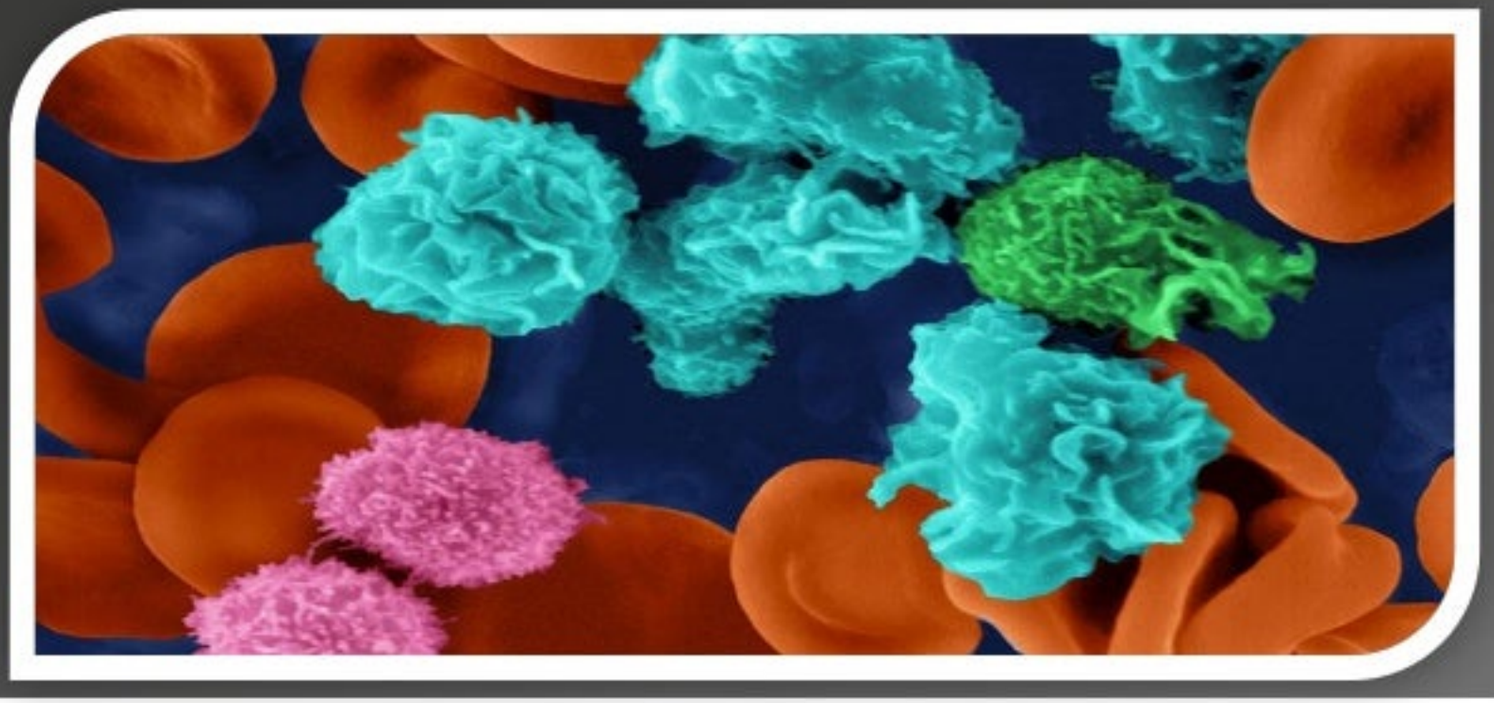


The Immune System

Structre, Artechtecutre and Functional Cells

Dr.T.V.Rao MD

What is Immune System

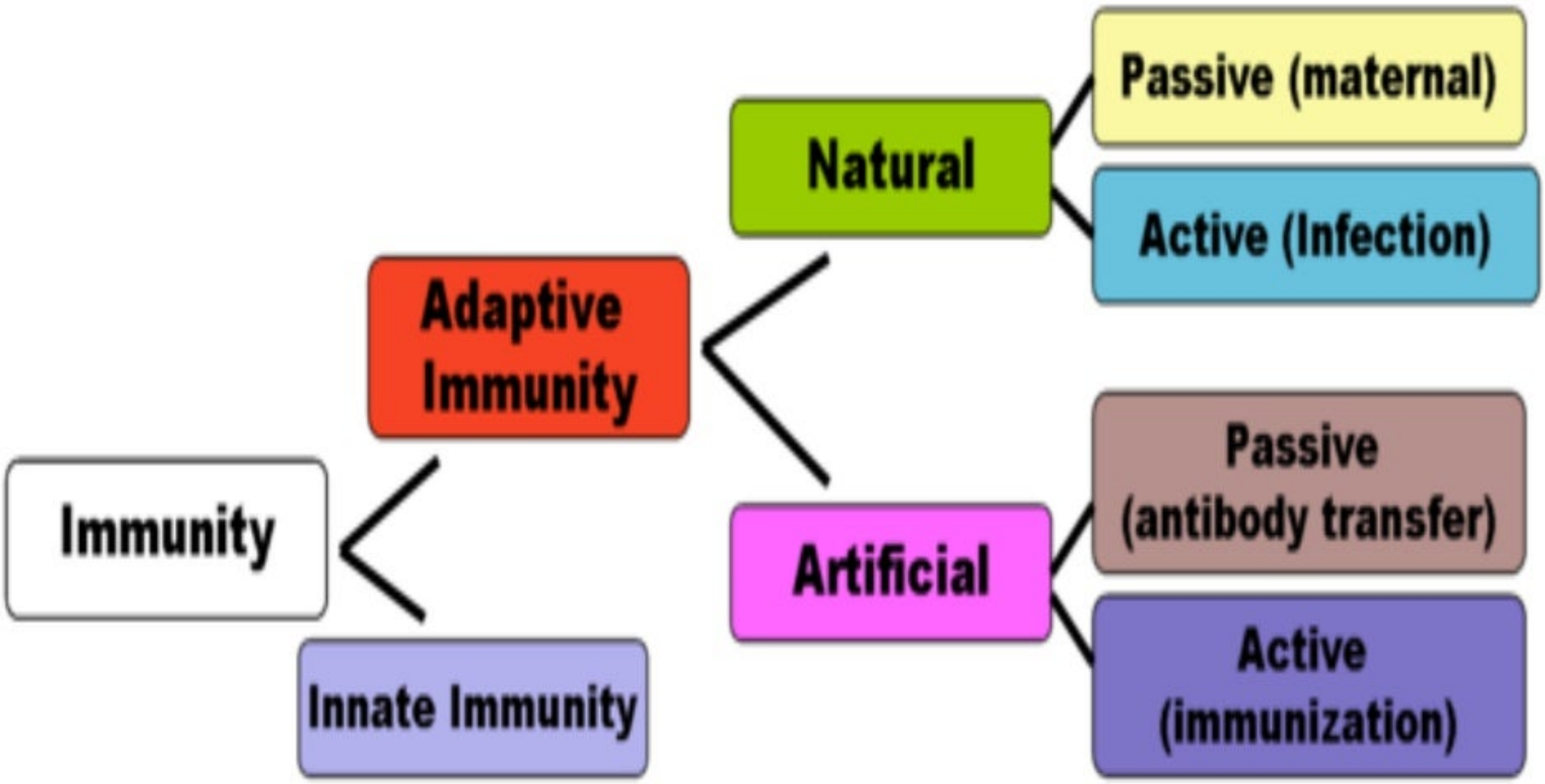
- Immune system is a biological structures and processes within an organism that protects against disease by identifying and killing pathogens and tumour cells. It detects a wide variety of agents, from viruses to parasitic worms, and needs to distinguish them from the organism's own healthy cells and tissues in order to function properly.

Immunity

The Latin term *"IMMUNIS"* means EXEMPT, referring to protection against foreign agents.

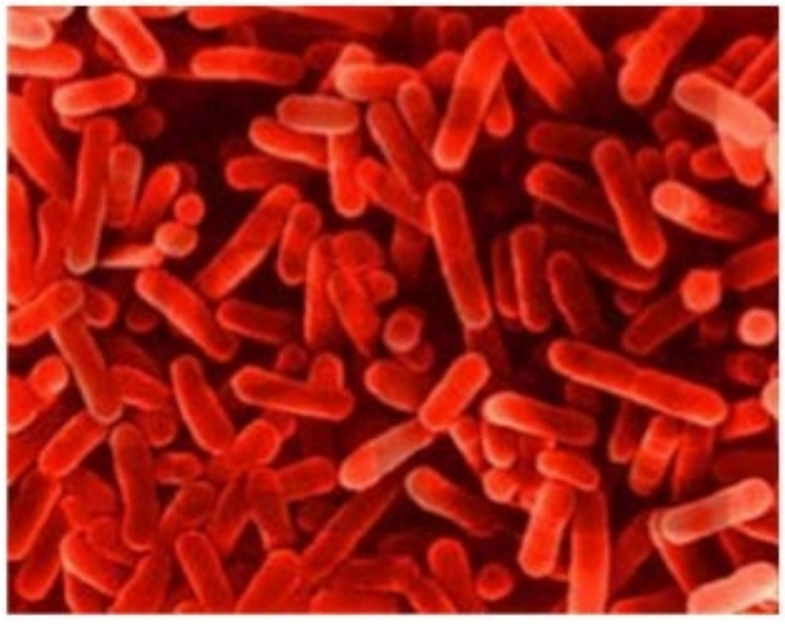
- DEFINITION: - The integrated body system of organs, tissues, cells & cell products that differentiates self from non – self & neutralizes potentially pathogenic organisms.
- *(The American Heritage Stedman's Medical Dictionary)*

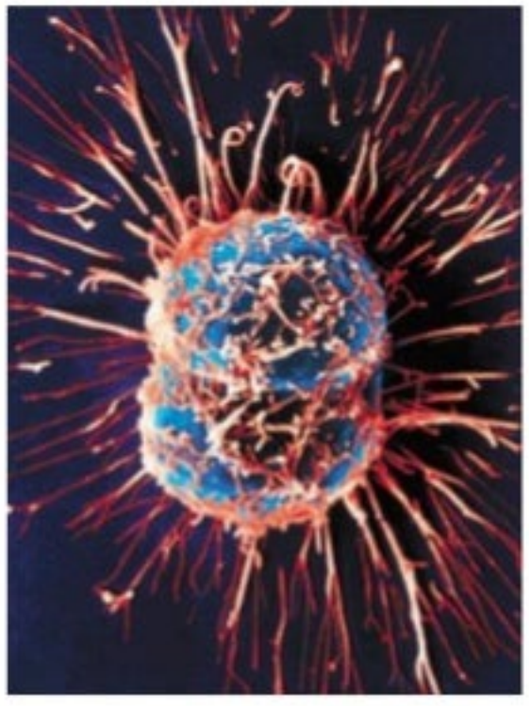
Basic classification of Immunity



What is the immune system?

- The body's defense against disease causing organisms, malfunctioning cells, and foreign particles





HISTORY OF IMMUNOLOGY

•**1798 Edward Jenner, Smallpox vaccination**

•1862 Ernst Haeckel, Recognition of phagocytosis

•1877 Paul Erlich, recognition of mast cells

•1879 Louis Pasteur, Attenuated chicken cholera vaccine development

•1883 Elie Metchnikoff Cellular theory of vaccination

•1885 Louis Pasteur, Rabies vaccination development

•1888 Pierre Roux & Alexandre Yersin, Bacterial toxin

•1888 George Nuttall, Bactericidal action of blood

•1891 Robert Koch, Delayed type hypersensitivity

•1894 Richard Pfeiffer, Bacteriolysis

bacteriolysis

•1900 Paul Erlich, Antibody formation theory

•1901 Karl Landsteiner, A, B and O blood groupings

•1901-8 Carl Jensen & Leo Loeb, Transplantable tumors

•1902 Paul Portier & Charles Richet, Anaphylaxis

•1903 Almroth Wright & Stewart Douglas, Opsonization reactions

•1906 Clemens von Pirquet, coined the word allergy

•1907 Svante Arrhenius, coined the term immunochemistry

•1910 Emil von Dungern, & Ludwik Hirszfeld, Inheritance of ABO blood groups

•1910 Peyton Rous, Viral immunology theory

•1914 Clarence Little, Genetics theory of tumor transplantation

•1915-20 Leonell Strong & Clarence Little, Inbred mouse strains

•1917 Karl Landsteiner, Haptens

•1921 Carl Prausnitz & Heinz Kustner, Cutaneous reactions

•1924 L Aschoff, Reticuloendothelial system

•1926 Lloyd Felton & GH Bailey, Isolation of pure antibody preparation

•1934-8 John Marrack, Antigen-antibody binding hypothesis

•1936 Peter Gorer, Identification of the H-2 antigen in mice

•1940 Karl Lansteiner & Alexander Weiner, Identification of the Rh antigens

•1941 Albert Coons, Immunofluorescence technique

•1942 Jules Freund & Katherine McDermott, Adjuvant

•1942 [illegible] Chase, Cellular transfer of sensitivity in guinea pigs (anaphylaxis)

•1944 Peter Medwar, Immunological hypothesis of allograft reaction

•1948 Astrid Fagraeus, Demonstration of antibody production in plasma B cells

•1948 George Snell, Congenic mouse lines

•1949 Macfarlane Burnet & Frank Fenner, Immunological tolerance hypothesis

•1950 Richard Gershon and K Kondo, Discovery of suppressor T cells

•1952 Ogden and Bretton, discovery of agammaglobulinemia (antibody immunodeficiency)

•1953 Morton Simonsen and W.J Hempster, Graft versus-host reaction

•1953 James Riley & Geoffrey West, Discovery of histamine in mast cells

•1953 Robert Billingham, Leslie Brent, Peter Medawar, & Marian Hasek, Immunological tolerance hypothesis

1955-1956 Niels Jerne, David Talmage, Macfarlane Burnet, Clonal selection theory

•1957 Ernest Witebsky et al., Induction of autoimmunity in animals

•1957 Alick Isaacs & Jean Lindemann, Discovery of interferon (cytokine)

•1958-62 Jean Dausset et al., Human leukocyte antigens

•1959-62 Rodney Porter et al., Discovery of antibody structure

•1959 James Gowans, Lymphocyte circulation

•1961-62 Jaques Miller et al., Discovery of thymus involvement in cellular immunity

•1961-62 Noel Warner et al., Distinction of cellular and humoral immune responses

•1963 Jacques Oudin et al., antibody idiotypes

•1964-8 Anthony Davis et al., T and B cell cooperation in immune response

1965 Thomas Tomasi et al., Secretory immunoglobulin antibodies

•1967 Kimishige Ishizaka et al., Identification of IgE as the reaginic antibody

•1971 Donald Bailey, Recombinent inbred mouse strains

•1974 Rolf Zinkernagel & Peter Doherty, MHC restriction

•**1975 Kohler and Milstein, Monoclonal antibodies used in genetic analysis**

•1984 Robert Good, Failed treatment of severe combined immunodeficiency (SCID, David the bubble boy) by bone marrow grafting. 1985 Tonegawa, Hood et al., Identification of immunoglobulin gene

•1985 Lenny Hood et al., Identification of genes for the T cell receptor

•1990 Yamamoto et al., Molecular differences between the genes for blood groups O and A and between those for A and B

•1990 NIH team, Gene therapy for SCID using cultured T cells.

•1993 NIH team, Treatment of SCID using genetically altered umbilical cord cells.

•1985-onwards Rapid identification of genes for immune cells, antibodies, cytokines and other immunological structures.

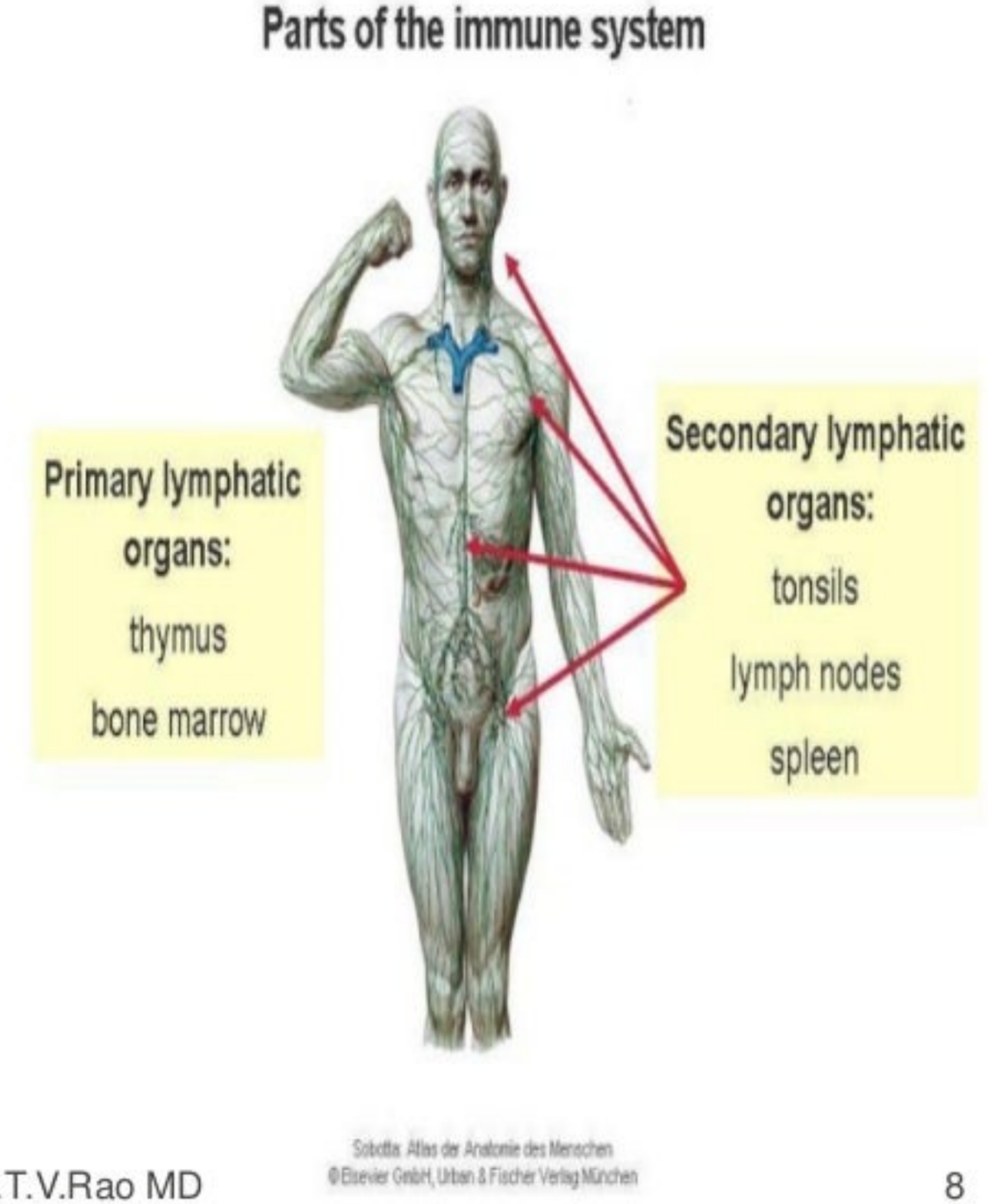
•1798 Edward Jenner, Smallpox vaccination
•1975 Kohler and Milstein, Monoclonal antibodies used in genetic analysis

Where is the Immune System

- Cells of the immune system are:
  - Distributed throughout the body in the blood, lymph, epithelial and CT.
  - Arranged in small spherical nodules (lymphoid nodules) found in CT and inside various organs.
    - Found in the mucosa of digestive (tonsils, Peyer's patches), respiratory, reproductive, urinary systems are MALT (mucosa-associated lymphoid tissue.
  - Organized as differently sized organs—lymphoid organs—the lymph nodes, spleen, thymus, bone marrow.

Immune System composed with

All parts of the body that help in the recognition and destruction of foreign materials. White blood cells, phagocytes and lymphocytes, bone marrow, lymph nodes, tonsils, thymus, and your spleen are all part of the immune system.

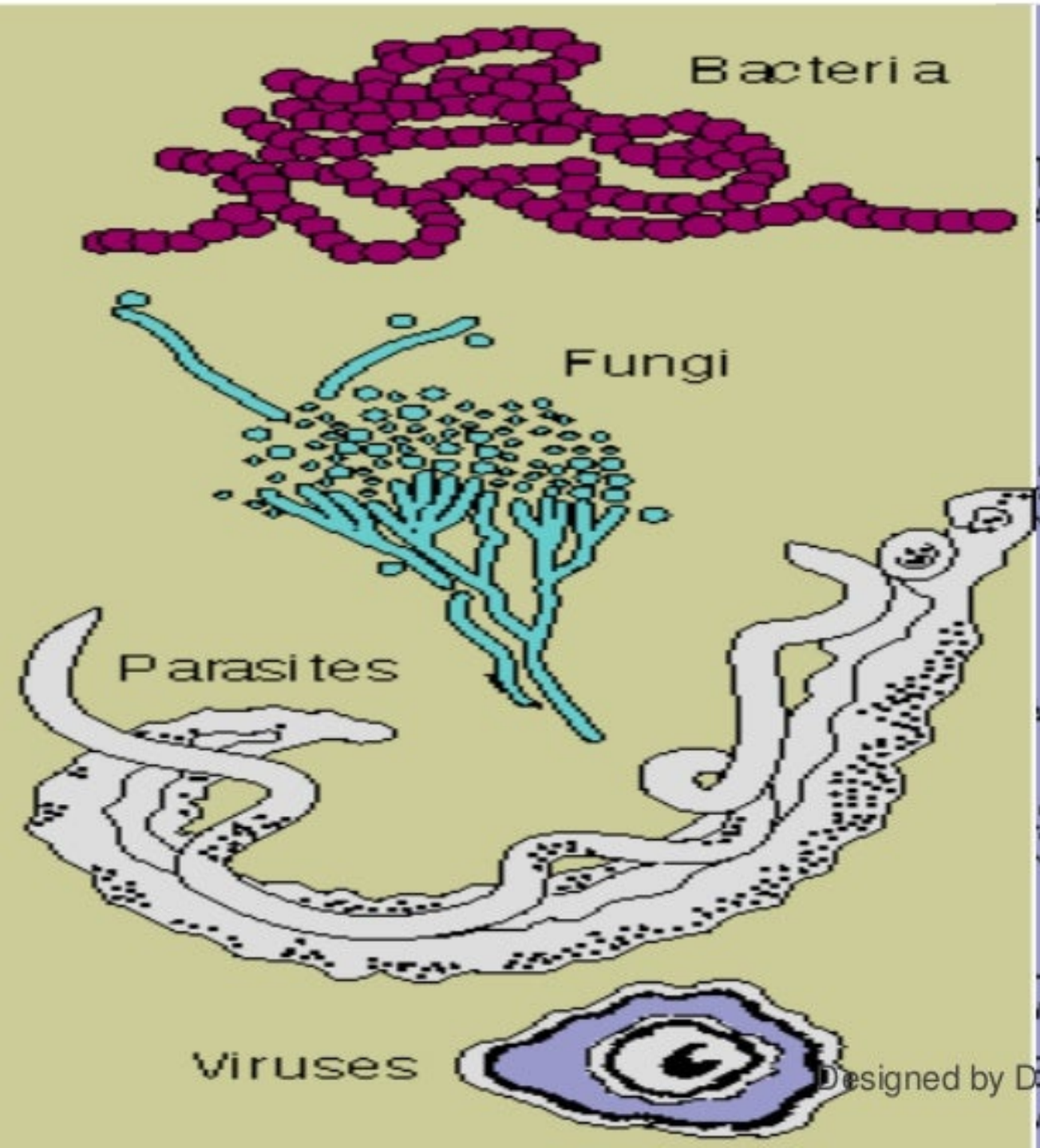


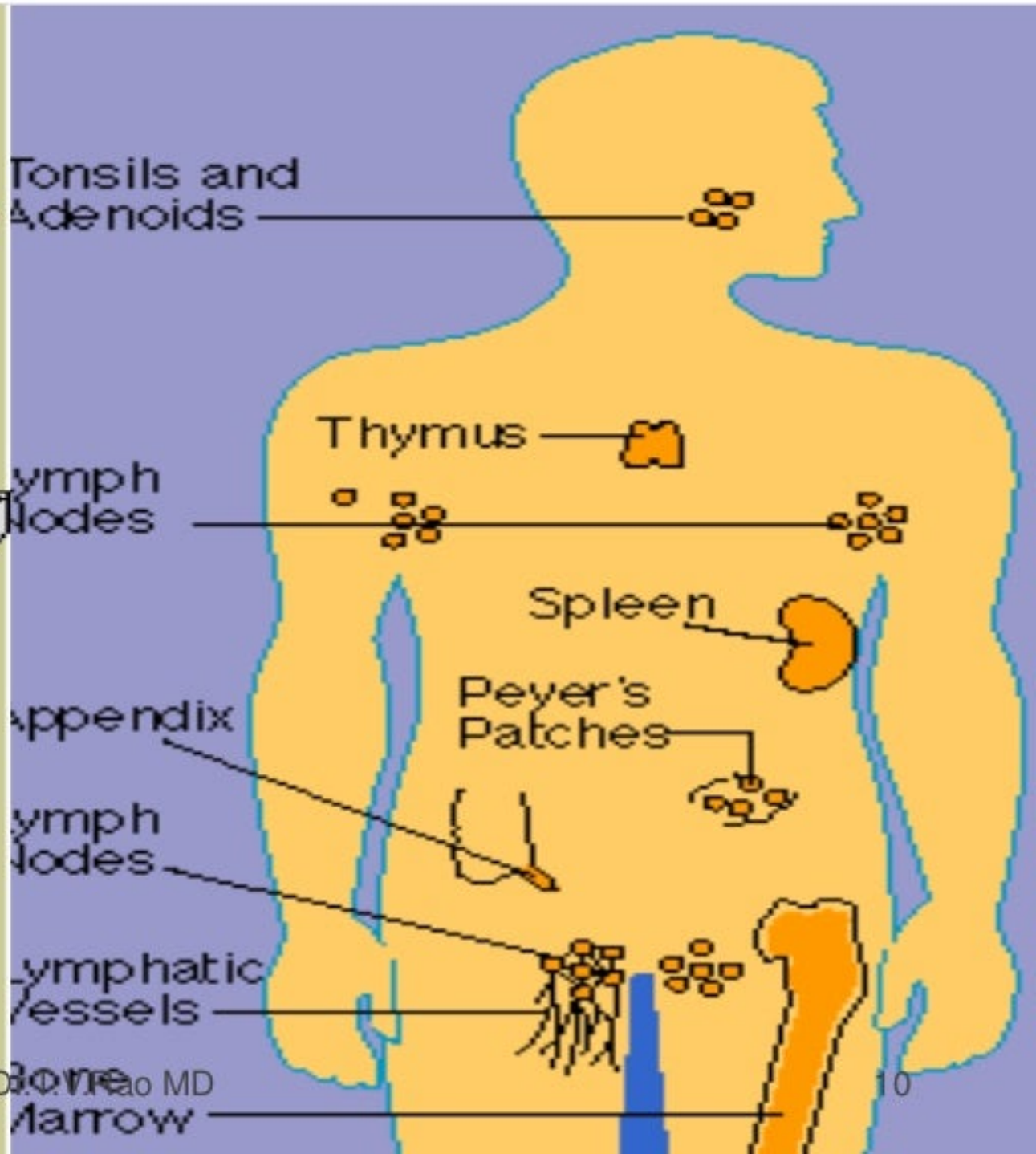
Life is a threat from everything in Nature

THE IMMUNE SYSTEM reacts to any foreign invasion

The Invaders

The Defender

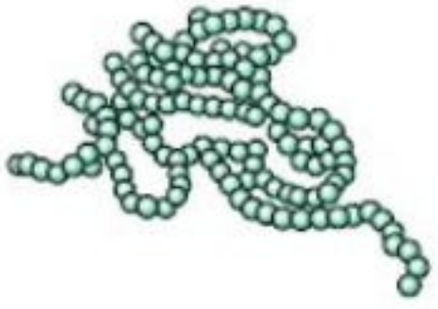


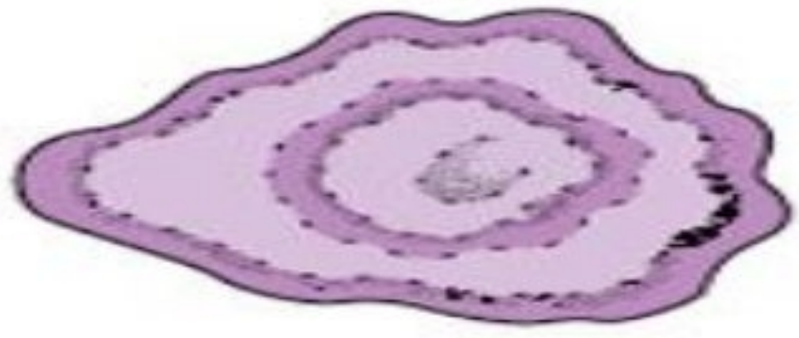


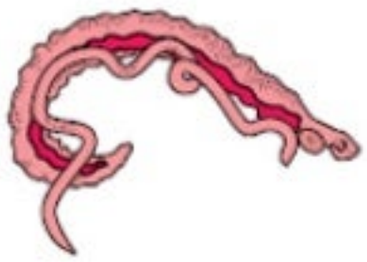
Life is Fight against Foreign Substance

- It has been estimated that during our lifetime, we will encounter a million foreign antigens capable of causing disease, and our bodies need the same amount of lymphocytes to defend against them

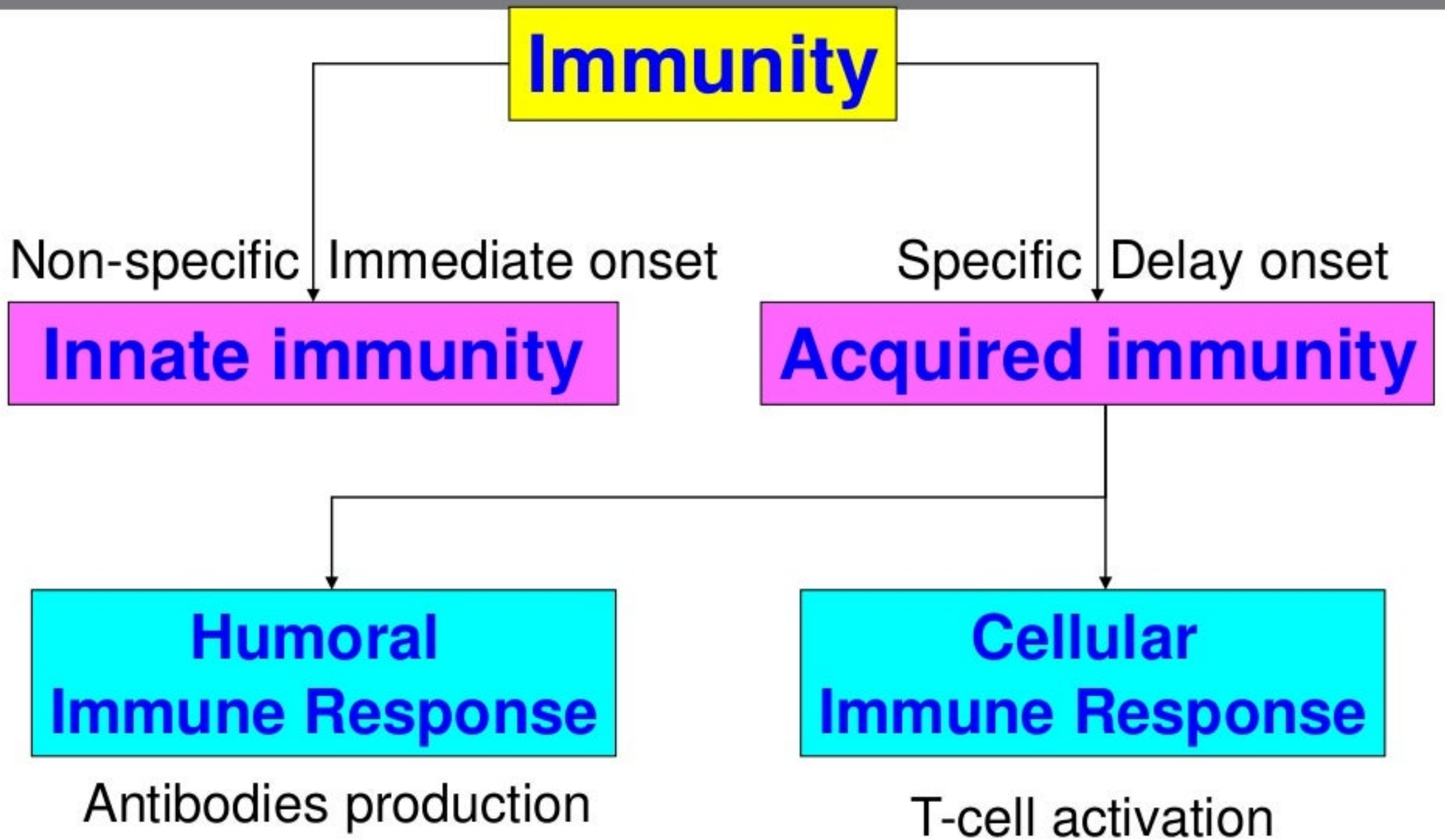
Every moment we are exposed too.







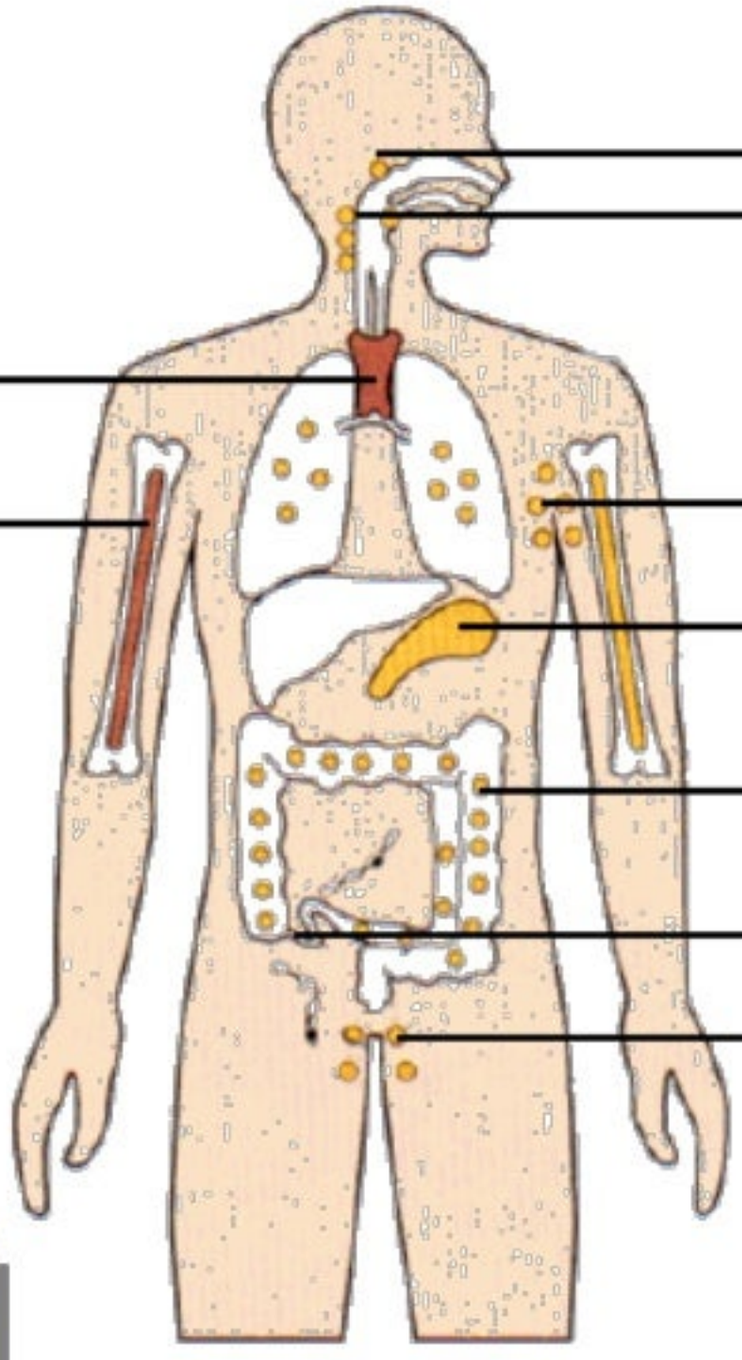
THE EVOLUTION OF IMMUNITY



Organs Of Immune System

- Primary Lymphoid Organs
  - Bone Marrow and Thymus
  - Maturation Site
- Secondary Lymphoid Organs
  - Spleen, lymph nodes,
  - MALT (mucosal associated lymph tissue)
  - GALT (gut associated lymph tissue)
  - Trap antigen, APC, Lymphocyte Proliferation

Lymphoid Organs

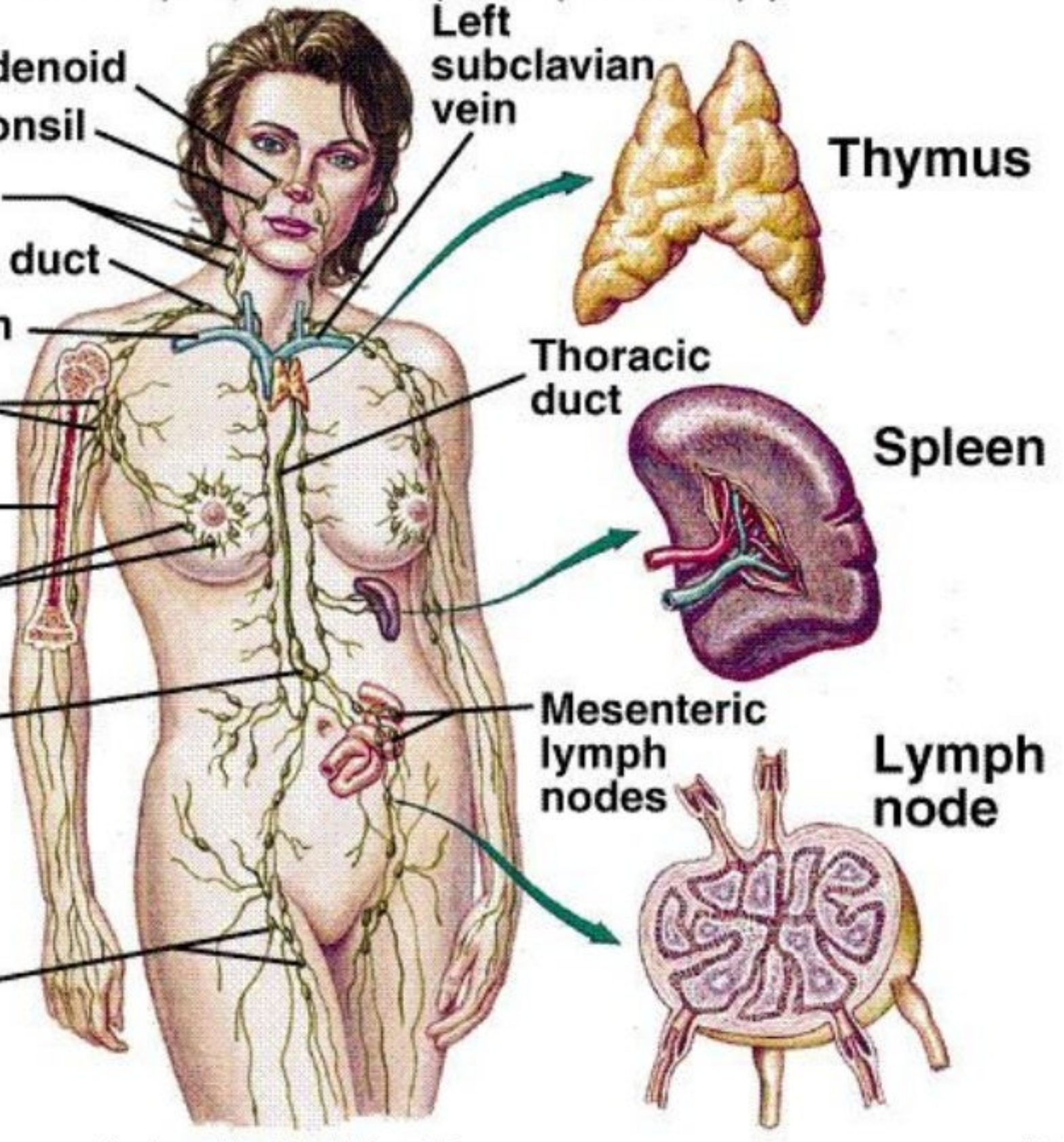


Adenoids
Tonsils
Thymus
Bone Marrow
Lymph nodes
Spleen
Peyer's patches
Appendix
Lymph nodes

Primary Organs

Secondary Organs

Lymph Nodes



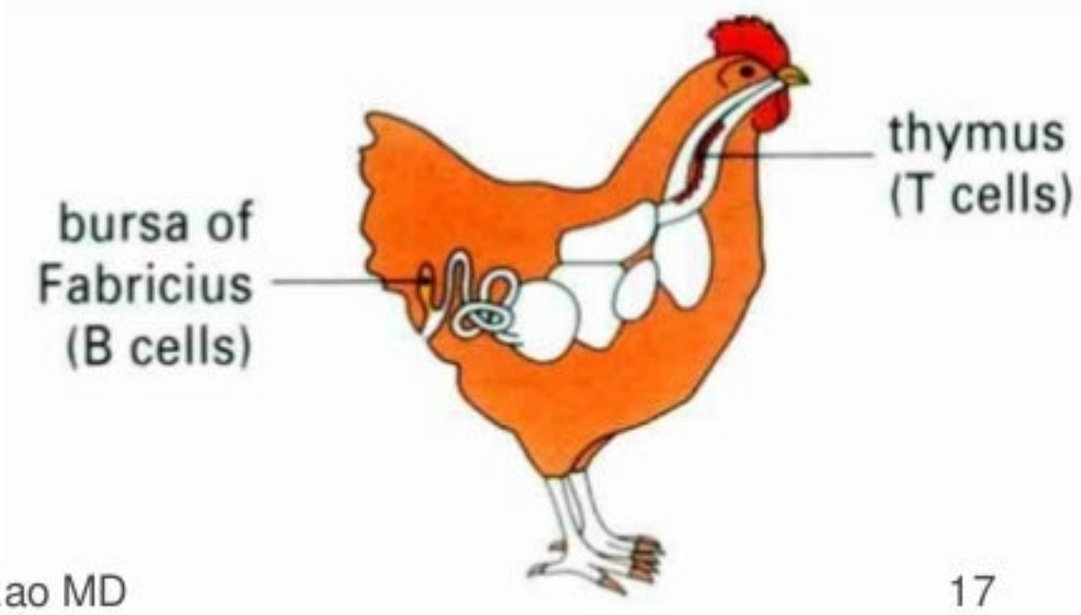
Central Immune organs

Central Immune Organs are the sites of generation, differentiation and maturation of immunocytes.

