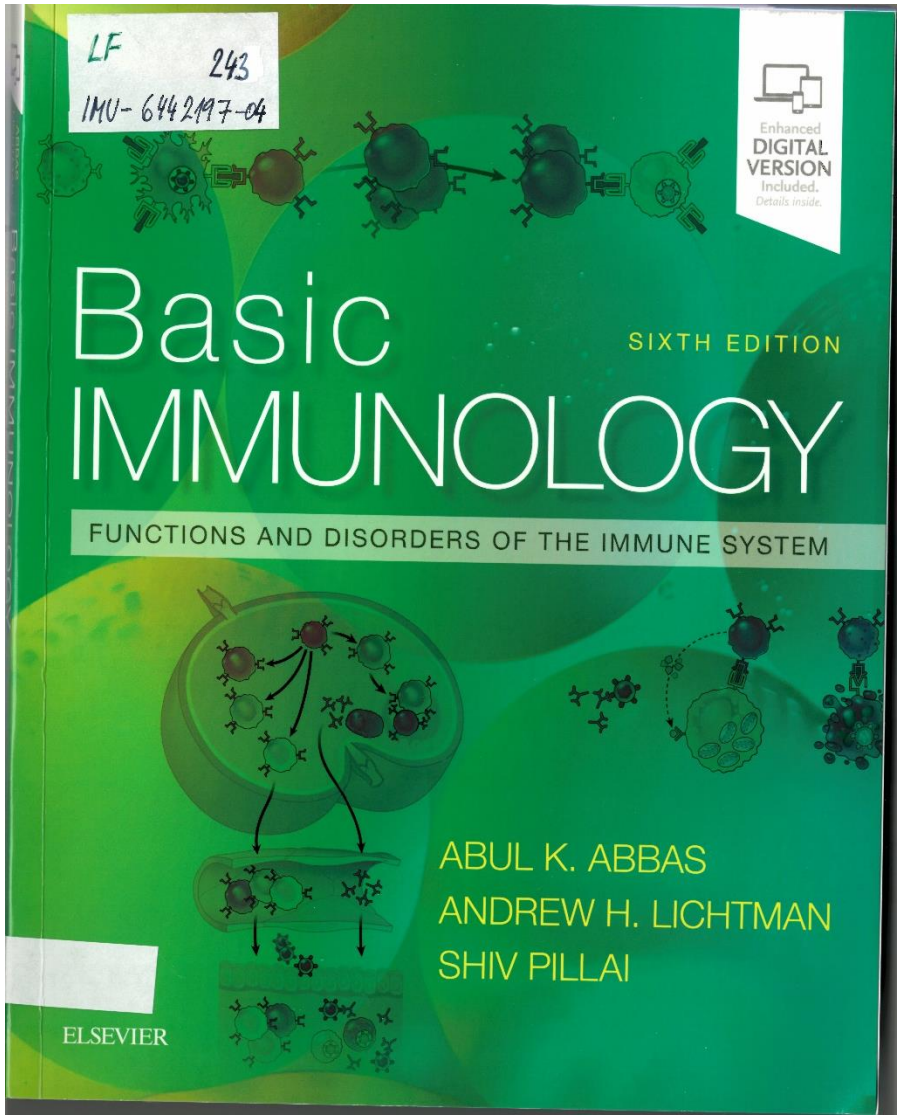
Immunology-introduction

Recommended textbook



Exams

- Examination period in winter semester
- 3 terms in examination period in summer semester
- 1 term in September
- No more, no less
- We accept cancellation of your examination slot even before you pull out the questions.

Immune system

- One of basic homeostatic mechanisms of the body.
- Its function is the recognition of foreign/dangerous substances.
- The dangerous substances trigger complex reactions which result in elimination of those substances.

Immune system

- Recognizes foreign/dangerous substances from the environment (mainly microbes)
- Is also involved in elimination of old and damaged cells of the body.
- Attacks tumor and virus-infected cells.

Functions of the immune system

- Deffence
- Autotolerance
- Immune surveillance

Antigen

- Substance, that is recognised by the immune system as a foreign and triggers immune reaction (immunogenicity).

- Products of the immune reaction (antibodies, T-lymphocytes) react with the antigen.

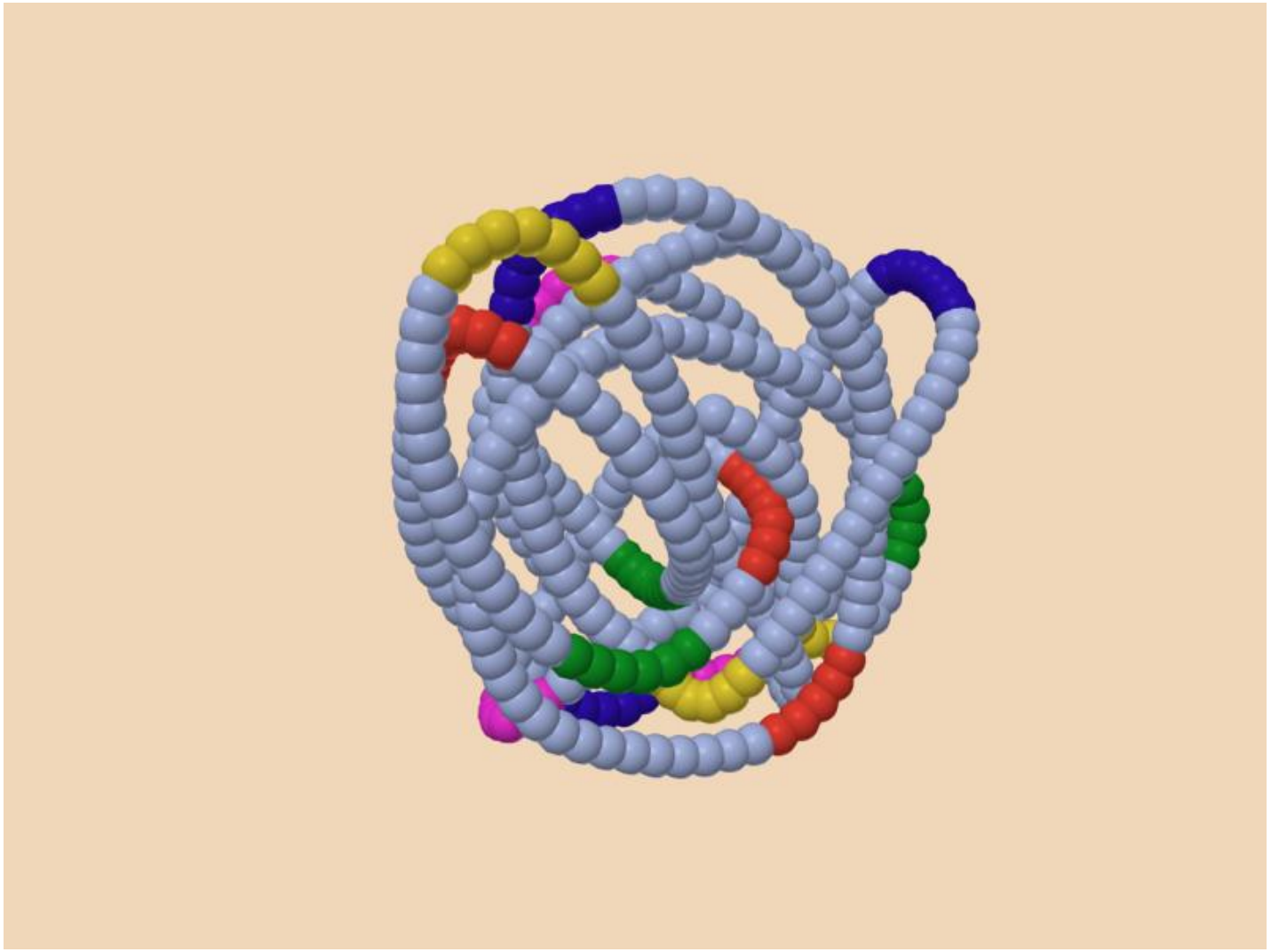
Chacteristics of immunogenicity

- Foreign (unknown) for the immune system
- High molecular weight (> 6 kDa)
- Chemical complexity

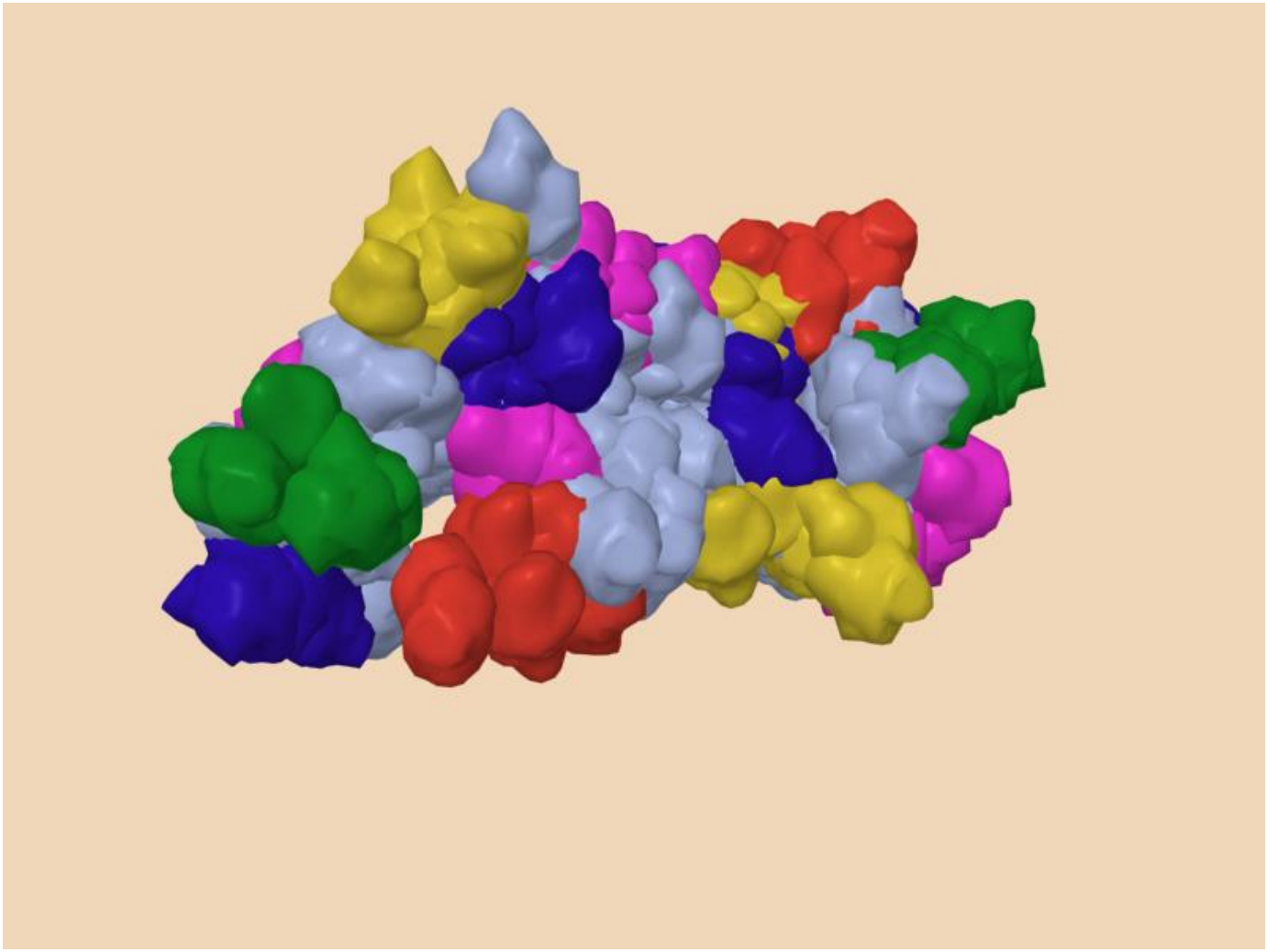
Antigen – functional components

- Carrier part of the molecule
- Antigenic determinant- epitope (cca 5-7 aminoacids)

