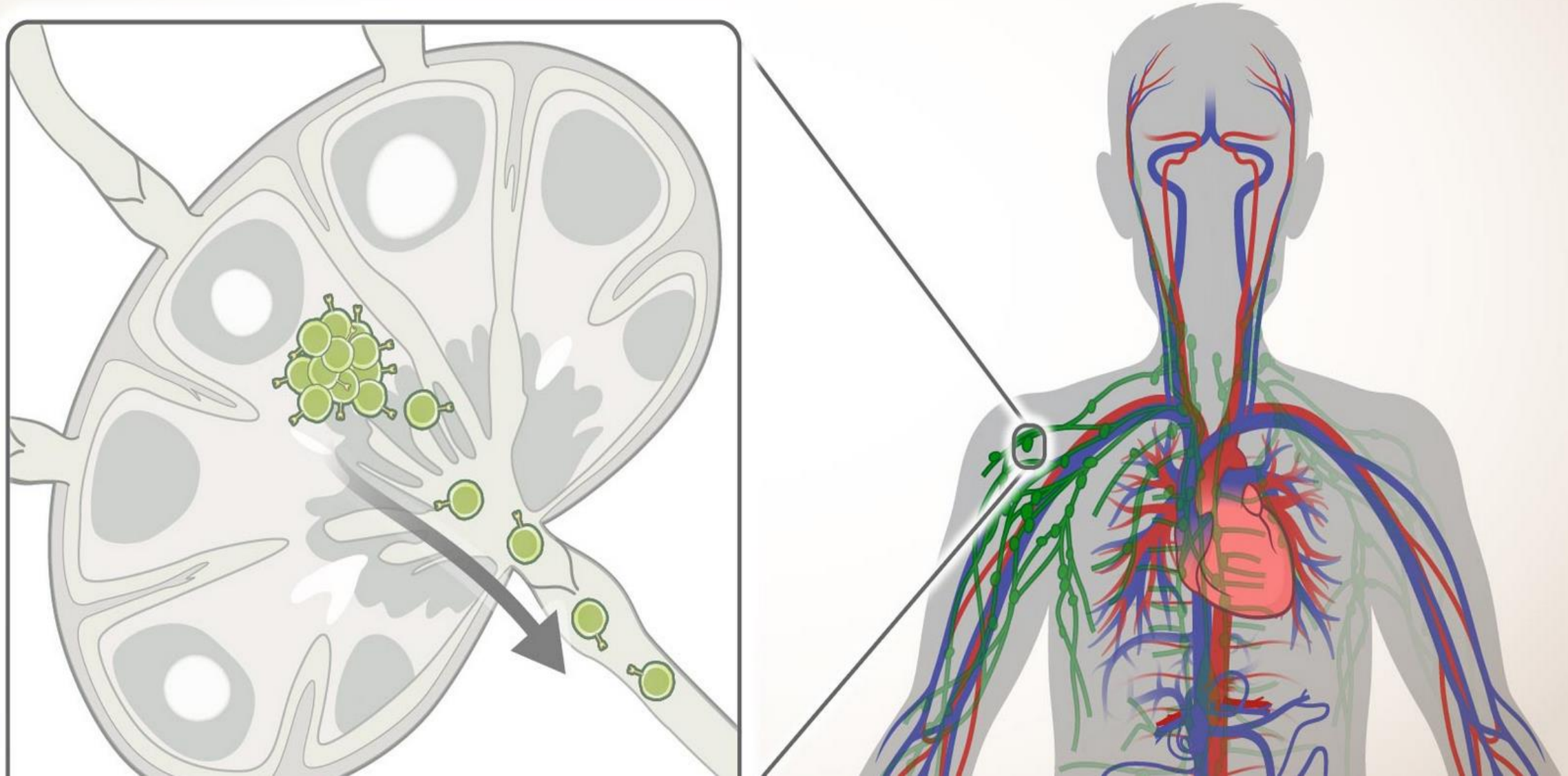


Signal 2 (or co-stimulation) is caused by the binding of B7 proteins on the dendritic cell to CD28 on the T cell. Without co-stimulation, the naive T cell will not be activated.

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.

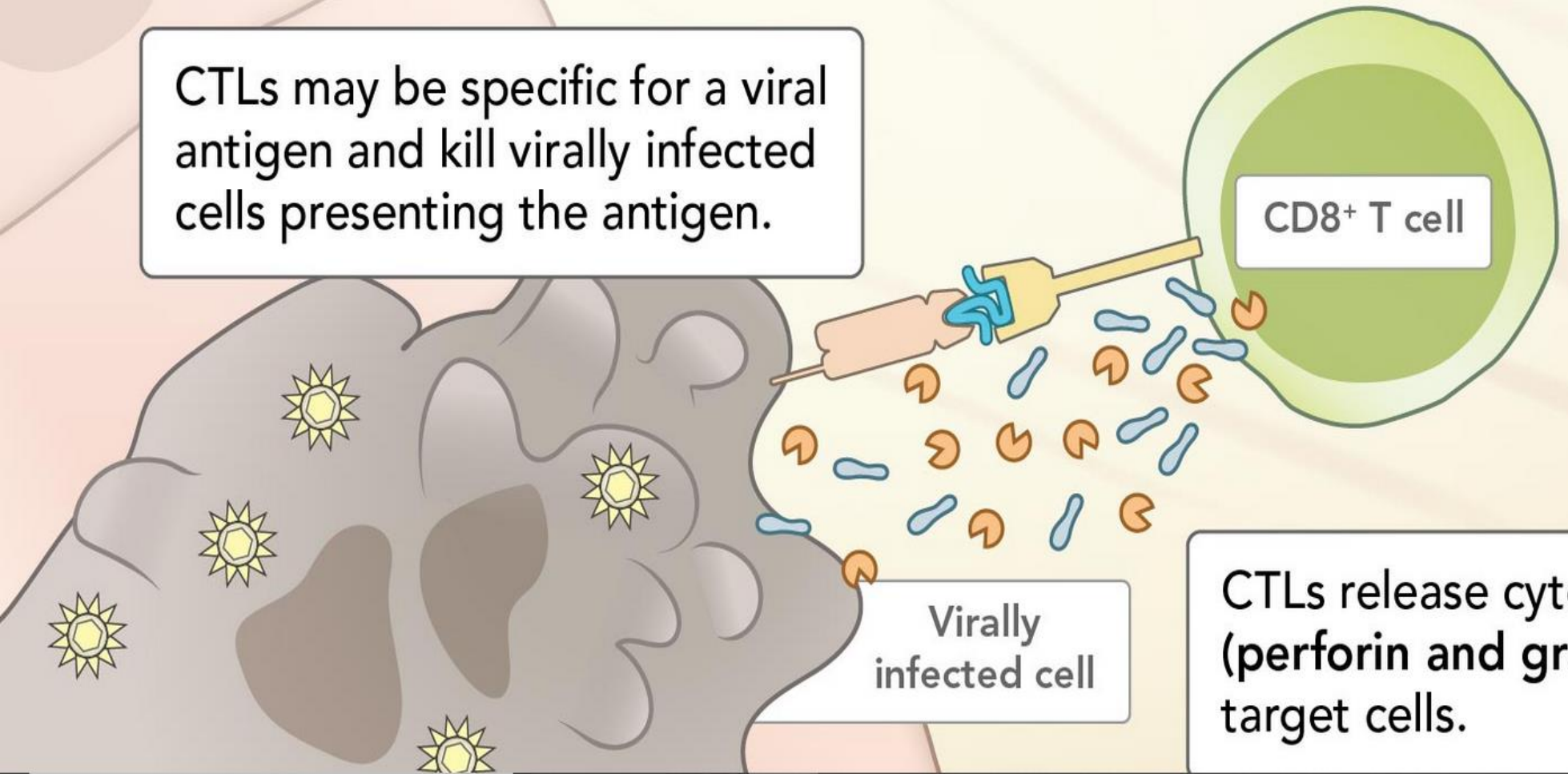


Effector cells can then leave the lymph node and travel through the circulation to carry out immune functions.

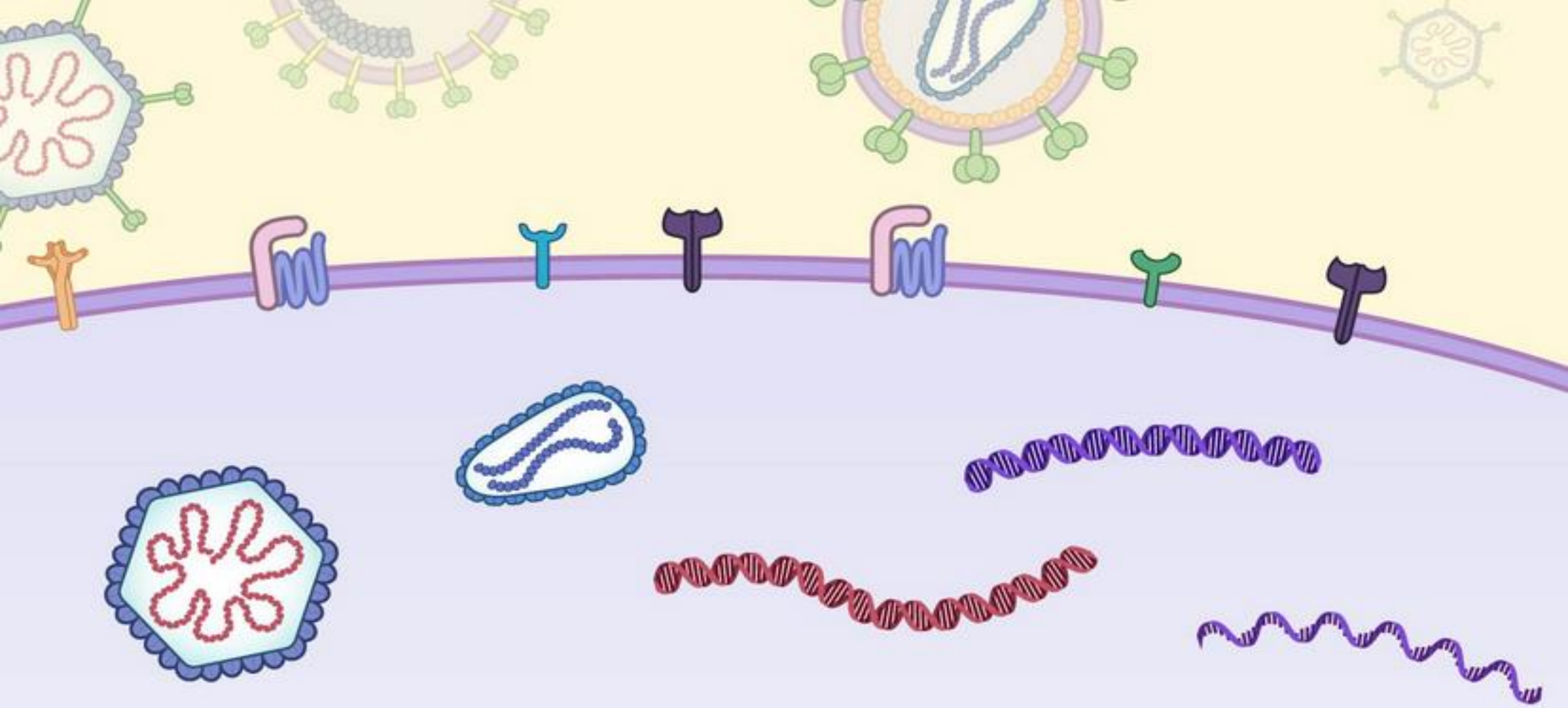


Effector $CD8^+$ cells are also called **cytotoxic T lymphocytes** (CTLs). These cells travel through the body and kill cells presenting the peptide–MHC I complex they recognize.

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.



Once a virus infects a host, the immune system responds.