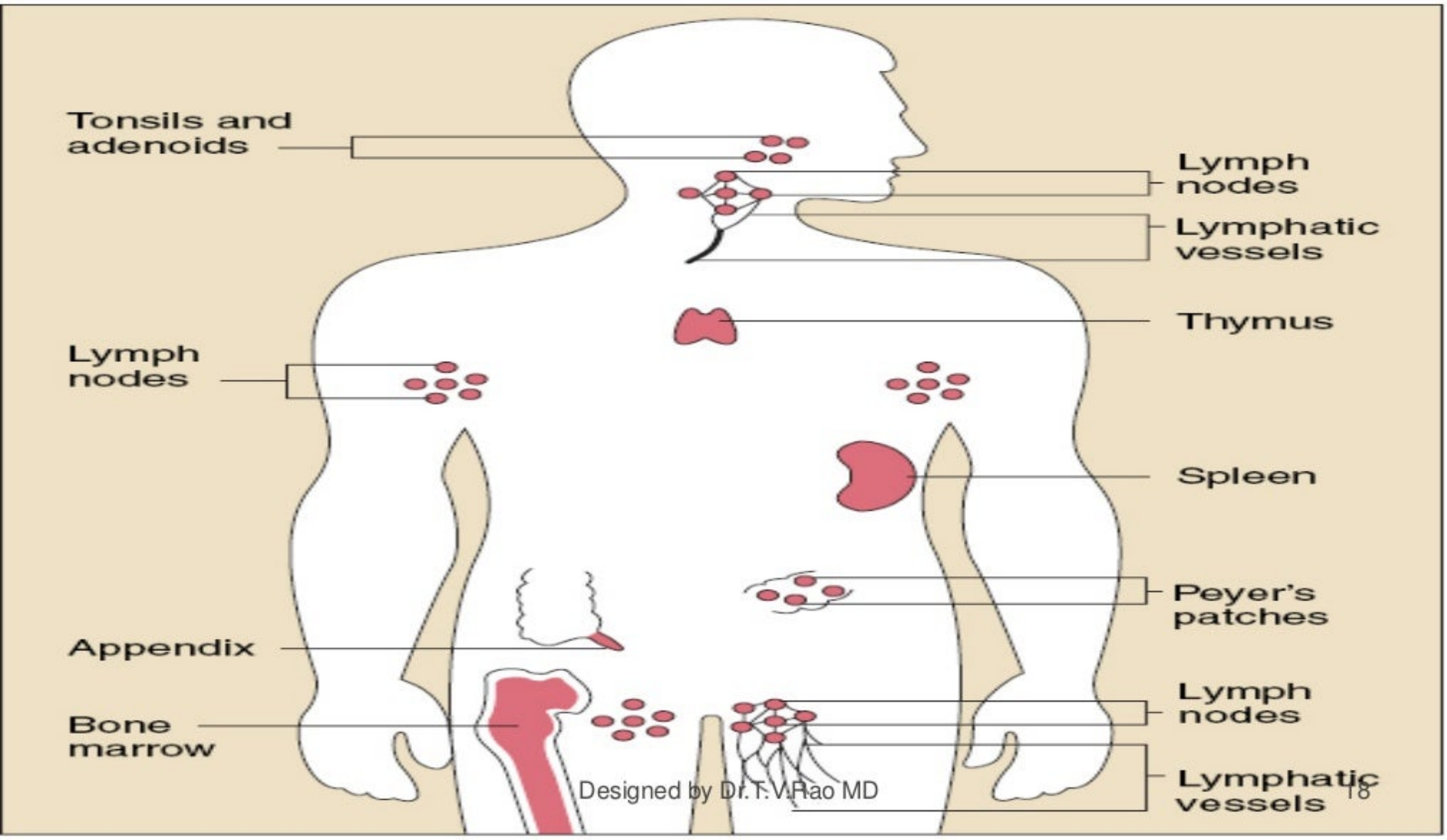
- Bone marrow
- Thymus
- Bursa of Fabricius

(the site of B cells maturation in birds)

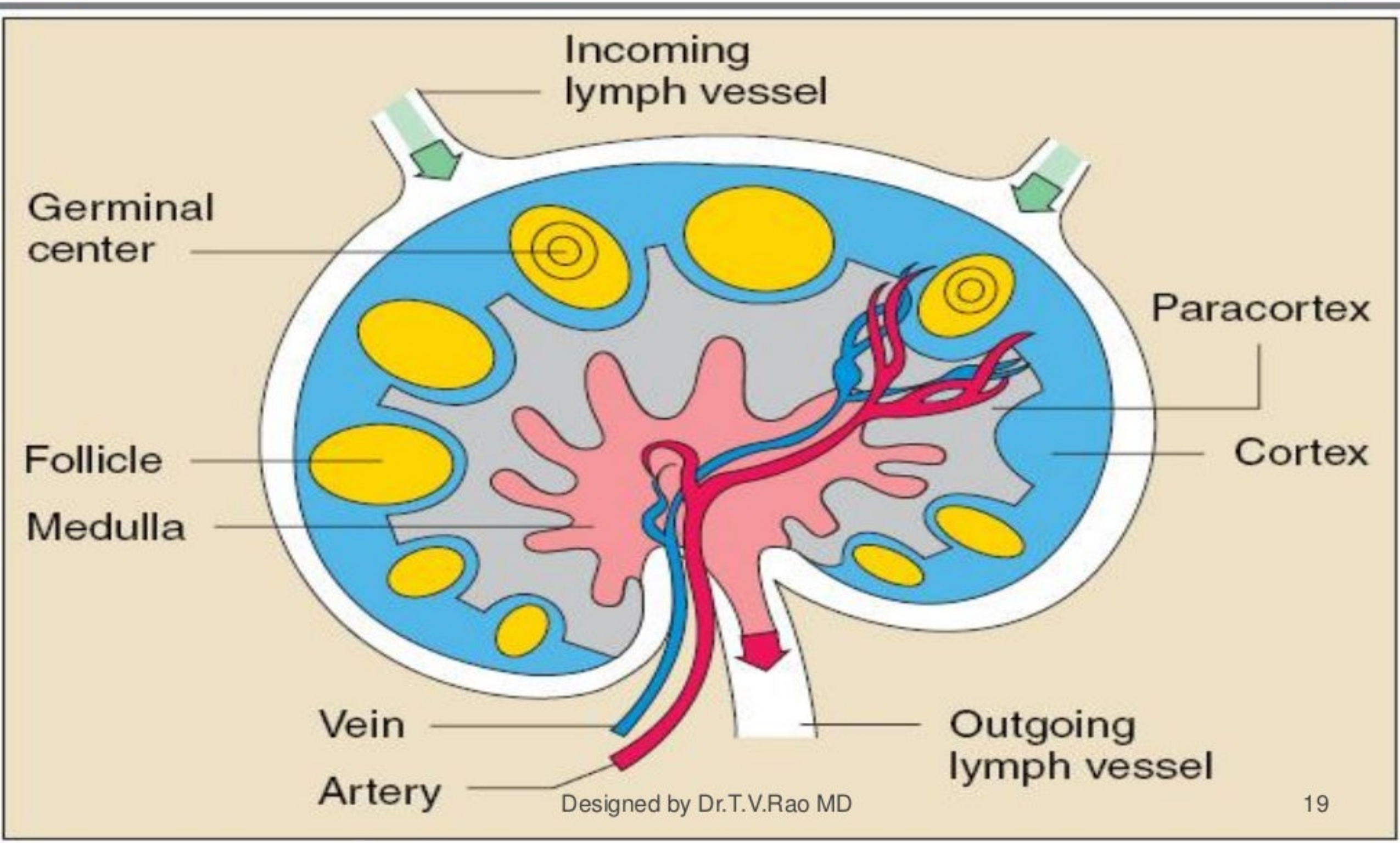
But absent in Humans



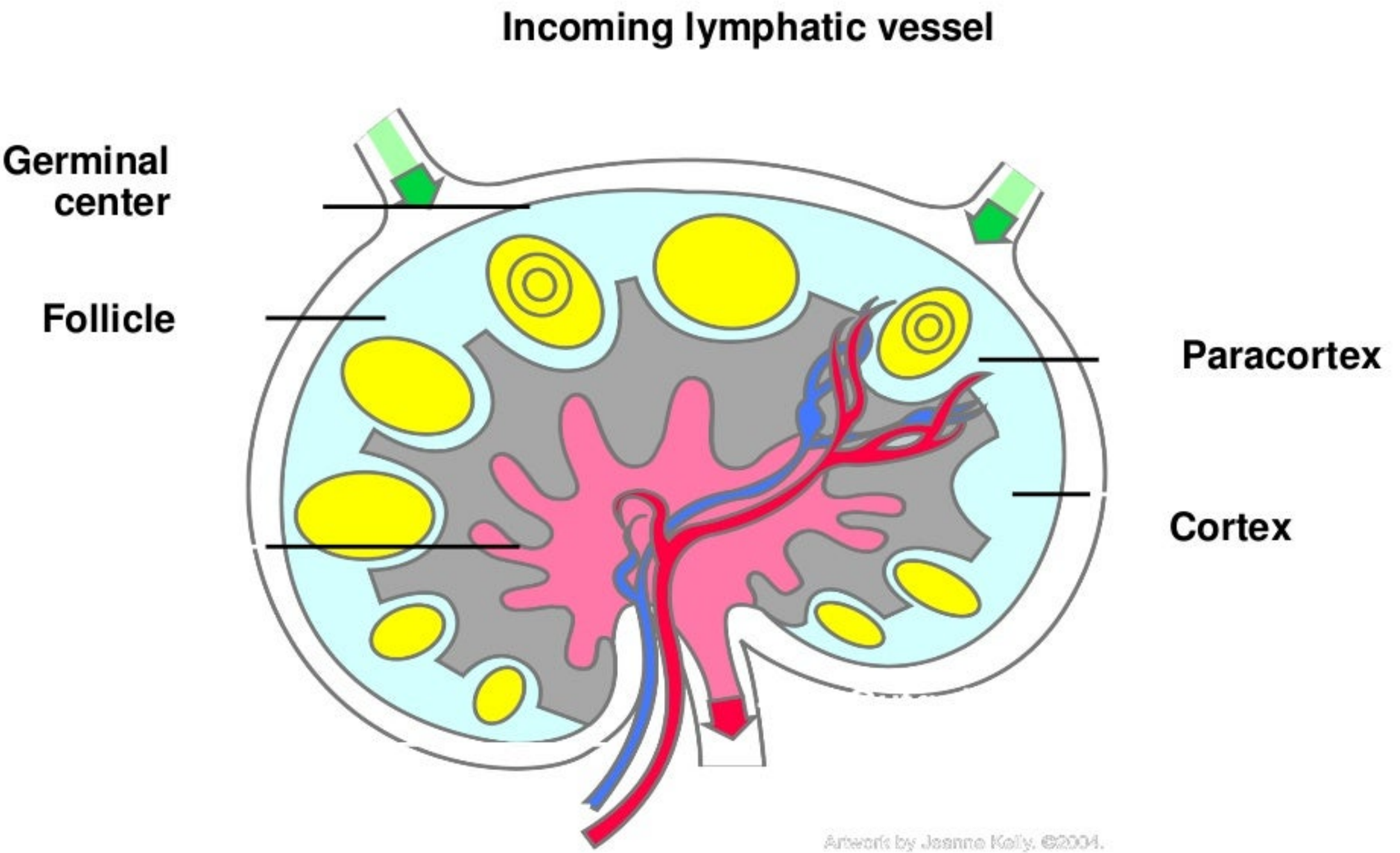
Organs of the Immune System



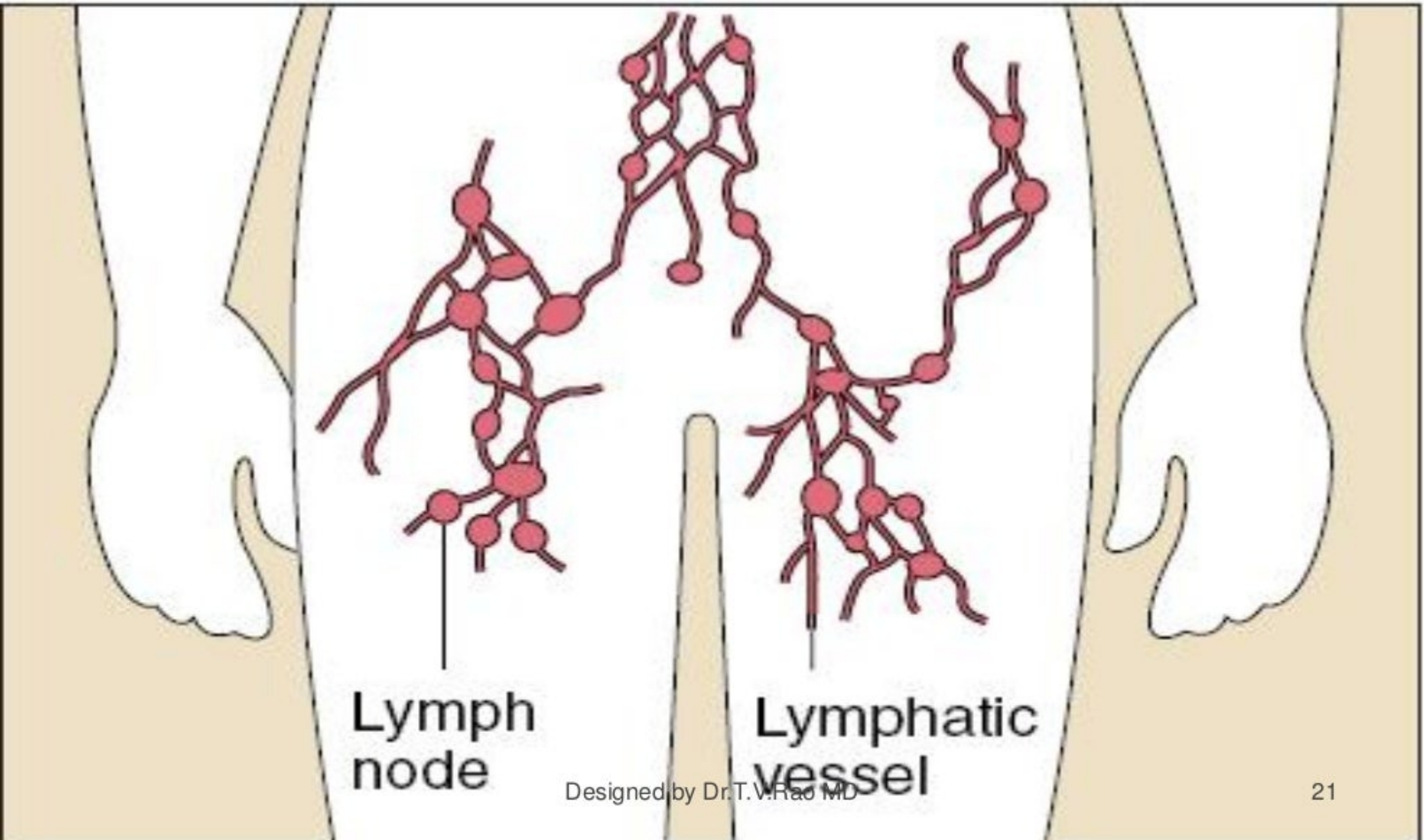
Lymph Node


Incoming
lymph vessel
Germinal
center
Paracortex
Follicle
Cortex
Medulla
Vein
Outgoing
lymph vessel
Artery

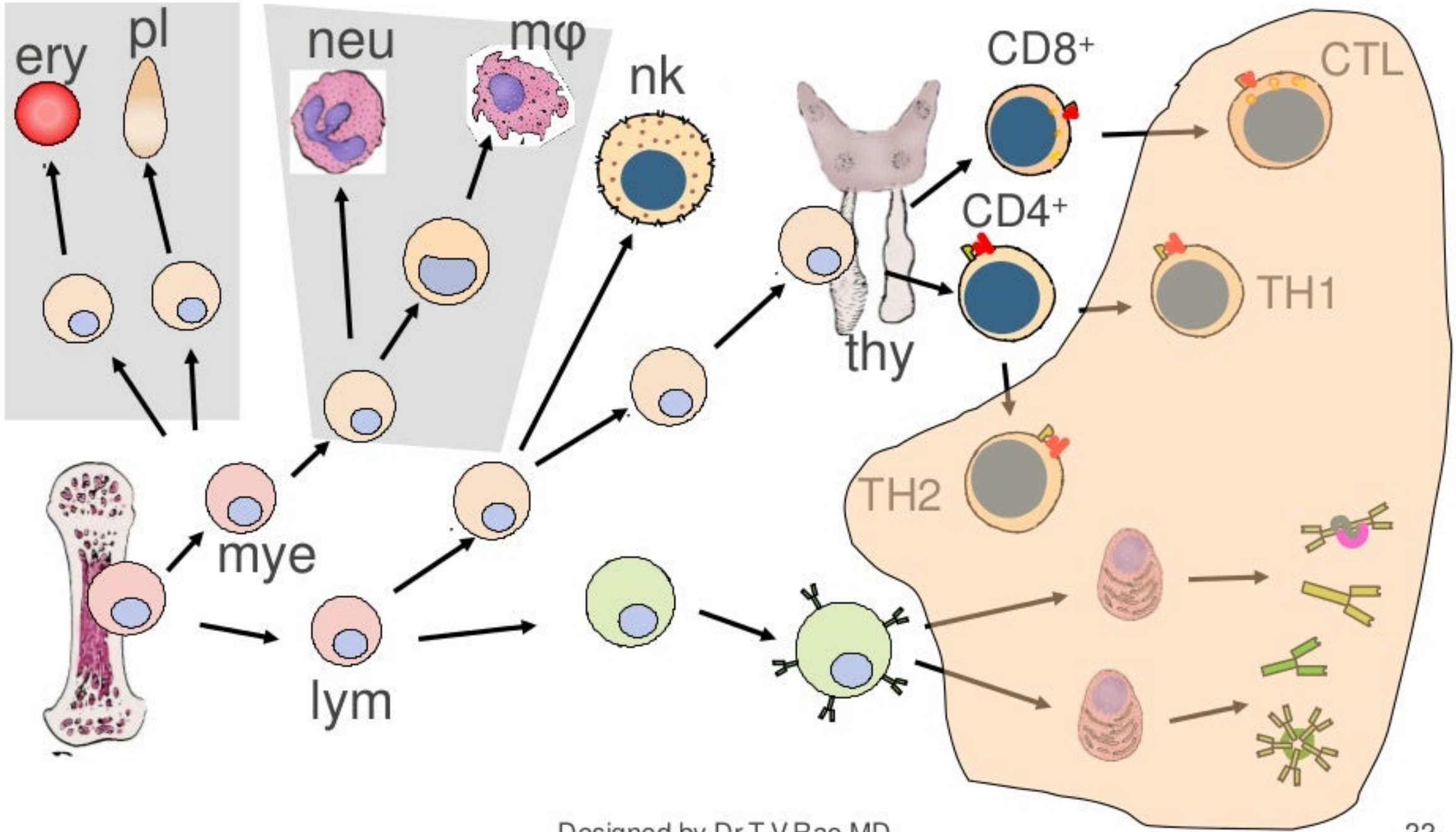
Lymph Node


Incoming lymphatic vessel
Germinal center
Follicle
Paracortex
Cortex
Artwork by Joanne Kelly. ©2004.

lymphatic Vessel



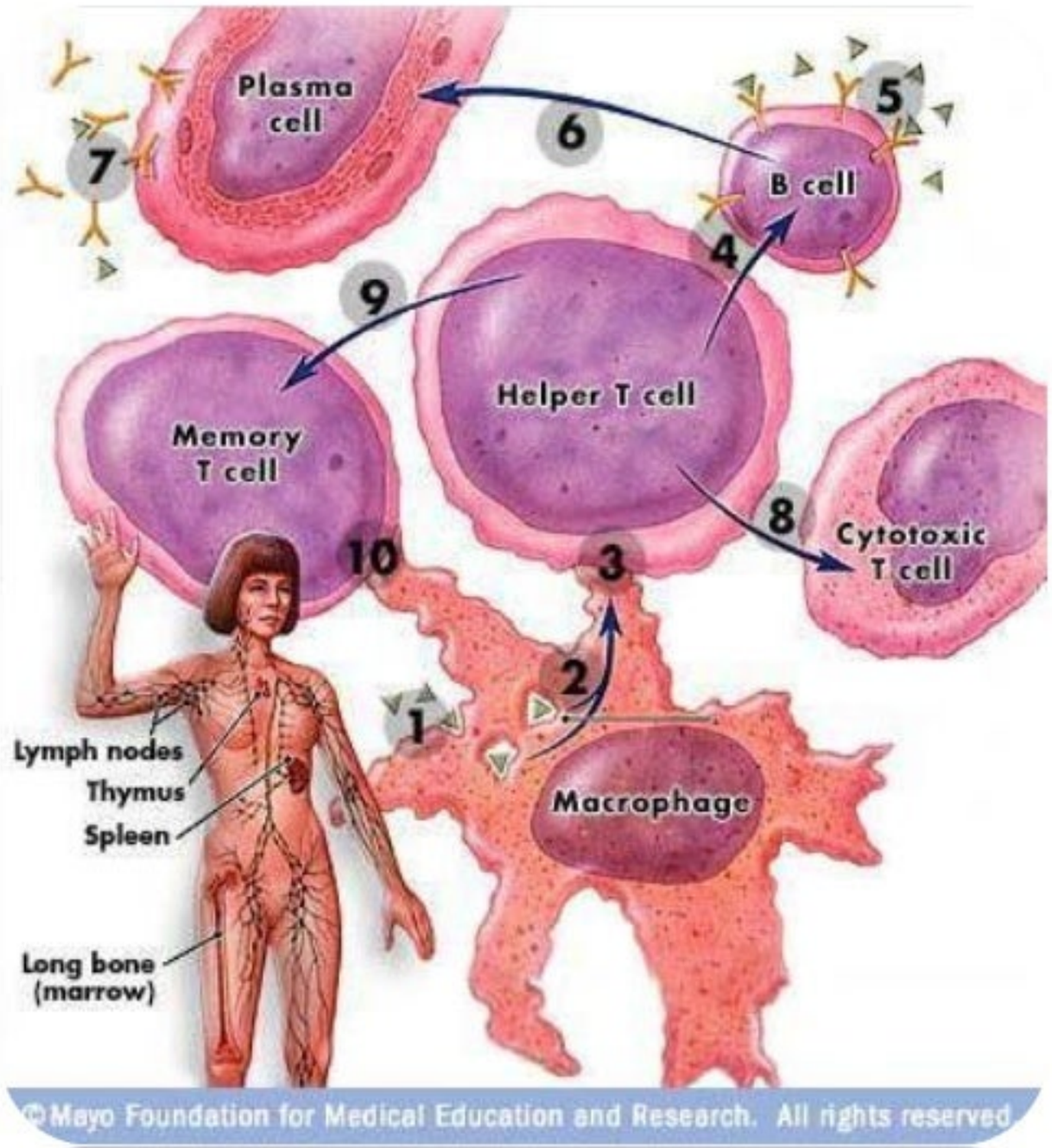
Development of the Immune System



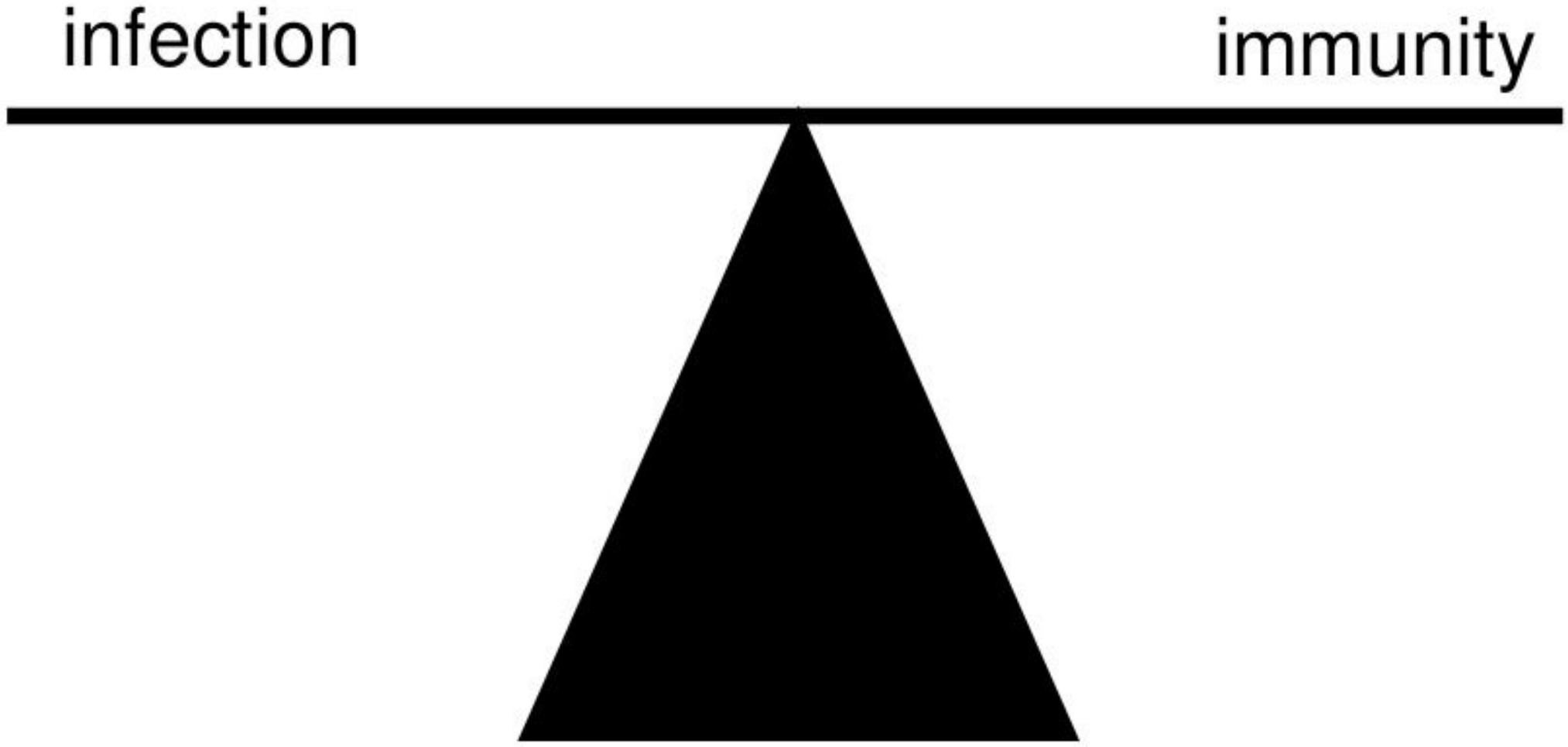
Function of the Immune System (Self/Non-self Discrimination)

- To protect from pathogens
  - Intracellular (*e.g.* viruses and some bacteria and parasites)
  - Extracellular (*e.g.* most bacteria, fungi and parasites)

- To eliminate modified or altered self



Infection and Immunity Balance

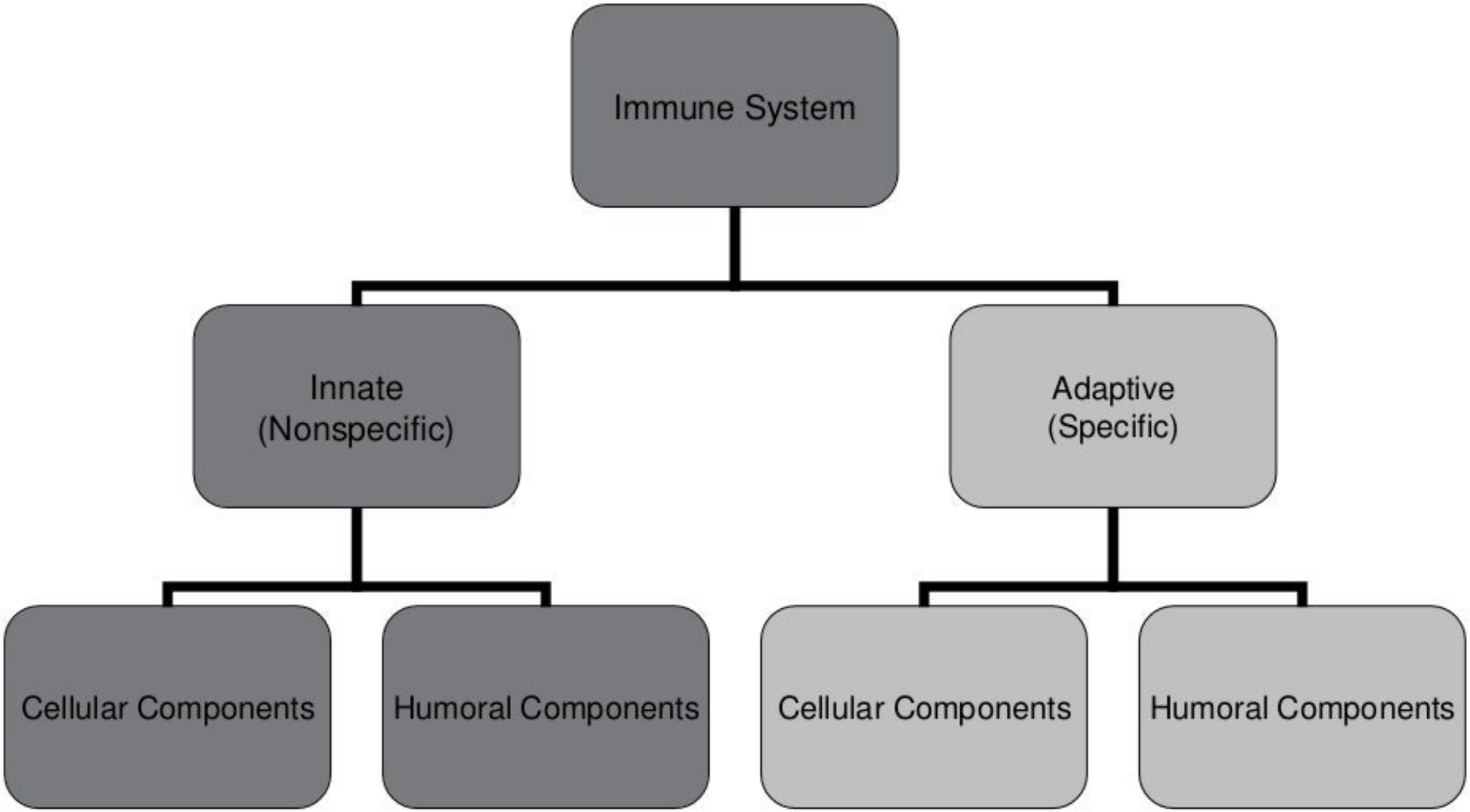


$$\text{Disease} = \frac{\text{Bolus of infection x virulence}}{\text{immunity}}$$

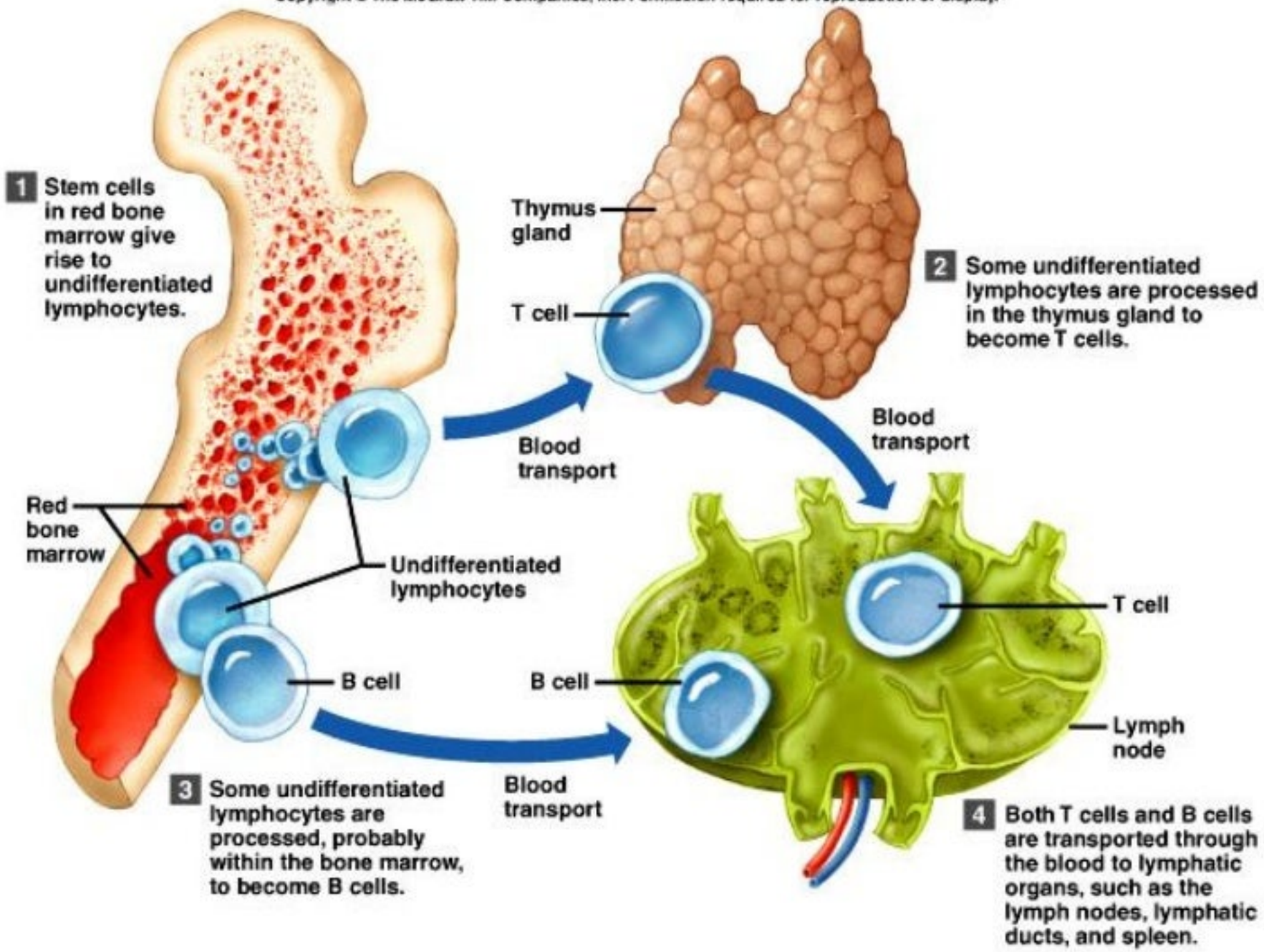
Effects of the Immune System

- Beneficial:
  - Protection from Invaders
  - Elimination of Altered Self
- Detrimental:
  - Discomfort and collateral damage (inflammation)
  - Damage to self (hypersensitivity or autoimmunity)

Overview of the Immune System



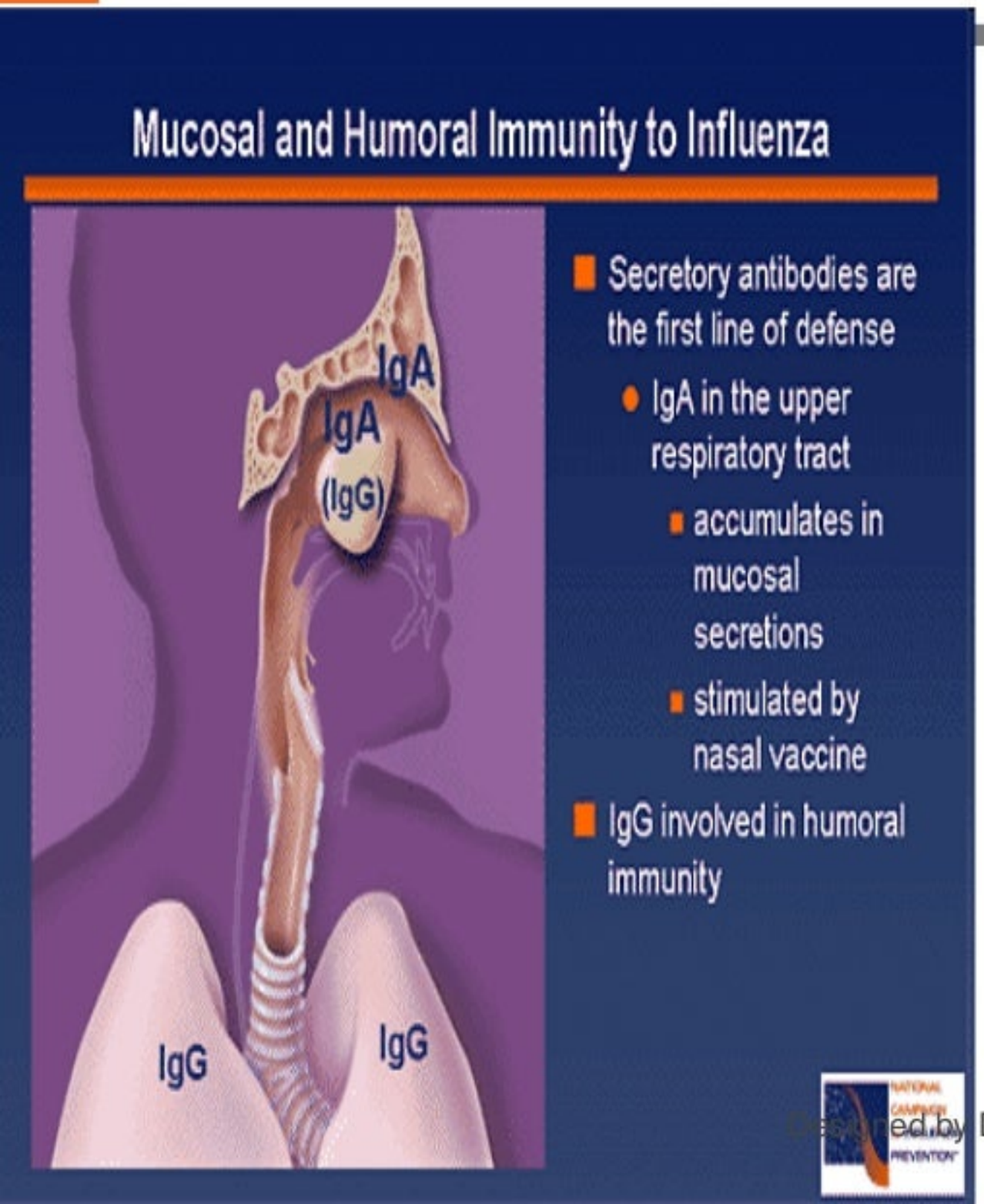
lymphocyte Origins



Functional Basis of immune System

- The **immune system** is composed of two major subdivisions, the innate or nonspecific immune system and the **adaptive or specific immune system.** The innate immune system is a primary defence mechanism against invading organisms, while the adaptive immune system acts as a second line of defence.

