Introduction to Immunology

Medical studies in English

Jan 7th 2020.

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Immunology

- Latin ***immunitas*** - exemption from civic duties and legal prosecution offered to Roman senators

- **Immunology** - experimental science in which explanation of immunological phenomena are based on **experimental** observations


History of Immunology

First knowledge

- China (10th century): vaccination with powdered scabs from cows infected with cowpox
- 16th century Girolamo Fracastoro proposed the theory about infectious diseases in a book

De Contagione et Contagiosis Morbis (1546)

History of vaccination

- Cowpox protect from smallpox.
- Lat. *vaccinus* = „vacca” = cow
- China and India (15th and 17th century): vaccination with powdered scabs from people infected with smallpox
- Lady **Mary Wortley Montagu** in 1711. described vaccination in Otoman empire
- **EDWARD JENNER, 1796. –** made first experiments
- **1979.** WHO erradication of smallpox

The Cow-Pock — or — the Wonderful Effects of the New Inoculation! — Vide. the Publications of y^e Anti-Vaccine Society.

Jenner experiment

Sarah Nelmes, milkmaid

↓

James Phipps, 8 years old, gardner's son

↓

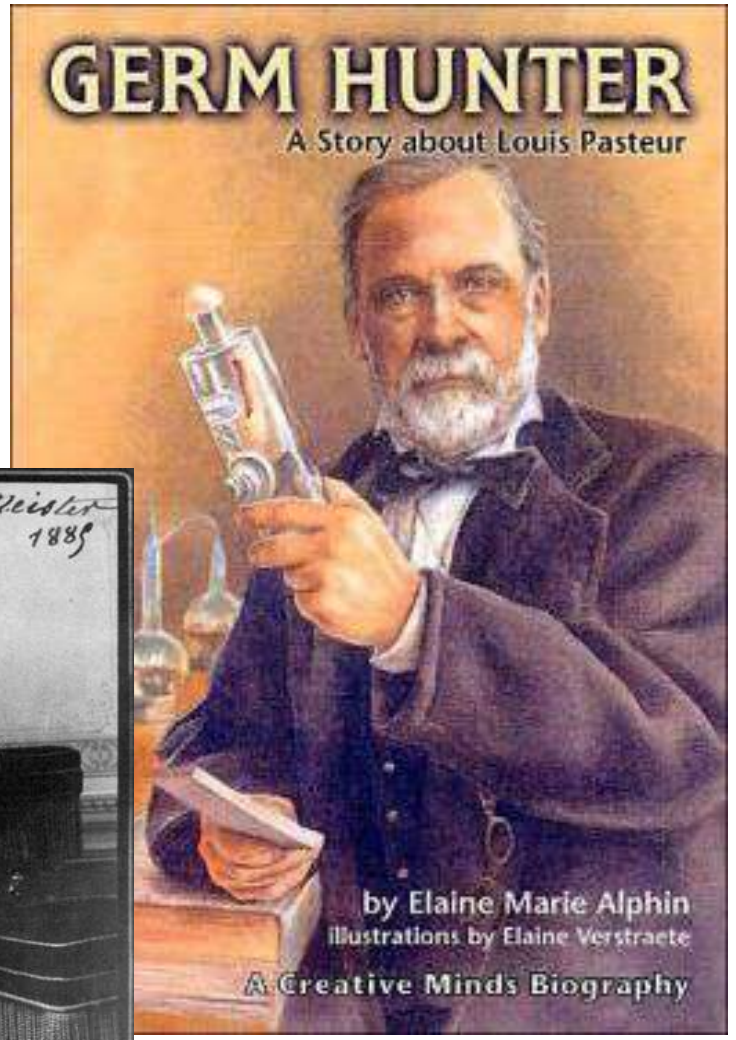
Diseased person →

↓

Cowpox – protection from smallpox

History of vaccination

Louis Pasteur,
1885.
- first rabies and antrax vaccine



Joseph Meister (9)

A bit more of history

R. Koch, 1880. Infectious diseases caused by microorganisms

L. Paster, 1885. rabies and cholera vaccination

E. Methchnikoff, 1883. described phagocytosis

E. von Behring i S. Kitasato, 1890. isolated antibodies (diphteria patients)

P. Erlich, 1900. – theory of antibodies (antiserum) and function of mastocites

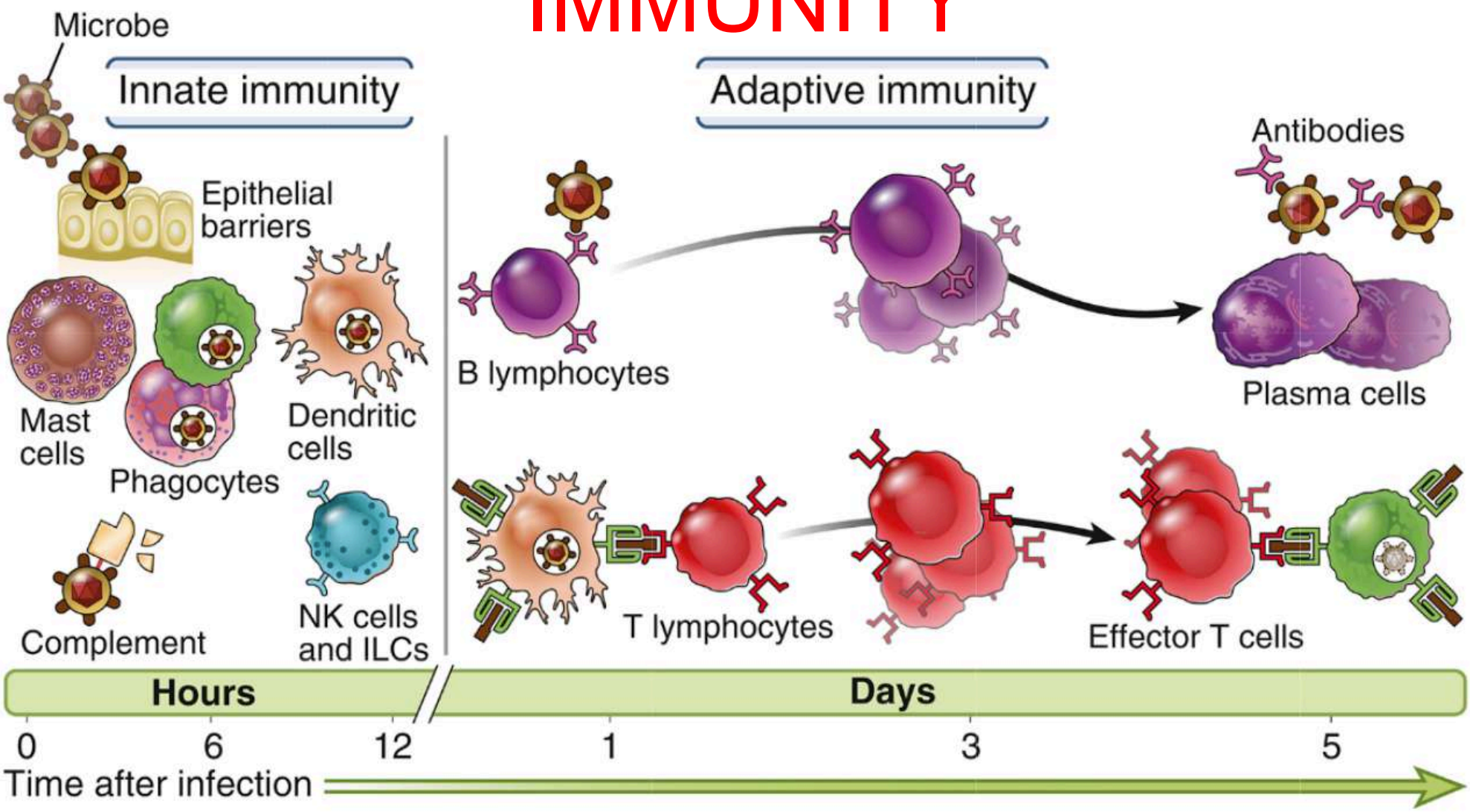
Disease	Maximum number of cases (year)	Number of cases in 2014	Percent change
Diphtheria	206,939 (1921)	0	–100
Measles	894,134 (1941)	669	–99.93
Mumps	152,209 (1968)	737	–99.51
Pertussis	265,269 (1934)	10,631	–95.99
Polio (paralytic)	21,269 (1952)	0	–100
Rubella	57,686 (1969)	2	–99.99
Tetanus	1560 (1923)	8	–99.48
Hemophilus influenza type B	~20,000 (1984)	34	–99.83
Hepatitis B	26,611 (1985)	1,098	–95.87

Role of the immune system	Implications
Defense against infections	Deficient immunity results in increased susceptibility to infections; exemplified by AIDS Vaccination boosts immune defenses and protects against infections
Defense against tumors	Potential for immunotherapy of cancer
The immune system can injure cells and induce pathologic inflammation	Immune responses are the cause of allergic, autoimmune, and other inflammatory diseases
The immune system recognizes and responds to tissue grafts and newly introduced proteins	Immune responses are barriers to transplantation and gene therapy

IMMUNE SYSTEM

- INNATE – ADAPTIVE
  nonspecific – specific
- HUMORAL – CELL MEDIATED
- ACTIVE – PASSIVE
- PRIMARY – SECONDARY

INNATE vs. ADAPTIVE IMMUNITY



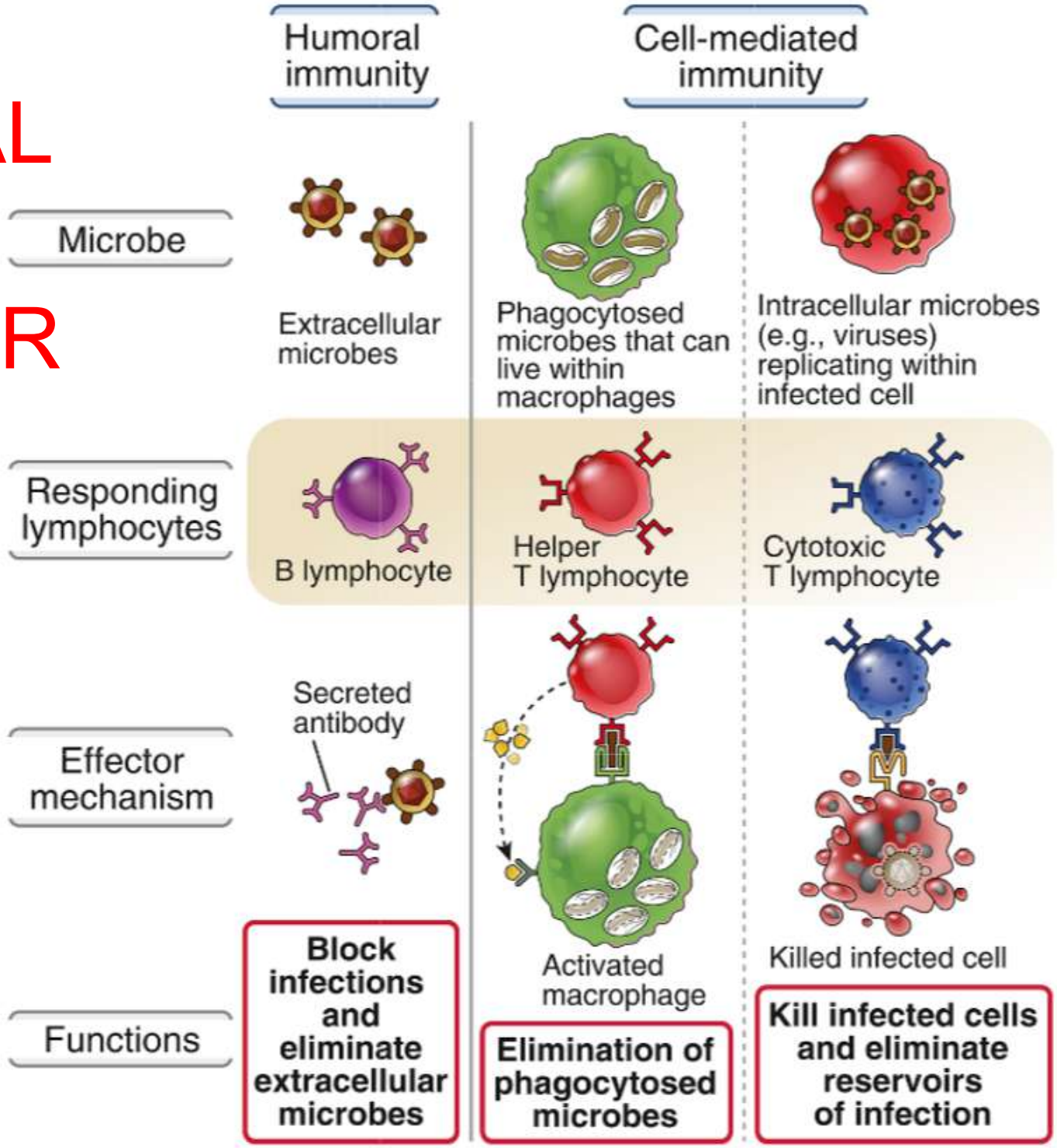
INNATE vs. ADAPTIVE

	Innate	Adaptive
Characteristics		
Specificity	For molecules shared by groups of related microbes and molecules produced by damaged host cells	For microbial and nonmicrobial antigens
Diversity	Limited; germline encoded	Very large; receptors are produced by somatic recombination of gene segments
Memory	None	Yes
Nonreactivity to self	Yes	Yes
Components		
Cellular and chemical barriers	Skin, mucosal epithelia; antimicrobial molecules	Lymphocytes in epithelia; antibodies secreted at epithelial surfaces
Blood proteins	Complement, others	Antibodies
Cells	Phagocytes (macrophages, neutrophils), natural killer cells, innate lymphoid cells	Lymphocytes

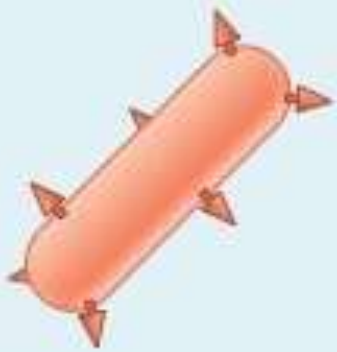
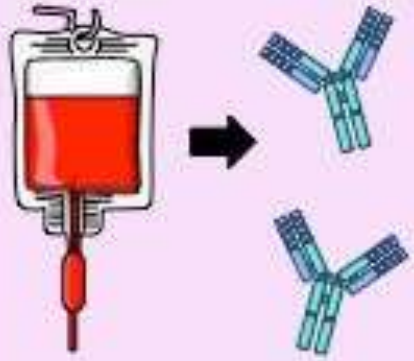
ADAPTIVE IMMUNITY