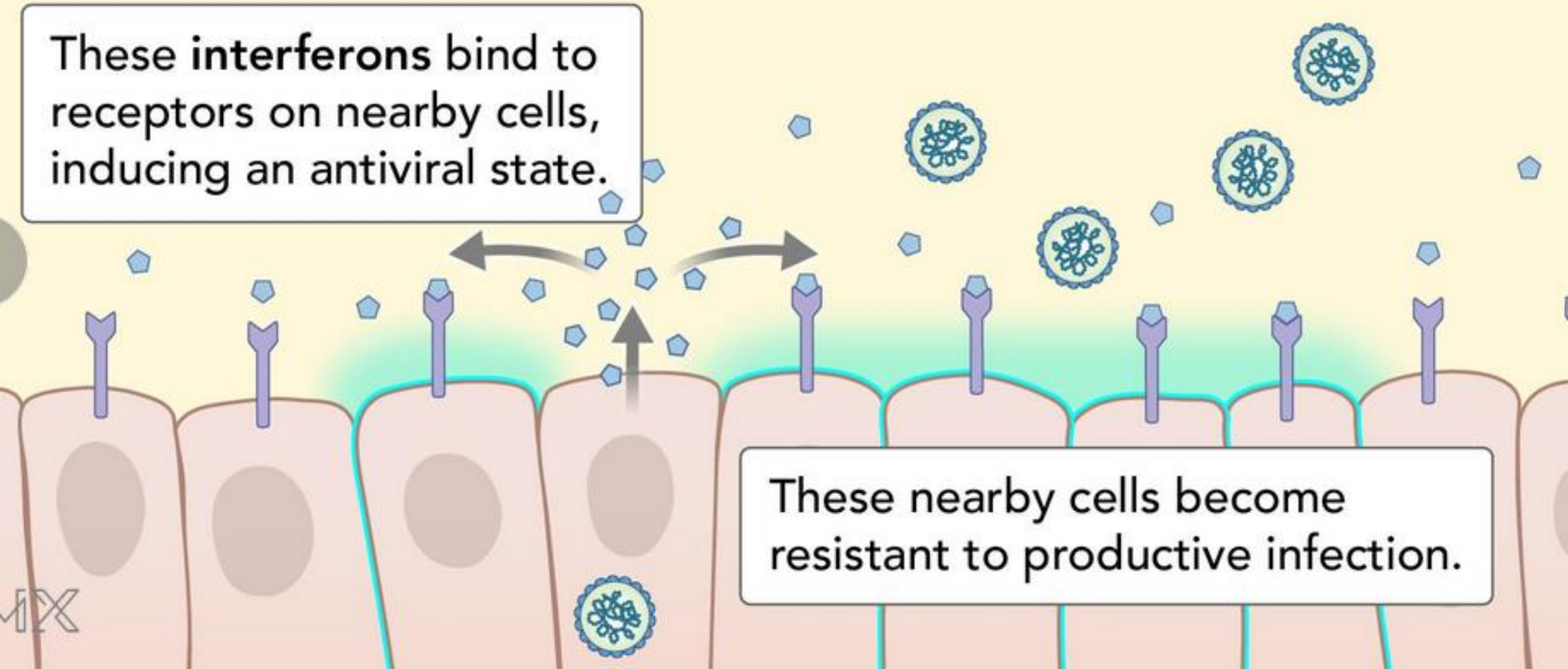
Viruses are detected by various **pattern recognition receptors** (PRRs). For example:

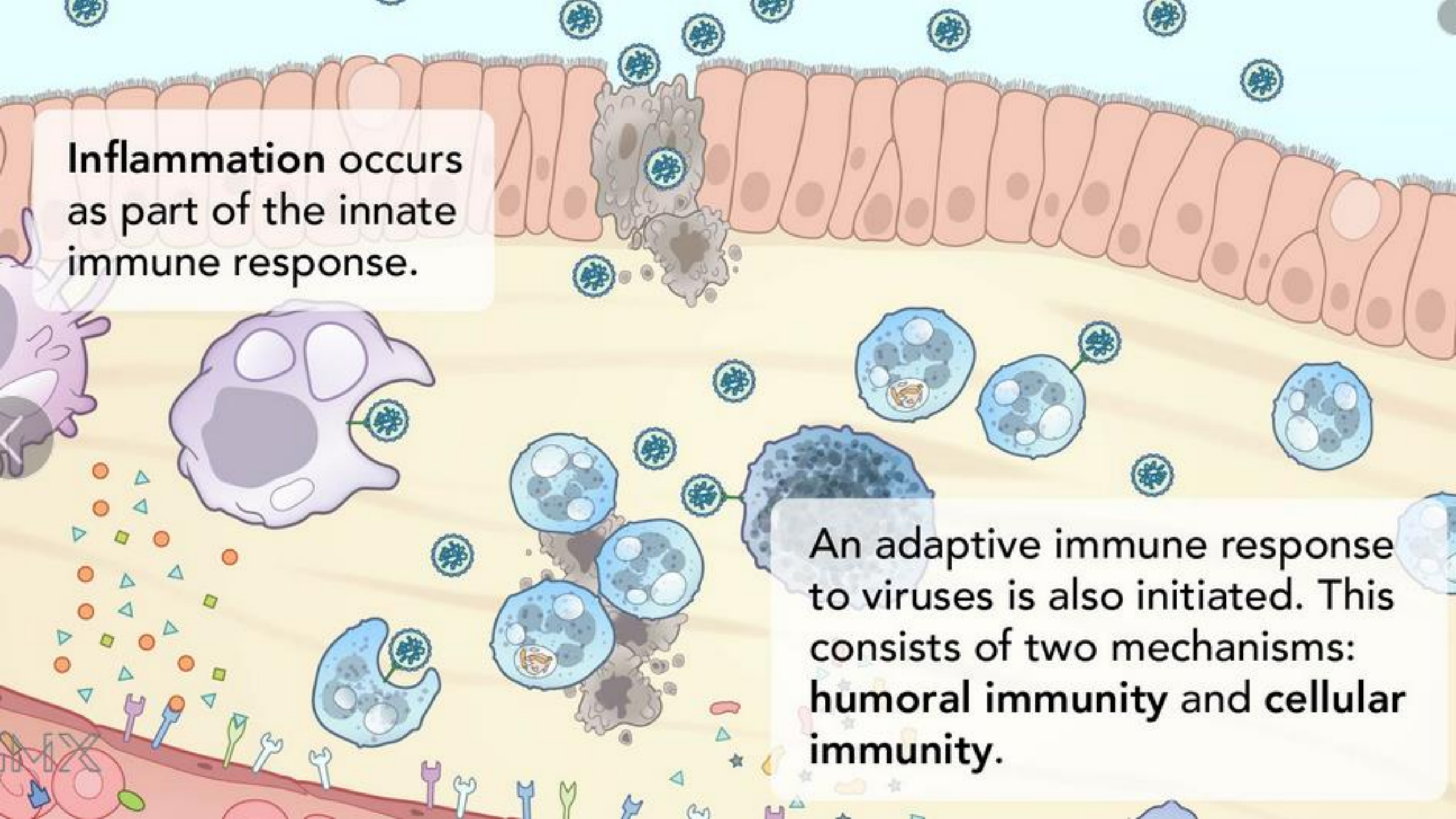
RIG-I and **MDA5** are sensors that bind viral dsRNA in the cytosol.

TLR3 is a toll-like receptor that binds viral dsRNA in endosomes.

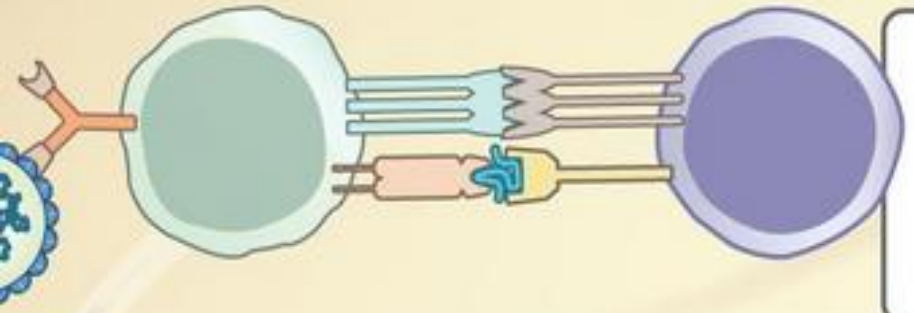
TLR7 and **TLR8** bind viral ssRNA in endosomes.

When PRRs bind to viral nucleic acids, a series of signals is initiated, leading to the expression of type 1 interferons by the host cell.



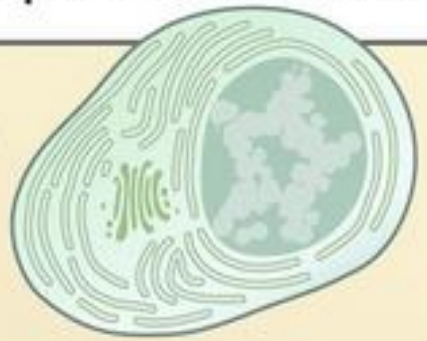

Inflammation occurs as part of the innate immune response.
An adaptive immune response to viruses is also initiated. This consists of two mechanisms: **humoral immunity** and **cellular immunity**.

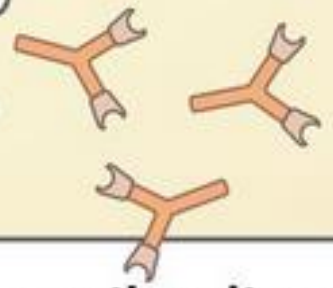
Humoral immunity is mediated by B cells and antibodies.



B cells are activated in response to viral antigens and helped by **helper T cells**...

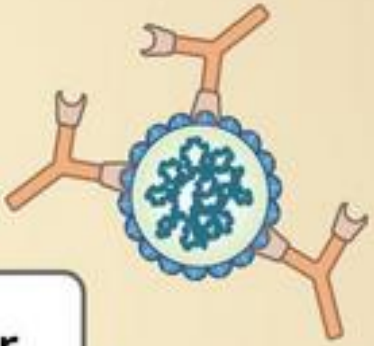
...which differentiate into long-lived **plasma cells** that produce antibodies.

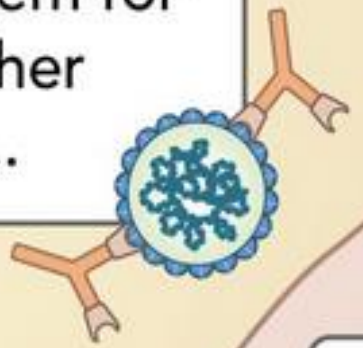




These **antibodies** block viruses from binding to and invading other cells...

...and mark them for removal by other immune cells...



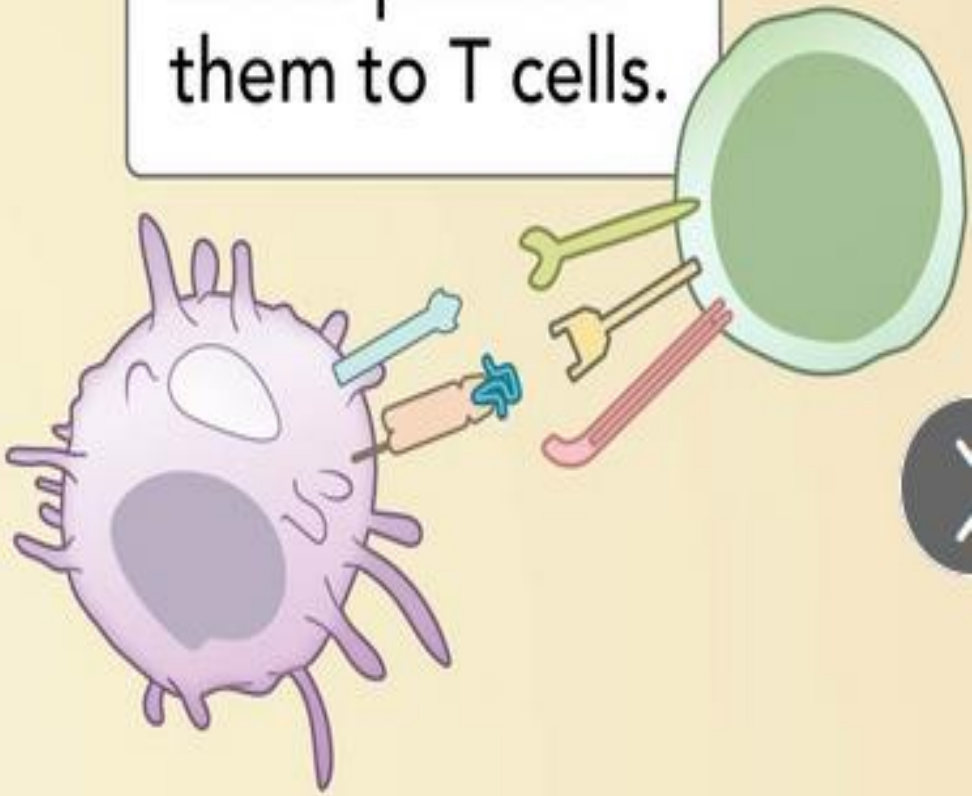


...thus preventing new cells from being infected.