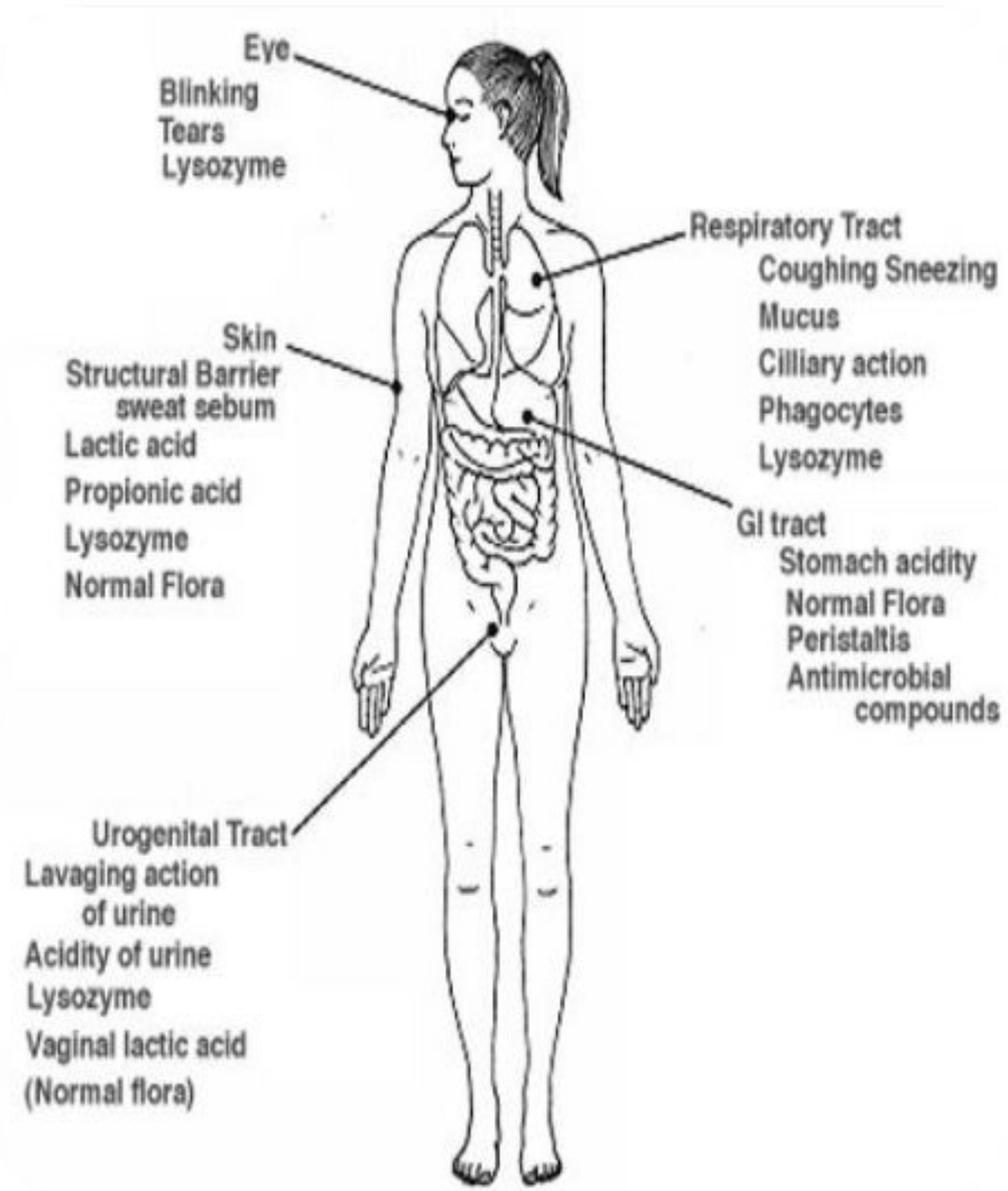
Innate Host Defenses Against Infection



- Anatomical barriers
  - Mechanical factors
  - Chemical factors
  - Biological factors
- Humoral components
  - Complement
  - Coagulation system
  - Cytokines

1st line of defenses

- Includes chemicals, Structure of skin/other epithelia, and mechanisms Cells – mainly neutrophils and macrophage

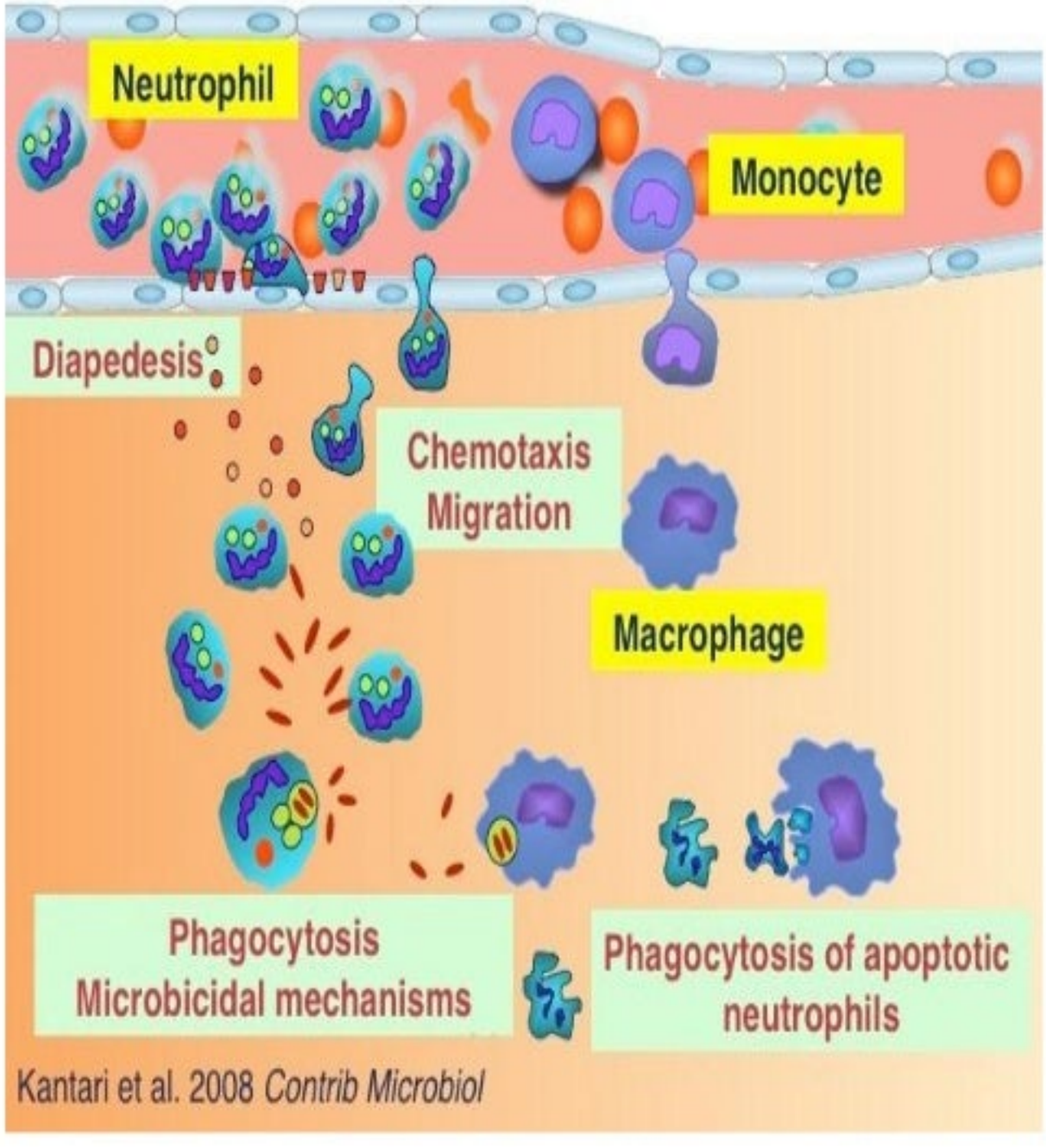


First-Line Defenses /Innate Immune System-

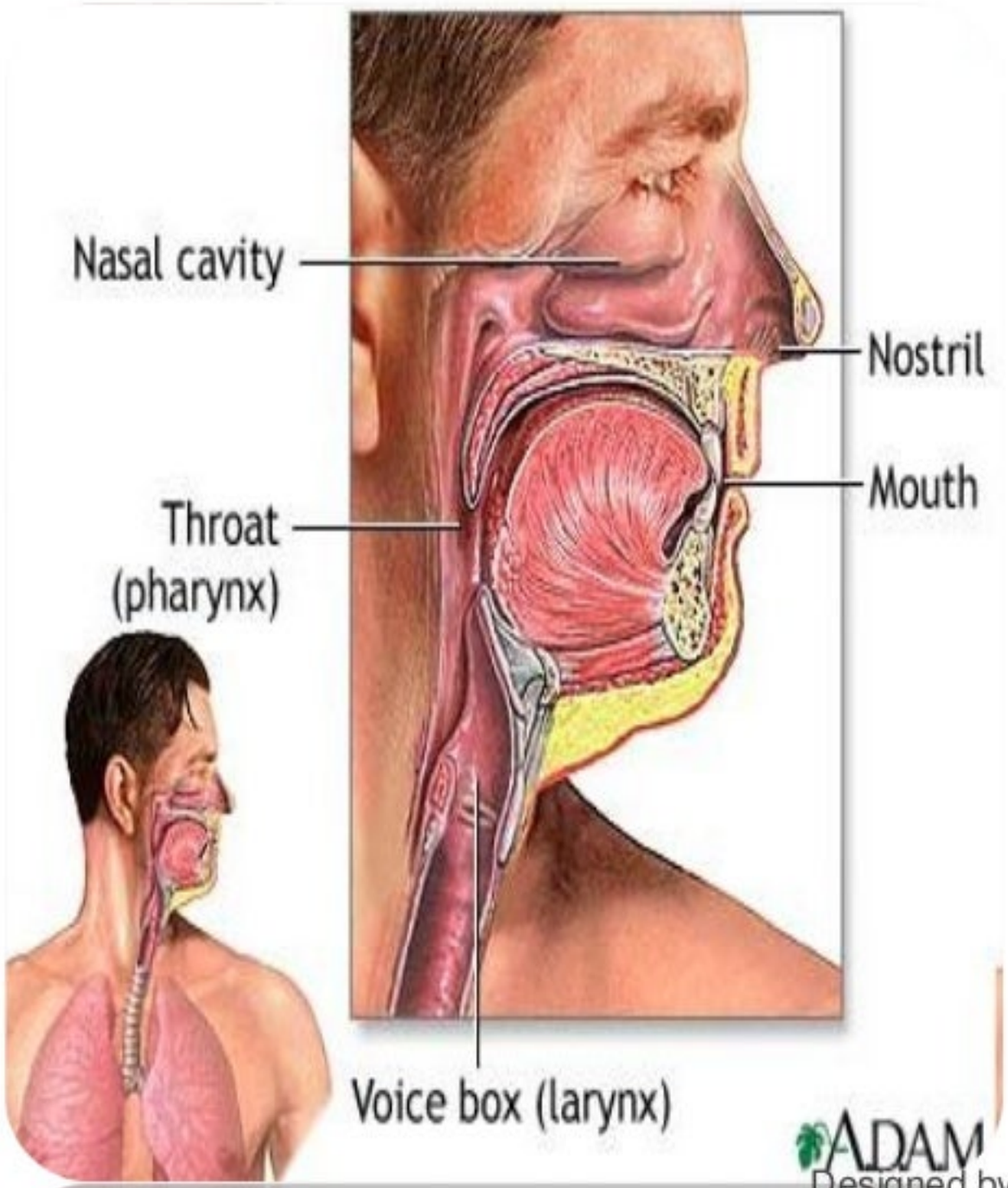
- *First-Line Defenses /Innate Immune System-* The body's first line of defense against pathogens uses mostly physical and chemical barriers such as
- Skin – acts as a barrier to invasion
- Sweat – has chemicals which can kill different pathogens.
- Tears - have lysozyme which has powerful digestive abilities that render antigens harmless.

Others – Innale Immunity

- Saliva – also has lysozyme.
- Mucus - can trap pathogens, which are then sneezed, coughed, washed away, or destroyed by chemicals.
- Stomach Acid – destroys pathogens



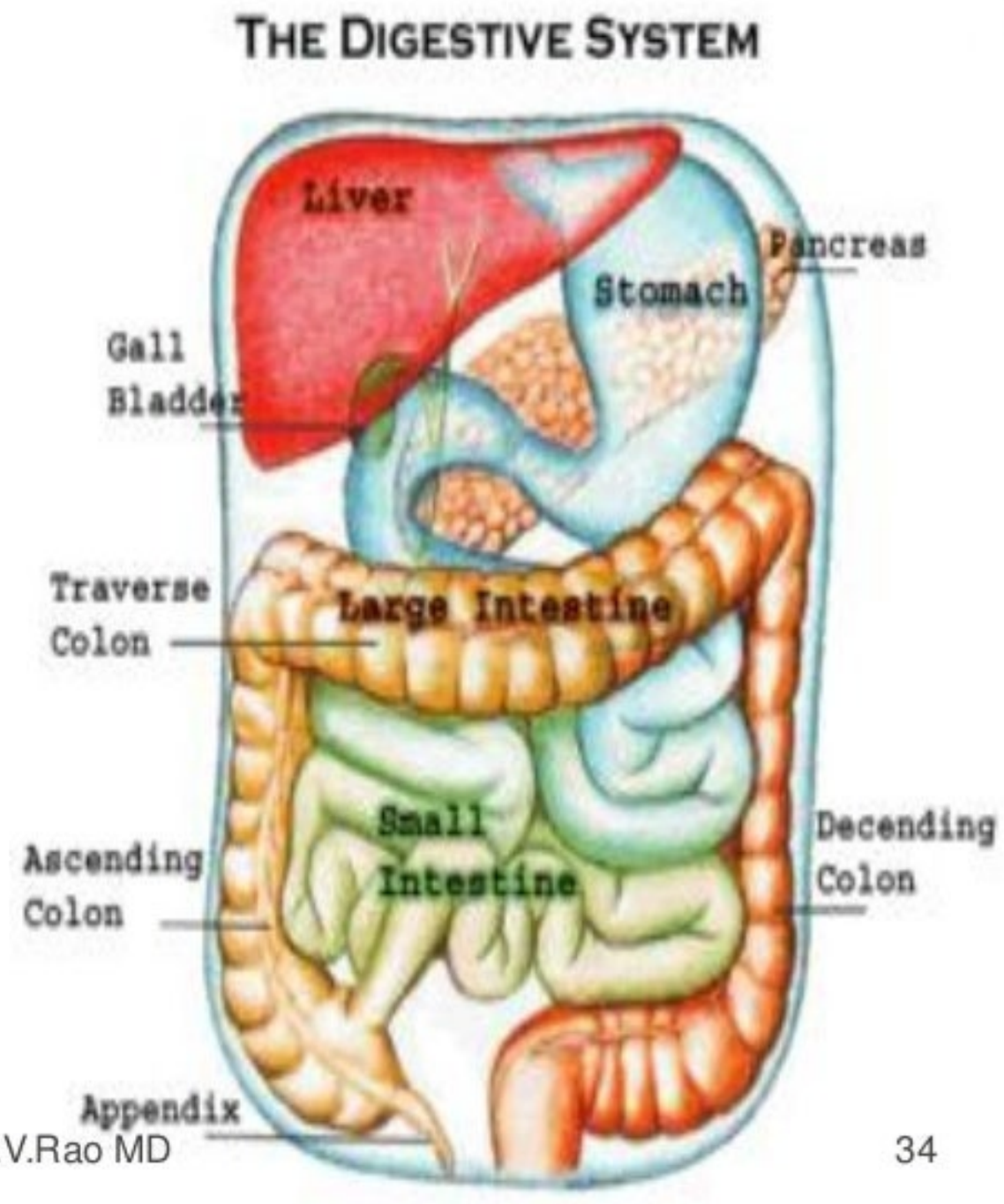
Life is at threat from what we breathe



Our 1st Line of Defense... Saves us from several threats

- The Integumentary System...
  - Skin
  - Mucous membranes
  - Mucous

- provides a physical barrier preventing microbial access



Bacteria

Viruses

Innate response

Physical barriers

Mucous membranes

Cytokines

Cilia

Antimicrobial secretions

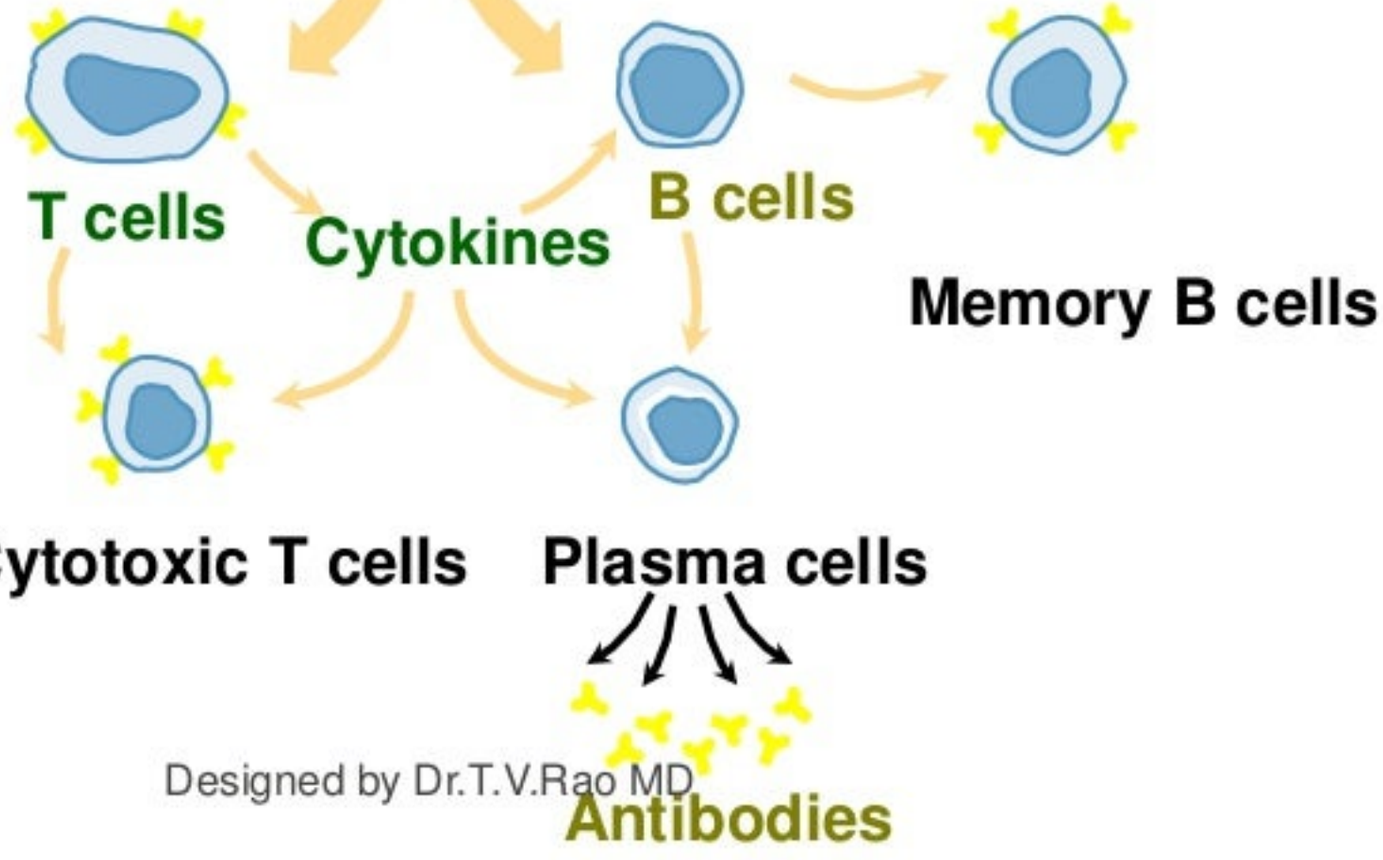
Macrophages

Acquired response

Macrophages present antigens

Cellular response

Humoral response



Inflammatory response

A non-specific response triggered by

- injury
- penetration of bacteria

-skin, respiratory, digestive, urinary or reproductive tract

Two main players

- histamine
- complement

Histamine

- dilates local blood vessels
- increases capillary permeability

Result is redness, heat and swelling

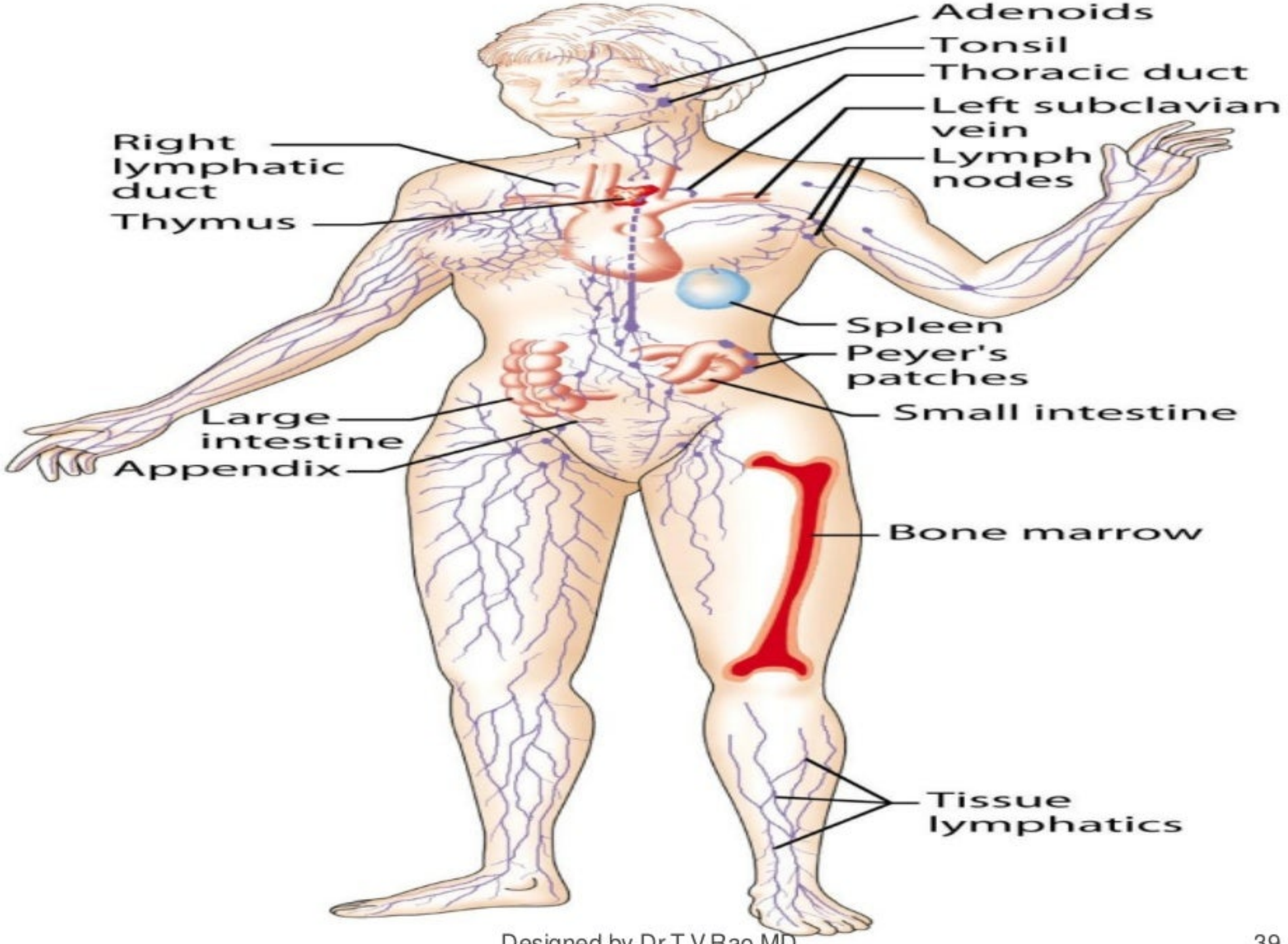
heat
- unfavorable to microorganisms
- mobilizes white blood cells (monocytes)
- raises metabolic rate of surrounding cells

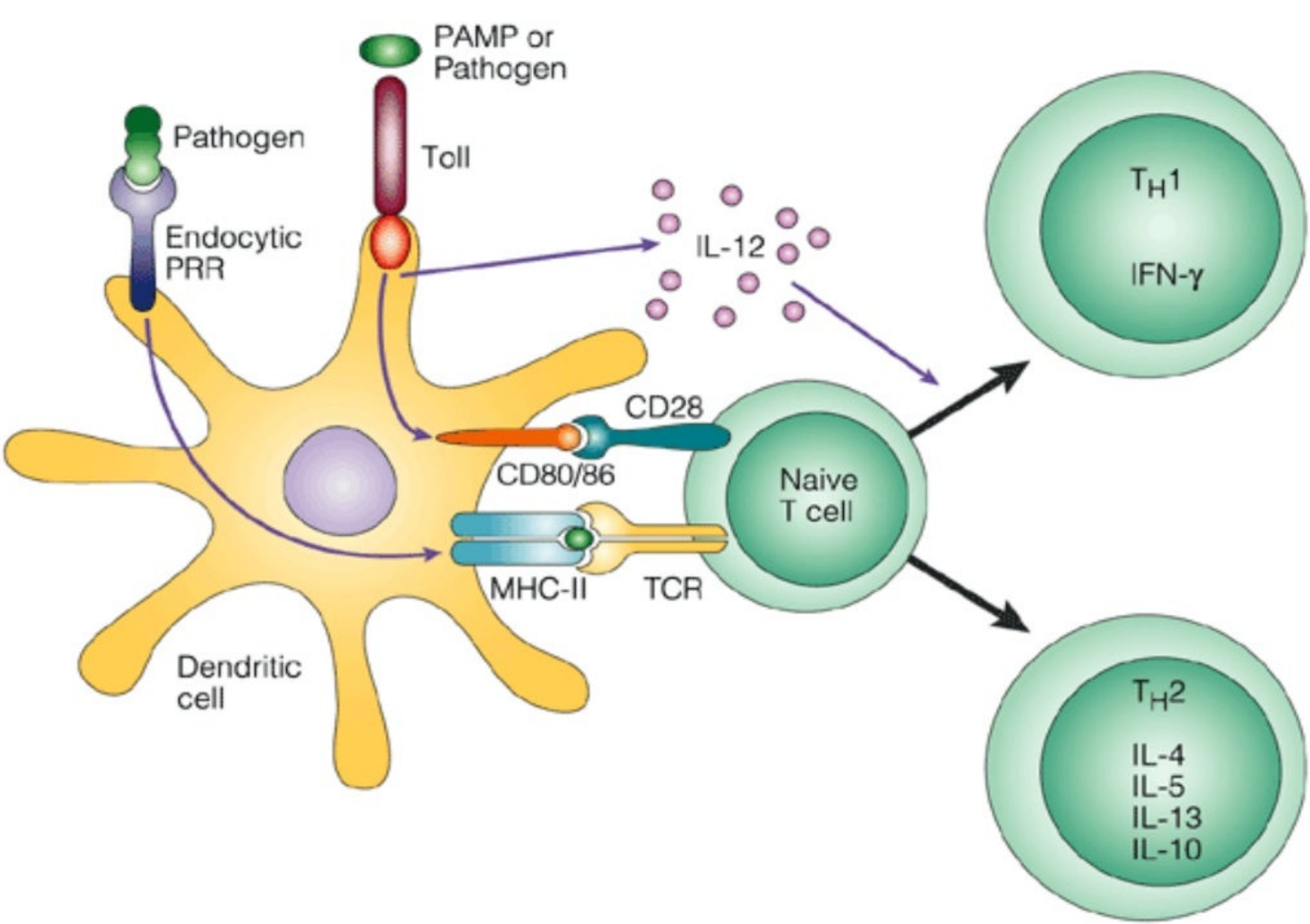
Complement - chemotaxsis agent
- recruits in WBC to injury site

The <u>Inflammatory Response</u>
- starts with release of histamine and other chemicals
- ends with WBC cleaning up the debris

Organs Of Immune System

- Primary Lymphoid Organs
  - Bone Marrow and Thymus
  - Maturation Site
- Secondary Lymphoid Organs
  - Spleen, lymph nodes,
  - MALT (mucosal associated lymph tissue)
  - GALT (gut associated lymph tissue)
  - Trap antigen, APC, Lymphocyte Proliferation

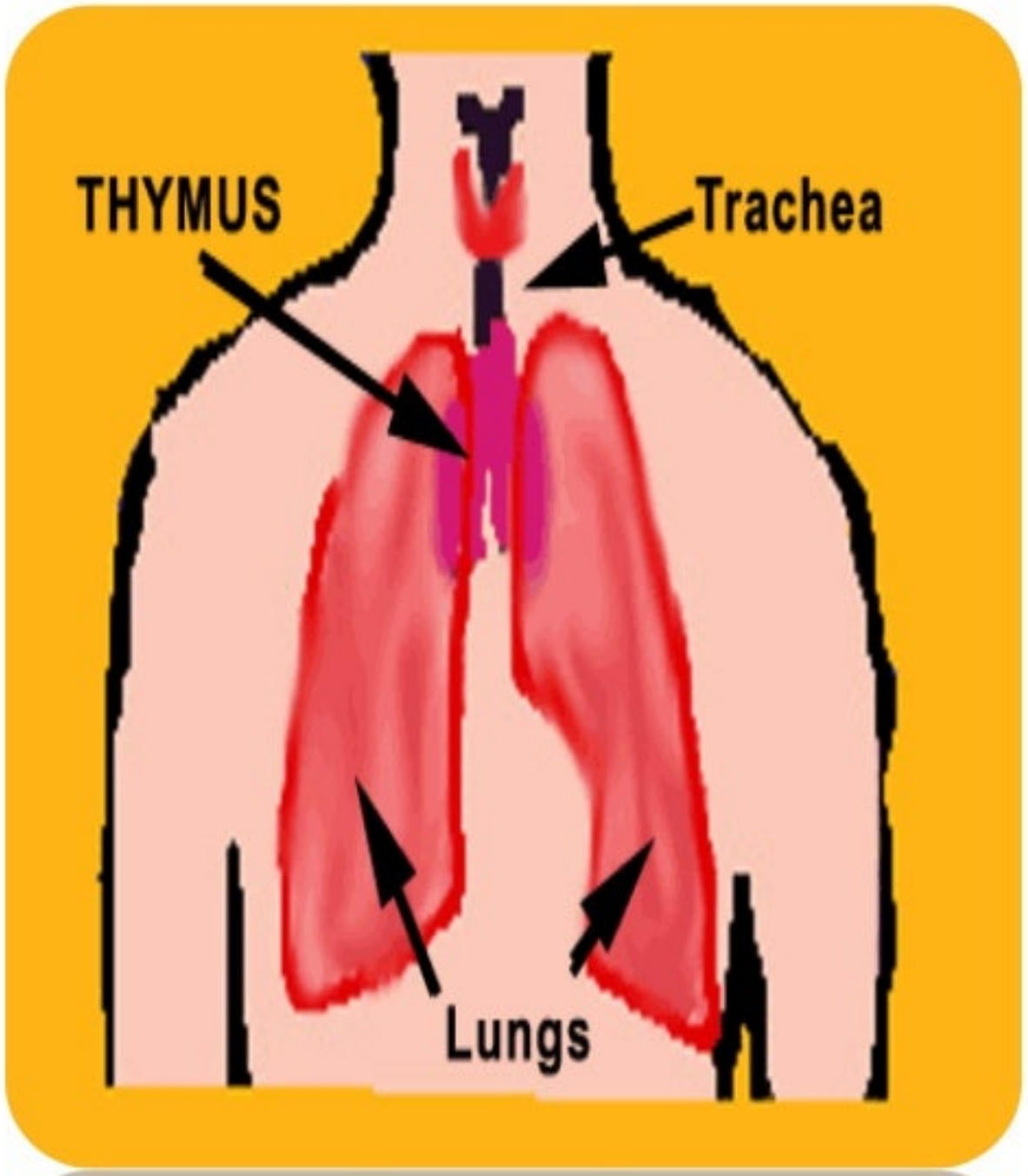

Adenoids
Tonsil
Thoracic duct
Left subclavian vein
Lymph nodes
Right lymphatic duct
Thymus
Spleen
Peyer's patches
Small intestine
Large intestine
Appendix
Bone marrow
Tissue lymphatics



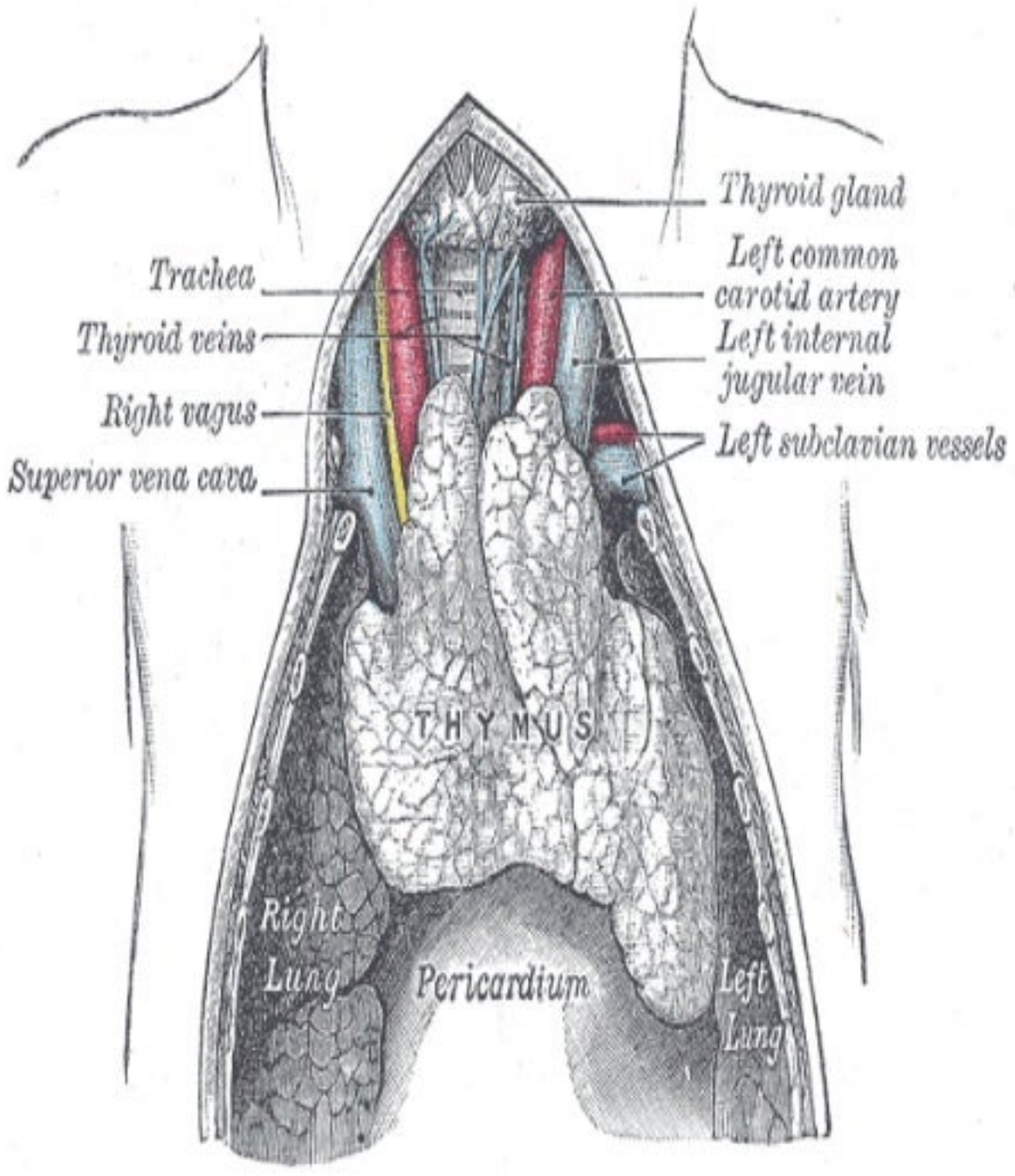
Nature Reviews | Immunology

Thymus

- Bilobed Organ on Top of Heart
- Reaches Max. Size During Puberty
  - 70g infants, 3 g in adults
- 95-99% Of T Cells Die in Thymus
  - self reactivity or no reactivity to Ag
- Consists of Cortex and Medulla
- Rat Thymocytes Sensitive to Glucorticoids

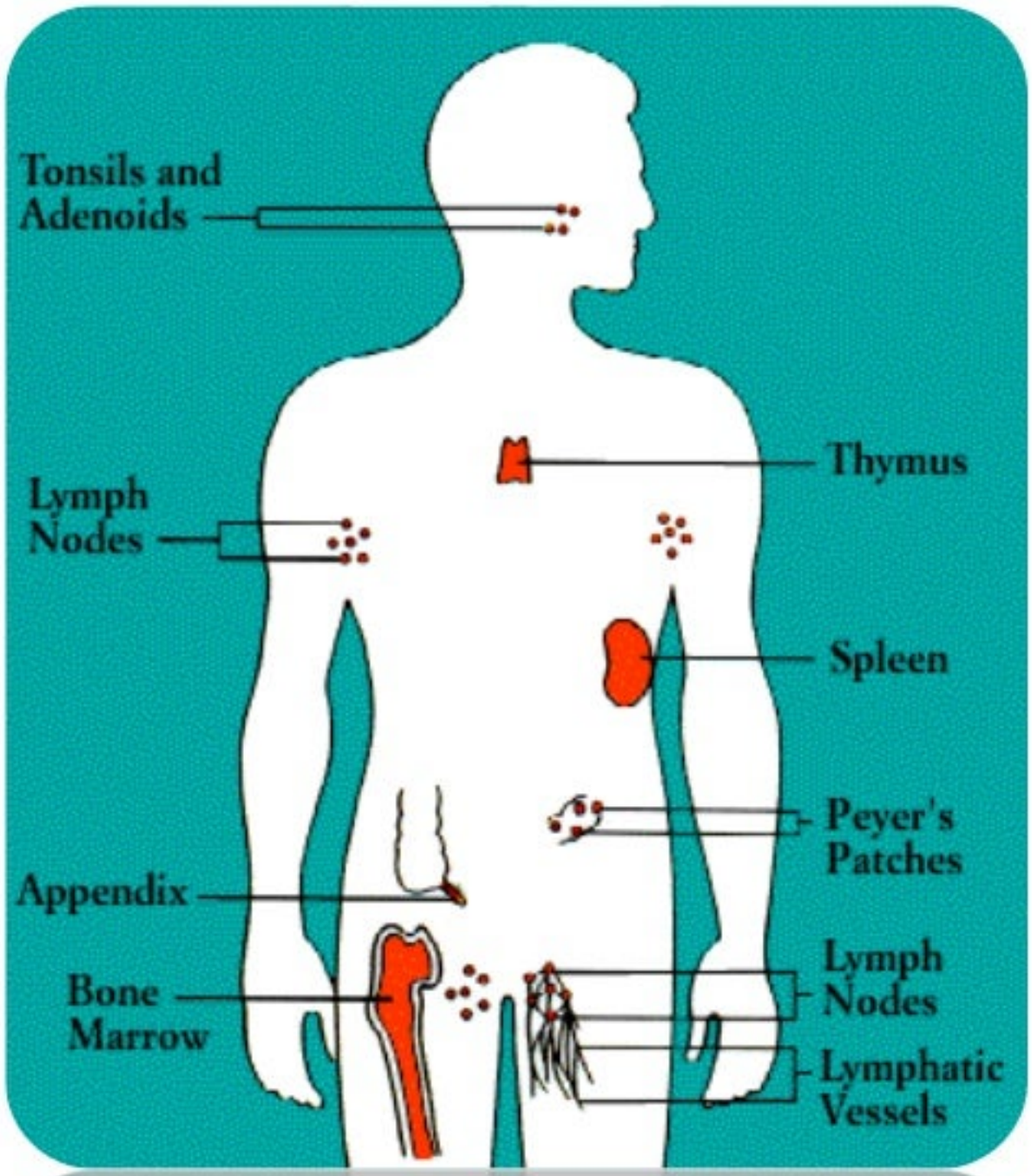


Anatomy



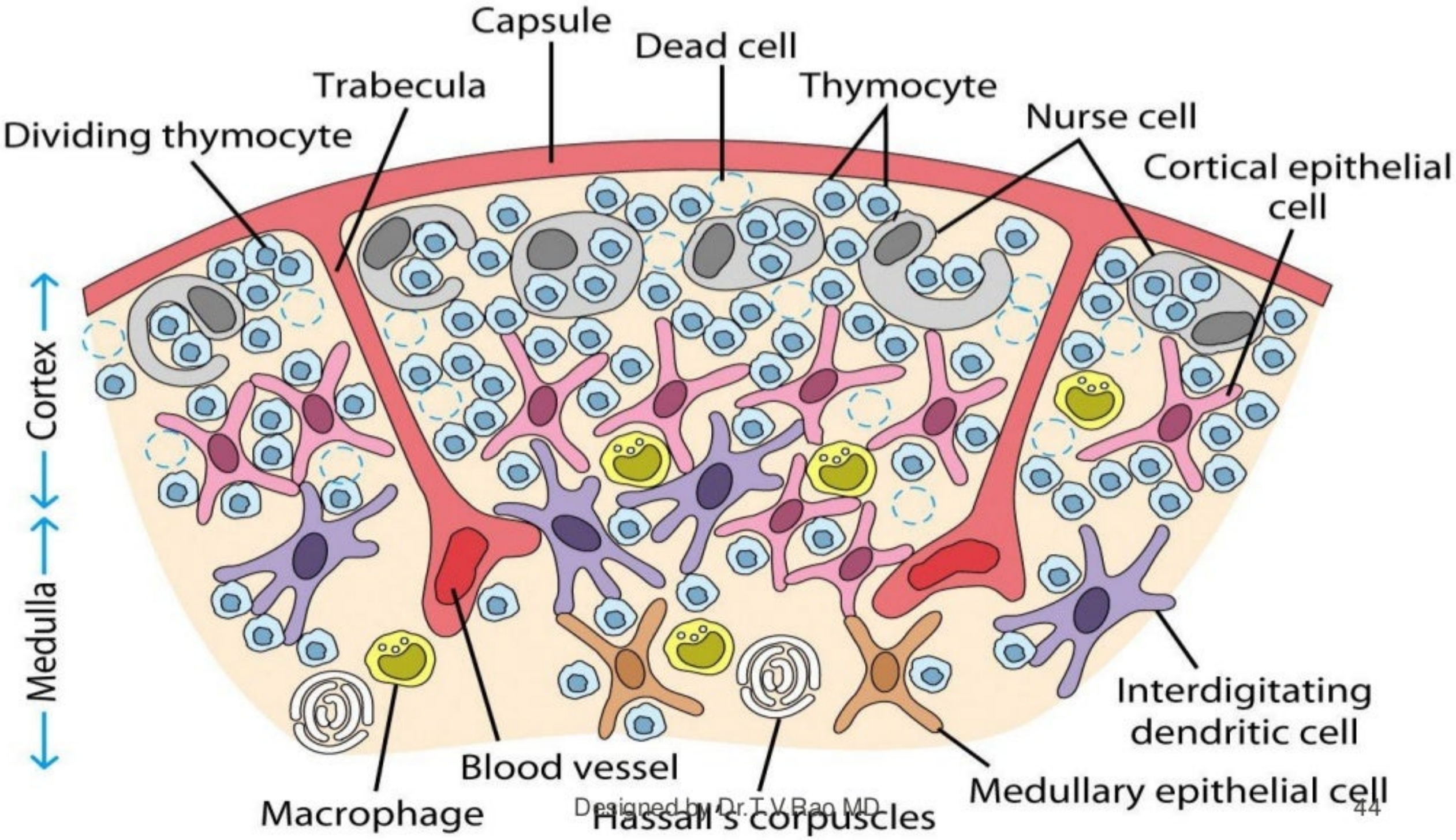
- The thymus gland is found in the thorax in the anterior mediastinum. It gradually enlarges during childhood but after puberty it undergoes a process of involution resulting in a reduction in the functioning mass of the gland. It continues to function throughout life, however

Anatomy



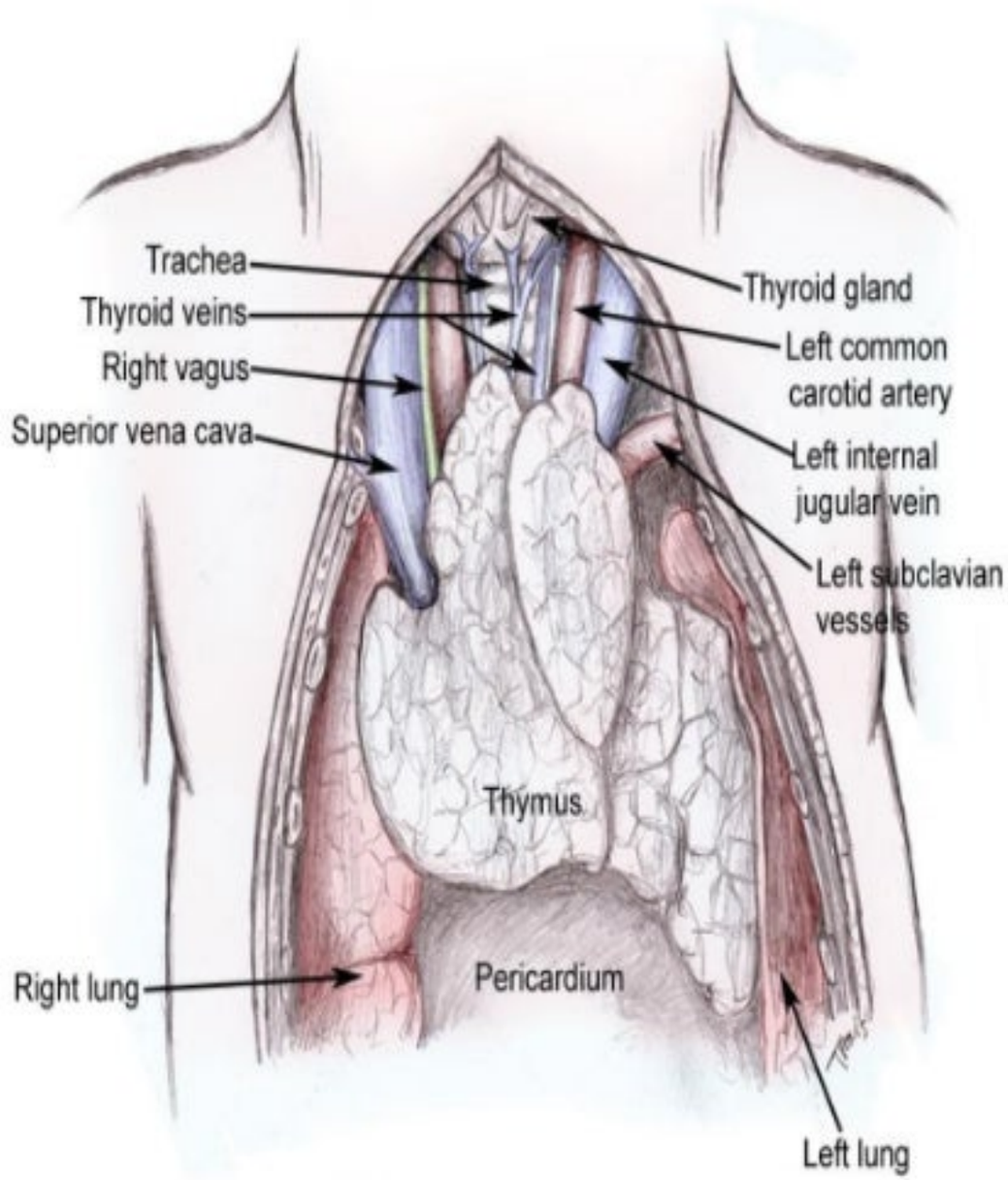
- The thymus gland is found in the thorax in the anterior mediastinum. It gradually enlarges during childhood but after puberty it undergoes a process of involution resulting in a reduction in the functioning mass of the gland. It continues to function throughout life, however

Structure - Functional



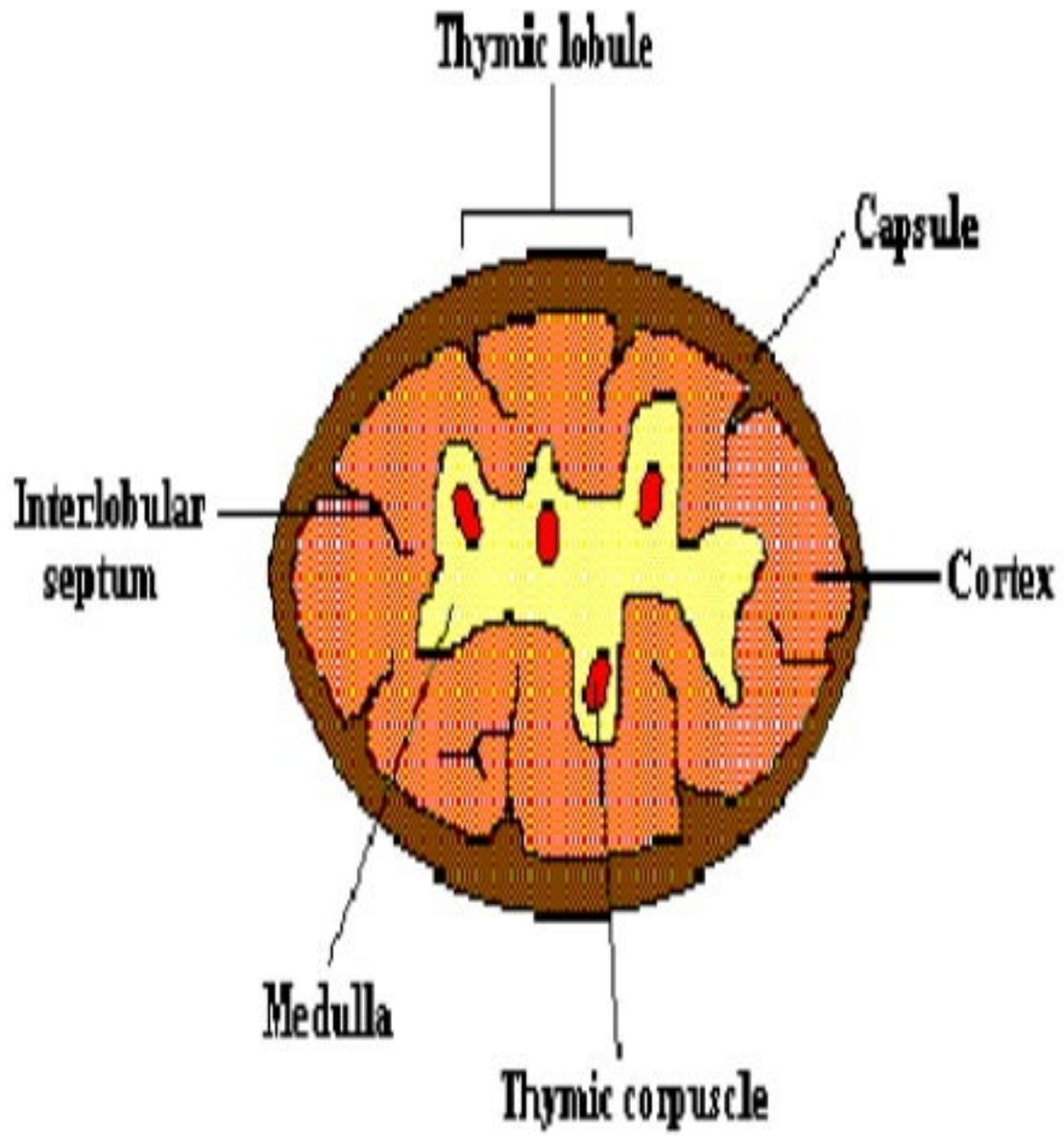
In Thymus
T lymphocytes are Educated

- In the thymus gland lymphoid cells undergo a process of maturation and education prior to release into the circulation. This process allows T cells to develop the important attribute known as self



Histology:

- The thymus gland is arranged into an outer, more cellular, cortex and an inner, less cellular, medulla. Immature lymphoid cells enter the cortex proliferate, mature and pass on to the medulla. From the medulla mature T lymphocytes enter the circulation.



