An overview of the immune system

1. Definitions

2. Innate and adaptive immunity

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Immunity means protection or exemption from something (infectious microbes, others foreign substances).
Ability to distinguish between *self* and *non self*

Immune response can be systemic

The immune system

is constituted by tissues, cells and molecules that are responsible for immunity

Innate and adaptive immunity

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Immunity is achieved by two strategies coordinated by positive and negative feedback

Innate immunity

Multicellular organisms, always present , ready to attack before adaptive immunity; many pathogenic microbes have evolved to resist innate immunity

Adaptive immunity

specific, stimulated by exposure to microbe; more potent,

vertebrates

Innate immunity

Rapid	Respond to danger signals	Transient

Recognition of shared structures in different microbes

- Pathogen Associated Molecular Patterns (**PAMPs**)

  Example: lipopolysaccharides (LPS) from Gram negative bacteria

- Damage Associated Molecular Patterns (**DAMPs**)

  Example: extracellularly released nuclear proteins

About 1000 conserved molecular patterns

Innate immunity

Rapid	Respond to danger signals	Transient

1. **Physical and chemical barriers (epithelia, mucous membranes, mucous)**

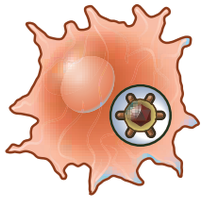
   - prevent pathogen invasion

2. **Innate immune cells and soluble factors**

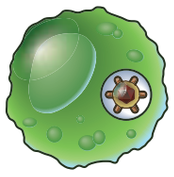
   - direct destruction of pathogen by phagocytosis or secretion of toxic enzymes
   - destruction of infected cells
   - secretion of soluble mediators of inflammation

Innate immune cells and soluble factors

Dendritic cells

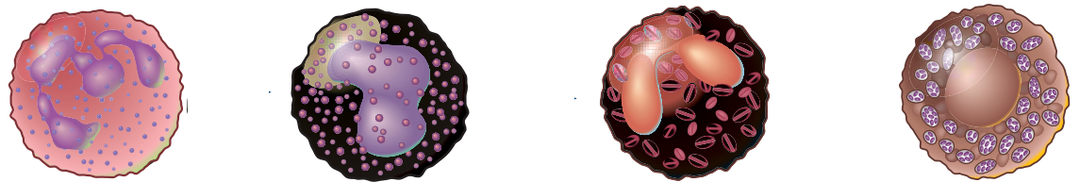


Macrophages



Complement system

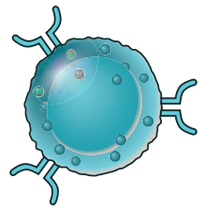
Granulocytes



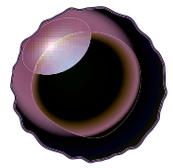
Neutrophiles Basophils Eosinophils Mast Cells

Granulocytes are named based on how they appear on Wright-Giemsa staining

Innate lymphocytes



Natural Killer



Innate Lymphoid Cells (ILCs)

Adaptive immunity

Slow	Recognizes “antigens” Specificity	Long lasting

Antigen: any molecule which can elicit an adaptive immune response; typically a protein, but can also be a small molecule, lipid or nucleic acid

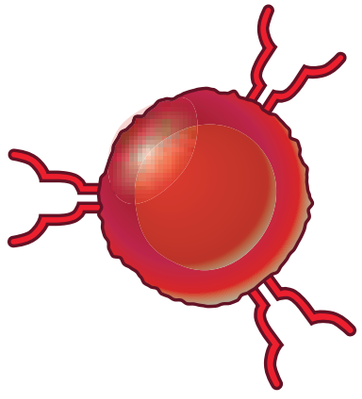
$> 10^7$ antigens

Adaptive immune cells and soluble factors

- direct and indirect neutralization of pathogen
- destruction of infected cells

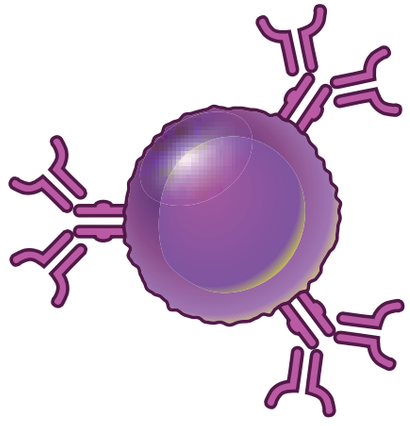
Adaptive immunity

Lymphocytes
Are the Effector cells



T cells

Cellular Immunity

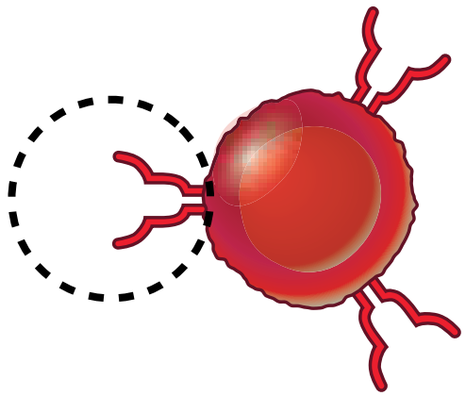


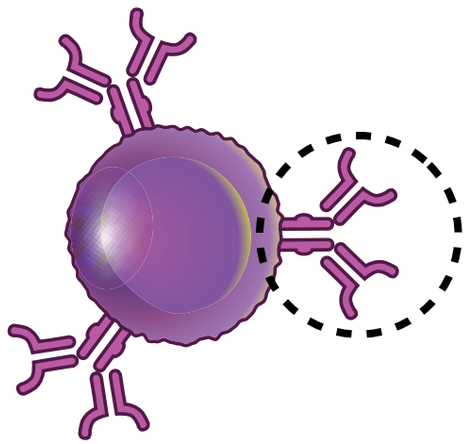
B cells

Humoral Immunity

What B and T cells have in common: SPECIFICITY

TCR
T Cell **R**eceptor





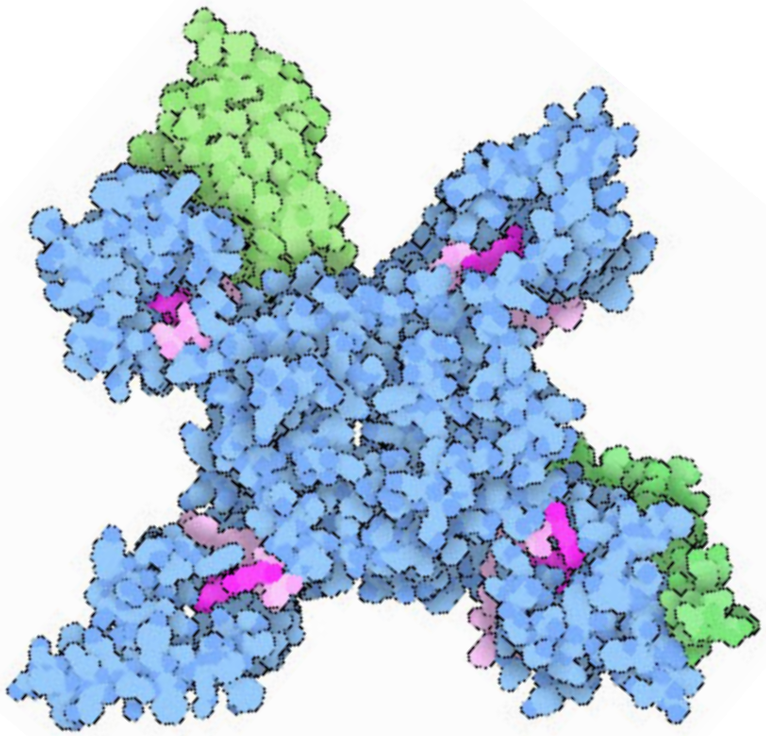
BCR
B Cell **R**eceptor

T cells

B cells

1. Express **membrane receptors** capable of recognizing a large variety of molecules. These molecules are defined as “**antigens**”.

