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Imunology 1

Self and not self

Antigens and receptors

Terminology

Immunity
complex, regulated, efficient system

- **Defense** against foreign structures (antigens)
  - anti infectious immunity
- **Recognition and discrimination** between self and not self structures
  – tumors, autoimmunity, transplantation
- **Regulation** of immune reactions, appropriate force (samoregulation)
  – anergy, allergy, hypersensitivity

Defense mechanisms

- Immunity system
- Nervous system
- Endocrinous system

Comunication systems – interaction, management, supervision

Immunity

- **Innate -** equal in all members, species specific, prepared
- **Adaptive** – gained with the help of own immune reaction after stimulation by antigen
- **Specific -** antigen dependent
- **Nonspecific** – functionally antigen non-dependent
- **Cell** – effectors are immunocompetent cells
- **Humoral** – effectors are soluble substances present in serum or body fluids
- **Systemic** – applicable for the whole body
- **Local** – applicable in a define place, (mucous membrane)

Know yourself

- I vs. they
- I and some others = we
- We vs. they

- Cells – my, not my, my but changed
- Microorganisms – foreign, pathogenic (threat)
  - foreign, not pathogenic (no threat)
  - physiological flora (no threat / threat

Today´s lecture

- Conception of self
- Immune memory
- Defense mechanisms
- Antigens
- Receptors

Foreign agenses, molecules, cells

- Viruses, bacteria, parasits, fungi, toxins, foreign cells (transplantation, grafts, transfusions), foreign molecules (pills, food....), tumorous cells – threats
- exogennous or endogennous

Elimination of threats by immunity system

- Isolation
- Disruption
- Engulfment and killing

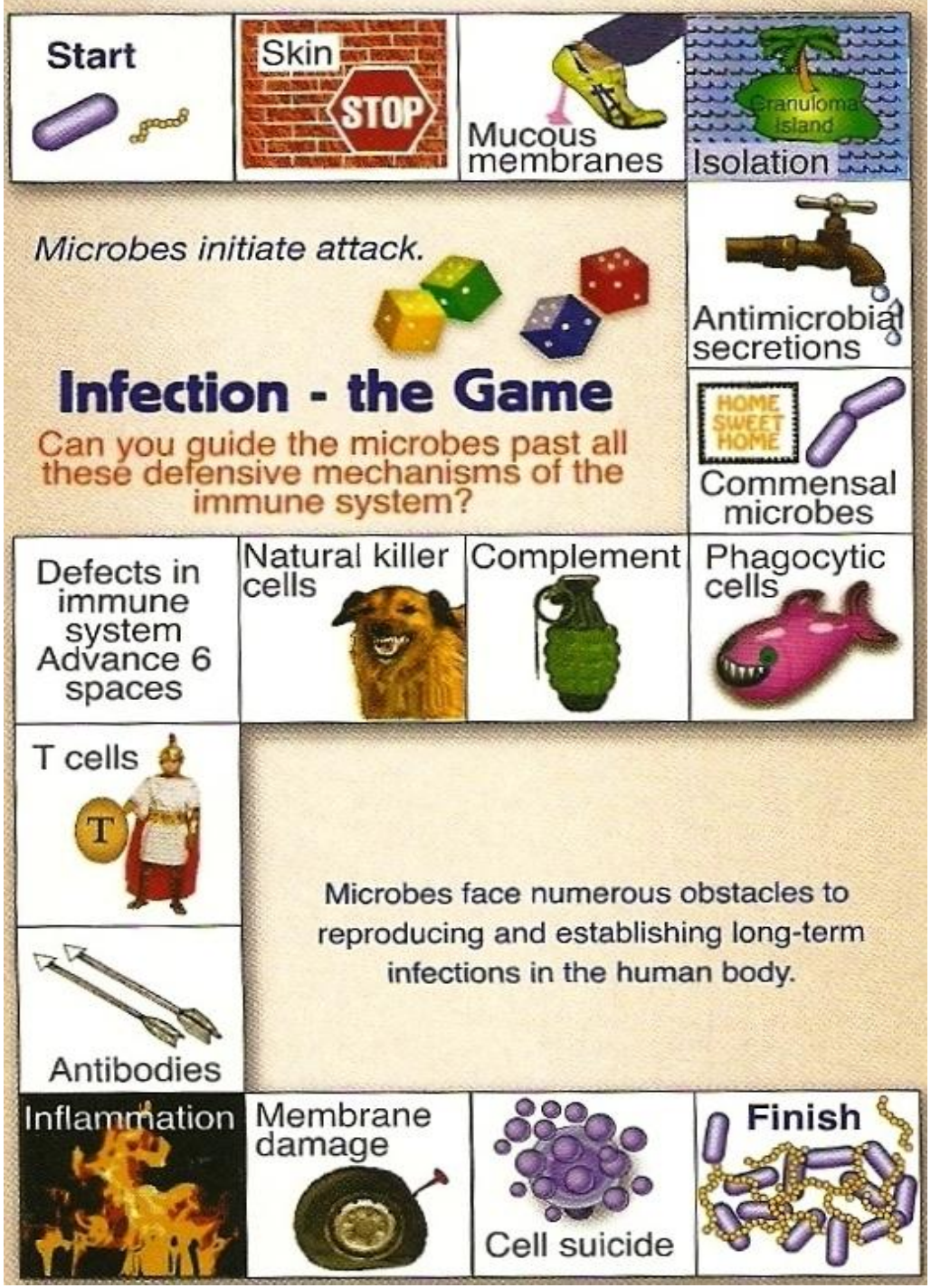
and combination

Microorganisms

- prevents spreading and growing, killing

Mechanical, biological, chemical bariéres, formation of granulomes, phagocytosis, appoptosis, complement, antibodies, natural killers, specific lymphocytes, cytokins production