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

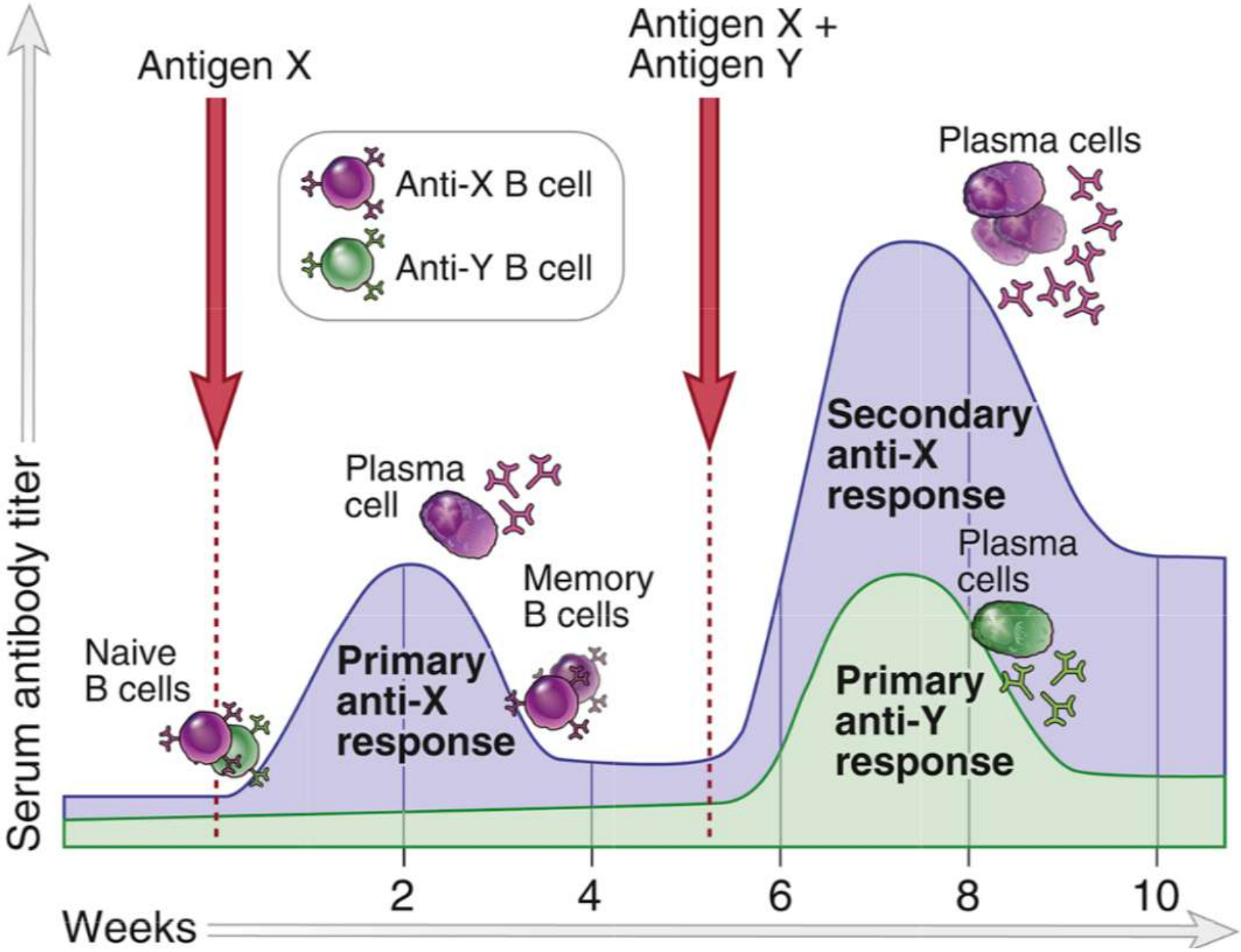
HUMORAL vs. CELLULAR



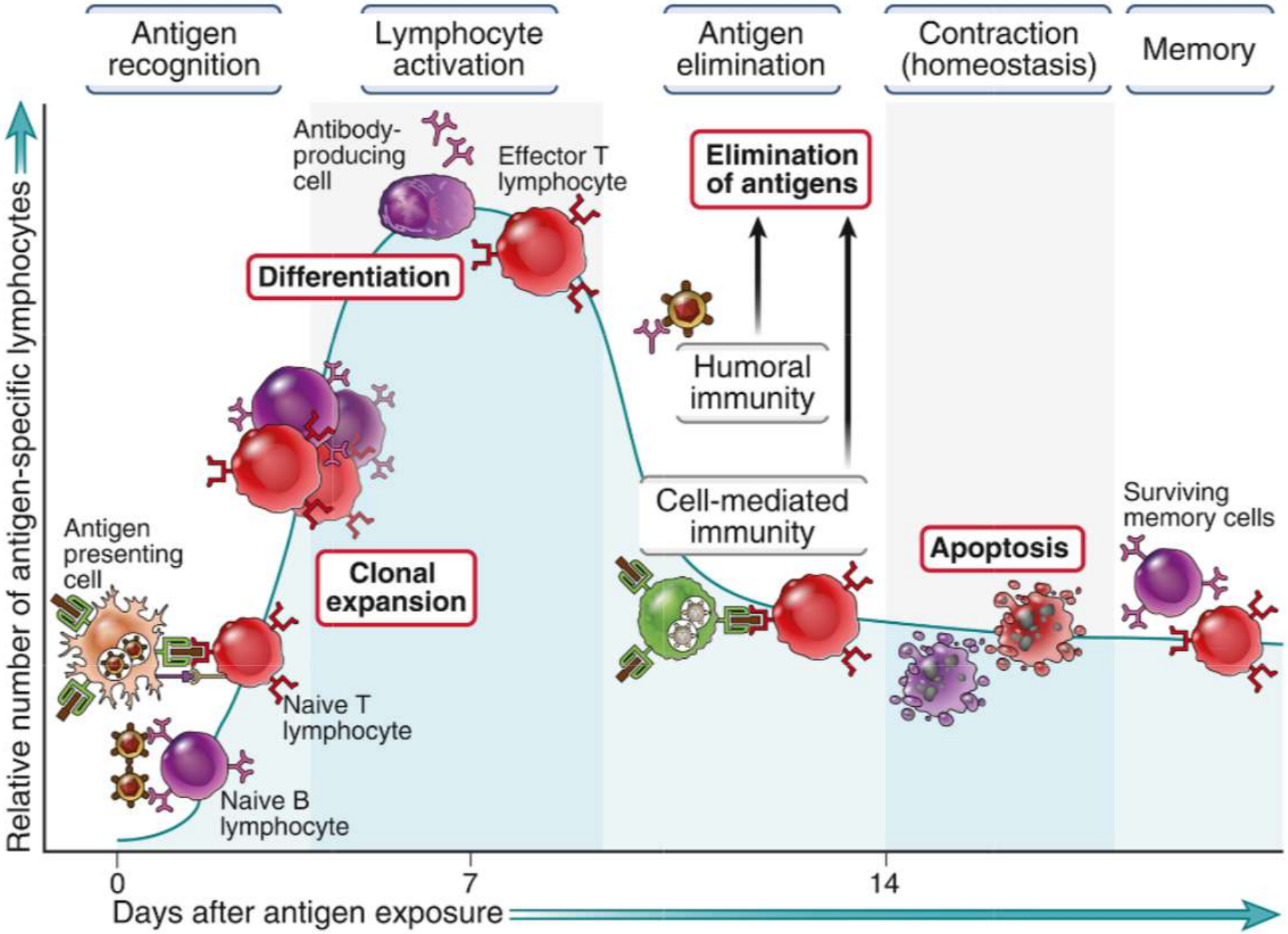
ACTIVE vs. PASSIVE

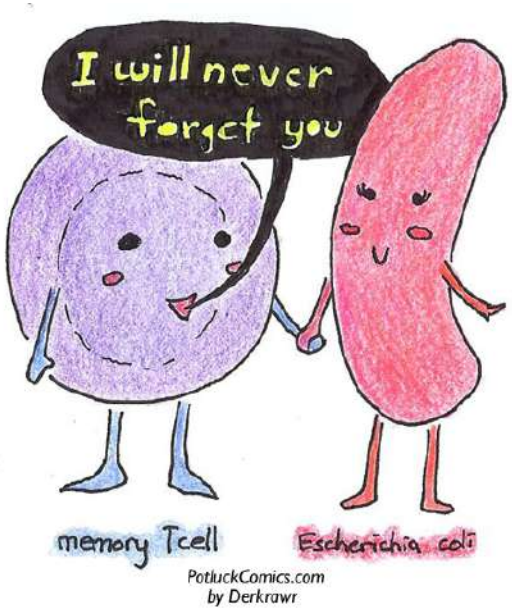
ACTIVE IMMUNITY		PASSIVE IMMUNITY	
Natural	**Artificial**	**Natural**	**Artificial**
			
Infection	Vaccination	Maternal antibodies	Monoclonal antibodies

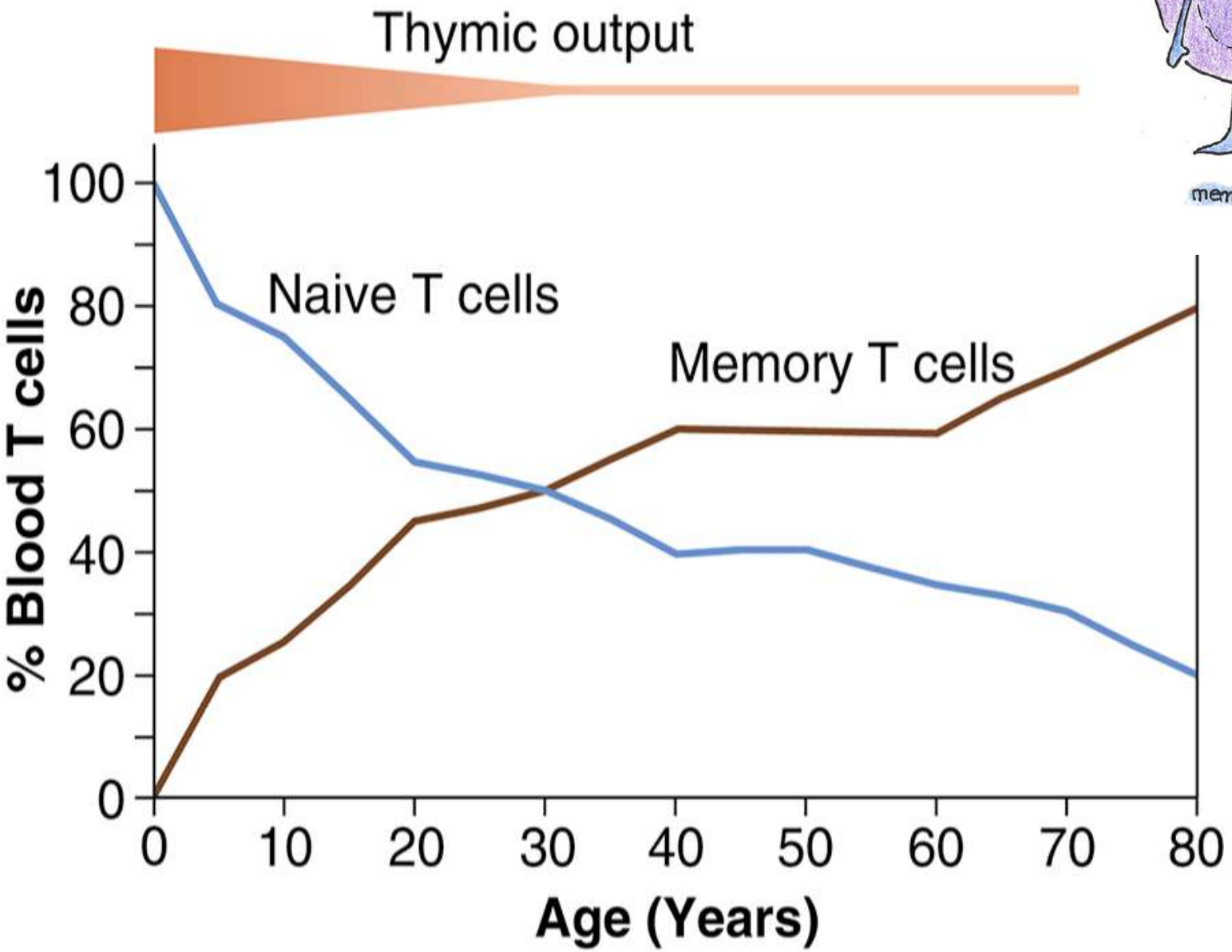
PRIMARY vs. SECONDARY



PHASES OF IMMUNE REACTION




I will never forget you
memory Tcell
Escherichia coli
PotluckComics.com
by Derkrawr


Thymic output
Naive T cells
Memory T cells
% Blood T cells
100
80
60
40
20
0
0
10
20
30
40
50
60
70
80
Age (Years)