Examples of antigens



Proteins

Sugars

Lipids

Nucleic acids

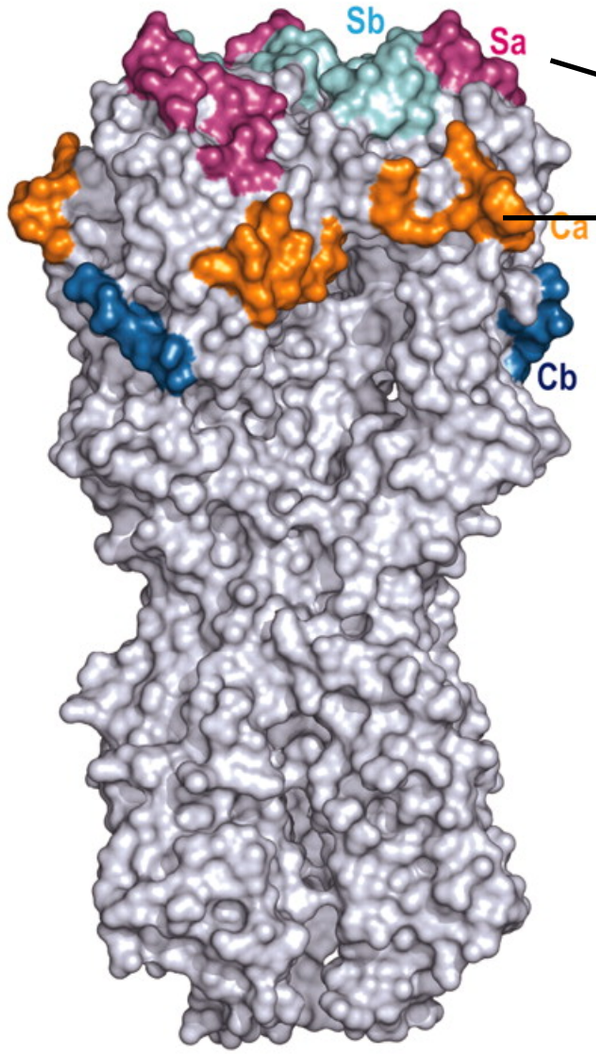
…actually EVERYTHING THAT BINDS

Antigen ≠ Immunogen

Antigen	a molecule that can be recognized by the BCR or TCR
Immunogen	a molecule that elicits an immune response

In physiological conditions, self-antigens can be recognized, but are not immunogenic

One antigen, multiple epitopes



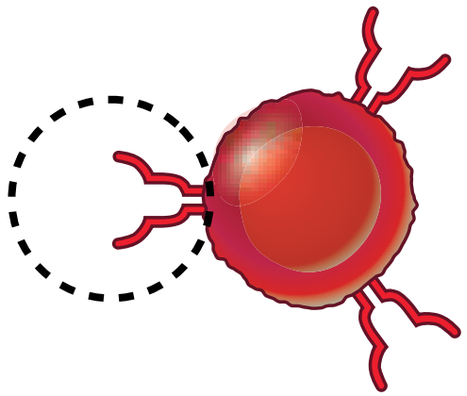
Influenza A H1N1 Hemagglutinin

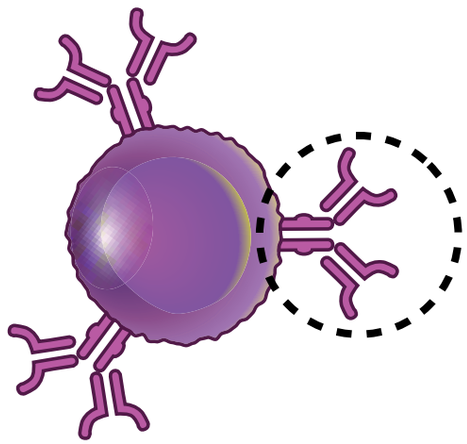
Epitopes

part of an antigen that is recognized by the immune system

What B and T cells have in common: SPECIFICITY

TCR
T Cell **R**eceptor





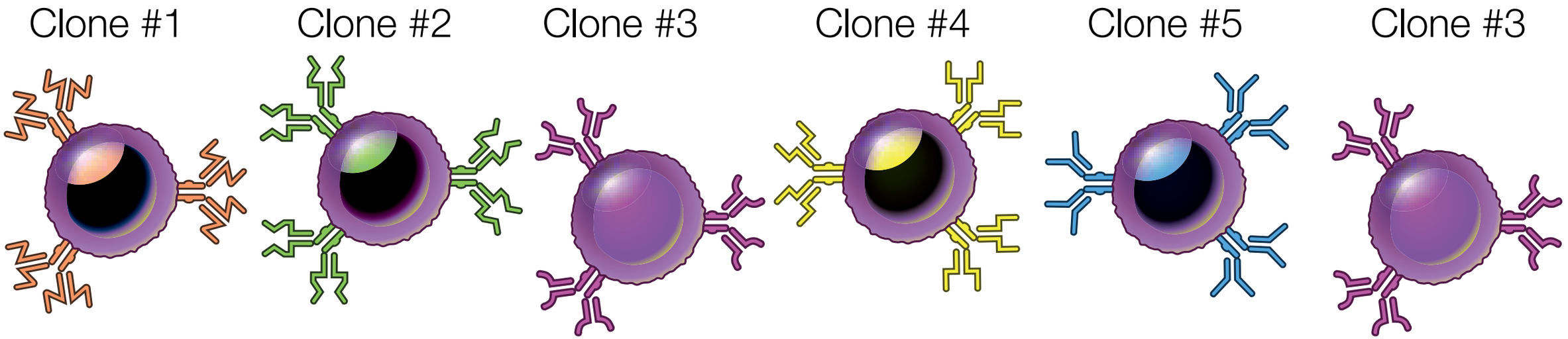
BCR
B Cell **R**eceptor

T cells

B cells

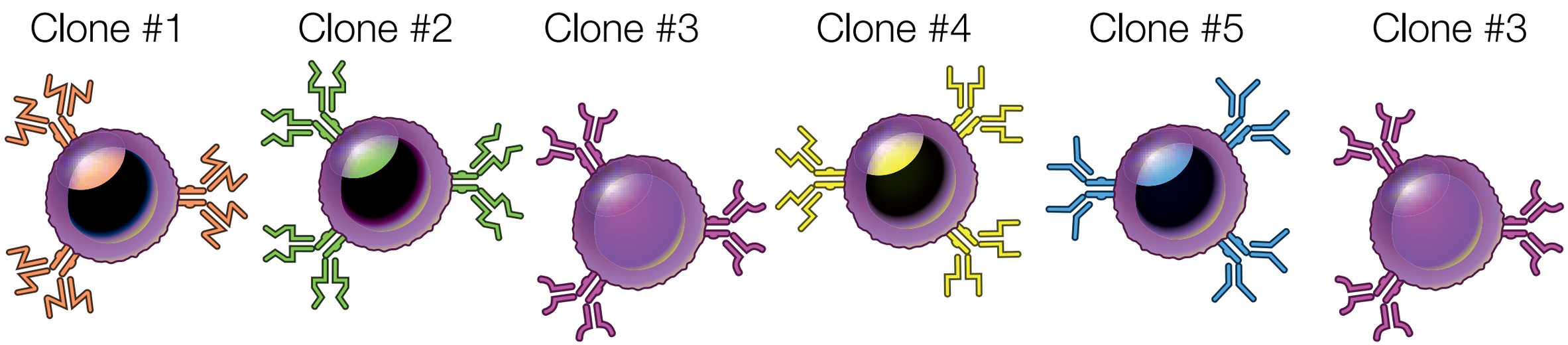
1. Express **membrane receptors** capable of recognizing a large variety of molecules. These molecules are defined as “**antigens**”.

What B and T cells have in common: DIVERSITY



2. Are a **diverse population**, composed by cells expressing different receptors. A cell with a given receptor is called **clone. Different antigens** recognized by **a specific clone.**