Additionally, **antigen-presenting cells** engulf viral proteins...

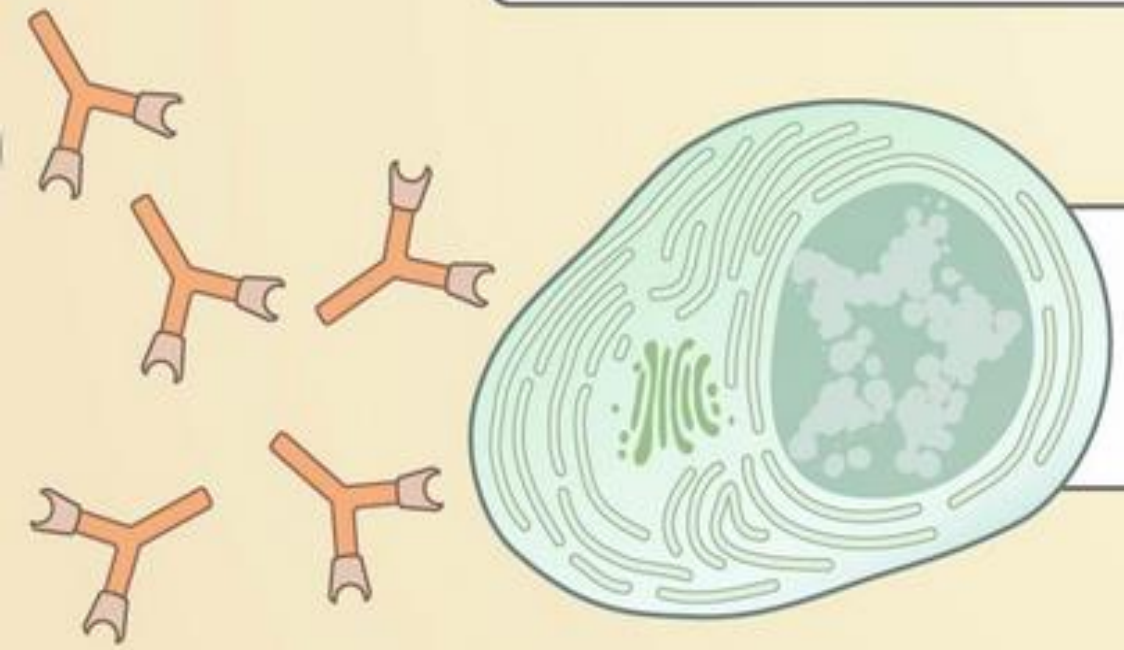
...process them into peptides...

...and present them to T cells.



Following infection or vaccination...

...memory cells derived from B and T cells...



...and antibodies produced by long-lived plasma cells...

...protect against future infections.

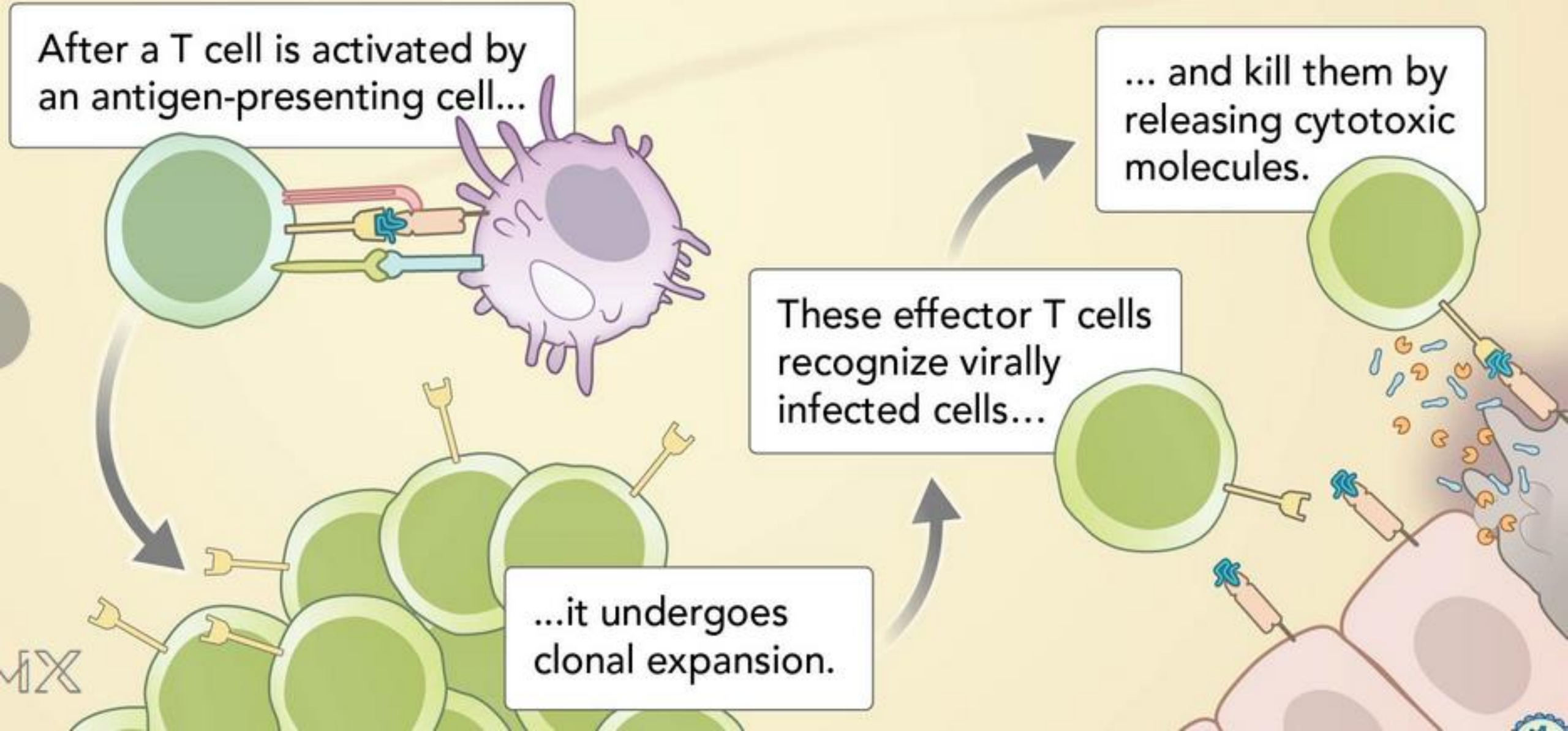
Cellular immunity is mediated in part by $CD8^+$ T cells.

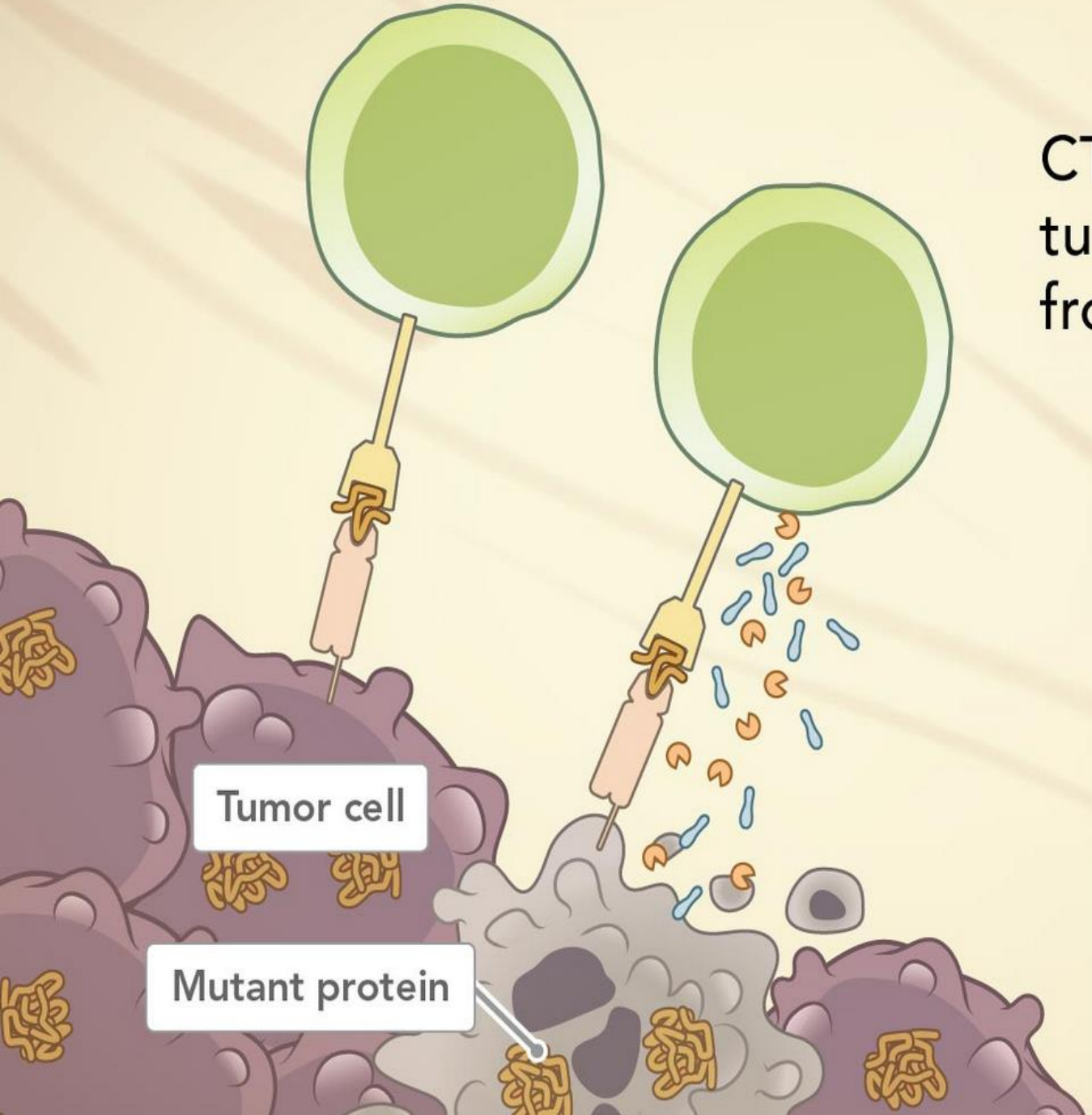
After a T cell is activated by an antigen-presenting cell...

...it undergoes clonal expansion.

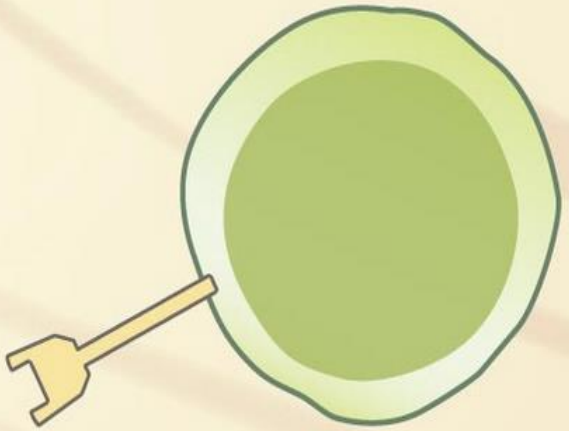
These effector T cells recognize virally infected cells...

... and kill them by releasing cytotoxic molecules.