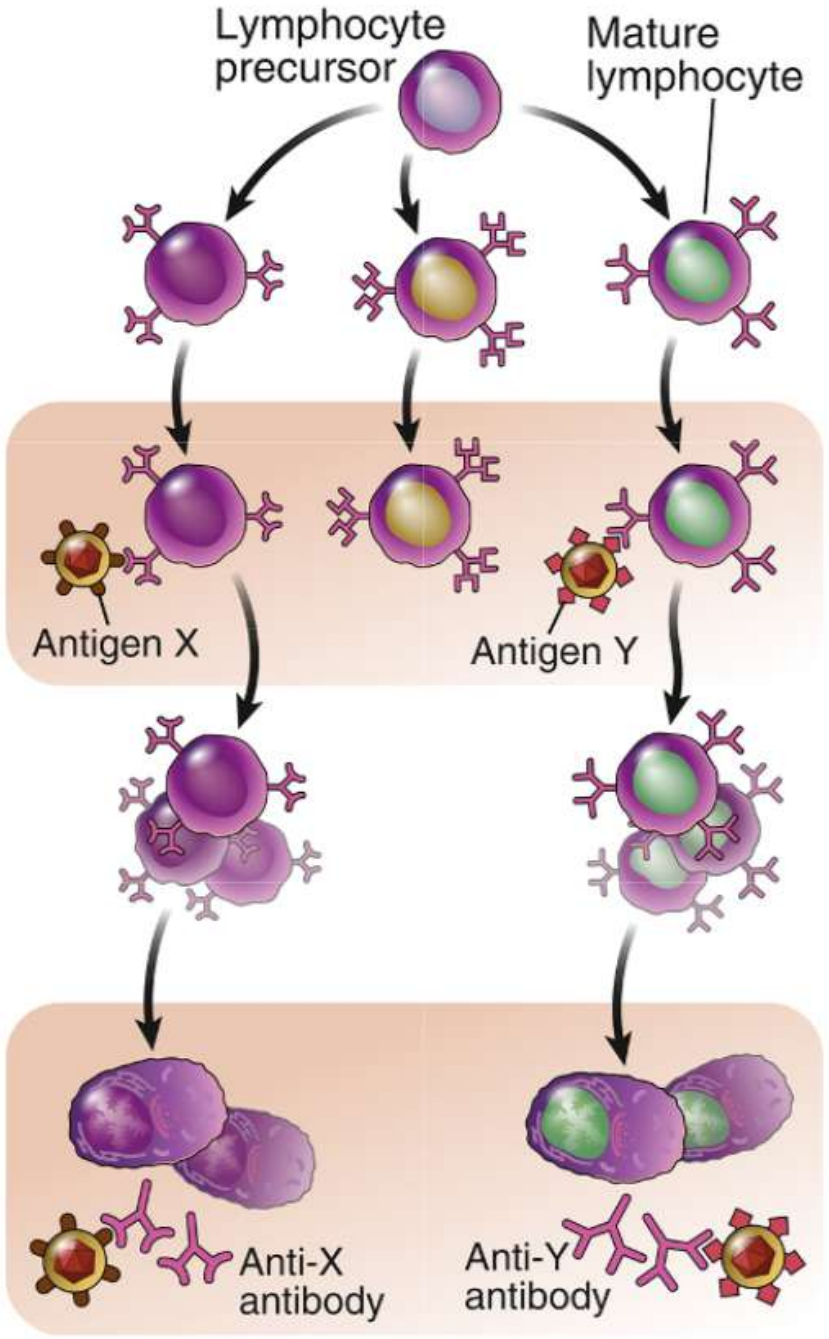
CLONAL SELECTION

Lymphocyte clones with diverse receptors arise in generative lymphoid organs

Clones of mature lymphocytes specific for many antigens enter lymphoid tissues

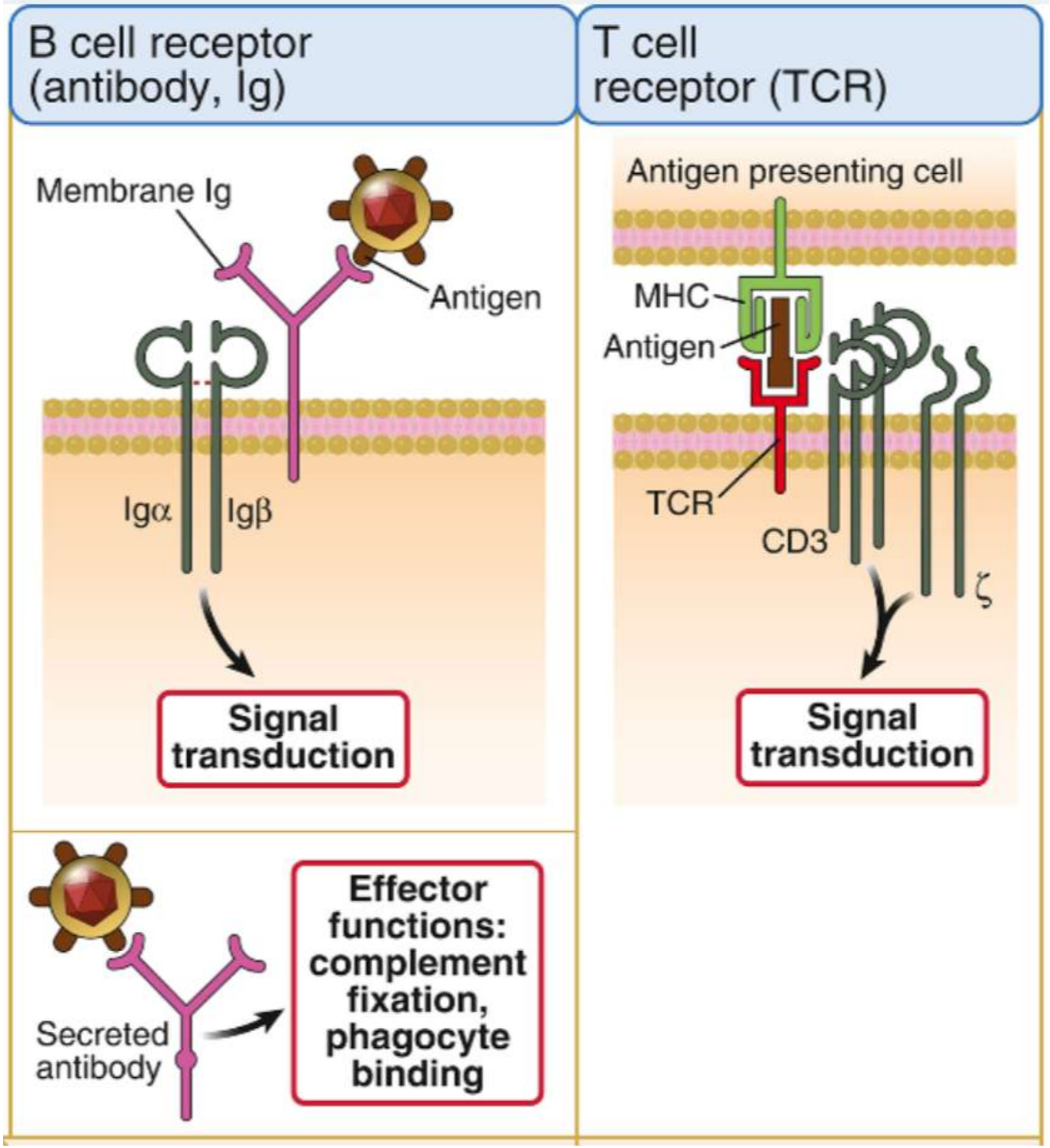
Antigen-specific clones are activated ("selected") by antigens

Antigen-specific immune responses occur



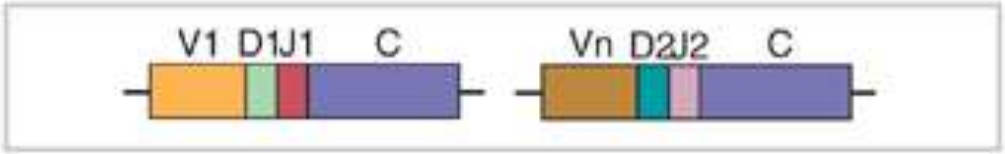
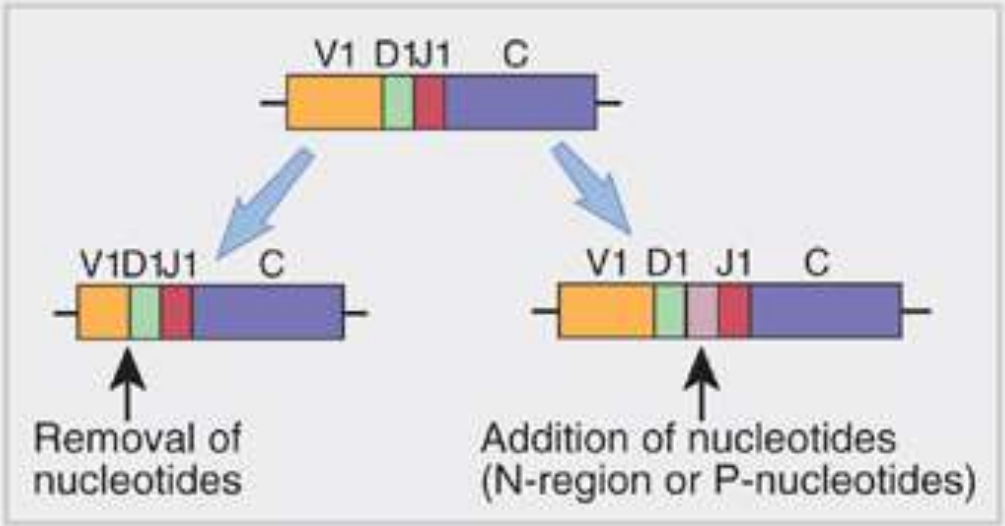
ANTIGEN RECEPTORS

B-CELL

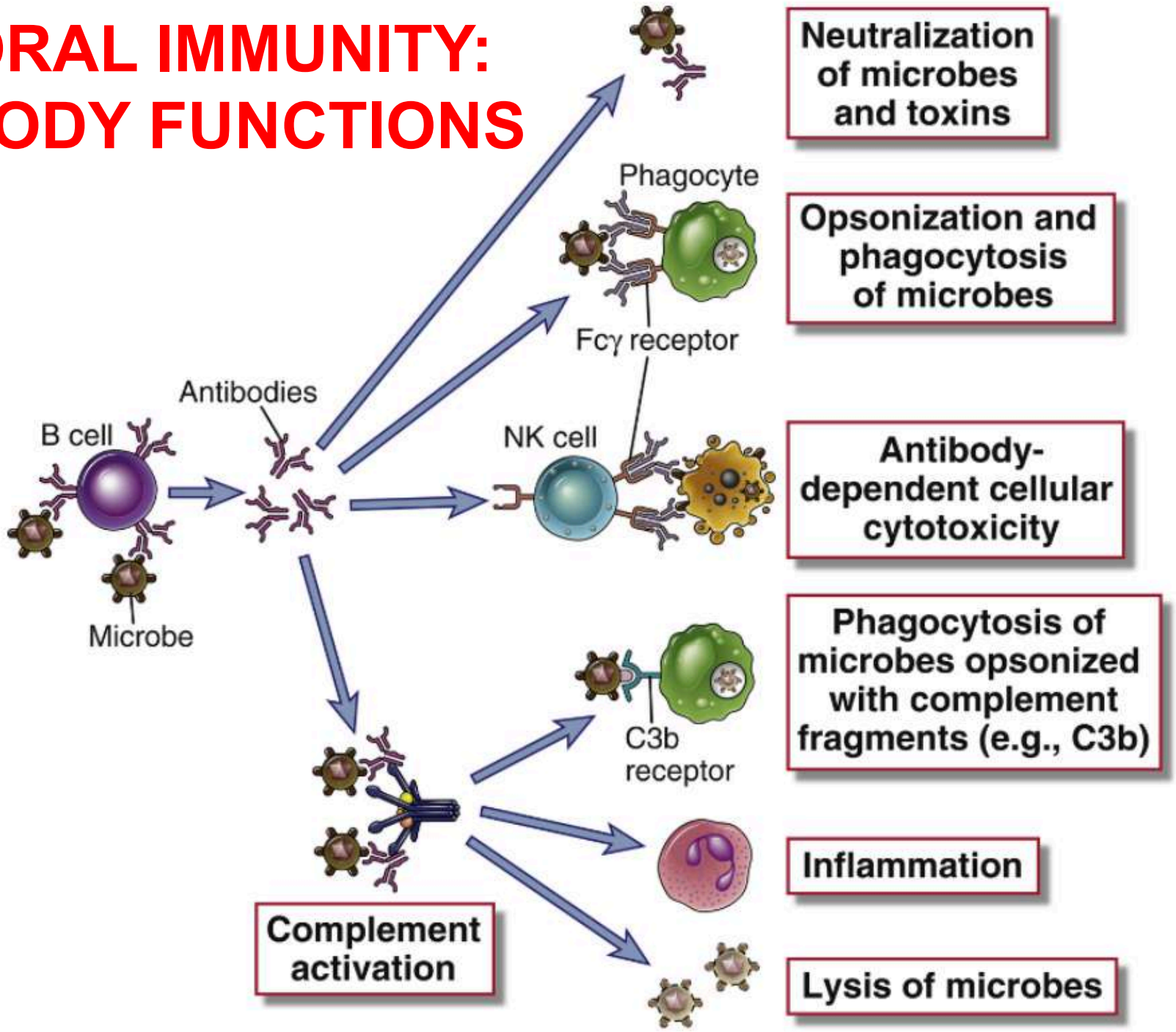

B cell receptor (antibody, Ig)
T cell receptor (TCR)
Membrane Ig
Antigen
Igα
Igβ
Signal transduction
Antigen presenting cell
MHC
Antigen
TCR
CD3
ζ
Signal transduction
Secreted antibody
Effector functions: complement fixation, phagocyte binding

T-CELL

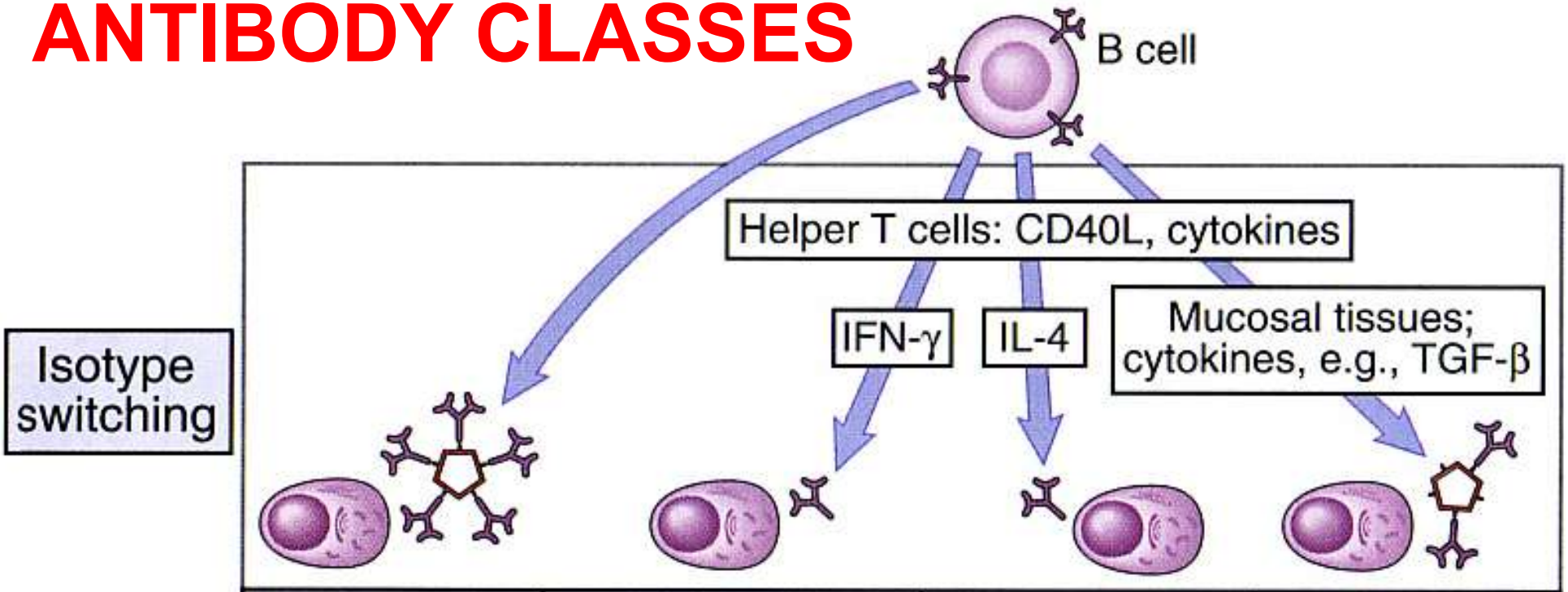
Mechanism of diversity

Mechanism	
Combinatorial diversity: Number of possible V-(D)-J combinations	 Ig: ~10^6 TCR: ~3×10^6
Junctional diversity: Total potential repertoire with junctional diversity	 Ig: ~10^{11} TCR: ~10^{16}