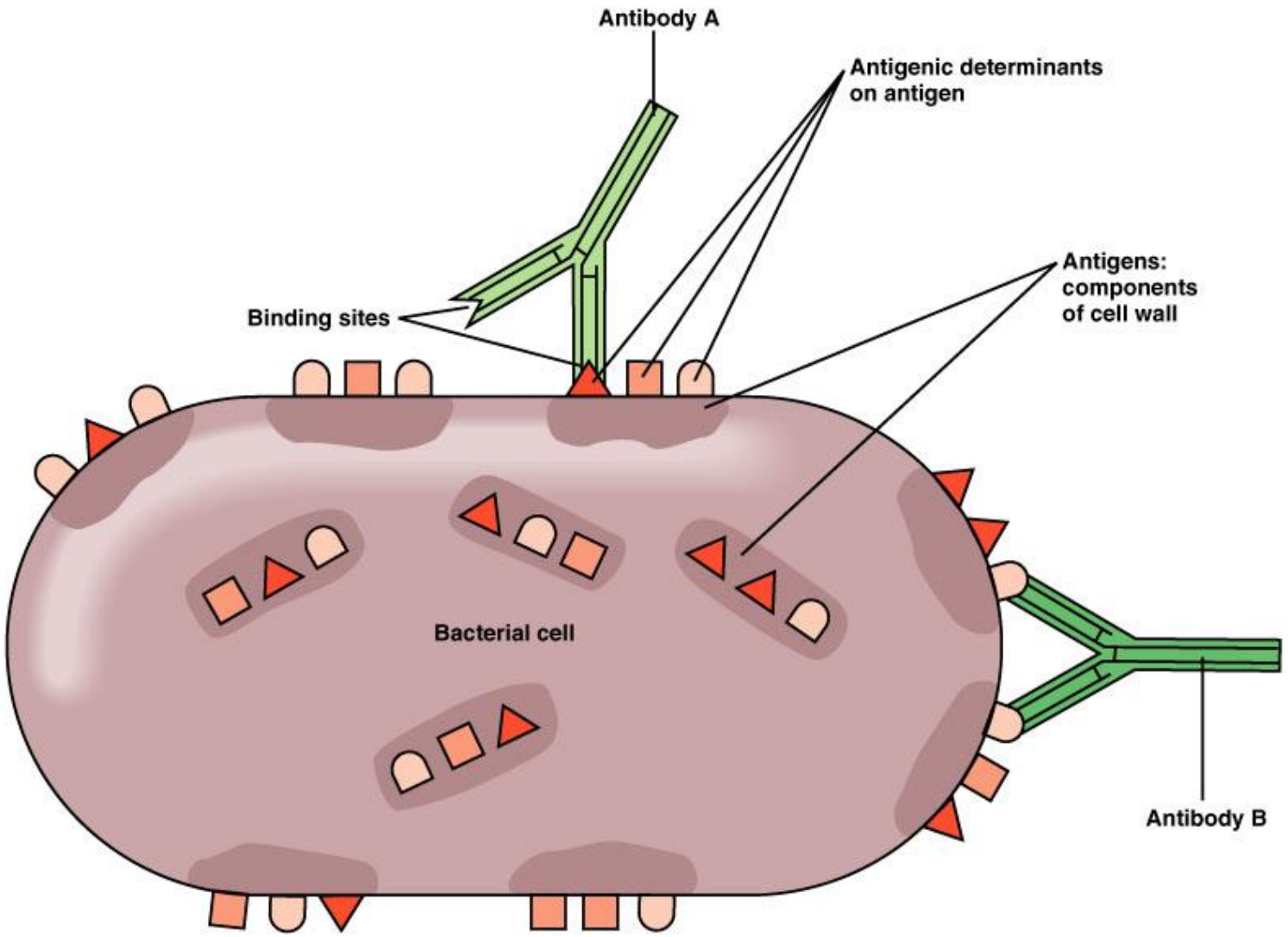
Antigen - epitopes, carrier part



Antigen - epitopes, carrier part



Antigen and epitope



Chemical composition of antigents

- Proteins – usually very good antigens.
- Polysacharides- usually only as a part of glycoproteins.
- Nucleic acids- poor antigenicity, limited to complexes with proteins.
- Lipids – only exceptionally, best known are sfingolipids.

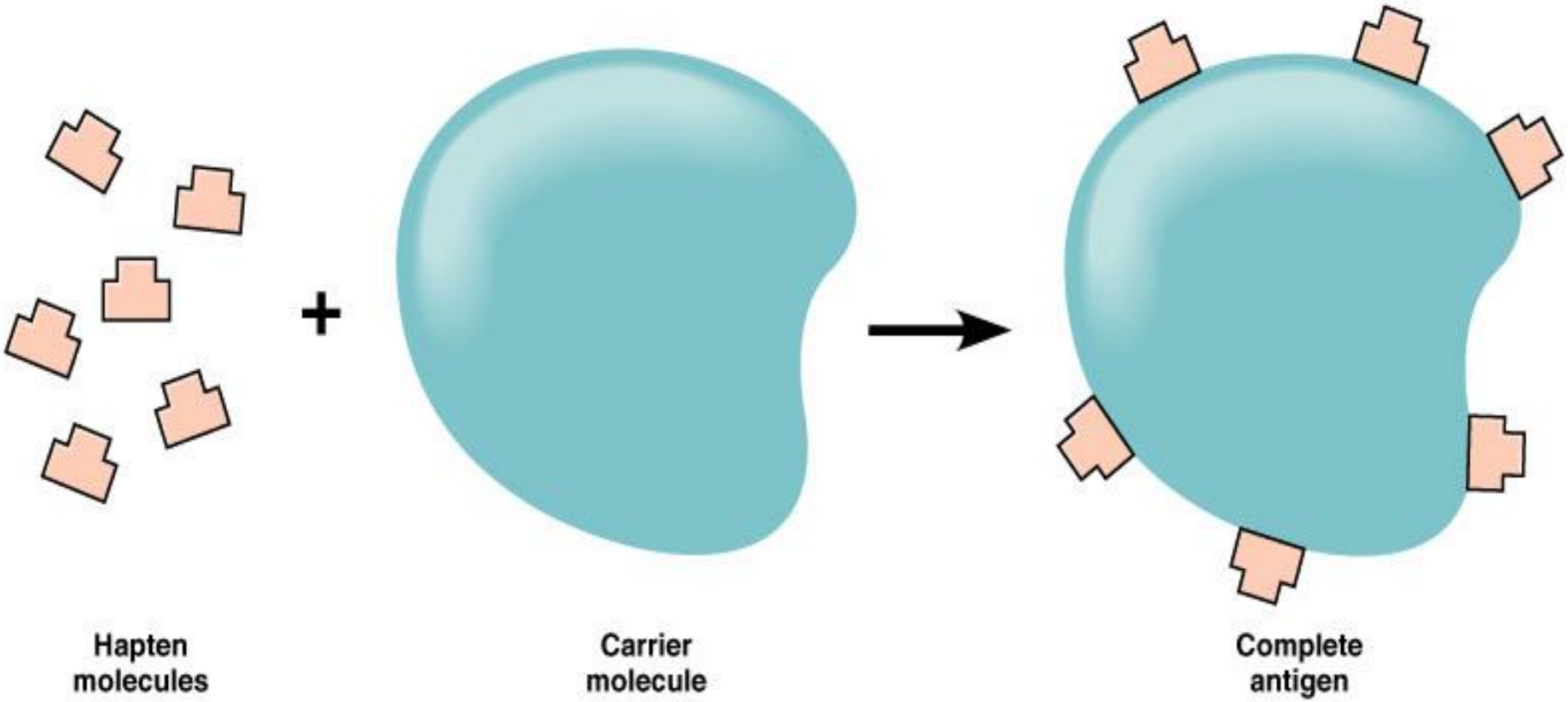
Protective and nonprotective antigens

- Protective antigens – elicit protective immune response that leads to elimination of the microbe.
- Non-protective antigens – elicit non-protective immune response, but it does not lead to elimination of the microbe (e.g. antibodies against HIV).

Hapten

- Low-molecular weight substances that trigger immune reaction after binding to various proteins of the body.
- They react with products of the immune reaction.
- Typical examples are metals (Cr, Ni) that trigger type IV immunopathological reactions. Drugs (antibiotics, local anestetics) cause type I immunopathological reaction.