Lymphatic System

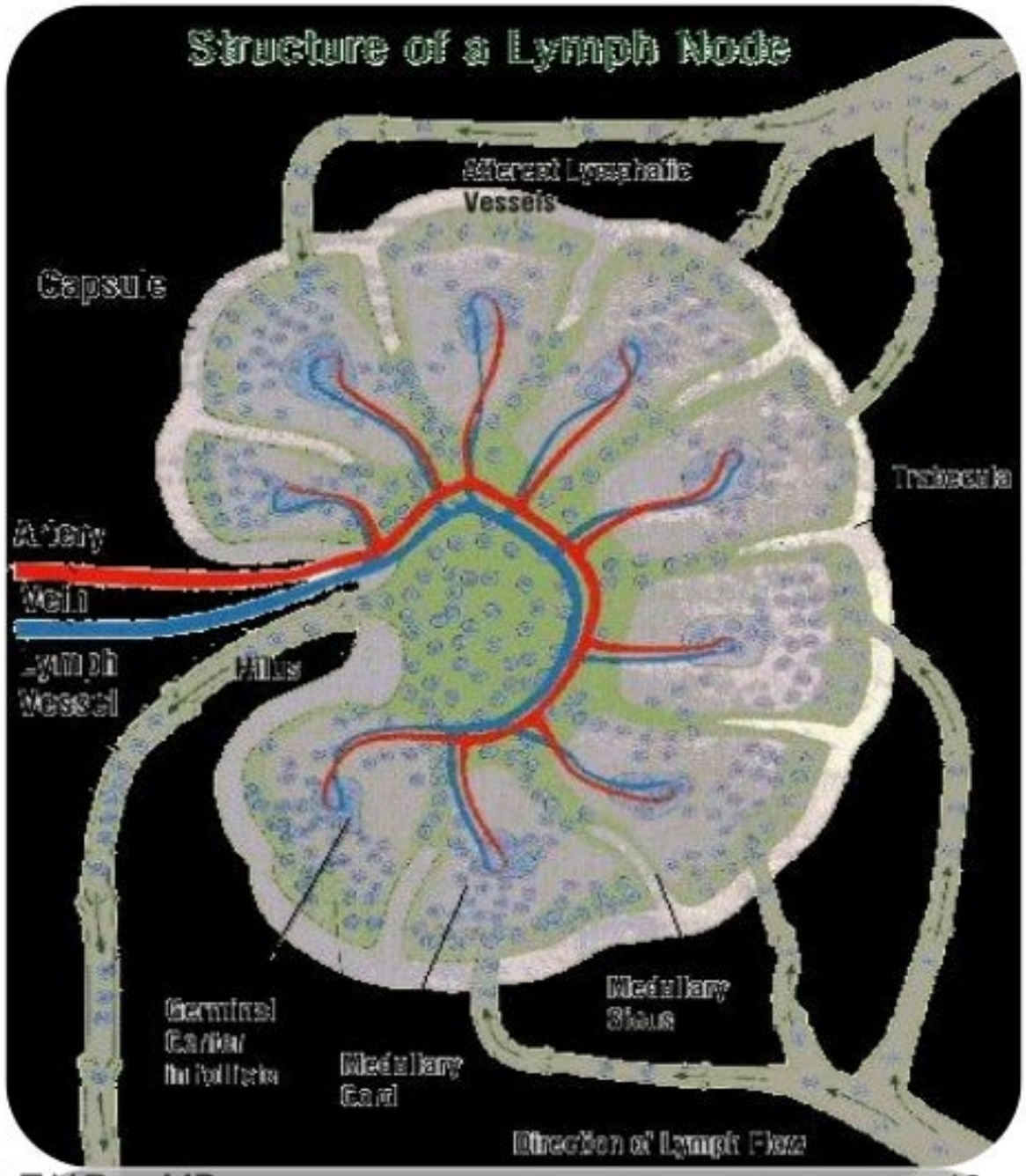
- Plasma From Blood Seeps Into Tissue
- Interstitial Fluid Either Goes Back or Becomes Lymph
- Lymph Enters Lymphatic Vessels
- Thoracic Duct Is Largest Lymphatic Vessel Empties Into Left Subclavian Vein
- Lymphatic Vessel Depends On Muscle Contractions For Movement
- One Way Valves Ensure One Direction
- Lymph Nodes Act As Filters For Antigens

Lymph Nodes

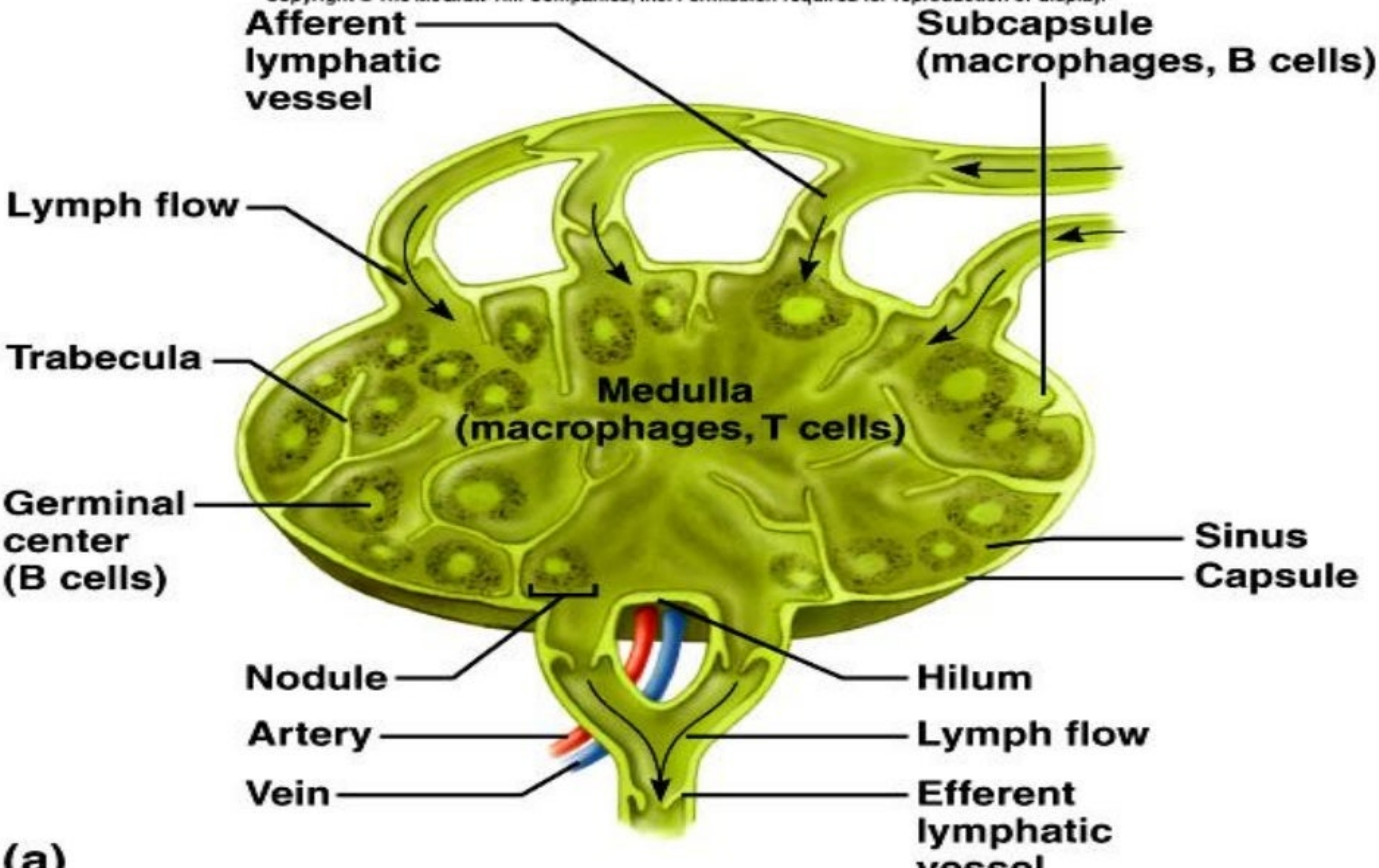
- Functions include:
- Filtration of particles and microorganisms to keep them out of general circulation.
- Interaction of circulating antigens in lymph with lymphocytes to initiate immune response.
- Activation, proliferation of B lymphocytes and antibody production.
- Activation, proliferation of T lymphocytes.

Cells of Lymph Node

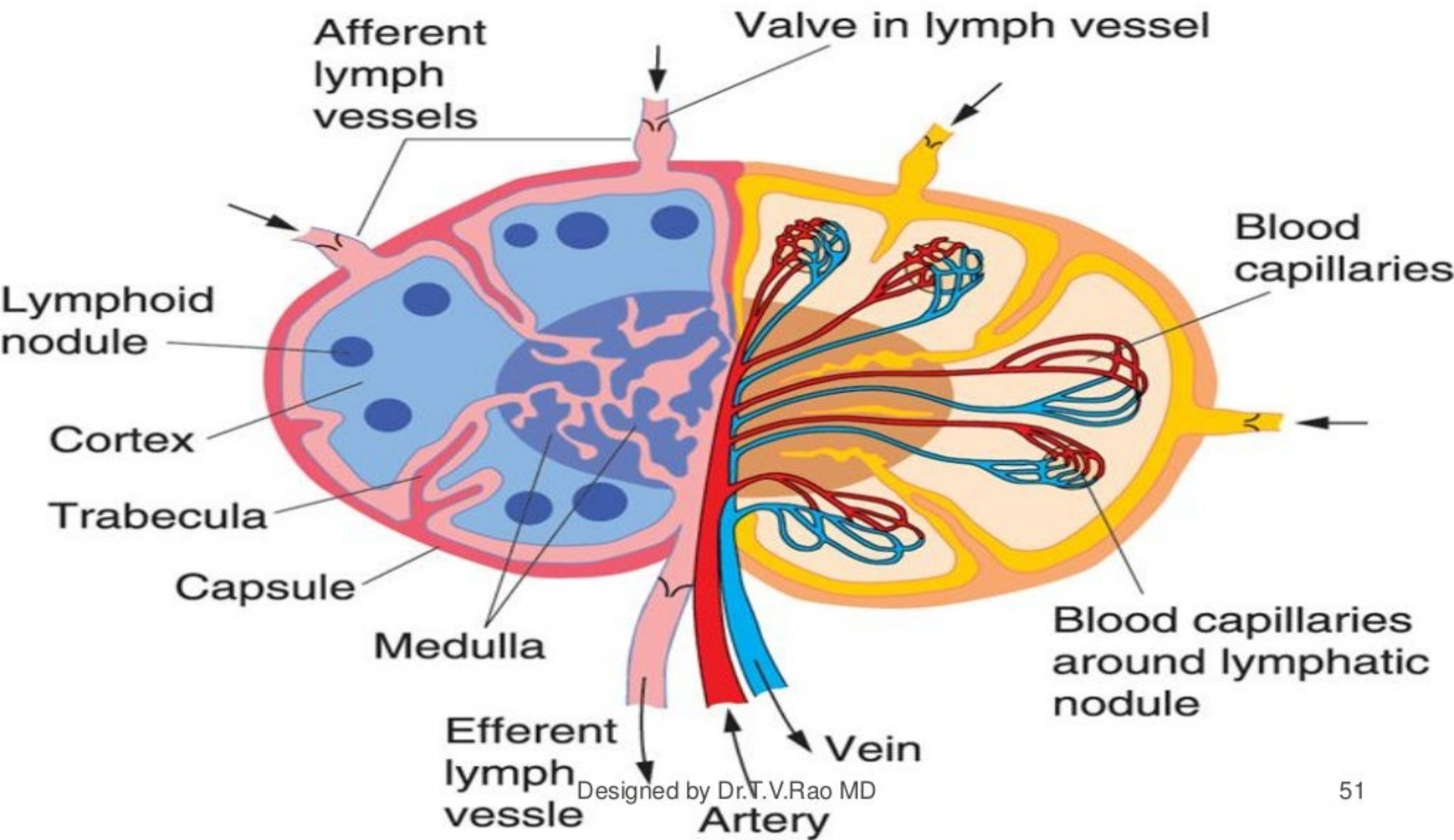
- Lymphoid cells
- Macrophages and other phagocytic antigen processing cells
- Lymphatic and vascular endothelial cells and fibroblasts responsible for lymph node supporting framework.



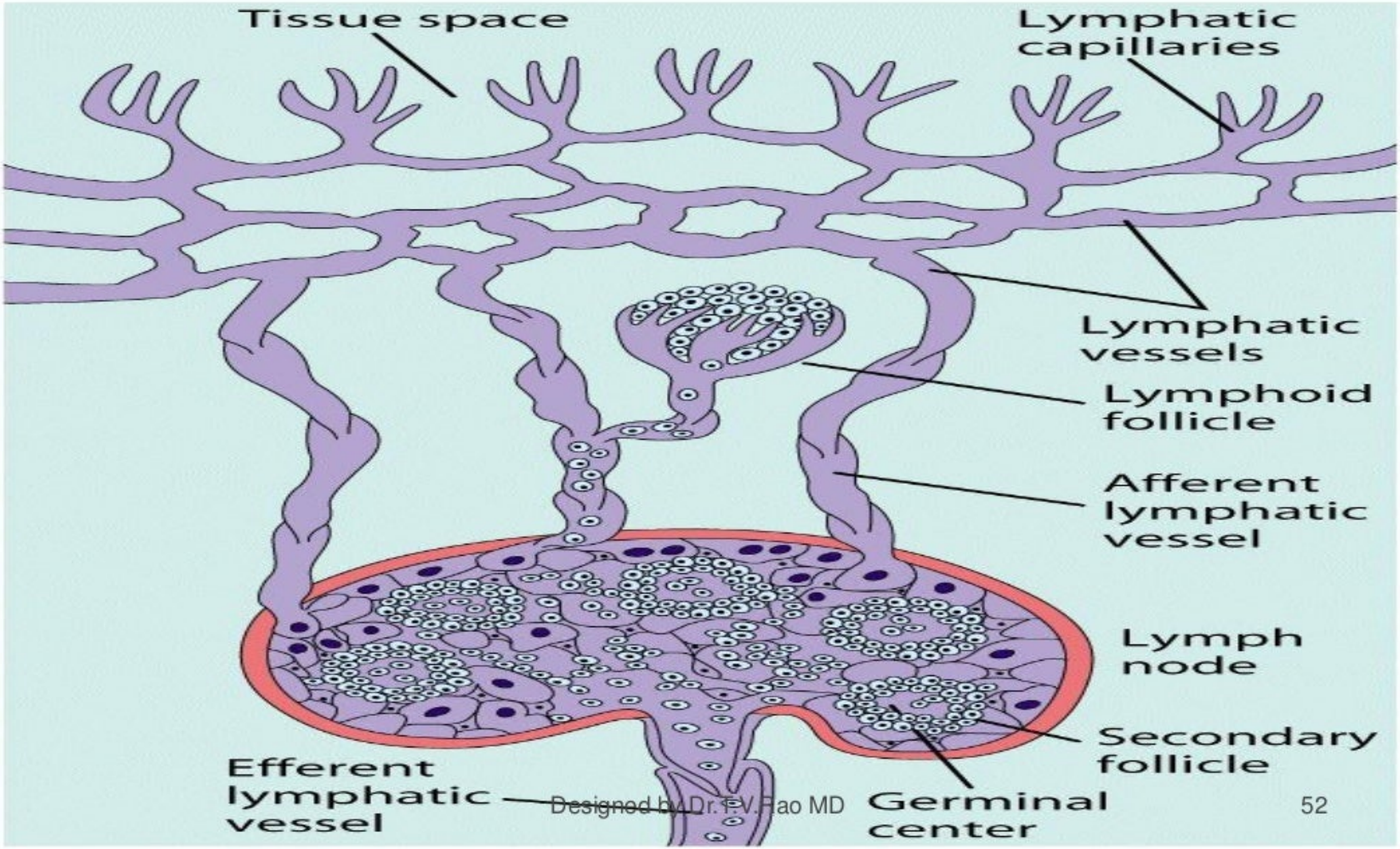
Lymph Nodes



Lymph Node

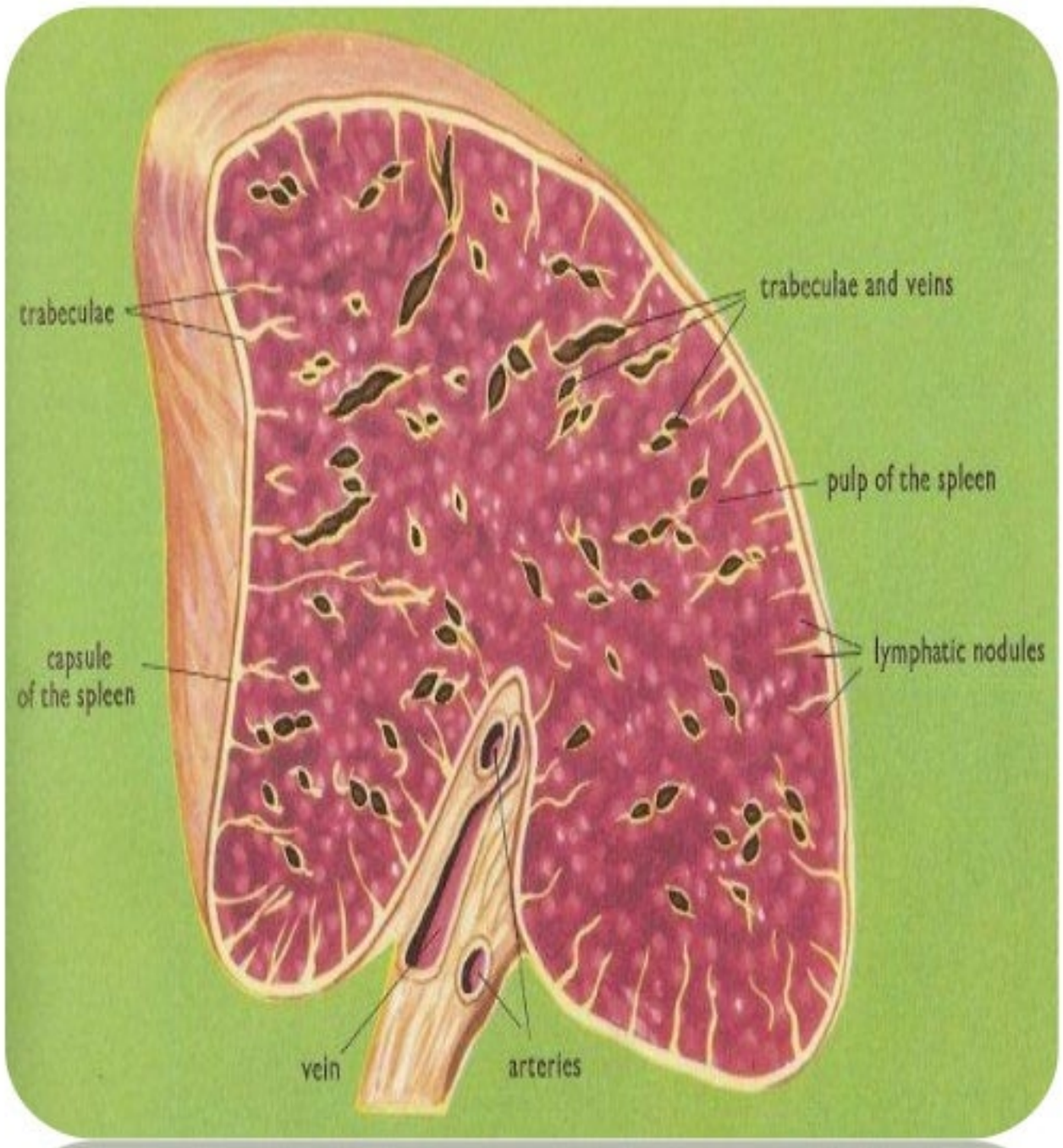

Afferent lymph vessels
Valve in lymph vessel
Blood capillaries
Lymphoid nodule
Cortex
Trabecula
Capsule
Medulla
Blood capillaries around lymphatic nodule
Efferent lymph vessle
Artery
Vein

Lymphatic System



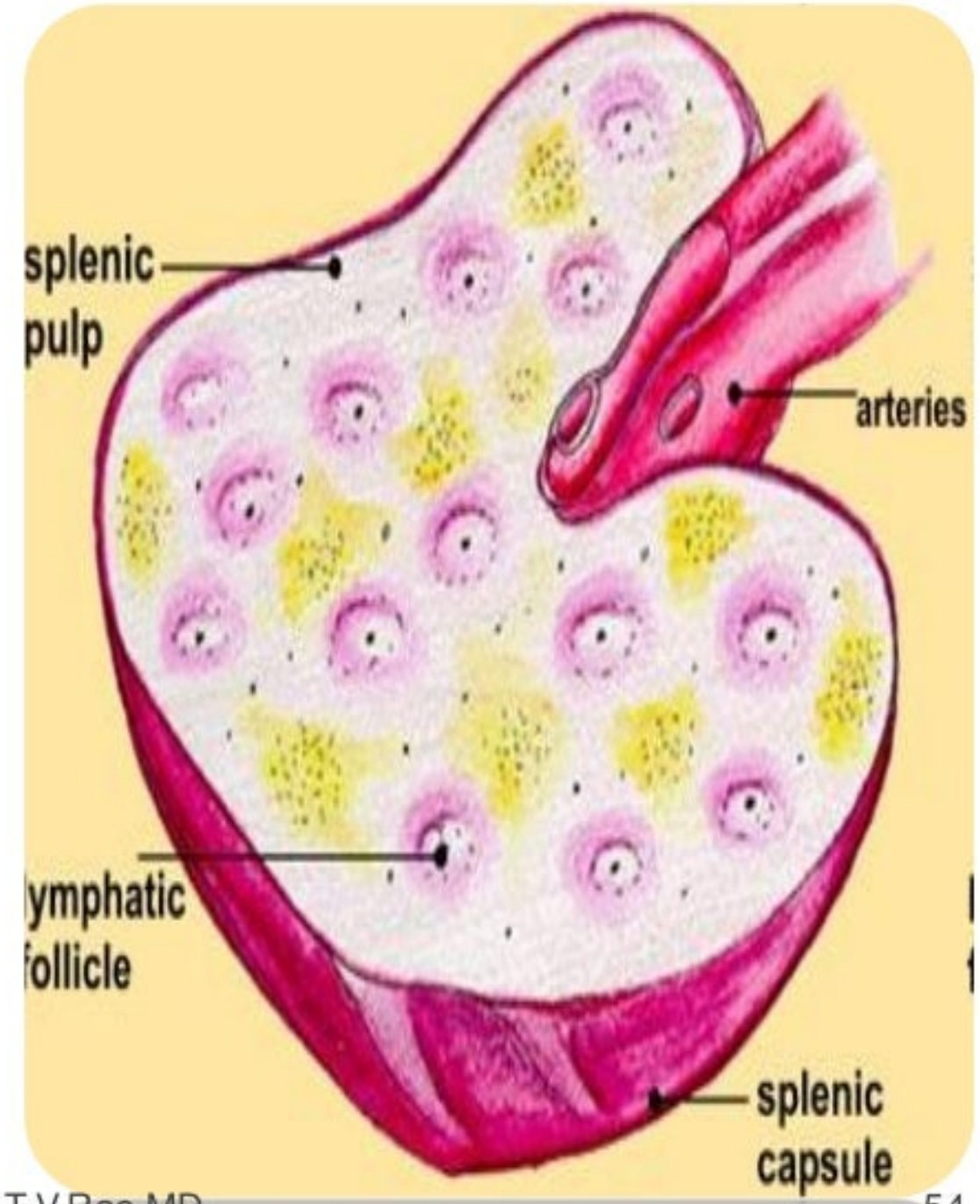
Spleen

- Largest accumulation of lymphoid tissue
- Abundant phagocytic cells—defense against antigens in blood
- Site of destruction of aged erythrocytes.
- Production site of activated lymphocytes which are delivered to the blood.
- THUS, an important blood filter and antibody-forming organ.

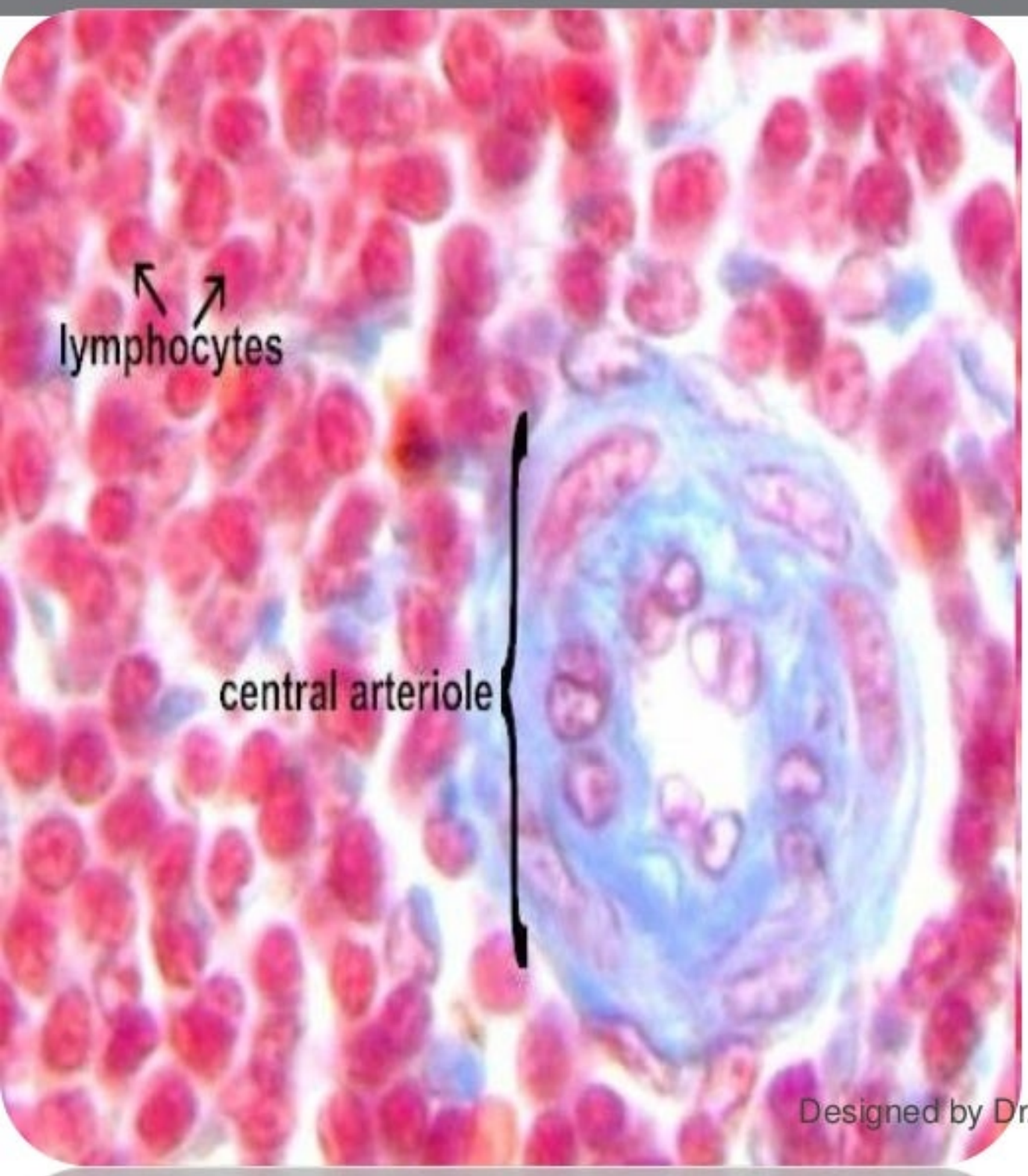


Spleen

- There are two distinct components of the spleen, the red pulp and the white pulp. The red pulp consists of large numbers of sinuses and sinusoids filled with blood and is responsible for the filtration function of the spleen. **The white pulp consists of aggregates of lymphoid tissue and is responsible for the immunological function of the spleen:**

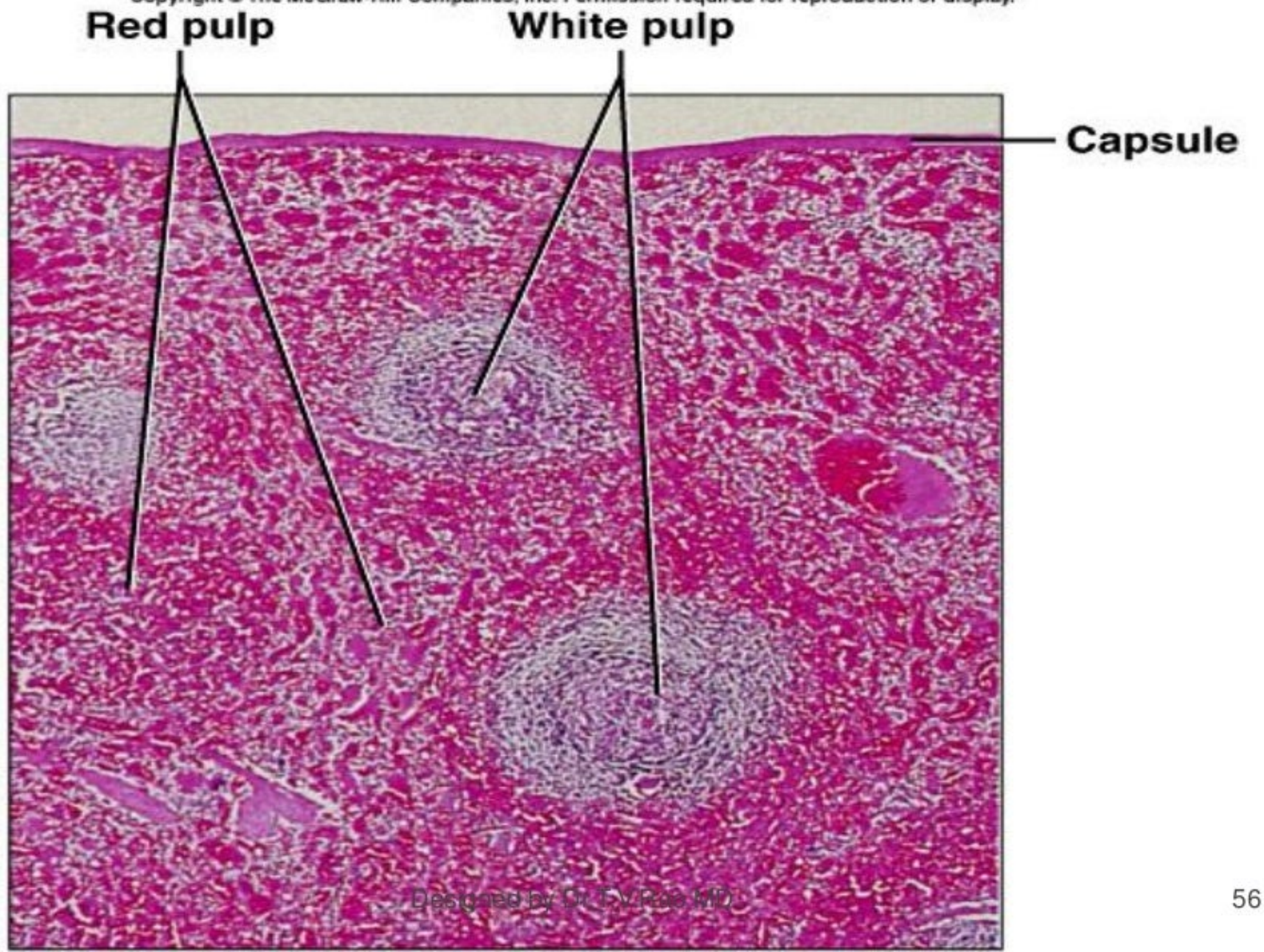


Spleen acts as filter through its vascular Arechleculre



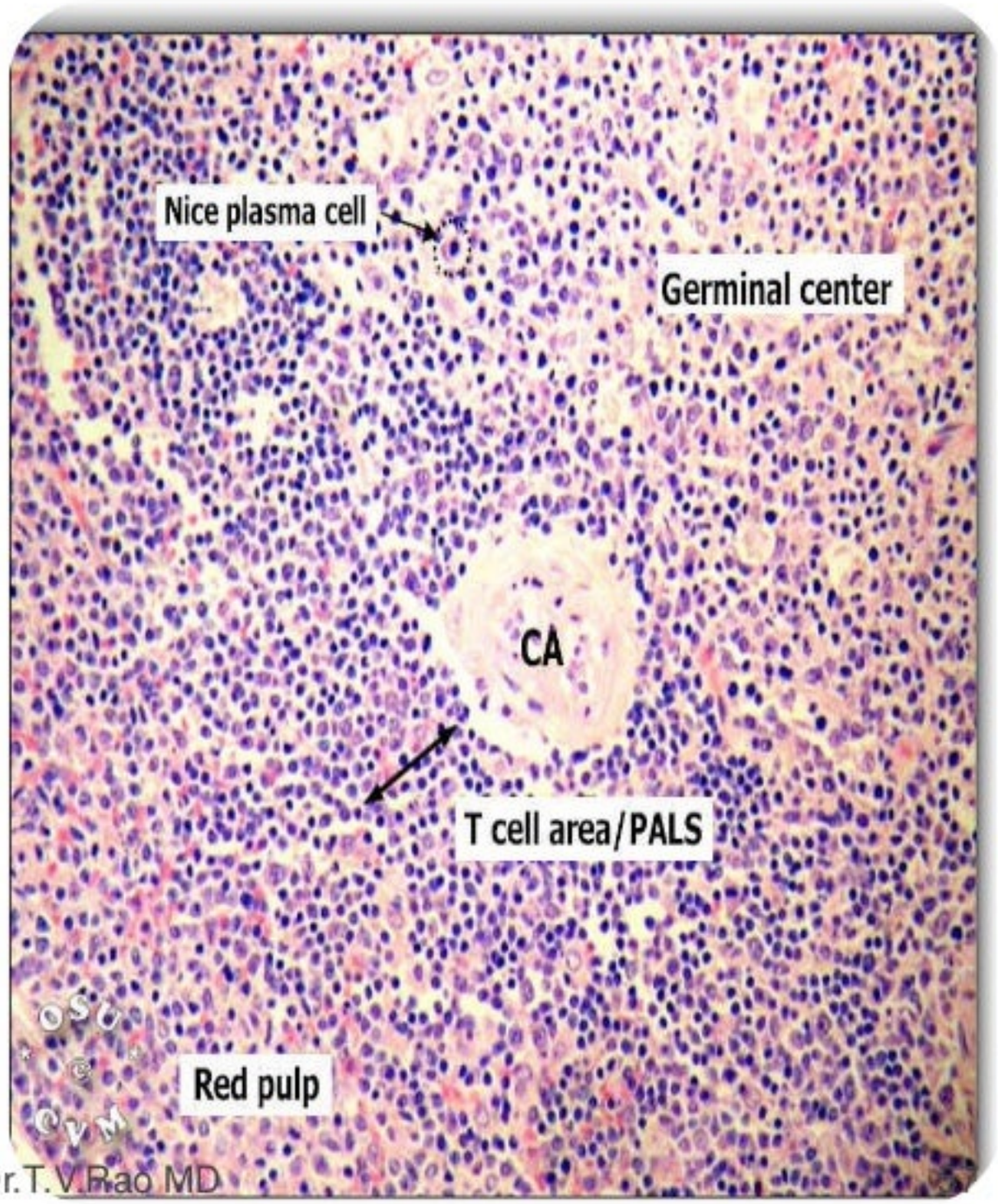
- There is a complex system of blood vessels within the red pulp arranged to facilitate removal of old or damaged red blood cells from the circulation. A small proportion of the splenic blood flow passes through more rapidly without undergoing this process of filtration.

Spleen



Functional aspects of spleen

- The white pulp contains T cells, B cells and accessory cells. There are many similarities with lymph node structure. The purpose of the white pulp is to mount an immunological response to antigens within the blood. The white pulp is present in the form of a per arteriolar lymphoid sheath.