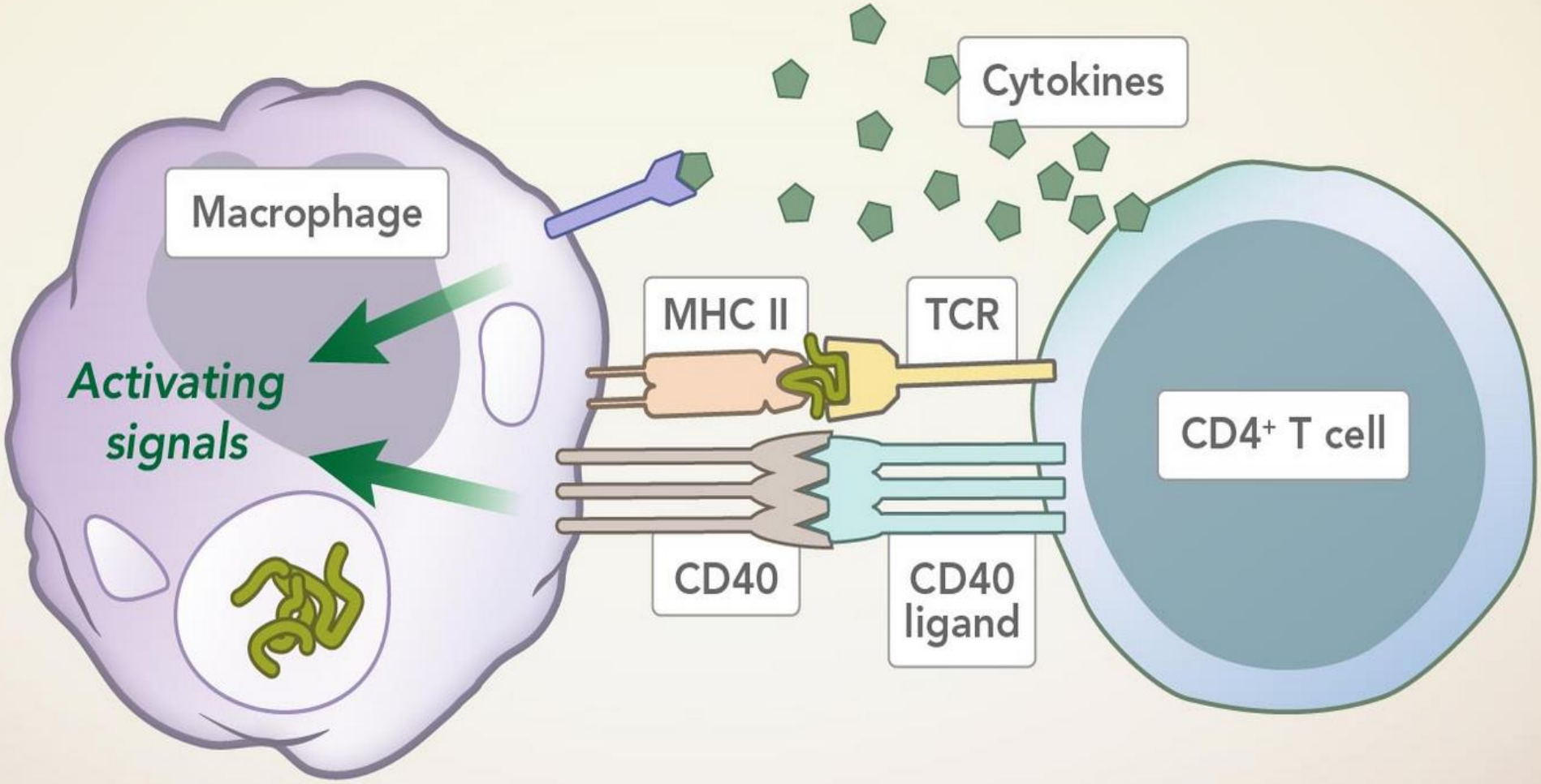


CTLs may also kill cells, such as tumor cells, presenting peptides from mutant proteins.



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.



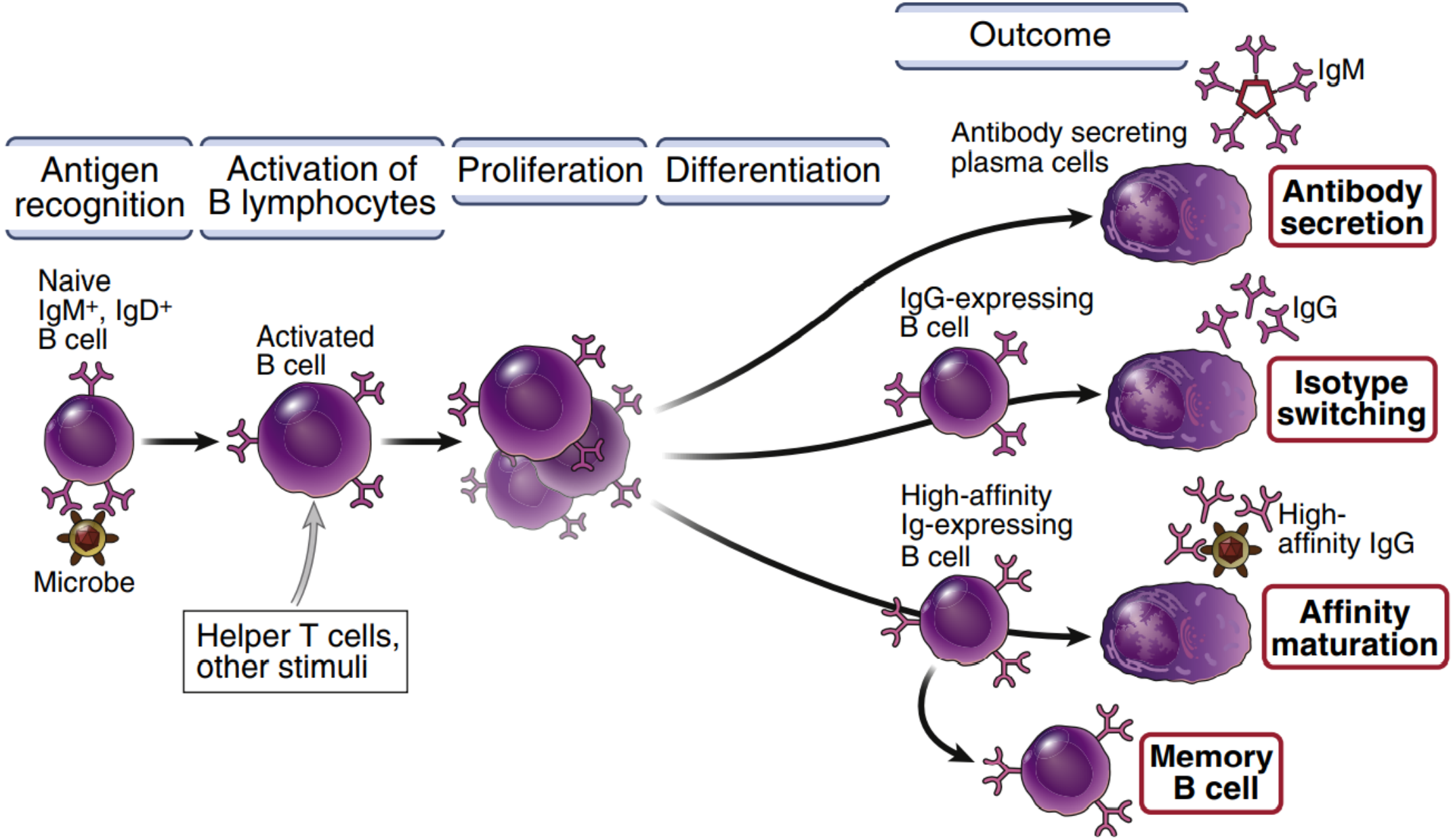


FIGURE 7-1 Phases of humoral immune responses. Naive B lymphocytes recognize antigens, and under the influence of helper T cells and other stimuli (not shown), the B cells are activated to proliferate, giving rise to clonal

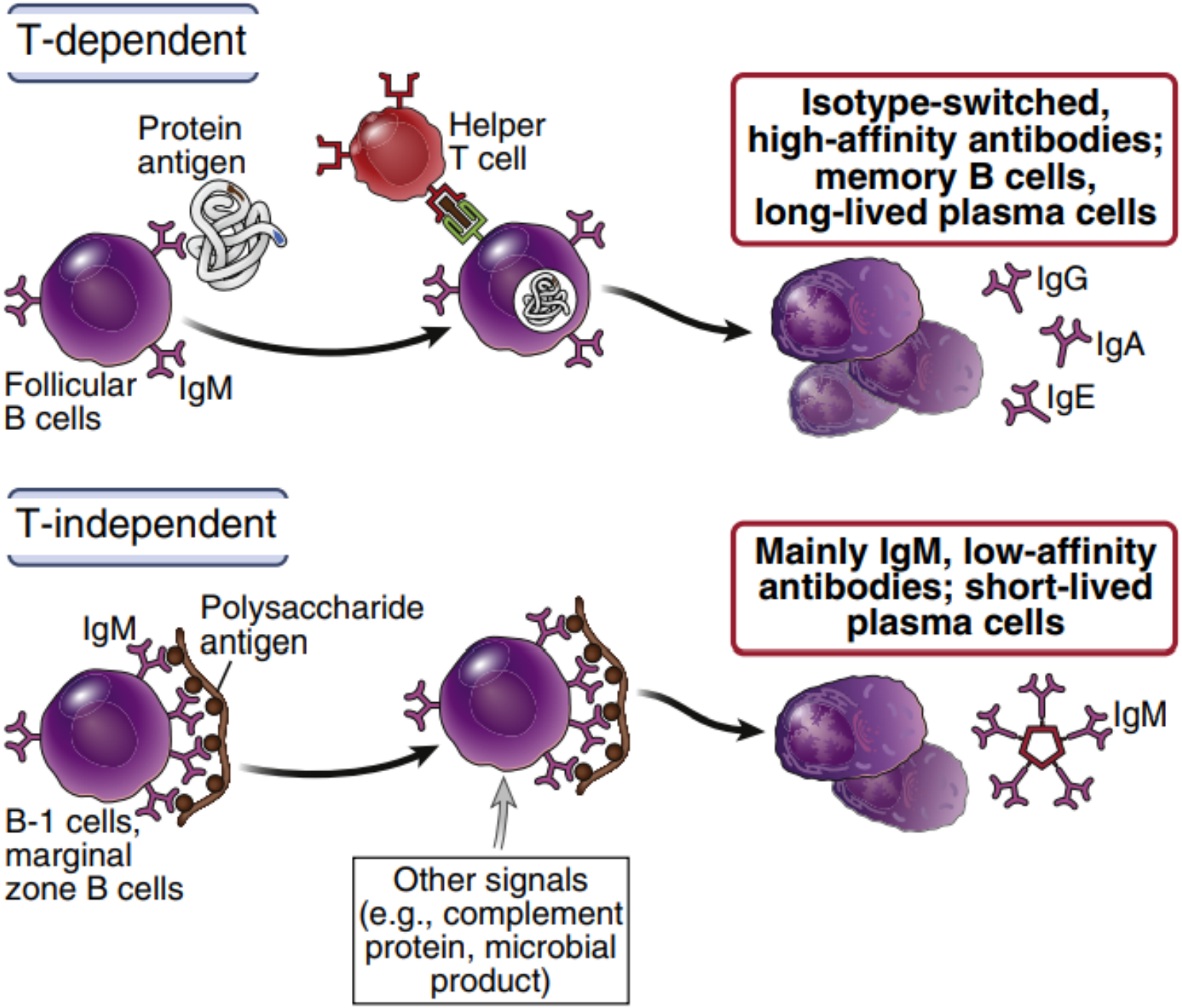


FIGURE 7-2 T-dependent and T-independent antibody responses. Antibody responses to protein antigens require T cell help, and the antibodies produced typically show isotype switching and are of high affinity. Non-protein (e.g., polysaccharide) antigens are able to activate B cells without T cell help. Most T-dependent responses are made by follicular B cells, whereas marginal zone B cells and B-1 cells play greater roles in T-independent responses. *Ig,* Immunoglobulin.