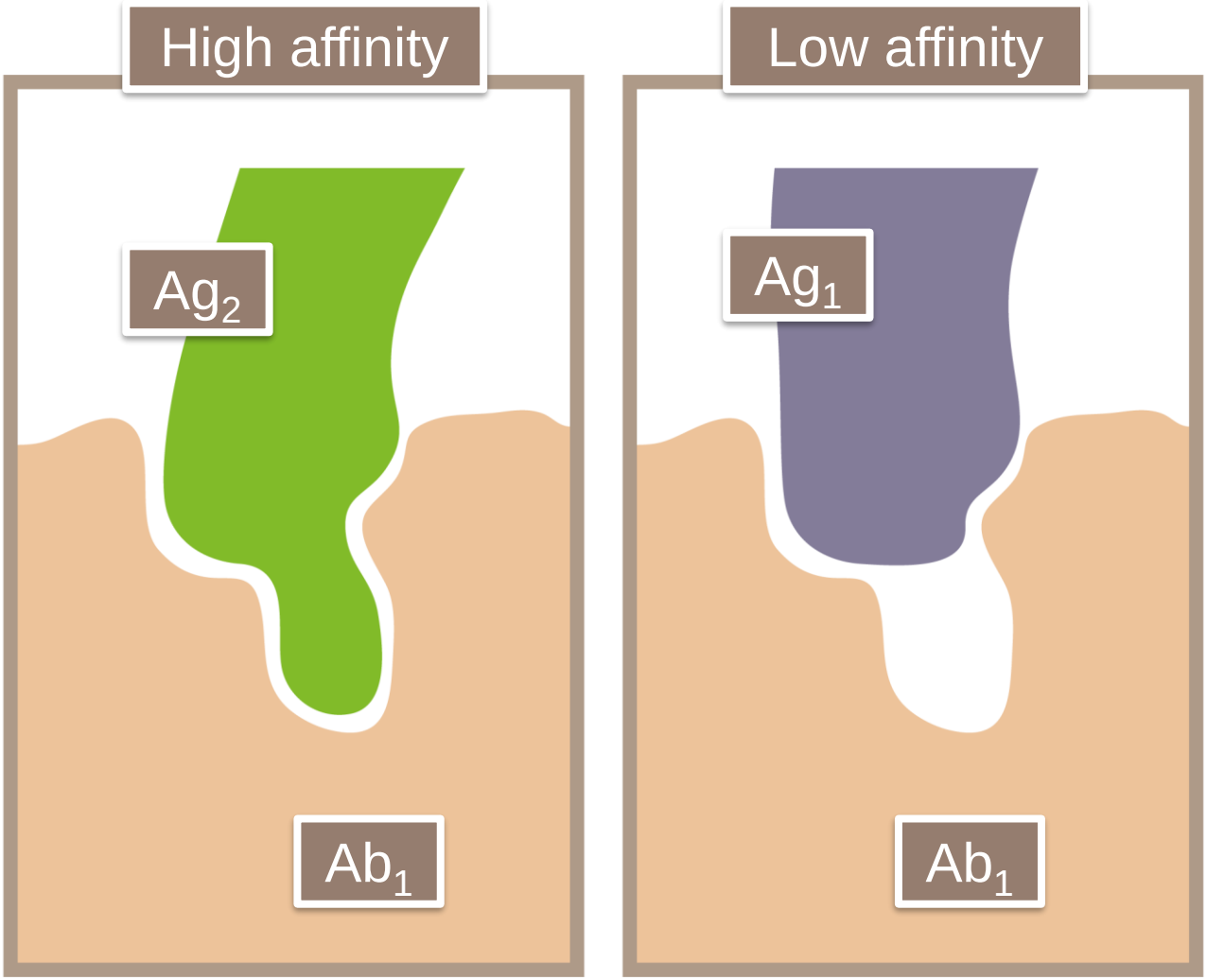
Immunogenicity of hapten



Cross reactivity of antigens

- Products of the immune reaction may, in some situations, react with substances that are very different from the initial immunogen.
- Immunological cross-reactivity not necessary mean similar chemical composition.
- The degree of cross reactivity may be different.
- Cross reactivity is important in pathogenesis of several autoimmune diseases (eg rheumatic fever).
- Cross reactivity of allergens is very important in allergology.

Cross reactivity of anntigens



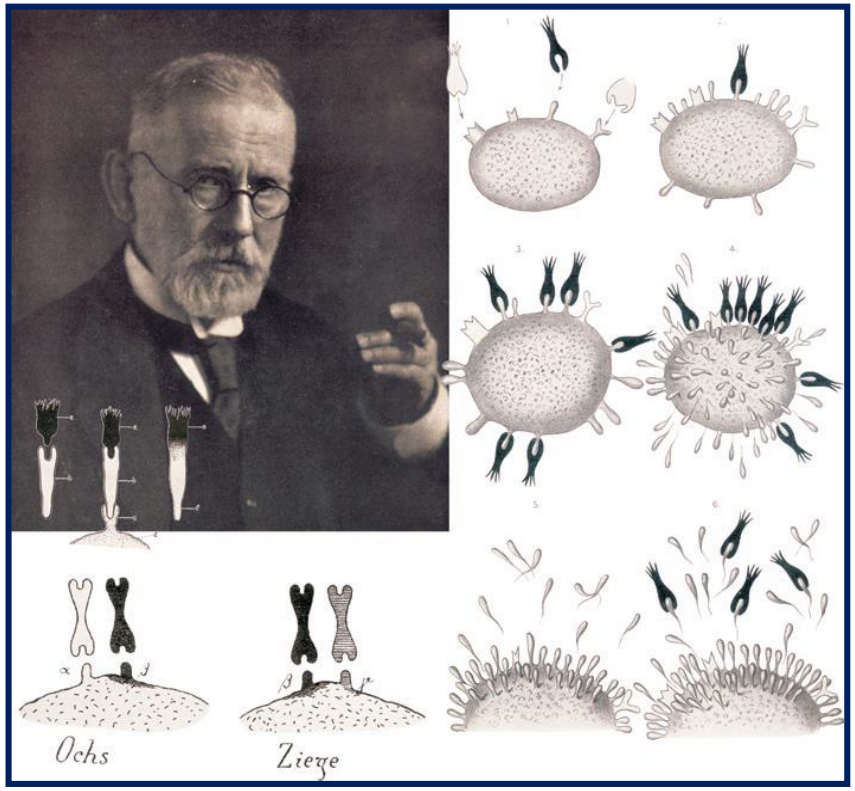
Adjuvants

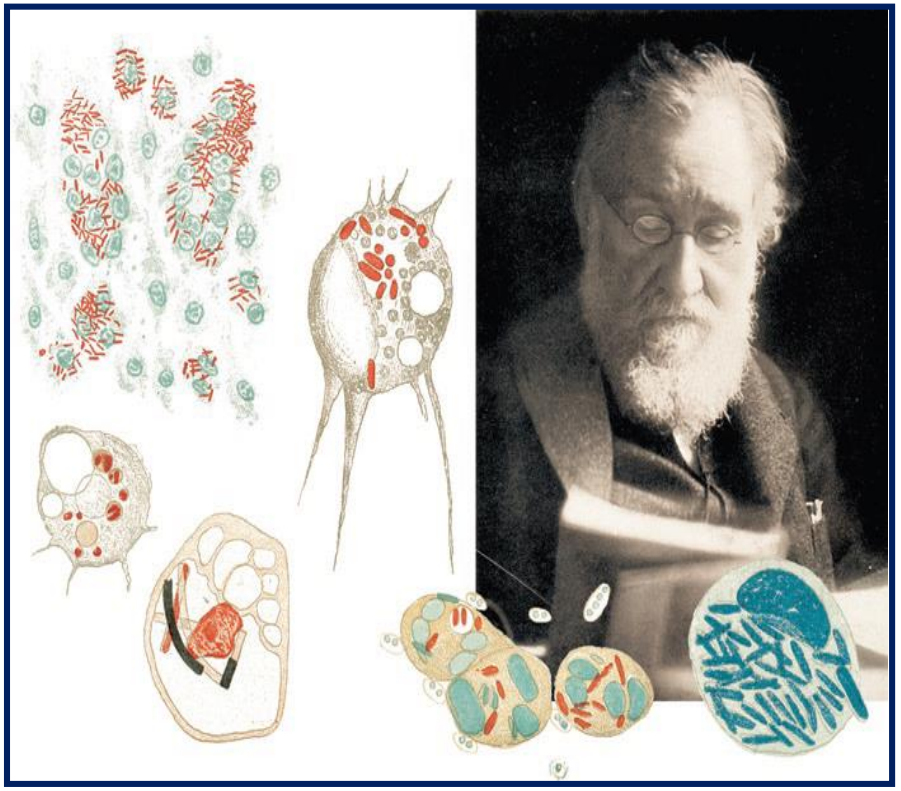
- Substances, that, when mixed with antigen, non-specifically enhance immune reaction against the antigen.
- Freud´s adjuvant: killed Mycobacterium tuberculosis + water-in-oil emulsion. Used in veterinary medicine.
- Alum precipitate - $AL(OH)_3$ - used in human medicine.
- Mechanisms: improved prezentaion of the antigen, fixation of the antigen in the place of application.

Two branches of the immune response

- Innate, nonspecific – very quickly recognizes several foreign substances and eliminates them. There is no memory.
- Adaptive, specific – high degree of specificity in distinction between self and non-self. The reaction requires several days to be effectively triggered. Immune memory is induced.

