



IMMUNOLÓGIAI ÉS  
BIOTECHNOLÓGIAI  
INTÉZET



# 3rd practice: Types and functions of lymphoid cells, CD markers

Basic Immunology

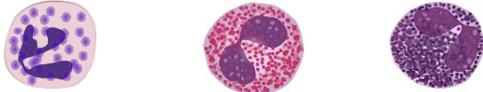
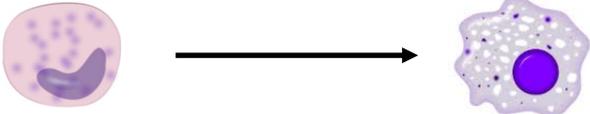
University of Pécs, Clinical Center

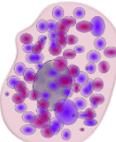
Department of Immunology and Biotechnology

Pécs

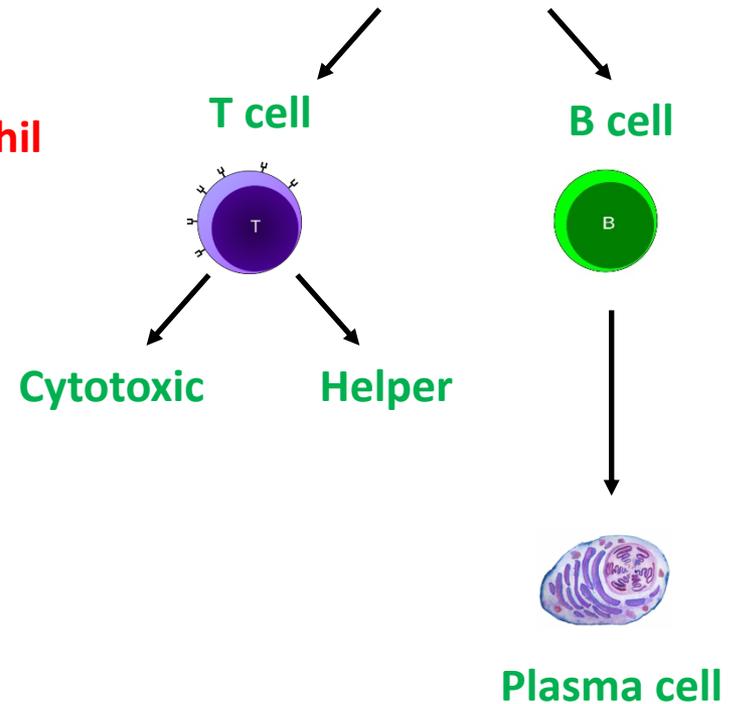
# Cells of the innate and adaptive immune system

## Innate:

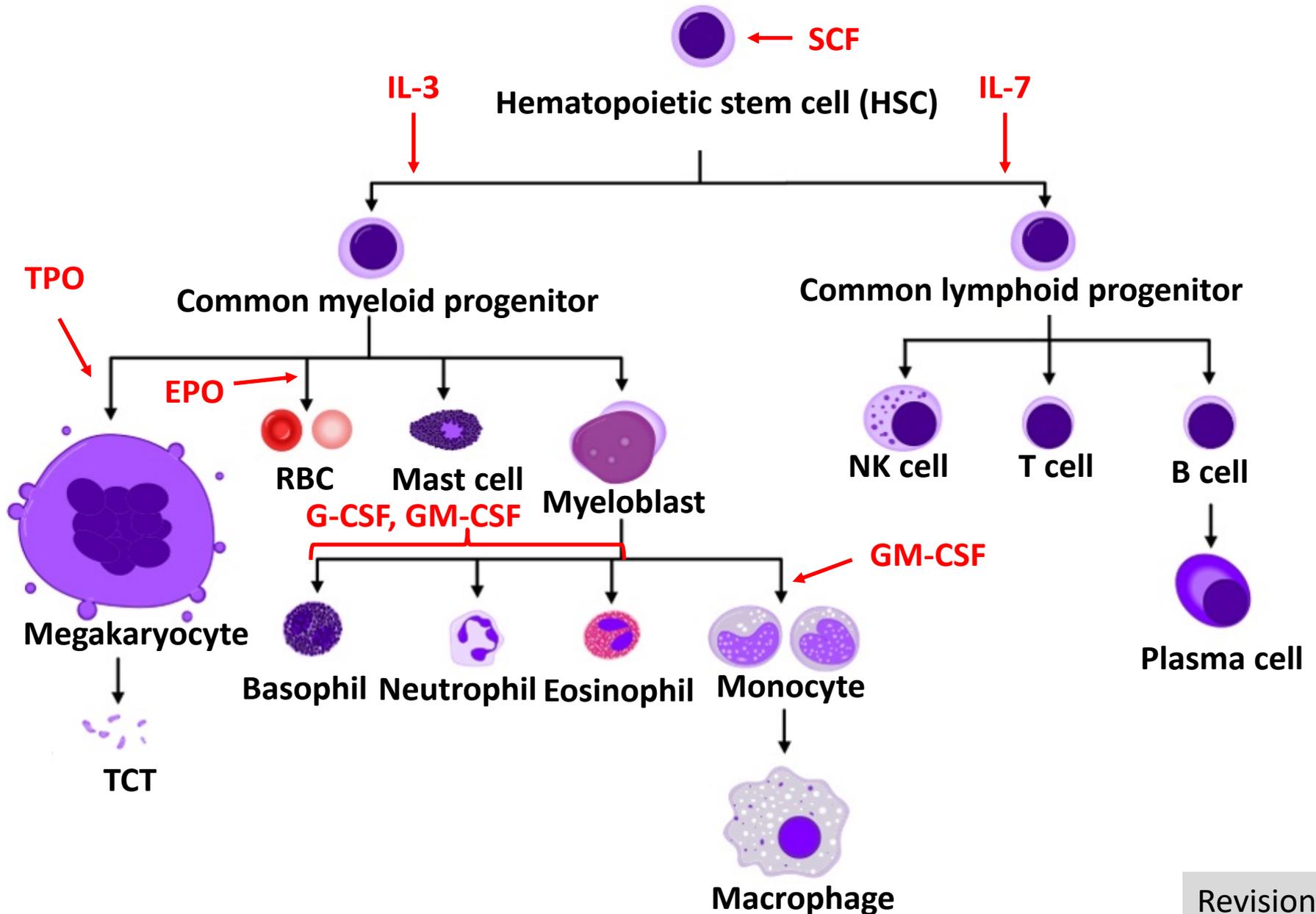
- 1. Granulocytes:**   
neutrophil, eosinophil, basophil
- 2. Monocyte (blood), macrophage (tissues)**  