Designed by Dr.T.V.Rao MD

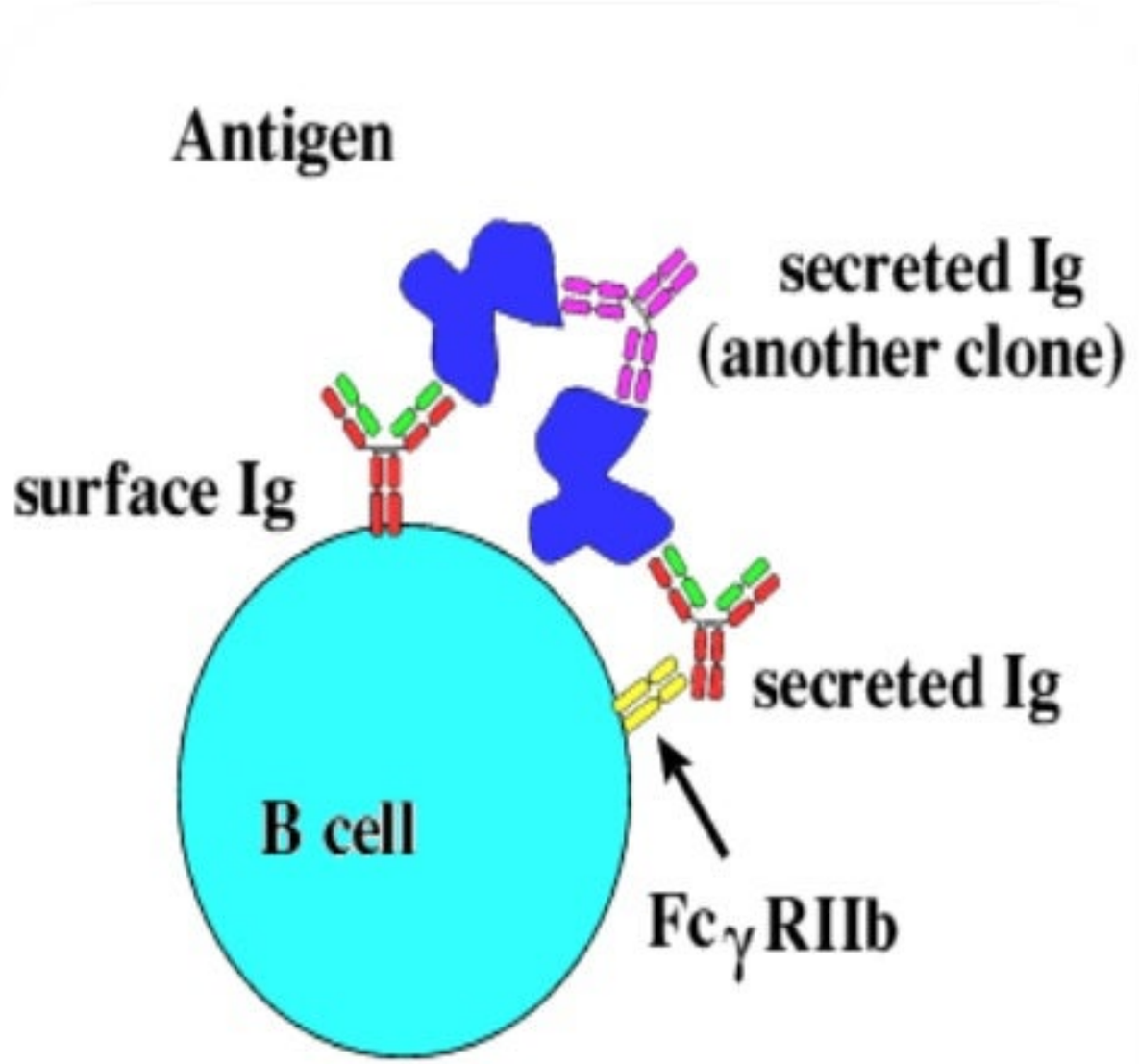
Mucosa-associated lymphoid tissue (MALT)

Gut-associated lymphoid tissue (GALT)

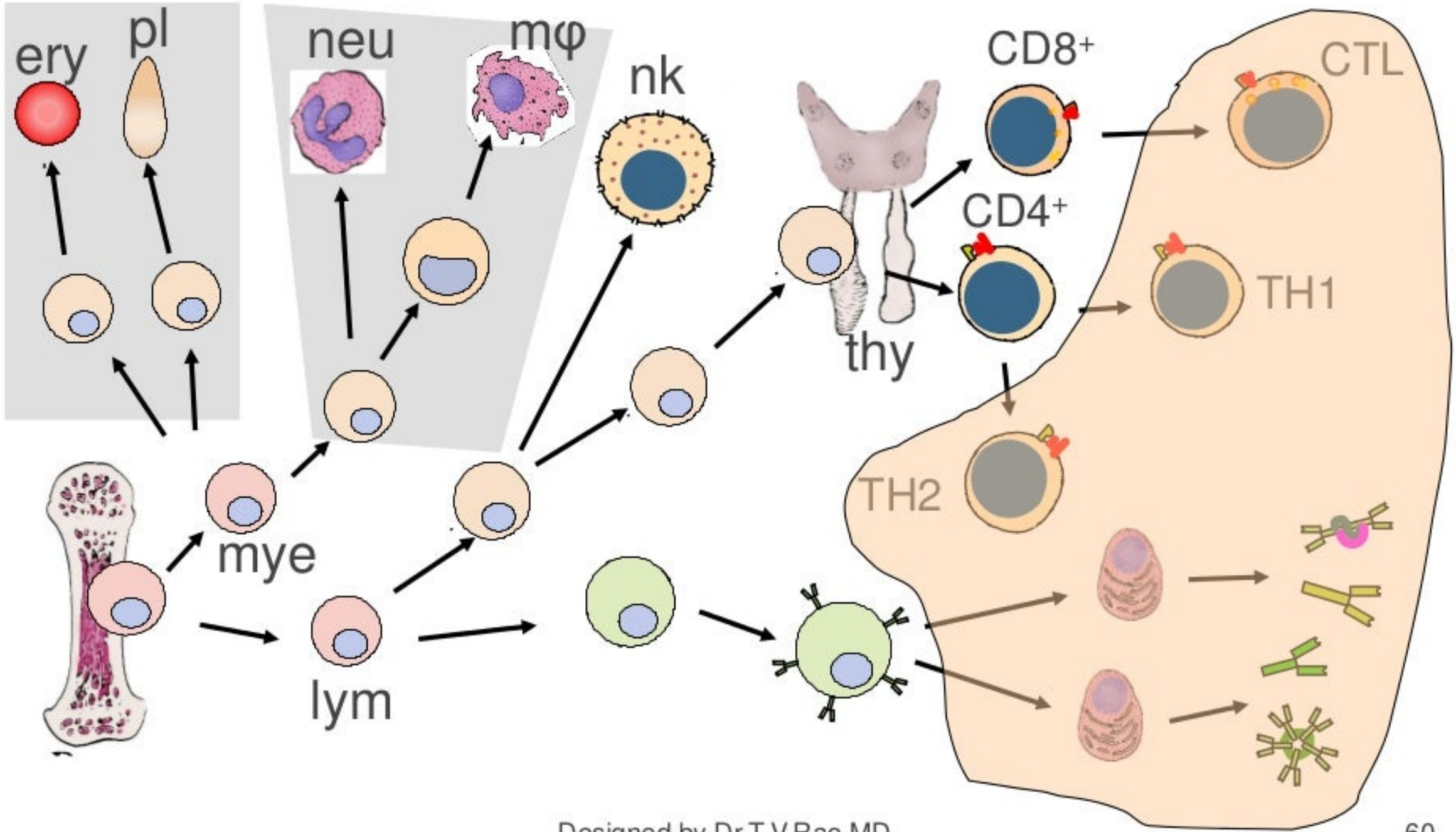
- Tonsils, adenoids (Waldeyer's ring)
- Peyer's patches
- Lymphoid aggregates in the appendix and large intestine
- Lymphoid tissue accumulating with age in the stomach
- Small lymphoid aggregates in the oesophagus
- Diffusely distributed lymphoid cells and plasma cells in the lamina propria of the gut

Cells of the Immune System

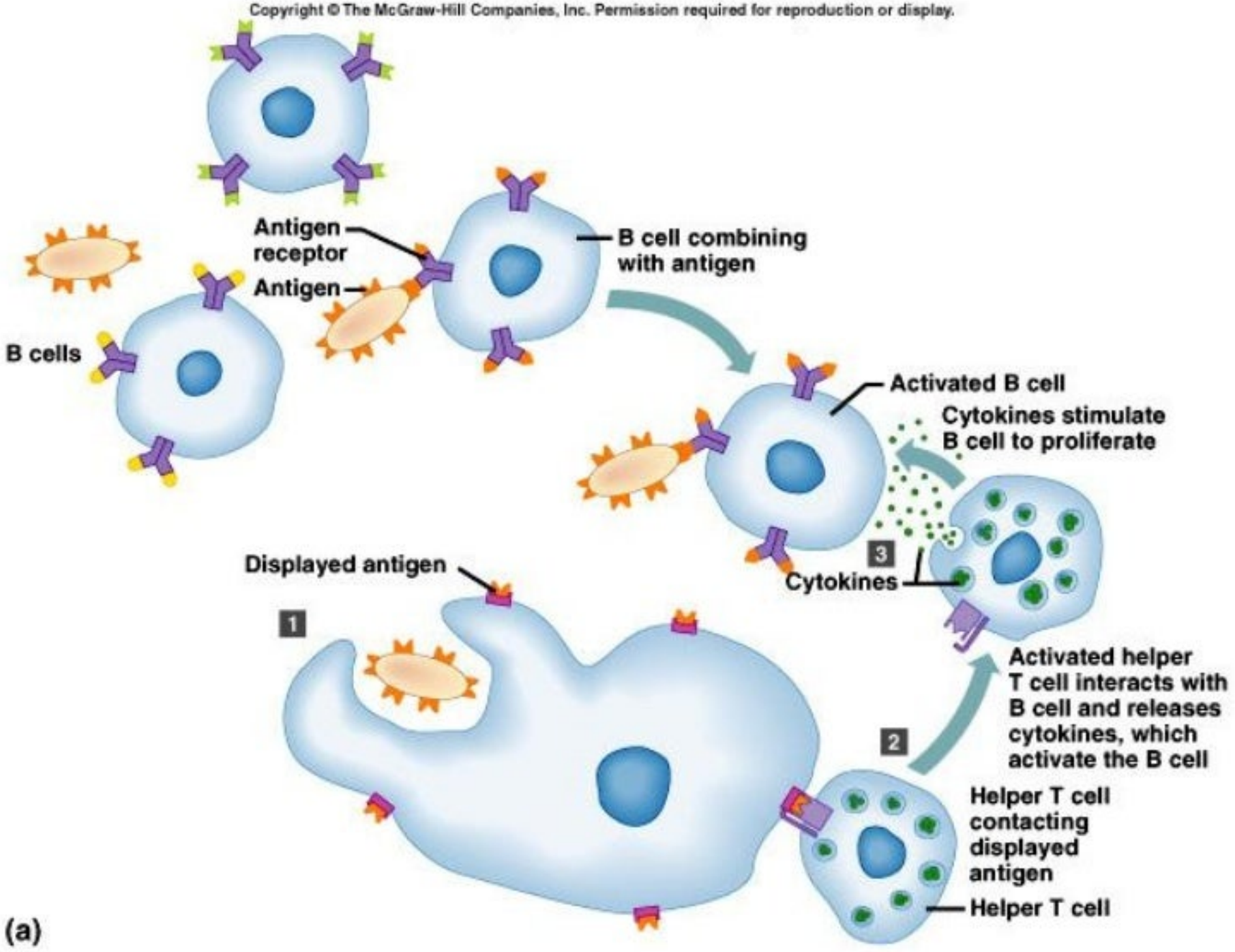
- Lymphoid Cells
  - B-cells, T-cells and Null cells (NK cells)
  - 20-40% of body's leukocytes
  - 99% of lymph node
  - If inactivated said to be naïve
  - Nucleus occupies almost entire cell
  - 6 μm diameter



Development of the Immune System



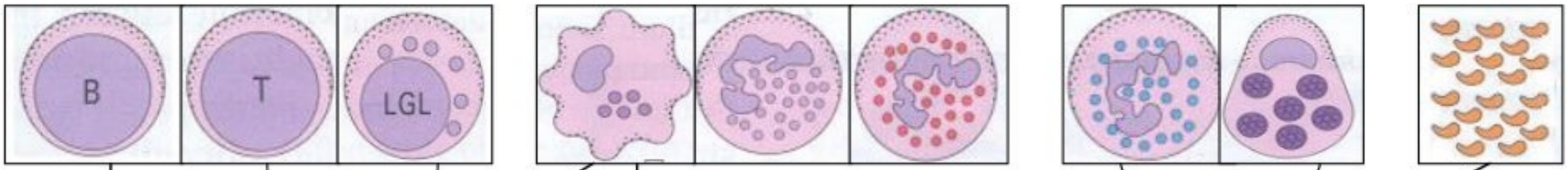
T Cell and B Cell Activation



COMPONENTS OF THE IMMUNE SYSTEM

Cellular components of the immune system

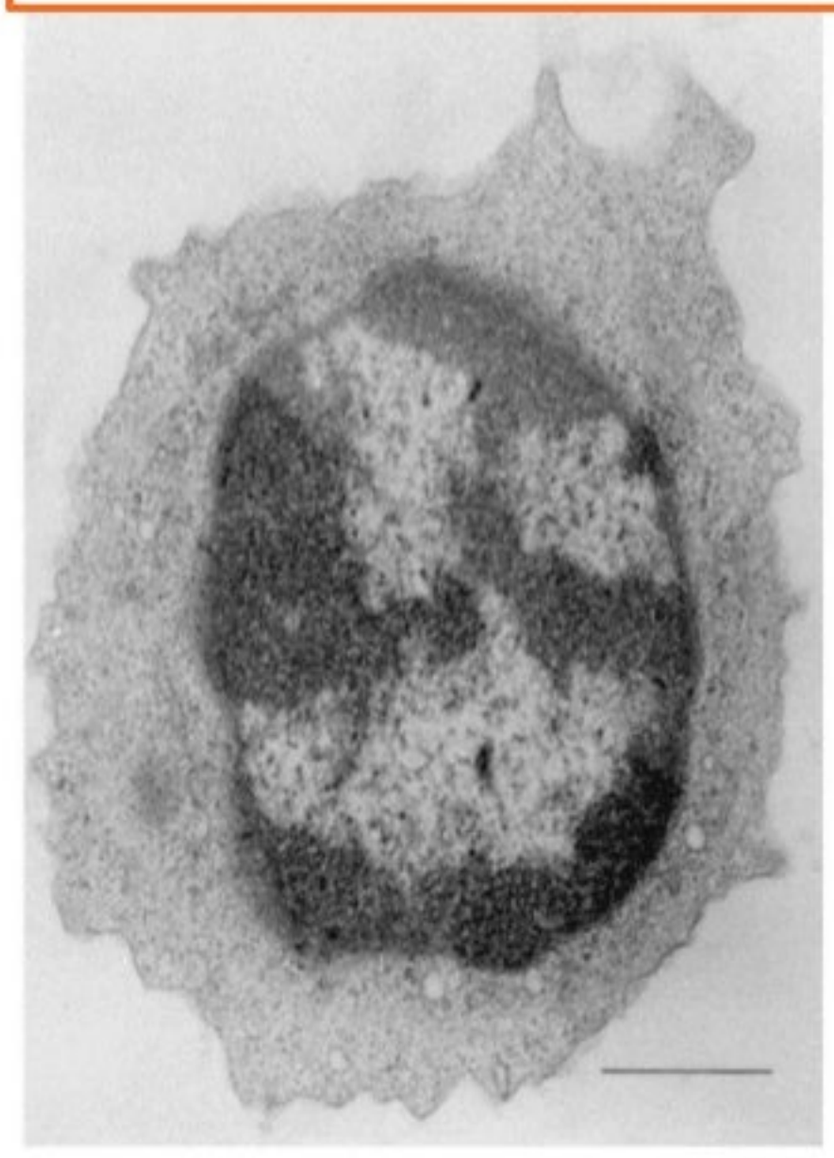
Lymphocytes	Phagocytes	Granulocytes	Others
B-cell	Mononuclear phagocyte	Basophil	Platelets
T-cell	Neurtrophil	Mast cell	
Large granular lymphocyte	Eosinophil		



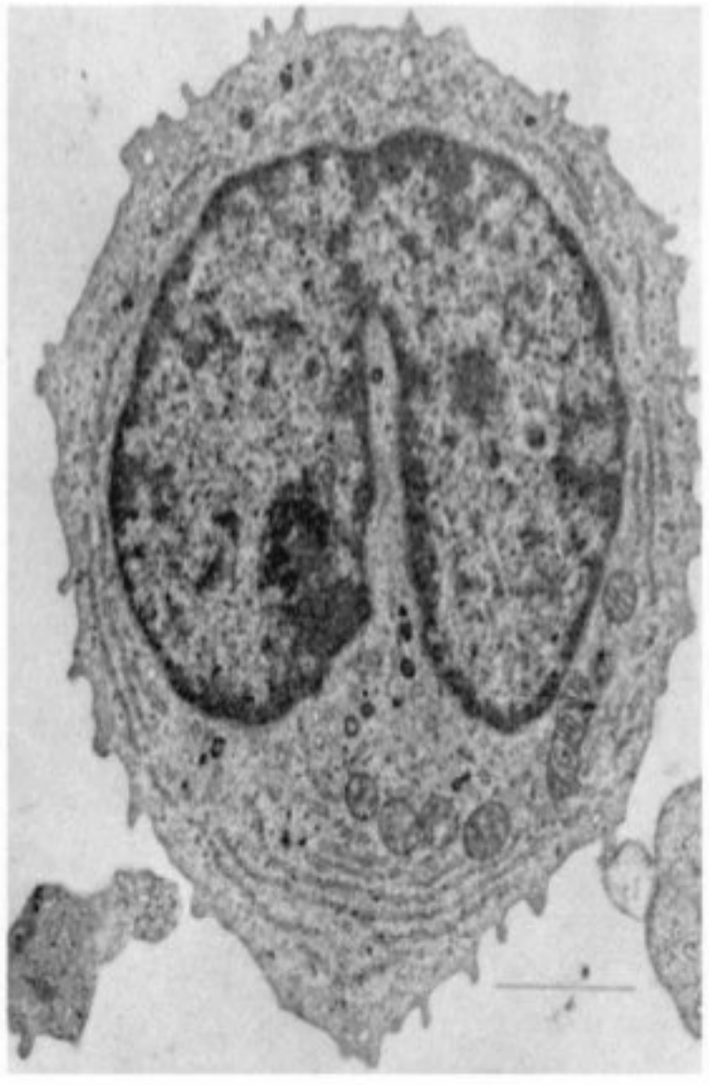
Antibodies | Cytokines | Complement | Inflammatory mediators

Soluble mediators of the immune system

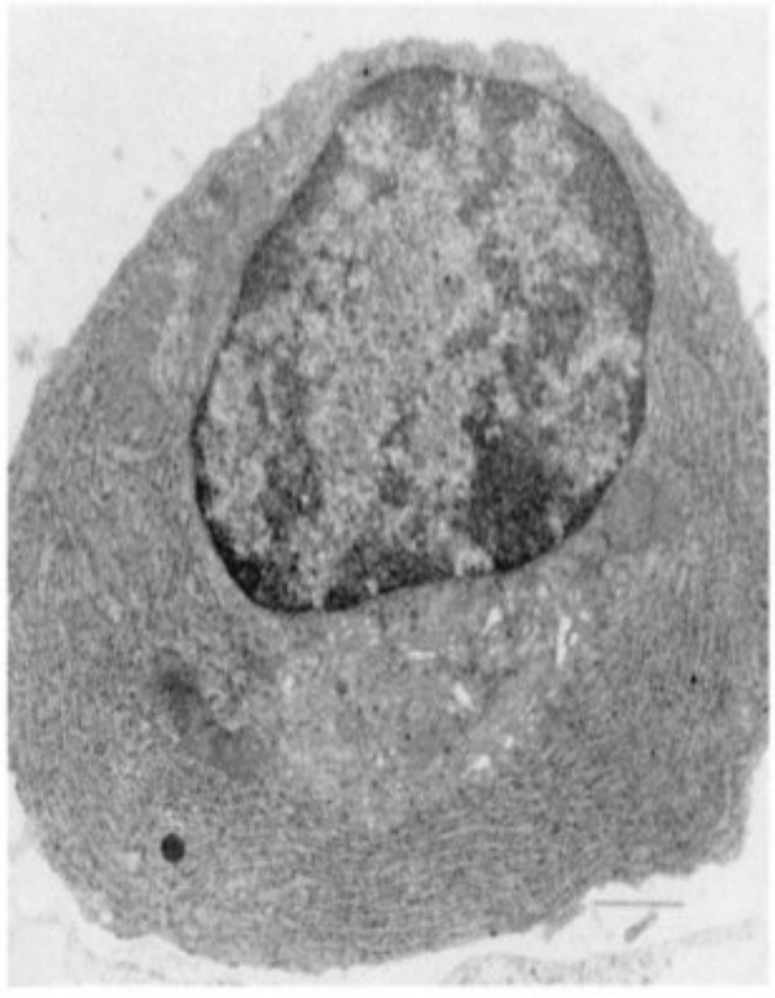
Lymphoid Cells



Small lymphocyte (T or B)
6 µm diameter



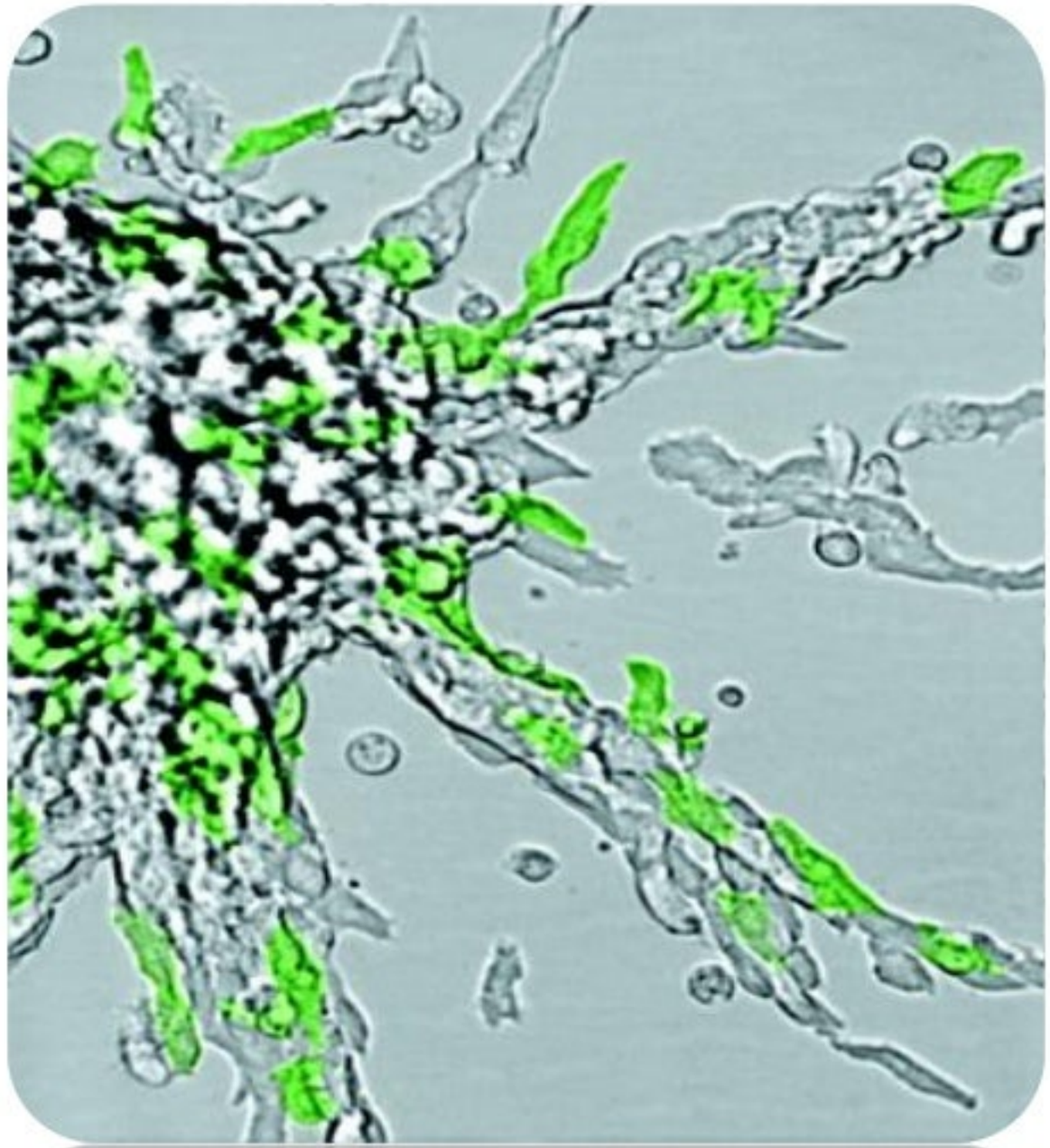
Blast cell (T or B)
15 µm diameter



Plasma cell (B)
15 µm diameter

Null Cells

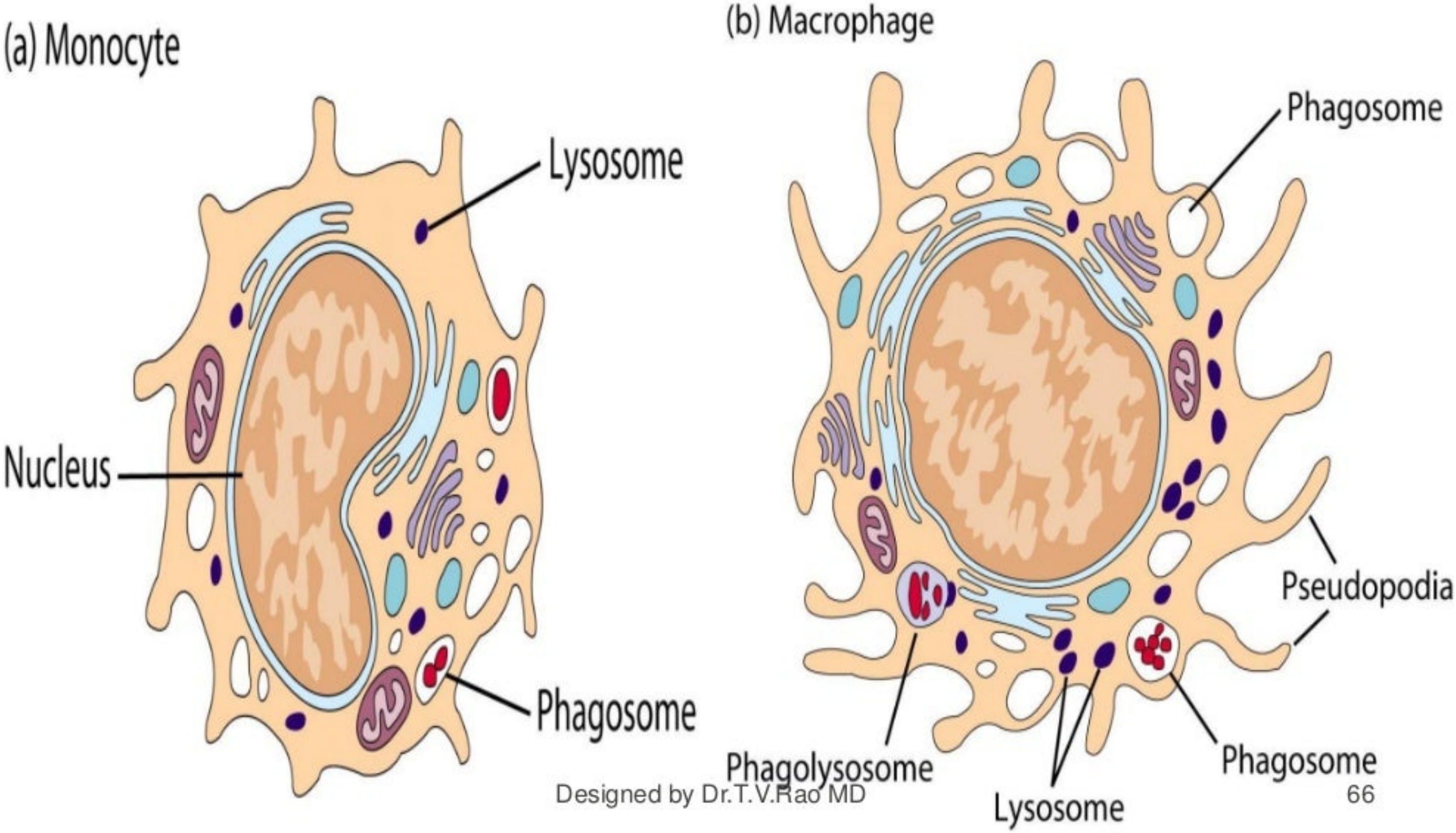
- Do Not Express Classical Lymphocyte Markers
- Predominantly NK Cells (CD56)
- Eliminate Tumor Cells and Virally Infected Cells
- Express Low Affinity FcγRIII (CD16)
- Using CD16 They Can Carry Out ADCC
- Reduction of MHC I Can Activate Them



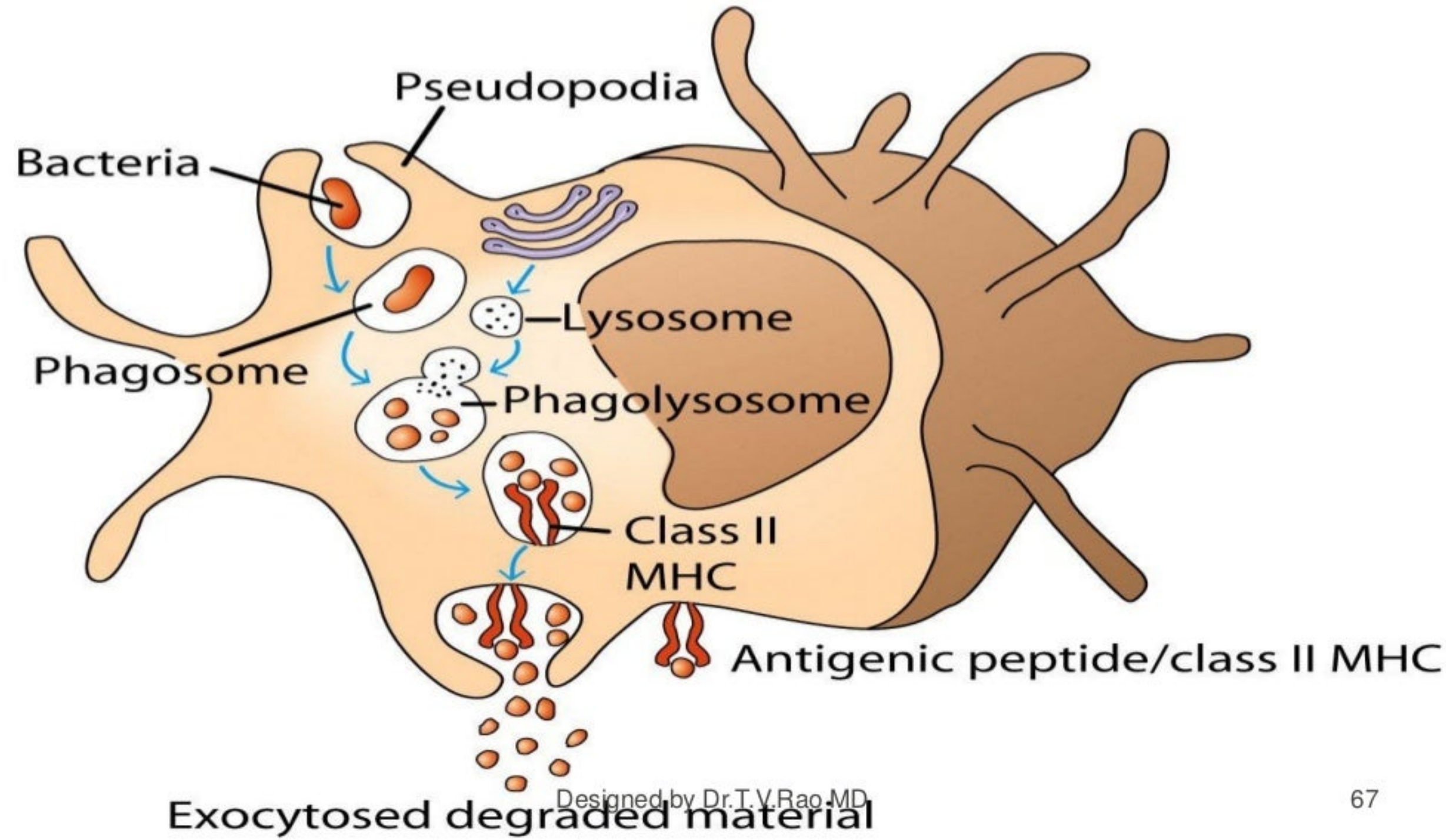
Mononuclear Cells

- Monocytes in Blood, MΦ in Tissues
  - Monocytes 5-10 times smaller than MΦ
- MΦ Increases Phagocytic Ability
- Secretes cytokines and Produces Hydrolytic Enzymes
- Named Based on Tissue They Reside
  - Alveolar (lungs), Kupffer (liver), Microglial (brain), Osteoclasts (bone)
- Activated By Phagocytosis or Cytokines (IFNγ)
- Antigen Presenting Capacity Thru MHC II

Monocyte vs Macrophages

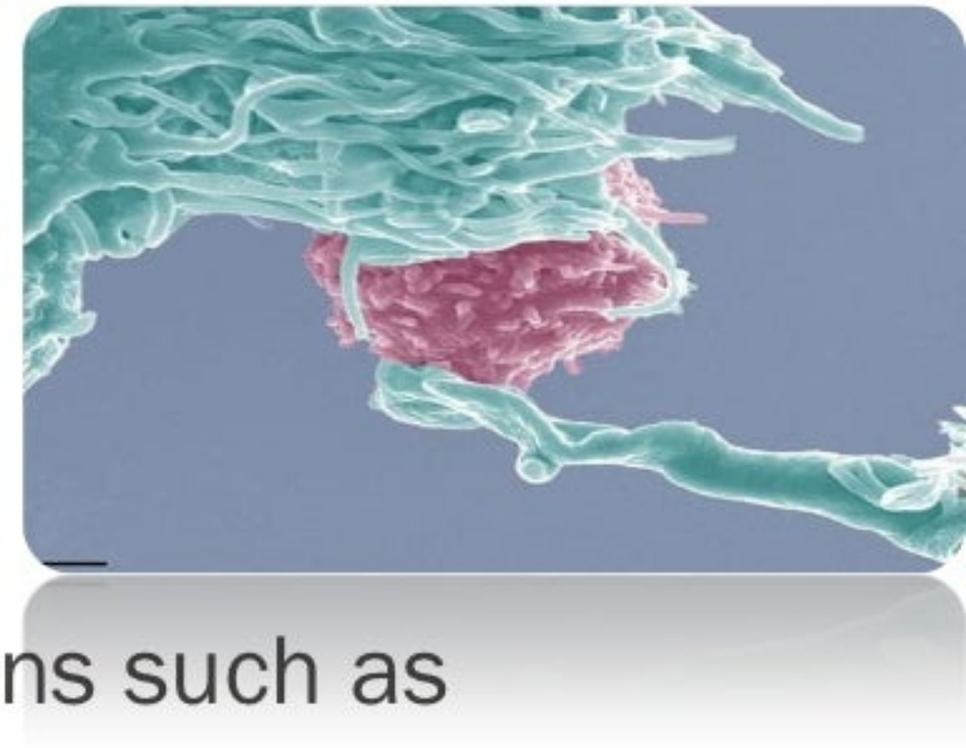


Macrophages are Effective APC

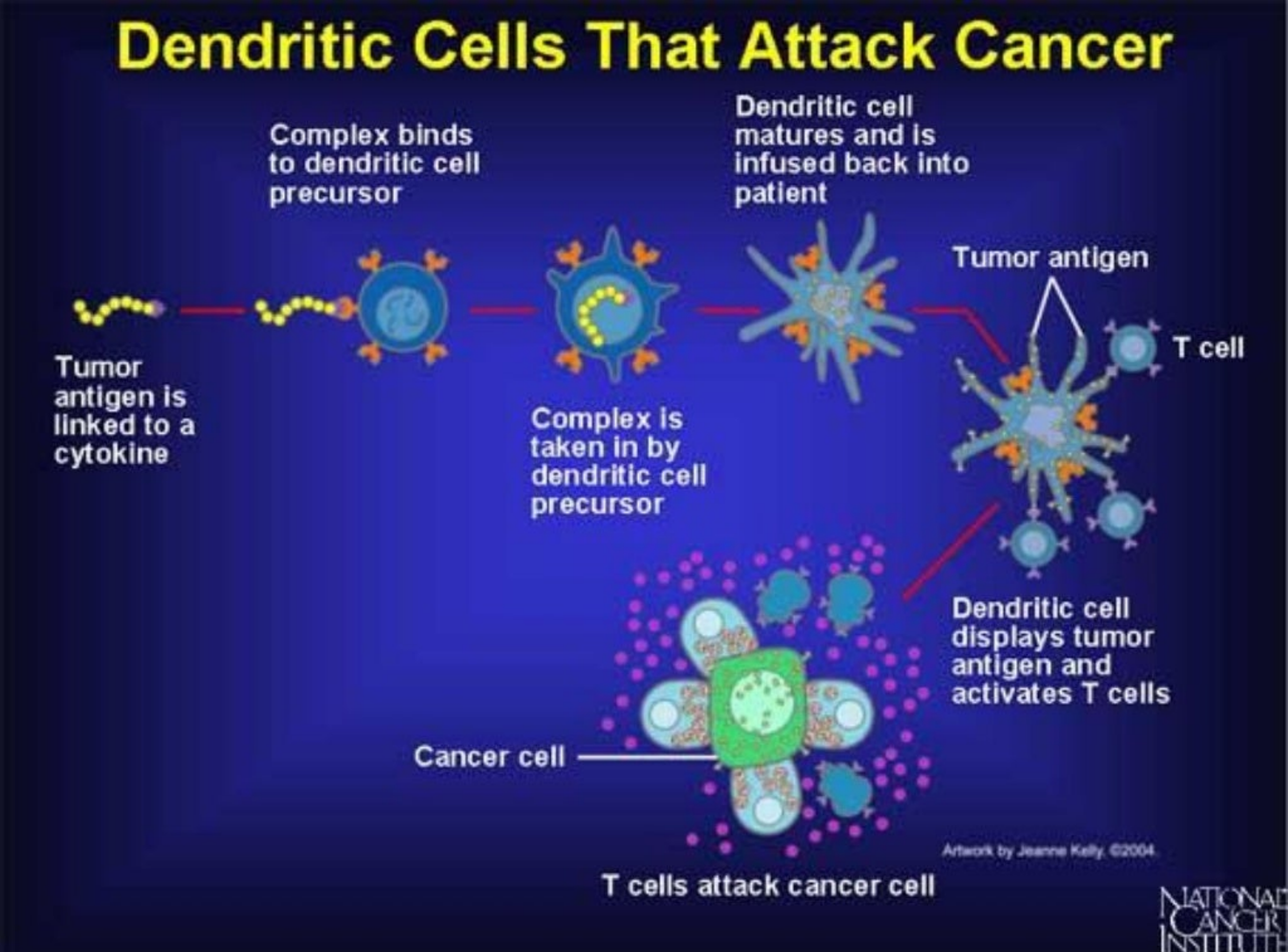


Dendritic Cells

- Professional APCs
- Several Types
  - Langerhans (LC) found in skin
  - Circulating DCs
    - Myeloid (MDC1 and MDC2)
    - Plasmacytoid
- Interstitial DCs, populate organs such as heart, lungs, liver, intestines
- Interdigitating DCs, T-cell areas of lymph nodes and Thymic medulla