Defensive mechanisms



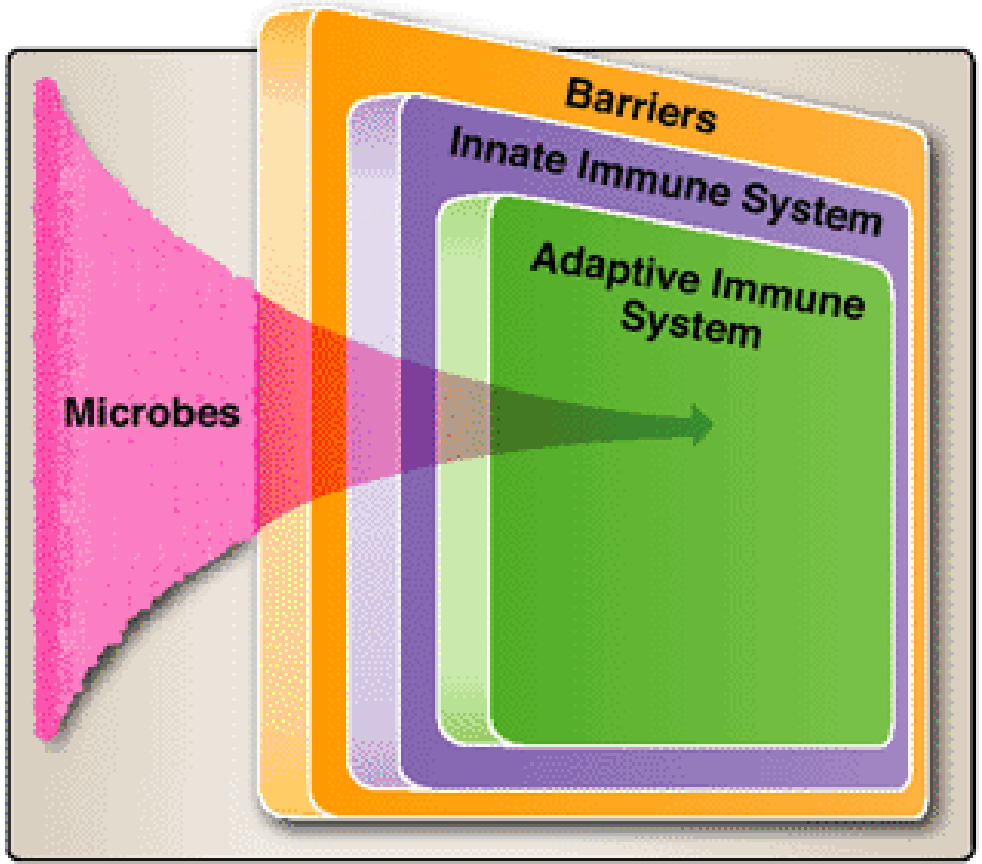
3 defensive lines

barrieres

innated mechanisms

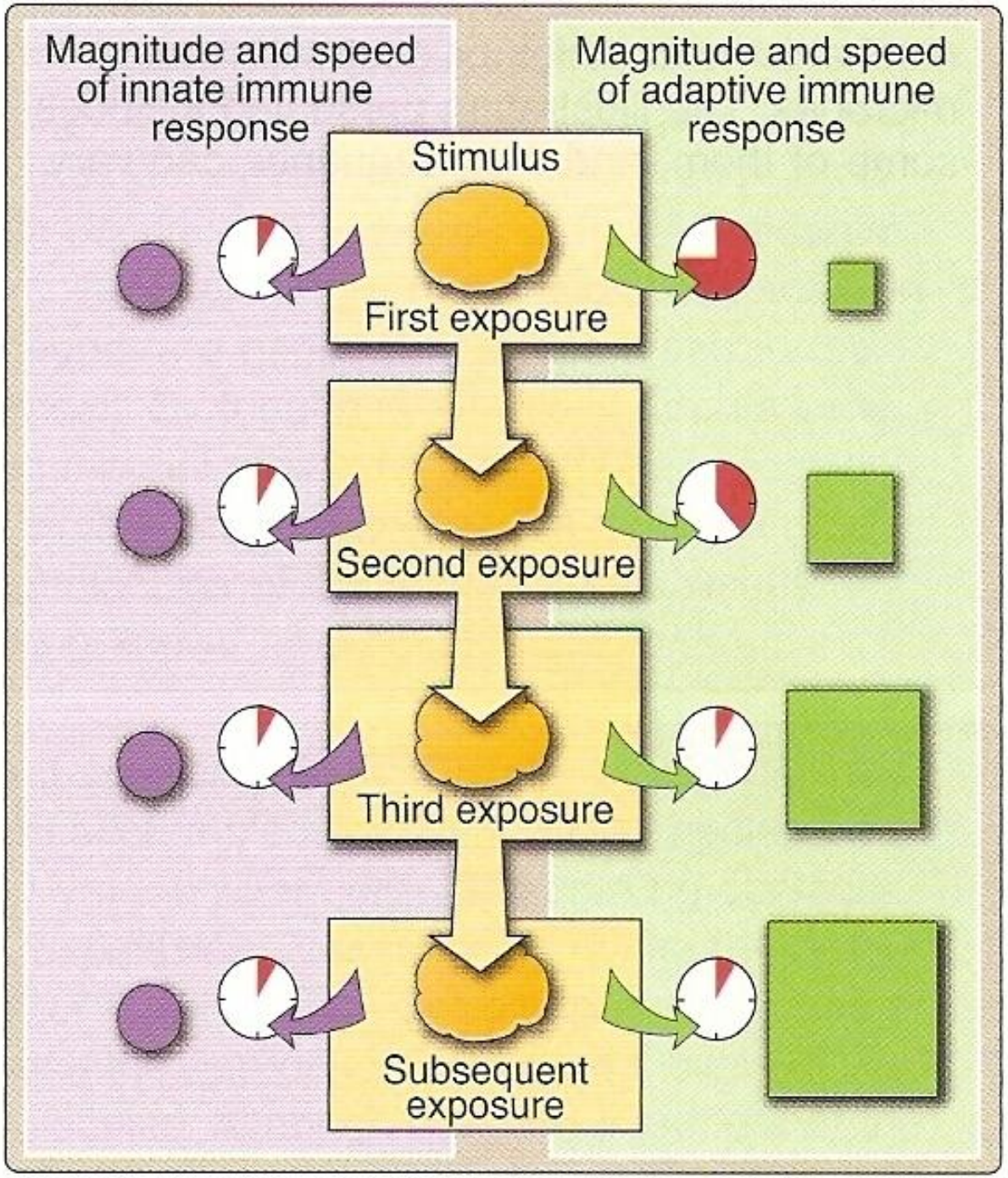
adaptive

immune mechanisms



Differences in innate and adaptive mechanisms

innate-nonspecific	**adaptive-specific**
	- prepared after exposition
- start without delay	- after time delay
- antigen not dependent	- antigen dependent
- same intensity	- different intensity if first, or any other



Differences innate and adaptive mechanisms

Immune memory

- Innate mechanisms – always as for the first time
- **Adaptive mechanisms** – in any next exposition:
  - more intense, rapid (microbial threats)
  - not reacting to common microorganisms, not threating molecules (physiological bacteria, molecules on skin, food, water)

Different reactions to safe and not safe molecules

Recognition of self - not self – foreign

- Receptor – ligand (antigen) reaction

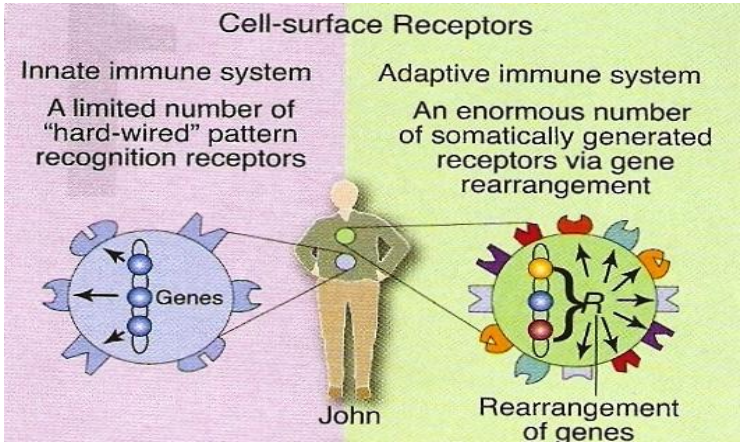
Recognition of not self - receptors

- **Recognition of self** – cell recognises environmental cells., important for appropriate functions
- **Identification of lack of self** – can start reaction (Ca decreases amount of MHC I molecules, that enable Natural Killers – NK cells – to destroy self cells)
- **Recognition of foreign** – via 2 types of receptors:
  - PRR – on idividual cell surface membrane or soluble molecules (cellular or humoral nonspecific immunity)
  - recognises structures other than self but broad-spread in microbes

  - SGR – are present on T a B lymfocytes, - recognises only 1 specificity (one of 10^{10} in 1 individual)