- 3. Dendritic cell (DC), follicular dendritic cell (FDC)**  

- 4. Mast cell**  

- 5. NK cell (natural killer)**  


## Adaptive:



# Hematopoiesis

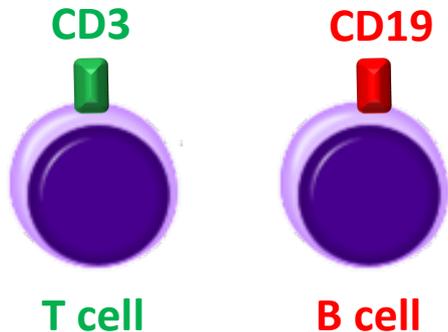


# CD markers



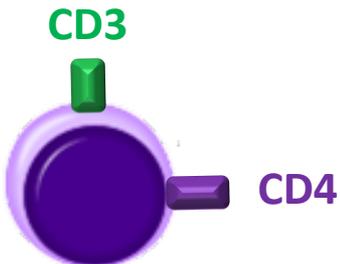
Certain cells (e.g. lymphocytes) cannot always be distinguished based on their morphology.

Different cells can be identified and distinguished by the molecules they express on the cell surface or in the cytoplasm.



**IMMUNOPHENOTYPE:** The characteristic molecular pattern of a cell type determined with the use of antibodies.

Such SURFACE MOLECULES were given a standardized nomenclature:



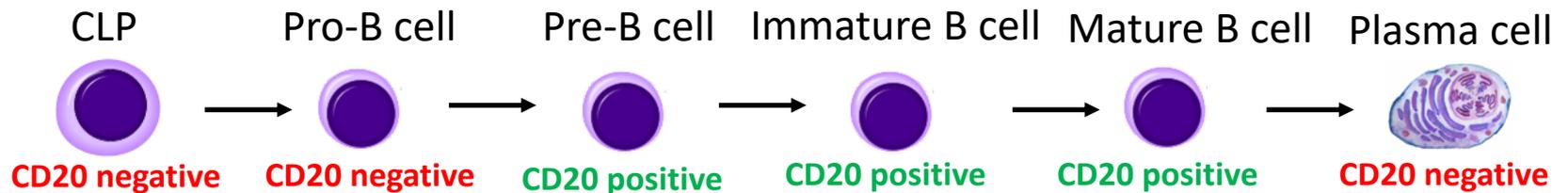
CD = **Cluster of differentiation**, usage: CD+number, e.g.: CD1, CD2, CD3, CD4, etc...

The structure and function of CD marker **varies!**

Example for immunophenotype:  
CD3+/CD4+/CD8- → Helper T cell

# Types of CD markers

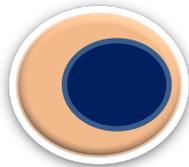
- **Lineage markers:** Molecules expressed exclusively on certain cell lineages.
  - E.g.: CD3 → found on all T cells                      CD19 → found on all B cells
- **Maturation markers:** The immunophenotype might differ in the phases of cell maturation, certain molecules are only expressed on immature cells, others on mature, fully functioning cells, etc.
  - E.g.: CD20 (It is also a lineage marker of B cells, cannot be found on any other cells)



- **Activation markers:** Molecules expressed by activated cells, whereas resting cells either lack them completely or express them at low levels, e.g.:
  - CD25 (The alpha chain of the interleukin-2 receptor, IL-2R $\alpha$ , see later)
  - CD80 and CD86 (B7-1 and B7-2, so-called costimulatory molecules expressed by activated antigen presenting cells, see later)

# Cells of the lymphoid lineage

Innate lymphoid cells (ILC)



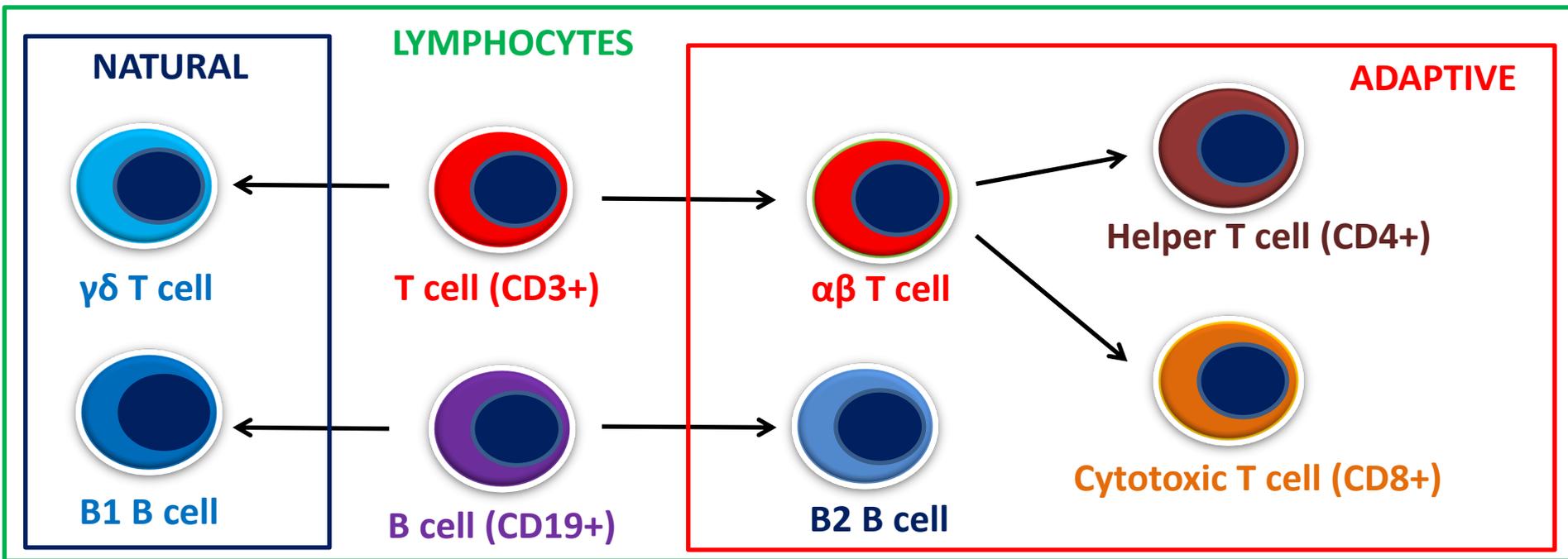
Lymphocyte



There is no difference  
in the morphology!