Nobel price 1908





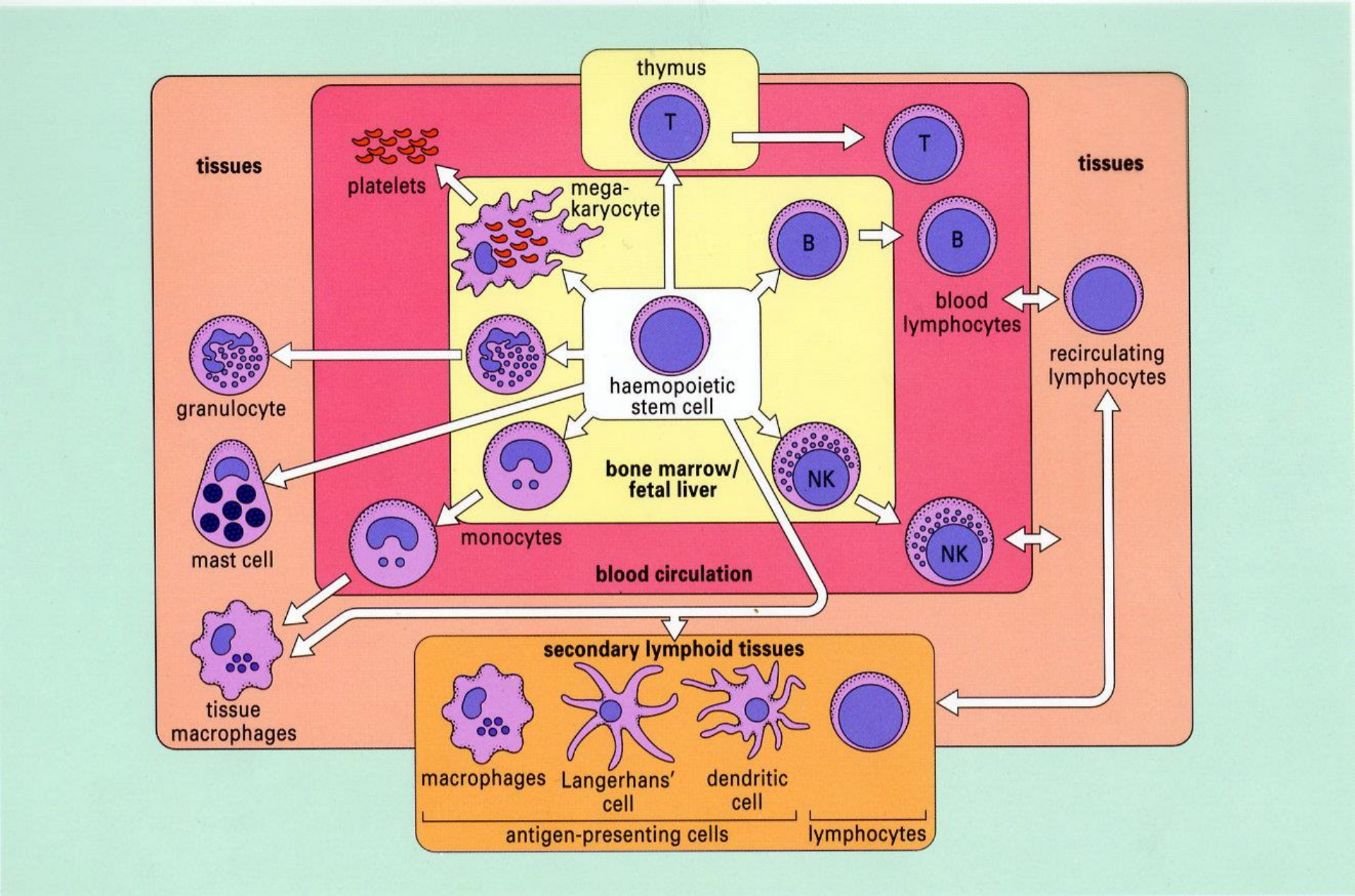
Paul Ehrlich
Adaptive immunity

Eli Metchnikoff
Inborn immunity

Cells of the immune system

- Main cells of the immune system
  - Lymfocytes (T a B)
- Accessory cells of the immune system
  - Granulocytes
  - Monocytes
  - Tissue macrophages
  - Mast cells
  - Dendritic cells
  - NK cells
  - Endotelial cells
  - Thrombocytes, erythrocytes, fibroblasts, epitelial cells

Majority of immune system cell originate in bone marrow



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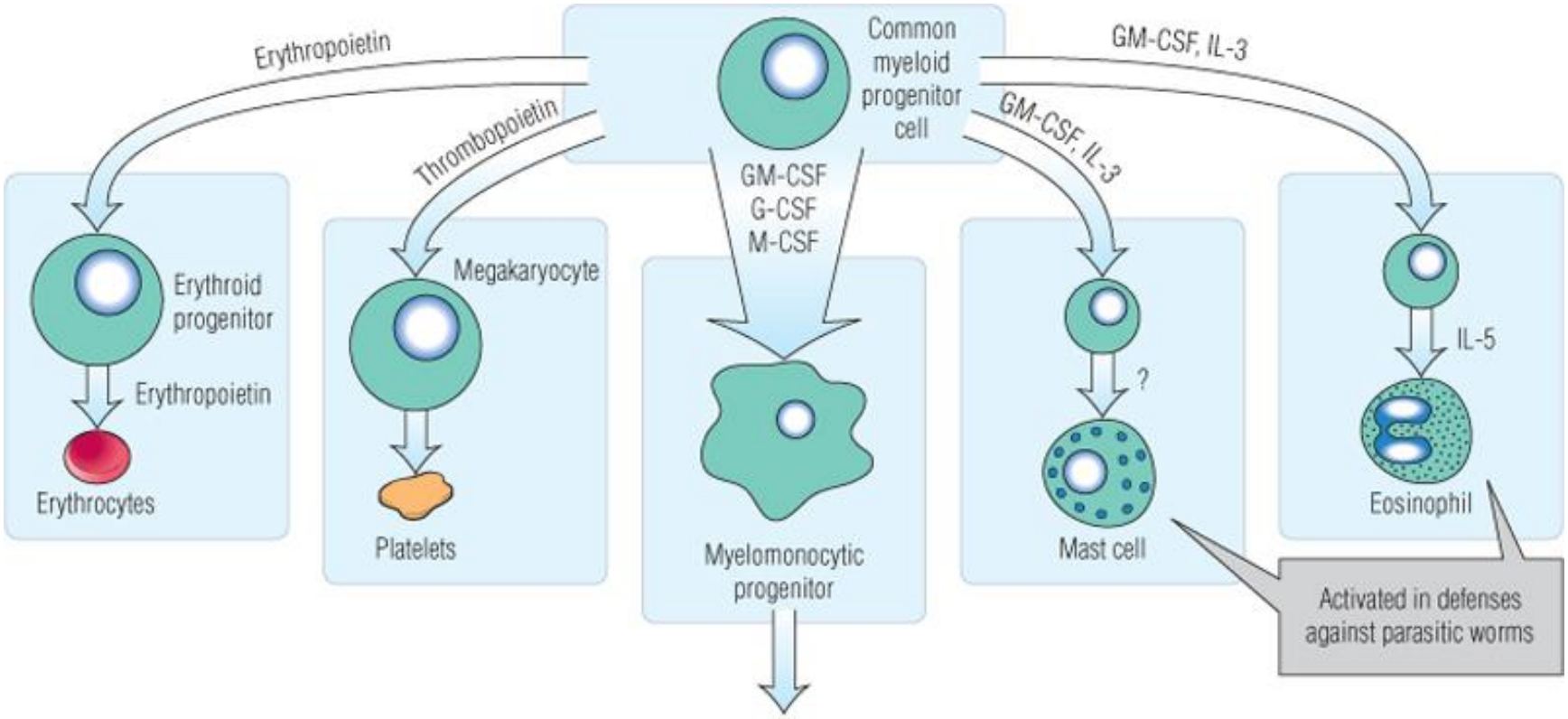
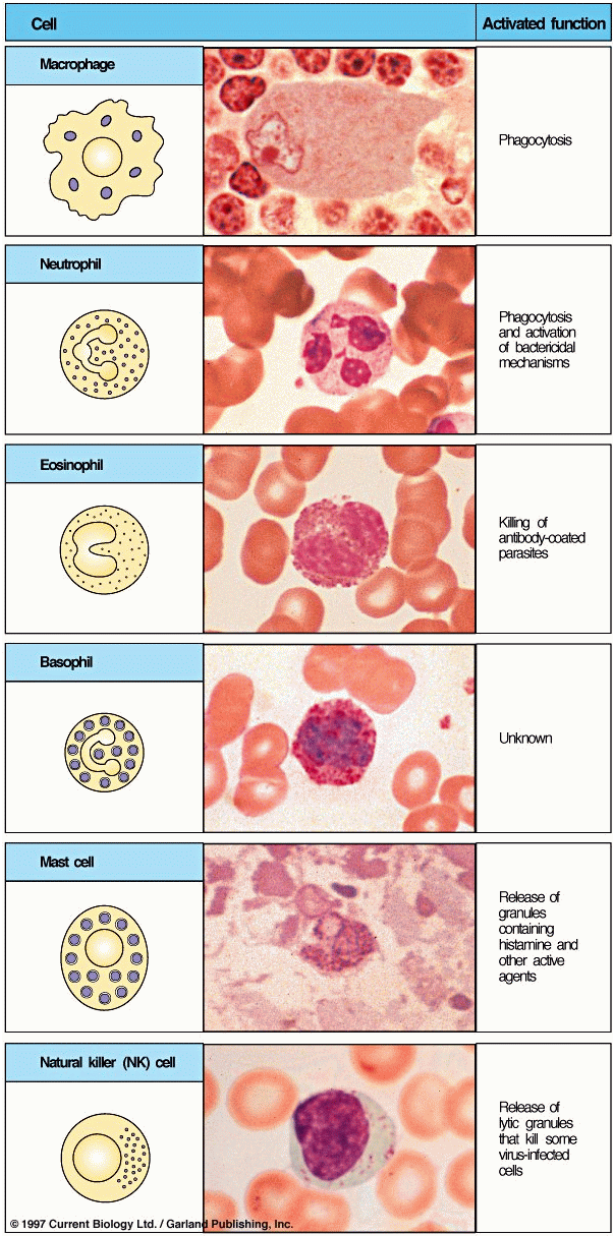
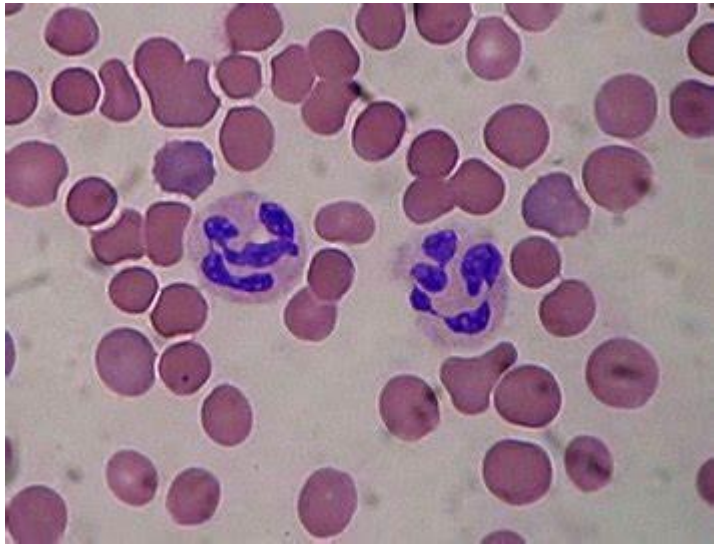
Differentiation of haematopoetic stem cell is influenced by the local environment



Auxiliary cells of the immune system

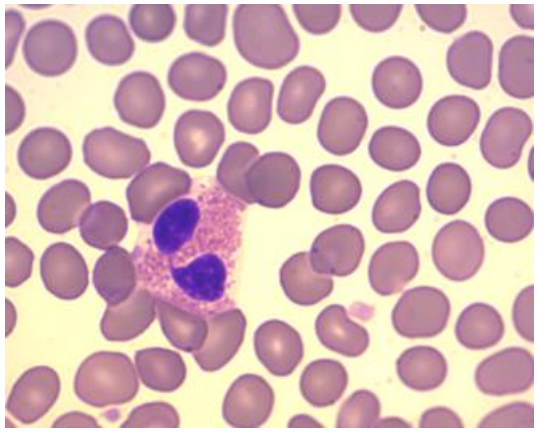


Polymorphonucler (neutrophil) granulocytes



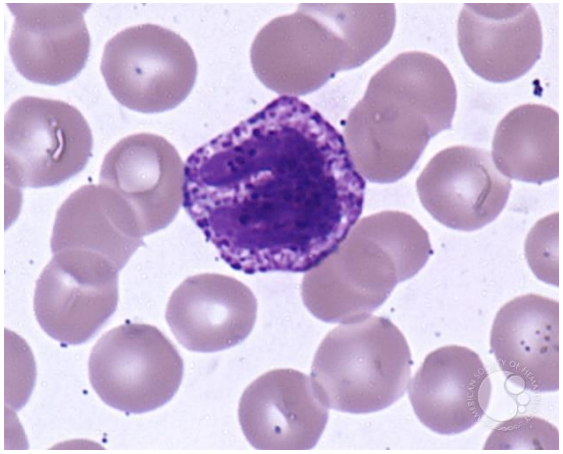
- Approx. 60-70% leukocytes in peripheral blood (in adults).
- Present in blood, but predominantly in various tissues (approx. 90%).
- Blood half life is several hours only.
- Important phagocytic cells that operate in early phases of inflammation
- Are important cytokine producers.
- The most significant component of pus.
- Do not present antigens.