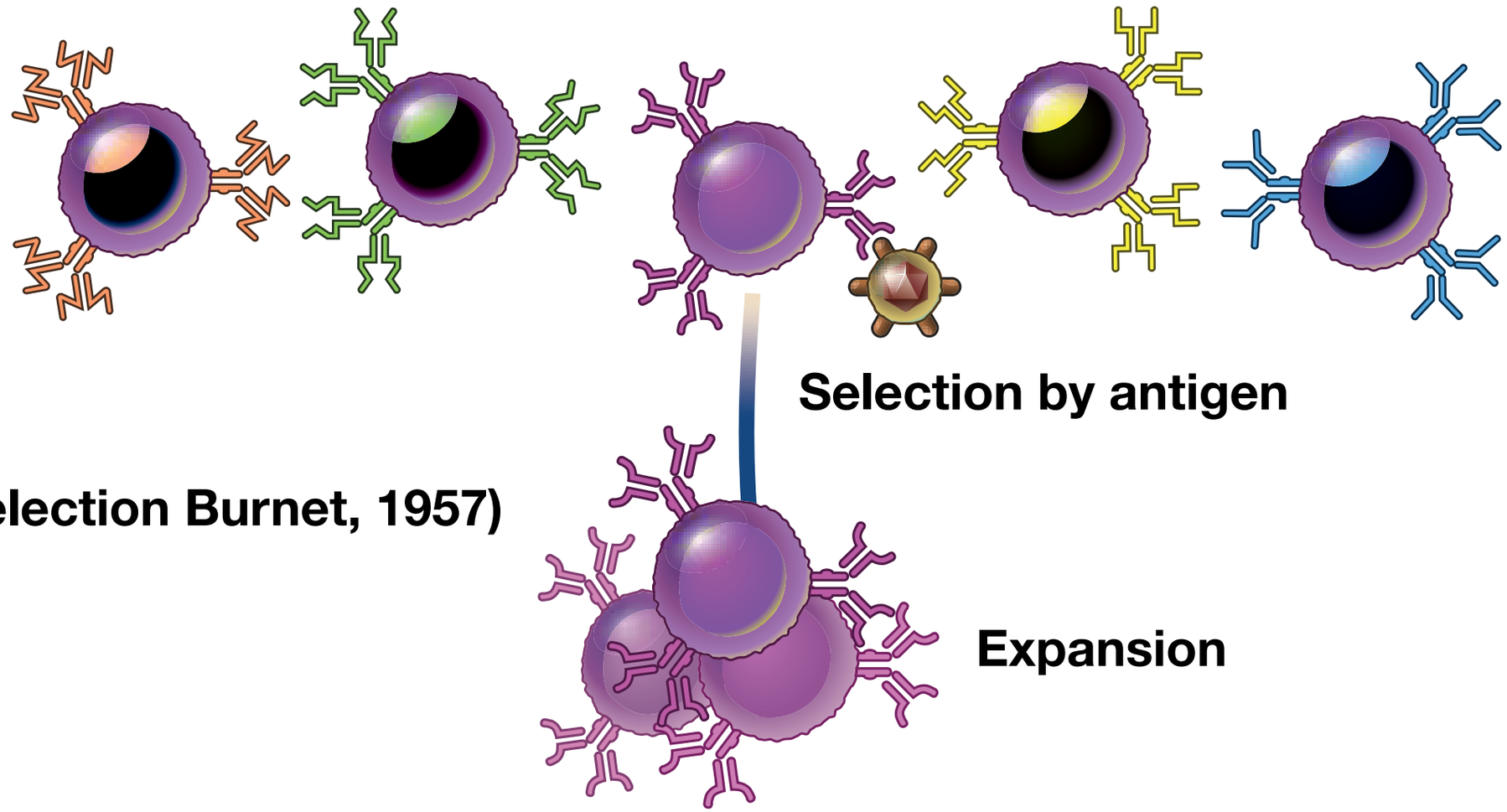
Diversity is very high…



~10^7-10^9 clones

but each clone is poorly represented in naïve individuals before the contact with the antigen

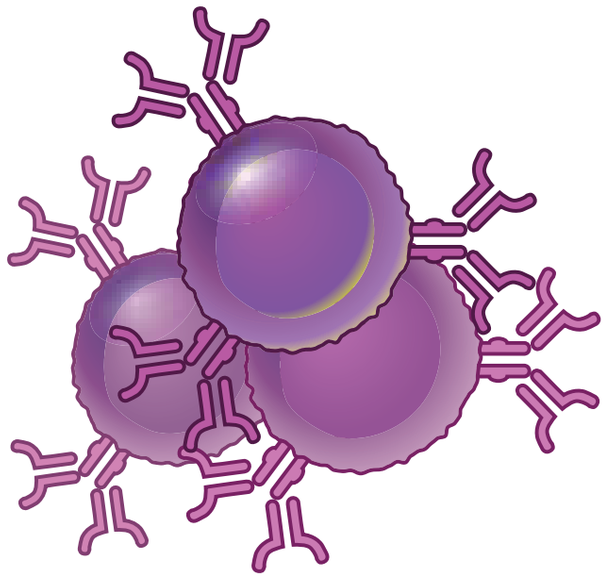
What B and T cells have in common: CLONAL SELECTION & EXPANSION



(Clonal selection Burnet, 1957)

3. **Antigen-specific clones** are **selected** and then **proliferate** massively (from few cells to millions)

What B and T cells have in common: MEMORY



Effector cells

Fight the pathogen; are short-lived cells and dye off after infection clearance.

Memory cells

Very **long-lived** cells; **rapidly reactivate** upon secondary antigen exposure. More effective against persisting antigens.

3. **Antigen-specific clones** differentiate into **effector** and **memory cells**

Works in pairs! To resume our findings:

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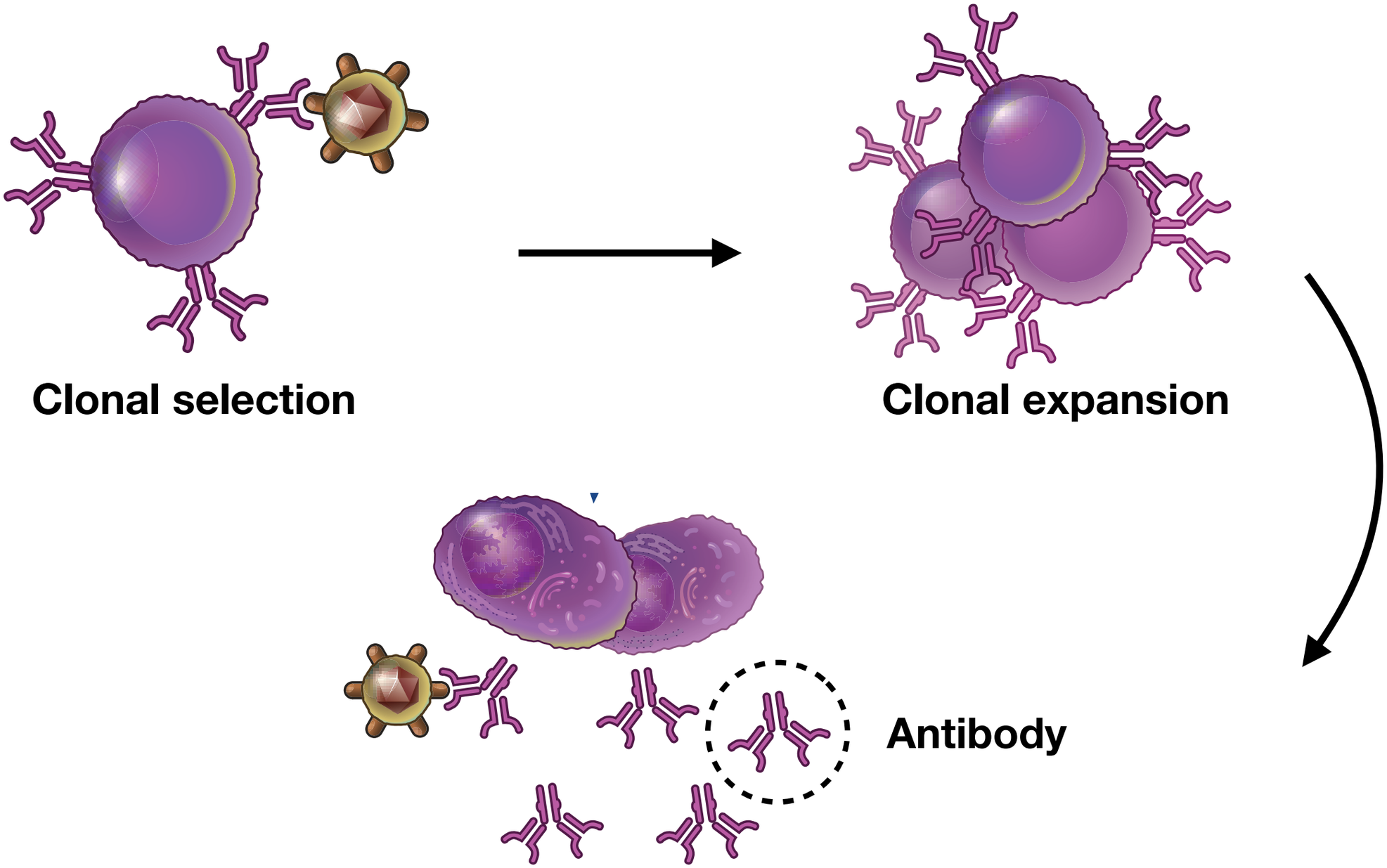
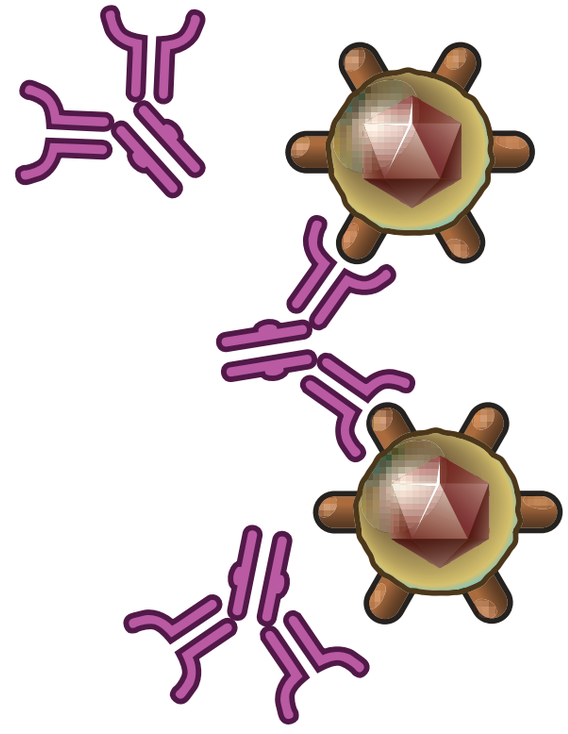
Innate Immunity		Adaptive Immunity
It is elicited rapidly	**Time**	It takes days to develop (clonal selection and expansion)
Recognize conserved microbial features	**Specificity**	Highly specific (antigens)
Transient	**Long-term consequences**	long-lived protection (immunological memory)

