Applied Immunology 2026’

1 – 2

Overview of the immune system: components, structure, functions. Immunological recognition.

Types of immune responses (elimination or tolerance).

What is the immune system?

- The immune system is a complex structural and functional NETWORK composed by molecular and cellular elements.
- The main function of the immune system is managing of the individual integrity with defence against outside parasites and against modifications of self structures (by viral infections, tumorous transformations or other mutations).
- The immune network is formed by balance of attacking and tolerating type immune responses.
- The immune system links to the other (endocrine, neural, metabolic) regulatory systems of the body in multiple levels influencing each other.

Composition of the immune system

- Individuals and species
- Organs
- Cells
- Molecules
- Functions

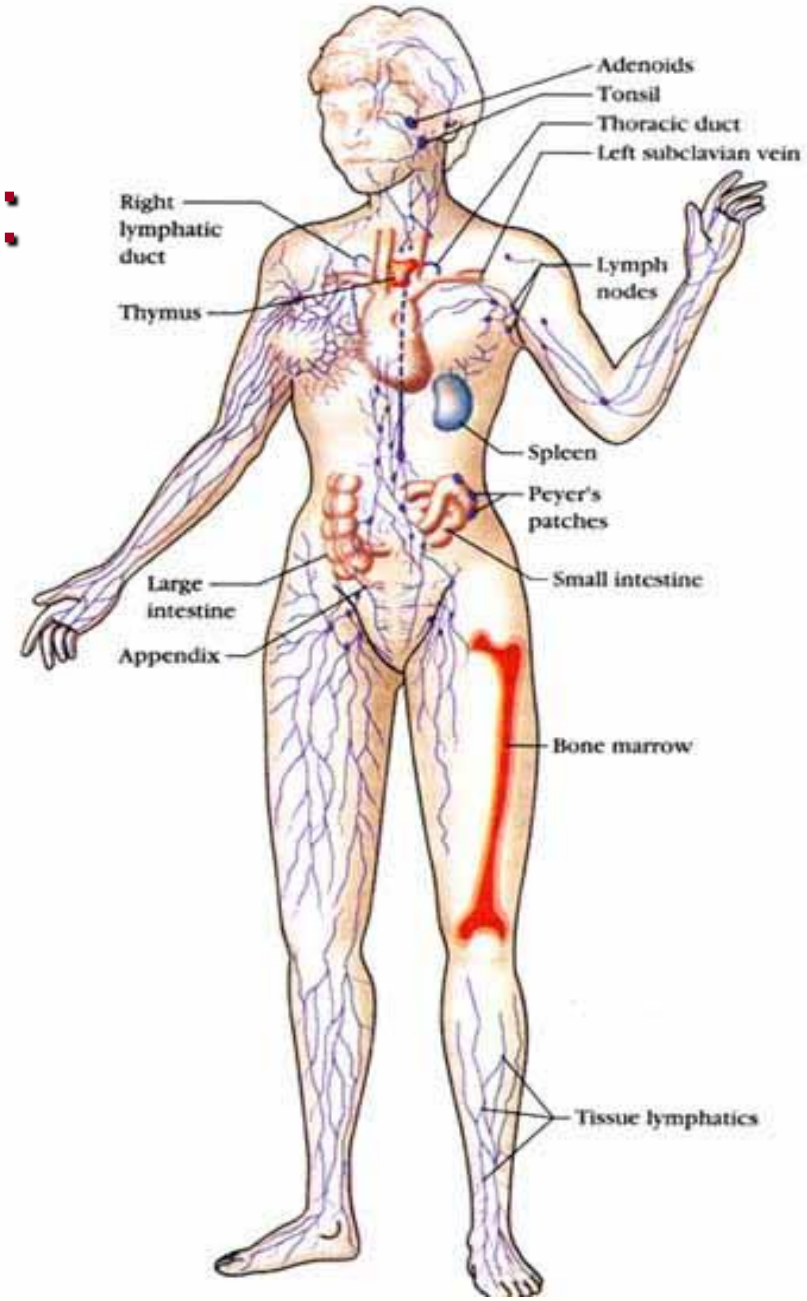
Structural and functional NETWORK

Central immune system:

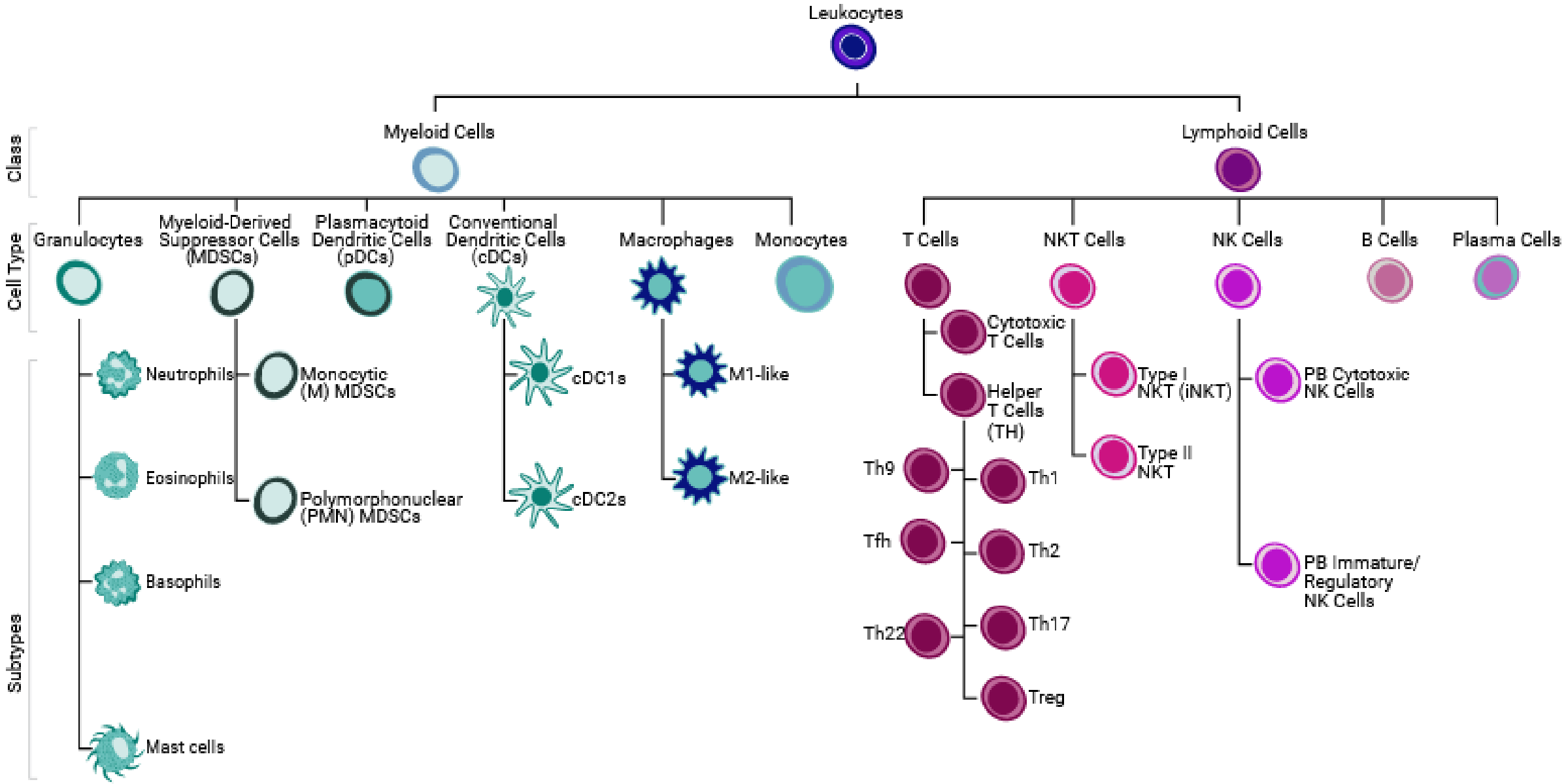
- bone marrow
- thymus
- spleen
- lymph nodes

Local immune system:

- SALT
- MALT



Main cellular components of the immune system



Composition of the immune system

Innate

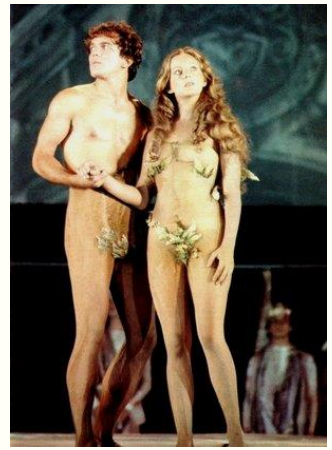
- None antigen specific
- No immunological memory
- Rapid reactivity
- Linear amplification of the reaction

Adaptive

- Antigen specific
- Immunological memory
- Activated after a latency
- Exponential amplification of the reaction

Natural

Innate-like immunity with adaptive features



Innate immune system

- Pattern recognition receptors (PRR)
- Recognition of pathogen associated molecular patterns (PAMP)
- First line of defence
- Low number of molecularly distinct receptors and high number of recognized patterns
- Main molecular components: Antibacterial peptides, Complement factors and their receptors, Heat shock proteins, Fc receptors, Inflammatory cytokines, Growth factors, Histamine
- Main cellular components: Macrophages, Monocytes, NK cells, Granulocytes, Mast cells

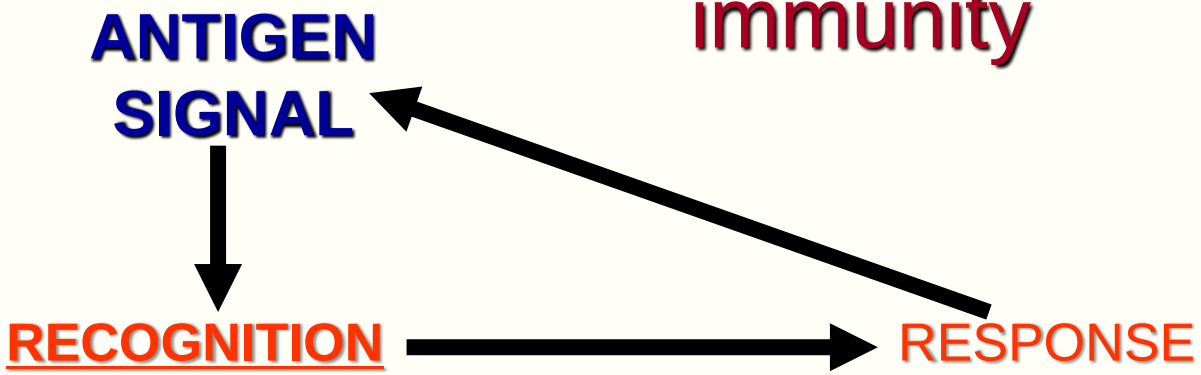
Adaptive immune system

- Antigen receptors (BCR,TCR)
- Epitope specific in a given antigen
- Adaptive type immune response
- High number of distinct antigen receptors and high number of recognized antigens
- It develops in a multistep differentiation process.
- Main molcelar components: Antibodies, T and B cell receptors, MHC, Lymphatic citokines
- Main cellular components: T cells (both αβ and γδ), B cells, antigen presenting cells

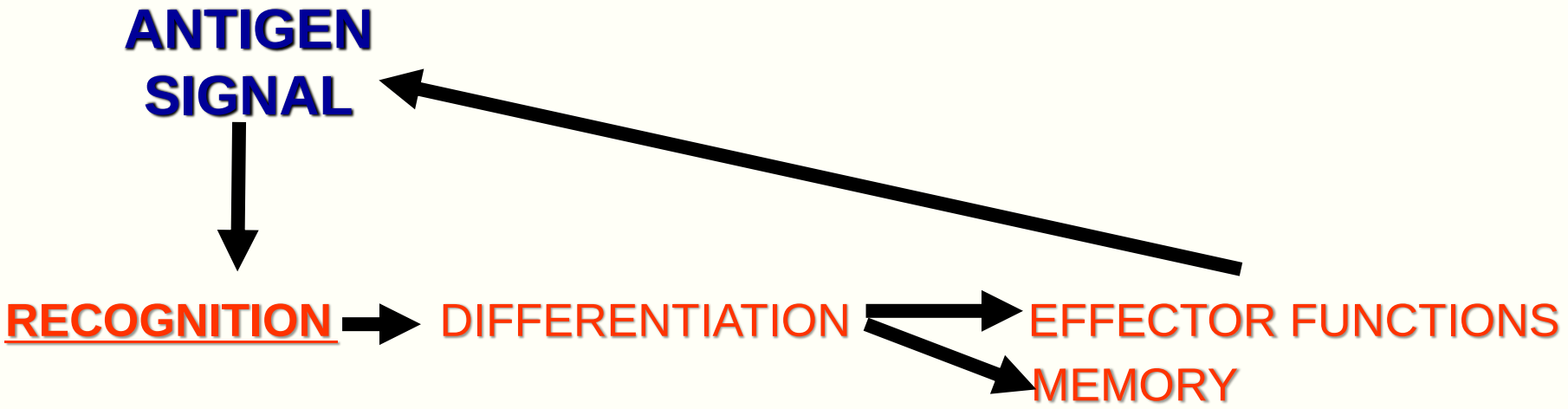
Natural immune system

- Antigen recognition receptors (BCR,TCR) with limited specificity
- Pattern recognition profile
- Innate-like immune response
- Limited number of distinct antigen receptors and high number of recognized antigens
- A prompt response to the antigen.
- Main cellular components: iNKT cells, iγδT cells, MAIT cells, IEL cells, CD5+ B cells
- Main molecular components: natural (auto)antibodies

Theoretical scheme of the innate and natural immunity



Theoretical scheme of the adaptive immunity



Definition of the antigen

Detre (Deutsch) László (1874-1939):

ANTIBODY GENERATOR: foreign substance induces antibody production (1899)

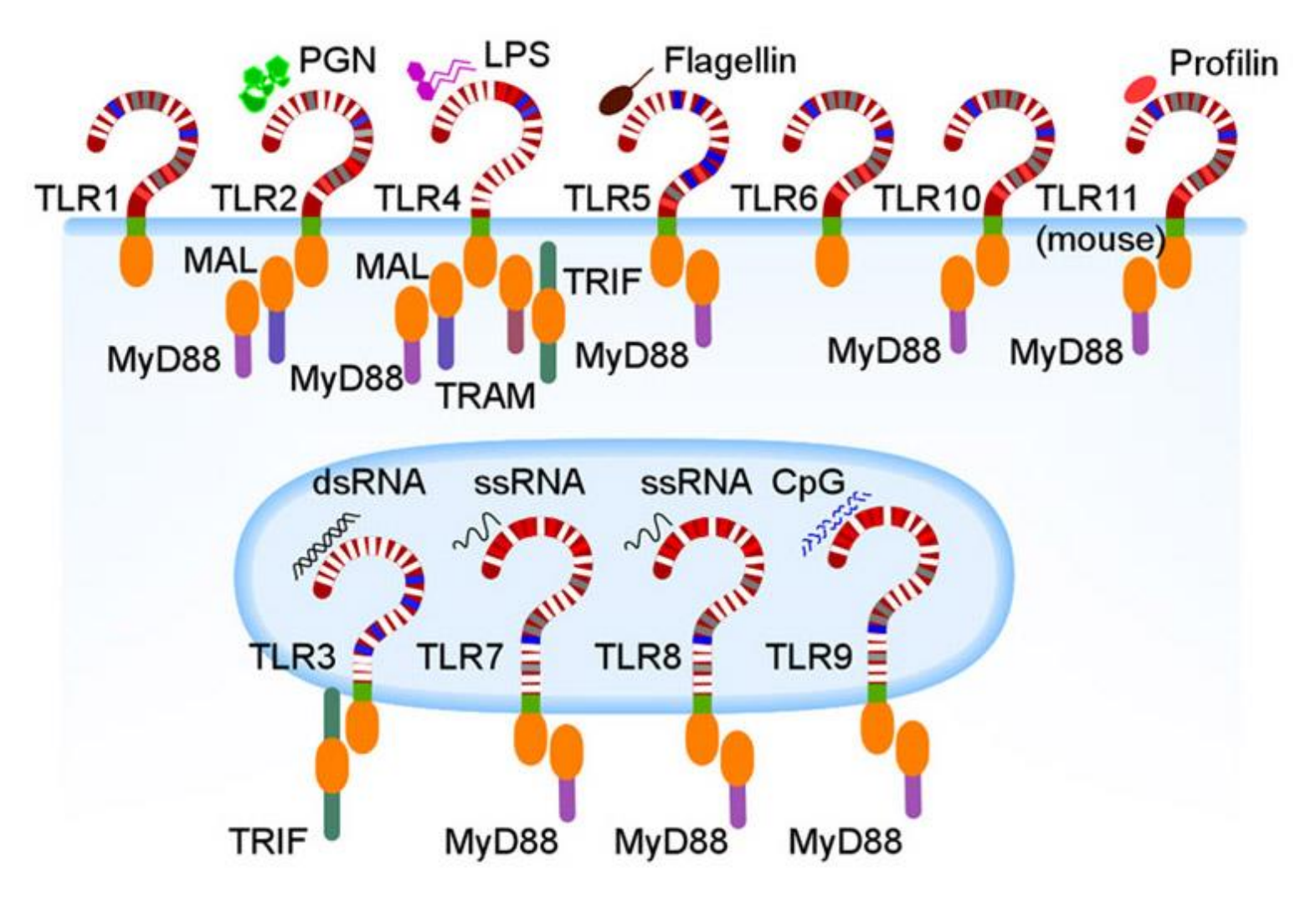
Modern definition: substance, which is recognized by different immune recognition molecules including T and/or B cell receptors, and it is able to induce *active immune response or tolerance* according to the host immunogenetic background (MHC haplotype).