Eosinophil granulocytes



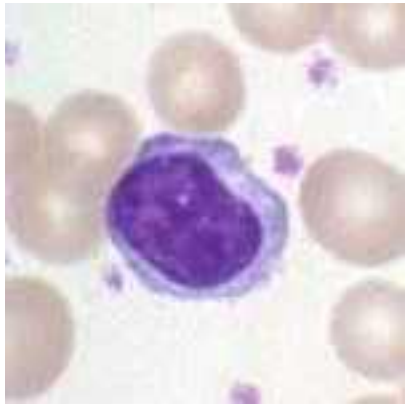
- 1-3% of leukocytes in healthy persons.
- Play a critical role in protection against parasites.
- Secrete many toxic substances affecting eucaryotic cells: MBP (major basic protein), eosinophil peroxidase, ECP (eosinophil cationic protein)…
- IL-5 is the most important stimulus for their formation.
- Synthetise various cytokines of the Th2 group.
- Involved inphagocytosis but do not present antigens
- Their number is increased in patients with parasitic and allergic diseases.
- Play a very significant role in allergic inflamation by destruction of cells and by production of cytokines.

Basophil granulocytes



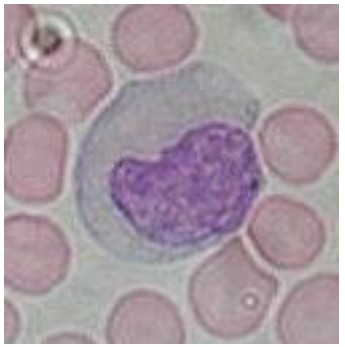
- Less than 1% of peripheral leukocytes.
- Similar functions as mast cells (binding of IgE, degranulation, secretion of pro-allergic cytokines).
- Previously considered as precursors of mast cells, currently these two cells types are considered as products of two different lineages.
- Enumeration of basophils has no clinical significance in immuno-allergology.

Lymphpcytes



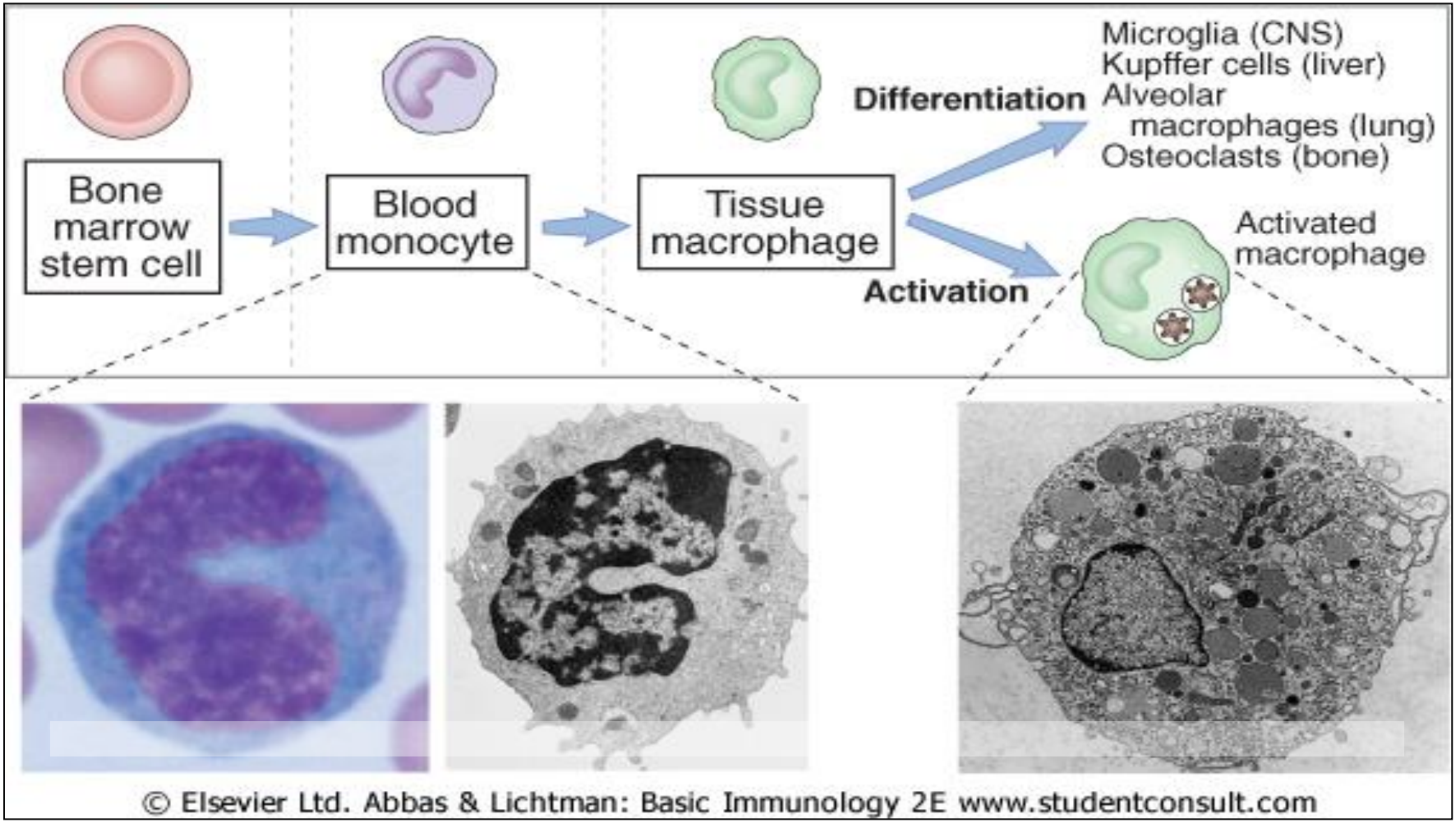
- 20-40% of leukocytes in adults.
- T- and B- lymphocytes ale the main cells of the immune response.
- Also NK cell appear like lymphocytes(LGL – large granulated lymphocytes).
- Not involved in phagocytosis.
- B-lymphocytes belong to the group of antigen-presenting cells.