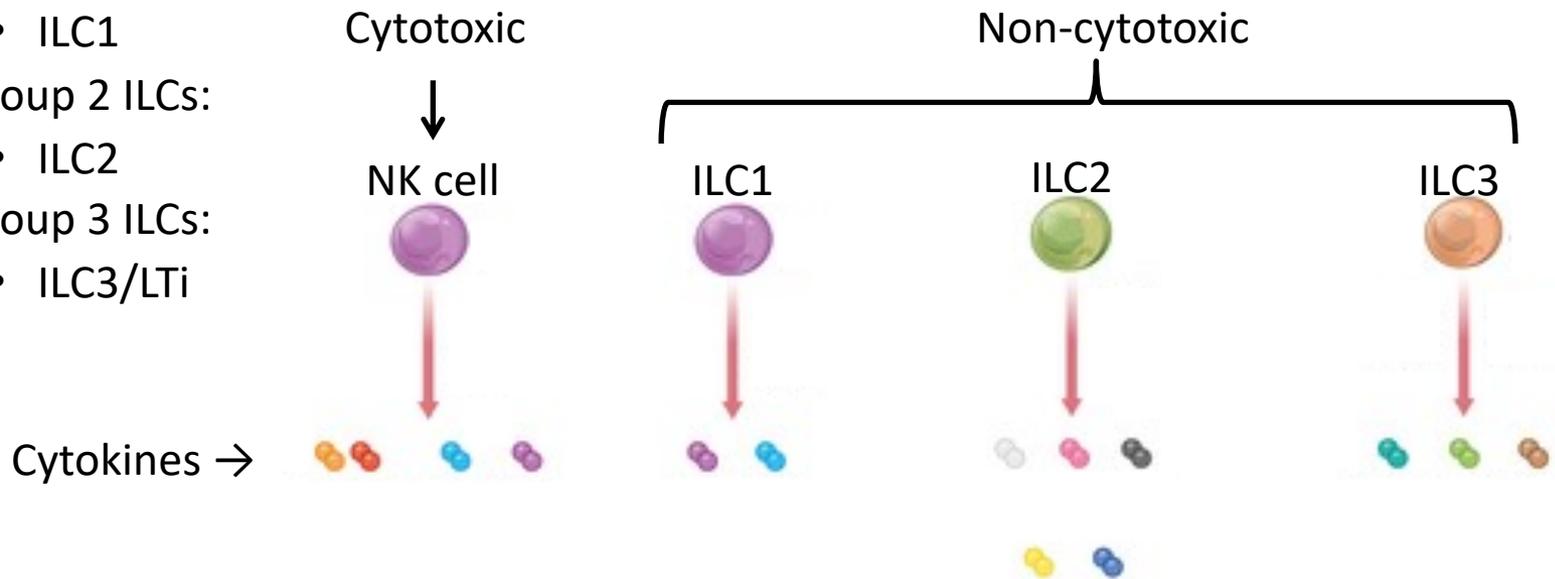
HAVE NO ANTIGEN-RECOGNITION  
RECEPTORS

HAVE ANTIGEN-RECOGNITION  
RECEPTORS

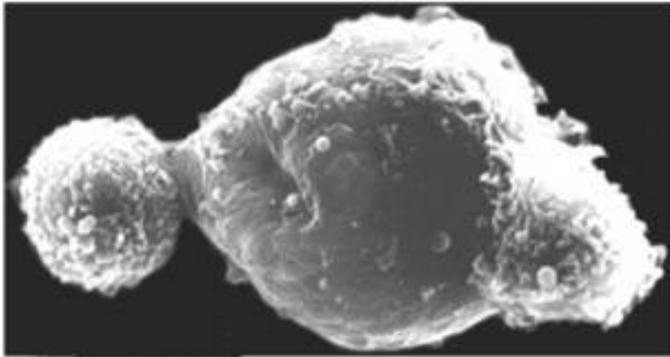


# Innate lymphoid cells (ILC)

- They cannot be distinguished from lymphocytes based on their morphology but unlike adaptive lymphocytes they cannot recognize antigens. → **They have no antigen recognition receptors.**
- They are classified based on the cytokines they produce and the transcription factors that are necessary for their formation. (see in the lectures):
  - Group 1 ILCs:
    - **NK cells**
    - ILC1
  - Group 2 ILCs:
    - ILC2
  - Group 3 ILCs:
    - ILC3/LTi

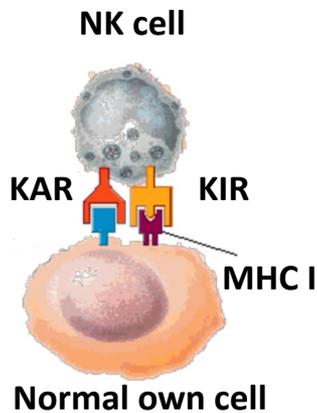


# Natural killer cells (NK cells)

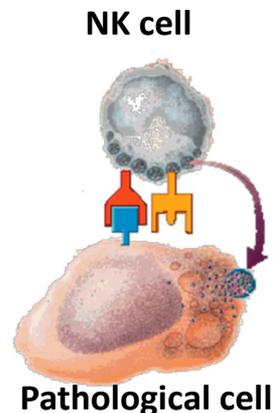


Two NK cells kill a cancerous cell.  
(Scanning electron microscopy image)

Blood lymphoid cells %:	≈ 10
Main function:	Killing cells infected with intracellular pathogens, Killing cancer cells
Recognition:	KAR → killing the target KIR → sparing the target <b>Fc receptor,</b> Complement receptor
Cytotoxicity:	Fas-FasL, Perforin, Granzymes
Produced mediators:	Cytokines
Fc receptor:	FcγR ( <b>binds IgG</b> )
Characteristic marker:	CD56