Recognition of not self - receptors

PRR pattern recognition receptors



SGR somatically generated receptors

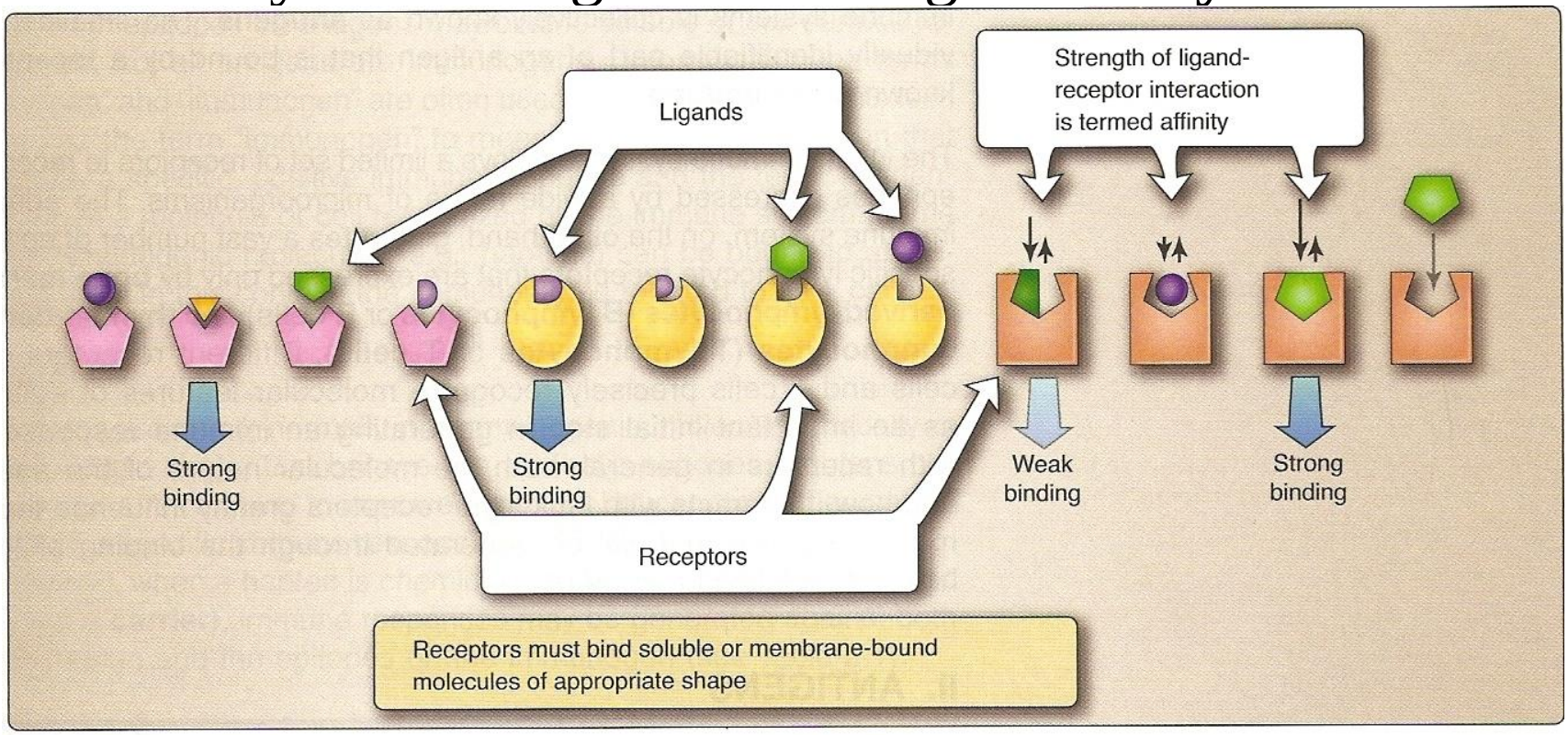
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Antigens and receptors

Immune system is stimulated by **receptor and ligand binding**

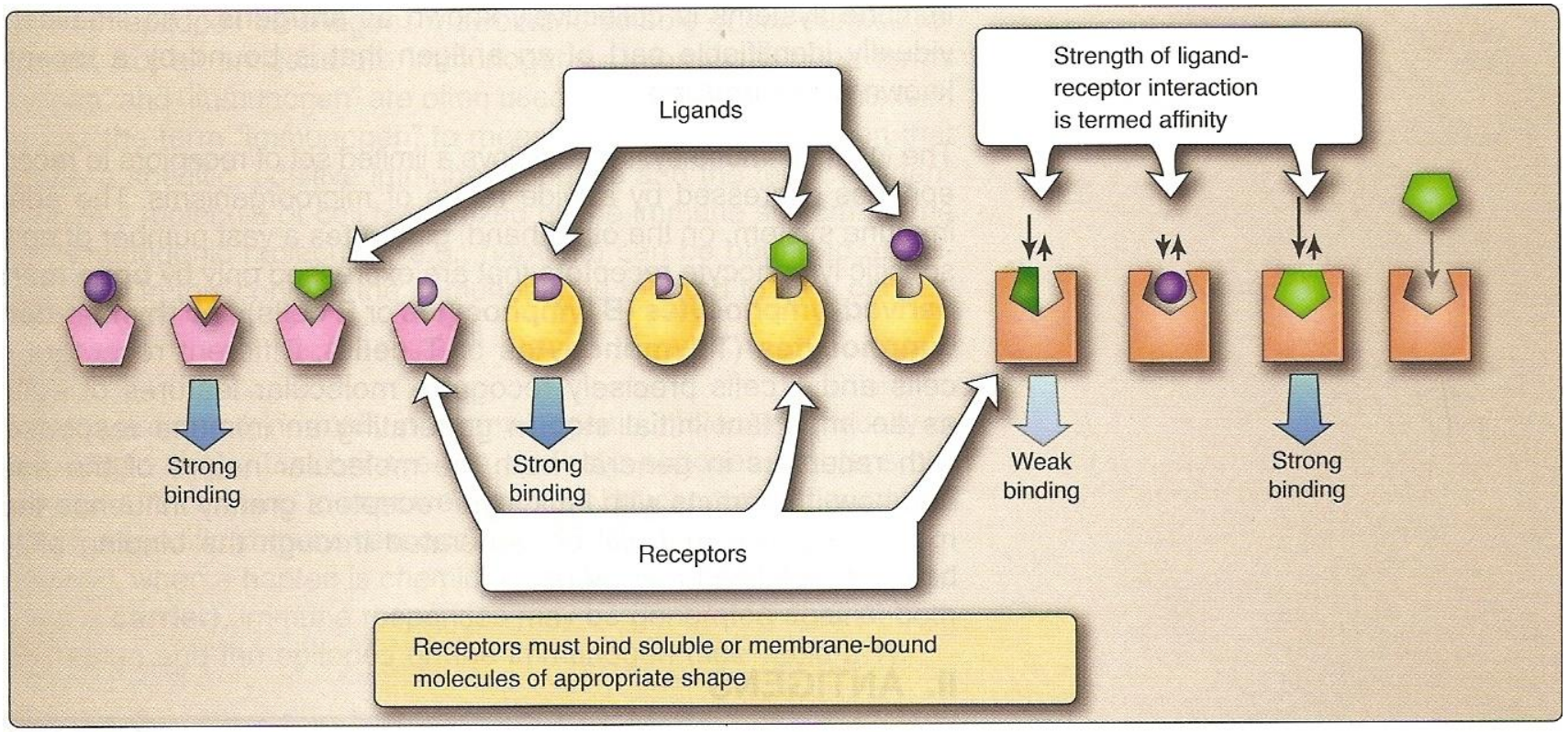
Shape and charge of receptor and ligand influence effectivity and strenght of binding **- affinity**



Antigens and receptors

Collective affinity – **avidity** – strenght of several bindings

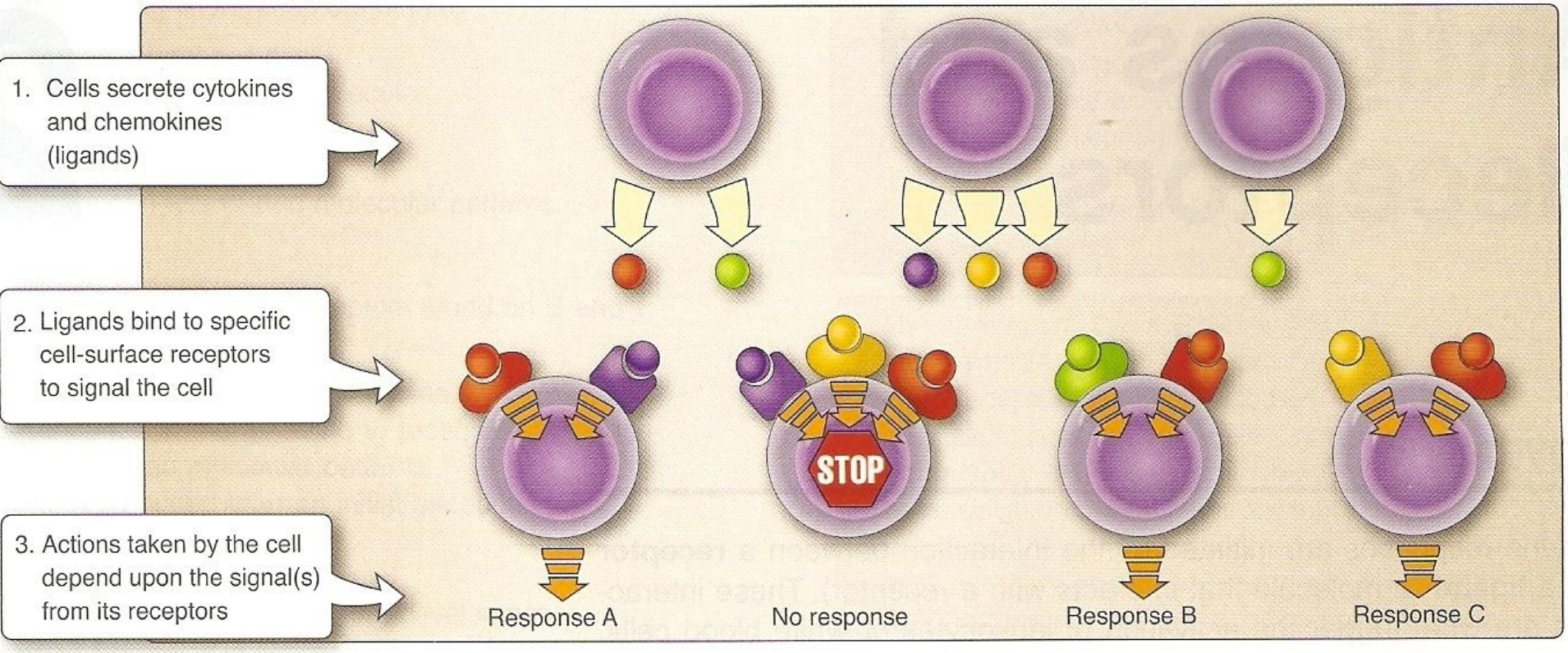
Sum of ligands recognised by cells of immune system on the **antigens**