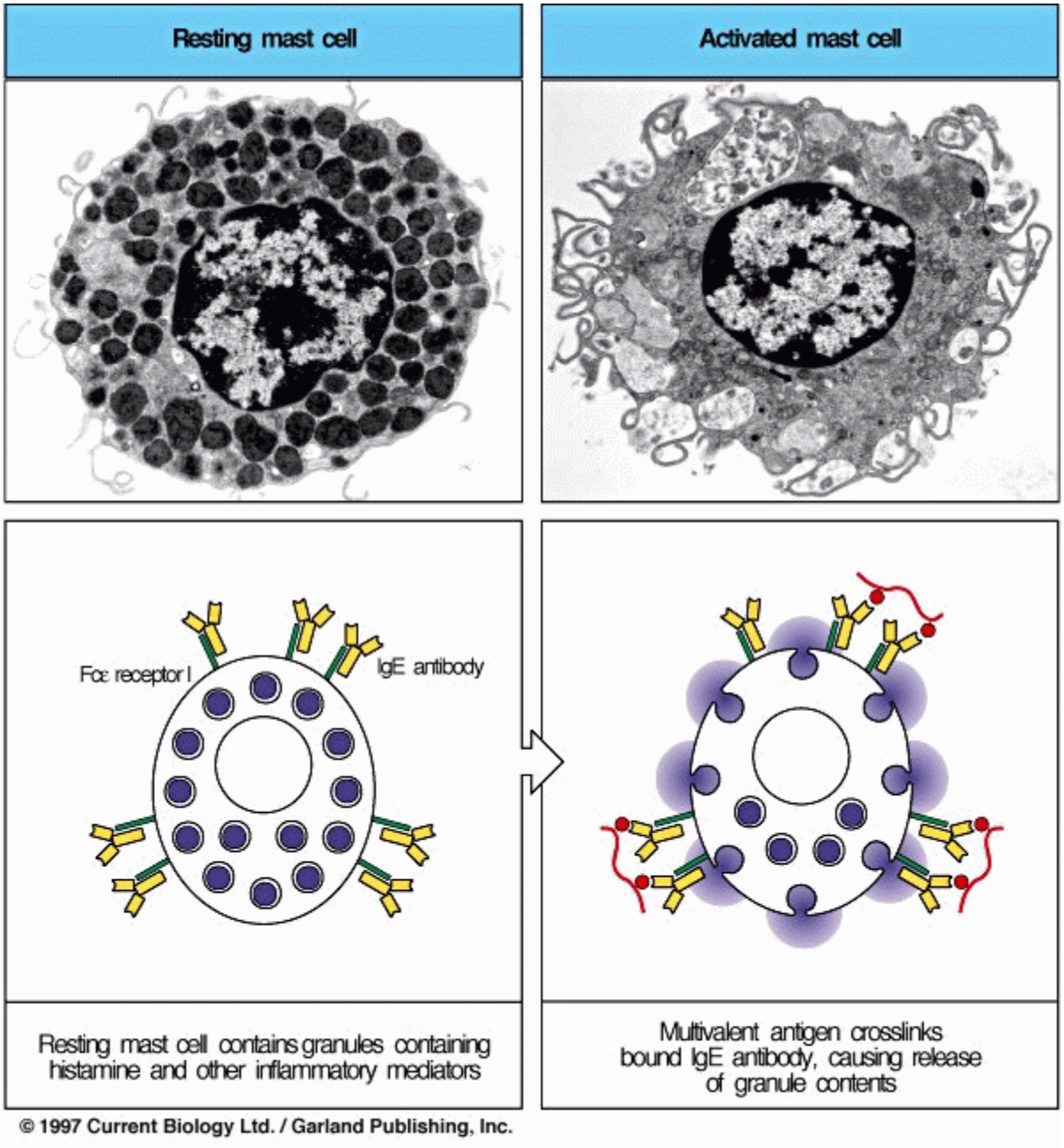
Monocytes



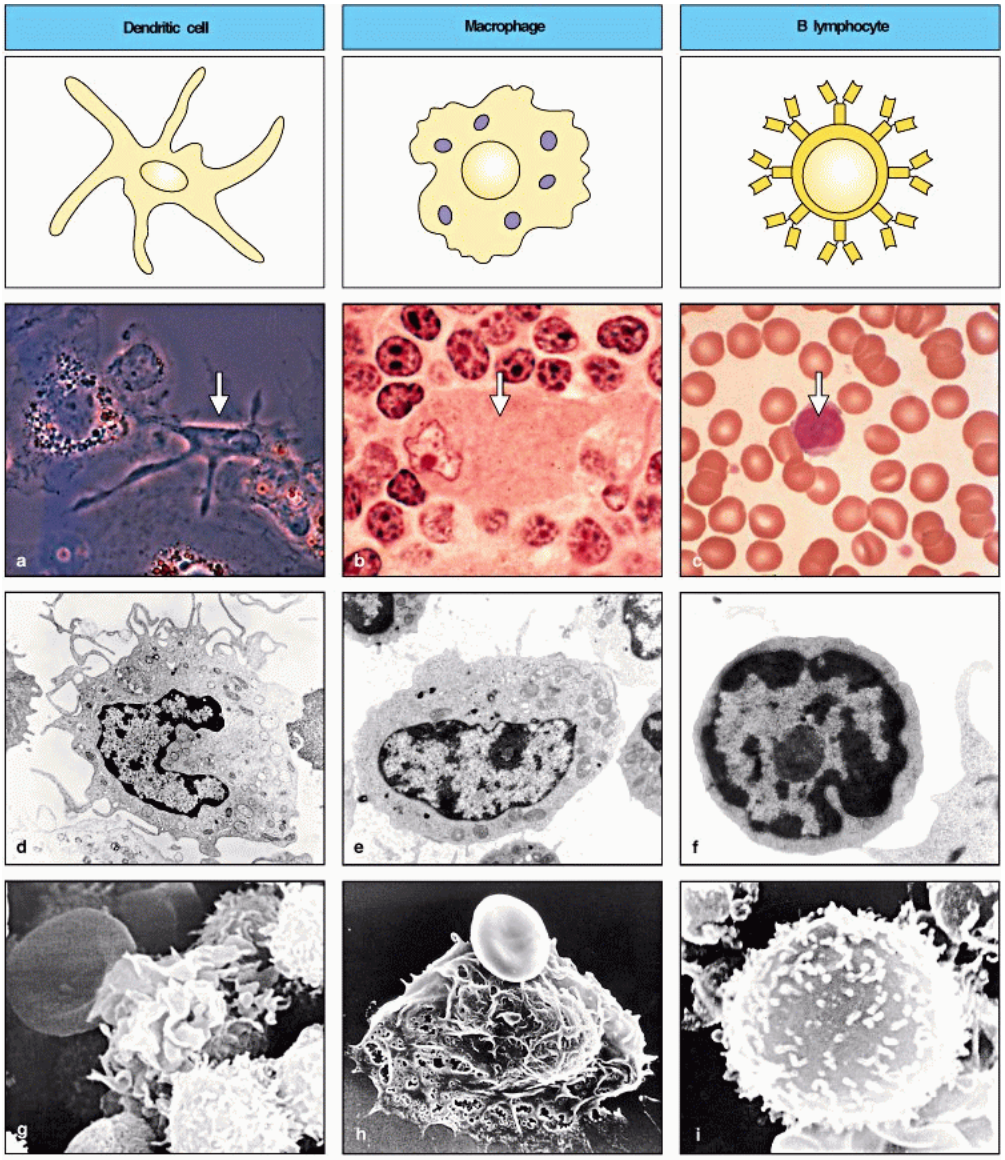
- 3-8% of leukocytes
- Circulating precursors of tissue macrophages and of some types of dendritic cells.
- Monocytes from the blood have very low biological activity.

Vývoj makrofágů z monocytů



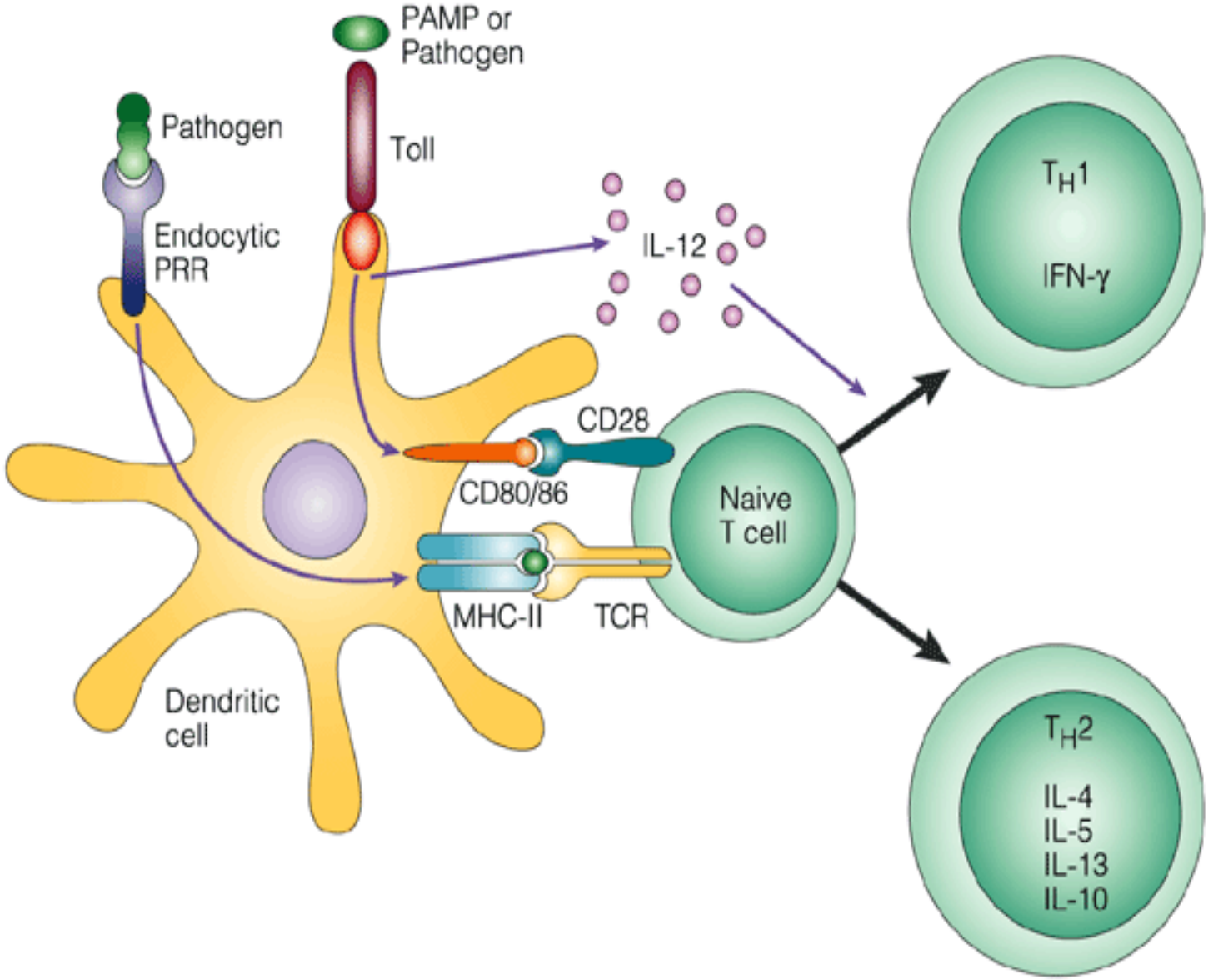


Antigen- presenting cells



Dendritic cells

- An important component of the innate immunity involved in activation of acquired immune system cells.
- The main function is antigen processing and its presentation to T-lymphocytes.
- They are also an important source of costimulatory signals.
- Langerhans dendritic cells are involved in the transfer of antigens from the epidermis of the skin.
- Non-activated dendritic cells also have a significant phagocytic capacity.



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Immature dendritic cells

- They phagocytose dead cells, various other molecules, as well as foreign particles and pathogenic organisms.
- TLRs are mainly involved in the uptake of viruses or bacteria.
- Immature dendritic prodominatly supress immune response leading to formation of regulatory T lymphocytes.

Mature dendritic cells

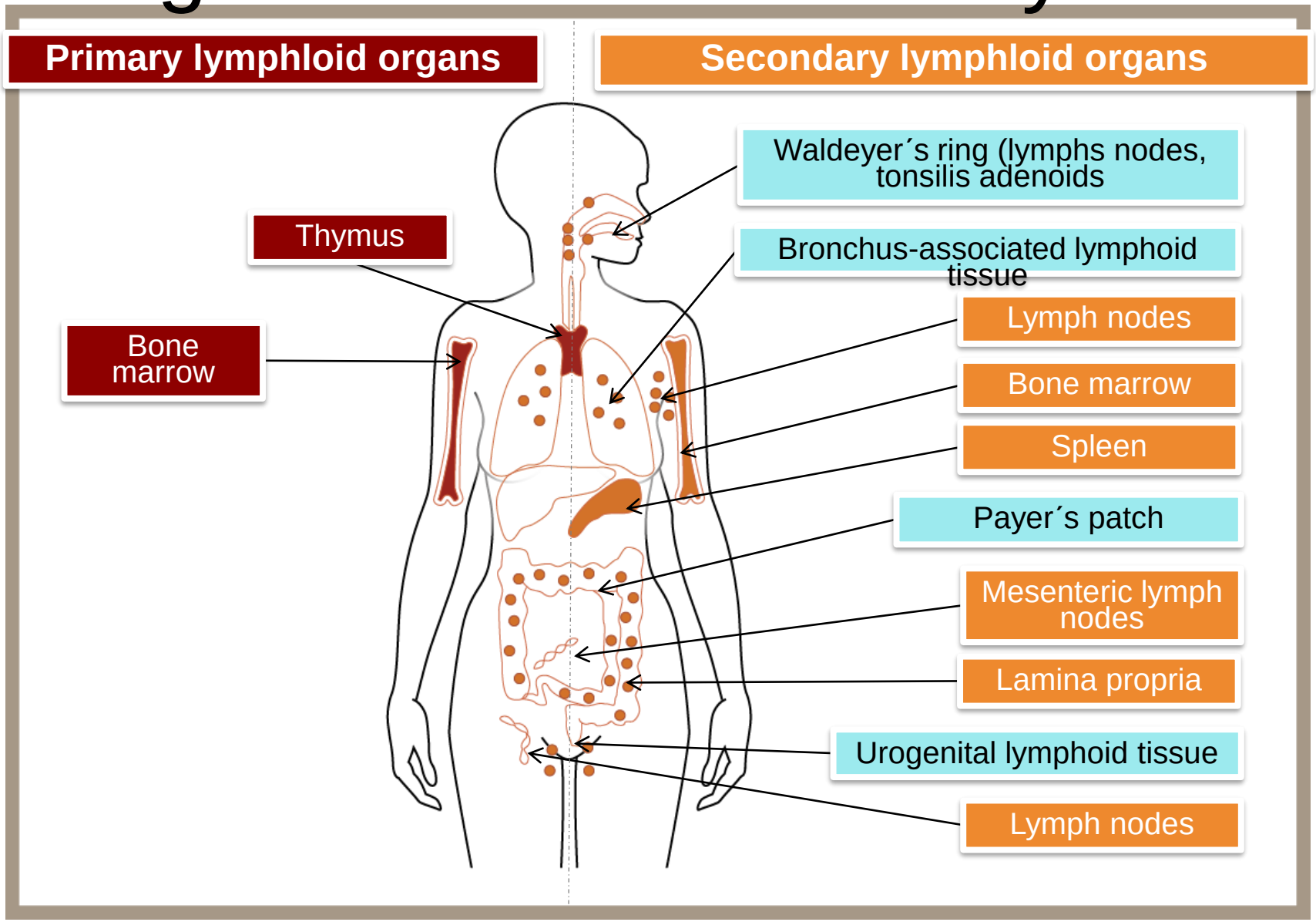
They are formed by the maturation of dendritic cells that have been activated by PRR.