**CELL IS LEFT ALIVE**



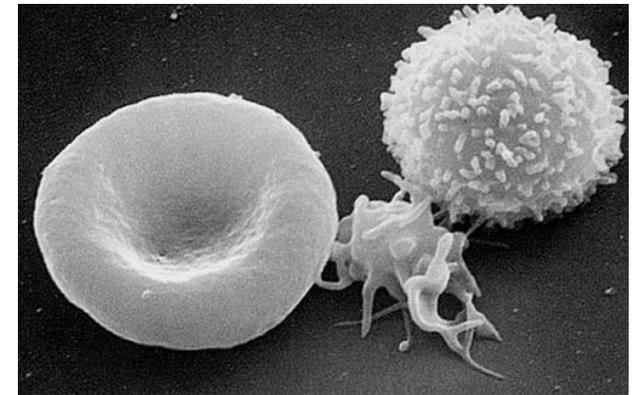
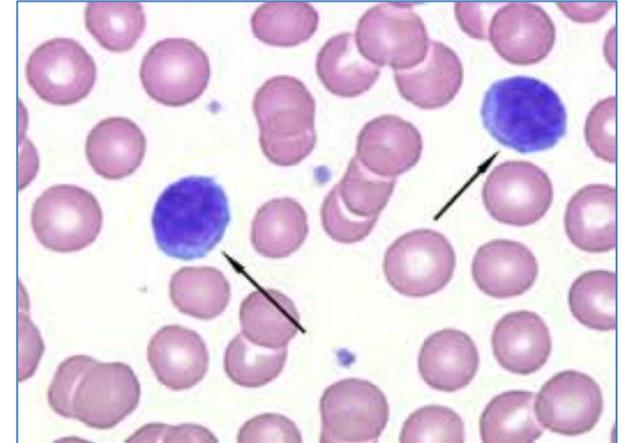
**CELL IS KILLED**

**Red: Only possible after the activation of the adaptive immunity**

# Lymphocytes

Leukocyte %:	25-40*
Main function:	ADAPTIVE IMMUNITY
Recognition	Antigen-specific receptors (TCR, BCR)

\* Including NK cells



A red blood cell, a platelet and a lymphocyte (SEM image)



B cell (CD19+)



Antibody production



Cytotoxic T cell (CD8+)



Direct killing of target cell (infected or cancerous)



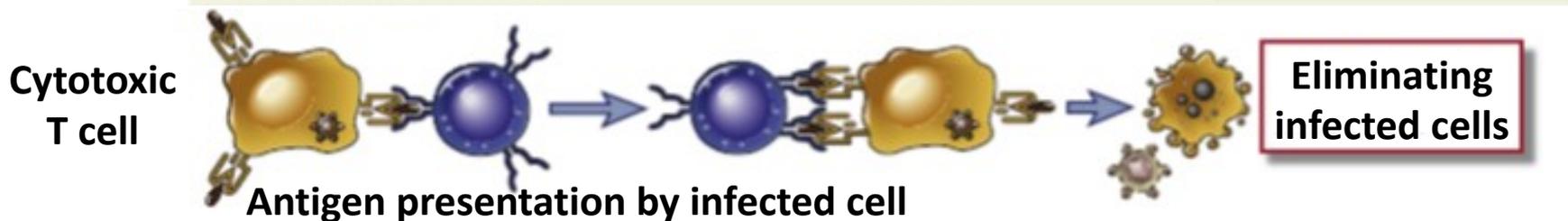
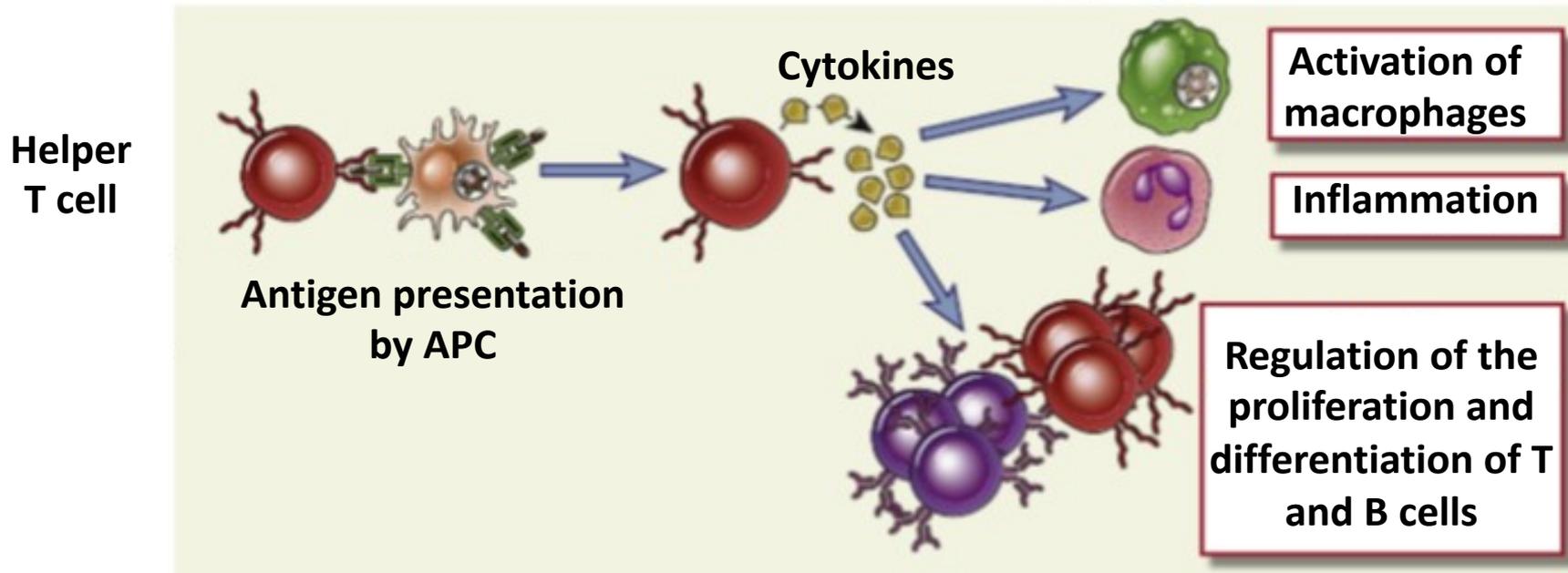
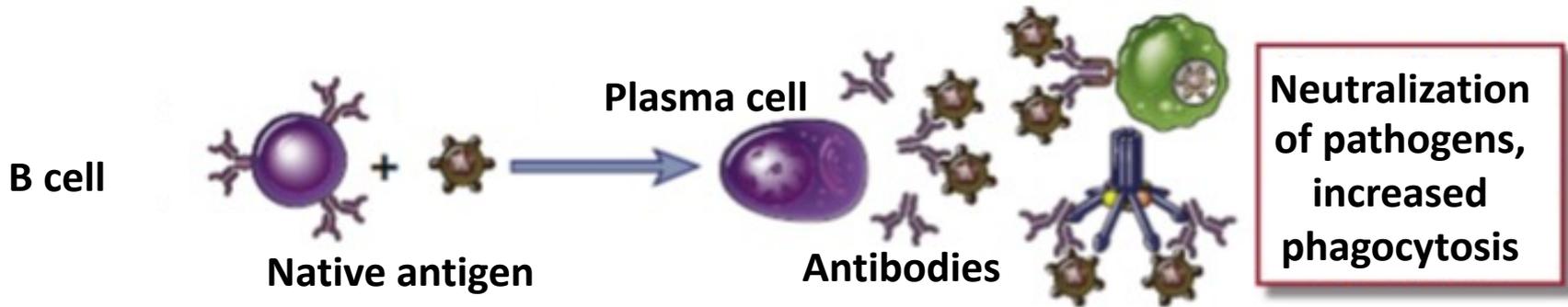
Helper T cell (CD4+)