B cells make antibodies



Immune functions of antibodies

1. Neutralization

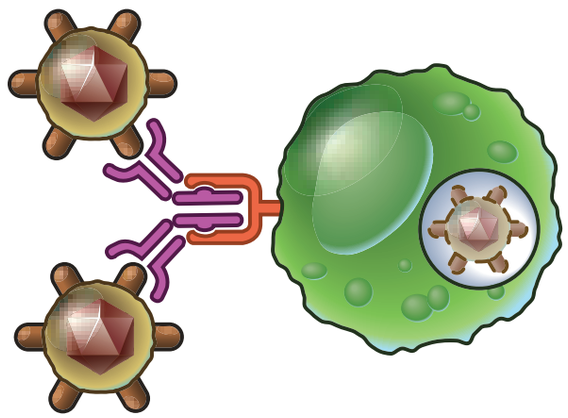


when the antibody binds to the microbe or toxin and makes it innocuous

Example: prevent viral entry into host cell

Immune functions of antibodies

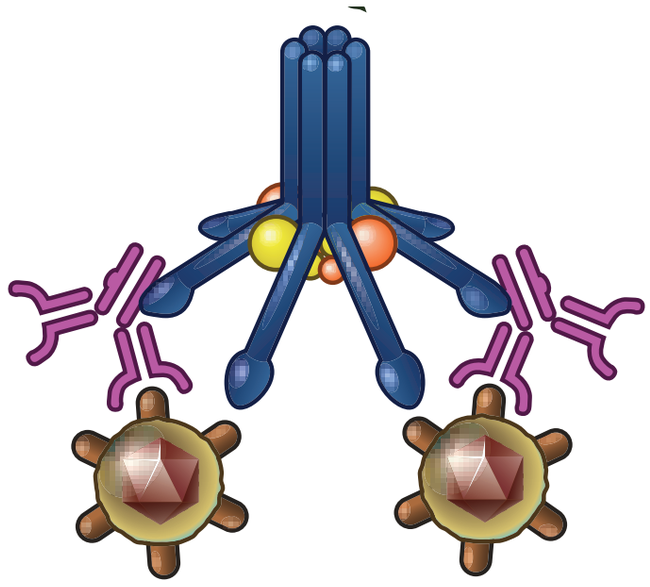
2. Opsonization



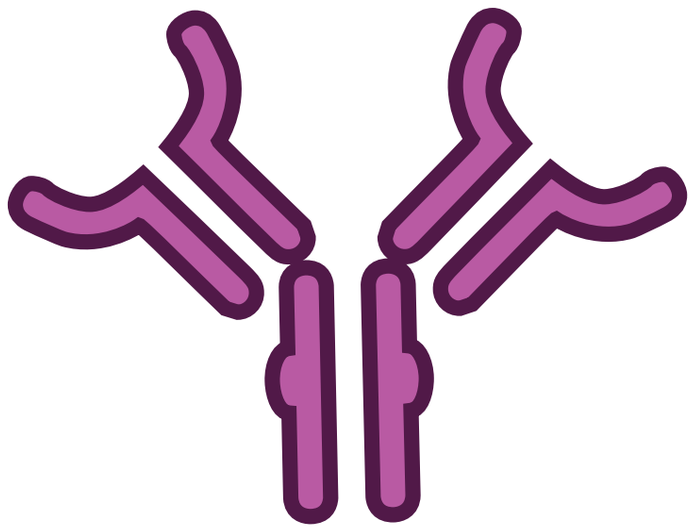
the antibody binds to the microbe, facilitating its phagocytosis by innate cells (macrophages and neutrophils)

Immune functions of antibodies

3. Complement activation



the antibody binds to the microbe, recruiting and activating the complement system which will destroy the pathogen



Antibody are soluble components found un the blood, tissues and mucosal surfaces

Humoral Immunity

Effective against extracellular pathogens

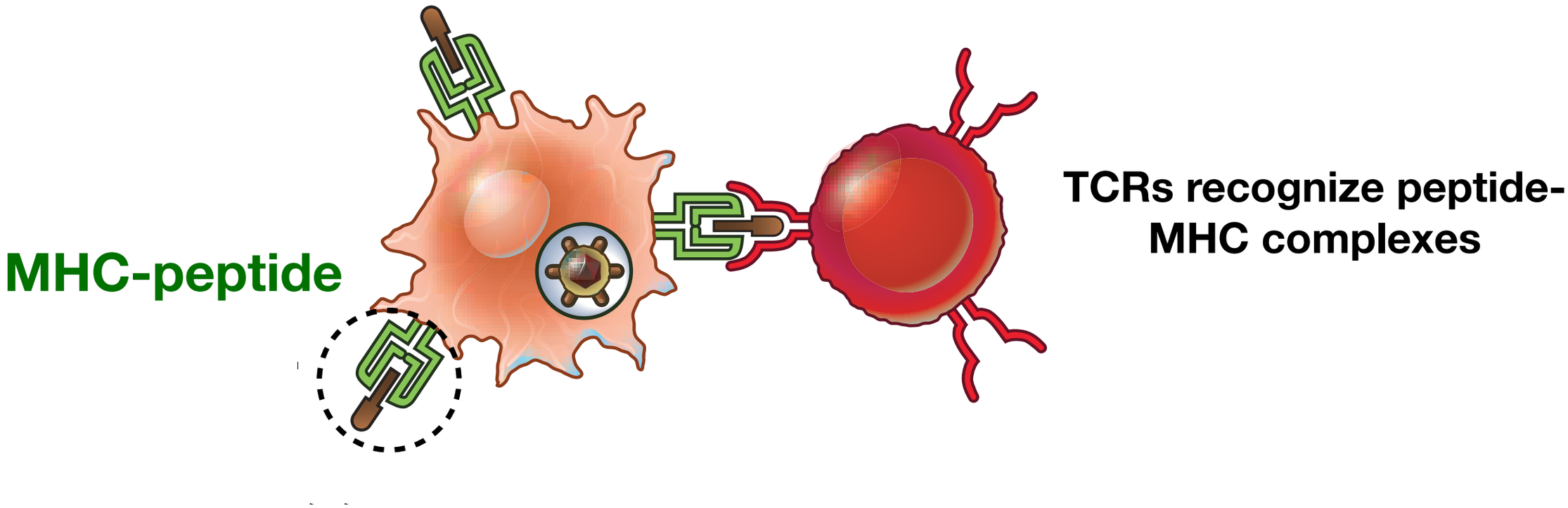
What happen if we have an intracellular pathogen?