Factors determining the immunogenity

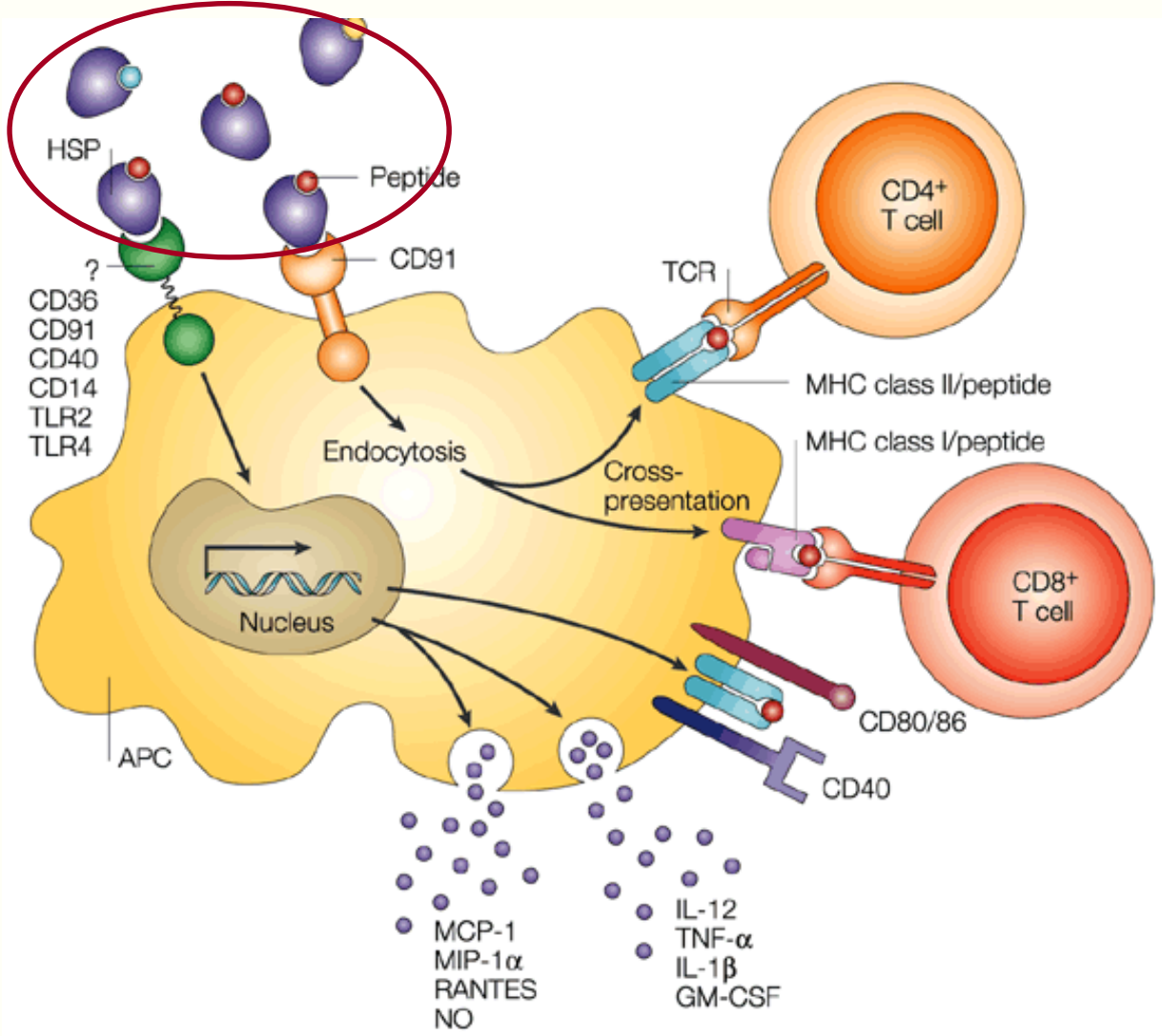
- **immunodominant regions**
- **chemical structure** (inorganic molecules are not antigens at general, but e.g. heavy metals in protein complex are able to induce specific metal allergies). The best antigens are proteins>polypeptides>polysaccharides>lipides>nucleic acids
- **physico-chemical nature** (D and L configuration; ortho-, para,- meta position; hydrophilic and hydrophobic amino acid sequence)
- **molecular weight** (not an absolute category)
- **conformation sensitivity** (folding and refolding)
- **Origin** auto-, allo-, xenoantigen
- **mode and anatomic region of the administration** (e.g. peripheral immune reaction and oral tolerance for the same antigen depending from the place of the antigen presentation)
- **dose dependence** (large and low dose)
- **Valency**: monovalent, bivalent, and multivalent antigens

Immunological recognition molecules

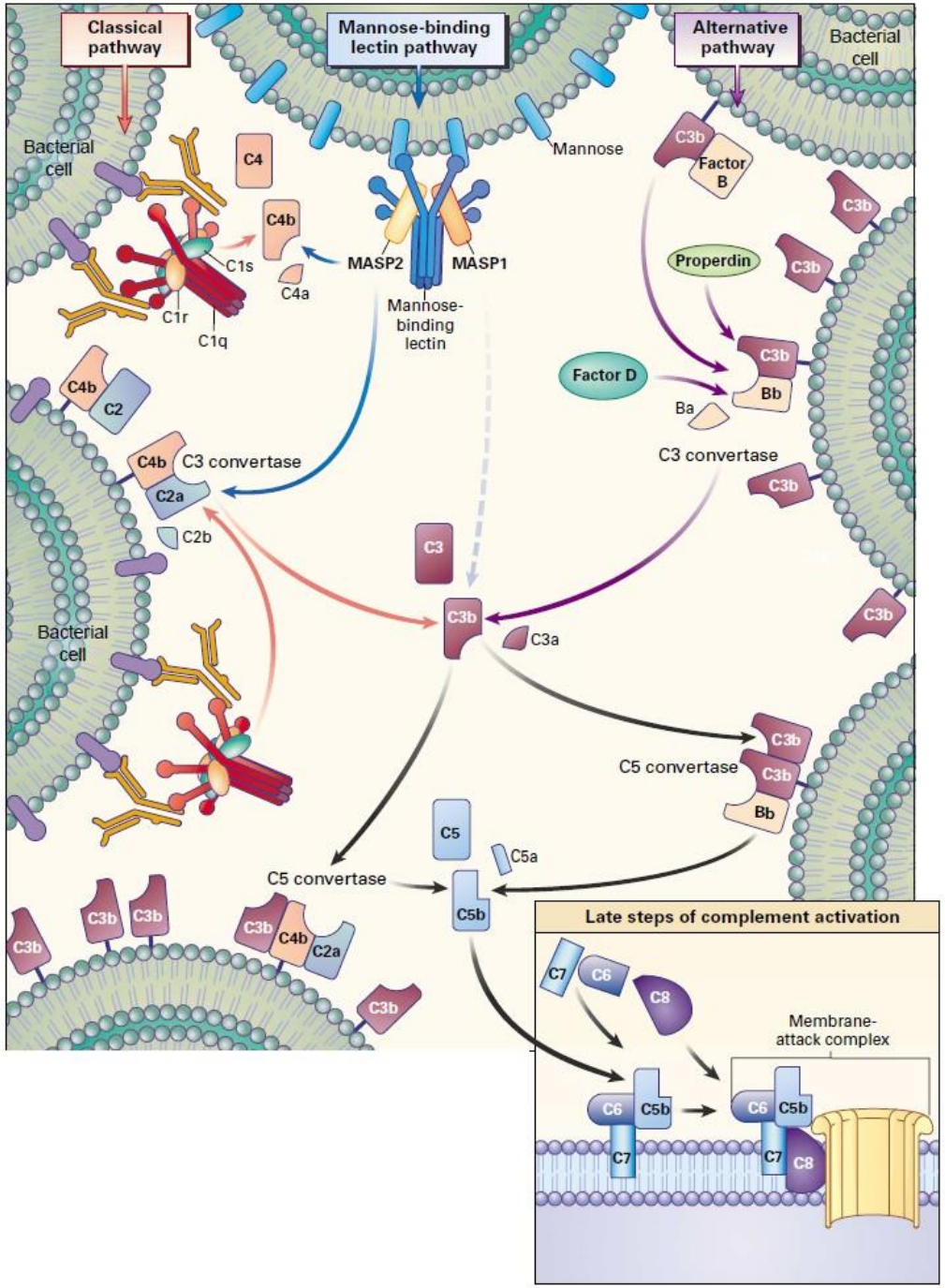
Innate	Natural	Adaptive
TLRs Heat shock proteins Complement	Invariant TcRs (both γδ and αβ) Natural (auto) antibodies	Immunoglobulins BcR TcR MHC I and MHC II