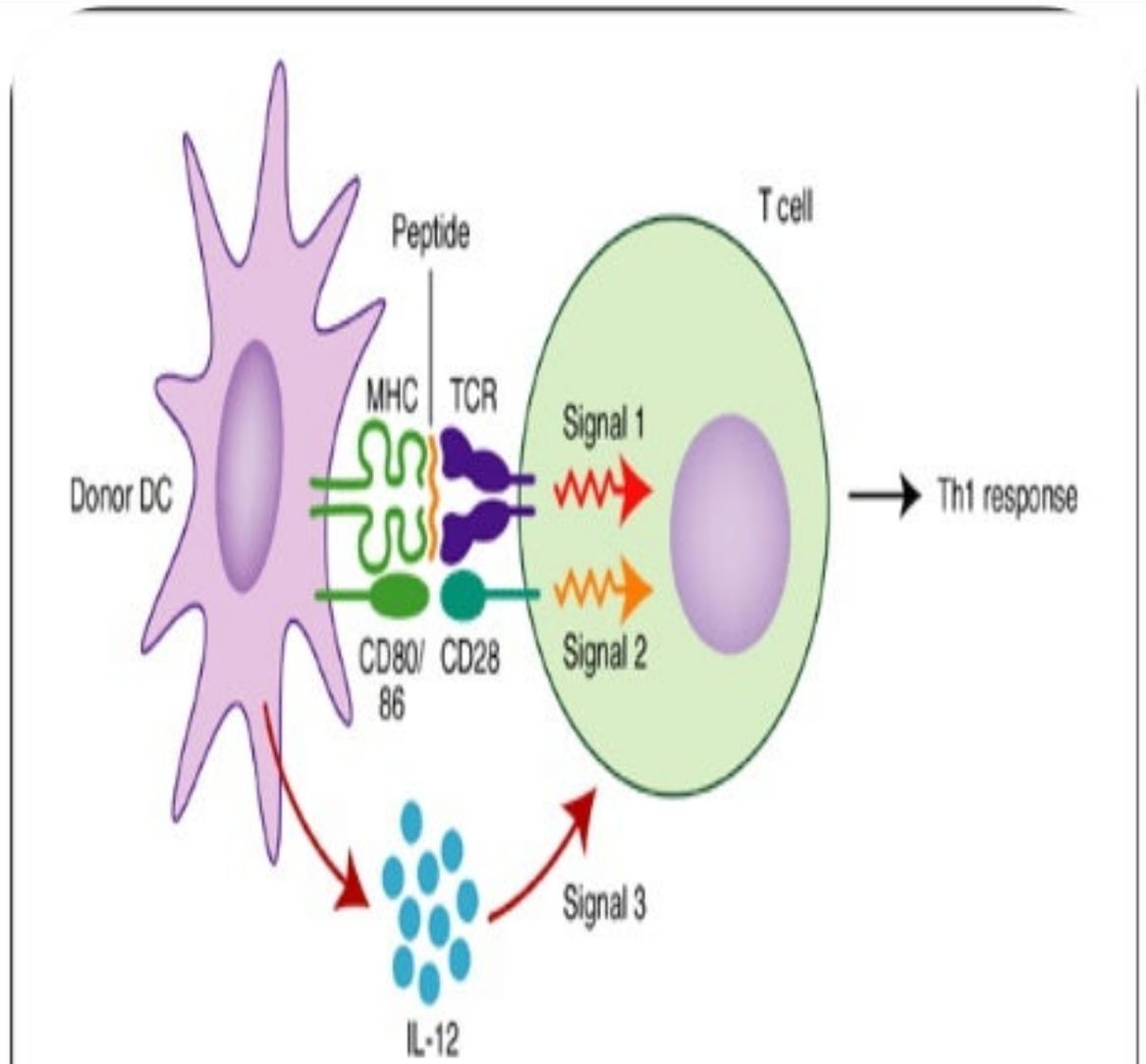


Dendritic Cells That Attack Cancer



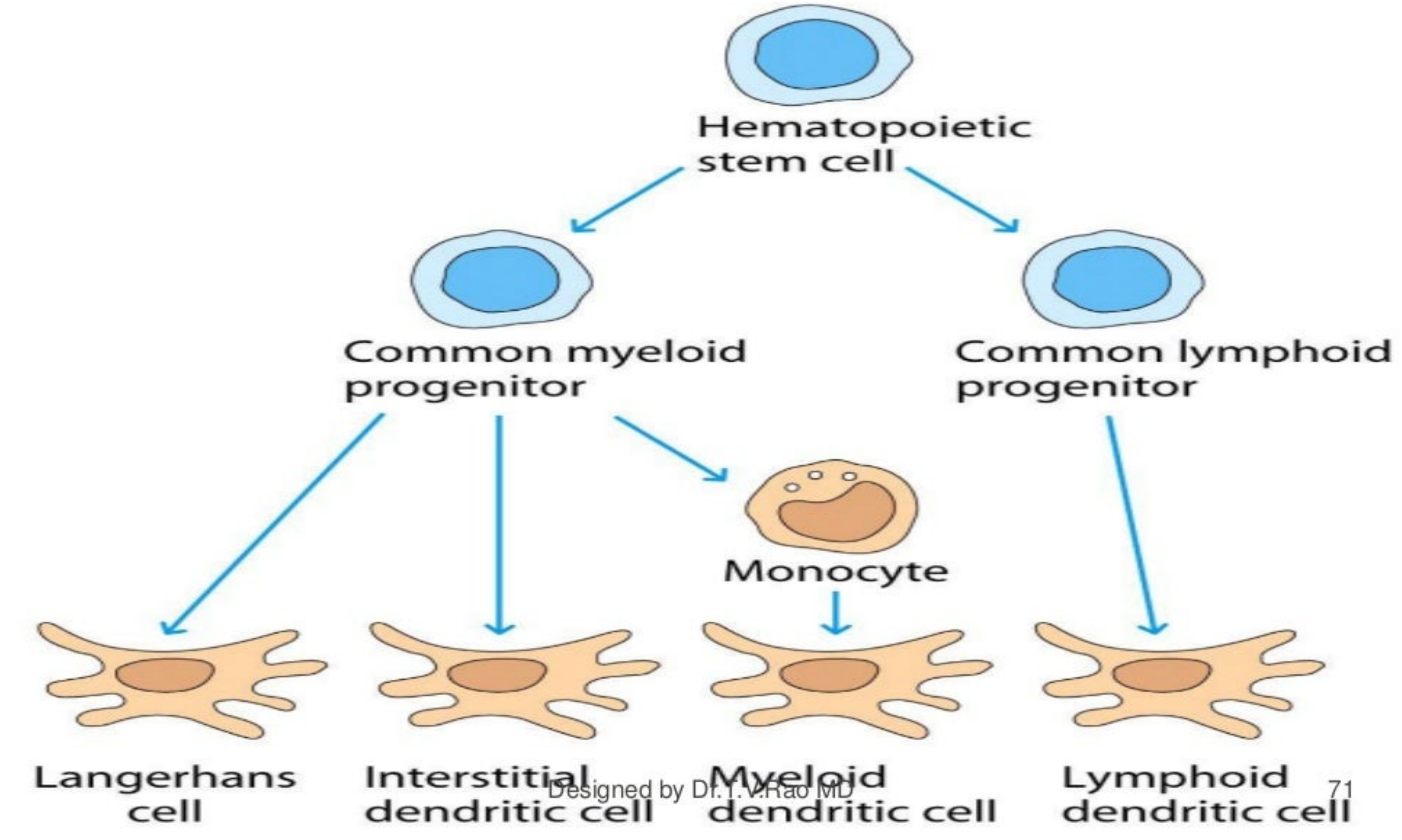
Dendritic Cells

- Scarce Cell Type
- Discovered in 1972
- Early 90s Using GM-CSF/IL4 and Later flt-3 limitation Was Overcome
- Intense Area of Research
- Seemed Promising for Tumor Treatment
- Maybe Better for Tolerance



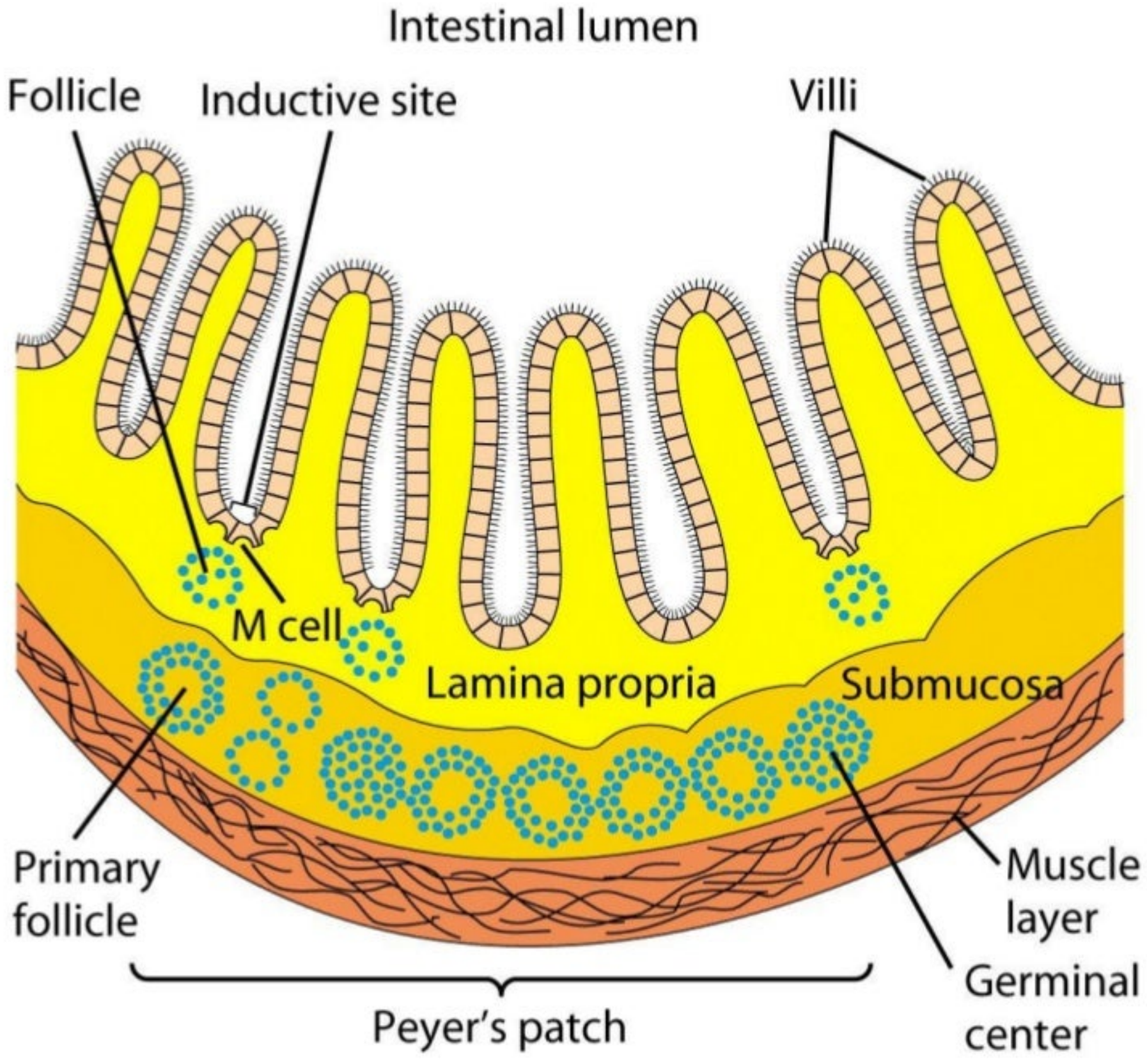
The interaction between dendritic cells (DCs) and T cells involves three signals

Developmental Pathway of Dendritic Cells

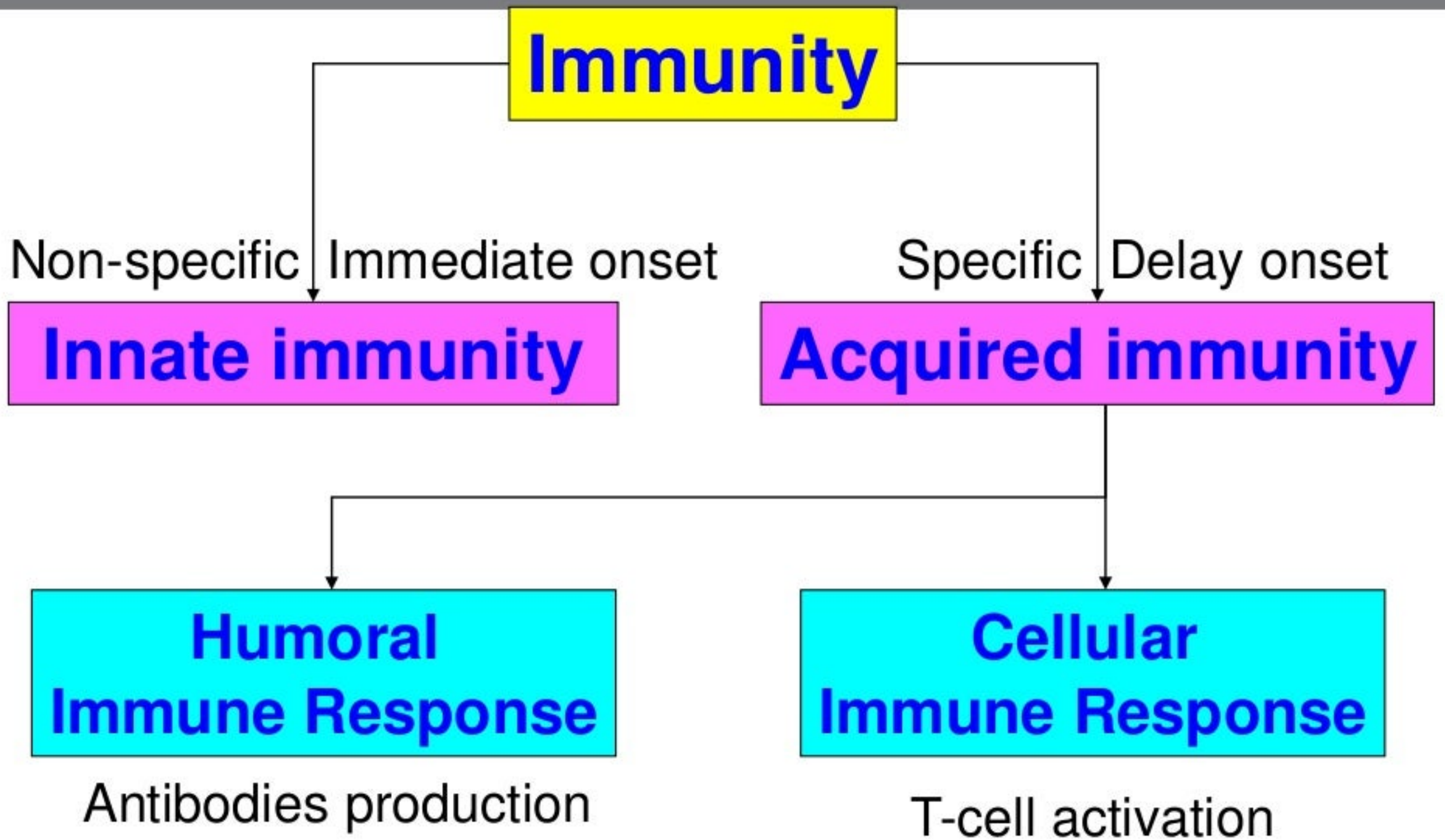


Mucosal Associated Lymphoid Tissue (MALT)

- Mucous Membranes S.A=400m^2
- Mucous Member. Most Common Pathogen Entry Site
- M.M Protected by MALT
- Organization Varies (most organized P.P, Tonsils, appendix
- GI Tract, IEL Unique $\gamma\delta$ TCRs
- Lamina Propia (below epithelium) MΦ, B cells, T_H
- M Cell Allows Ag Entry, Unique Architecture


Intestinal lumen
Follicle
Inductive site
Villi
M cell
Lamina propria
Submucosa
Primary follicle
Muscle layer
Germinal center
Peyer's patch

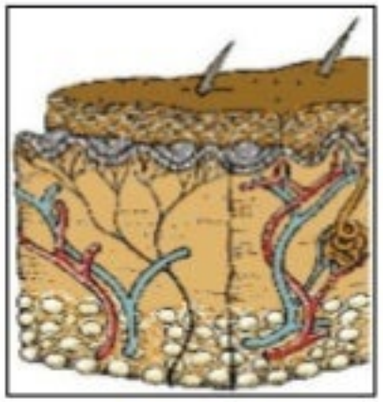
THE EVOLUTION OF IMMUNITY



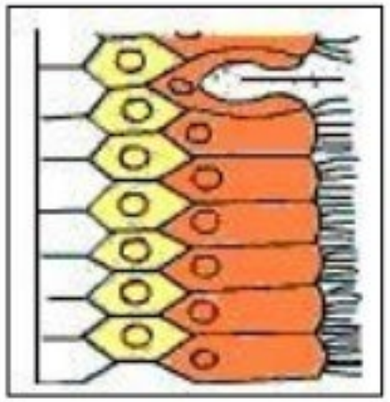
INNATE IMMUNITY

Pathogenic invasion → Bacteria Viruses

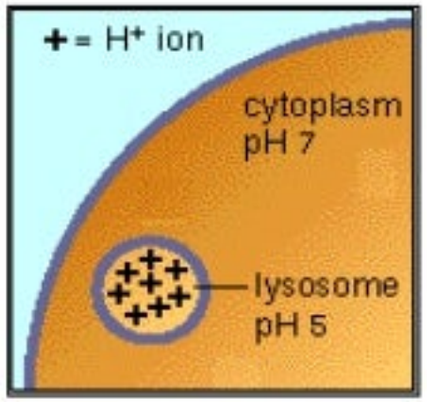
1st Line Defense



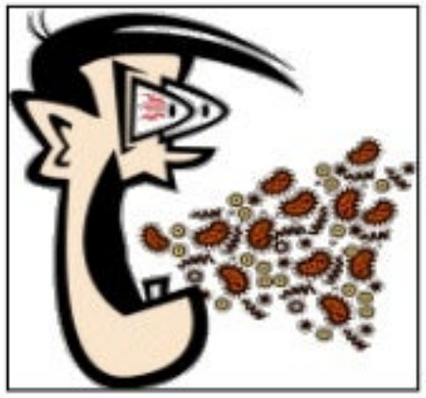
Skin



Ciliated cells



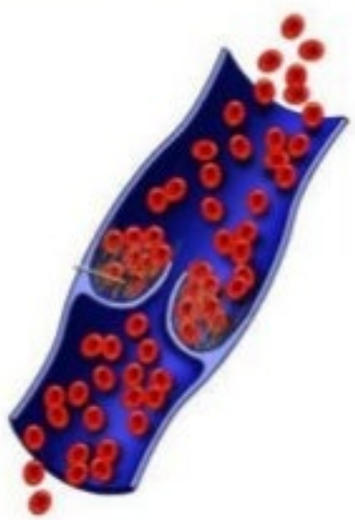
Lysozyme



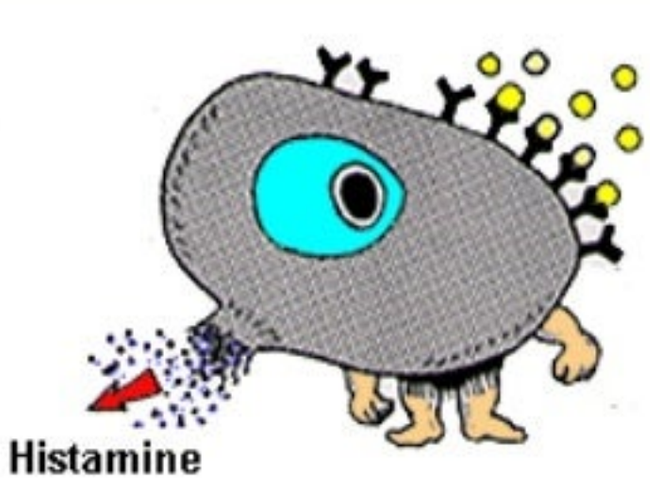
Coughing

Vomiting

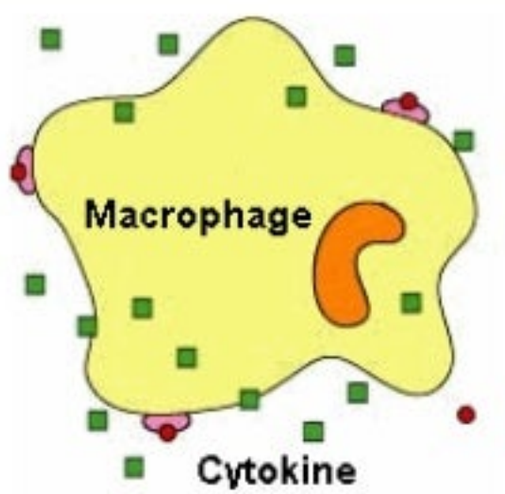
2nd Line Defense



Blood clot



Mast cell



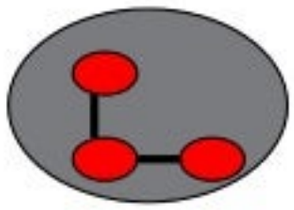
Cytokines

Leukocytes

Innate vs. Adaptive

Innate

stem



Cytotoxicity
Phagocytosis

Adaptive

CD4+

CD8+

Cytotoxicity

stem

Macrophage

Cytolysis

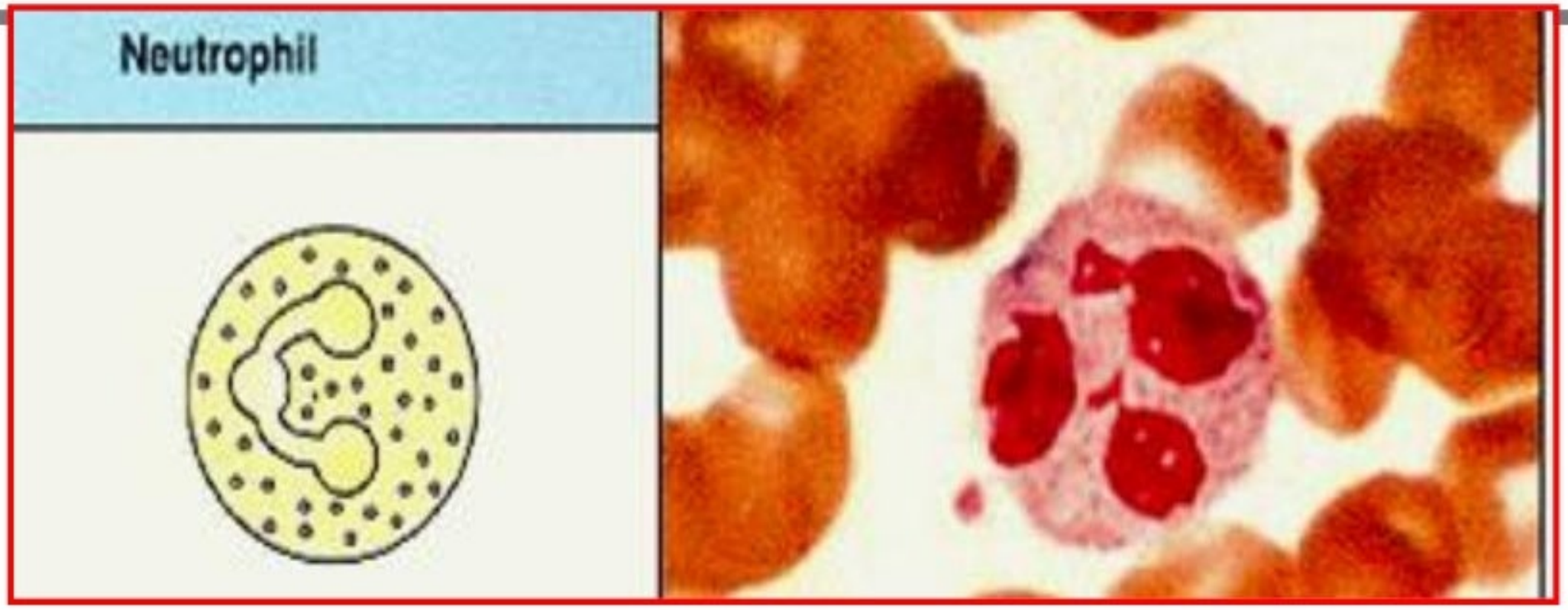
B-cell

Cytolysis

Innate immunity

- Front line of defense
- Not specific
- No immunologic memory

Innate Immune System



Immediate response
No memory
No specific recognition

ADAPTIVE IMMUNE SYSTEM

T-lymphocytes

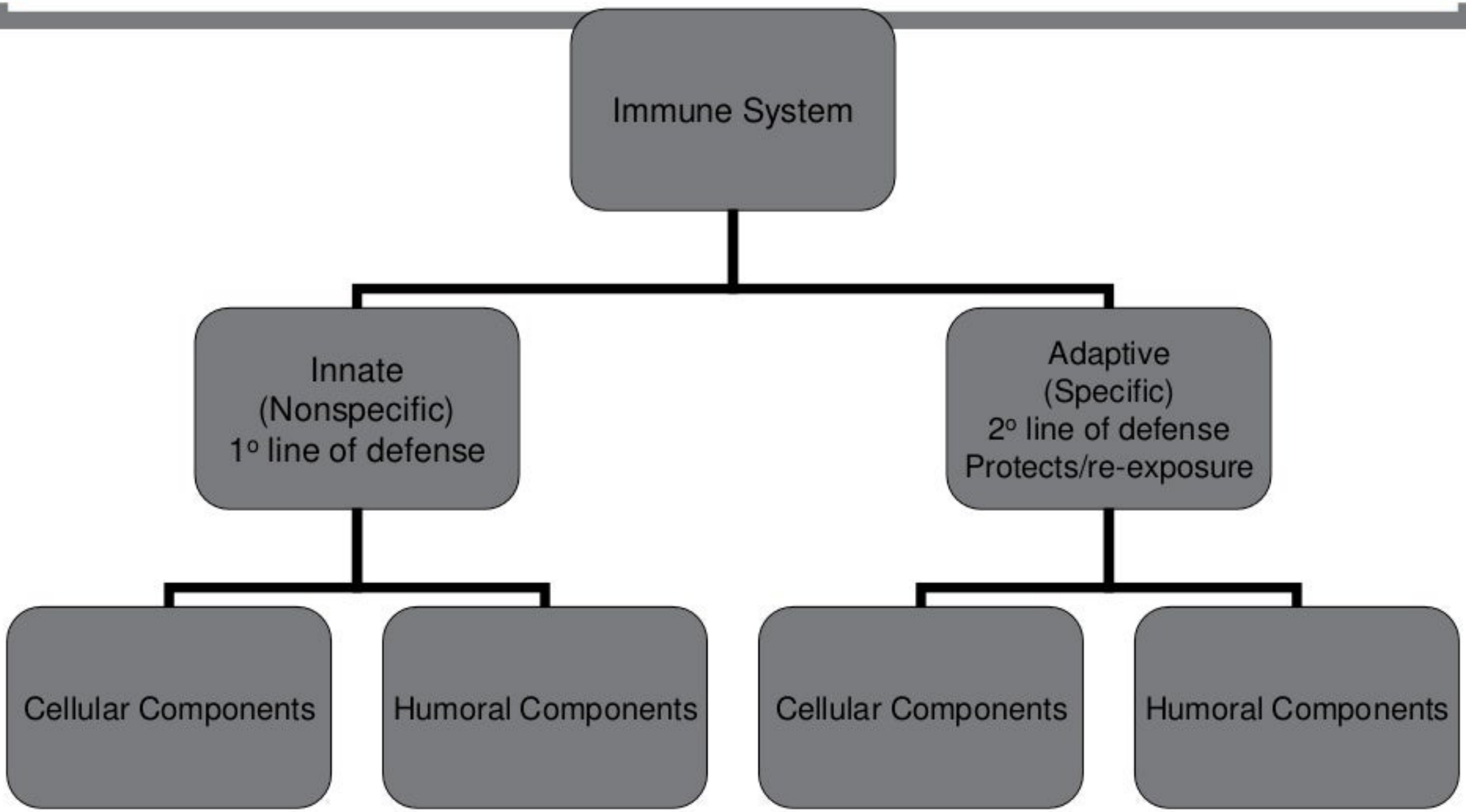
T-cytotoxic → Cytotoxic

B-lymphocytes

Plasma cells → Antibodies

Response takes 7 to 10 days

Overview of the Immune System

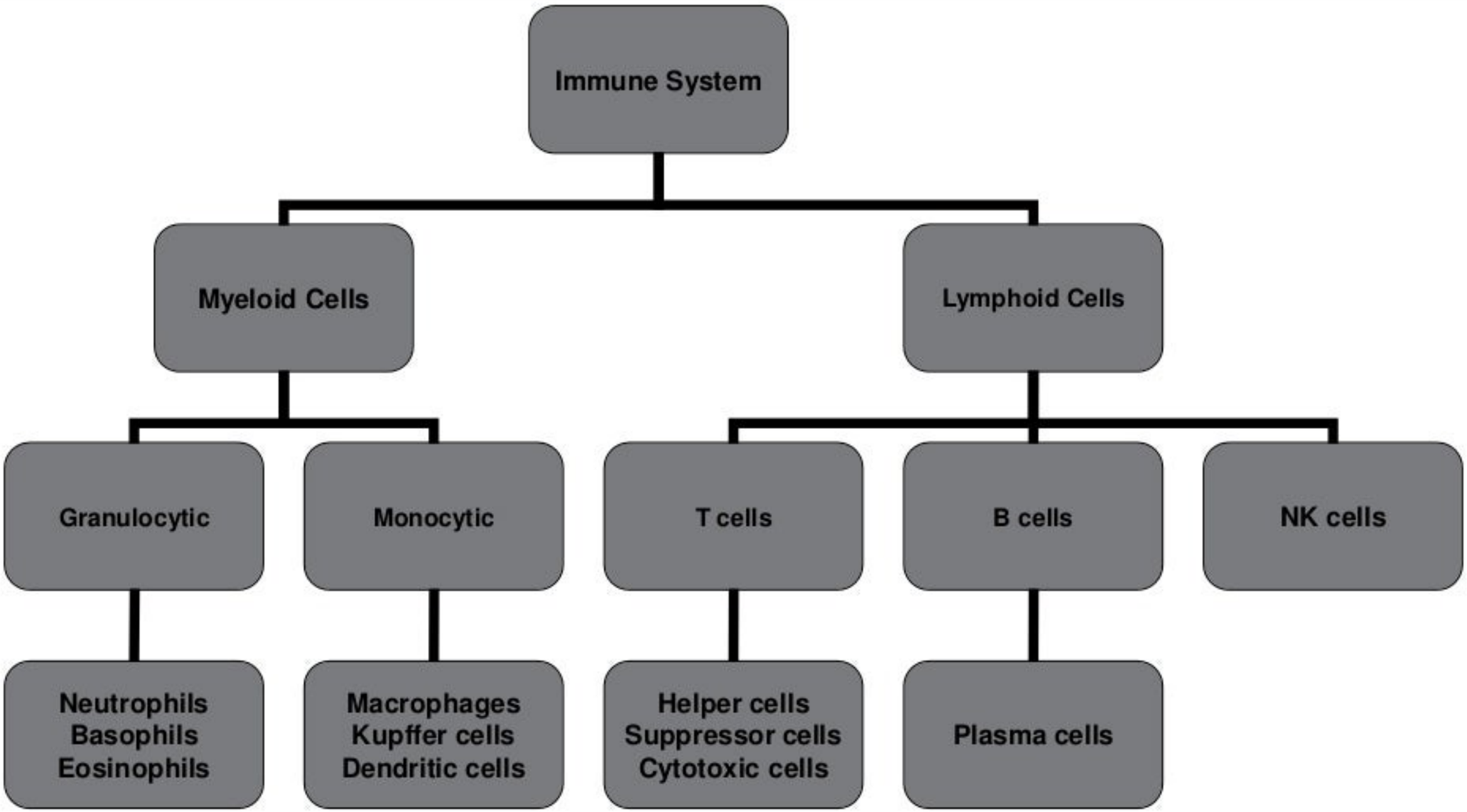


Interactions between the two systems

Comparison of Innate and Adaptive Immunity

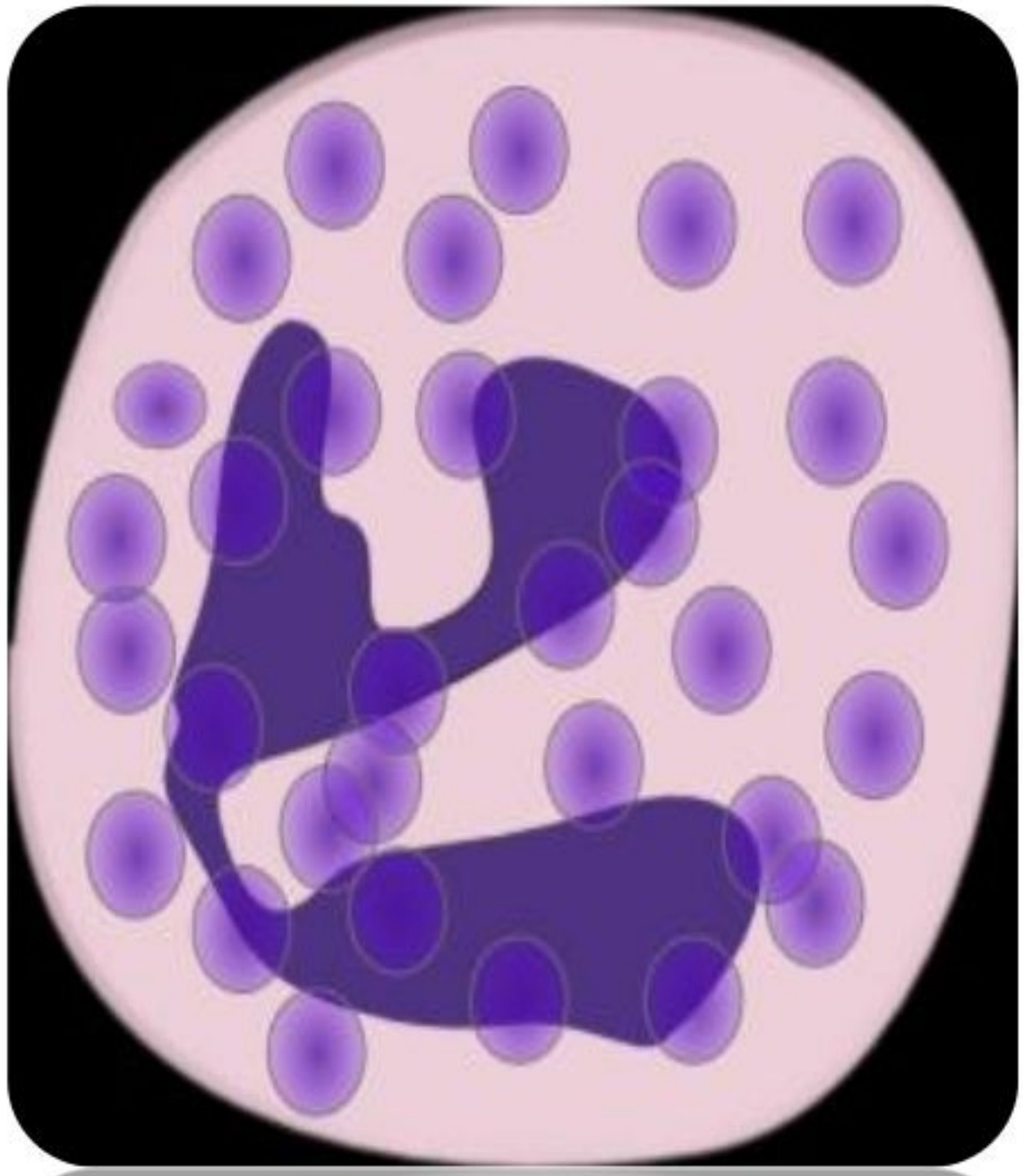
Innate Immunity	Adaptive Immunity
No time lag	A lag period
Not antigen specific	Antigen specific
No memory	Development of memory

Cells of the Immune System



Cellular components

- Neutrophils
- Monocytes and macrophages
- NK cells
- Eosinophils



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  - 20-40% of body's leukocytes
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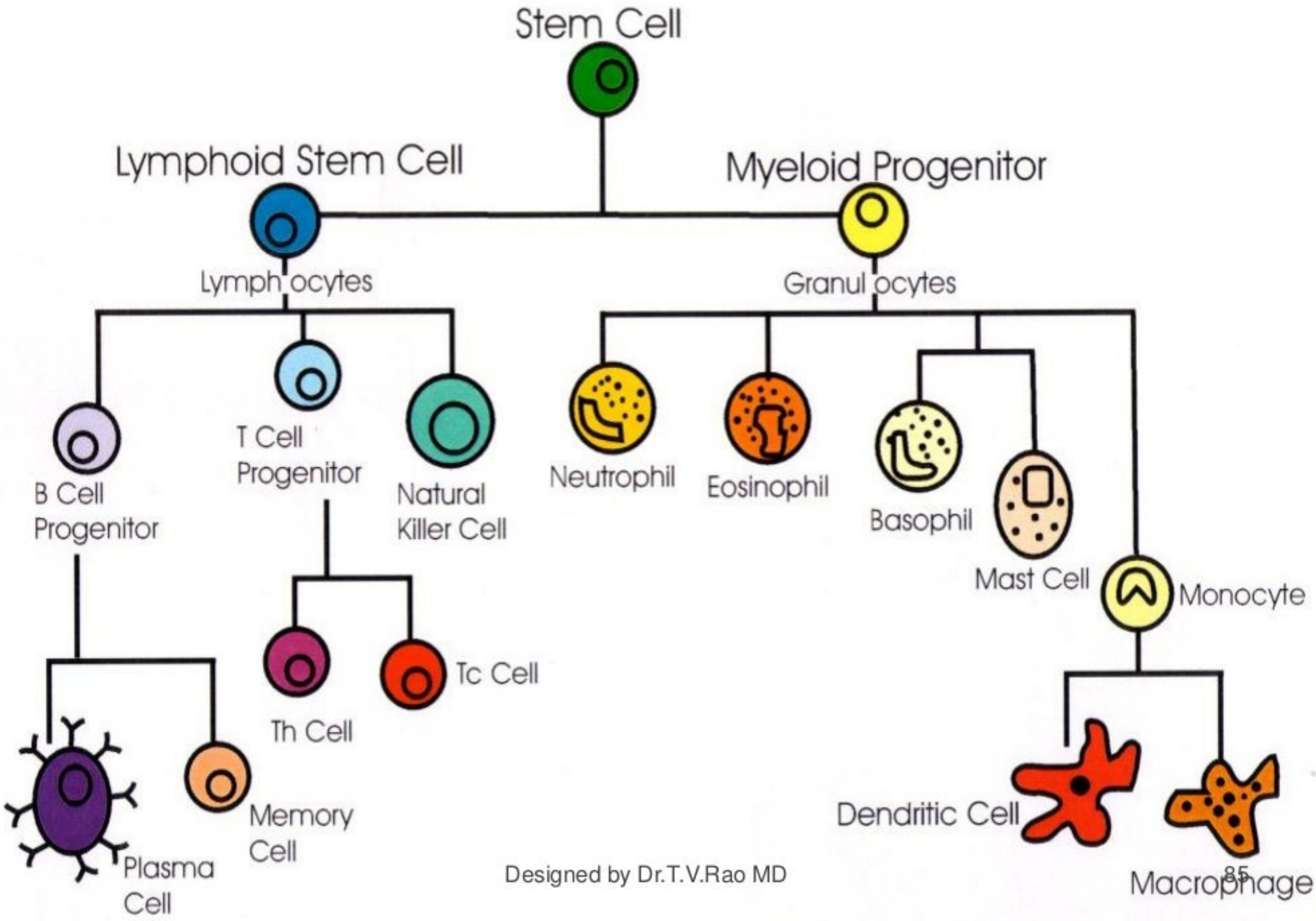
Cells of the Immune System



Identifying Cell Using the CD Nomenclature

- CD Cluster Of Differentiation
- Over 300 CD Markers
- T cells, CD4 or CD8 and CD3
- B cells, CD19
- NK cells, CD56
- Monocytes/Macrophages CD14
- Dendritic Cells, CD1c (Human), CD11c (mouse)

Mononuclear Cells

- Monocytes in Blood, MΦ in Tissues
  - Monocytes 5-10 times smaller than MΦ
- MΦ Increases Phagocytic Ability
- Secretes cytokines and Produces Hydrolytic Enzymes
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  - Alveolar (lungs), Kupffer (liver), Microglial (brain), Osteoclasts (bone)
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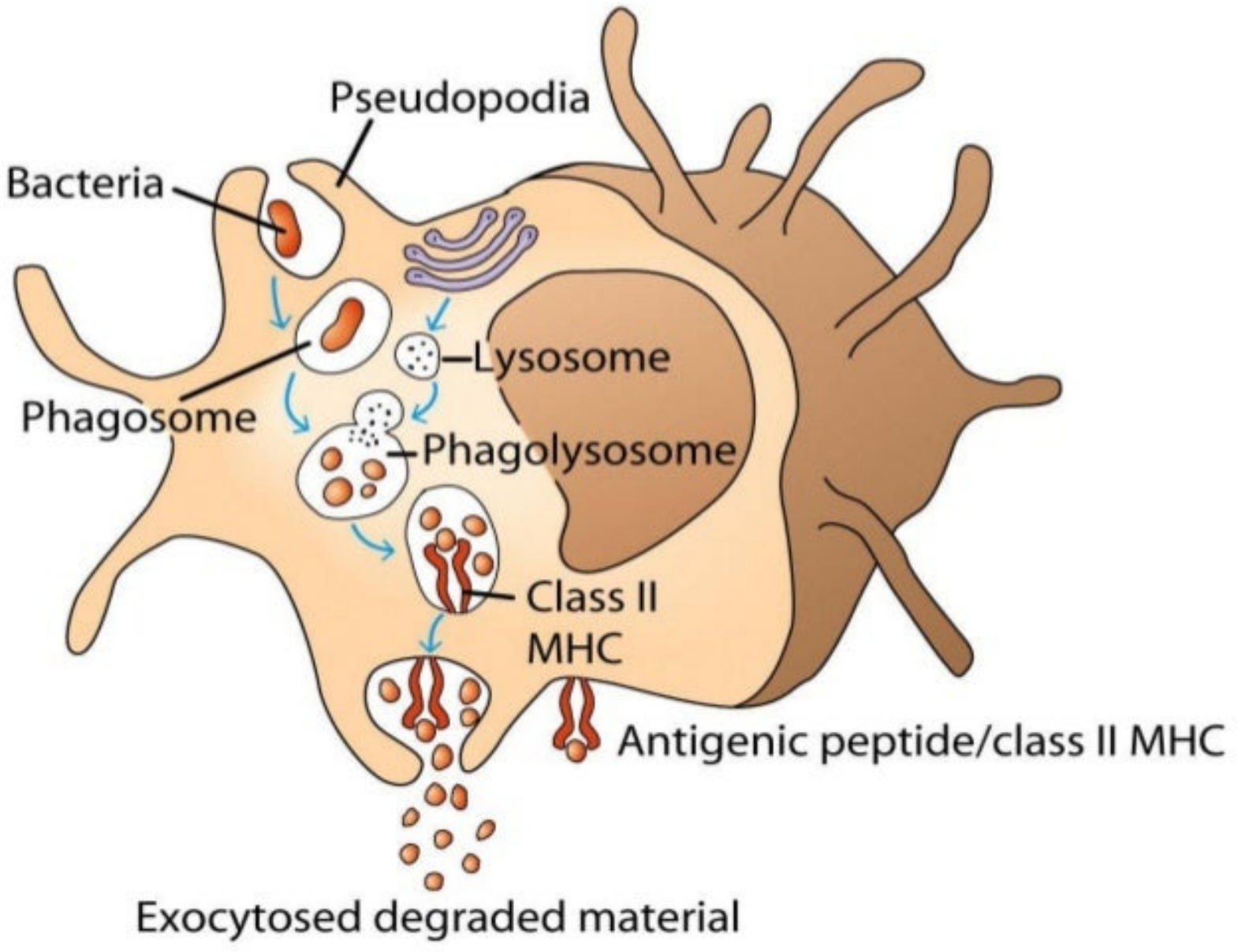
- Antigen Presenting Capacity Thru MHC II

MΦ Effective APC



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- Maybe Better for Tolerance

Anatomical Barriers - Mechanical Factors

System or Organ	Cell type	Mechanism
Skin	Squamous epithelium	Physical barrier Desquamation
Mucous Membranes	Non-ciliated epithelium (*e.g.* GI tract)	Peristalsis
	Ciliated epithelium (*e.g.* respiratory tract)	Mucociliary elevator
	Epithelium (*e.g.* nasopharynx)	Flushing action of tears, saliva, mucus, urine

Anatomical Barriers - Chemical Factors

System or Organ	Component	Mechanism
Skin	Sweat	Anti-microbial fatty acids
Mucous Membranes	HCl (parietal cells) Tears and saliva	Low pH Lysozyme and phospholipase A
	Defensins (respiratory & GI tract)	Antimicrobial
	Surfactants (lung)	Opsonin

Anatomical Barriers - Biological Factors

System or Organ	Component	Mechanism
Skin and mucous membranes	Normal flora	Antimicrobial substances Competition for nutrients and colonization

Humoral Components

Component	Mechanism
Complement	Lysis of bacteria and some viruses Opsonin Increase in vascular permeability Recruitment and activation of phagocytic cells
Coagulation system	Increase vascular permeability Recruitment of phagocytic cells B-lysin from platelets – a cationic detergent
Lactoferrin and transferrin	Compete with bacteria for iron
Lysozyme	Breaks down bacterial cell walls
Cytokines	Various effects

Cellular Components

Cell	Functions
Neutrophils	Phagocytosis and intracellular killing Inflammation and tissue damage
Macrophages	Phagocytosis and intracellular killing Extracellular killing of infected or altered self targets Tissue repair Antigen presentation for specific immune response
NK and LAK cells	Killing of virus-infected and altered self targets
Eosinophils	Killing of certain parasites

Innate (non-specific) Immunity

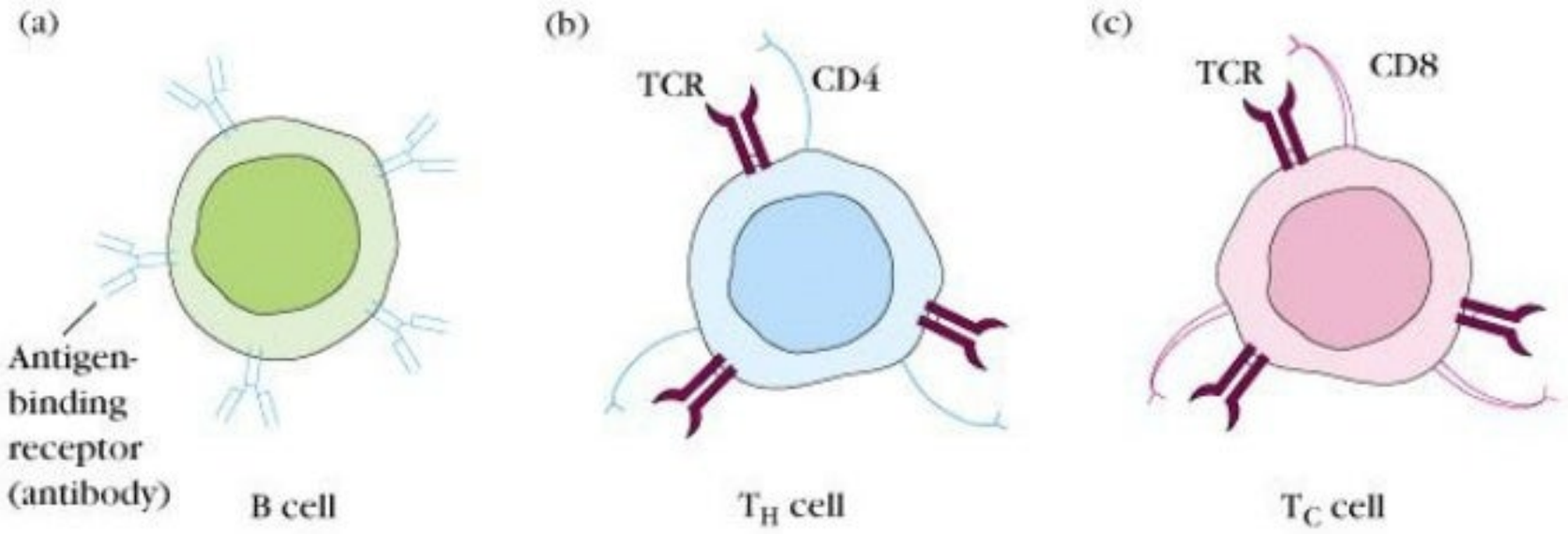
- 4 barriers to infection
  - Anatomic
  - Physiologic
  - Phagocytic
  - Inflammatory

Specific Defenses

- An *antigen* is any foreign substance that stimulates the immune system to react to it.
- The body does not consider its own proteins foreign; therefore the immune system must distinguish *self* from *nonself*.
- Lymphocytes have a large number of *antigen receptors*.