Regulation of the immune response

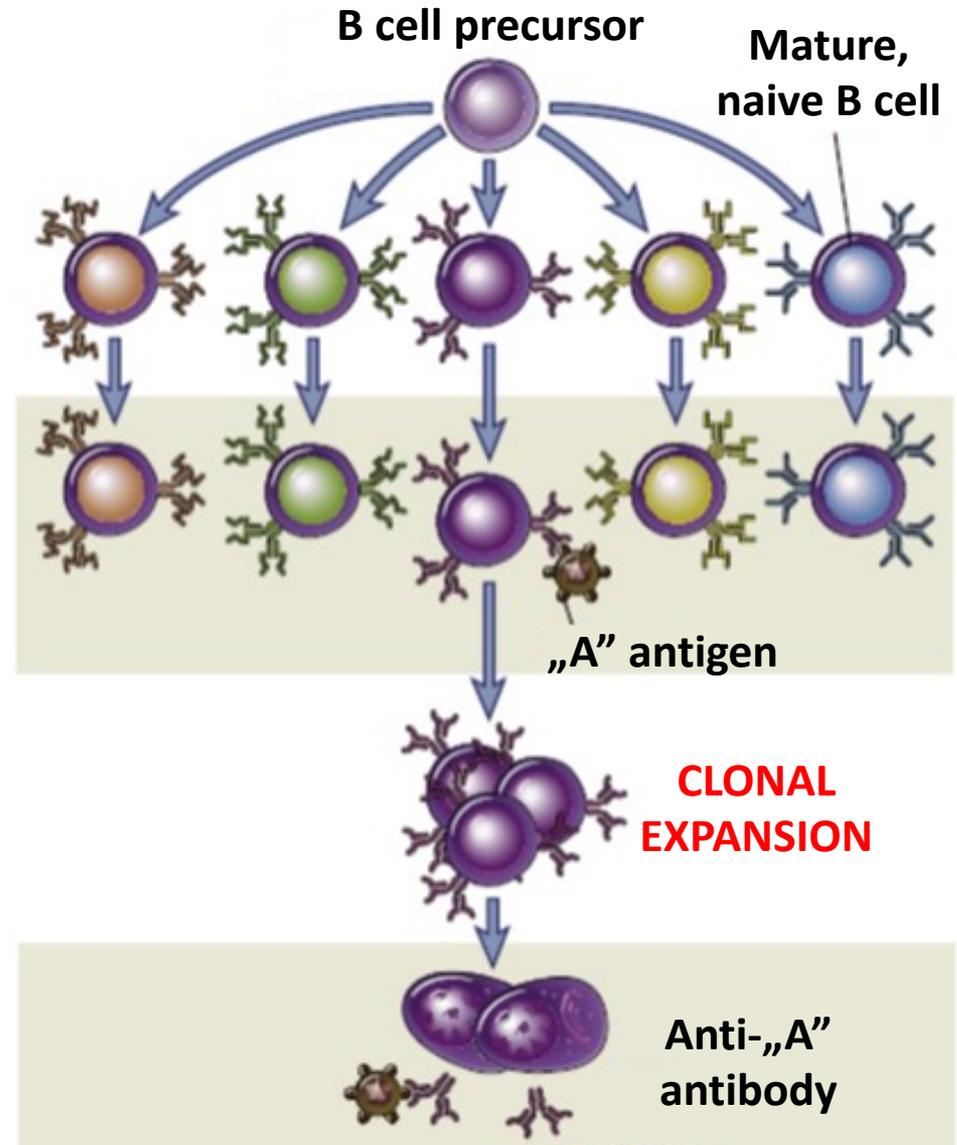
All of the above are done in an ANTIGEN-SPECIFIC manner!

# Main groups of lymphocytes



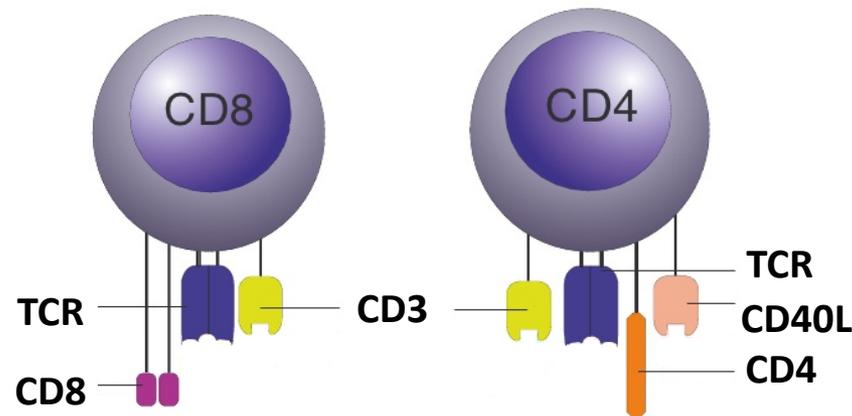
# Clonality

1. Each newly produced lymphocyte expresses a **unique antigen-binding receptor**.
2. **Only those lymphocytes will become activated which recognize an antigen.** These selected cells will proliferate and produce **clones** of themselves with each sister cell having the same antigen-recognition receptor.
3. These clones will differentiate into **effector cells** which will participate in the immune response. (e.g. effector plasma cells produce antibodies)