Toll Like Receptors (TLR) recognize molecular patterns associated with a broad range of lipid-based cell wall components on pathogens including bacteria, fungi, protozoa and viruses.



Heat shock proteins (Hsp60, 70, 90, gp96) play important role in antigen presentation, activation of macrophages, lymphocytes and dendritic cells. As part of their molecular chaperone functions play role in antigen presentation by MHC molecules.



Complement system

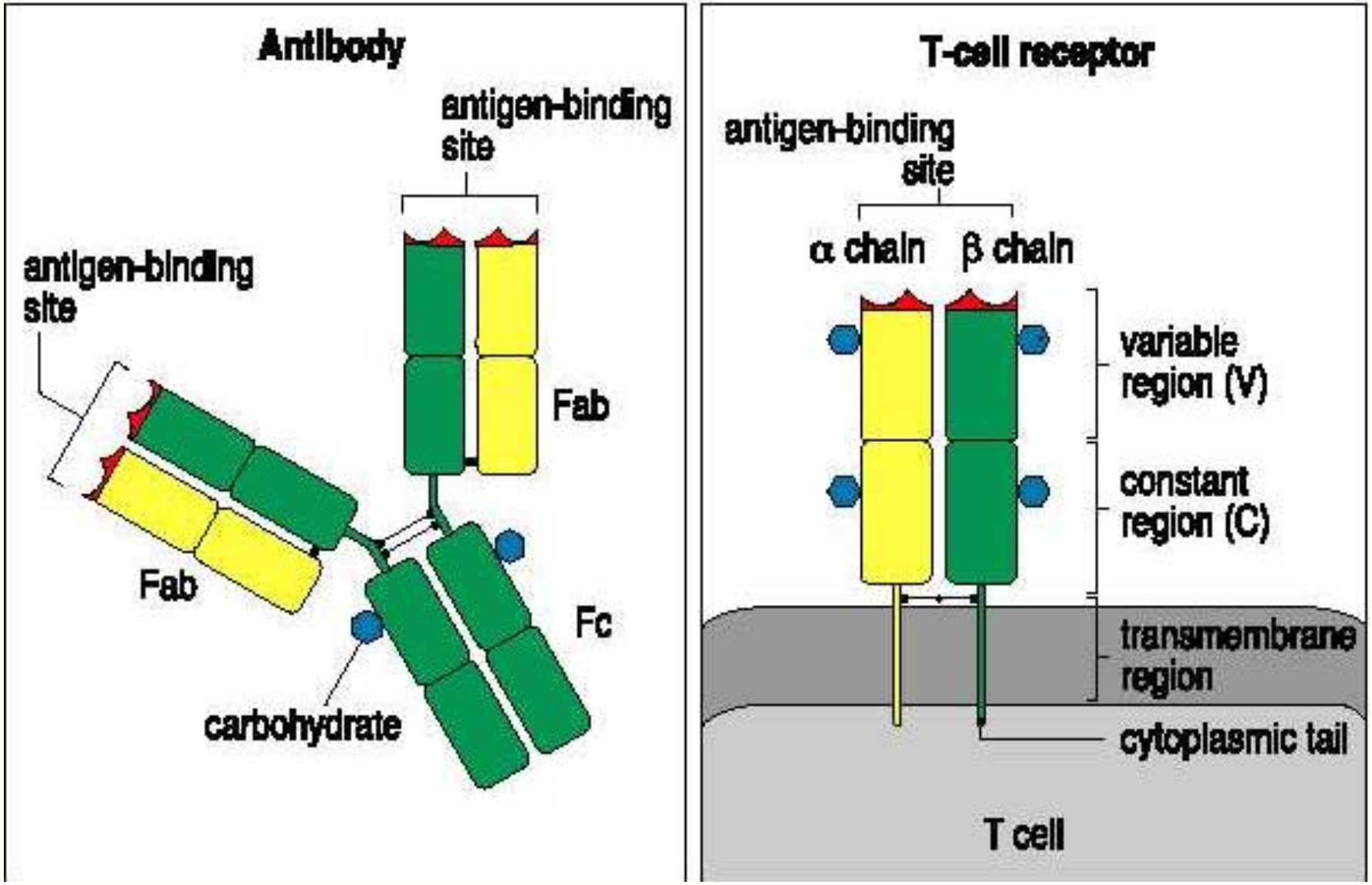
The complement system is a part of the immune system that enhances (complements) the ability of antibodies and phagocytic cells to clear pathogens from an organism. It is part of the innate immune system, which is not adaptable and does not change over the course of an individual's lifetime. However, it can be recruited and brought into action by the adaptive immune system.

Recognition molecules in the adaptive immune system

Immunoglobulins
B cell receptors (BcR)
T cell receptors (TcR)
MHC class I and class II

Specialized molecules manage antigen recognition. The common structural features of these molecules are the well-conserved (constant) basic elements (designed by 110 amino acids domain units) containing variable, antigen specific parts (binding sites) for the recognition and ligand formation.