The mature dendritic cell migrates to the lymph nodes and exposes fragments of bacterial / viral antigens to both HLA-II and HLA-I, thereby activating naïve CD4 + or CD8 + lymphocytes.

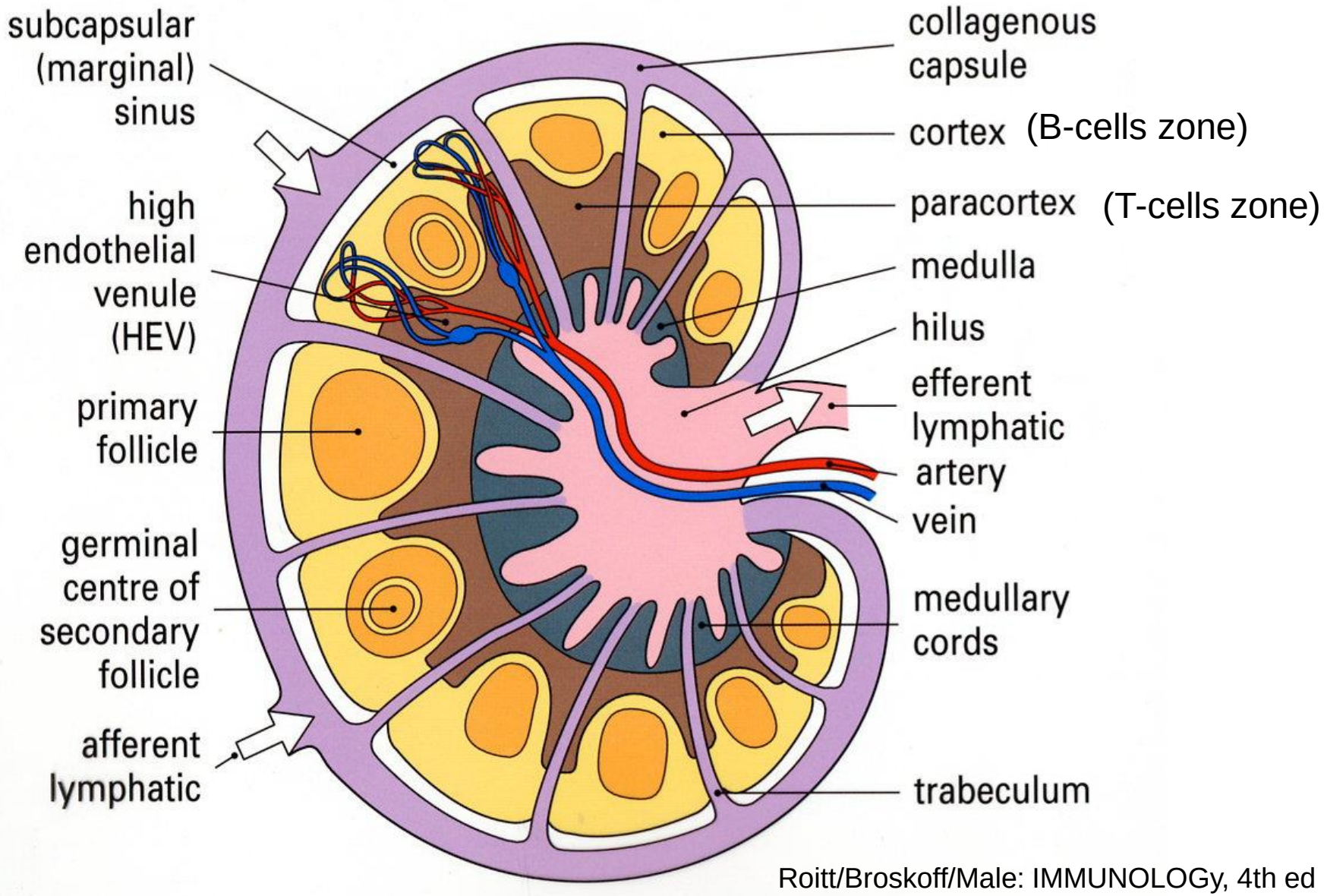
Another cell involved in immune reactions

- Epithelial cells: produce various cytokines, antibacterial substances, are part of MALT.
- Endothelial cells: are important in regulation of leukocyte extravasation and other parts of the inflammatory process.
- Erythrocytes: express receptors for C3b and C4b – they are involved in immune complexed elimination.
- Thrombocytes – important in inflammation , mainly as a source of vasoactive substances.
- Fibroblasts: produce various cytokines.