HUMORAL IMMUNITY: ANTIBODY FUNCTIONS

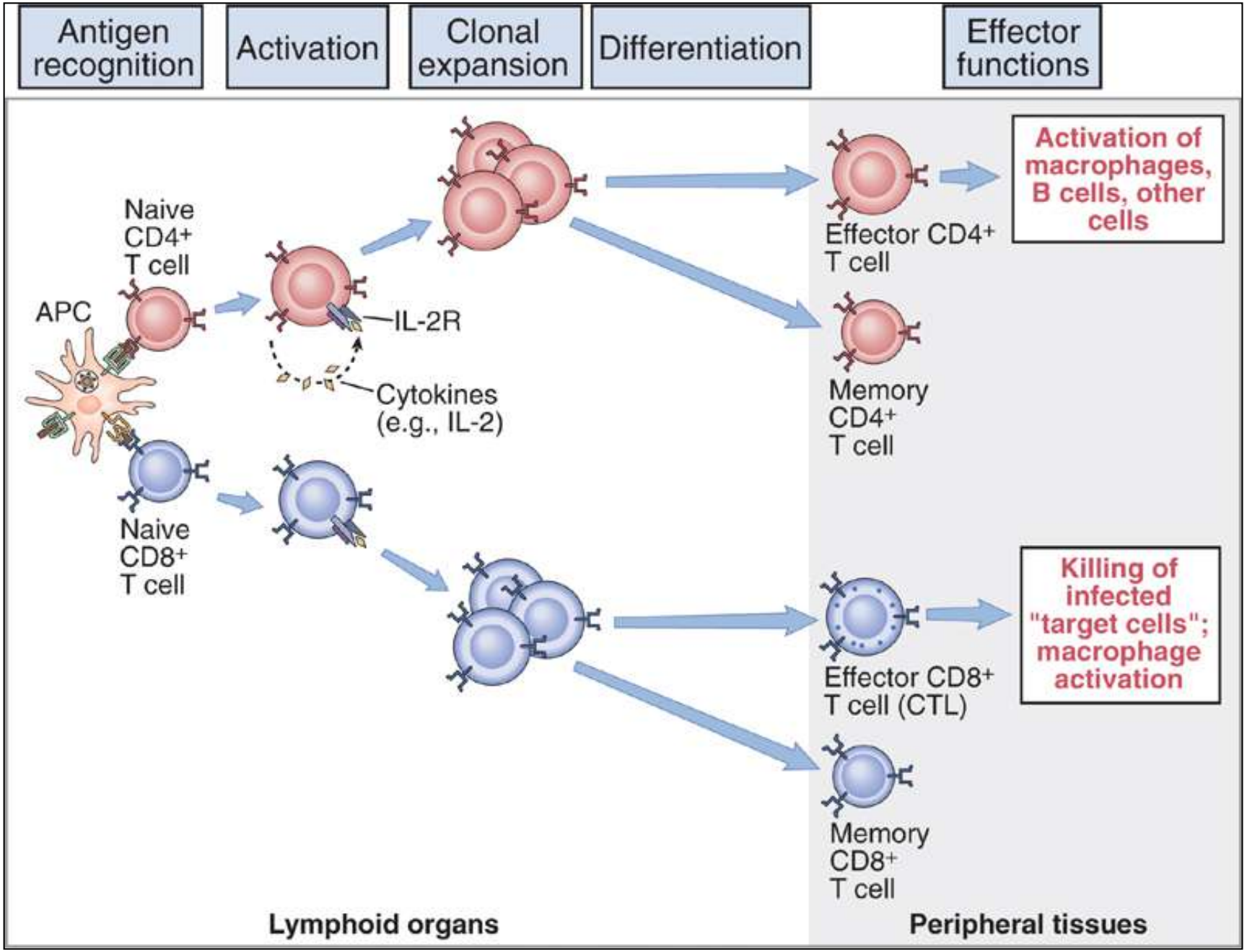


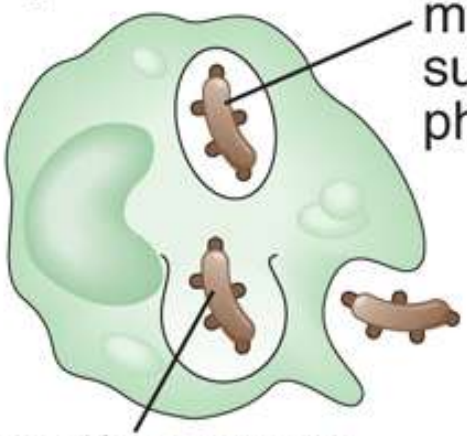
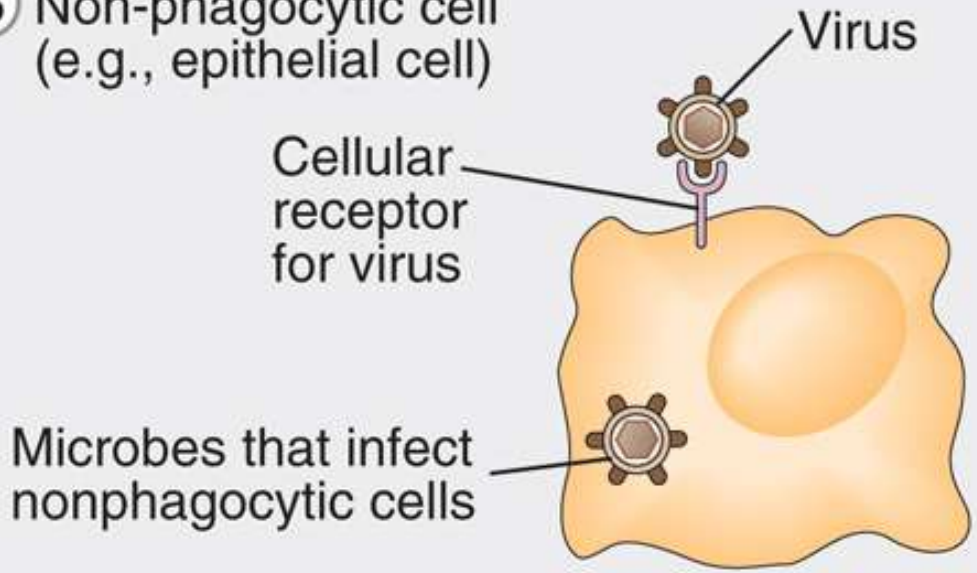
ANTIBODY CLASSES

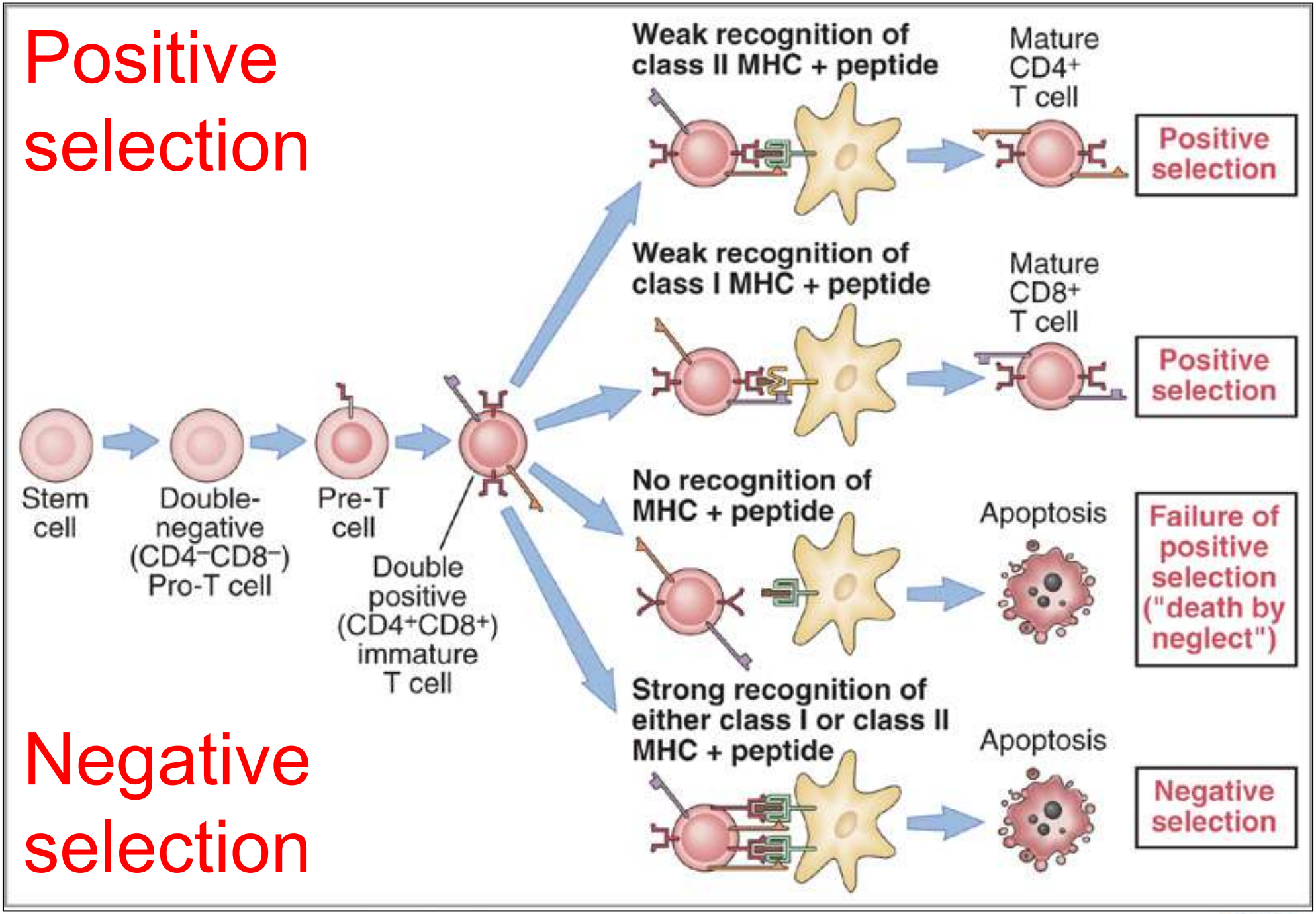


	IgM	IgG subclasses (IgG1, IgG3)	IgE	IgA
Principal effector functions	Complement activation	Fc receptor–dependent phagocyte responses; complement activation; neonatal immunity (placental transfer)	Immunity against helminths Mast cell degranulation (immediate hypersensitivity)	Mucosal immunity (transport of IgA through epithelia)

CELLULAR IMMUNITY



Intracellular microbes	Examples
A Phagocyte  	Intracellular bacteria: Mycobacteria *Listeria monocytogenes* *Legionella pneumophila* Fungi: *Cryptococcus neoformans* Protozoa: *Leishmania* *Trypanosma cruzi*
B Non-phagocytic cell (e.g., epithelial cell)  	Viruses: All Rickettsiae: All Protozoa: *Plasmodium falciparum* *Cryptosporidium parvum*

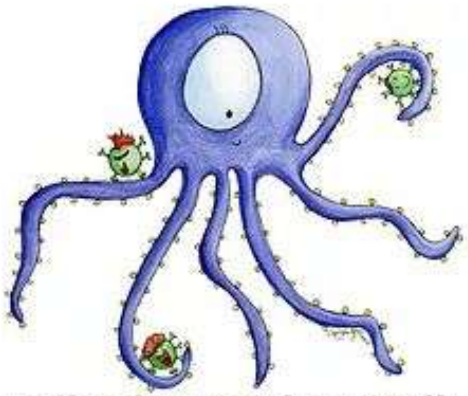

Positive selection
Weak recognition of class II MHC + peptide
Mature CD4+ T cell
Positive selection
Weak recognition of class I MHC + peptide
Mature CD8+ T cell
Positive selection
Stem cell
Double-negative (CD4−CD8−) Pro-T cell
Pre-T cell
Double positive (CD4+CD8+) immature T cell
No recognition of MHC + peptide
Apoptosis
Failure of positive selection ("death by neglect")
Strong recognition of either class I or class II MHC + peptide
Apoptosis
Negative selection
Negative selection