Antigens and receptors

Presence of other bindings on the same cell can influence its activity.

Cell must correlate information from several receptors – sometimes antagonistic signals



Antigens and receptors

Receptors

- are on surfaces of cells (surface receptors)
- or are soluble molecules (products of leukocytes)

Ligands

- are (antigens) on surfaces of cells (surface molecules of microbes)
- or are soluble molecules (products of cells)

Antigens

- Are molecules, organisms or parts of molecules recognised by immune system
- They are simple, complex,
  proteins, carbohydrates, synthetic

Epitope, Immunogen, Hapten, Tolerogen

Immunogenicity

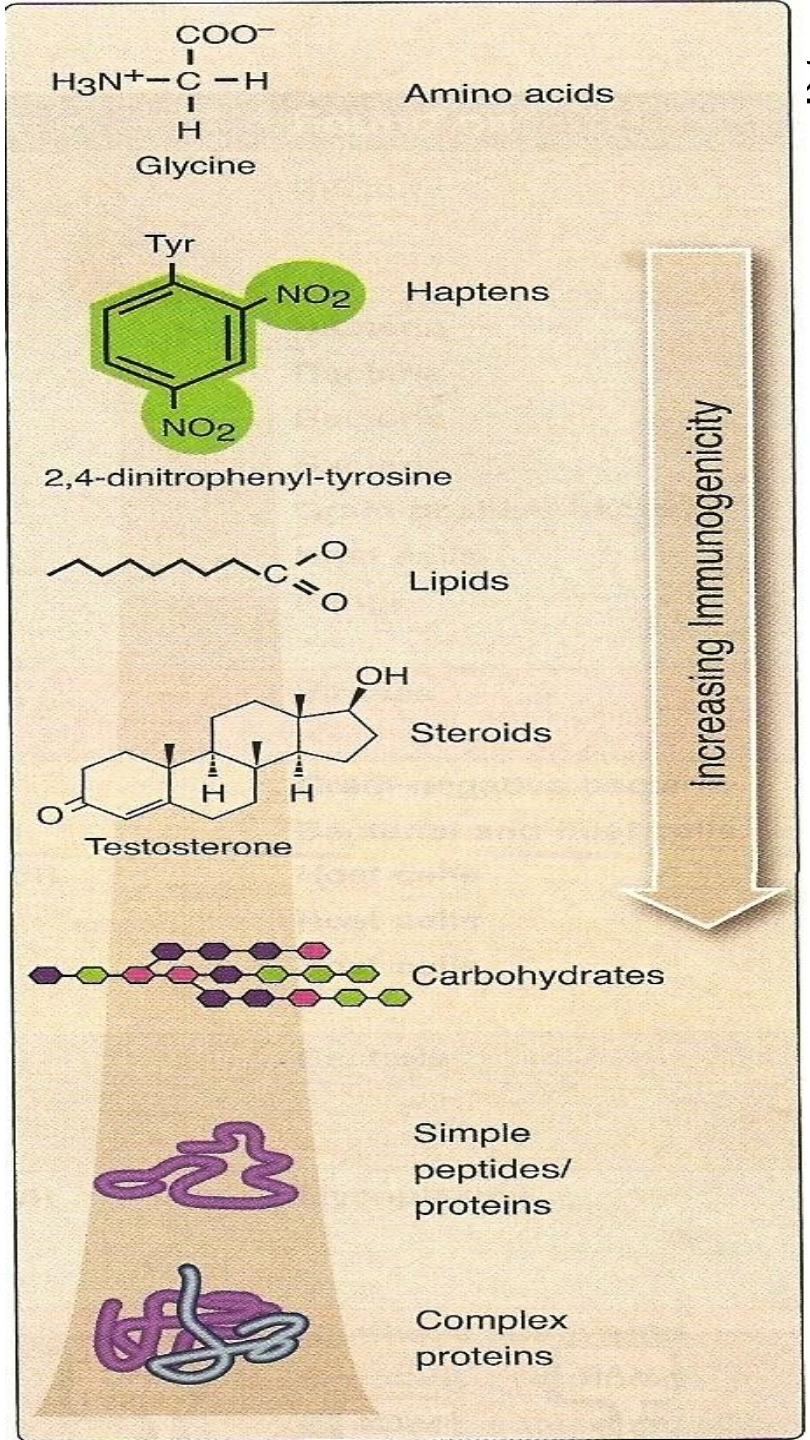
2.4

size- 10kDa

complexity - more different epitopes, polysacharid (is many same molecules – faible immunogen)

conformation – epitopes reachable by receptors

chemical structure – proteins> carbohydrates> steroids> lipids> NK - faible (ex. D-aminoacids > L-aminoacids)