Antigen specific recognition molecules

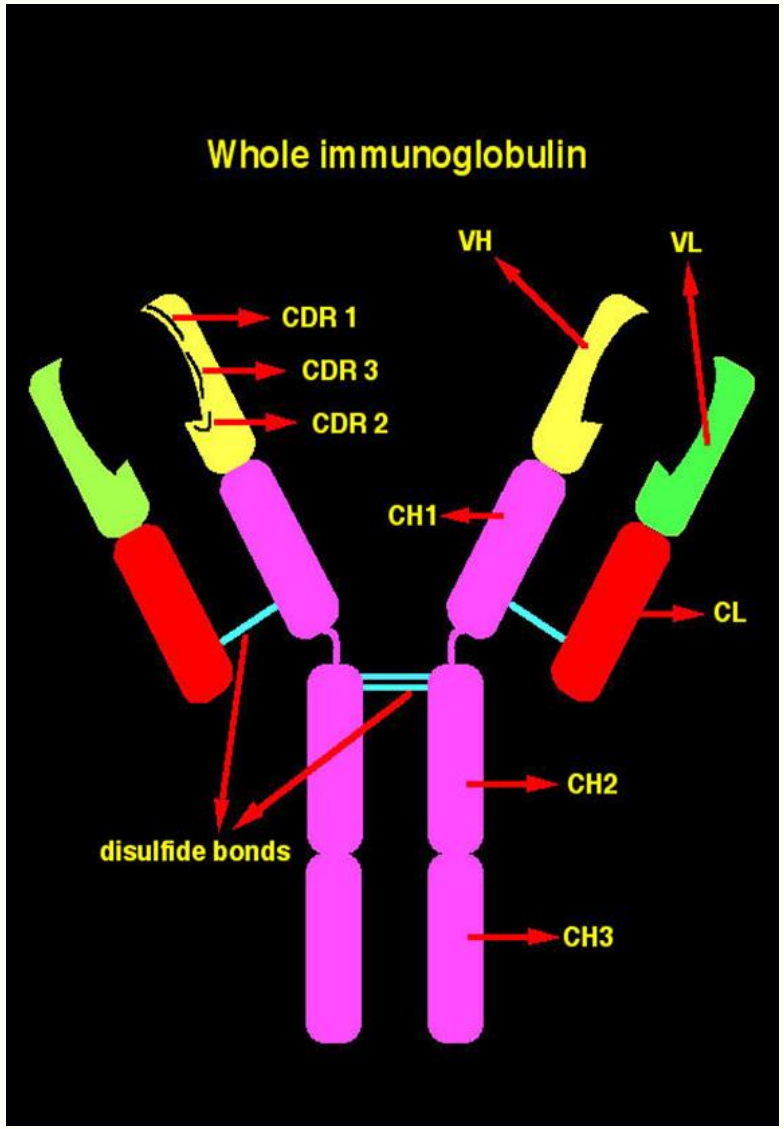


Antigen recognition in adaptive immunity

Native antigens are recognized by immunoglobulins or B cell receptors.

T cells can recognize exclusively in denatured (presented) forms of the antigens.

Immunoglobulin idiotype



Individual determinants in **V regions**, specific for each antibody.

The N terminal Ig domain contains V region forming the antigen binding site: clustering the 3 hyper variable sequences close to each other on both chains - the variation of 3 x 3 results tremendous diversity.

Construction of idiotype by immunoglobulin rearrangement

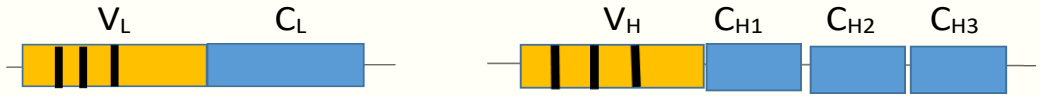
Génátrendeződés

1 2 3 Szomatikus hipermutációk 1 2 3

Gene rearrangement

Somatic hypermutations

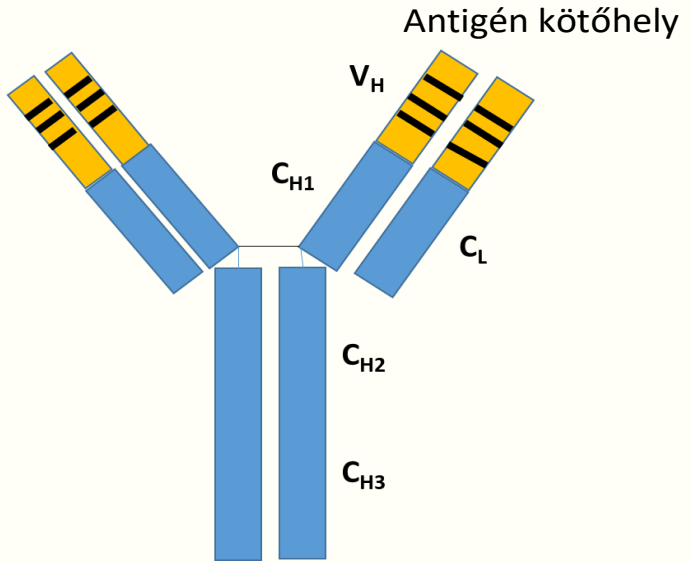
Hírvivő RNS



CDR 1 2 3 1 2 3

Messenger RNA

Immunglobulin fehérje



Immunoglobulin protein

Antigen bindingsite

Human immunoglobulins

IgG – blood, lymph, make up 80% of Ig only Ig of maternal origin to pass the placenta wall give newborns (Mw 150 kD) neutralize toxins and viruses

IgM – Blood, lymph (cell surface) pentamer structure (Mw 900 kD) first antibodies formed in response to initial infection.

IgA – Mucosal surfaces, blood (active in dimeric or tetrameric form) (Mw 150-600 kD)

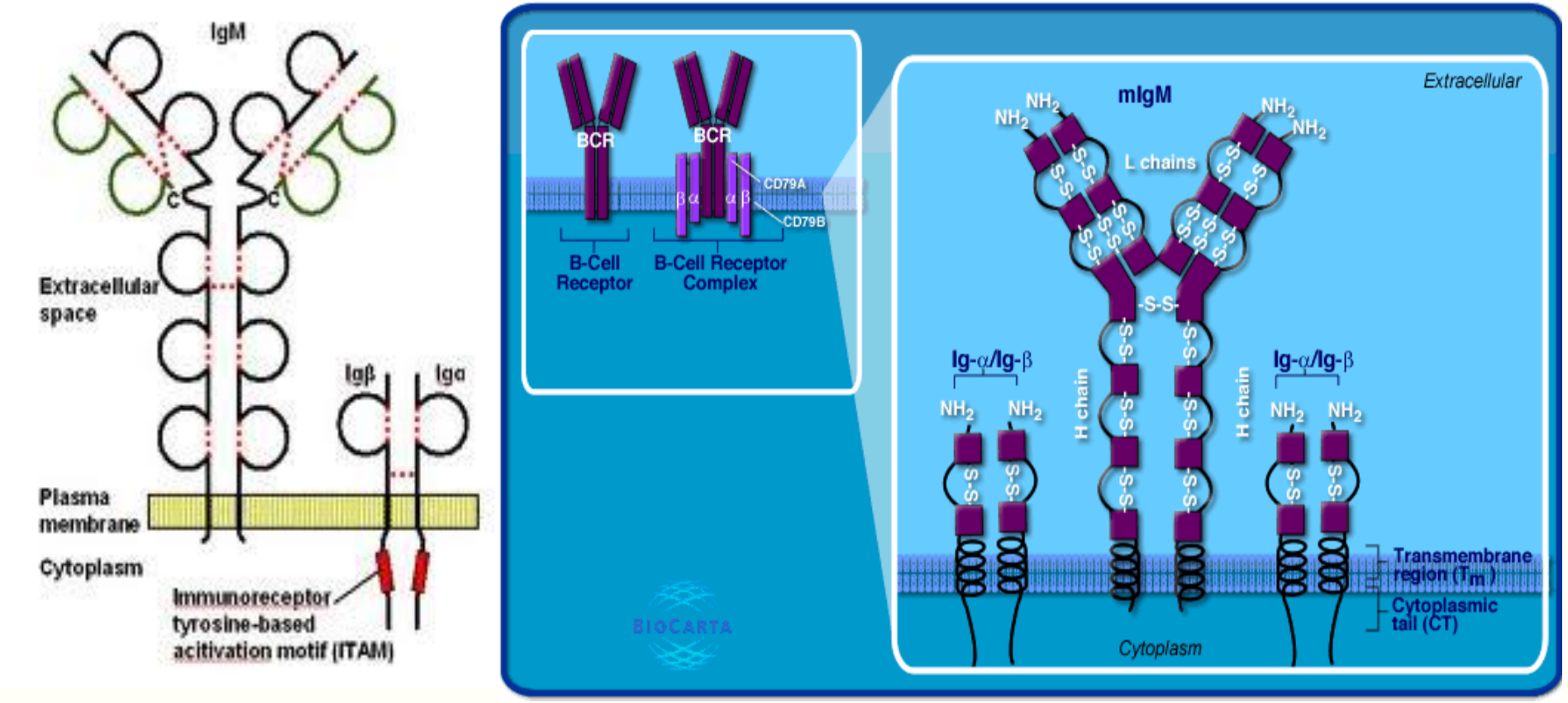
IgD – only membrane-bounded form in B-cell surfaces (Mw 150 kD) may function in initiation of antibody-antigen response

IgE – blood, in perifery can bound to basophiles and mast cells (Mw 190 kD) plays role in defence agains parasites and initiation of and allergic reactions