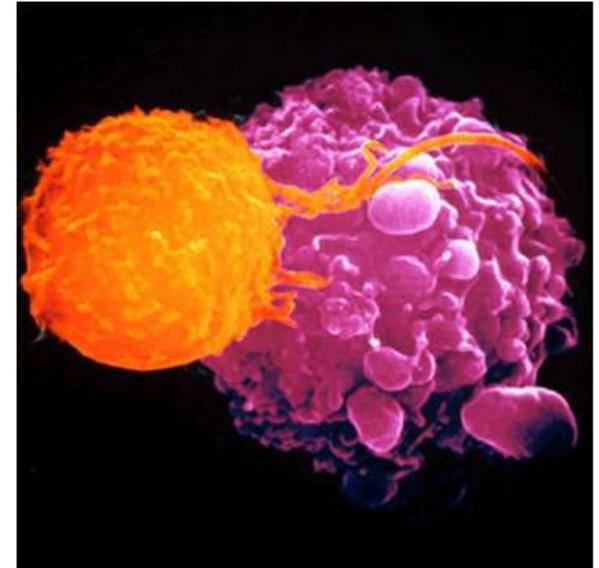
# T cells

<b>Main function:</b>	<b>Antigen-specific killing of target cell (CD8+), Regulation of the immune response through cytokines (CD4+)</b>
<b>Recognition:</b>	<b>Through MHC, antigen-specific TCR</b>
<b>Possible type of TCR:</b>	<b><math>\alpha\beta</math> and <math>\gamma\delta</math></b>
<b>Produced mediators:</b>	<b>Cytokines</b>
<b>Main types of <math>\alpha\beta</math> T cells:</b>	<b>CD4+ Helper CD8+ Cytotoxic</b>
<b>Site of production:</b>	<b>Bone marrow, thymus</b>
<b>Characteristic marker:</b>	<b>CD3 (Makes a complex with the TCR)</b>



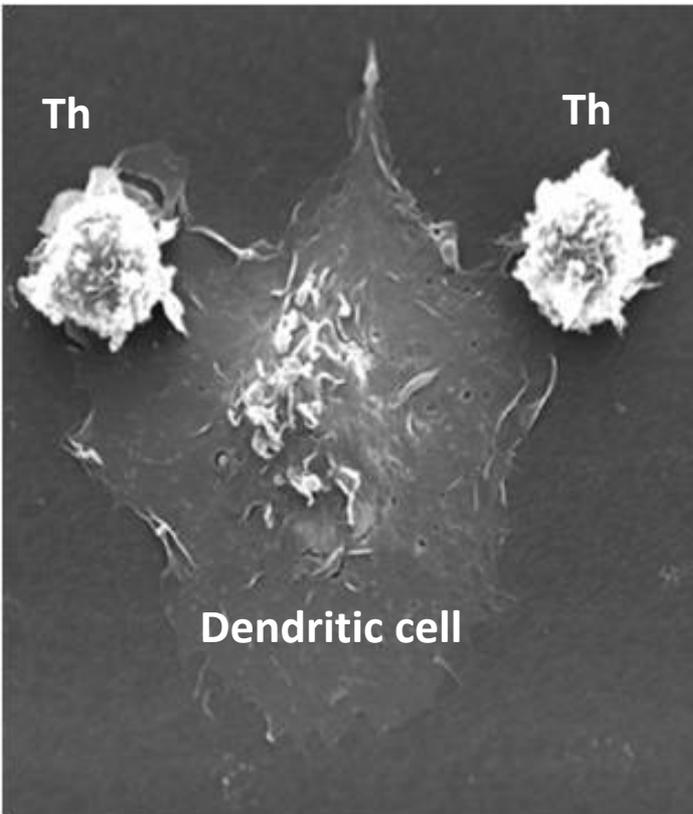
# Cytotoxic T cells (Tc or CTL)

<b>Blood T cells:</b>	<b>1/3</b>
<b>Main function:</b>	<b>Effector cell of the cellular immunity</b>
<b>Recognition:</b>	<b>Through MHC I, antigen-specific TCR</b>
<b>Target cells to kill:</b>	<b>Infected with IC pathogens, Cancerous, Foreign (transplantations!)</b>
<b>Recognized antigens:</b>	<b>Endogenous (from the cytoplasm of the target cell)</b>
<b>Cytotoxicity:</b>	<b>Fas-FasL, Perforin, Granzyme</b>
<b>Immunophenotype:</b>	<b>CD3+/CD8+/CD4-</b>



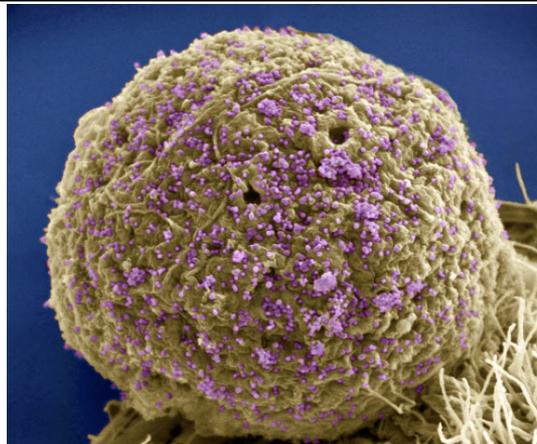
A cytotoxic T cell kills a cancer cell. (SEM image)