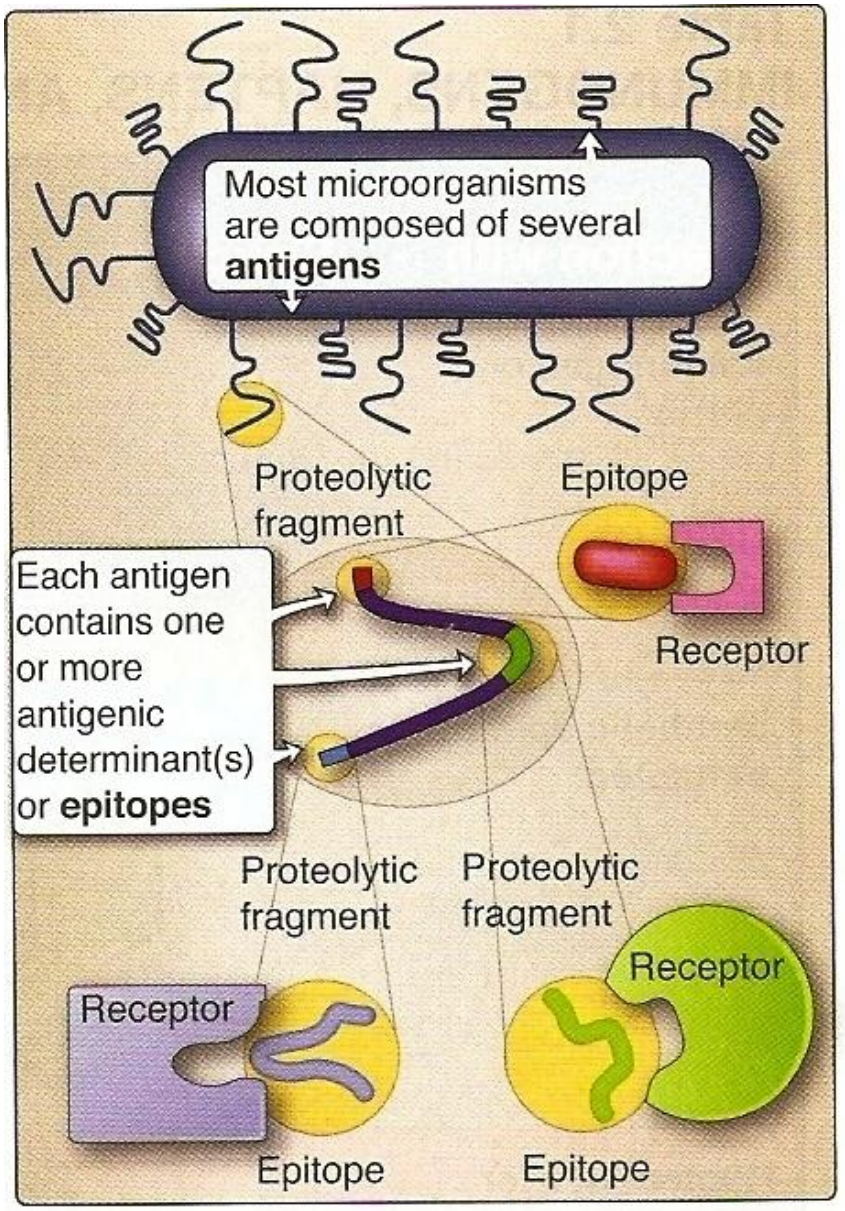
Epitop – basic unit of immunogenicity

- area of antigenic molecule, that is recognisable and can be bound by receptors (on B and T lymfocytes)
- different types
  - part of soluble surface molecules, surface molecule, degradated (proteolysed) fragments of antigens (B cells)
  - small fragments on surfaces of specialised host molecules (MHC) – (T cells)

Acc. to characteristics of immune reaction they can stimulate, they are **immunogens, haptens, tolerogens**

Antigens and receptors

Epitop – the smallest identificable part of antigen that can be bound to the receptor – **antigenic determinant**

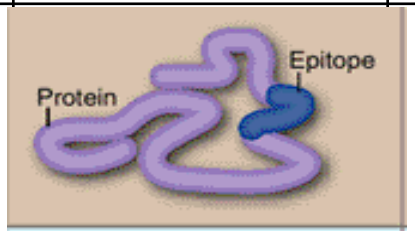
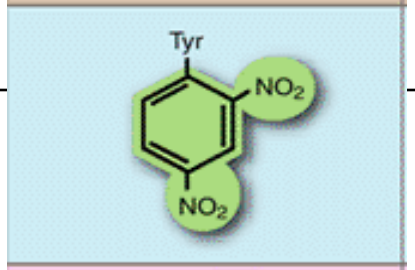
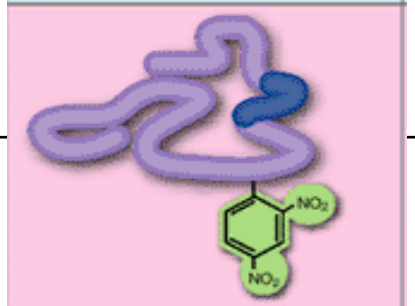
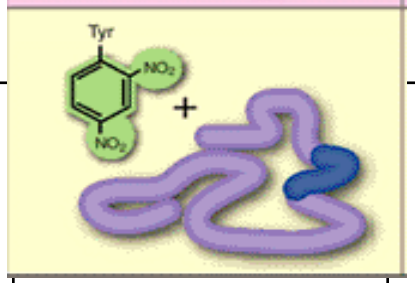


Immunogen

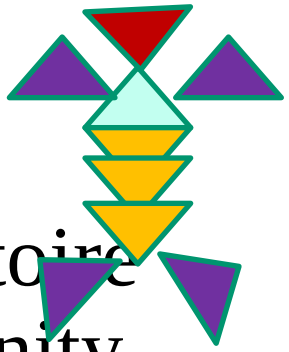
- contains epitopes, that induce immune reaction and are the target immune reaction
- not every antigen is immunogenic
- Antigen is a molecule recognised by immune system
- non-immunogenic molecules (haptens) can be bound on immunogen (called carrier)

Hapten

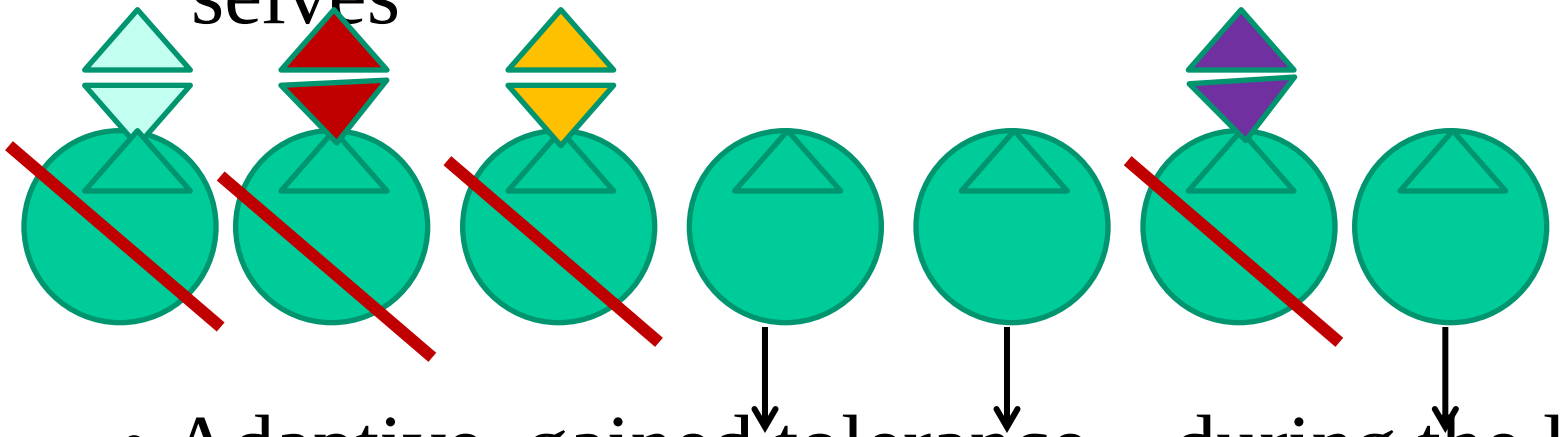
- Is small, not immunogenic molecule, commongy not of biological ethiology (synthetic epitopes)
- Is antigen able to bind immunity receptors and not able to induce immunity reaction, **not immunogenic**
- Hapten + immunogen (carrier) = immunity reaction against both

injection	structure	answer to epitop	answer to hapten	comments
imunogen (carrier)		+		protein stimulating production of im. reaction is immunogen
hapten synthetic epitop			+	molecule not able to stimulate production of im.reaction – is hapten
hapten-carrier conjugate		+	+	hapten chem. bound to carrier stimulates im. reaction to both
hapten, carrier not conjugated		+	-	hapten and carrier not bound will not start im.reaction

Tolerogen



- During evolution of immunity repertoire (sum of all epitopes, to which immunity receptors were generated) first the tolerance against self molecules is generated (innate tolerance). No immunity reactions against selves



- Adaptive, gained tolerance – during the life depends on different conditions (ex. p.o.)

Receptors

Engagement of receptors is the event, that leads to different activities, acc. to the type of ligand, molecule or cell, that the receptor will bind.