Examples: viral infections, intracellular bacteria

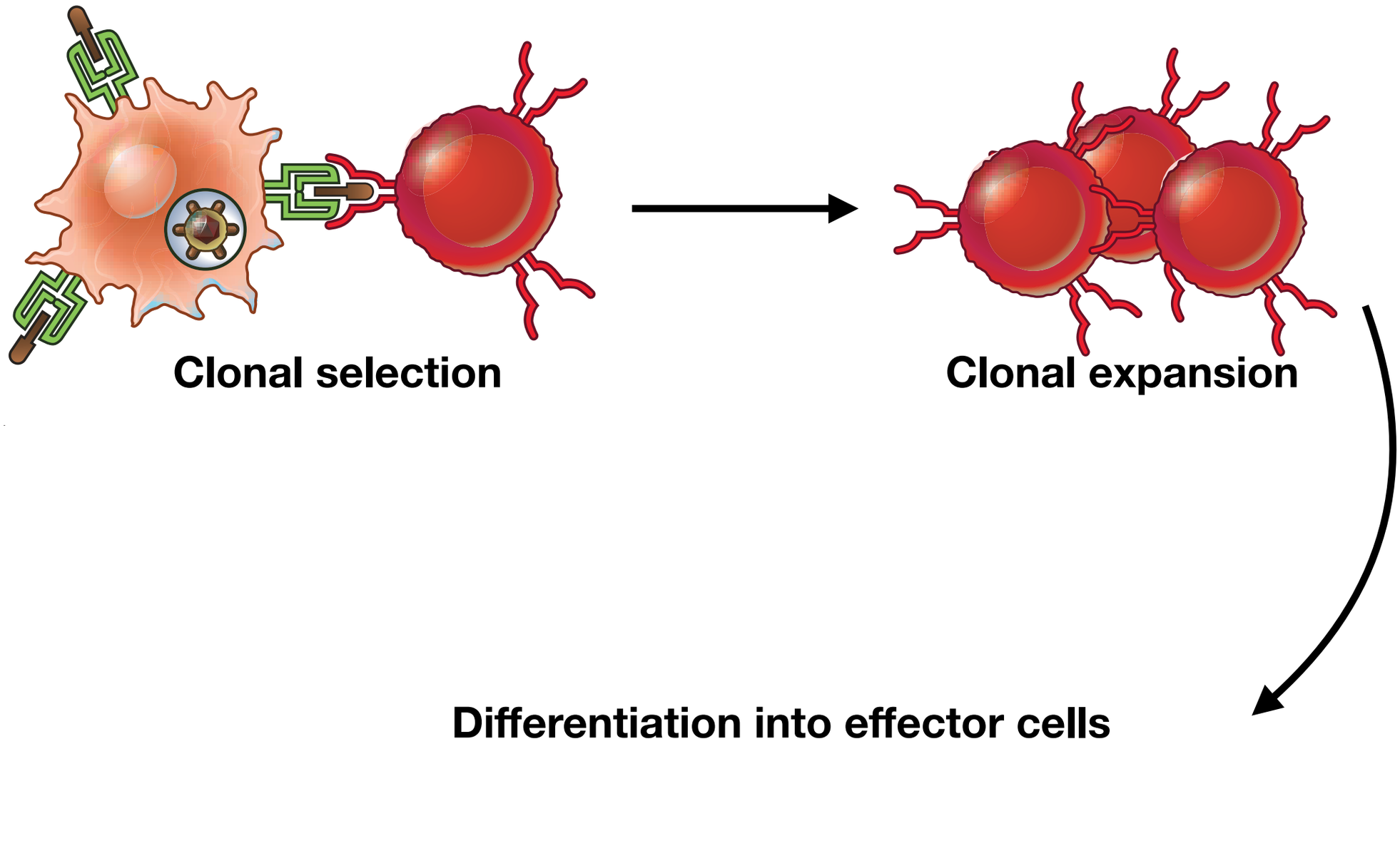
Antibodies are not effective!

A window to check what's inside the cell: MHC presentation

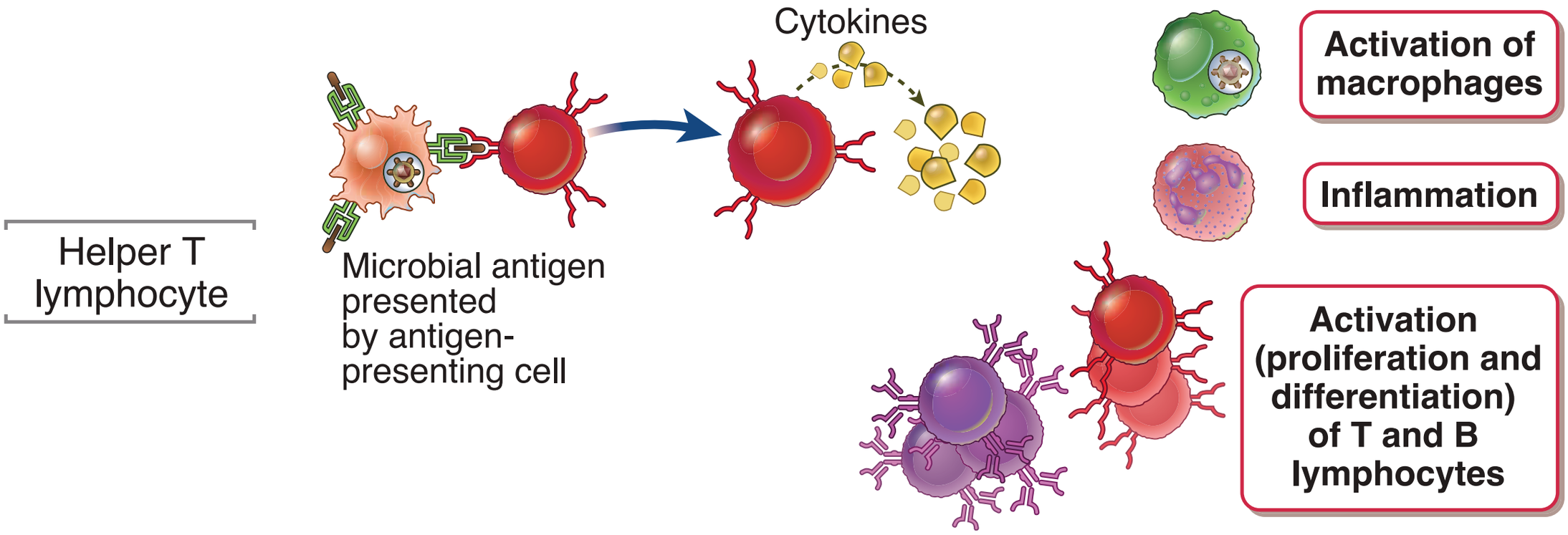
Cells display on their surface a protein complex called **MHC**, loaded with **peptides** derived from "digested" phagocytosed microbes or internally synthesized protein.



T cells differentiate into different effectors



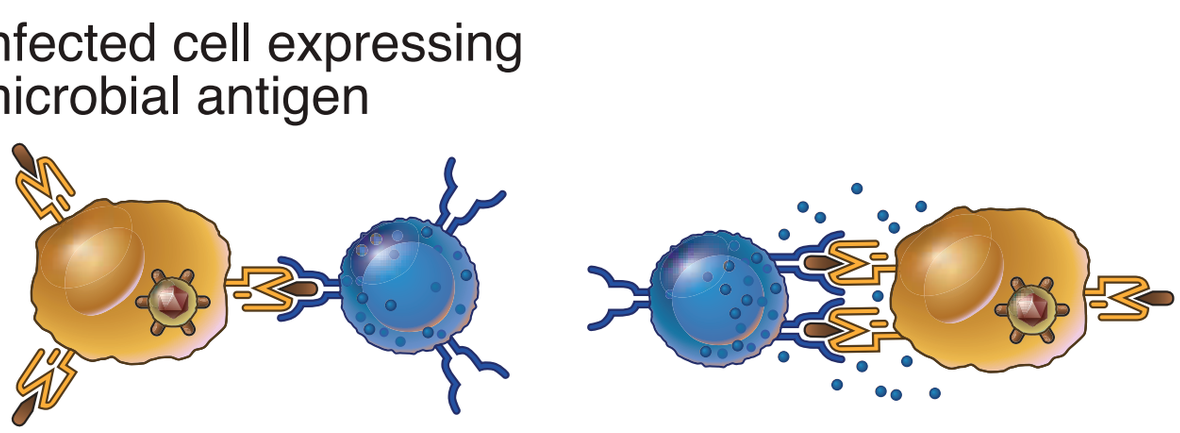
T cells effectors: Helper

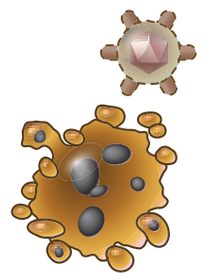


T cells effectors: Cytotoxic

Cytotoxic T lymphocyte (CTL)

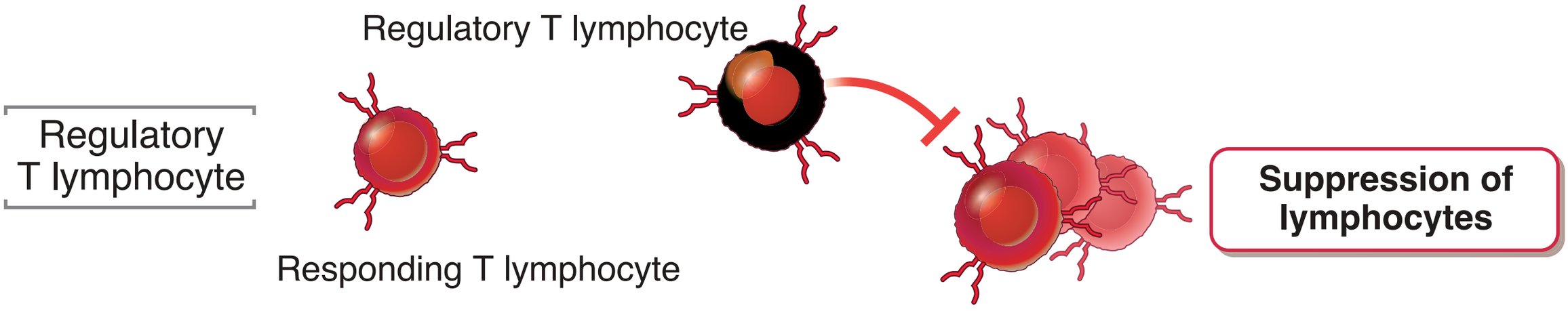
Infected cell expressing microbial antigen