CELLS OF THE IMMUNE SYSTEM

NK Cell

Cytotoxic T Cell

Helper T Cell



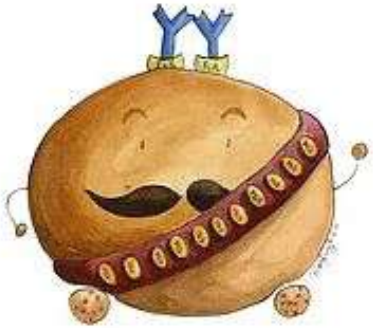
Follicular Dendritic Cell

Macrophage

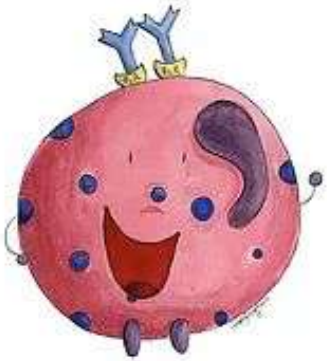
Treg

B Cell

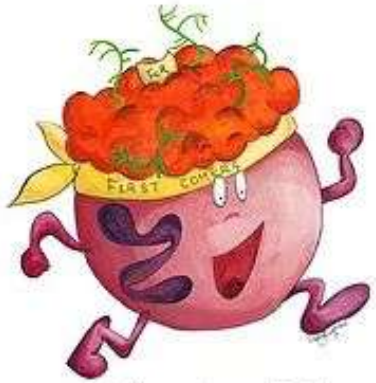
Plasma Cell



Mast Cell

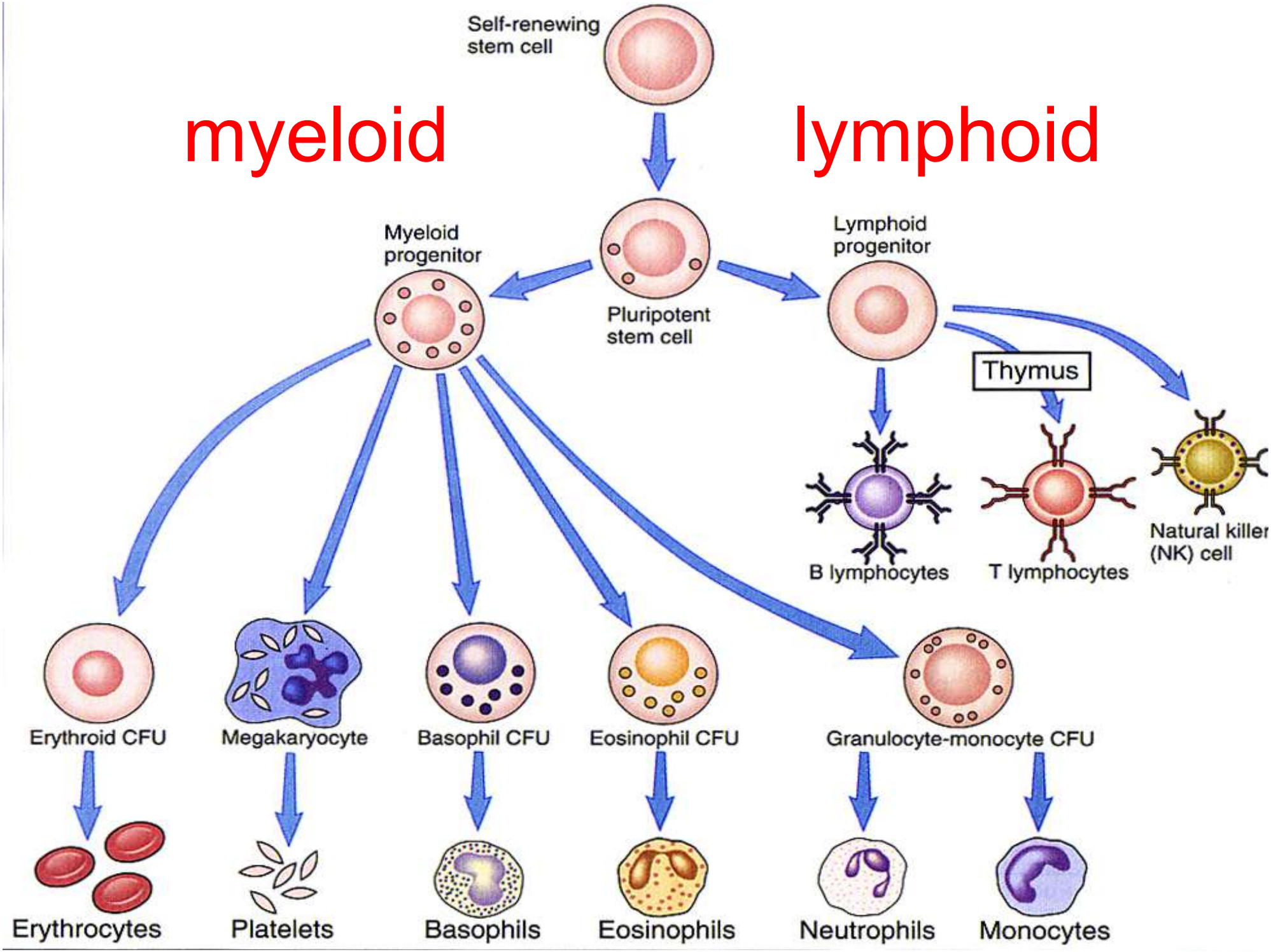


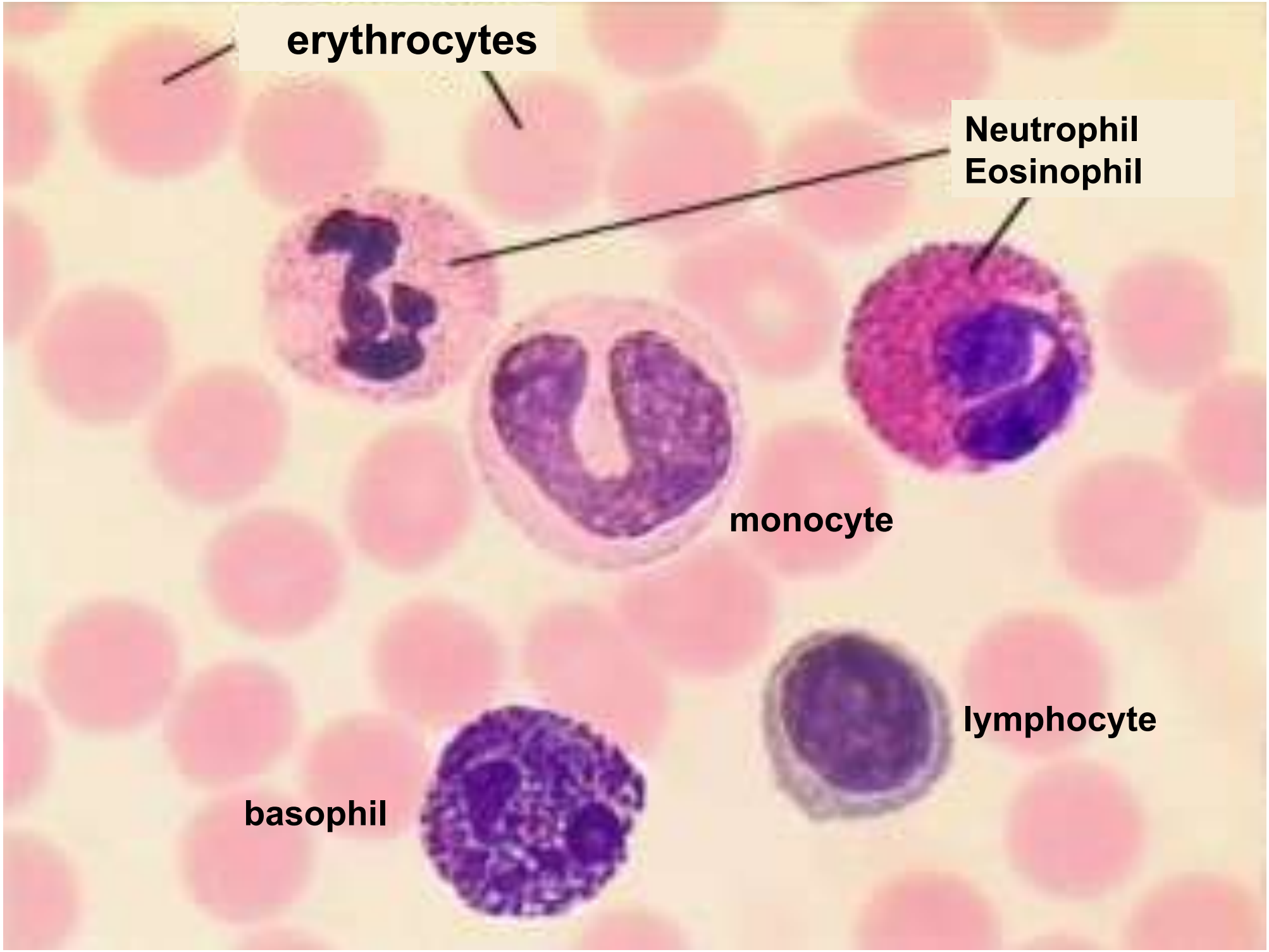
Basophil

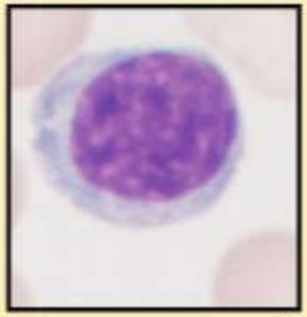
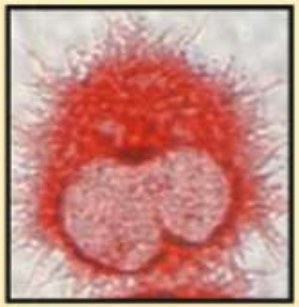
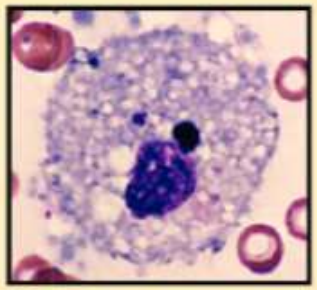


Neutrophil

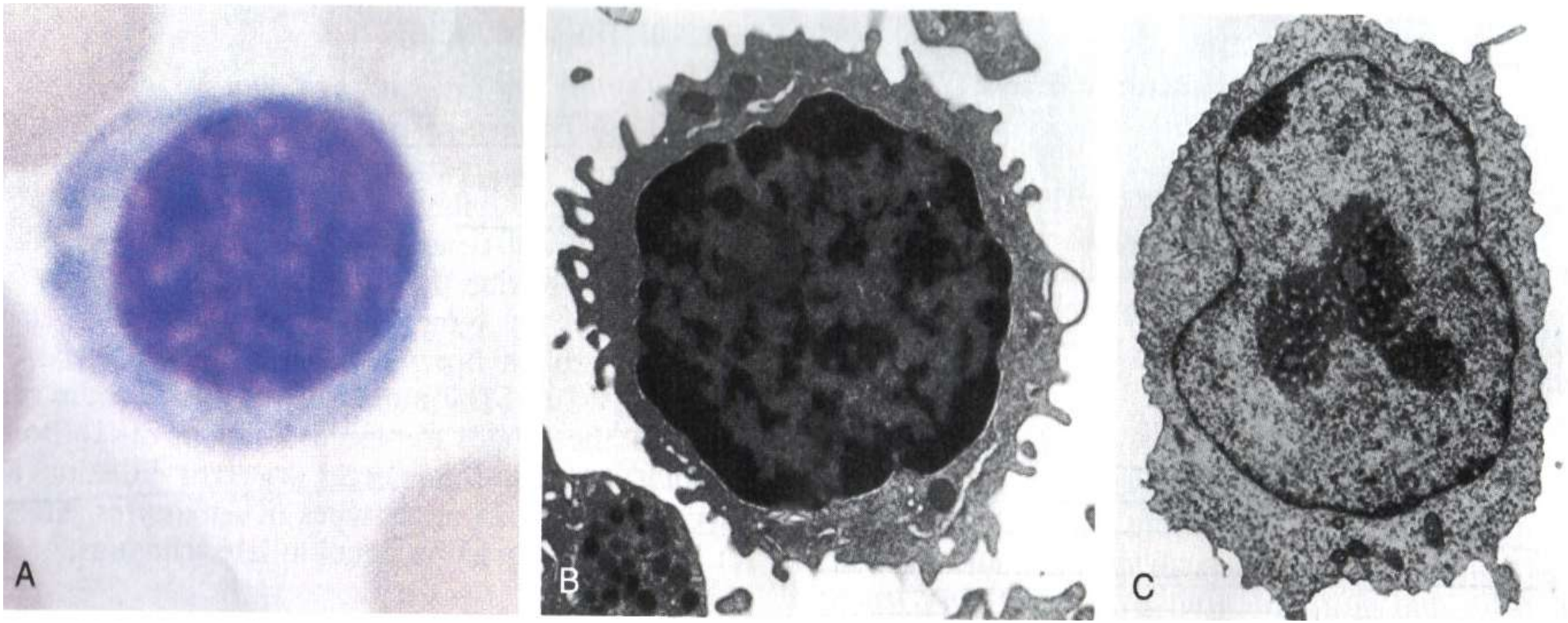
Eosinophil

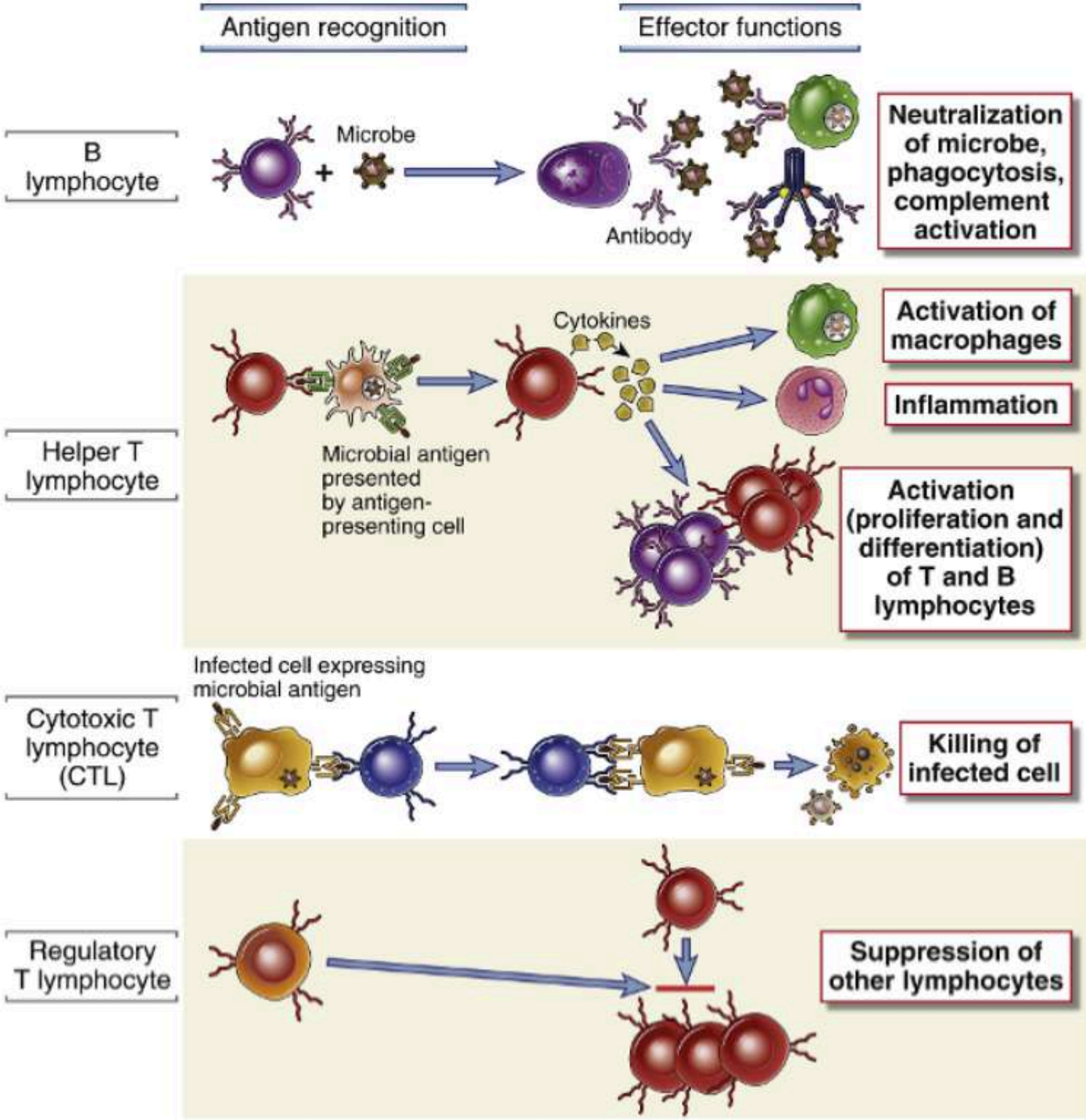

myeloid
lymphoid
Self-renewing stem cell
Pluripotent stem cell
Myeloid progenitor
Lymphoid progenitor
Thymus
B lymphocytes
T lymphocytes
Natural killer (NK) cell
Erythroid CFU
Megakaryocyte
Basophil CFU
Eosinophil CFU
Granulocyte-monocyte CFU
Erythrocytes
Platelets
Basophils
Eosinophils
Neutrophils
Monocytes


erythrocytes
Neutrophil
Eosinophil
monocyte
lymphocyte
basophil

Cell type	Principal function(s)
Lymphocytes: B lymphocytes; T lymphocytes  *Blood lymphocyte*	Specific recognition of antigens • B lymphocytes: mediators of humoral immunity • T lymphocytes: mediators of cell-mediated immunity
Antigen-presenting cells: dendritic cells; macrophages; B cells; follicular dendritic cells  *Dendritic cell*	Capture of antigens for display to lymphocytes: • Dendritic cells: initiation of T cell responses • Macrophages: effector phase of cell-mediated immunity • Follicular dendritic cells: display of antigens to B lymphocytes in humoral immune responses
Effector cells: T lymphocytes; macrophages; granulocytes  *Macrophage*	Elimination of antigens: • T lymphocytes: activation of phagocytes, killing infected cells • Macrophages: phagocytosis and killing of microbes • Granulocytes: killing microbes