Adaptive Immunity requires 2 major groups of cells:

a. B and T Lymphocytes (B or T cells)

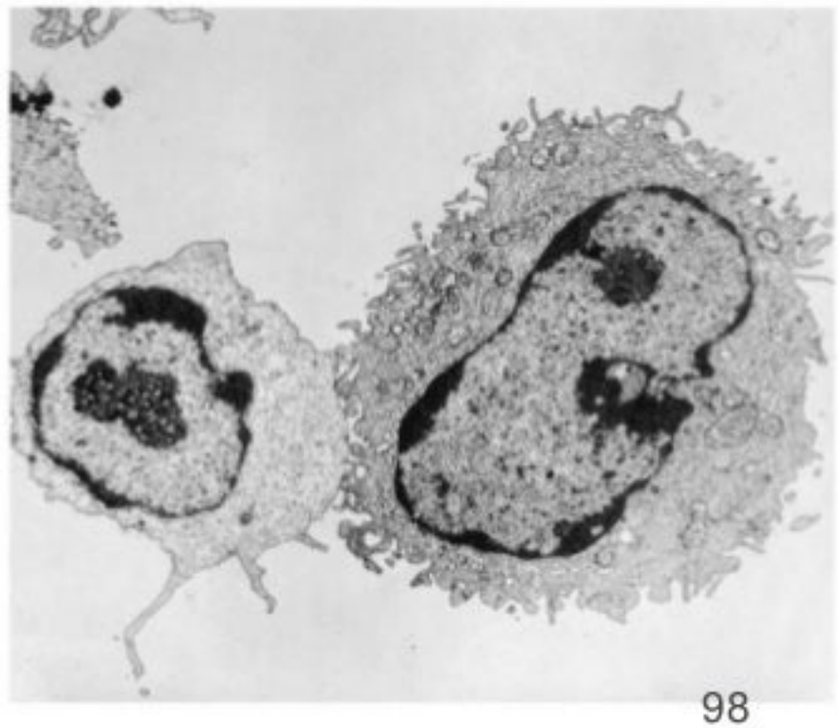


b. Antigen presenting cells (APC's)

-macrophage (MØ)

-dendritic cells (DC)

-B cells



Adaptive Immunity

Displays four (4) attributes:

1) antibody specificity – distinguishes minute differences in molecular structure to determine non-self antigens.

2) diversity – the immune system can produce a hugely diverse set of recognition molecules which allows us to recognize literally billions of molecular shapes

3) memory – once it has responded to an antigen, the system maintains a memory of that Ag

4) **self-nonself recognition** –the system typically responds only to foreign molecules

***adaptive IR is not independent of innate IR – they're connected**

Humoral vs Cell-mediated Immune Response:

Humoral IR: occurs when Ag becomes coated with Ab which brings about the elimination of the foreign body

-cross-link several Ag's to form clumps -> more easily phago'd

-bind complement proteins

-neutralize toxins, viruses, and bacteria from binding target cells

Cell-Mediated IR: occurs when effector T cells are activated

-activated T_H cells → activate phagocytic cells
activate B cells to produce Ab

-activated T_C cells → kill altered self cells (viral infected and tumor cells)

Specific defences require B and T Lymphnodes

- Specific defenses require *B lymphocytes* (*B cells*) and *T lymphocytes* (*T cells*), which are both produced in the bone marrow; however, T cells mature in the thymus, while B cells mature in bone marrow.
- B cells give rise to *antibodies* that are shaped like antigen receptors and are capable of combining with and neutralizing antigens.
- T cells do not produce antibodies but instead attack foreign antigens directly.

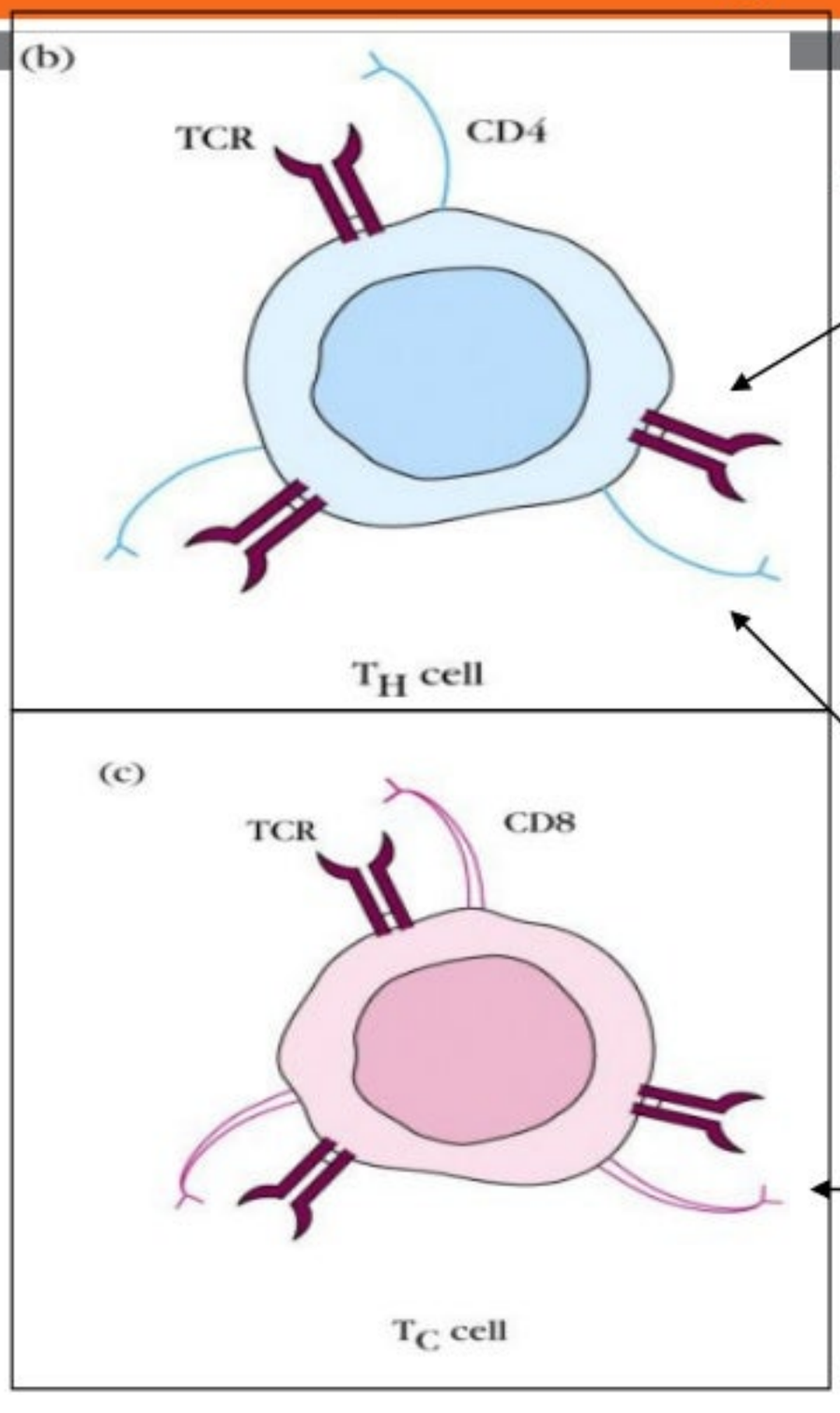
Types of T Cells

- *Cytotoxic T cells* kill infected cells that bear a foreign antigen on contact. Cytotoxic T cells provide *cell-mediated immunity*.

- *Helper T cells* stimulate other immune cells and produce cytokines.

- Some T cells are *memory T cells* that will jump-start an immune reaction upon re-infection.

T Lymphocytes



- Formed in bone marrow; migrate to and mature in Thymus gland
- Exhibit unique T-cell Antigen receptors (**TCR**'s) on surface
- **TCR**'s can only recognize Ag with associated with MHC glycoproteins
  - **MHC I** – found on nearly all nucleated cells
  - **MHC II** – found only on APC's

Once T cell binds to Ag, it triggers cell division to form both memory T cells and effector T cells

There are 2 populations of T cells characterized by the type of **CD glycoprotein** found on surface:

T_H – exhibits **CD4**

T_C – exhibits **CD8**

B Cells and Antibody-Mediated Immunity

- A *toxin* is a chemical produced by certain bacteria that is poisonous.
- As a B cell encounters a bacterial cell or a toxin with a specific antigen in a lymph node or spleen, it is activated to divide.
- The resulting cells are *plasma cells*, mature B cells that mass-produce antibodies.
- Defense by B cells is thus called *antibody-mediated immunity*.

Structure of IgG

- The most common type of antibody, the *IgG antibody*, is a Y-shaped molecule that has two binding sites for a specific antigen.

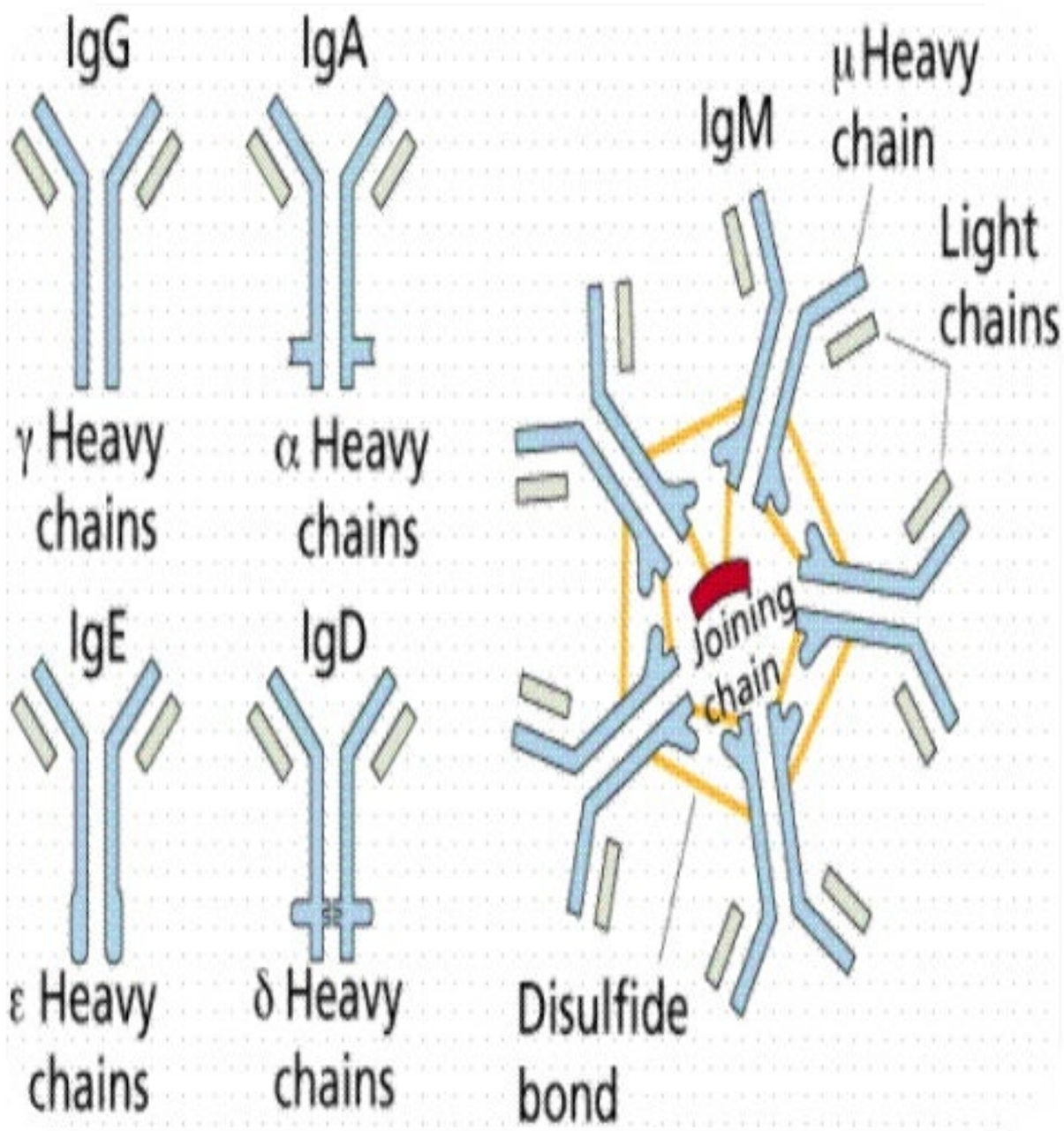
- Antigen-antibody complexes often mark the antigen for destruction by neutrophils or macrophages, or they may activate complement.

Other Types of Antibodies

- There are five types of antibodies:
- *IgG* – the main type in circulation, binds to pathogens, activates complement, and enhances phagocytosis
- *IgM* – the largest type in circulation, activates complement and clumps cells
- *IgA* – found in saliva and milk, prevents pathogens from attaching to epithelial cells in digestive and respiratory tracts

Immunoglobulin's (Cont)

- *IgD* – on surface of immature B cells, its presence signifies the readiness of a B cell
- *IgE* – found as antigen receptor on basophils in blood and on mast cells in tissues, responsible for immediate allergic response and protection against certain parasitic worms.
- The different classes of antibodies vary in structure.



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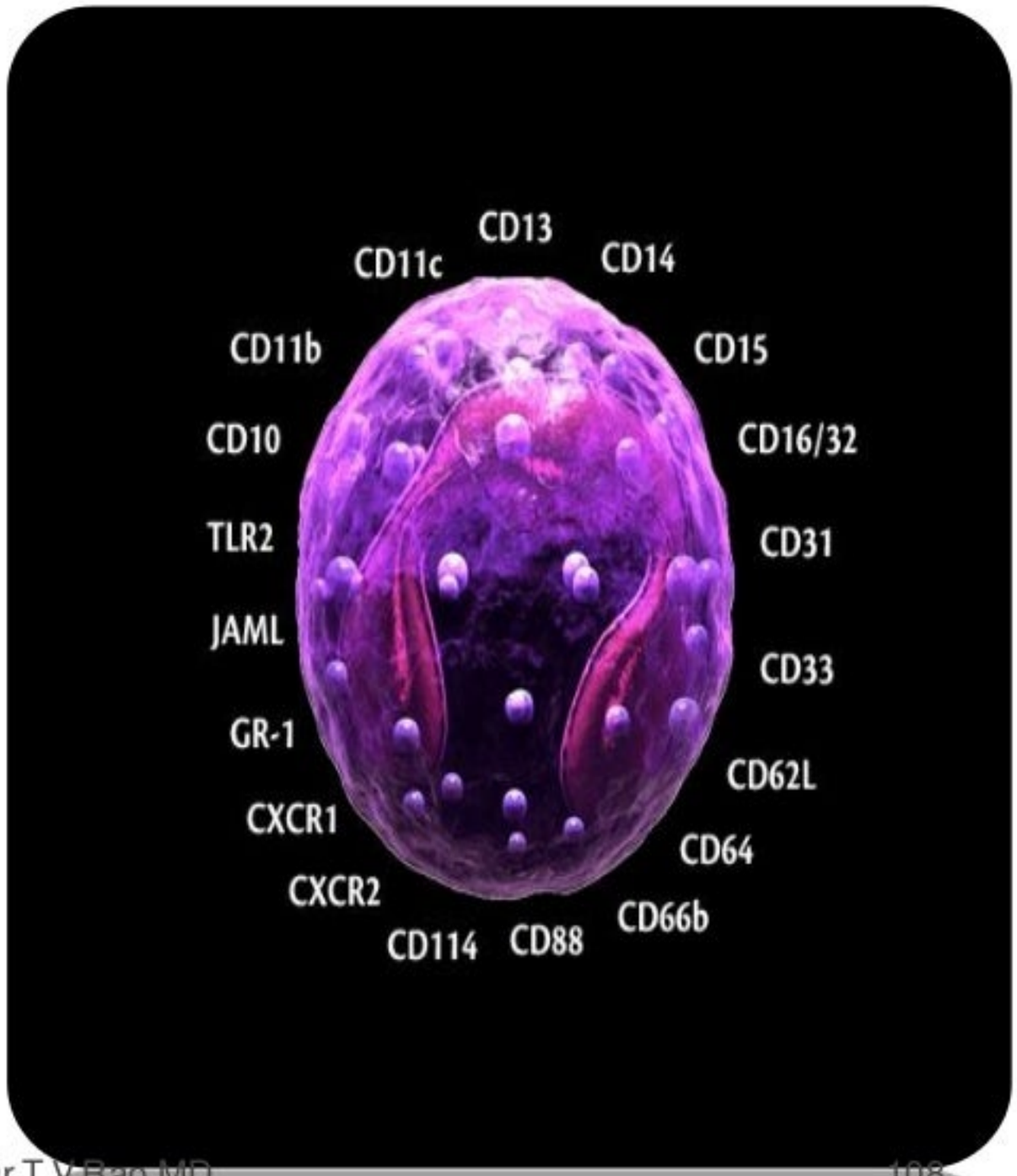
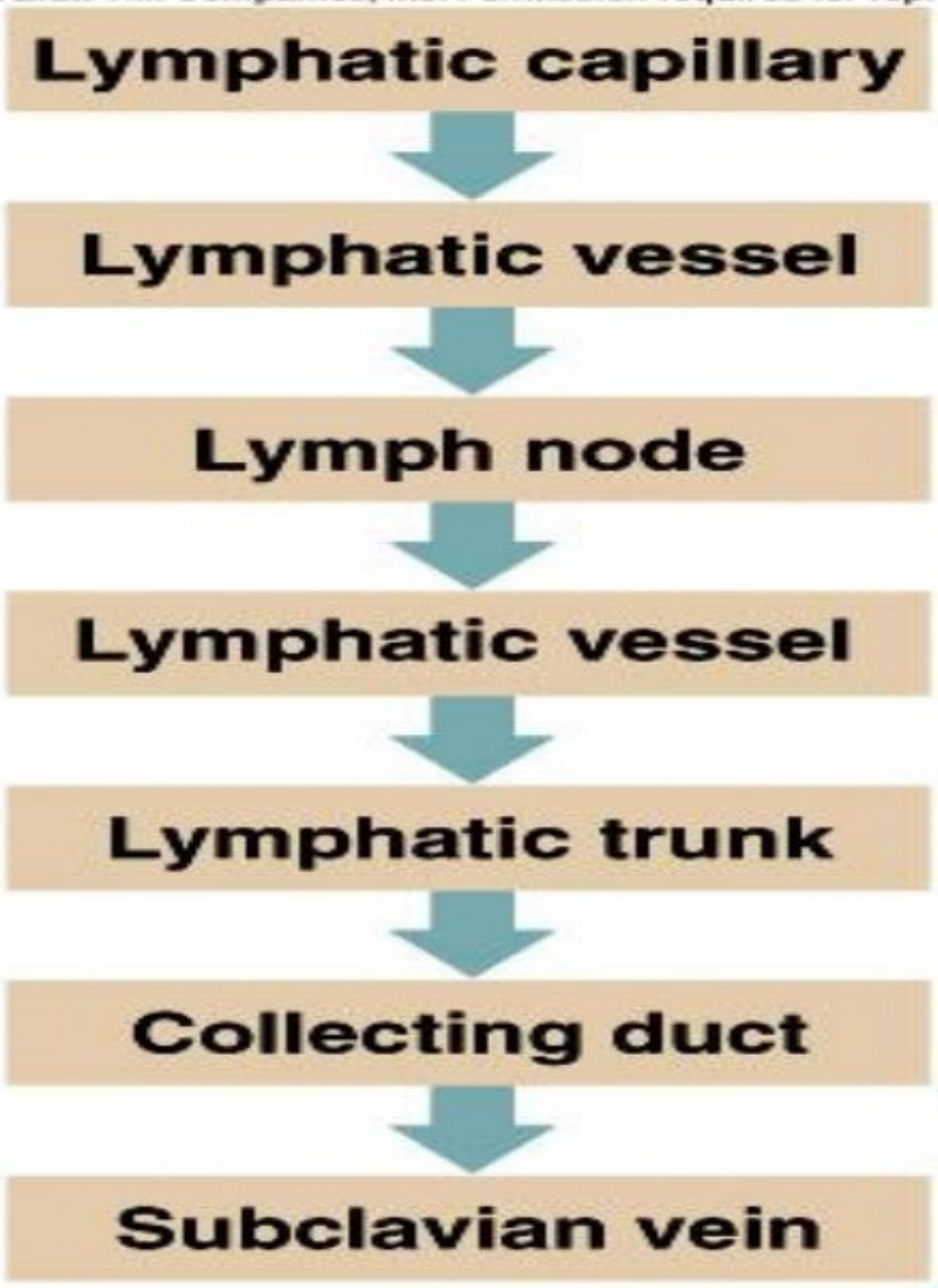


Induced Immunity

- Immunity occurs naturally by infection or is induced by medical intervention.
- The two types of *induced immunity* are active immunity and passive immunity.
- In *active immunity*, the individual produces the antibodies against an antigen.
- In *passive immunity*, the individual is given prepared antibodies.

Lymphatic Pathways



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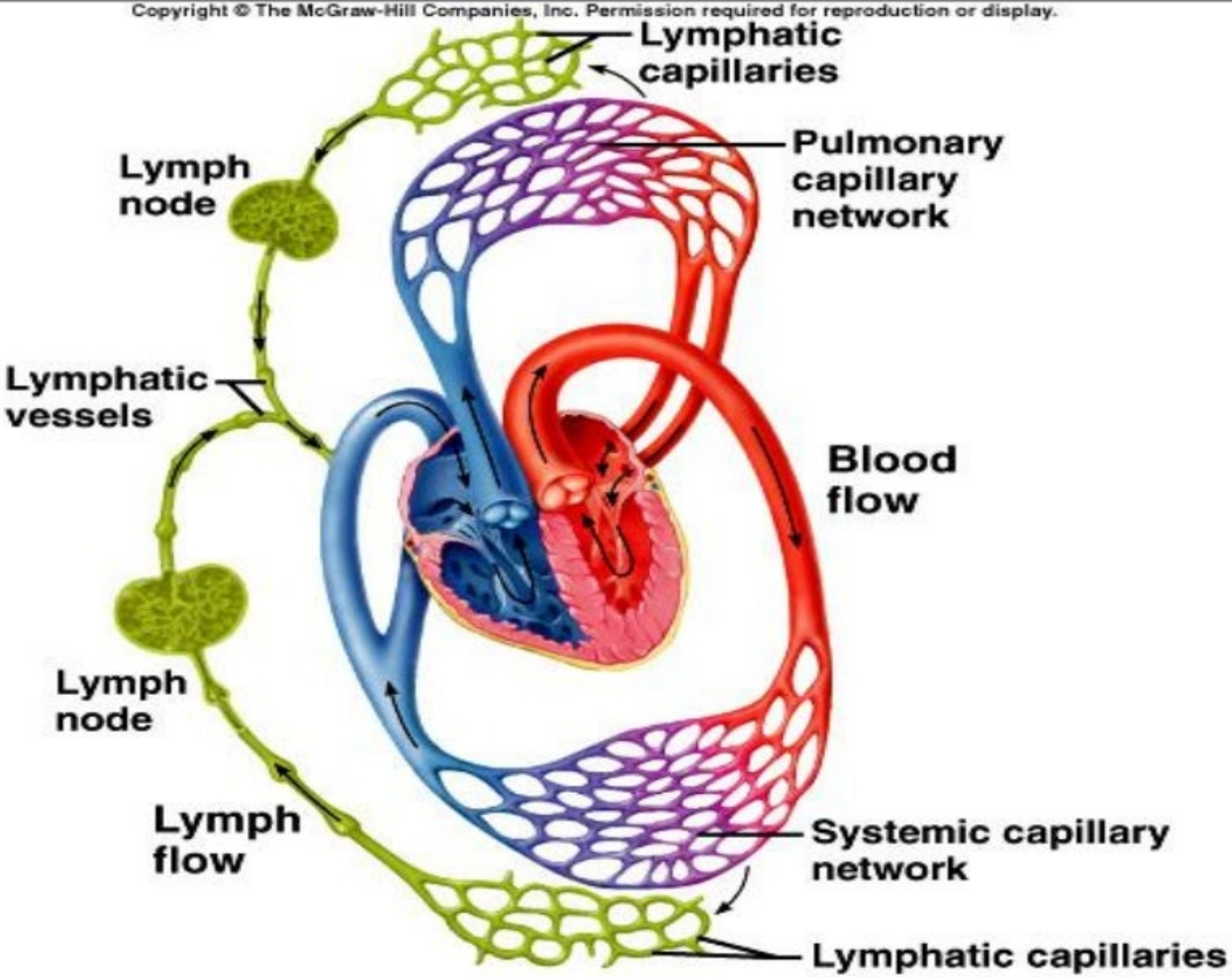
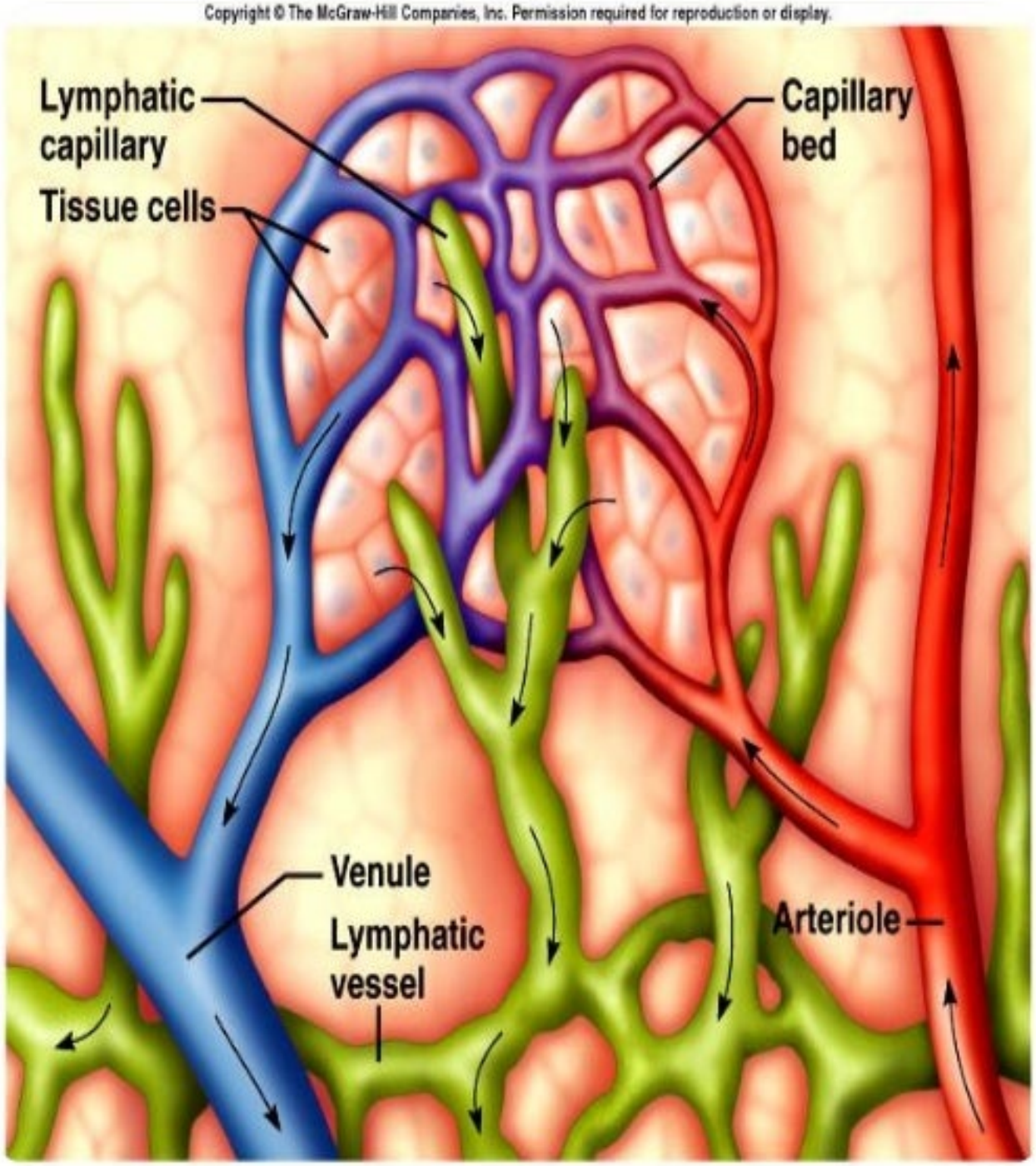


Lymphatic Capillaries

- microscopic
- closed-ended tubes
- in interstitial spaces of most tissues

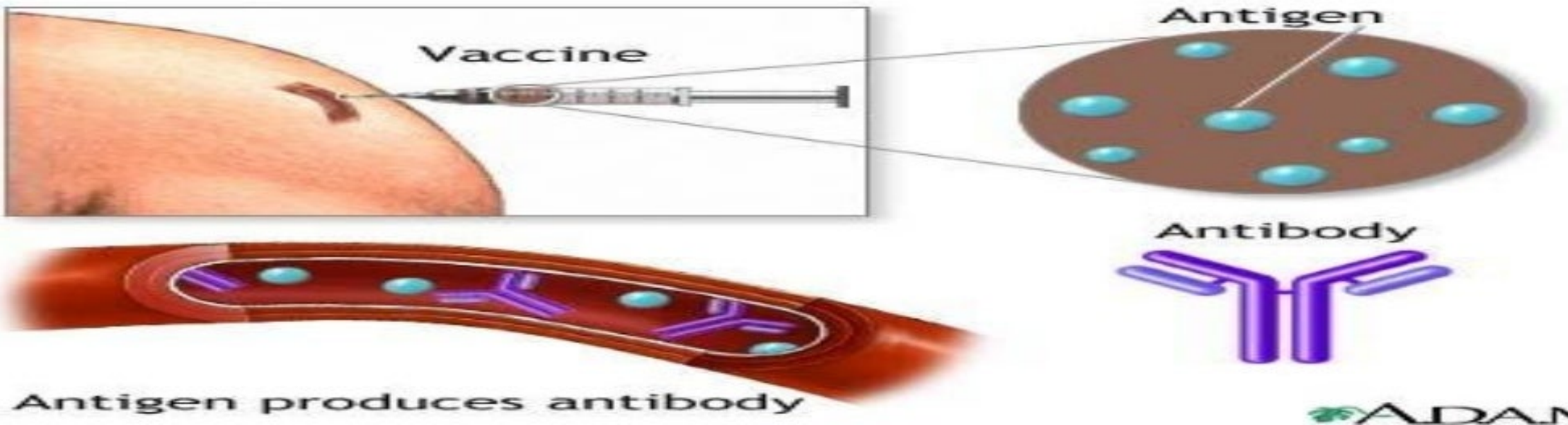


Active Immunity

- A person naturally develops *active immunity* after infection.
- *Immunization* involves the use of *vaccines*, substances that contain an antigen to which the immune system responds.
- Vaccines are available to induce long-lived active immunity in a well person.

Active Immunity

- After exposure to a vaccine, which is a non-virulent disease agent, antibodies are produced.
- With a booster shot or second exposure, the antibody titer rises to a much higher level.
- Active immunity is long-lived because there are memory B cells and memory T cells that will respond to lower doses of antigen in the body.



Passive Immunity

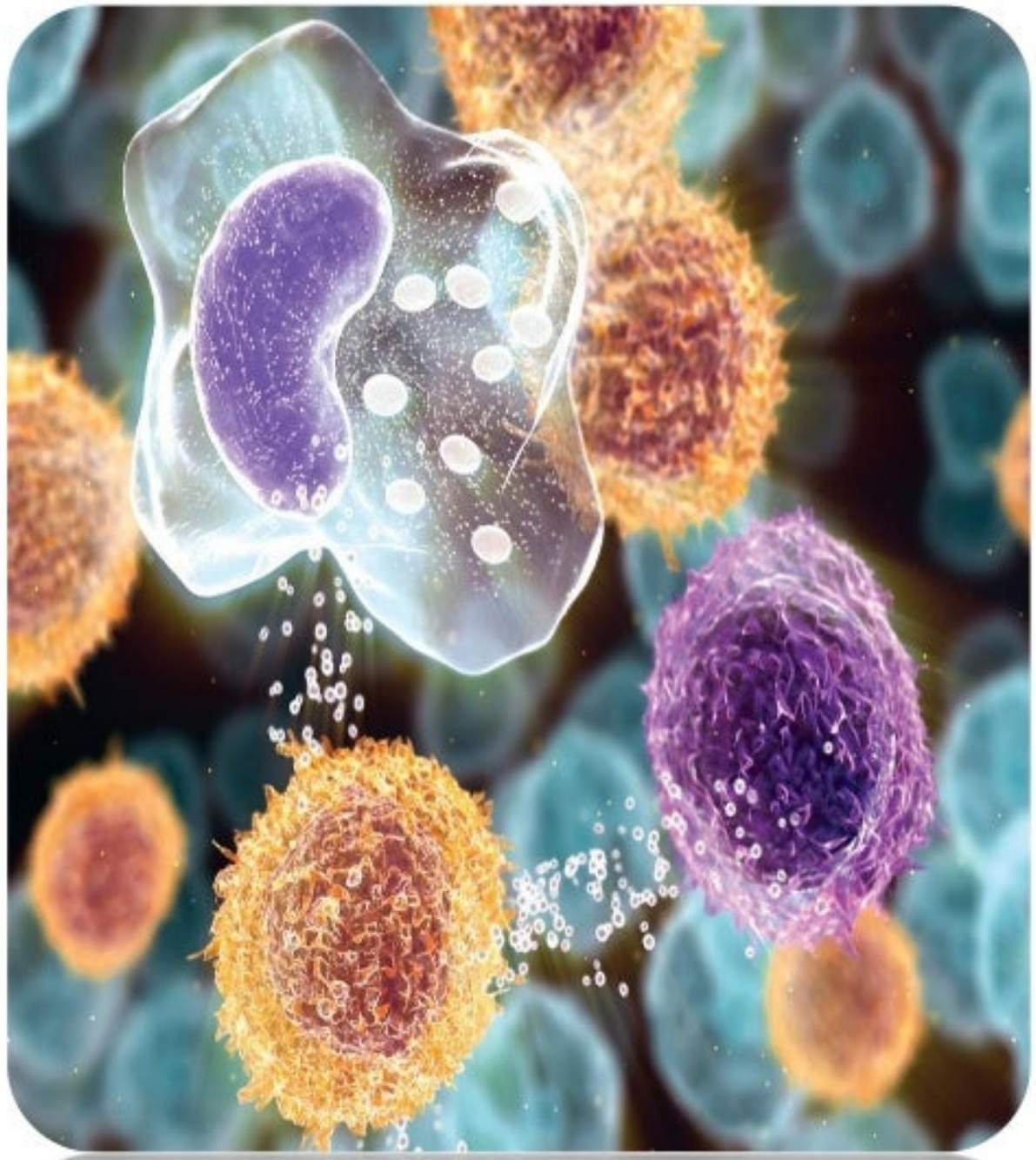
- You **don't** produce the antibodies
  - A mother will pass immunities on to her baby during pregnancy - through what organ?
  - These antibodies will protect the baby for a short period of time following birth while its immune system develops. What endocrine gland is responsible for this?
  - Lasts until antibodies die

Passive Immunity

- *Passive immunity* occurs when an individual is given prepared antibodies.
- For example, a newborn has antibodies that passed from its mother through the placenta.
- Breast-feeding passes antibodies from mother to child.
- However, passive immunity is short-lived since the antibodies were not produced by the person's own B cells.

Cytokines and Immunity

- *Cytokines* are signaling molecules produced by T lymphocytes, monocytes, and other cells.
- Both *interferon* and *interleukins* are cytokines used to improve a person's own T cell performance in fighting cancer.
- Interleukins show promise in the treatment of chronic infectious diseases.



ANTIBODIES

POLYCLONAL.

Derived from different B Lymphocytes cell lines

Batch to Batch variation affecting Ab reactivity & titre

NOT Powerful tools for clinical diagnostic tests

MONOCLONAL.

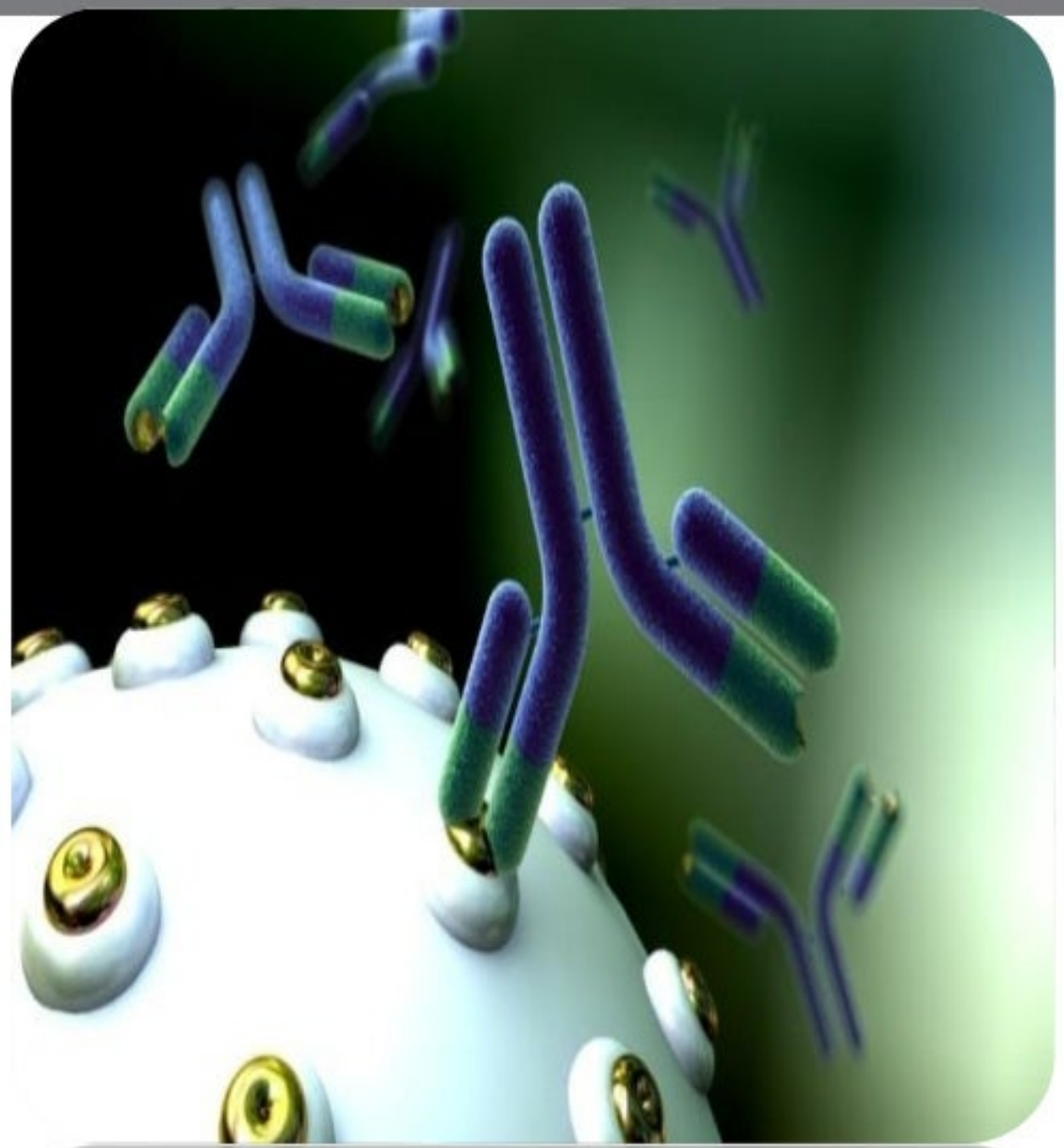
Derived from a single B cell clone

mAb offer Reproducible, Predictable & Potentially inexhaustible supply of Ab with exquisite specificity

Enable the development of secure immunoassay systems.