Killing of infected cell

T cells effectors: Regulatory

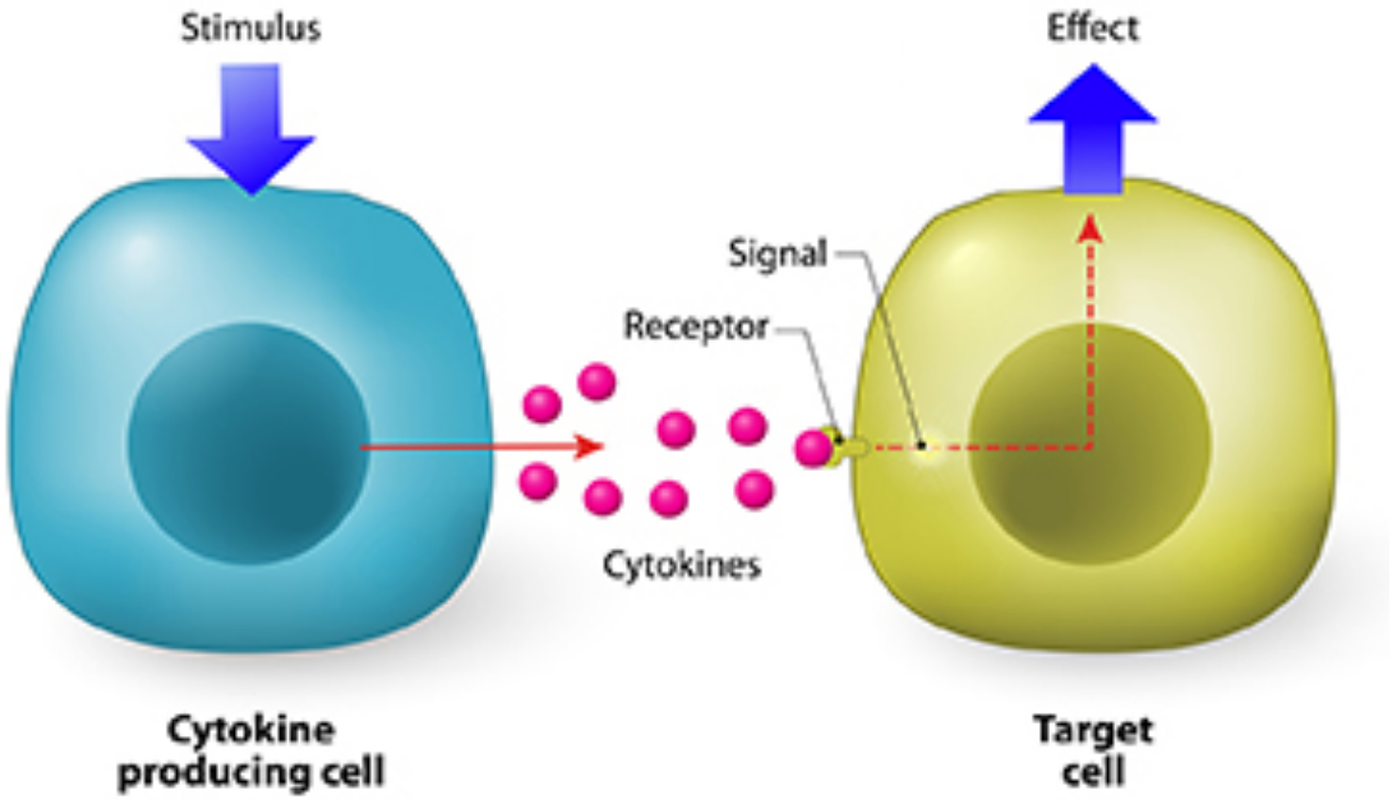


Immune cells need to communicate with each other to cooperate

1. Soluble factors

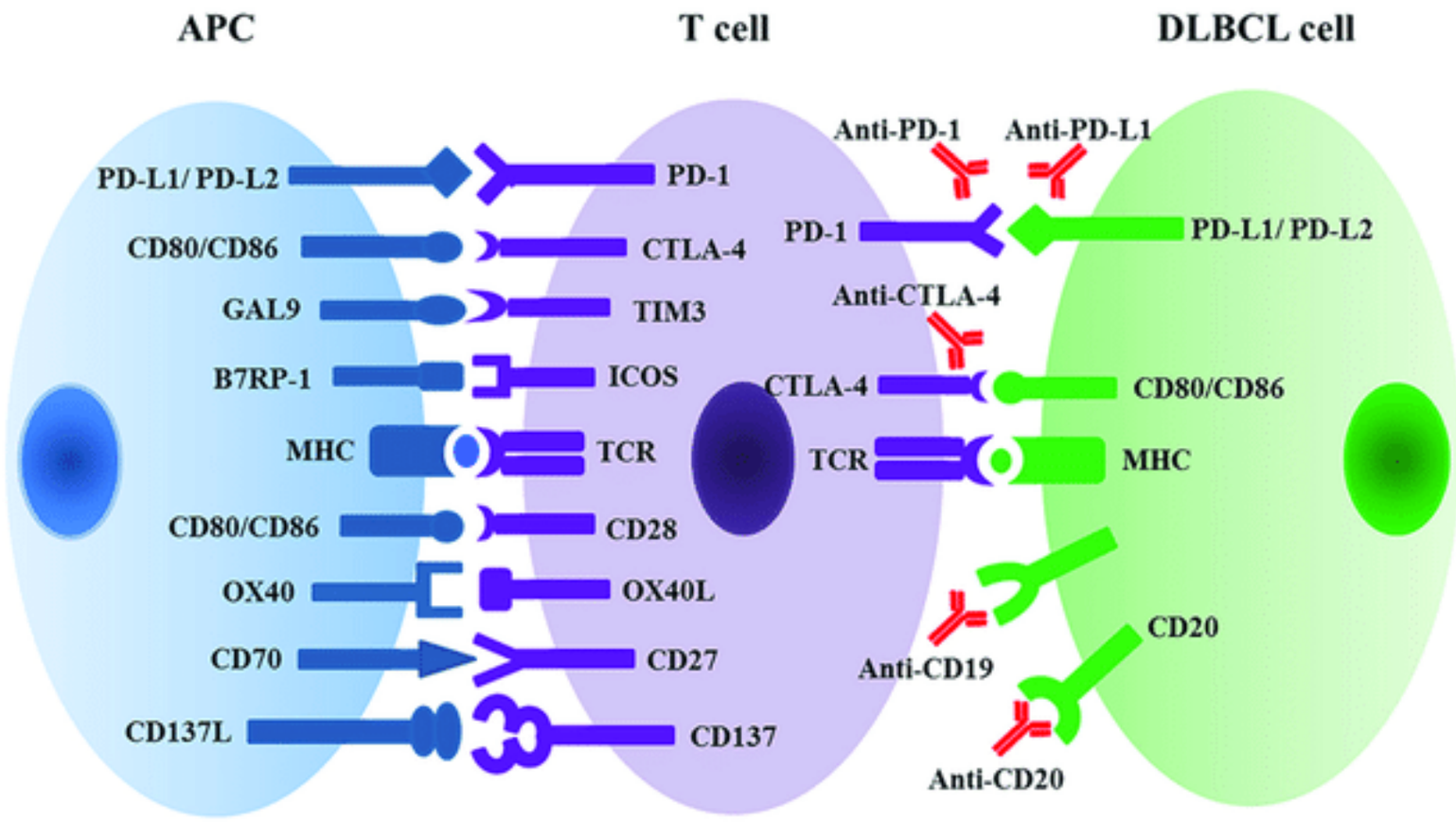
2. Ligand-receptor interactions

Soluble factors



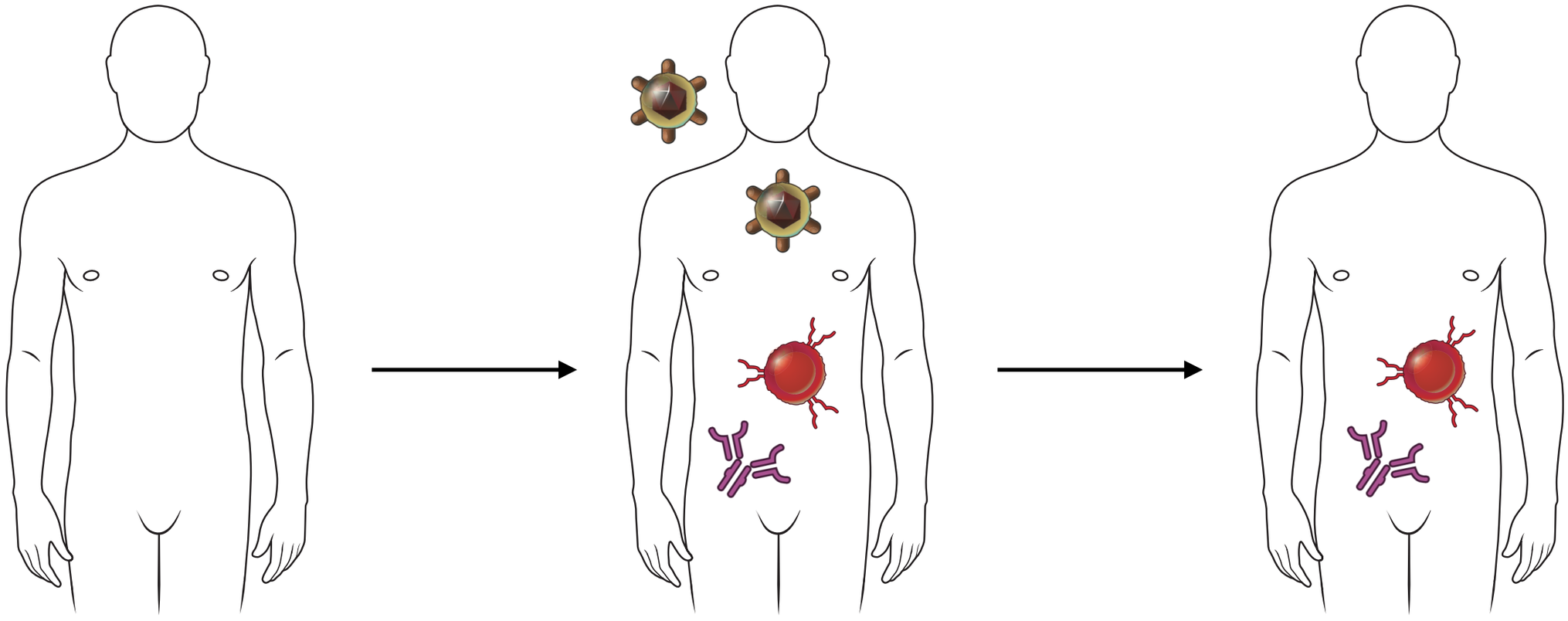
Cytokines and chemokines

Ligand-receptor interactions



Active immunity

Host response to a microbial antigen