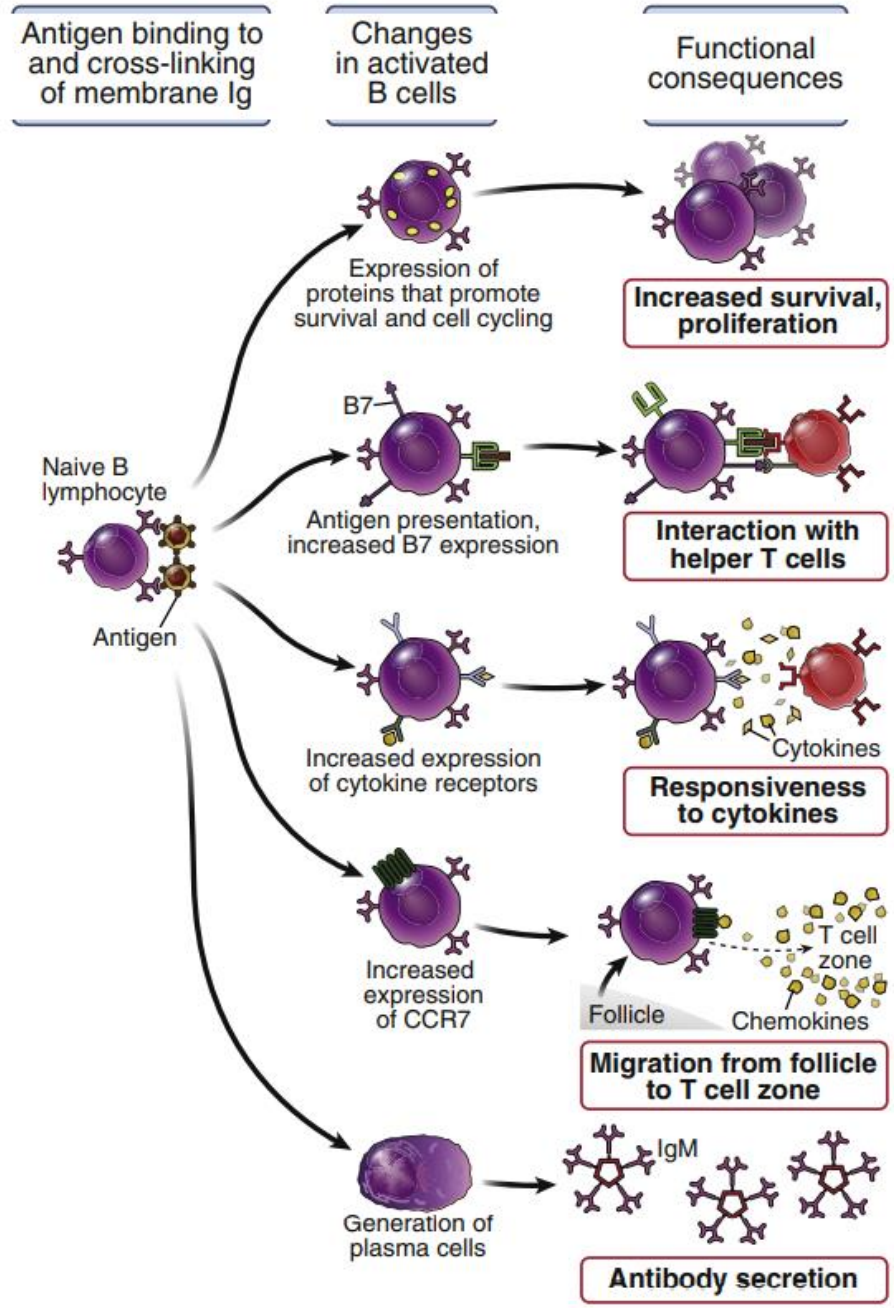


FIGURE 7-6 Functional consequences of antigen receptor-mediated B cell activation. The activation of B cells by antigen in lymphoid organs initiates the process of B cell proliferation and IgM secretion and prepares

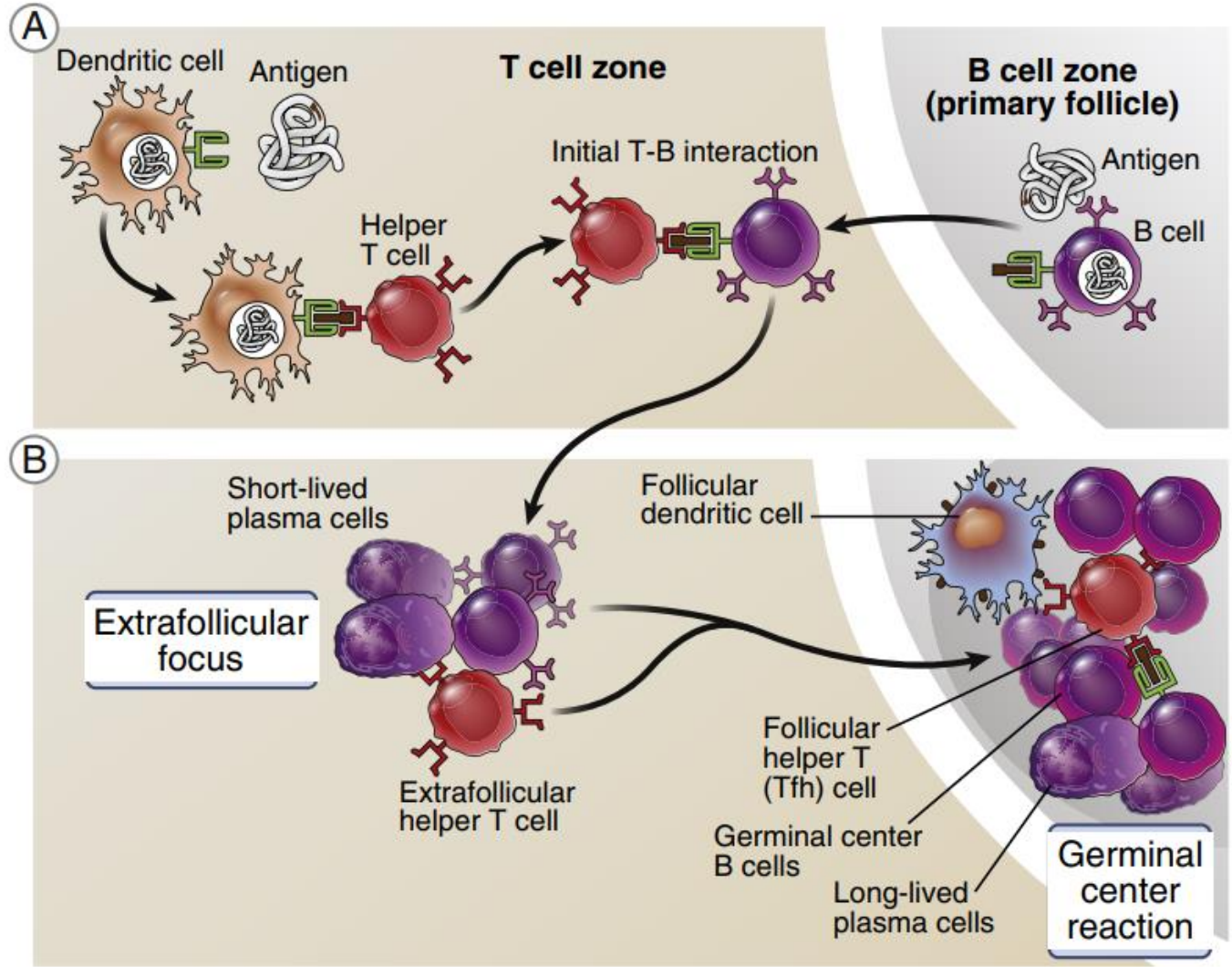


FIGURE 7-7 Sequence of events in helper T cell–dependent antibody responses. **A,** T and B lymphocytes independently recognize the antigen in different regions of peripheral lymphoid organs and are activated. The activated cells migrate toward one another and interact at the edges of lymphoid follicles. **B,** Antibody-secreting plasma cells are initially produced in the extrafollicular focus where the antigen-activated T and B cells interact. Some of the activated B and T cells migrate back into the follicle to form the germinal center, where the antibody response develops fully.

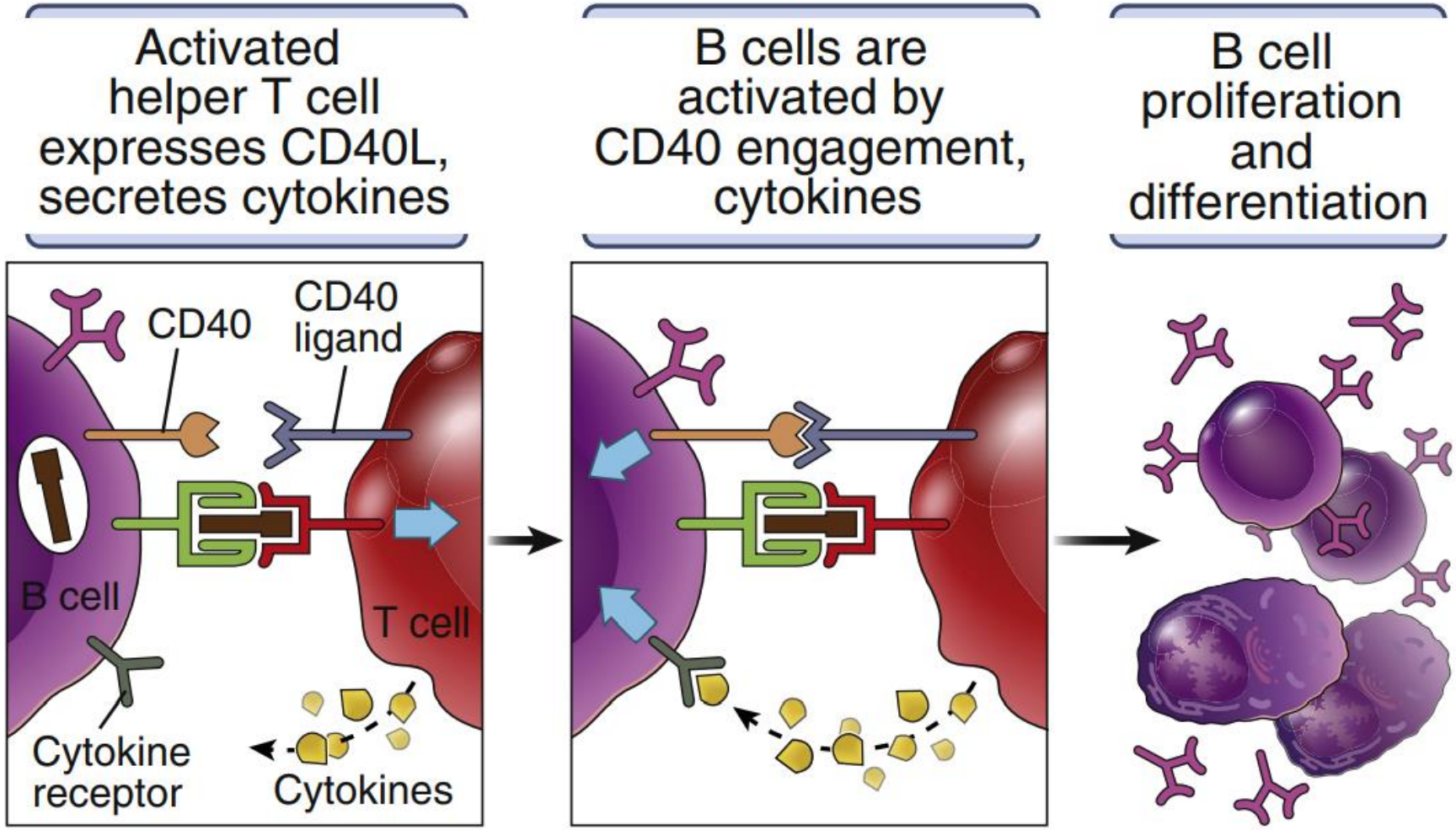
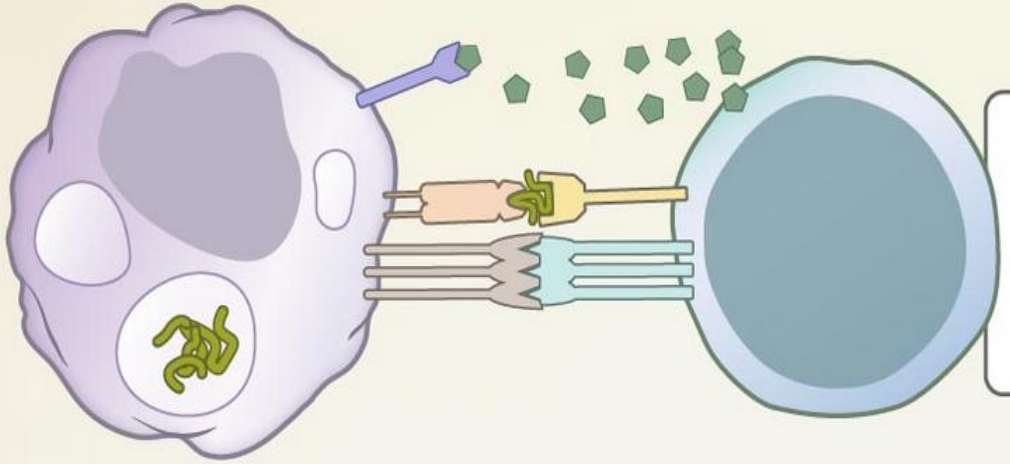
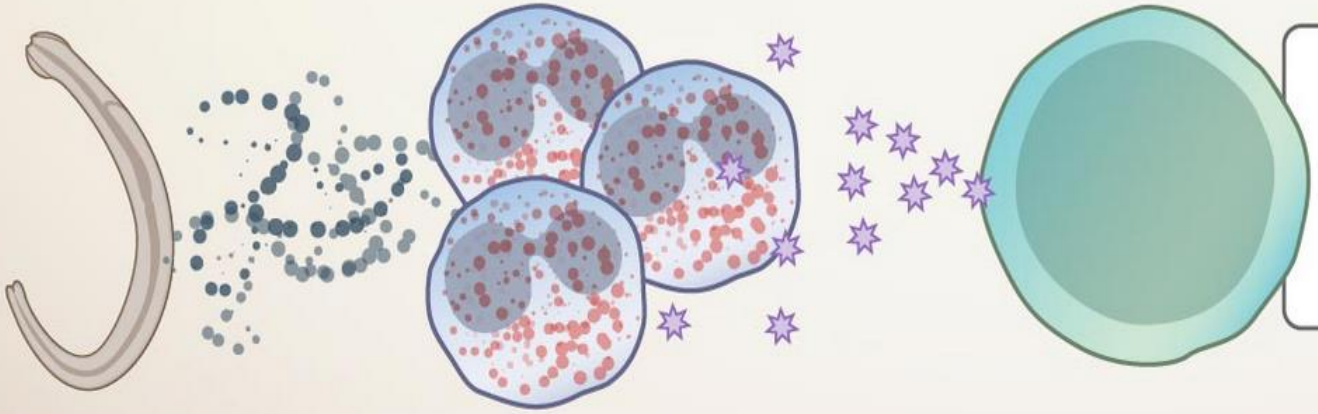