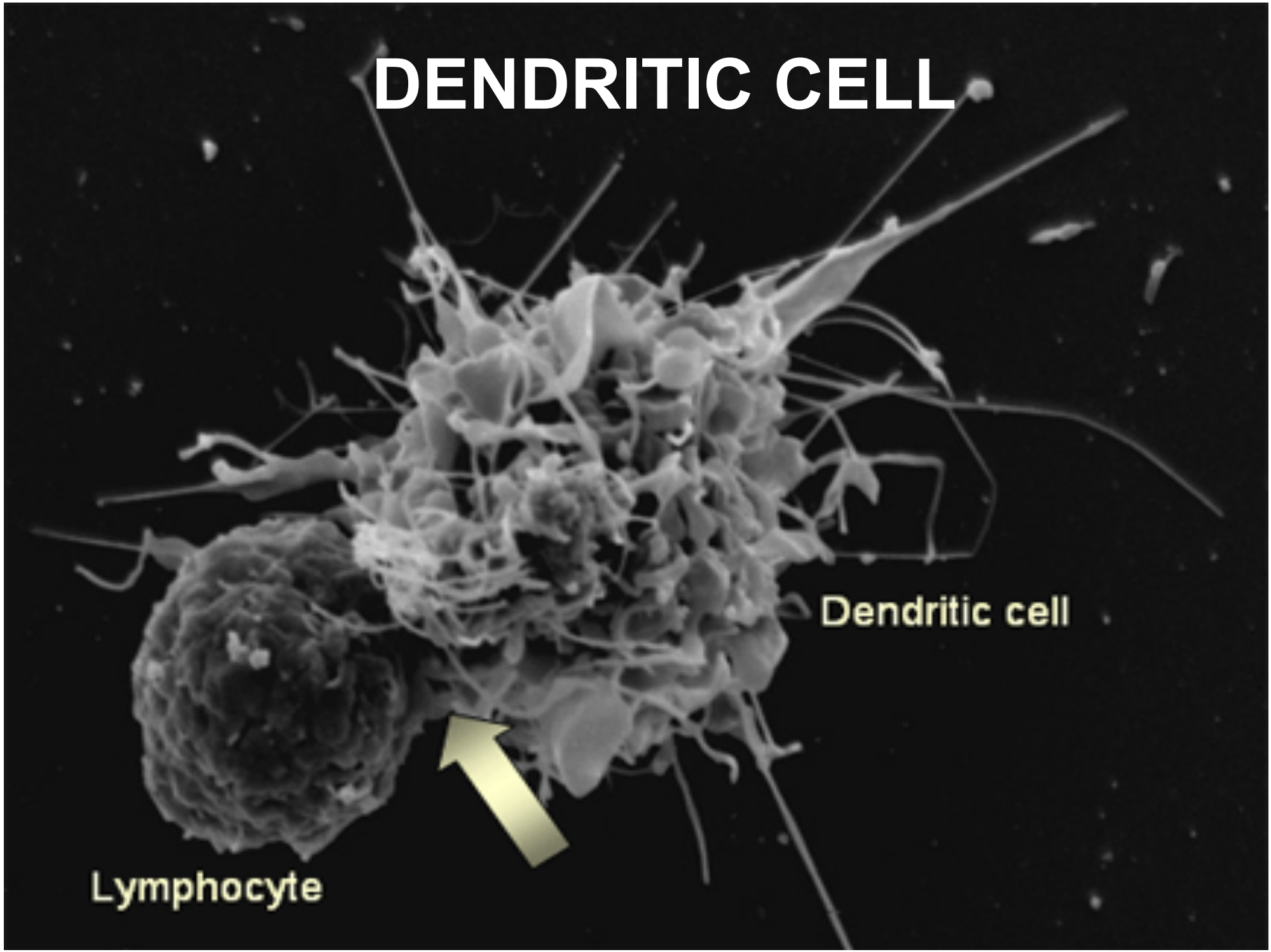
Lymphocytes

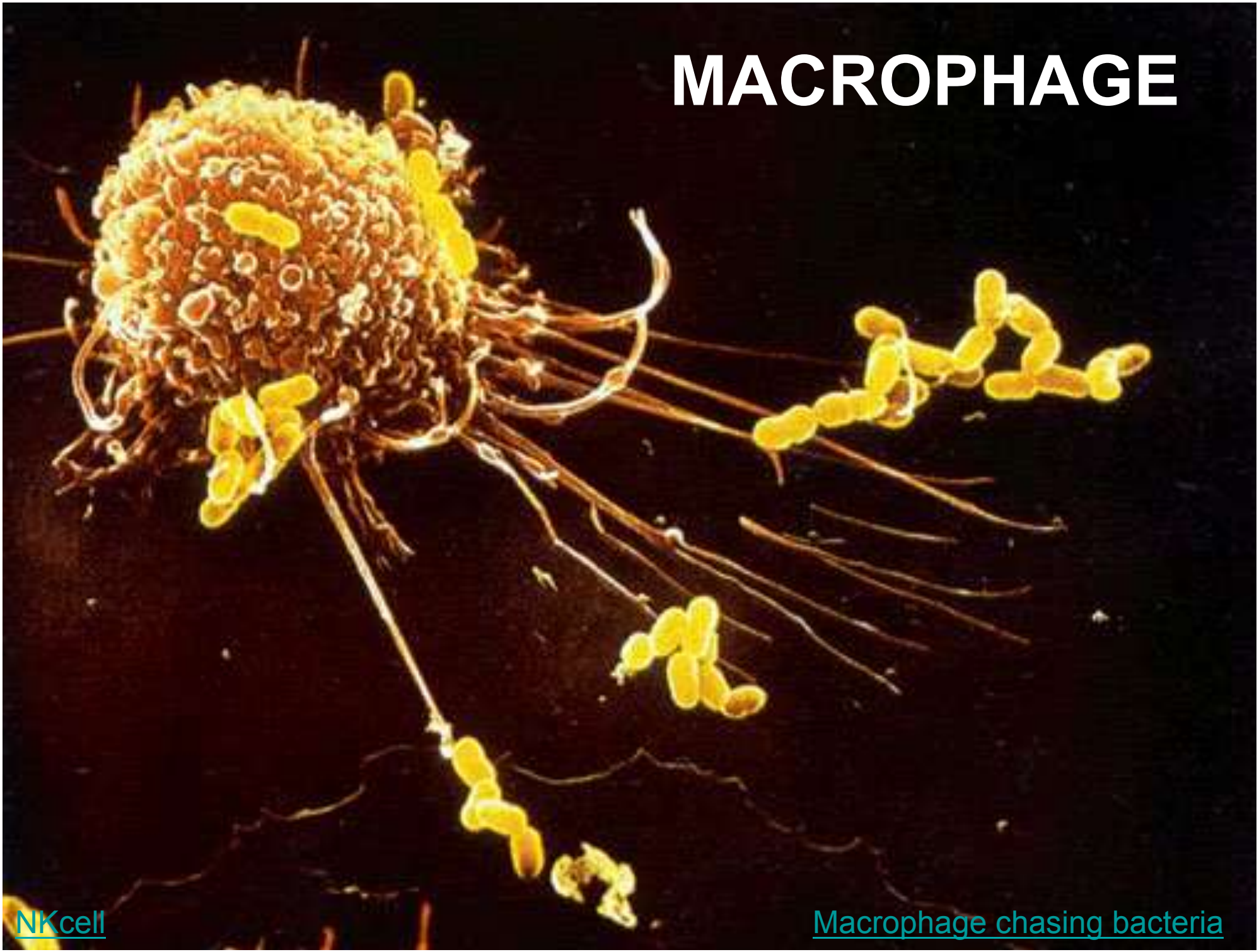



Antigen recognition
Effector functions
B lymphocyte
Microbe
Antibody
Neutralization of microbe, phagocytosis, complement activation
Helper T lymphocyte
Cytokines
Activation of macrophages
Inflammation
Microbial antigen presented by antigen-presenting cell
Activation (proliferation and differentiation)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

Tissue	Number of lymphocytes
Spleen	70×10^9
Lymph nodes	190×10^9
Bone marrow	50×10^9
Blood	10×10^9
Skin	20×10^9
Intestines	50×10^9
Liver	10×10^9
Lungs	30×10^9