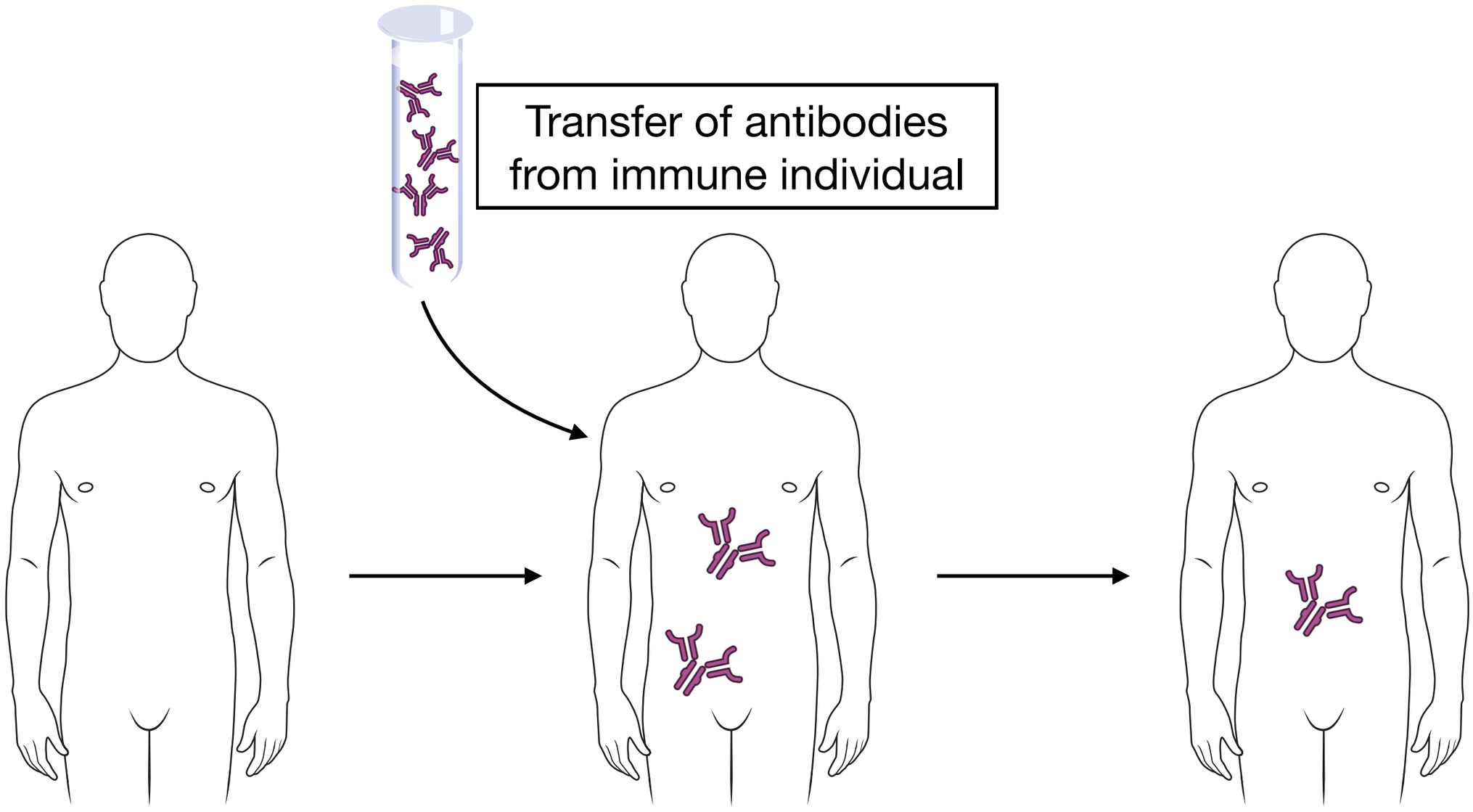
naïve

(has never seen the antigen before)

immune

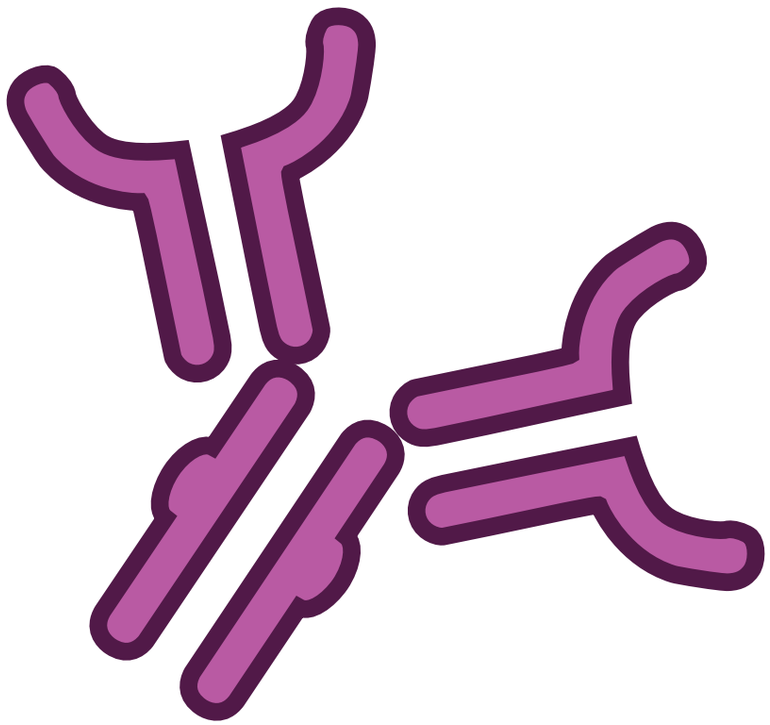
(is protected from subsequent exposure to the same microbe)

Passive immunity



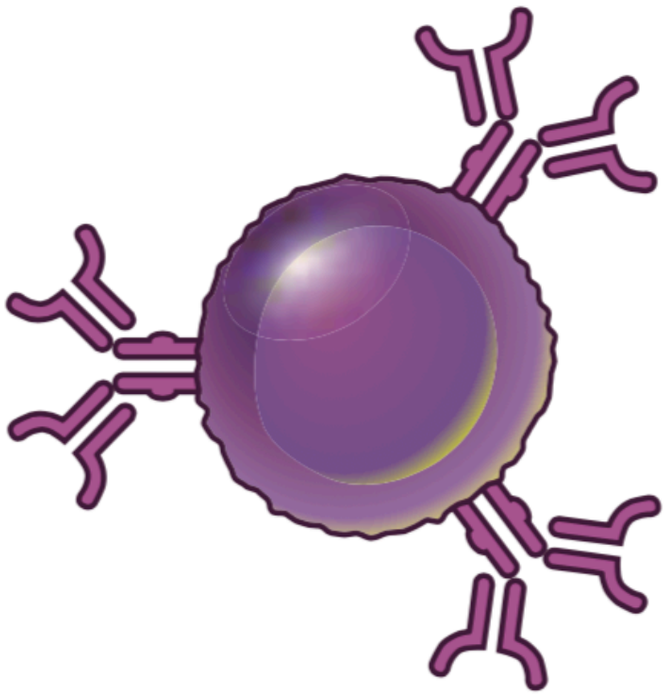
naïve
(has never seen the antigen before)

immune
(is protected from exposure to the same microbe)



How long do antibodies stay in circulation after transfer?