Monoclonal Antibodies

- All plasma cells derived from the same B cell secrete an identical antibody.
- B lymphocytes can therefore be exposed to a particular antigen and will produce *monoclonal antibodies* to the specific antigen.



Major Histocompatibility Complex (MHC)

- **There are two major classes of MHC molecules associated with T-cell function, namely:**

MHC Class I

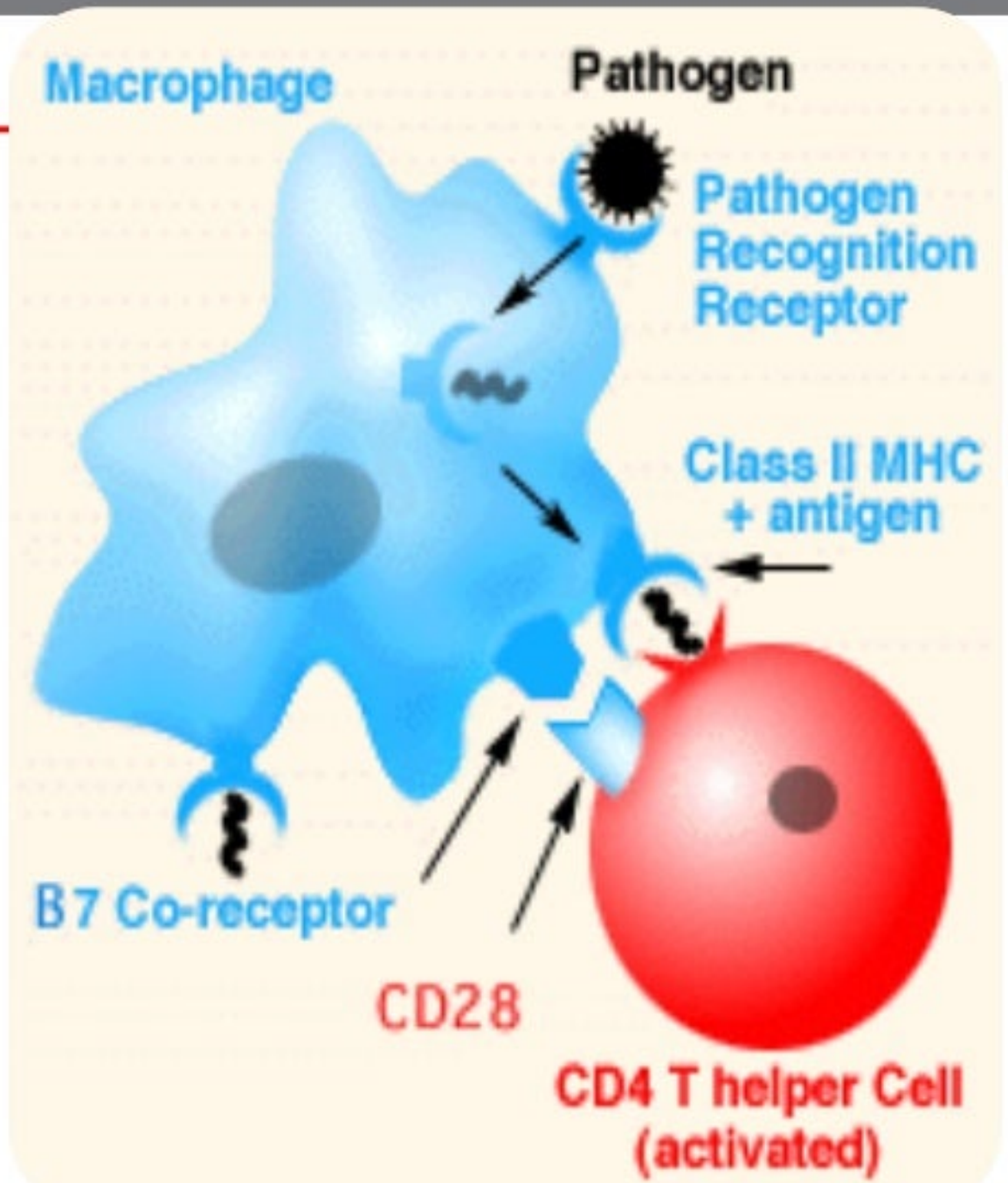
MHC Class II.

HUMAN LEUKOCYTE ANTIGEN (HLA)

- The HLA is related to MCH Class I and II expression
- HLA is related to risk for autoimmune diseases and allograft transplantation survival.

Major Histocompatibility Complex

- The major function of the molecules encoded by the *Mhc* is to facilitate the display of unique molecular fragments on the surface of cells in an arrangement that permits their recognition by immune effectors such as T-lymphocytes.



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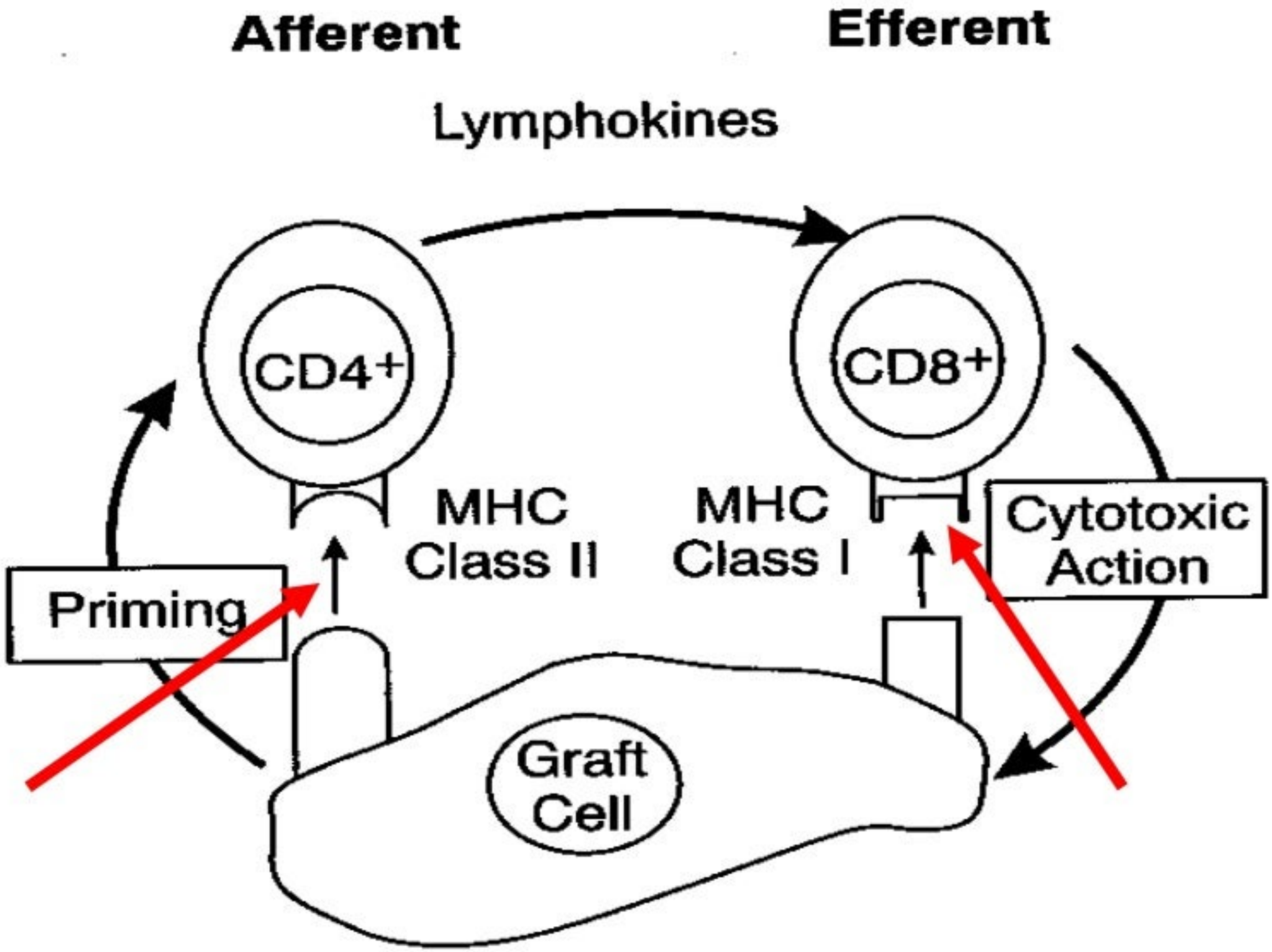

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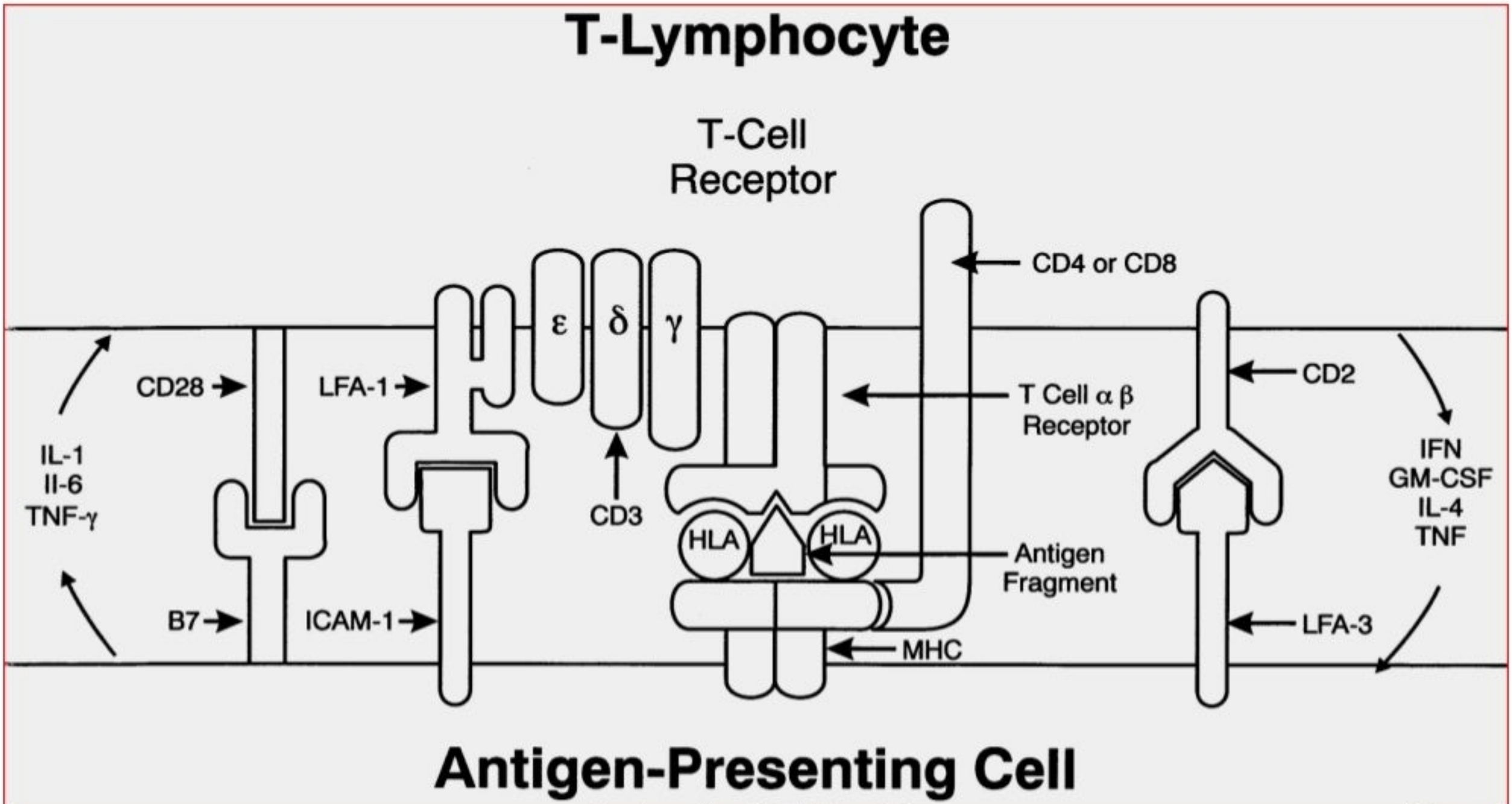
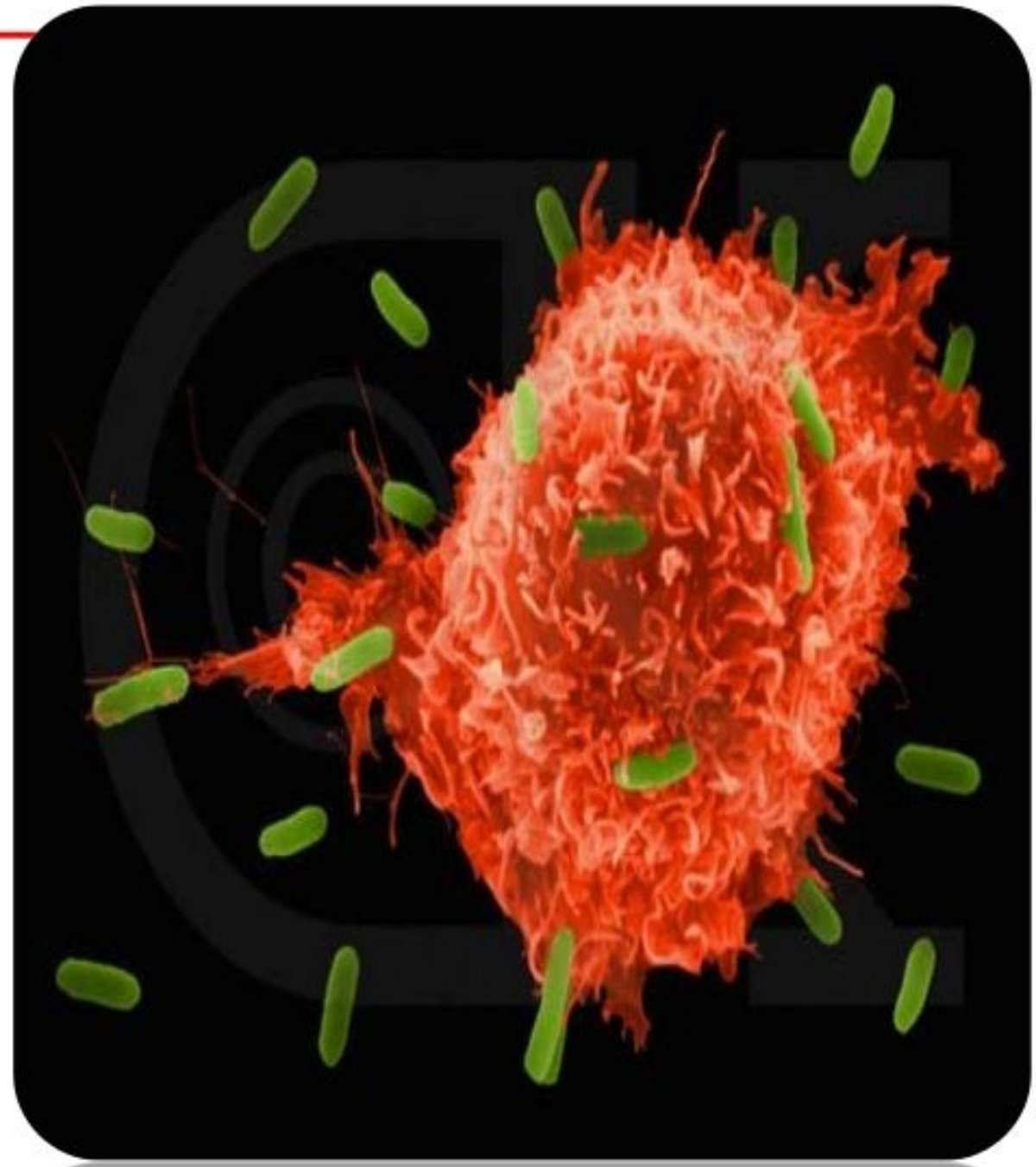


Antigen Presenting Cell

- Macrophages,
- Vascular endothelial cells,
- B-cells, and
- Dendritic cells (Heart)
- Express the major histocompatibility complex (MHC) molecules and can present antigen to the T-cells.



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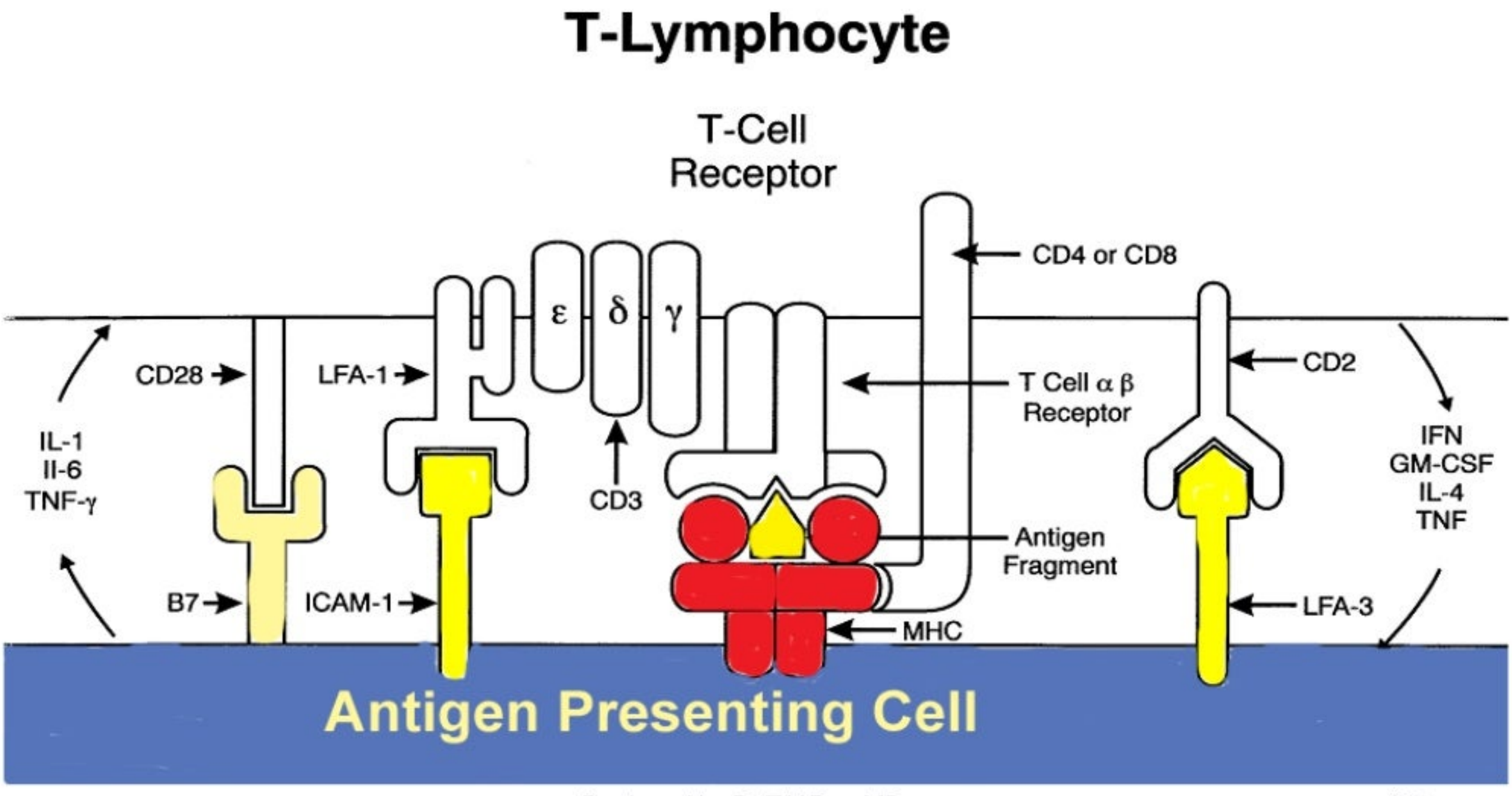

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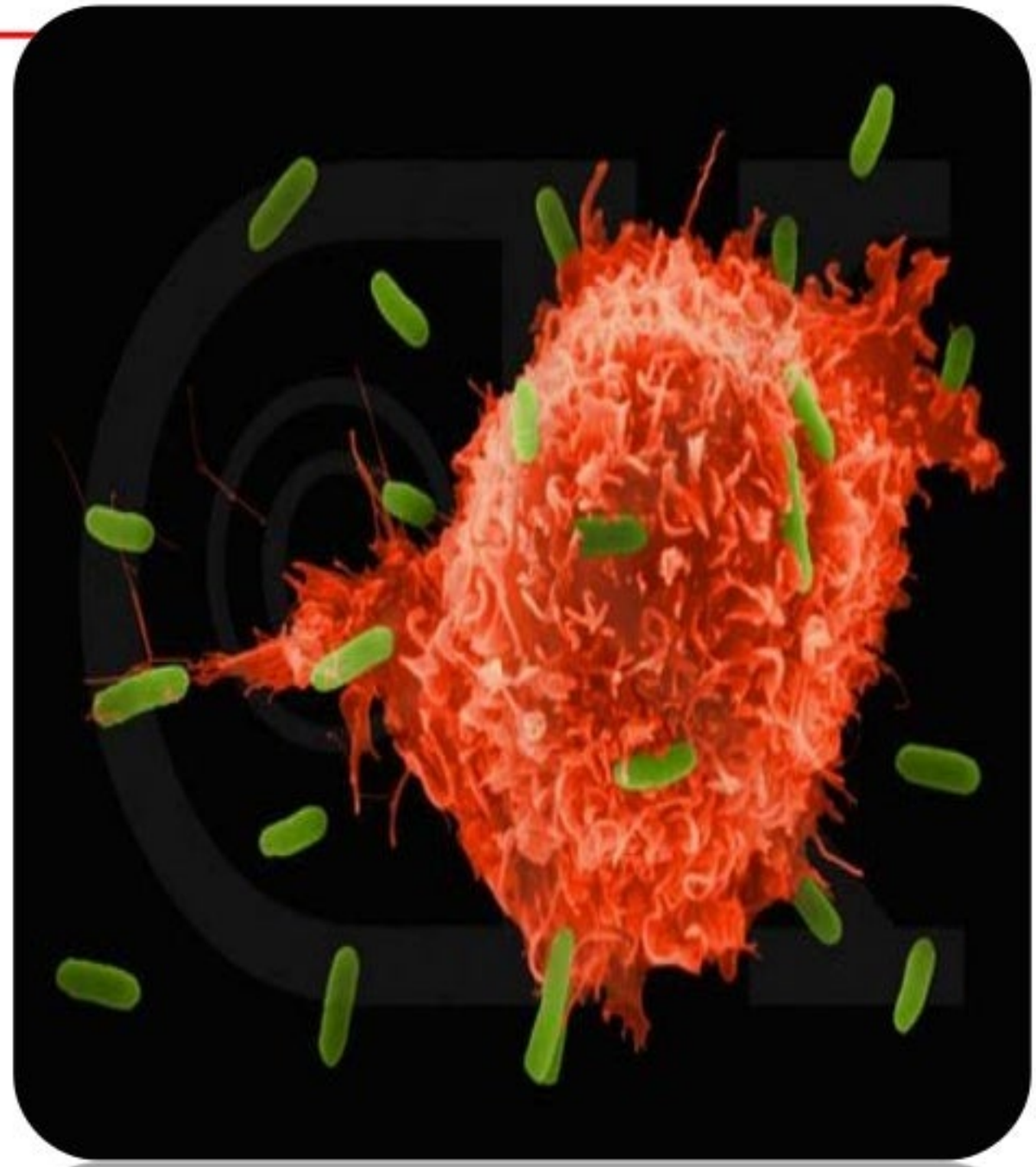

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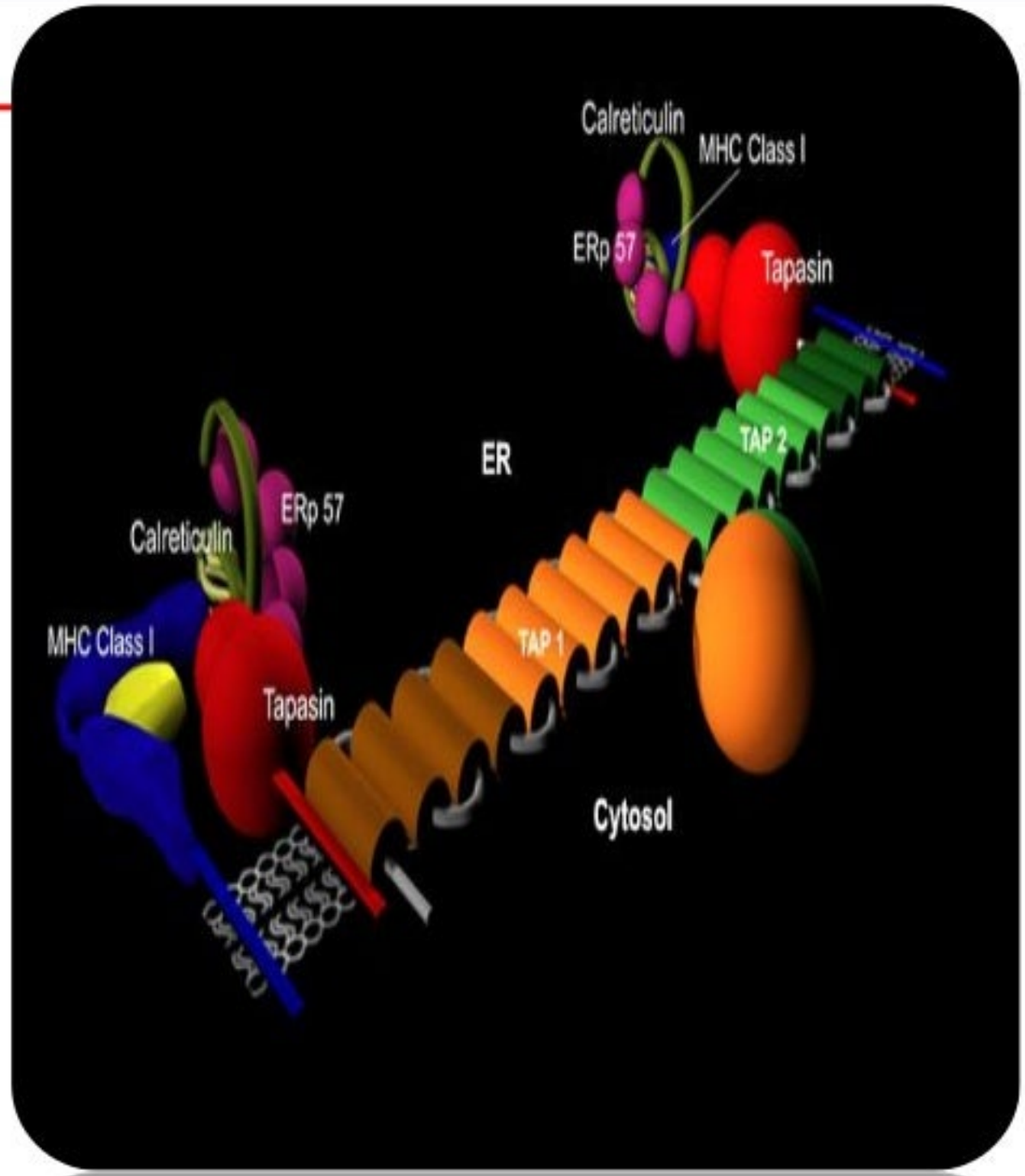
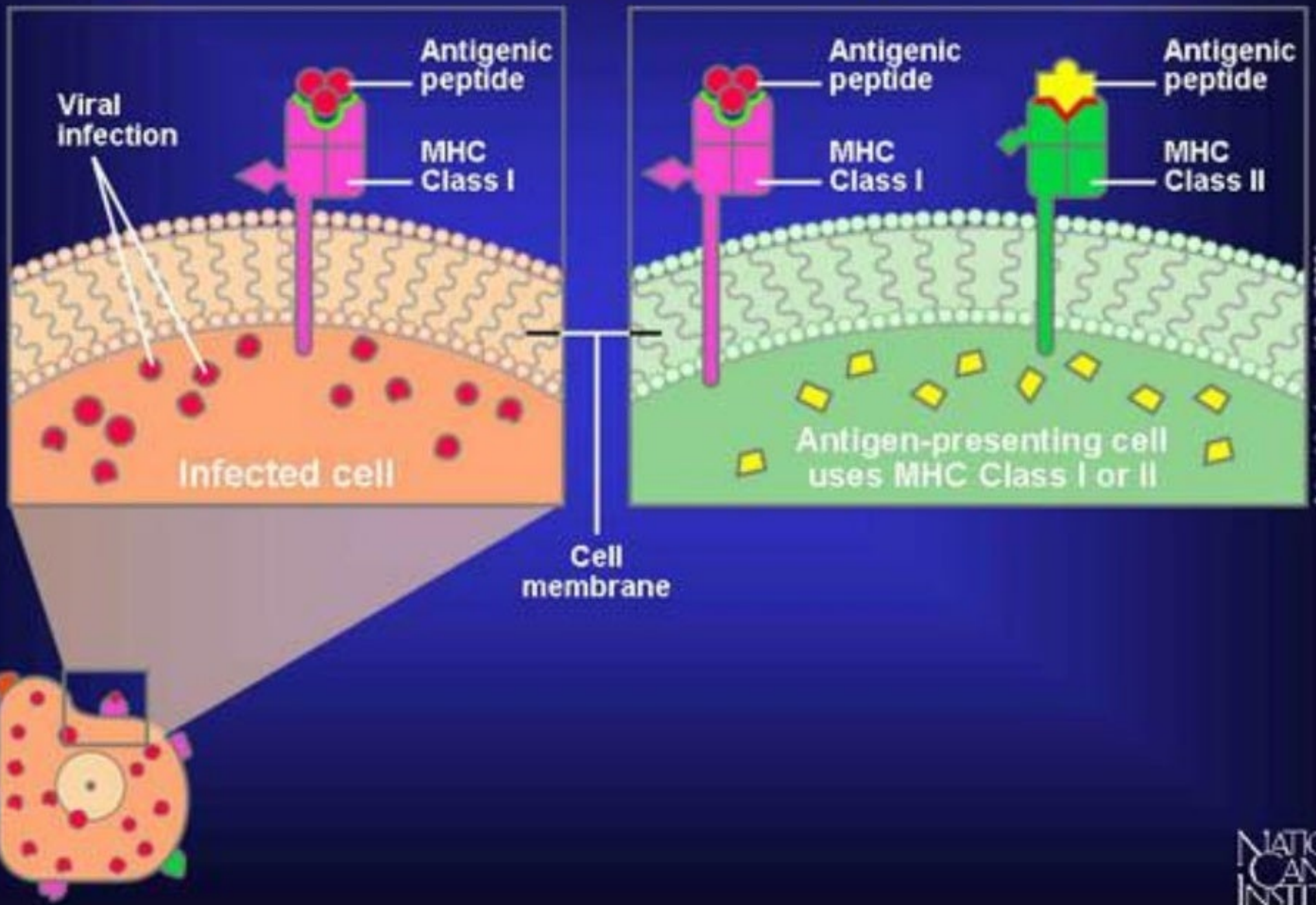


Markers of Self: Major Histocompatibility Complex



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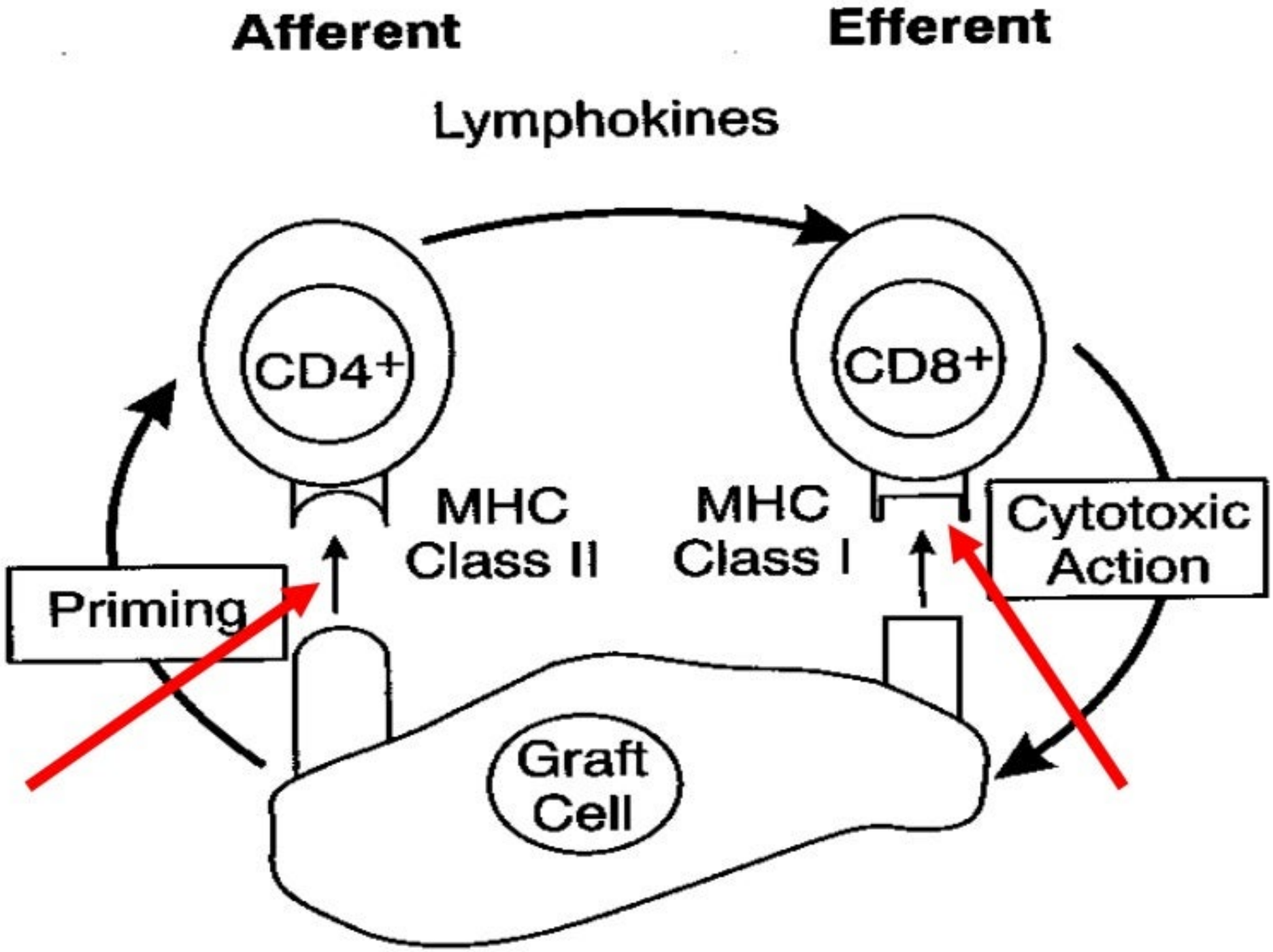

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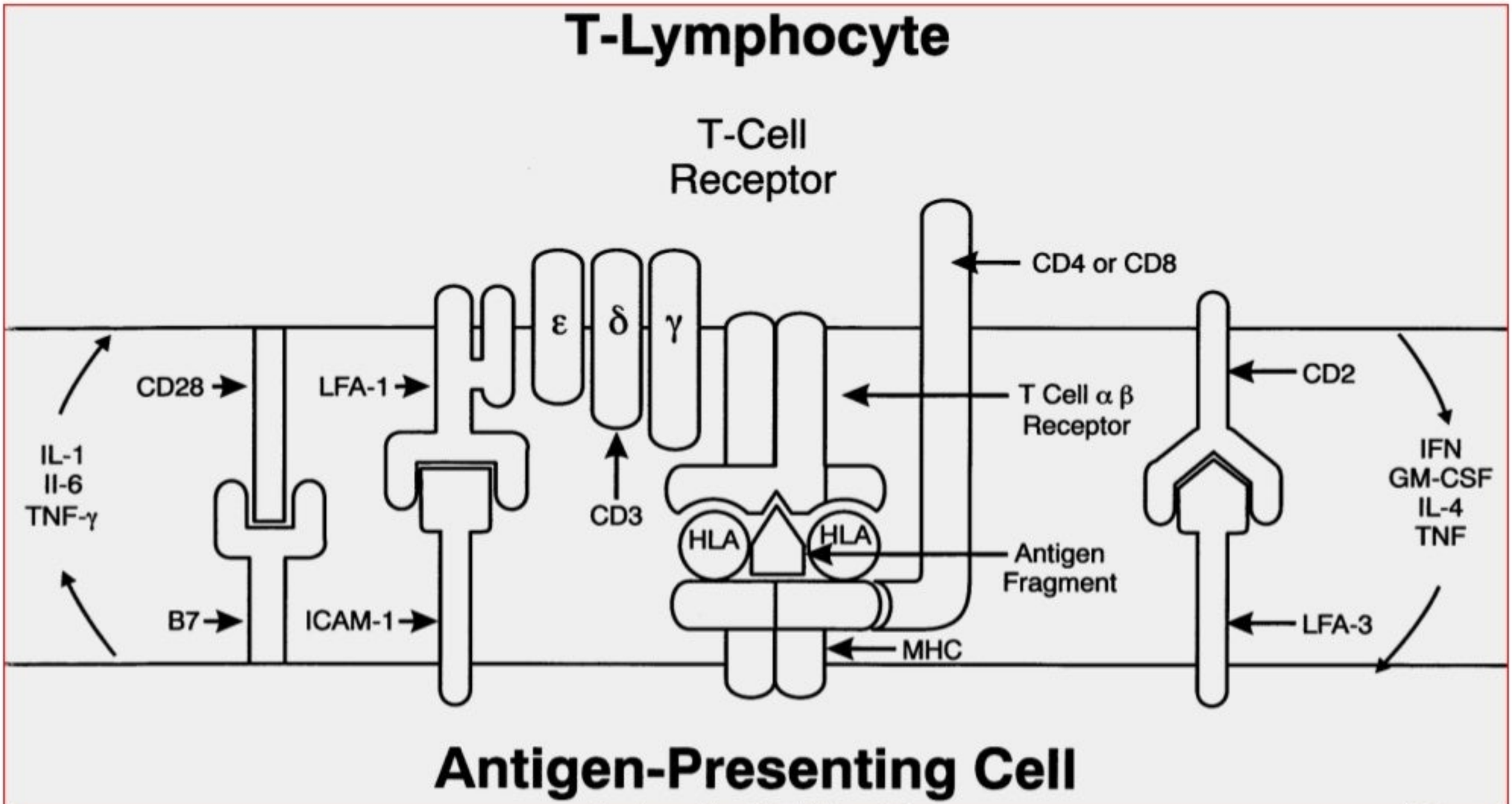

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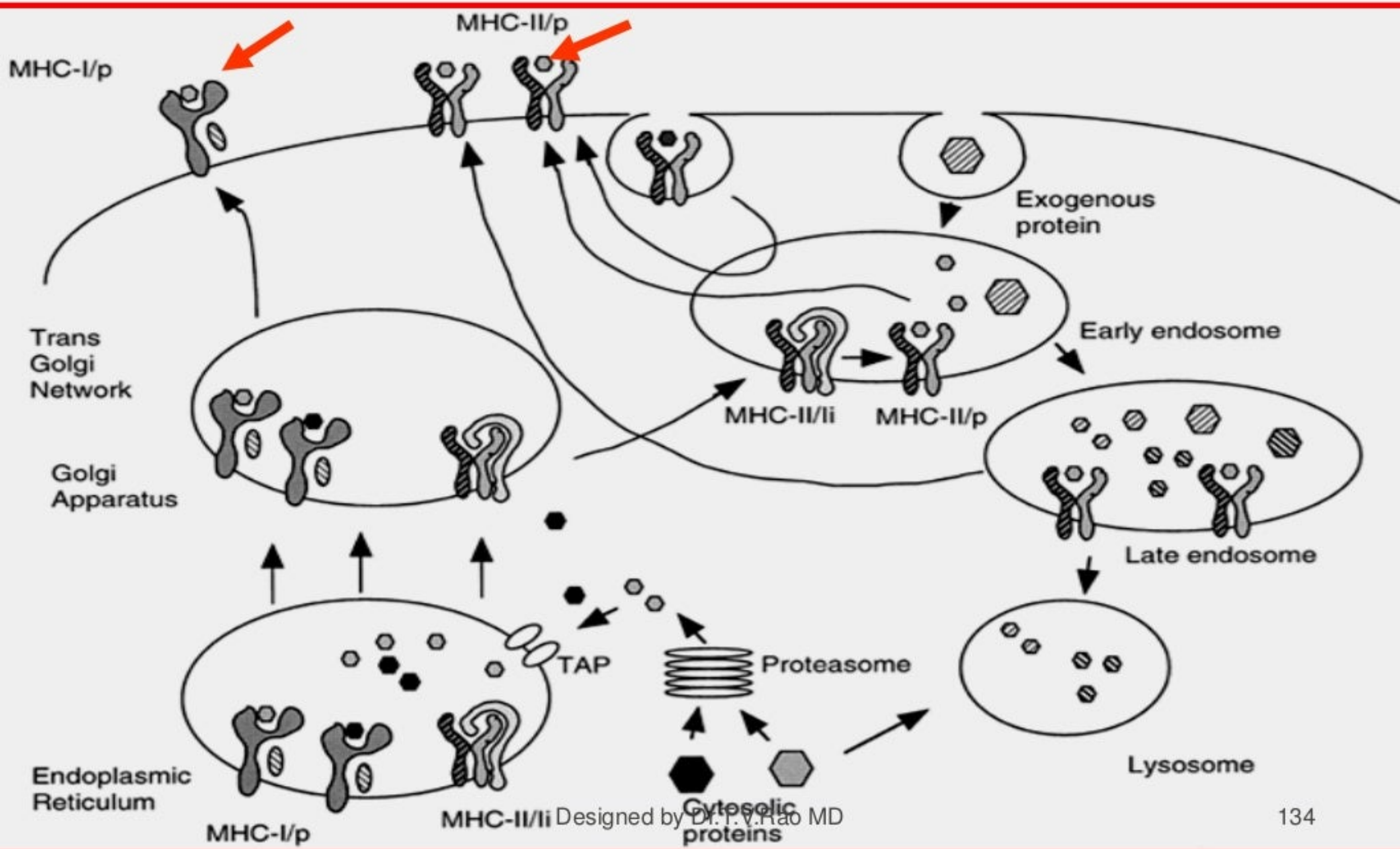

Programme created by Dr.T.V.Rao MD for Medical and Paramedical Students in the Developing world

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