~ 2%

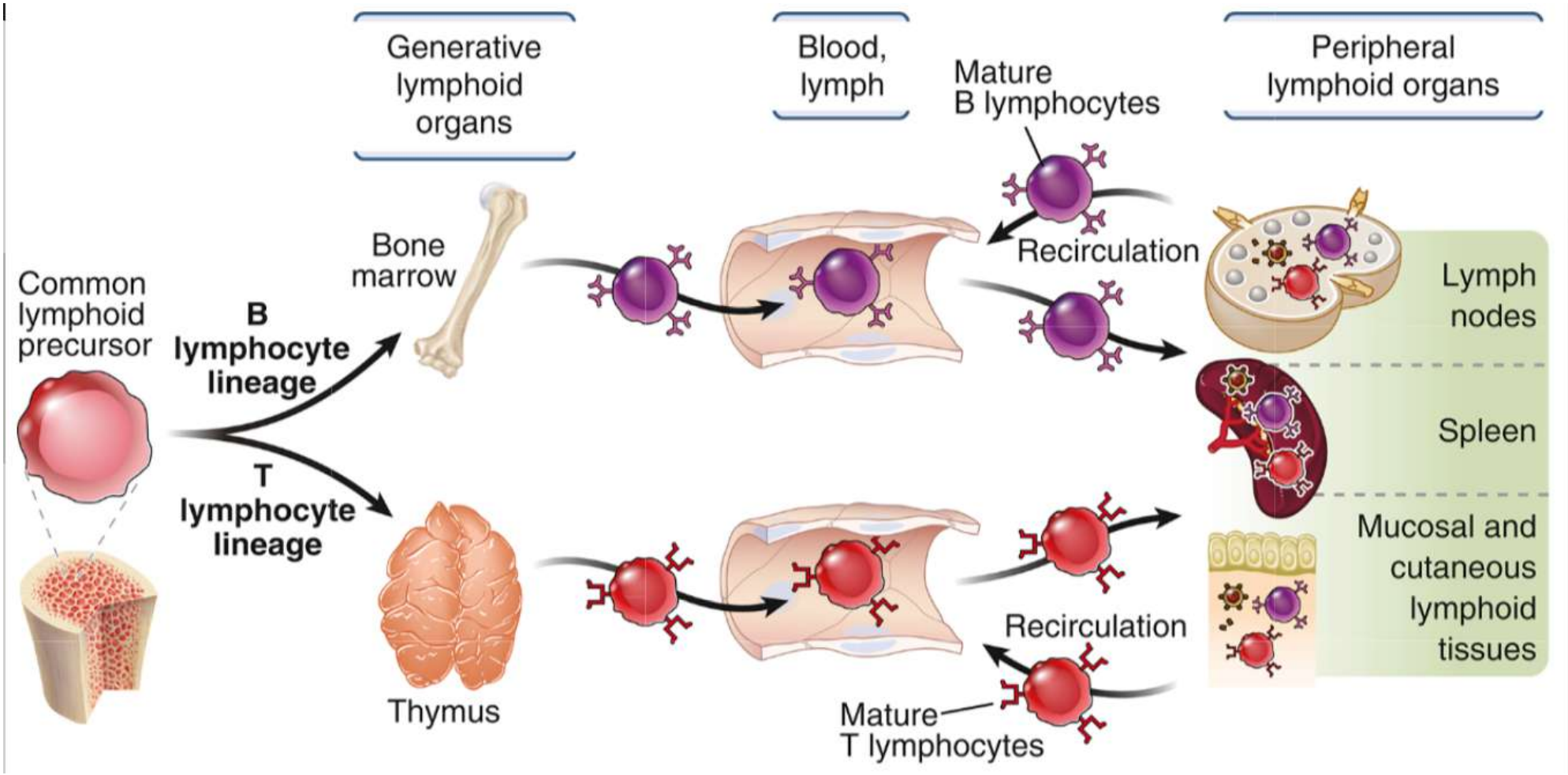

DENDRITIC CELL
Dendritic cell
Lymphocyte


MACROPHAGE
NKcell
Macrophage chasing bacteria

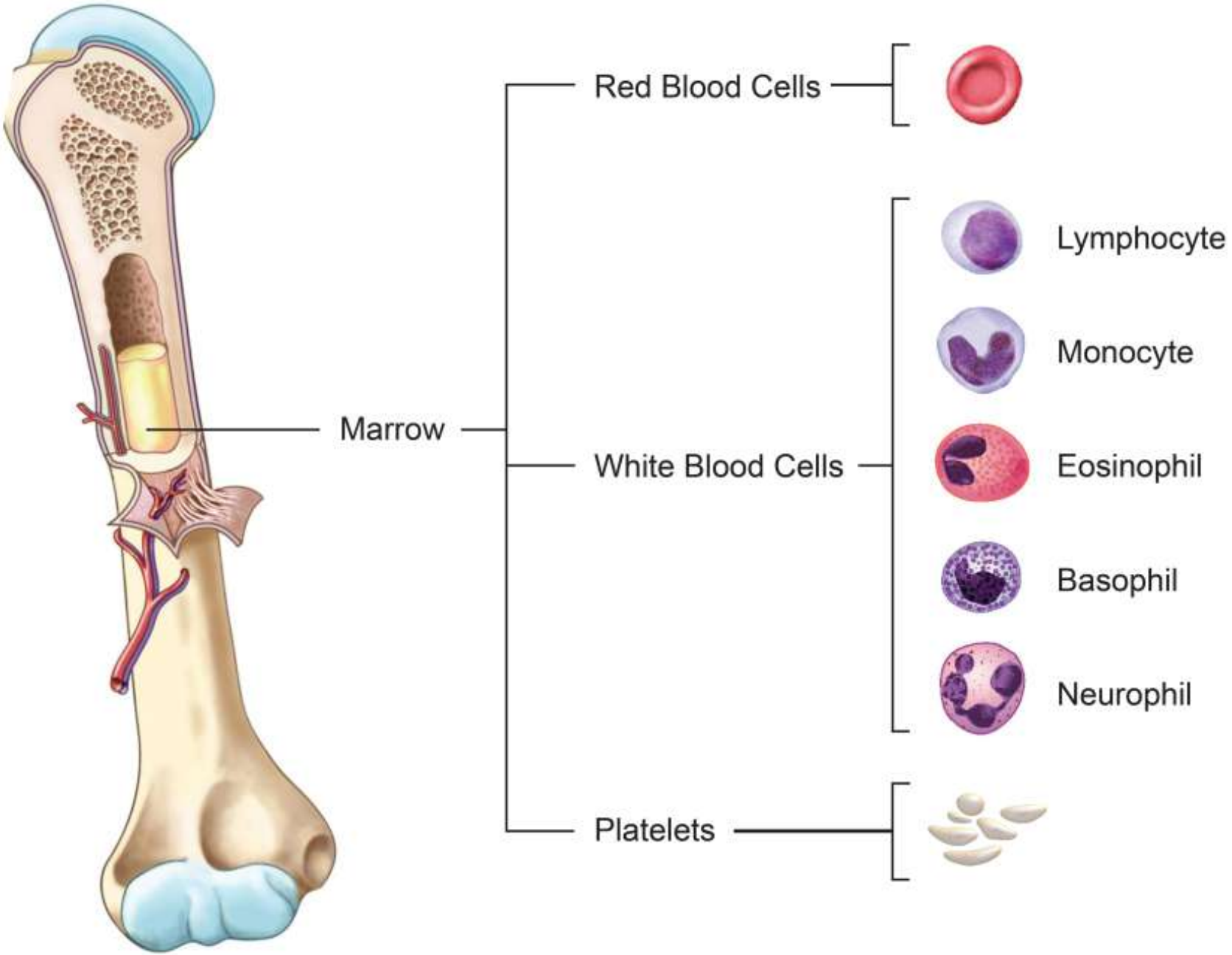
LYMPHOID TISSUES

- **Primary** (generative, central)
  - Bone marrow
  - Thymus
- **Secondary** (peripheral)
  - Lymph nodes
  - Spleen

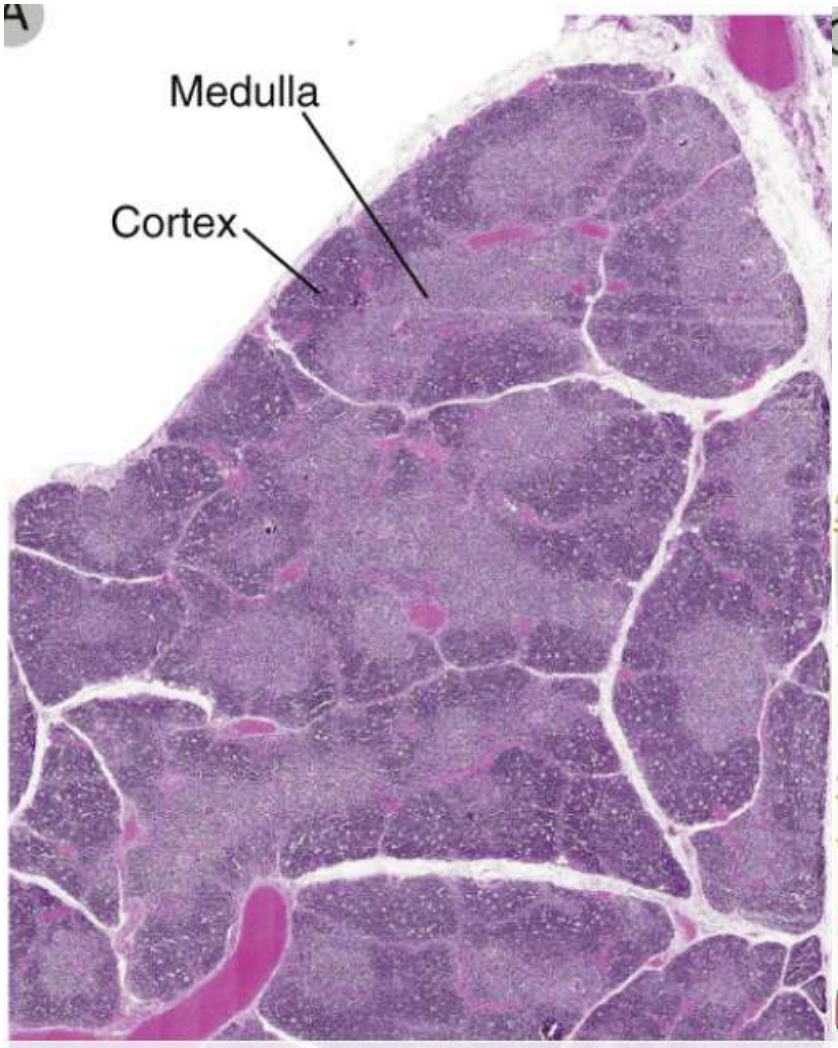
LYMPHOID TISSUES

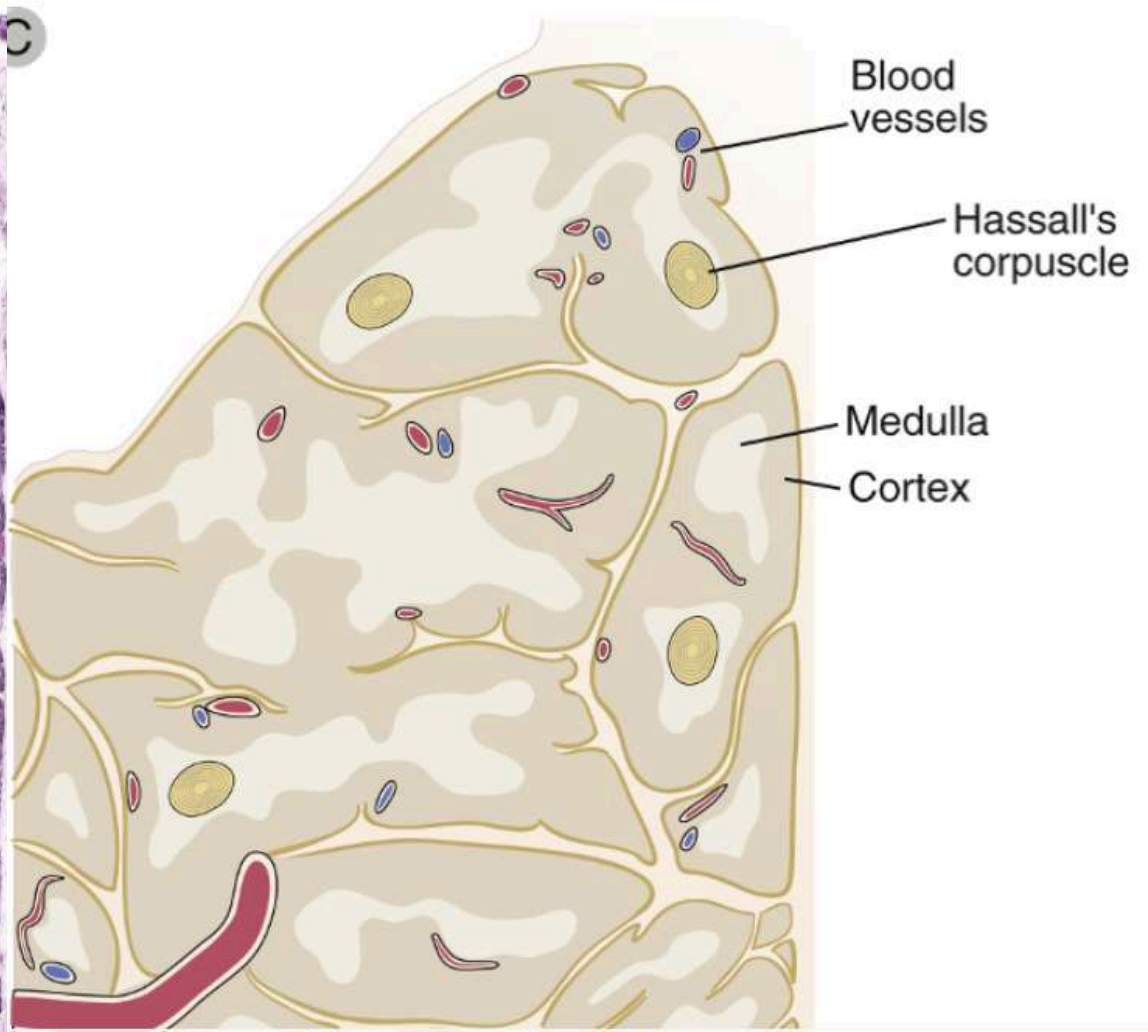


Bone marrow


Marrow
Red Blood Cells
White Blood Cells
Platelets
Lymphocyte
Monocyte
Eosinophil
Basophil
Neurophil