FIGURE 7-9 Mechanisms of helper T cell–mediated activation of B lymphocytes. Helper T cells recognize peptide antigens presented by B cells (and costimulators, e.g., B7 molecules, not shown) on the B cells. The helper T cells are activated to express CD40 ligand (CD40L) and secrete cytokines, both of which bind to their receptors on the same B cells and activate the B cells.

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

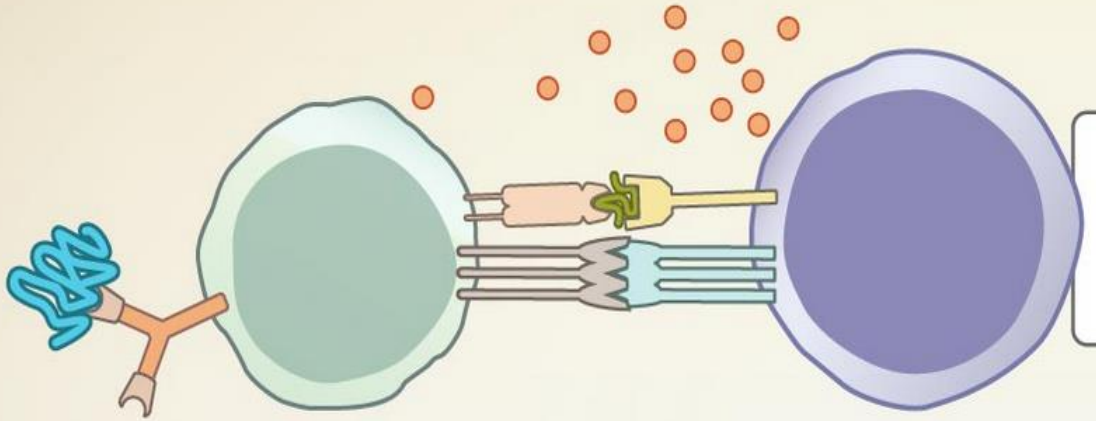


Th1 cells activate macrophages to enhance their ability to kill intracellular microbes.

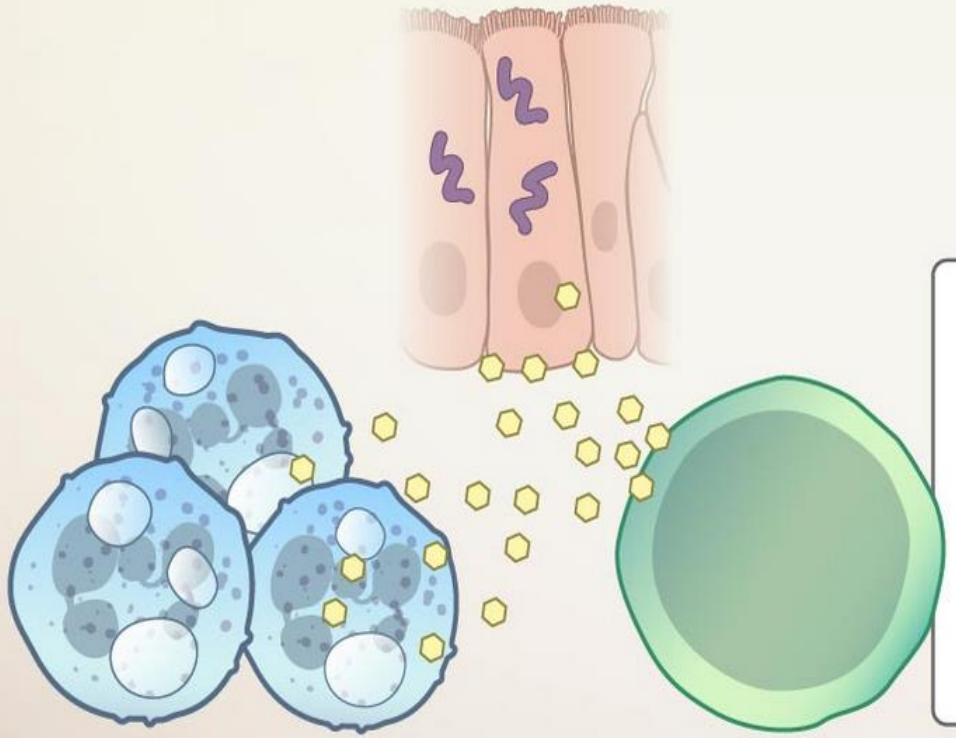


Th2 cells activate eosinophils that kill parasites and macrophages to promote tissue repair and fibrosis.

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

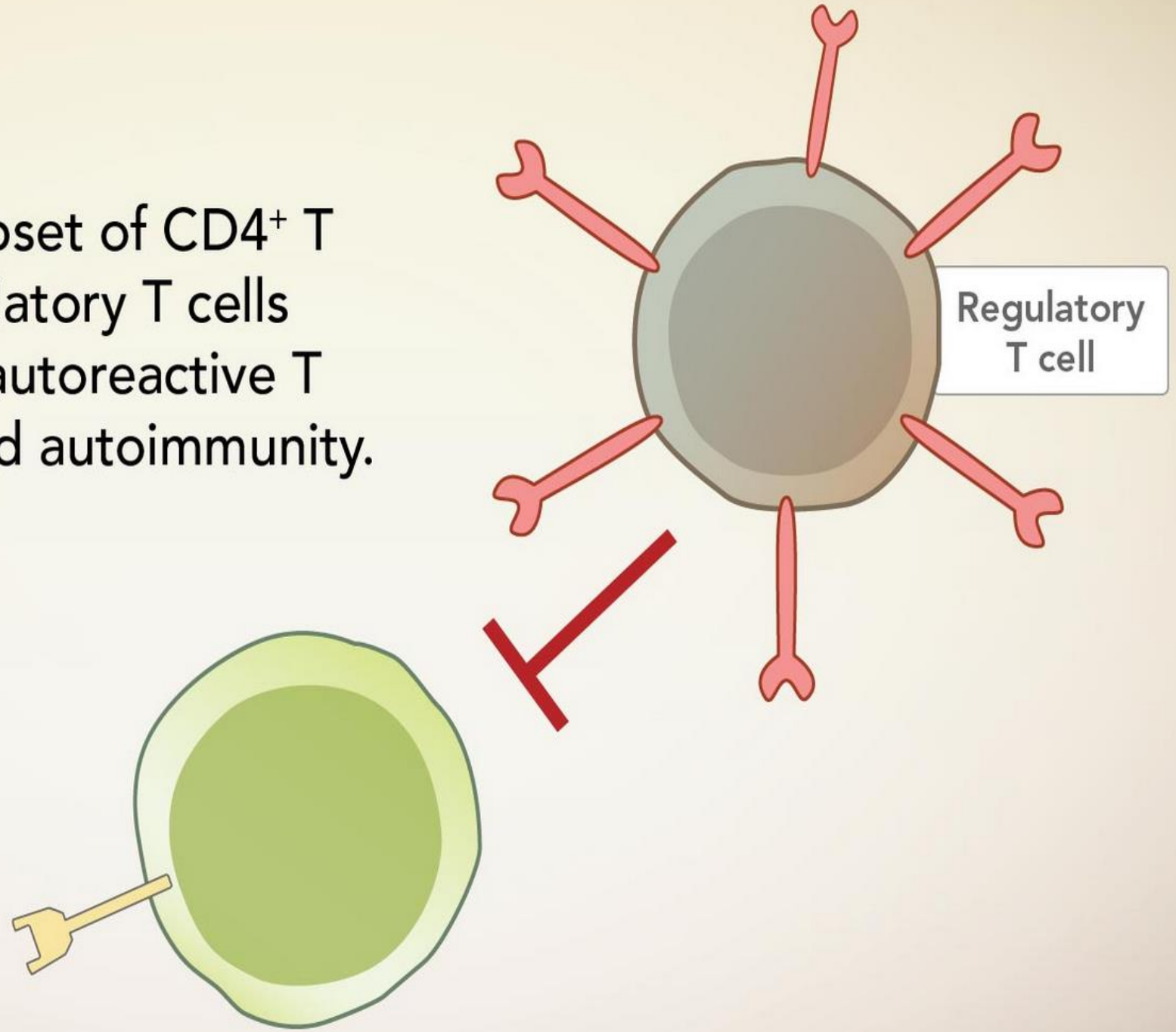


T follicular helper (Tfh) cells help B cells generate effective antibody responses.



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.