- bind molecules and **induce generation of signals** by which cells communicate
- recognise particules from envirenment and **detect invaders**
- **watch environment** (neighbours), to be sure that they are part of self and do not represent the threat

Preformed receptors

- present as part of **innate immunity**
- enable rapid reaction

PRR – on soluble molecules and host (human) cells

TLR – present on host cells

KAR – on NK cells

KIR – on NK cells

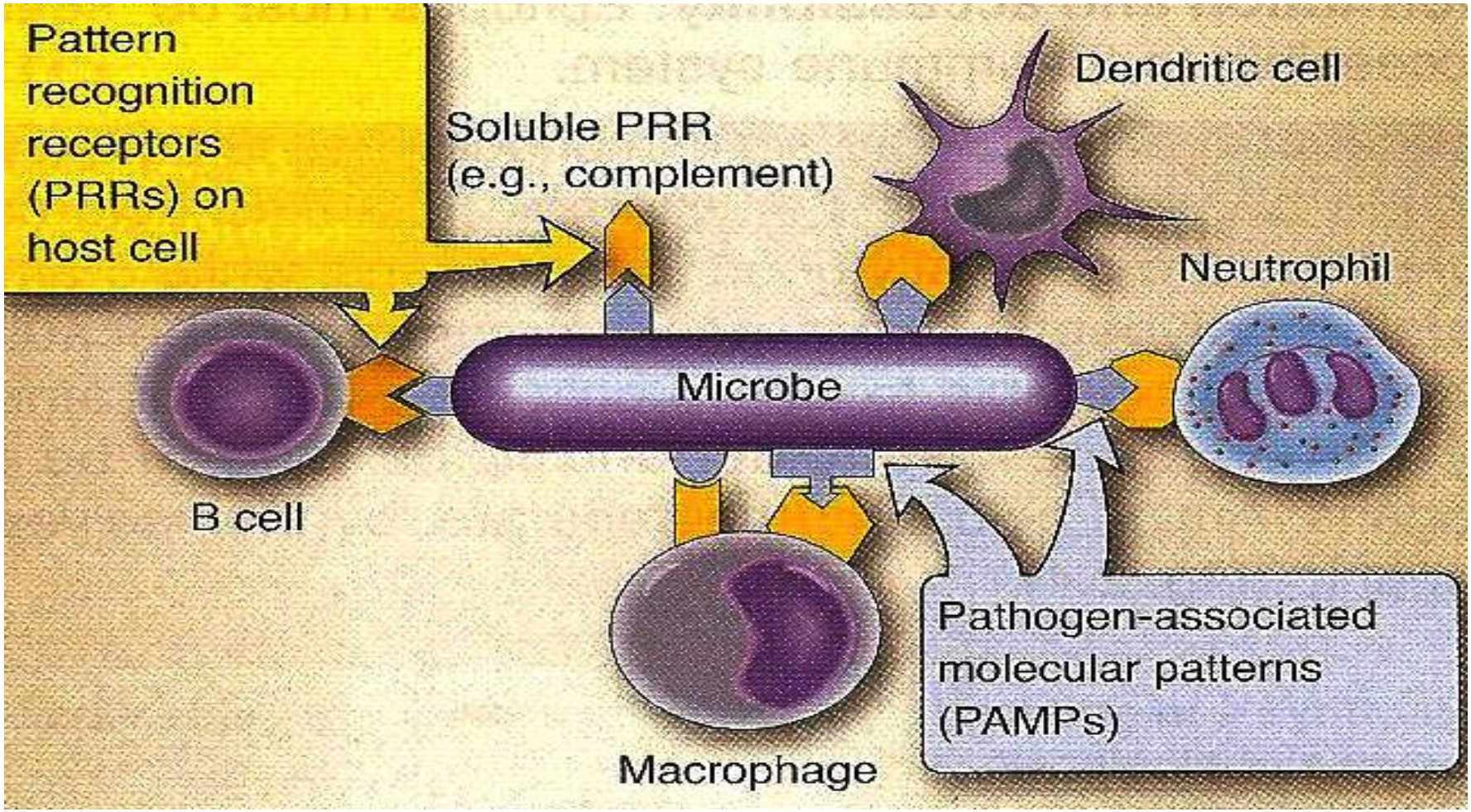
CR – on soluble molecules, phagocytes, on B cells

FcR – on phagocyting cells

PRR – pattern recognition receptors

- present on host cells or in soluble forme (proteins of complement)
- recognise different motives (patterns) present on microbes and not on self cells (e.g. PAMP – pathogen associated molecular patterns)
- this bound starts different forms of inflamation with the aime to kill the pathogen

PRR – pattern recognition receptors

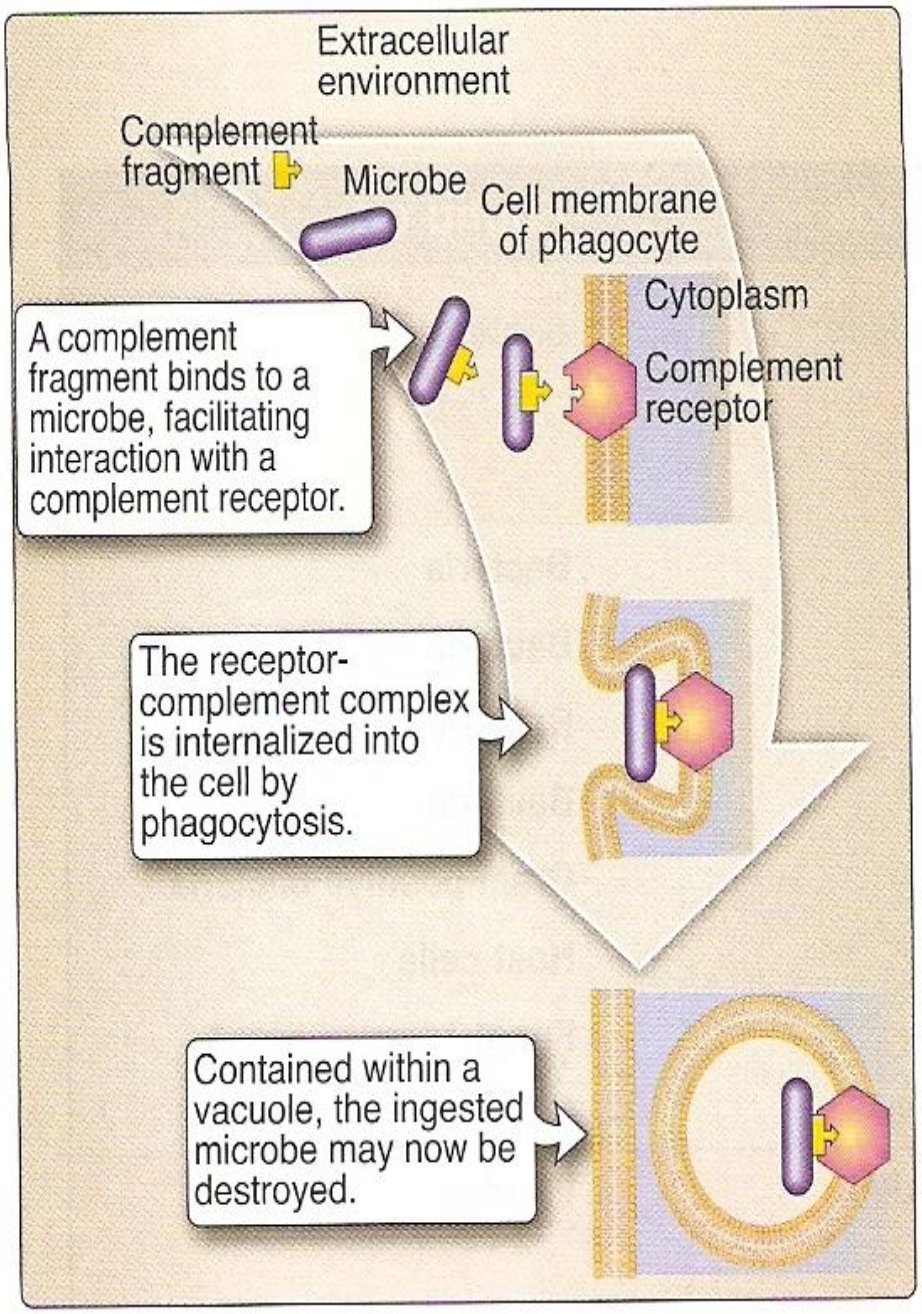


TLR – toll like receptors

- present on host cells
- bind PAMP of microbes
- start **transcription**, synthesis and secretion of cytokins stimulating inflamation and attraction of macrophages, NK cells, neutrofils and dendritic cells to the site of infection