Depends on the isotype, at best (IgG) the half-life is 21 days



How long do memory B cells survive?

Years!

Active vs passive immunity

Active immunity

Immunity is provided by the host's response after microbe exposure

Long-term immunity

Passive immunity

Immunity is provided by the transfer of antibodies, without exposure to the microbe

Instantaneous but short-term immunity

Examples of passive immunity

1. Transfer of maternal antibodies to the fetus
   IgG: last trimester of gestation through the placenta
   IgA: also after birth, through maternal milk

Protection to the newborn for the first few months of life

Examples of passive immunity

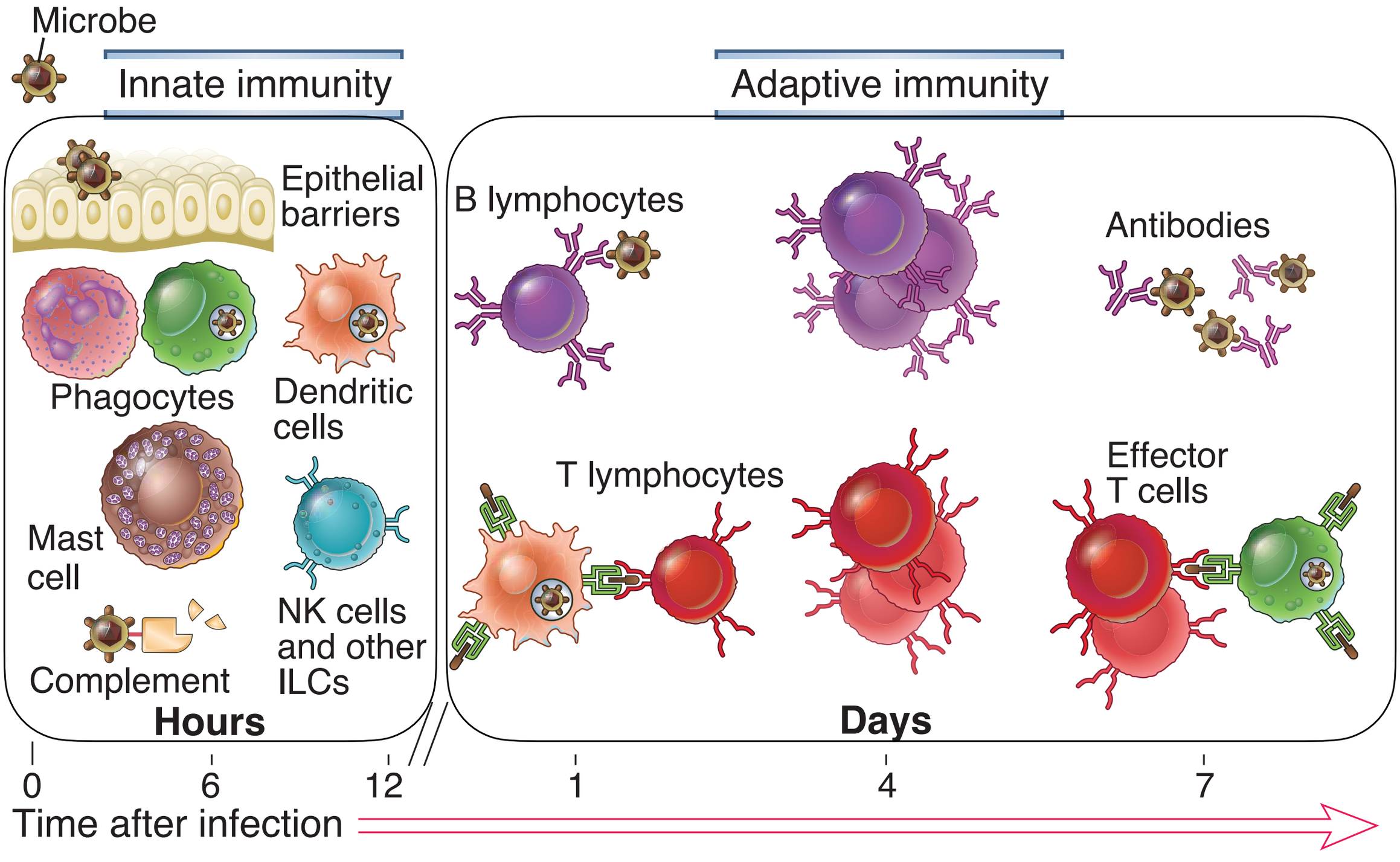
2. Transfer of antibodies as treatment or prophylaxis in individuals at risks

Snake venom

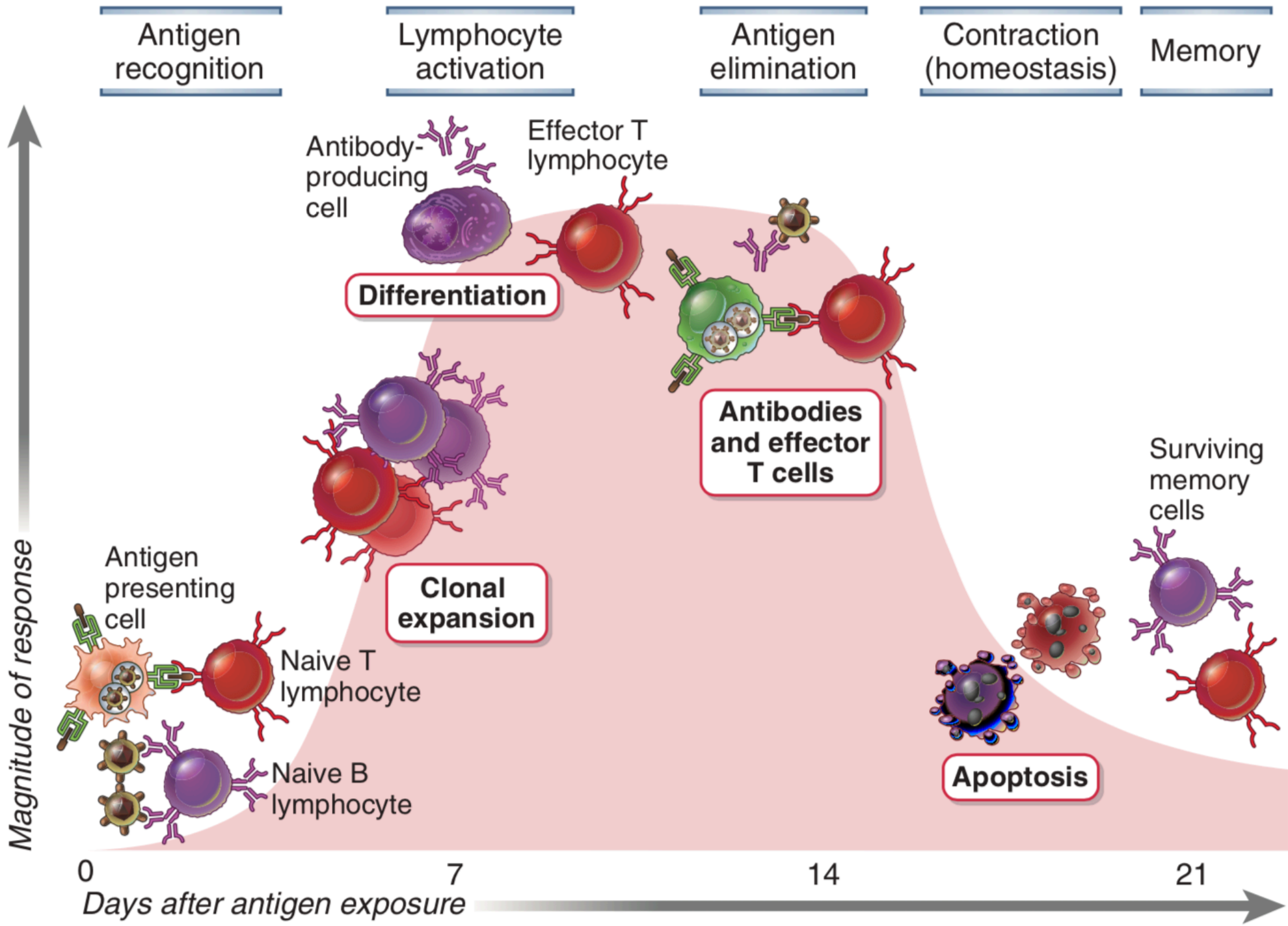
Rabies virus

Tetanus toxin

All in one slide



Steps of an adaptive response



Immunological memory