# Helper T cells (Th)



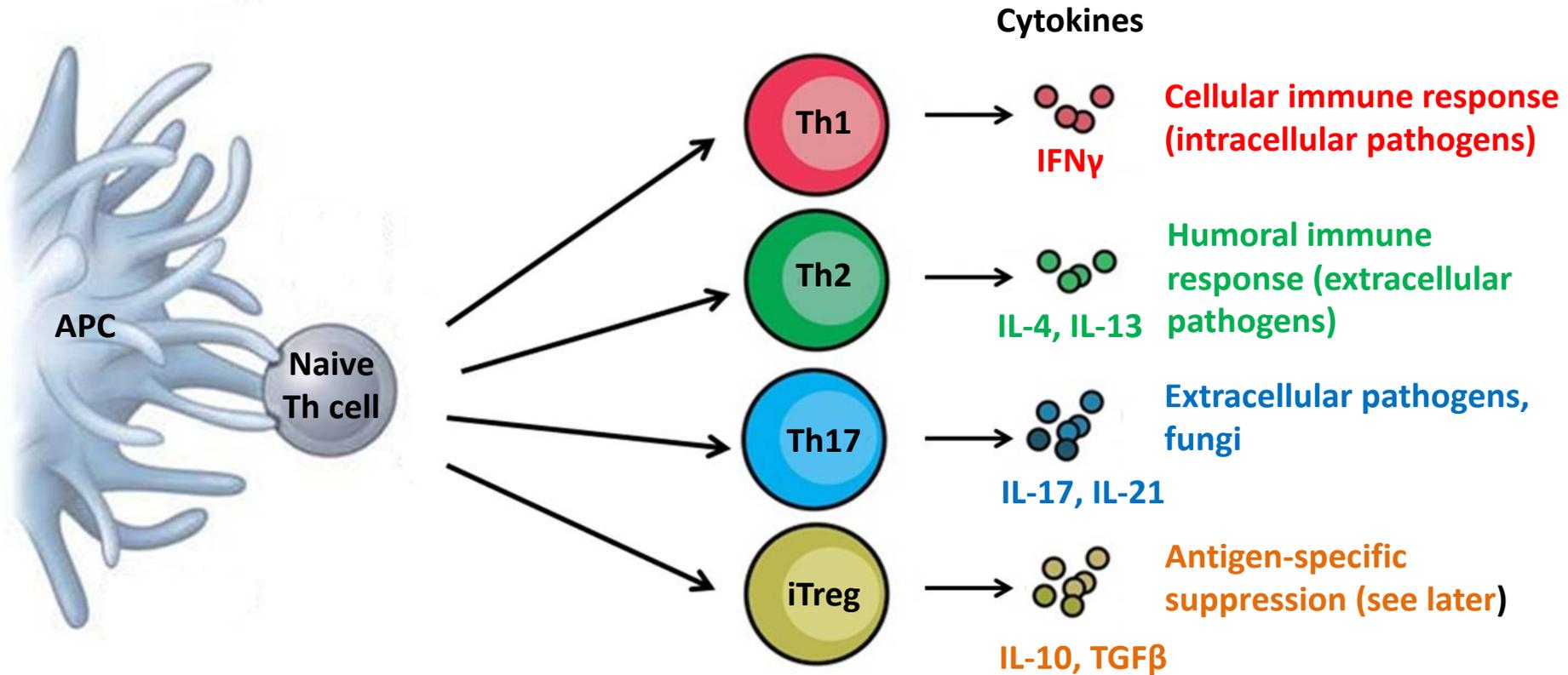
Two helper T cells attached to a dendritic cell. (Scanning electron microscopy image)

<b>Blood T cells:</b>	<b>1/3</b>
<b>Main function:</b>	<b>Regulation of immune response</b>
<b>Recognition:</b>	<b>Through MHC II, antigen-specific TCR</b>
<b>Recognized antigens:</b>	<b>Exogenous (degraded in phagolysosomes)</b>
<b>Immunophenotype:</b>	<b>CD3+/CD4+/CD8-</b>
<b>Role in diseases:</b>	<b>Autoimmunity, HIV infection</b>



Yellowish-brown: Th cell  
purple: **HIV** virions  
(SEM image)

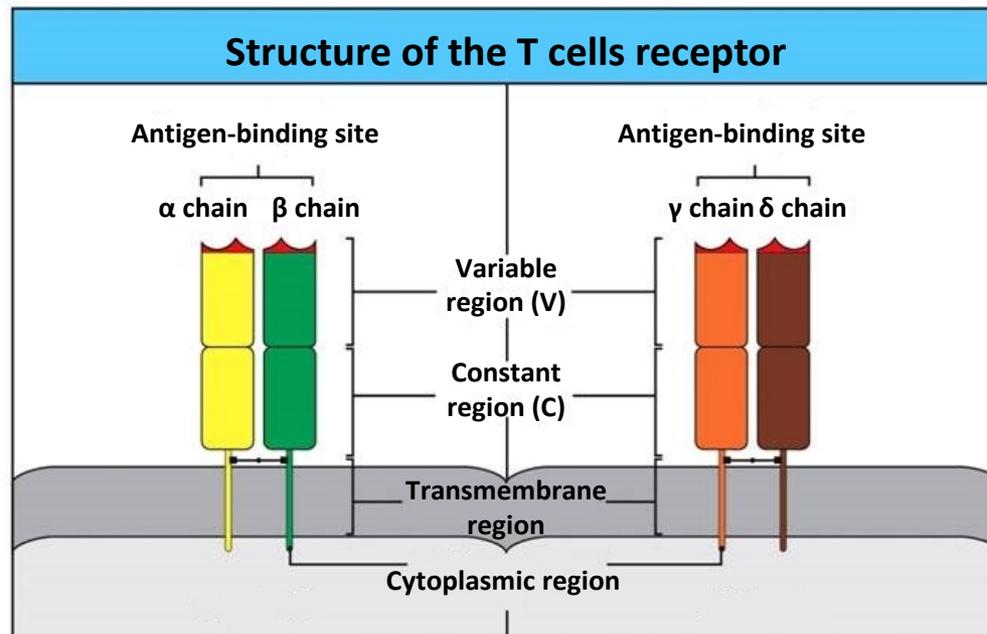
# Main subtypes of Th cells



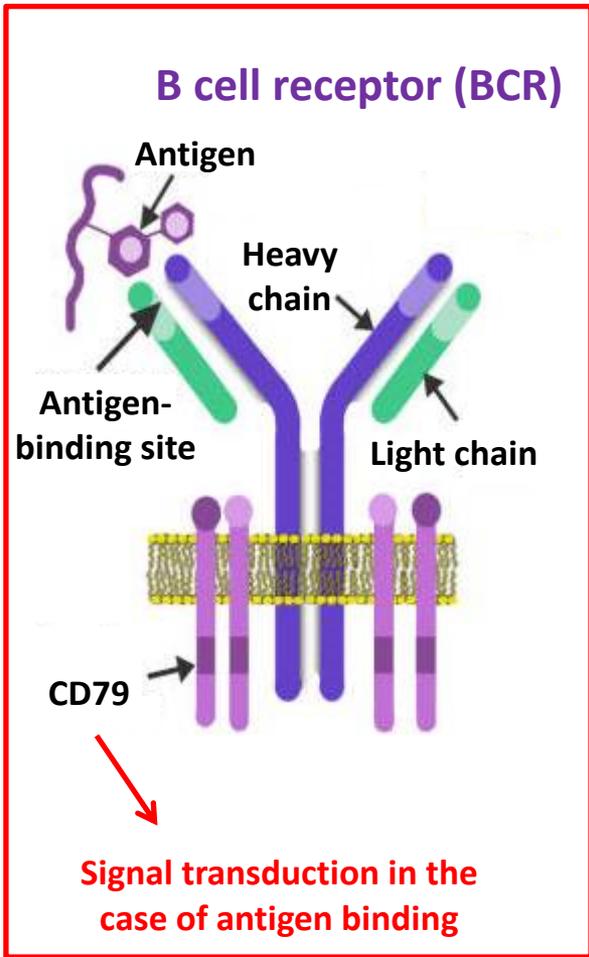
- Th17 cells play an important role in **inflammatory disorders**. (see later)
- **Regulatory T cells** (Treg): They can inhibit other immune cells (**suppression**, see later), their immunophenotype is: **CD4<sup>+</sup>/CD25<sup>+</sup>/Foxp3<sup>+</sup>**