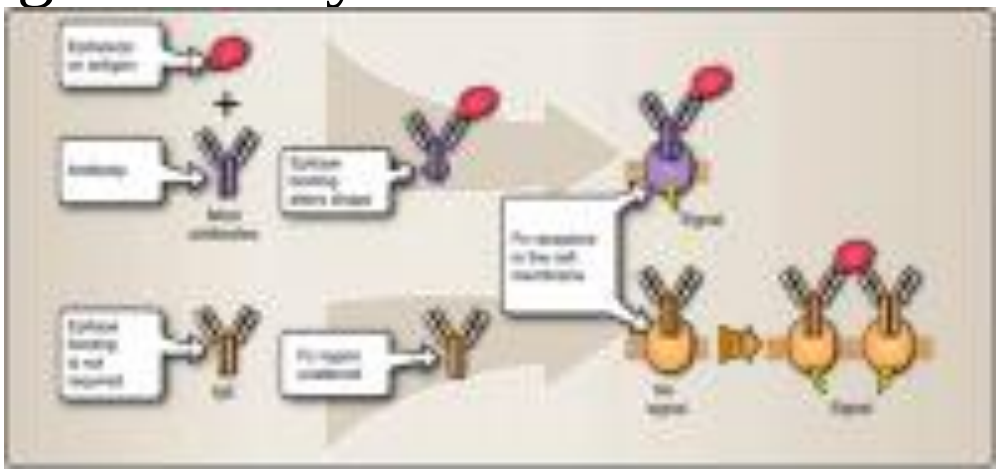
CR – receptor for complement

- Complement – comples of soluble proteins activated with the aime to kill pathogen.
- Parts of complement bind microbes
- CR – Receptors for complement on the surface of phagocyting and B cells bind fragments of C´and enable phagocytosis of microbes bound on C´

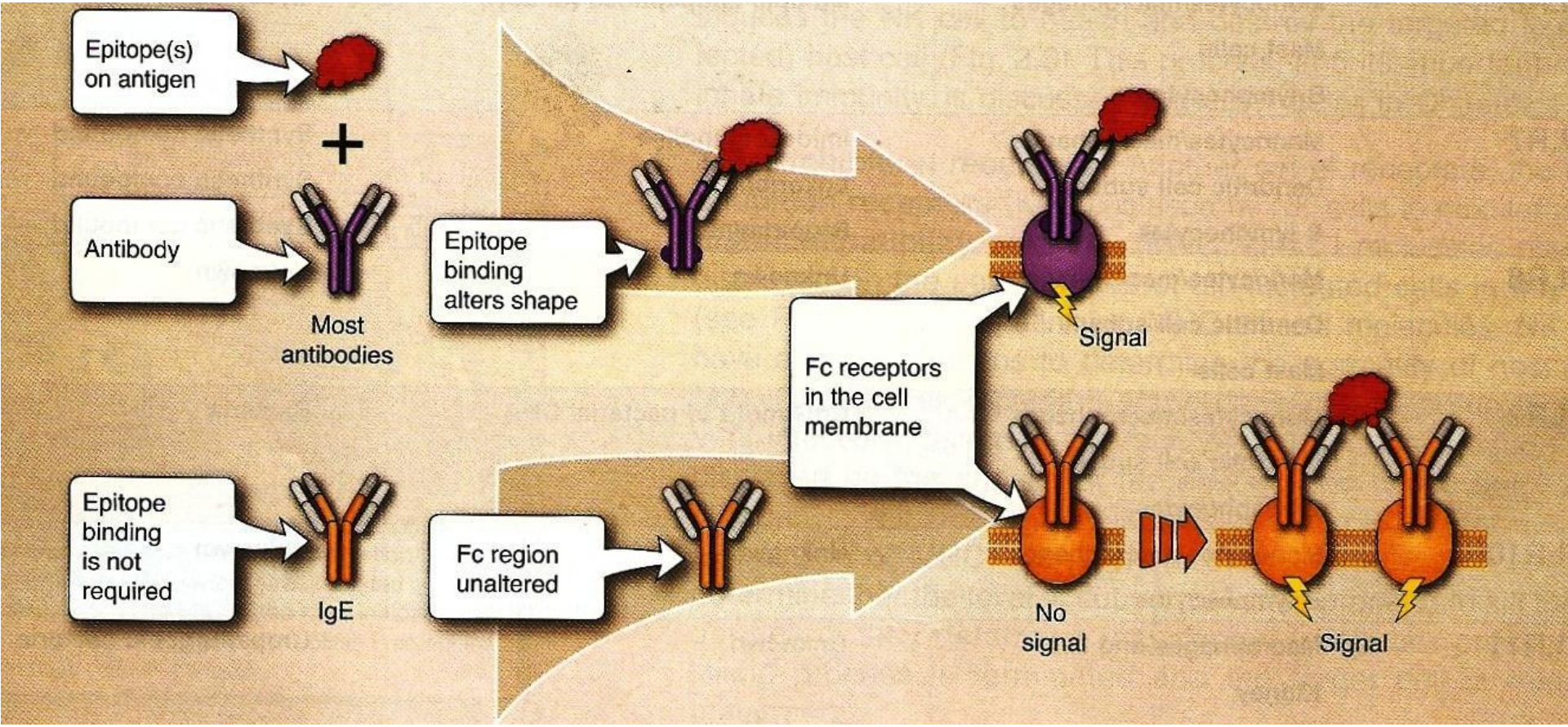


FcR – receptors for Fc fragment of immunoglobulins

- Imunoglobulins IgG, IgA, IgM – are able to bind antigens (by their Fab fragments) and then are bound by their Fc fragment on FcR receptors on the surface of fagocyting cells.
- IgE can bind to FcR on mastocyts by its Fc fragment even when the antigen is not yet bound on its Fab