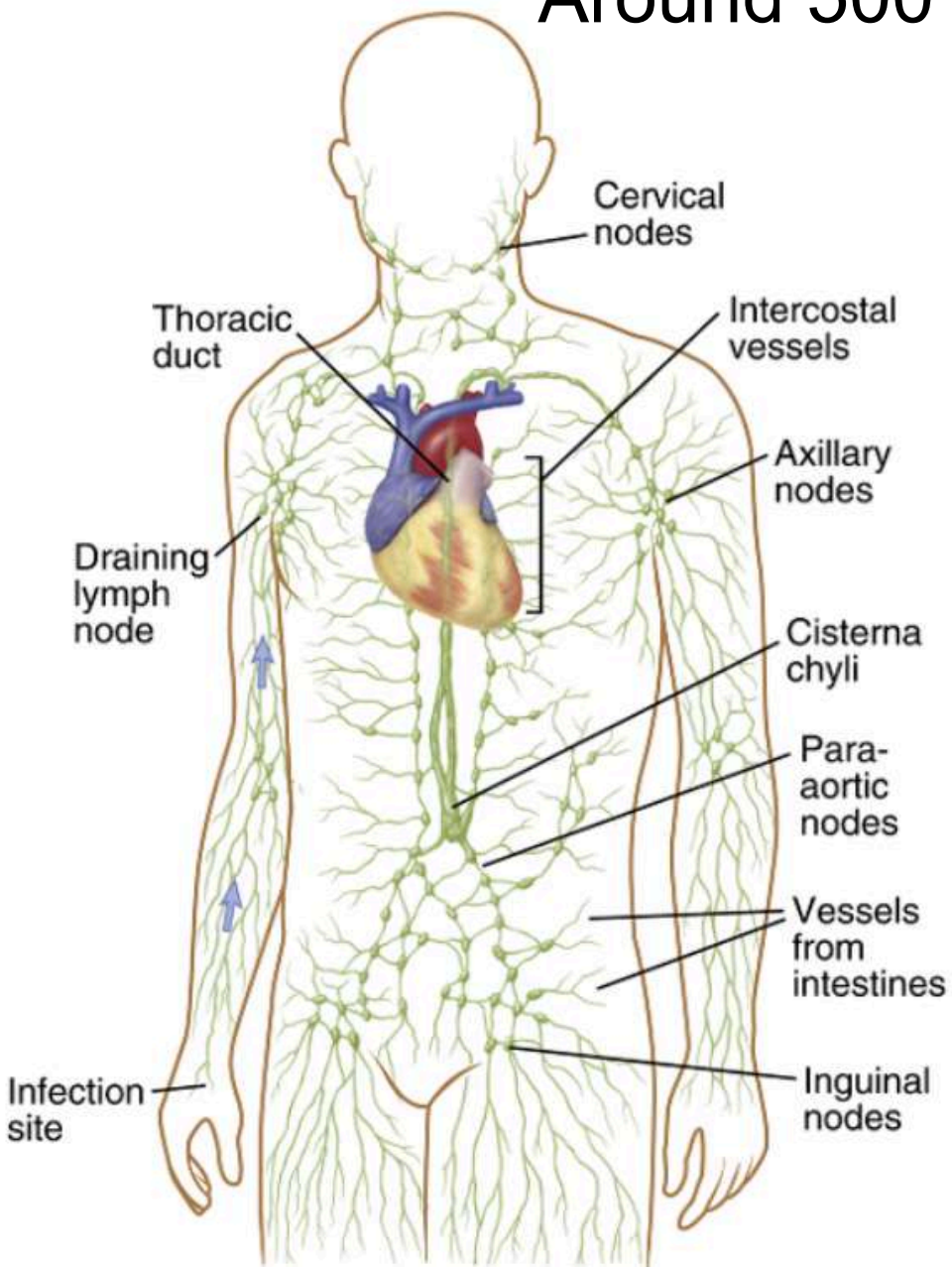
Thymus


A
Medulla
Cortex

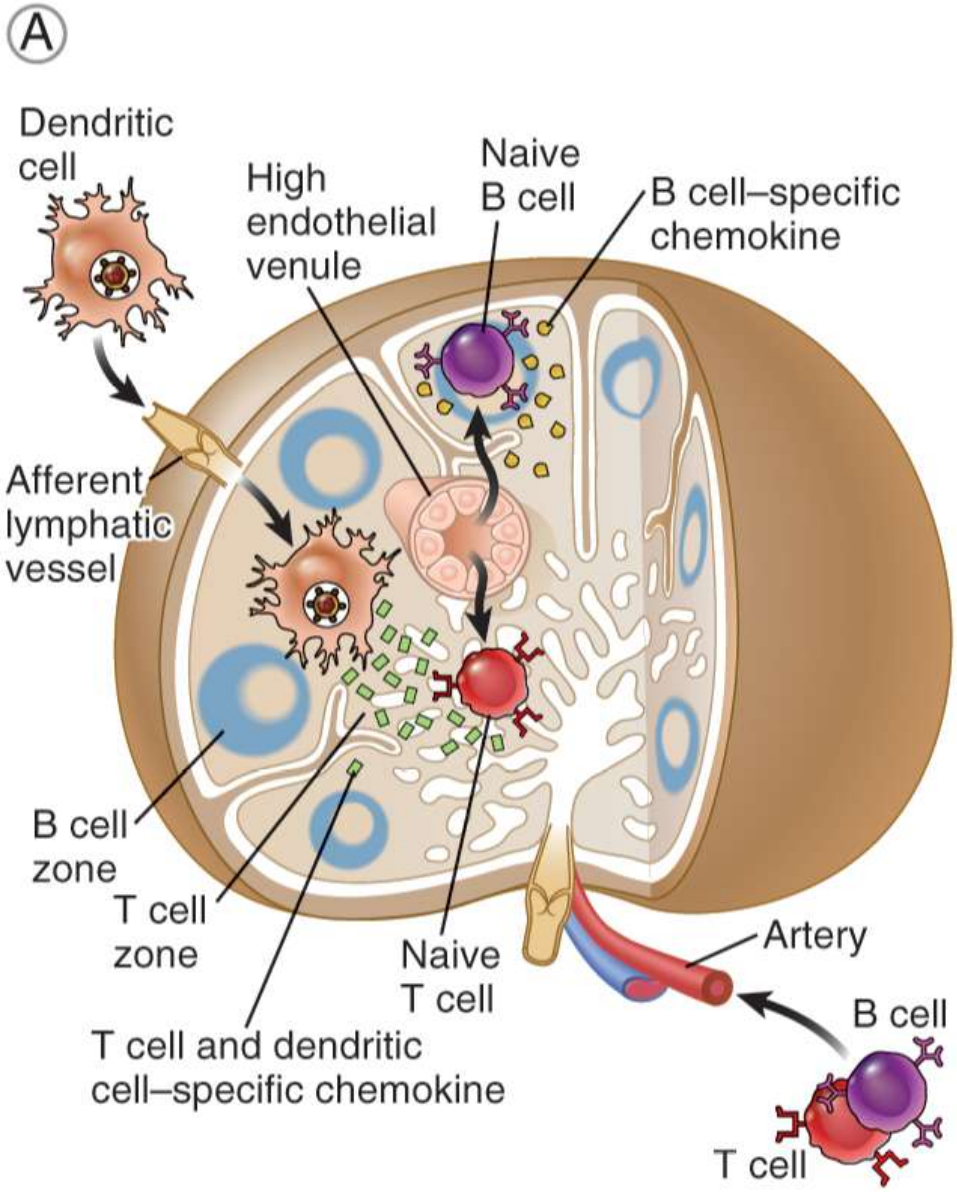

C
Blood vessels
Hassall's corpuscle
Medulla
Cortex

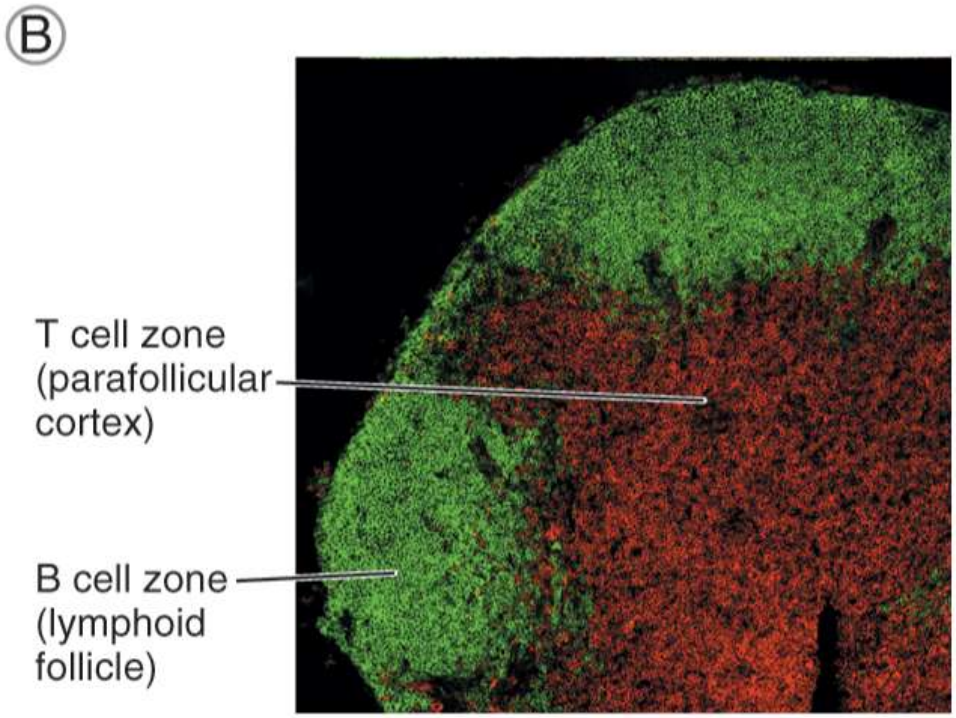
Lymph nodes

Around 500 in human body

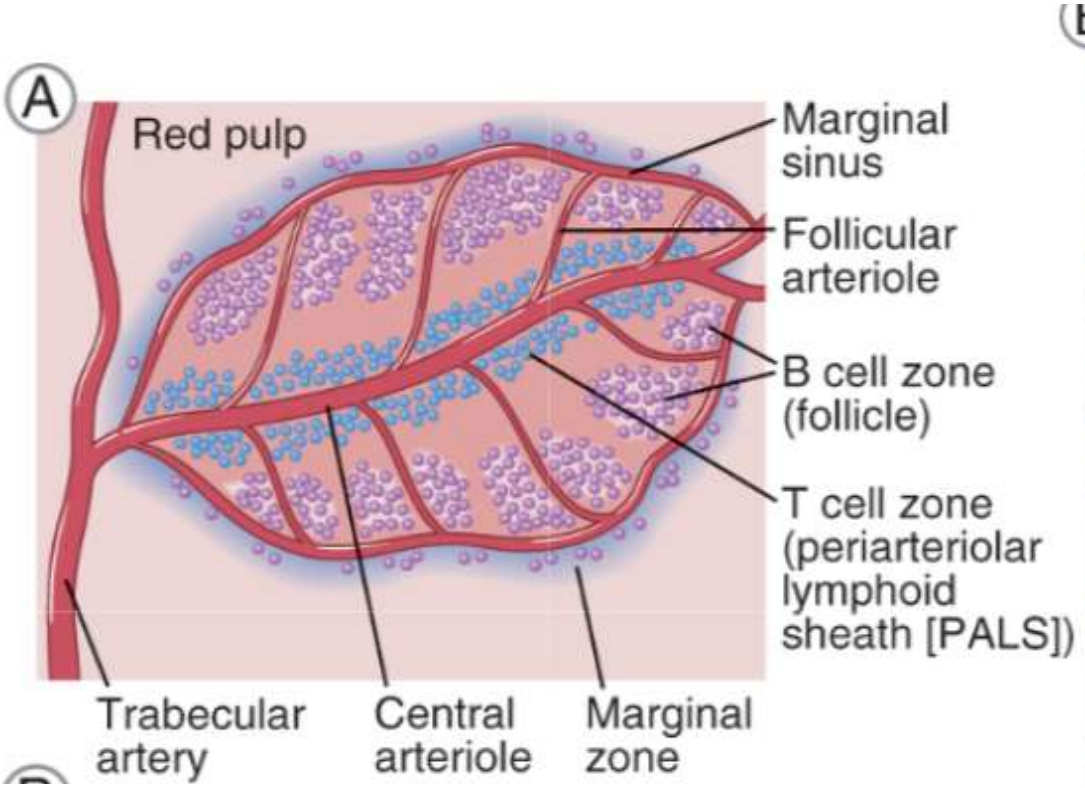


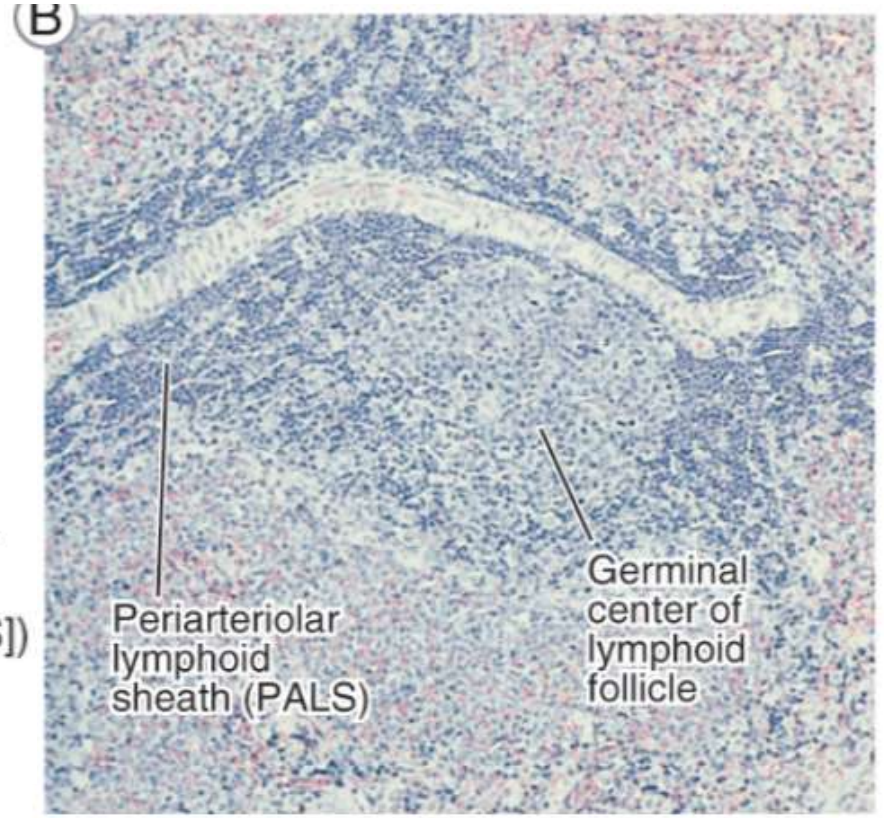
Lymph nodes


A
Dendritic cell
High endothelial venule
Naive B cell
B cell–specific chemokine
Afferent lymphatic vessel
B cell zone
T cell zone
Naive T cell
Artery
T cell and dendritic cell–specific chemokine
B cell
T cell


B
T cell zone (parafollicular cortex)
B cell zone (lymphoid follicle)

Spleen

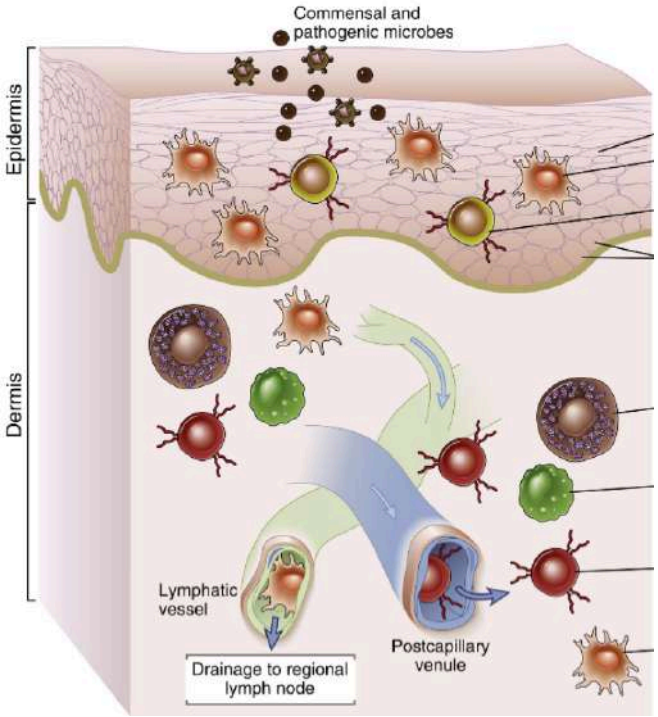

A
Red pulp
Marginal sinus
Follicular arteriole
B cell zone (follicle)
T cell zone (periarteriolar lymphoid sheath [PALS])
Trabecular artery
Central arteriole
Marginal zone

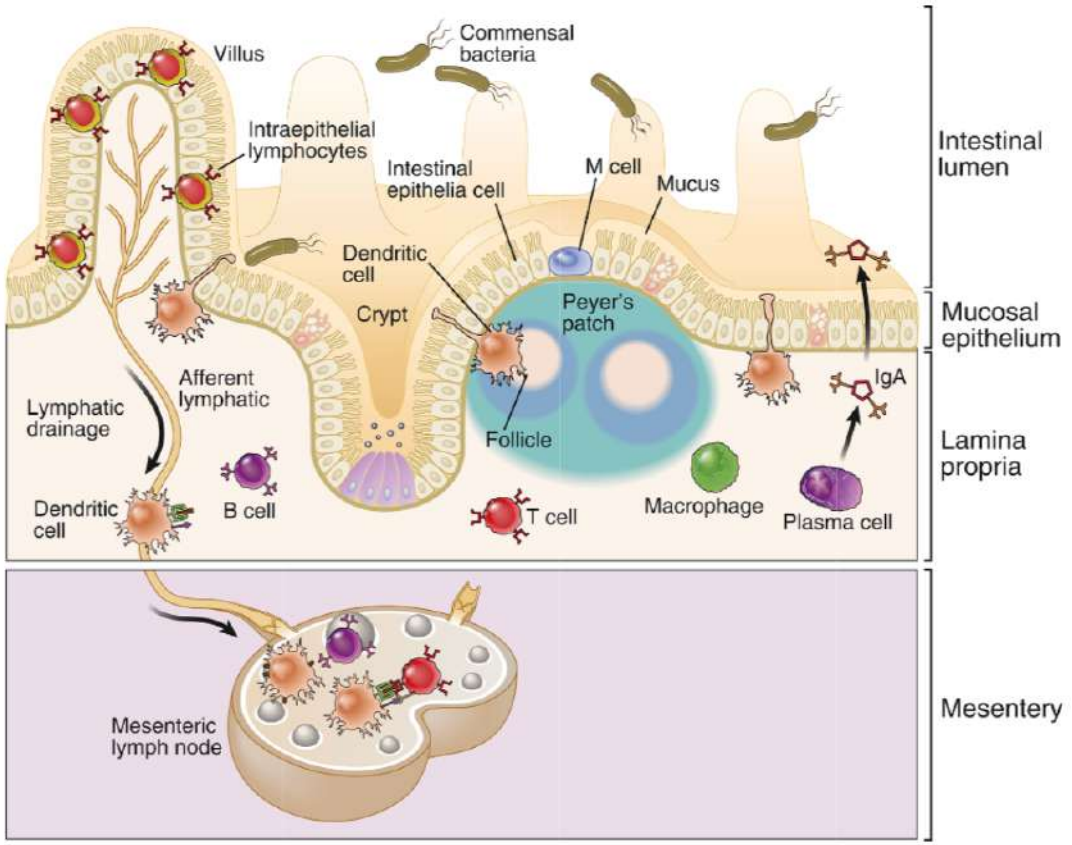

B
Periarteriolar lymphoid sheath (PALS)
Germinal center of lymphoid follicle

Regional immune systems

1. Skin
2. Gastrointestinal mucosa
3. Bronchial mucosa

(Immune privileged tissues - eye, brain, testes, pregnant uterus)





IMMUNE SYSTEM DEFORMATIONS

- Too strong:
  - **HYPERSENSITIVITY** (ALLERGY)
- Too weak:
  - **IMMUNODEFICIENCY**
- Wrongly directed:
  - **AUTOIMMUNITY**


THE IMMUNE SYSTEM
We owe it our lives!
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