# $\gamma\delta$ T cells

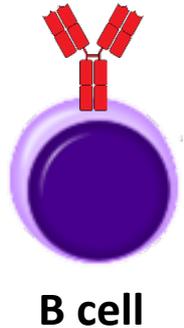
- They express TCRs that consist of  $\gamma$  and  $\delta$  chains.
- They are **innate-like lymphocytes**, they are not as well-characterized as  $\alpha\beta$  T cells.<sup>[17.]</sup>
- They are mainly found in the **skin** and the **mucosa**; usually as intraepithelial lymphocytes (IELs). They can be detected in the peripheral blood in low numbers.
- They participate in the early phases of the immune response against invasive pathogens.
- Their antigen-recognition is **MHC-independent**.
- They mainly recognize **lipid antigens**.



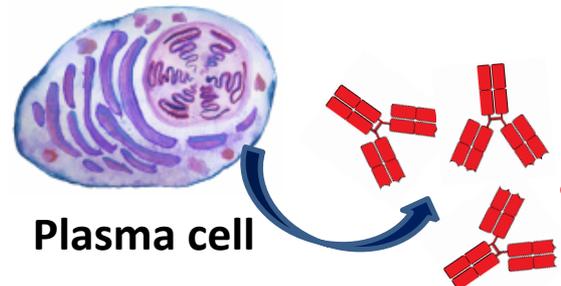
# B cells



<b>Blood lymphoid cells %:</b>	<b>10-15</b>
<b>Main functions:</b>	<b>Antibody production, Antigen presentation</b>
<b>Recognition:</b>	<b>Native antigens with antigen-specific BCR</b>
<b>Main types:</b>	<b>B1 and B2</b>
<b>Site of production:</b>	<b>Bone marrow</b>
<b>Characteristic marker:</b>	<b>CD19 (makes a complex with BCR)</b>



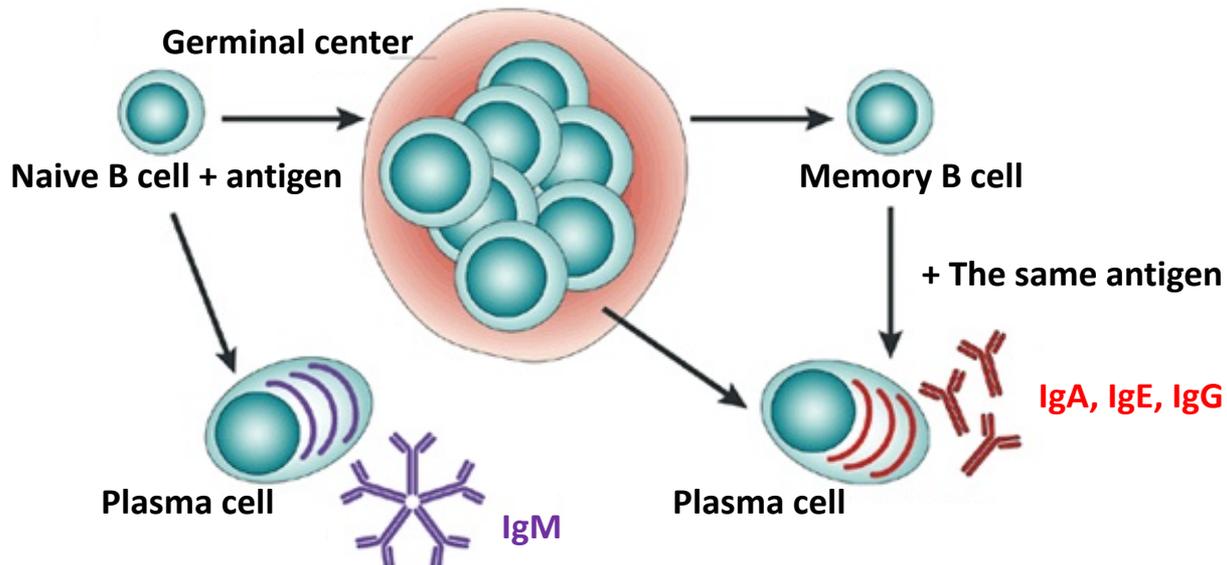
**BCR = surface immunoglobulin**



**Antibody against the same antigen recognized by the BCR (secreted immunoglobulin)**

# B2 B cells

<b>Found in:</b>	<b>Follicles in secondary lymphoid organs, blood</b>
<b>Main functions:</b>	<b>Antibody production, Antigen presentation</b>
<b>Recognition:</b>	<b>Native antigens with antigen-specific BCR</b>
<b>Site of primary maturation:</b>	<b>Bone marrow</b>
<b>Site of antigen-dependent maturation:</b>	<b>Germinal center</b>
<b>Produced antibodies:</b>	<b>Monospecific, high-affinity, with varying isotype</b>



# B1 B cells

- Only few can be found in the peripheral blood.
- **They are innate-like lymphocytes**, most of them reside on serous membranes. (e.g. peritoneum, pleura, pericardium)
- They are first produced in the fetus and later undergo self-renewal in the periphery, not in the bone marrow, as B2 cells do.
- They produce **natural autoantibodies** that can bind that can bind evolutionarily **conserved self-antigens**.
- They were first described as CD5+ B cells in mice.
- The immunophenotype of the human B1 cells is still controversial.

	B1 cells	B2 cells
Spontaneous antibody production	Significant	Minimal
Isotype of produced antibodies	<b>IgM</b>	IgM/IgG/IgA/IgE
Affinity and specificity of antibodies	<b>Polyspecific with low affinity</b>	Monospecific with high affinity
Affinity maturation, memory	No	Yes

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