FcR – receptors for Fc fragment of immunoglobulins

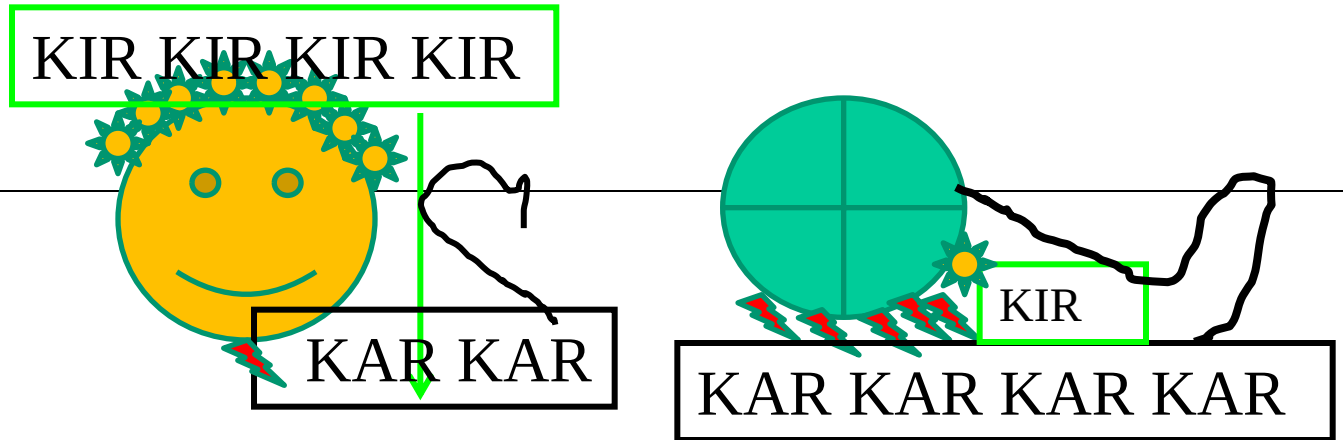


KIR, KAR on NK- natural killers

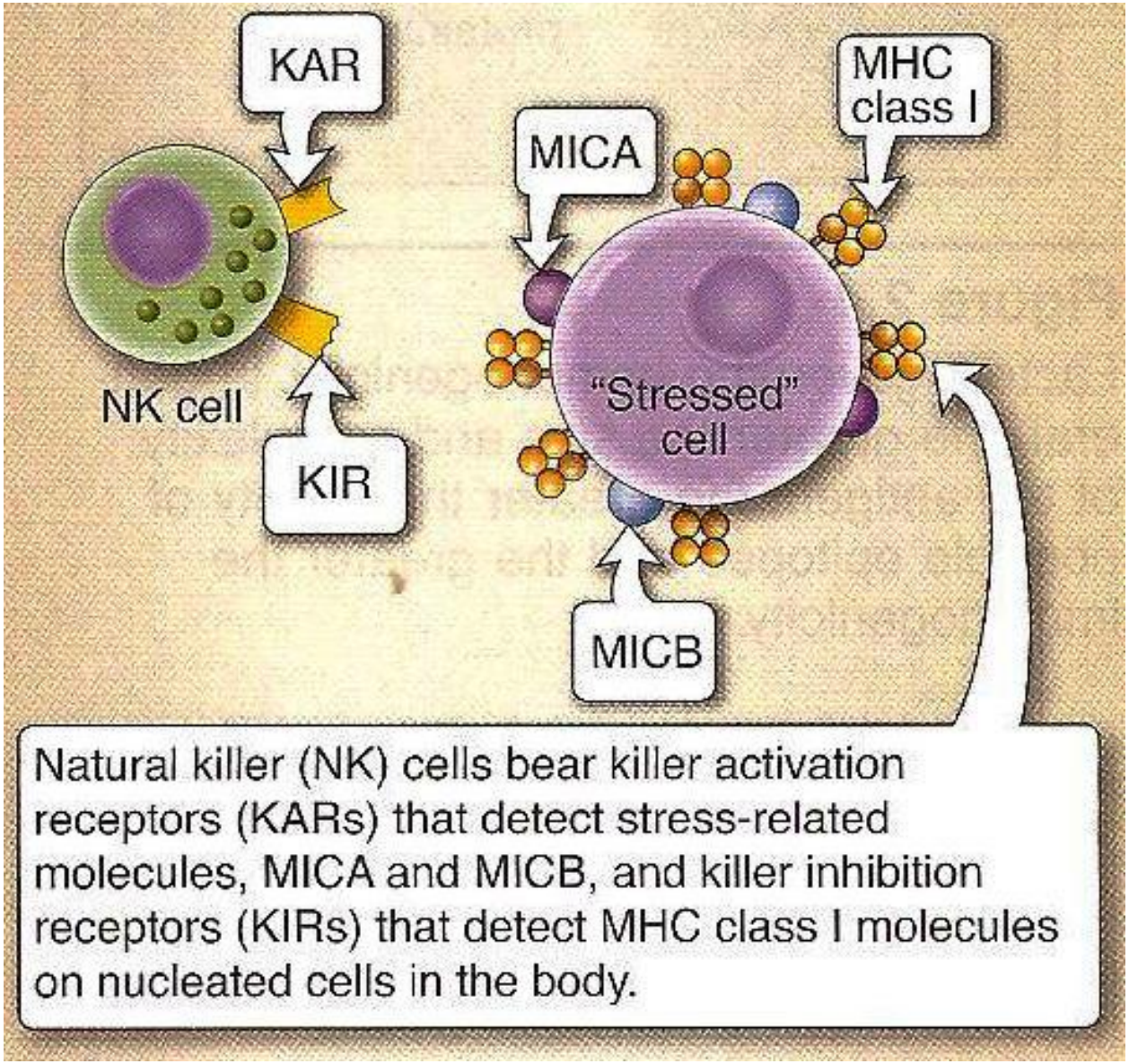
- NK cells – part of lymphocytic line
- Receptors recognising changes on self cells molecules (after viral infection, or changed by Ca-gennic processes)
- **KAR** – **killer activation receptors** – recognise MICA, MICB (stress molecules) on self cells that activates NK cells to kill self cell.
- **KIR** – **killer inhibition receptors** – monitors MHC I molecules. Tumor and virus infected cells decrease number of MHC I, that decrease the possibility of binding to MHC I molecules and decrease the inhibítion of killers

KIR, KAR on NK- natural killers

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KIR, KAR – on natural killers NK



Generated receptors

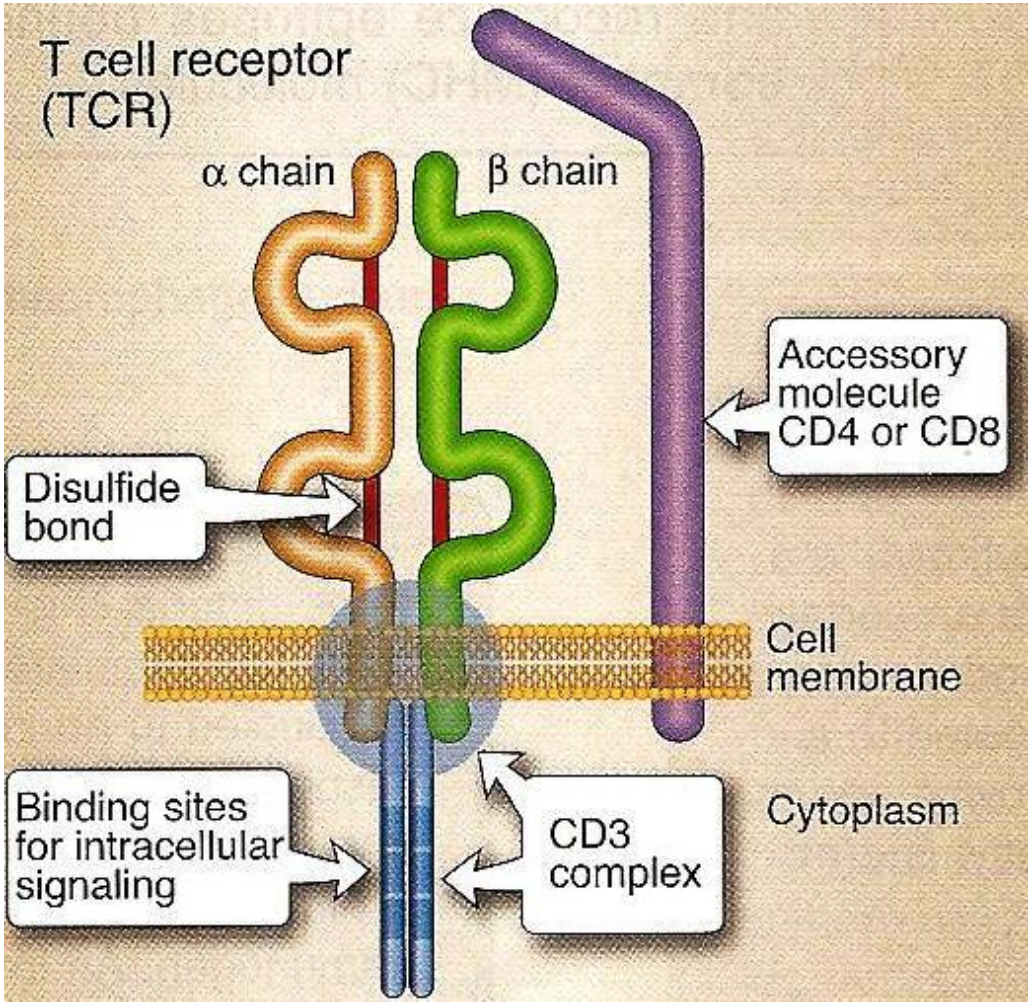
- specialised reeptors on B an T lymphocytes of adaptive immunity
- generated by chromosomal rearrangement and mutations in each individual = big ammount of specificities that the individuum can ever meet – individual variability

BCR – B cell receptor

TCR – T cell receptor

TCR

- structurally like immunoglobulin
- heterodimer consisting of αβ or χδ pair of chains.
  Bound on cell membrane and combining with other receptors (CD3) and recognising epitops in MHC molecules (cooperation with CD4 or CD8, that works like coreceptors)



BCR – B cell receptor

- monomer of immunoglobulin
- bound to transmembran heterodimer Igα a Igβ
- after binding of epitop to BCR cytoplasmatic part of Igα a Igβ will start cascade of i.c. signals leading to activation of B cell and its transformation to plasmatic cell, that will synthesise Ig of the same specificity as that of BCR