Antigen – antibody reactions

- Neutralization (e.g. viruses, toxins)
- Precipitation (soluble molecules)
- Agglutination (particles, cells)
- Opsonization (large particles)
- Complement fixation

B cell Receptor (BcR) Complex



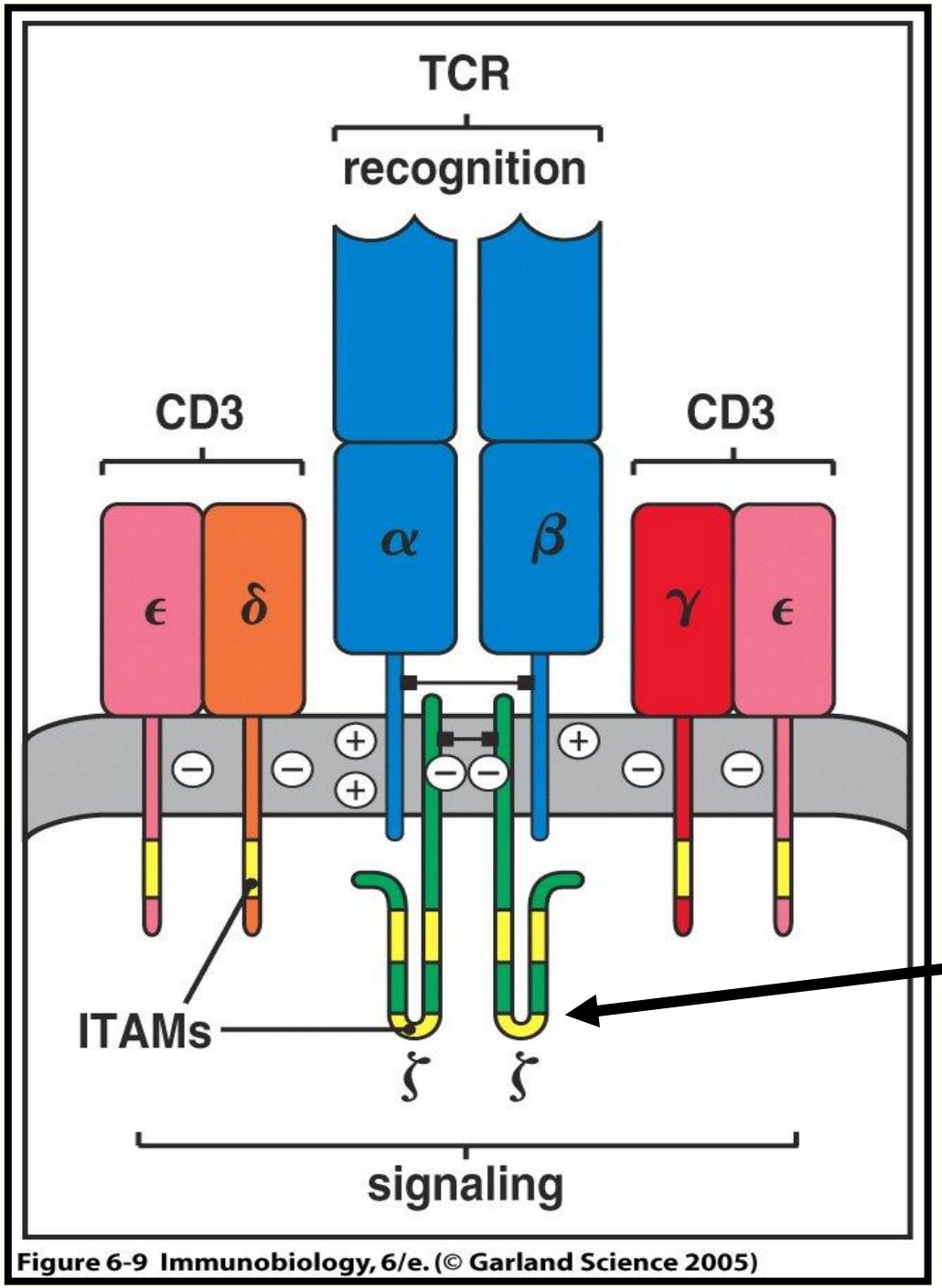


Figure 6-9 Immunobiology, 6/e. (© Garland Science 2005)

T Cell Receptor complex

ITAMs
Immunoreceptor
Tyrosine-based
Activation
Motifs

Antigen Recognition by T Cells

-T cells recognize antigens only displayed on surfaces of the body's own cells as MHC and peptide complexes

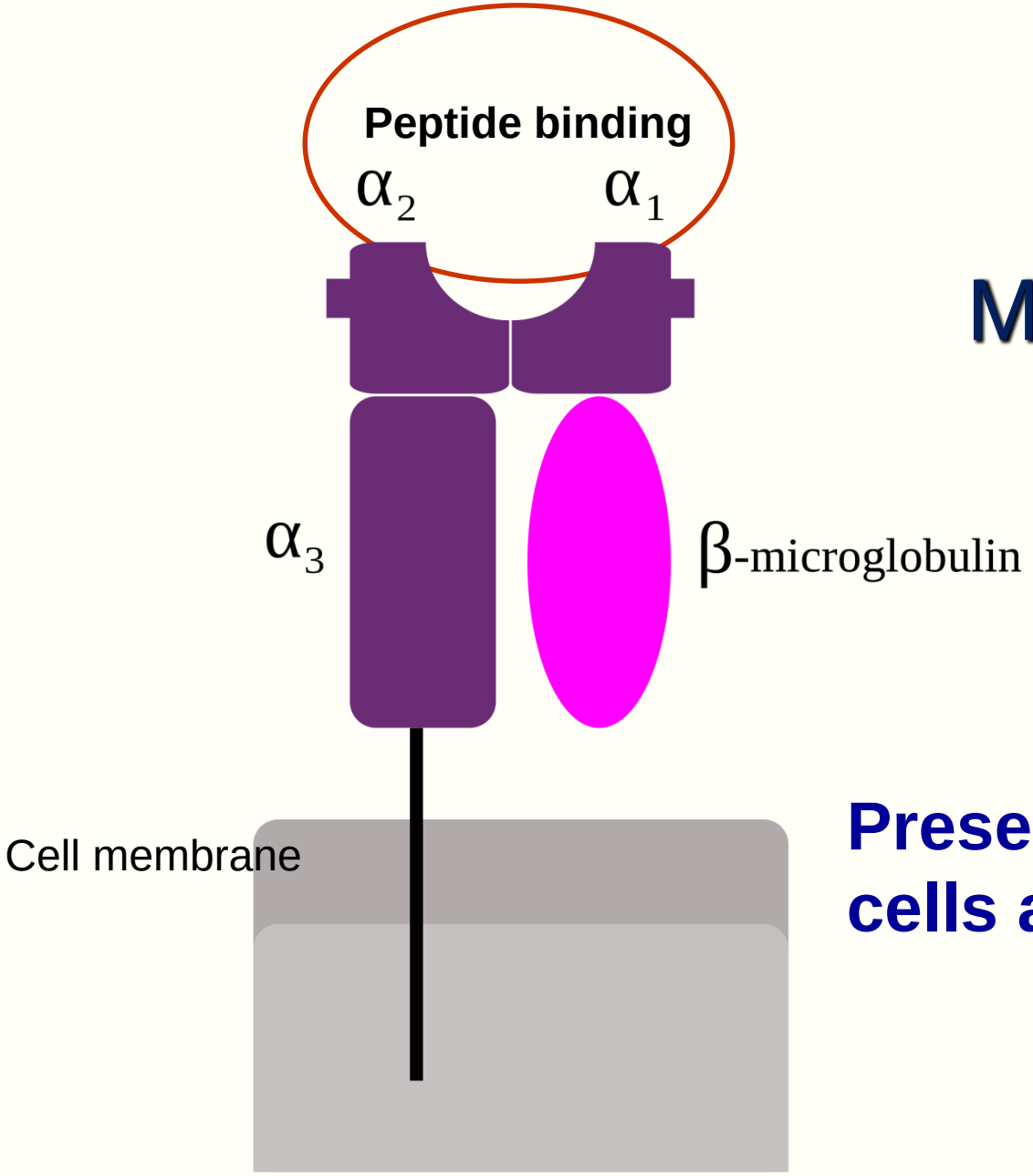
Main T cell types:

-CD8+ (cytotoxic) T-cells

MHC Class I - peptide complex

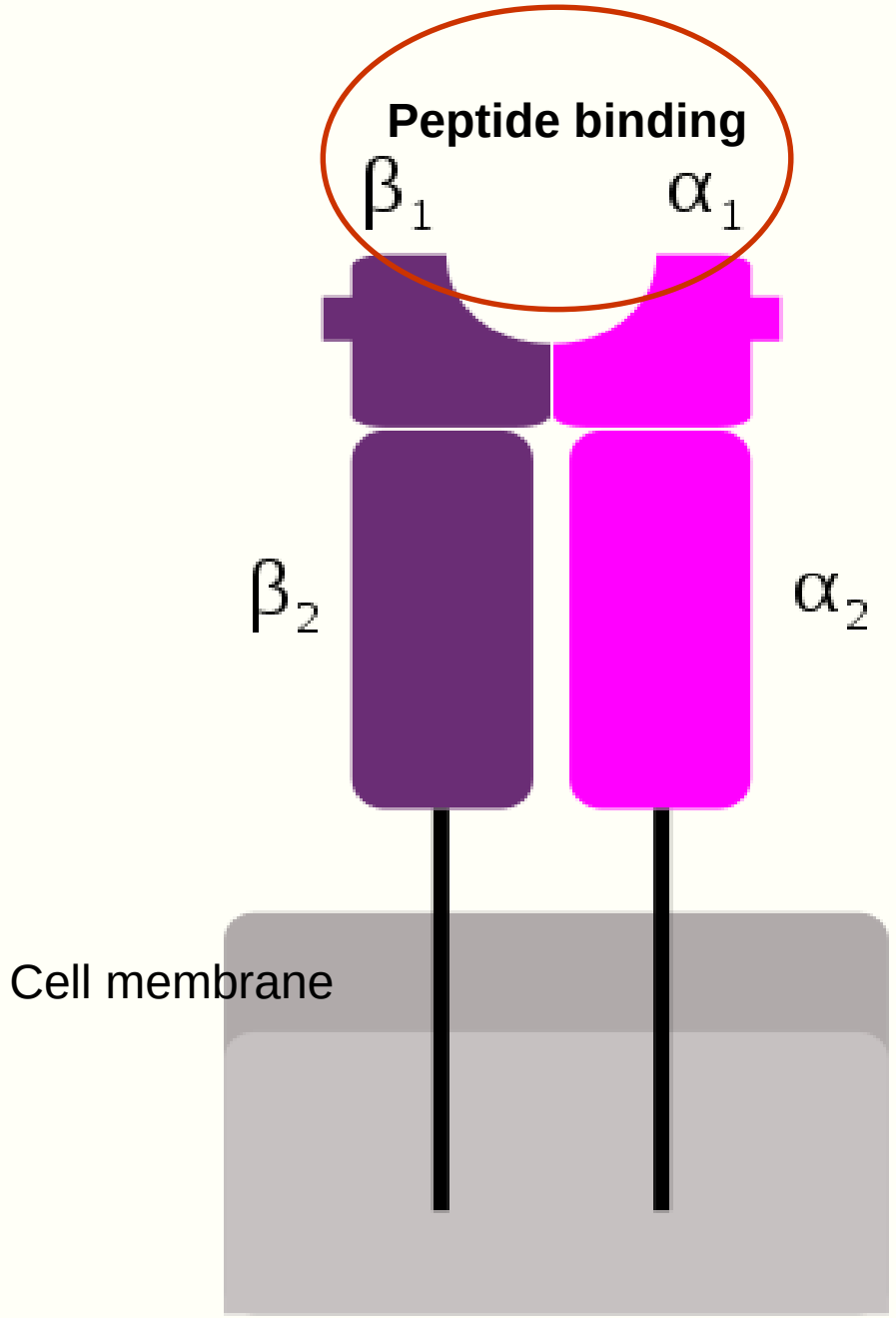
-CD4+ (helper) T-cells

MHC Class II - peptide complex



MHC Class I

Present in all nucleated cells and platelets



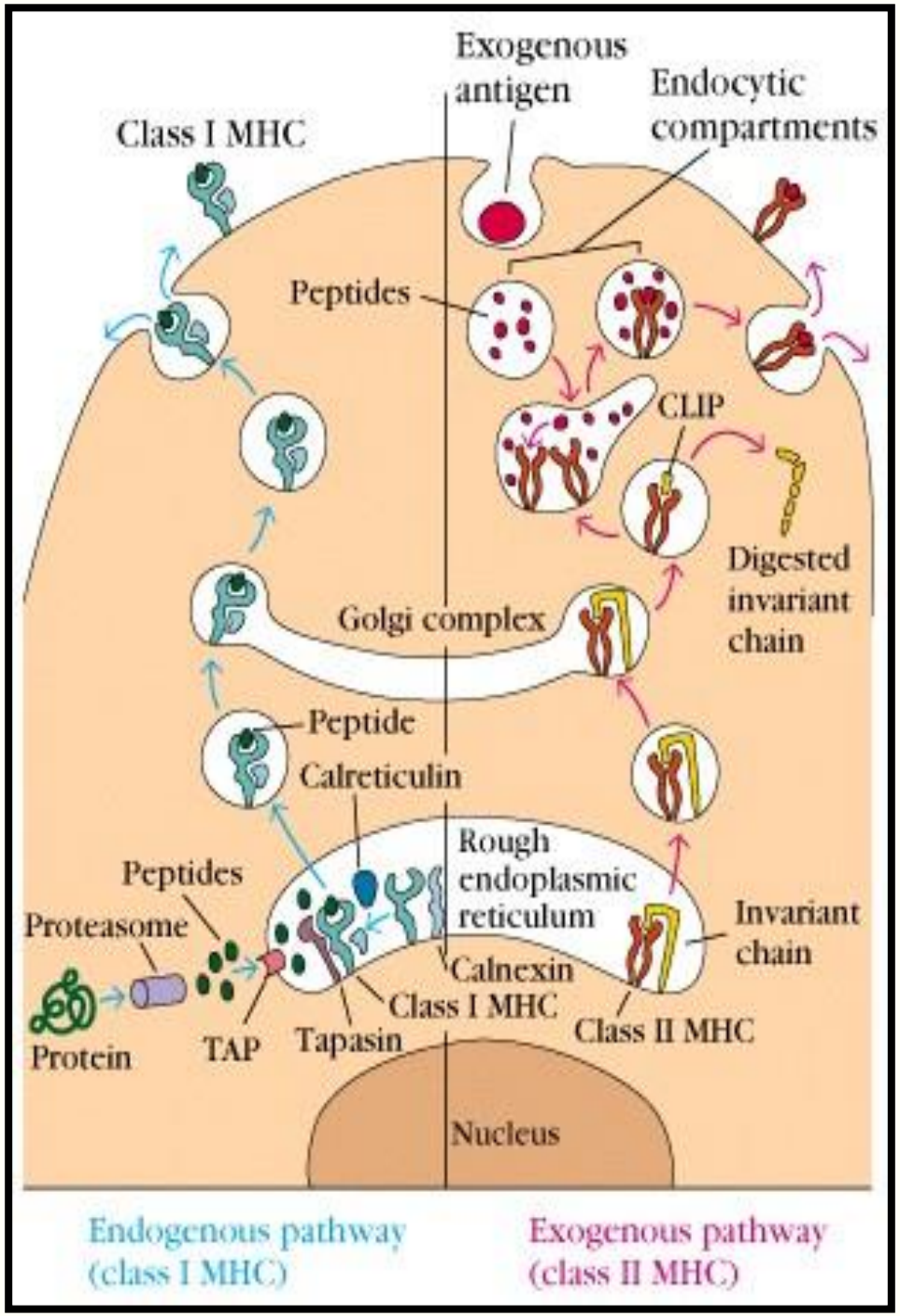
MHC Class II

Present in professional or facultative antigen presenting cells (APC)

Professional antigen presenting cells: dendritic cells, monocytes, macrophages, B cells, thymus epithelial cells

Facultative antigen presenting cells: inflammatory epithel and endothel in pathologic conditions

Presentation of intracellular antigens by MHC I:
continous in all cells and platelets