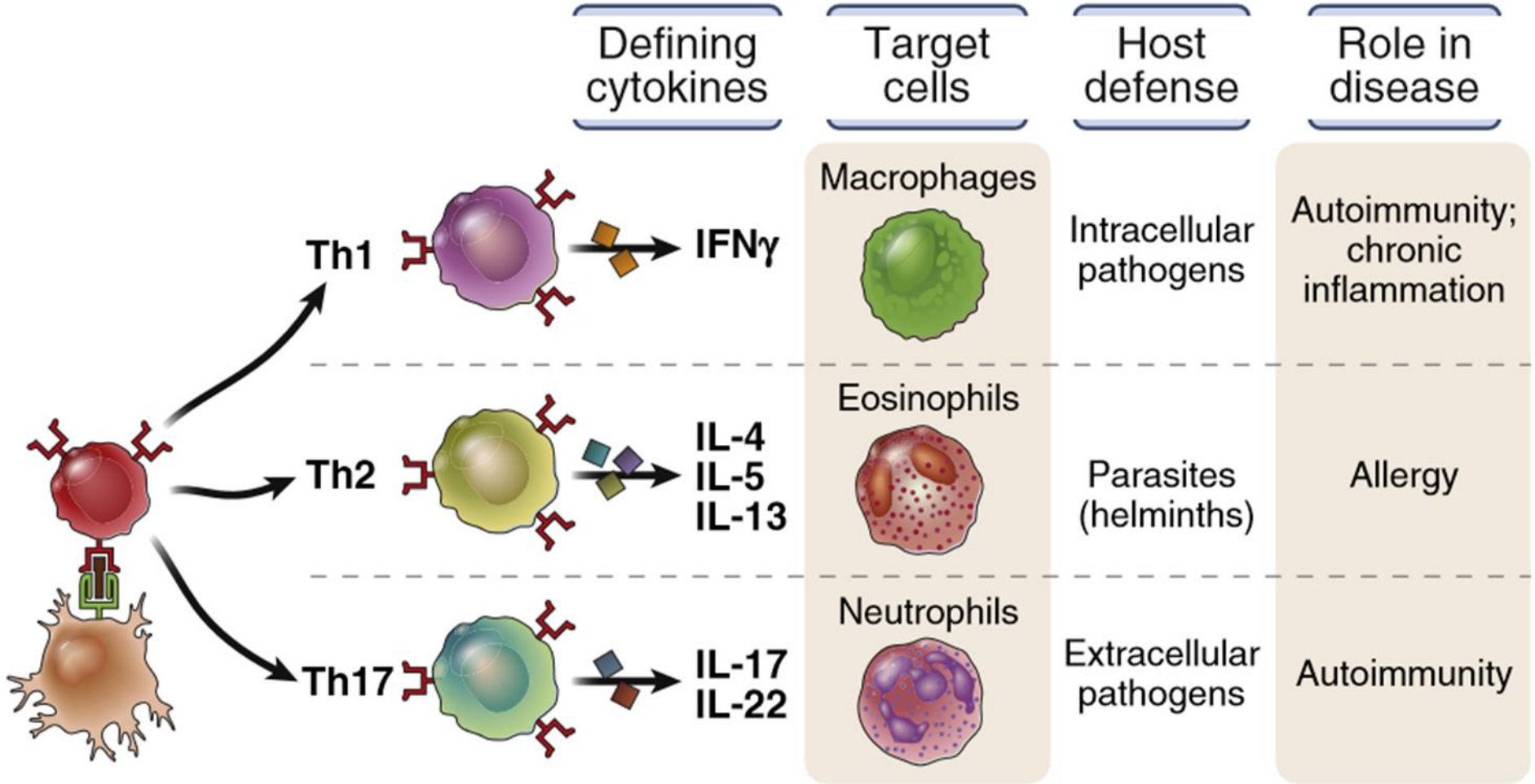
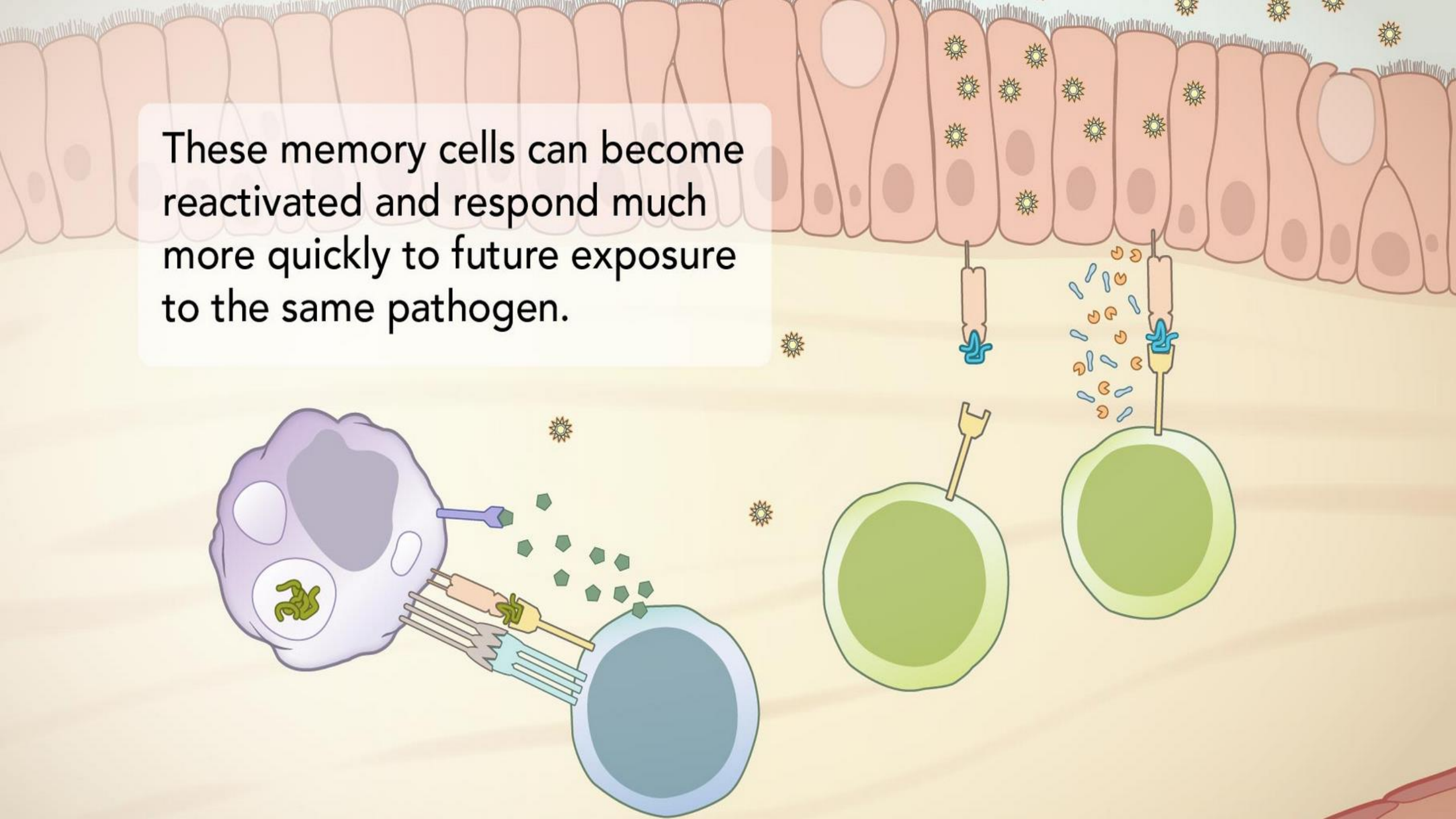
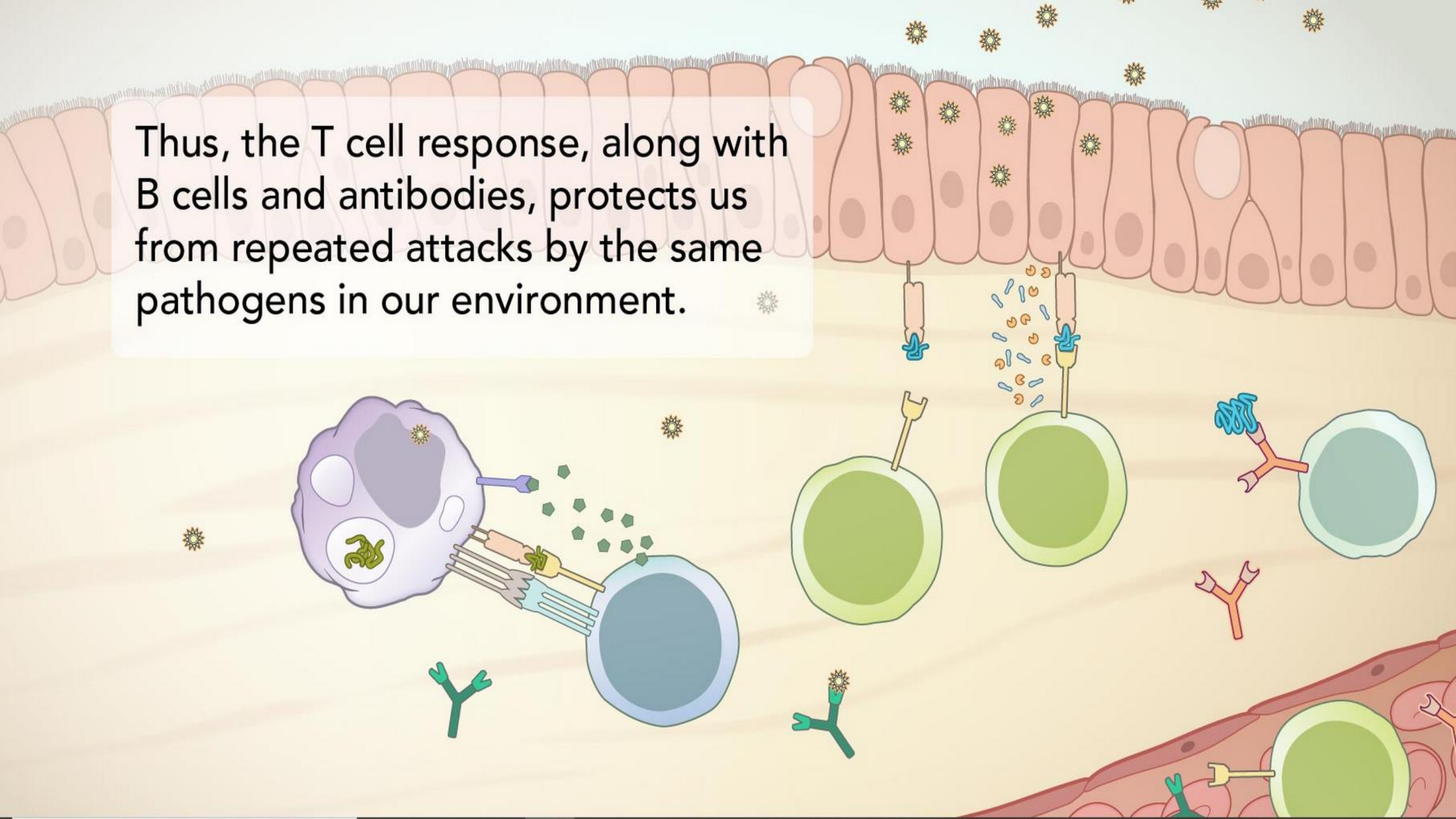


FIGURE 6-3 Characteristics of subsets of CD4⁺ helper T lymphocytes. A naive CD4⁺ T cell may differentiate into subsets that produce different cytokines that recruit and activate different cell types (referred to as *target cells*) and combat different types of infections in host defense. These subsets also are involved in various kinds of inflammatory diseases. The table summarizes the major differences among Th1, Th2, and Th17 subsets of helper T cells. *IFN*, Interferon; *IL*, interleukin.

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.