Organs of the immune system



Lymph node



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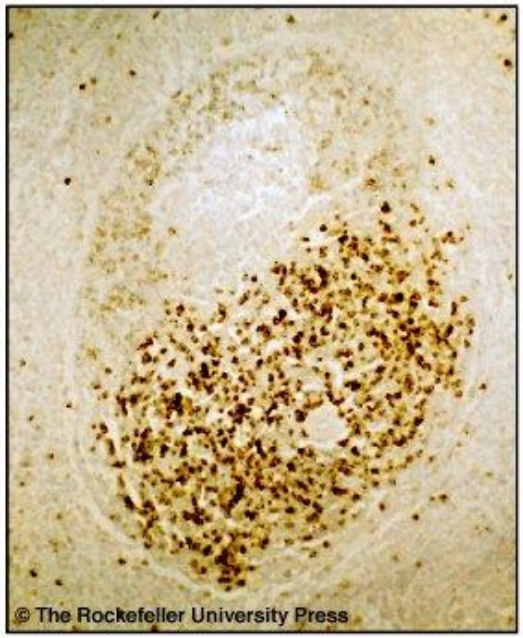
The Spleen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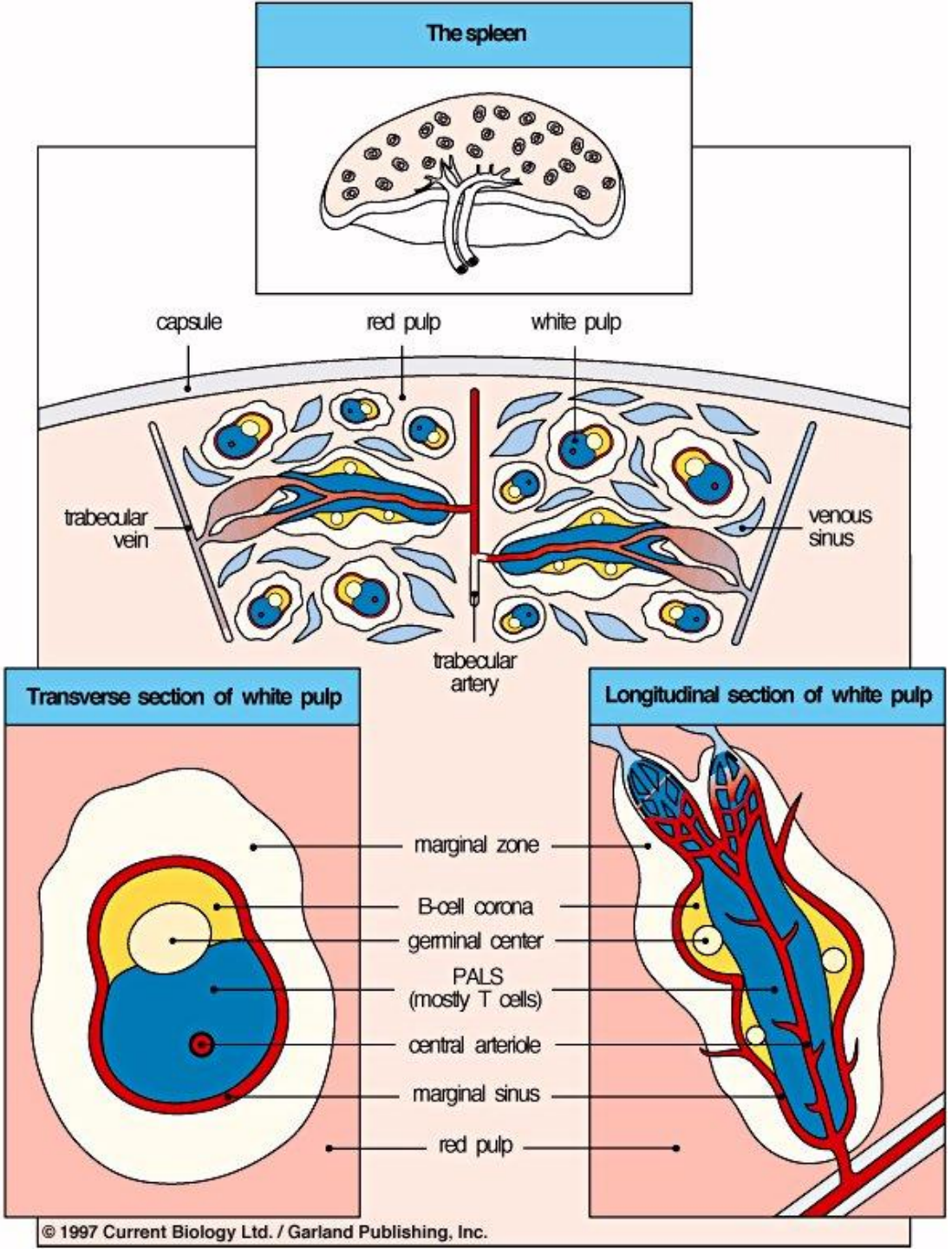
The spleen
capsule
red pulp
white pulp
trabecular vein
venous sinus
trabecular artery
Transverse section of white pulp
Longitudinal section of white pulp
marginal zone
B-cell corona
germinal center
PALS (mostly T cells)
central arteriole
marginal sinus
red pulp
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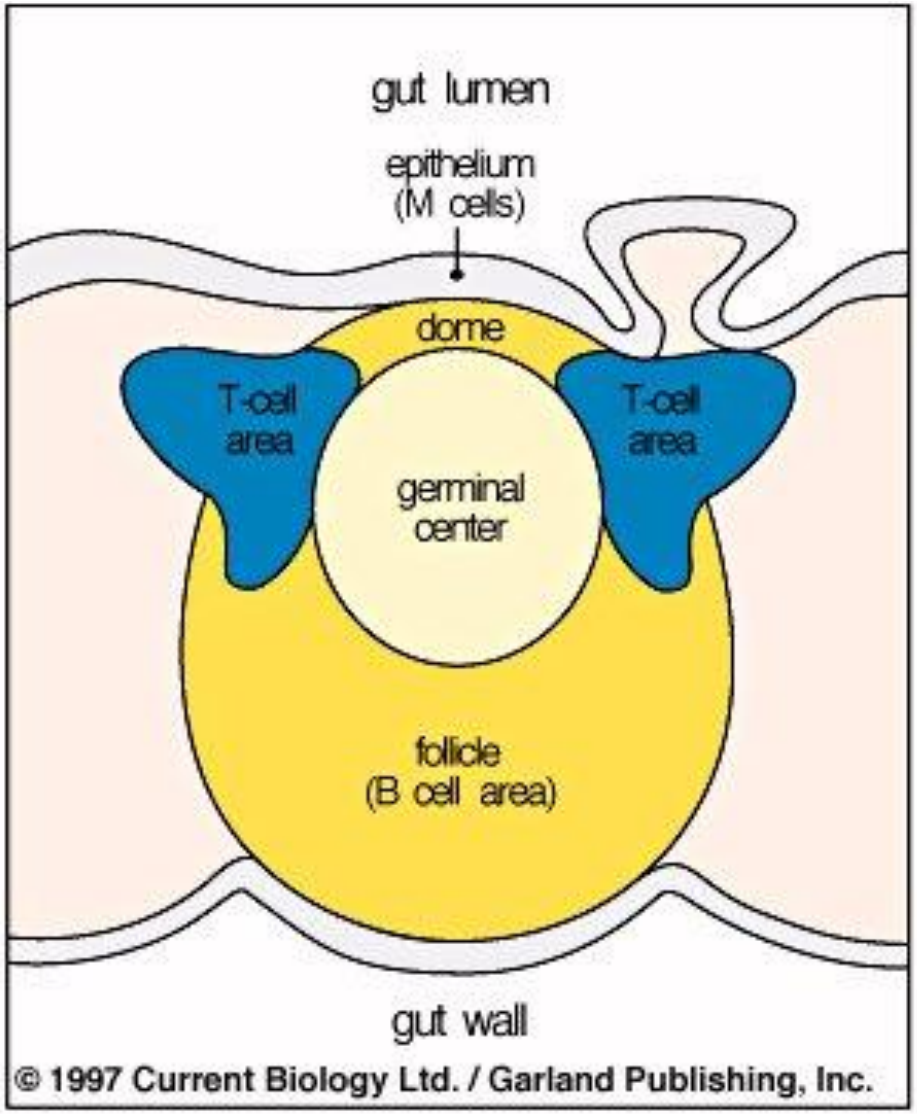
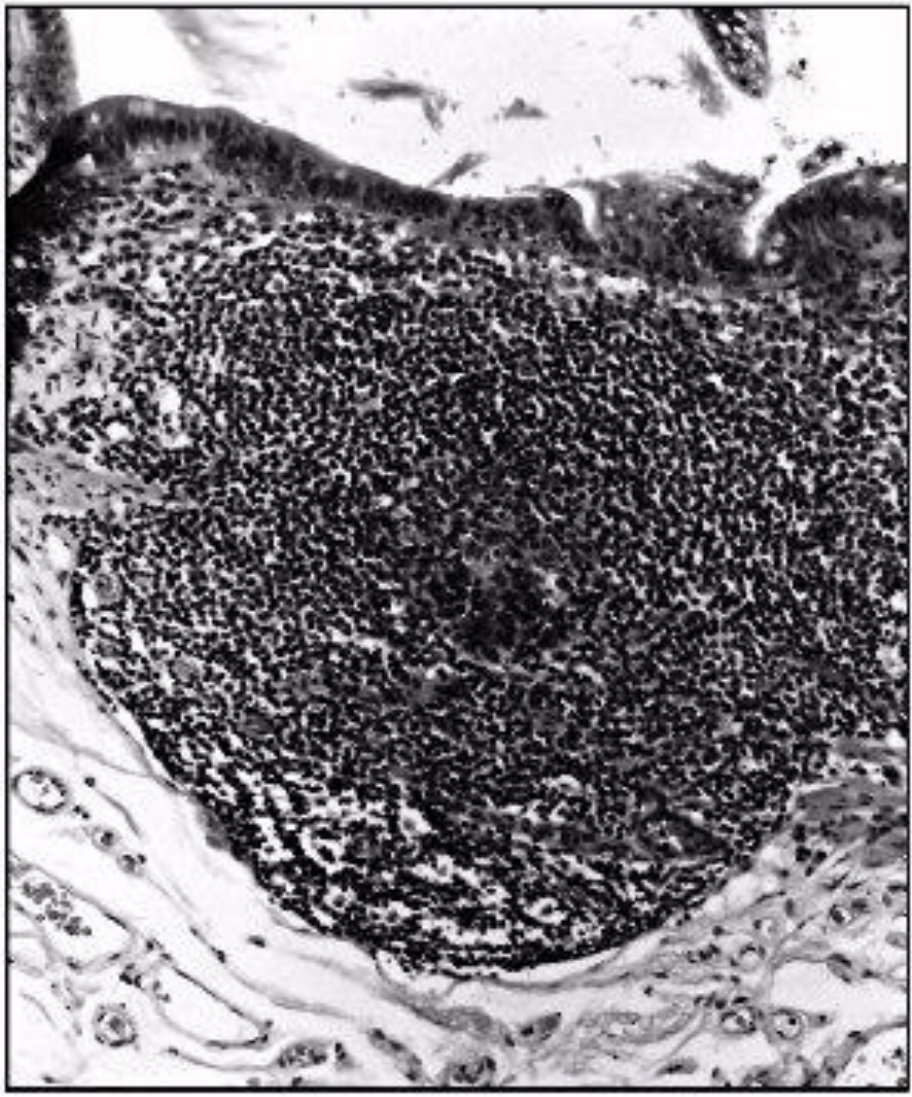
Marginal zone of the spleeen

- Localized between white and red pulp.
- B-lymphocytes of the marginal zone are responsible for quick response to T- cell independent, polysacharide antigens.
- The response is mainly in IgM.

Payer ´s Patches

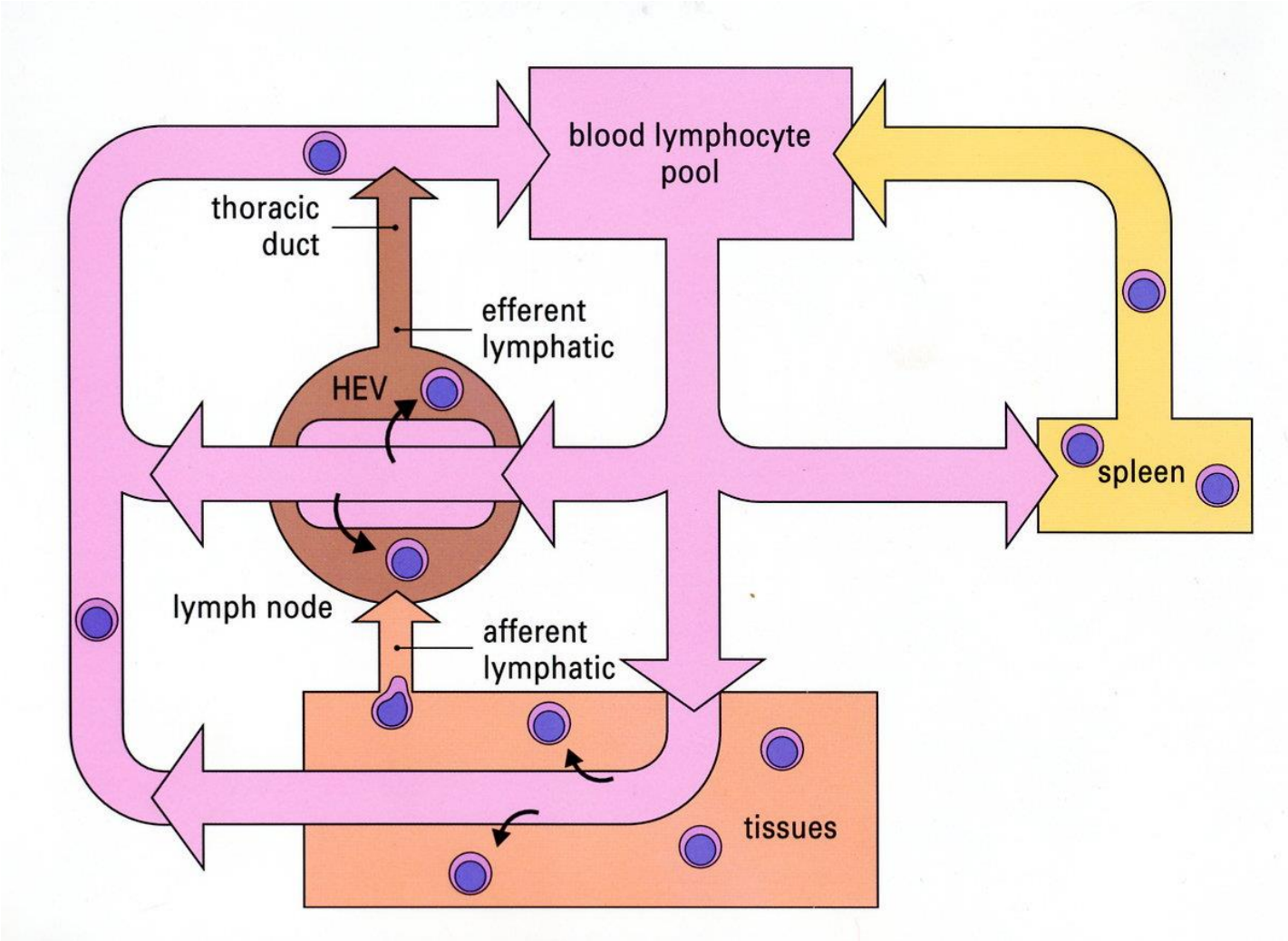




High endotelial venules

- Specialized venules. The site where lymphpocytes leave the blood stream and migrate into lymph nodes, spleen, organs of MALT.
- Adhesion molecules enable selective attachment of various types of lymphocytes.

Circulation of Lymphocytes in the body
The role of High Endotelial Venules



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