Presentation of extracellular antigens by MHC II:
in APCs, after phagocytosis

MHC Restriction

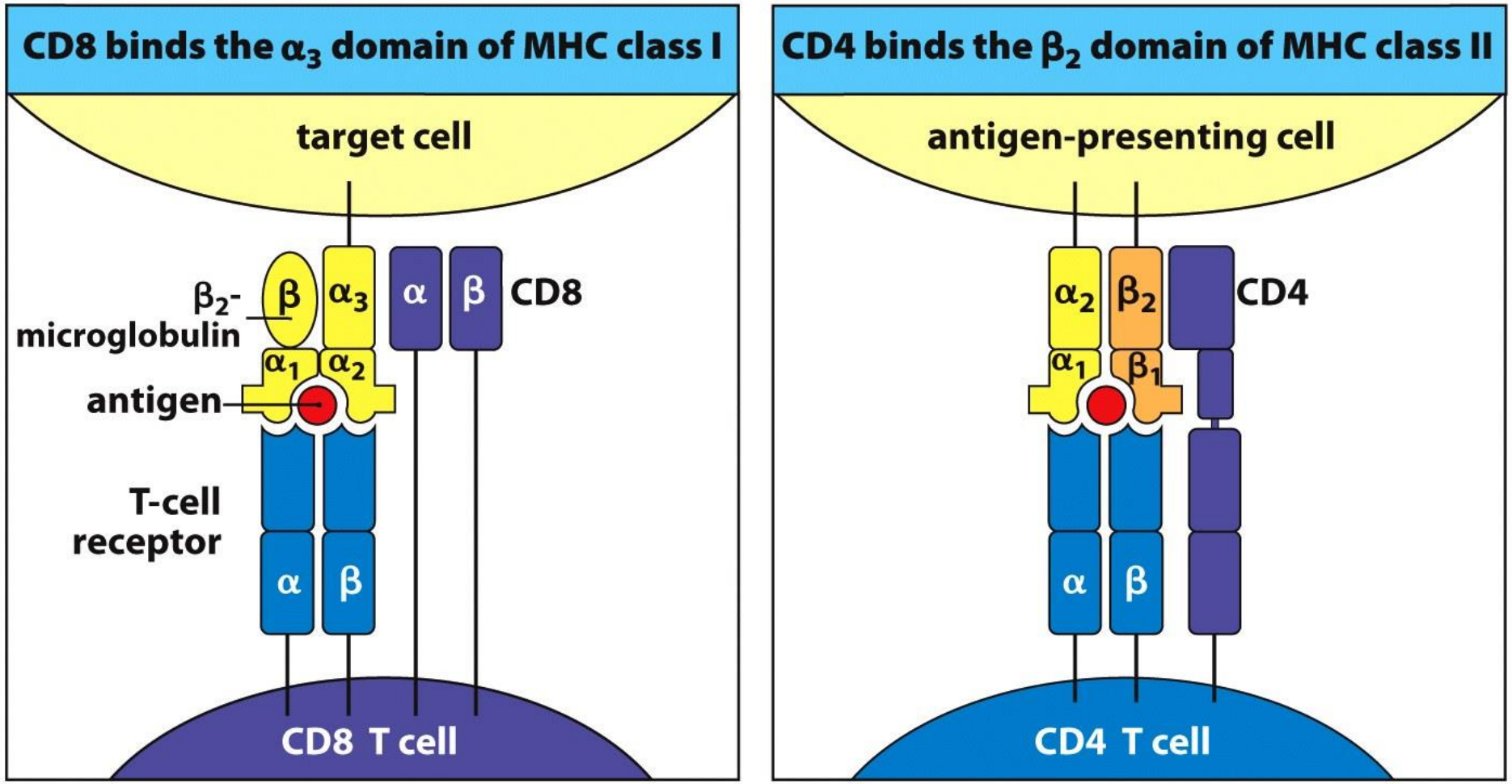


Figure 5.14 The Immune System, 3ed. (© Garland Science 2009)

MHC I – CD8

MHC II – CD4

Septicemia (toxic shock syndrome) caused by superantigens

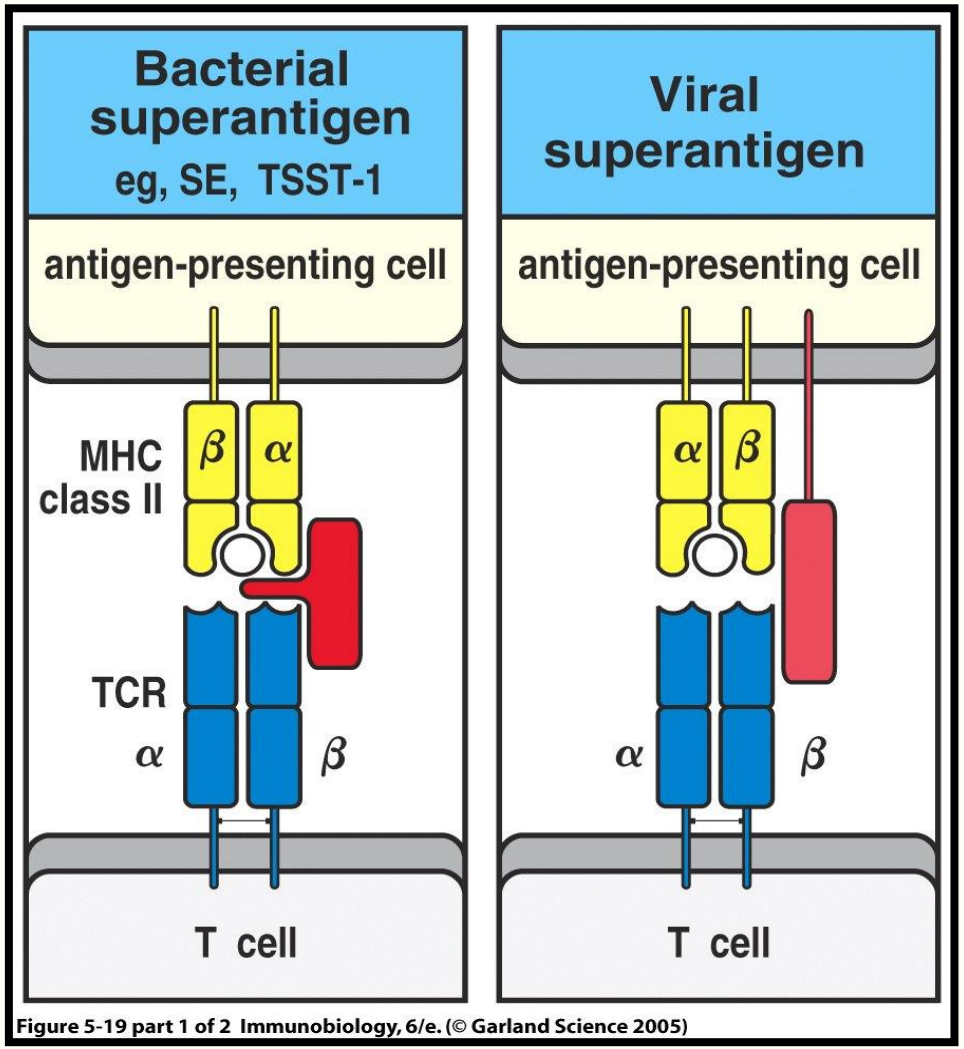


Figure 5-19 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

Compared to a normal antigen-induced T-cell response the endotoxins (Sags) are capable of activating much higher number of the T-cells in *nonspecific* manner. This causes a massive immune response with irregular cytokine production (toxic shock syndrome) that is not specific to any epitope on the SAg.

T cells activated nonspecifically overproduce cytokines resulting systemic toxicity with general catastrophe of bioregulation, („Cytokine tsunami")

TARGETING TYPE IMMUNE RESPONSE & TOLERANCE

- Upon encountering an antigen, **the immune system can either develop a targeting type immune response or** enter a state of unresponsiveness called **tolerance**.
- Immunological tolerance is thus the lack of ability to mount an immune response to epitopes to which an individual has the potential to respond.
- **Targeting type and tolerating type immune responses composed by the same cellular and molecular components, the differences are in the effector phase only.**
- Targeting type immune response or tolerance needs to be carefully regulated since an inappropriate response – whether it be **autoimmune** reaction to self-antigens or tolerance to a potential pathogen – can have serious and possibly life-threatening **immunodefficiencies**.