Humoral Immunity

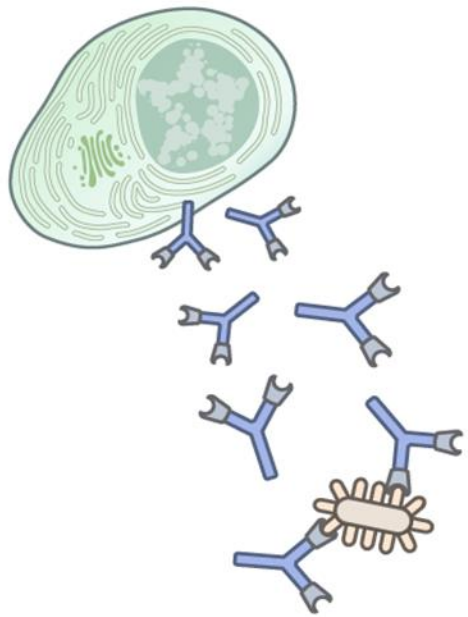
B cells

↓

Plasma cells

↓

Antibodies

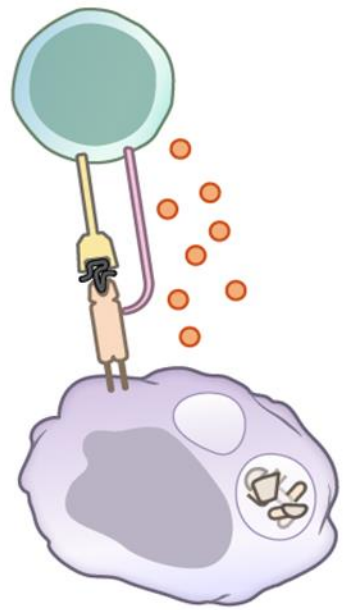


Can bind to virtually any molecule

Cell-Mediated Immunity

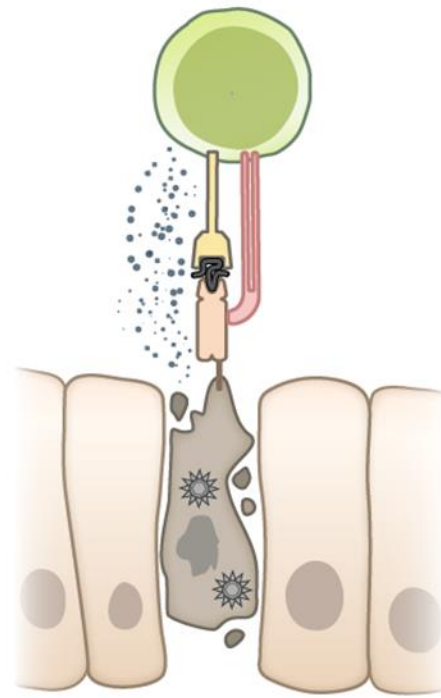
T cells

Helper T cells

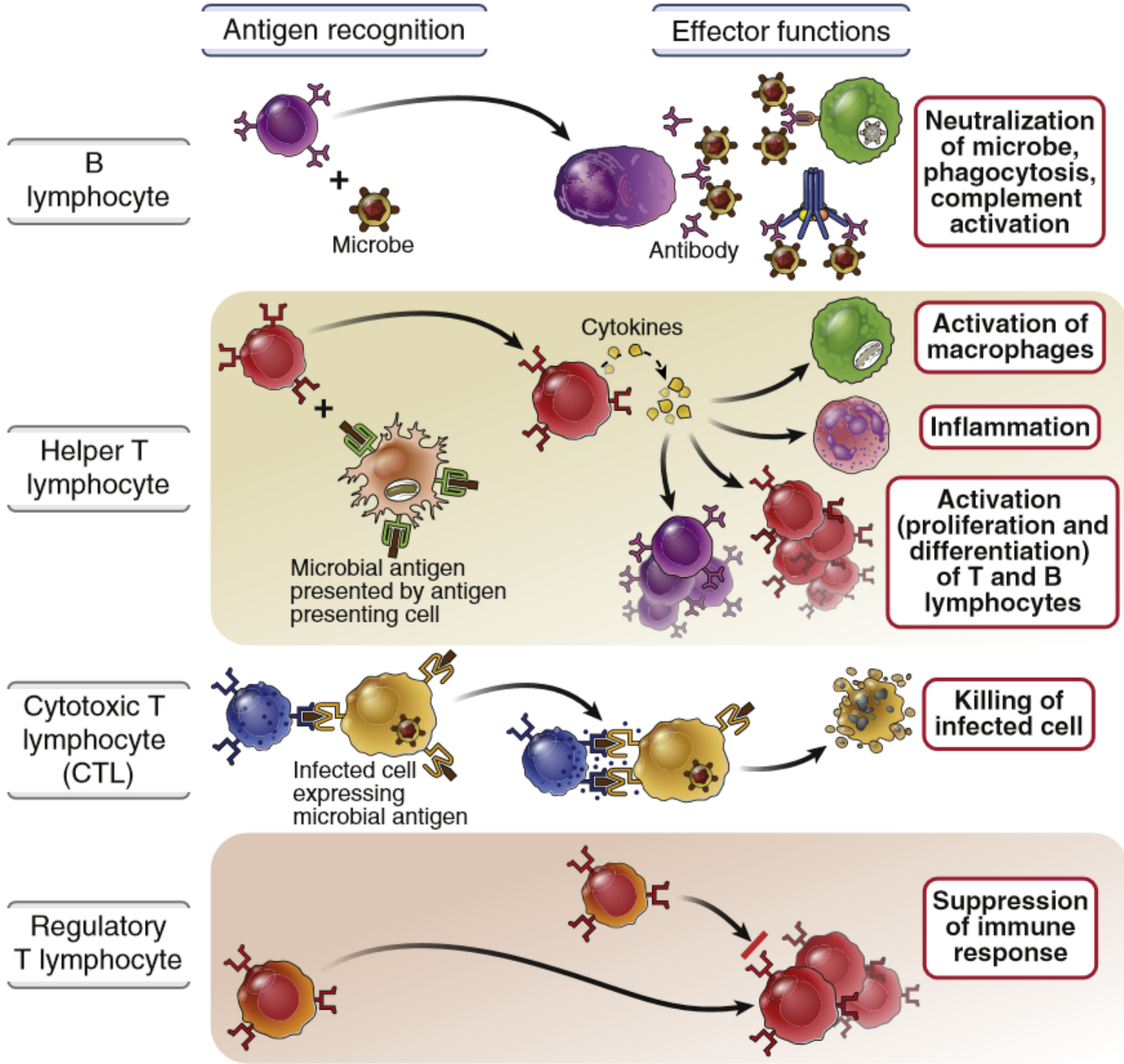


Activate other immune cells

Cytotoxic T cells



Directly kill infected cells


Antigen recognition
Effector functions
B lymphocyte
Microbe
Antibody
Neutralization of microbe, phagocytosis, complement activation
Helper T lymphocyte
Cytokines
Activation of macrophages
Inflammation
Activation (proliferation and differentiation) of T and B lymphocytes
Microbial antigen presented by antigen presenting cell
Cytotoxic T lymphocyte (CTL)
Killing of infected cell
Infected cell expressing microbial antigen
Regulatory T lymphocyte
Suppression of immune response

Both innate and adaptive immune responses defend against microbial infection. Which of the following is a correct statement about innate immunity?

A The innate immune system usually responds more rapidly and with greater magnitude following repeated exposure to the same pathogen.

B Innate immune responses to infections occur quickly and take place before adaptive immune responses.

C Innate immune responses only occur in response to a subset of microbial pathogens.

D Innate immunity is only mediated by secreted cytokines and not by cells.

Lymphocytes of the adaptive immune system utilize receptors that recognize and target molecules produced by pathogens, called antigens. Millions of different receptors, each with a different specificity, are randomly generated by genetic events in developing lymphocytes. Given the wide variety of molecules that can be recognized by lymphocytes, why doesn't the immune system generally develop strong responses to self antigens?

A Lymphocytes with receptors that strongly recognize self antigens during development are caused to die by apoptosis, change their receptor specificity, or become regulatory T cells.

B The genes that code for antigen receptor variable regions do not contain DNA sequences that would encode receptors that bind to self antigens.

C Human lymphocyte receptors are unable to recognize antigens from human beings, excluding all self antigens from recognition.

D All self antigens are proteins, and lymphocyte receptors are unable to recognize protein antigens.

The adaptive immune response includes B cells that secrete antibodies. Antibodies perform multiple functions to protect us from pathogens. Which of the following antibody functions does not depend on the binding of additional molecules or cells to the non-antigen binding end (Fc region) of an antibody molecule?

A Antibody-dependent killing of an infected cell by natural killer cells

B Opsonization of a microbe to enhance phagocytosis

C Complement-mediated lysis of a microbe

D Neutralization of a bacterial toxin

There are multiple subsets of T lymphocytes that participate in the adaptive immune response. The two largest classes of T cells are CD4+ and CD8+ T cells, distinguished by the co-receptor molecules that they express. How do the functions of CD4+ and CD8+ T cells differ from each other?

A CD4+ T cells are naive T cells that have not been activated and require activation before participating in an immune response, while CD8+ T cells are effector T cells that have been activated and are ready to perform their immune function.

B CD4+ T cells are memory T cells that are long lived and respond quickly to repeated challenge by the same pathogen, while CD8+ T cells are mature T cells that are short lived and only activated during an infection.

C CD4+T cells produce antibodies that bind to pathogens and aid in their removal, while CD8+ T cells are natural killer T cells that directly kill infected cells by releasing the contents of cytotoxic granules.

D CD4+ T cells are helper T cells that provide signals to other immune cells to increase their immune function, while CD8+ T cells are cytotoxic T cells that directly kill infected cells by inducing apoptosis.

Both B and T cells are lymphocytes that participate in the adaptive immune response. However, the receptors expressed by B and T cells differ in significant ways. What is one difference between antigen recognition by B and T cells?

A B cells can recognize extracellular or cell surface antigens of any molecular type, while T cells can only recognize peptide fragments of proteins displayed by a specific cell surface molecule.

B B cells secrete antigen receptors, but do not express antigen receptors on their membranes, while T cells can both secrete antigen receptors and express antigen receptors on their membranes.

C B cells can only recognize antigens that have been processed inside cells before display on the cell surface, while T cells can only recognize intact cell surface or intact secreted molecules.

D B cell antigen receptors are lipid molecules, while T cell antigen receptors are proteins.

Before B and T lymphocytes can perform their immune functions, they must pass through multiple developmental steps that lead to the activation of the lymphocytes. Which of the following statements describes the molecular signals required to activate a naive T lymphocyte?

A Naive T lymphocytes need to encounter the antigen they recognize, bind a costimulatory molecule, and detect pathogen-specific danger signals in order to become activated.

B Naive T lymphocytes need to encounter the antigen they recognize and bind a costimulatory molecule in order to become activated.

C Naive T lymphocytes only need to encounter the antigen they recognize in order to become activated.

D Naive T lymphocytes are ready to perform their effector function, but have not yet done so.

1

Both innate and adaptive immune responses defend against microbial infection. Which of the following is a correct statement about innate immunity?

YOUR ANSWER: Innate immune responses to infections occur quickly and take place before adaptive immune responses.

2

Lymphocytes of the adaptive immune system utilize receptors that recognize and target molecules produced by pathogens, called antigens. Millions of different receptors, each with a different specificity, are randomly generated by genetic events in developing lymphocytes. Given the wide variety of molecules that can be recognized by lymphocytes, why doesn't the immune system generally develop strong responses to self antigens?

YOUR ANSWER: Lymphocytes with receptors that strongly recognize self antigens during development are caused to die by apoptosis, change their receptor specificity, or become regulatory T cells.

3

The adaptive immune response includes B cells that secrete antibodies. Antibodies perform multiple functions to protect us from pathogens. Which of the following antibody functions does not depend on the binding of additional molecules or cells to the non-antigen binding end (Fc region) of an antibody molecule?

YOUR ANSWER: Neutralization of a bacterial toxin

4 There are multiple subsets of T lymphocytes that participate in the adaptive immune response. The two largest classes of T cells are CD4+ and CD8+ T cells, distinguished by the co-receptor molecules that they express. How do the functions of CD4+ and CD8+ T cells differ from each other?

YOUR ANSWER: CD4+ T cells are helper T cells that provide signals to other immune cells to increase their immune function, while CD8+ T cells are cytotoxic T cells that directly kill infected cells by inducing apoptosis.

5 Both B and T cells are lymphocytes that participate in the adaptive immune response. However, the receptors expressed by B and T cells differ in significant ways. What is one difference between antigen recognition by B and T cells?

YOUR ANSWER: B cells can recognize extracellular or cell surface antigens of any molecular type, while T cells can only recognize peptide fragments of proteins displayed by a specific cell surface molecule.

6 Before B and T lymphocytes can perform their immune functions, they must pass through multiple developmental steps that lead to the activation of the lymphocytes. Which of the following statements describes the molecular signals required to activate a naive T lymphocyte?

YOUR ANSWER: Naive T lymphocytes need to encounter the antigen they recognize and bind a costimulatory molecule in order to become activated.

SUMMARY

- The physiologic function of the immune system is to protect individuals against infections.
- Innate immunity is the early line of defense, mediated by cells and molecules that are always present and ready to eliminate infectious microbes.
- Adaptive immunity is mediated by lymphocytes stimulated by microbial antigens, requires clonal expansion and differentiation of the lymphocytes before it is effective, and responds more effectively against each successive exposure to a microbe.
- Lymphocytes are the cells of adaptive immunity and are the only cells with clonally distributed receptors with fine specificities for different antigens.
- Adaptive immunity consists of humoral immunity, in which antibodies neutralize and eradicate extracellular microbes and toxins, and cell-mediated immunity, in which T lymphocytes eradicate intracellular microbes.
- Adaptive immune responses consist of sequential phases: antigen recognition by lymphocytes, activation of the lymphocytes to proliferate and to differentiate into effector and memory cells, elimination of the microbes, decline of the immune response, and long-lived memory.

SUMMARY

❖Different populations of lymphocytes serve distinct functions and may be distinguished by the surface expression of particular membrane molecules.

❖B lymphocytes are the only cells that produce antibodies. B lymphocytes express membrane antibodies that recognize antigens, and the progeny of activated B cells, called plasma cells, secrete the antibodies that neutralize and eliminate the antigen.

❖T lymphocytes recognize peptide fragments of protein antigens displayed on other cells. Helper T lymphocytes produce cytokines that activate phagocytes to destroy ingested microbes, recruit leukocytes, and activate B lymphocytes to produce antibodies. Cytotoxic T lymphocytes (CTLs) kill infected cells harboring microbes in the cytoplasm.

❖Antigen-presenting cells (APCs) capture antigens of microbes that enter through epithelia, concentrate these antigens in lymphoid organs, and display the antigens for recognition by T cells.

❖Lymphocytes and APCs are organized in peripheral lymphoid organs, where immune responses are initiated and develop.

❖Naive lymphocytes circulate through peripheral lymphoid organs, searching for foreign antigens. Effector T lymphocytes migrate to peripheral sites of infection, where they function to eliminate infectious microbes. Plasma cells remain in lymphoid organs and the bone marrow, where they secrete antibodies that enter the circulation and find and eliminate microbes.