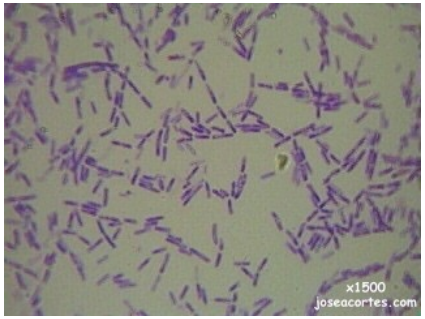
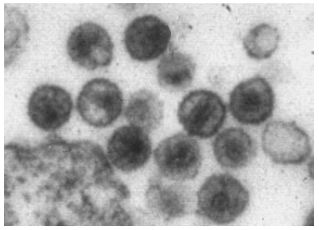
Lecture 11
23 Aug 2023

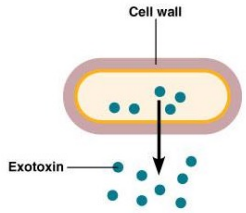
What can be an Antigen?

- Ags can be:
  - Foreign substances like microrganisms & its products, toxins etc.

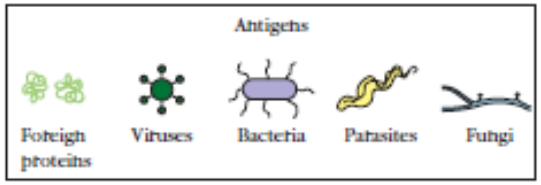


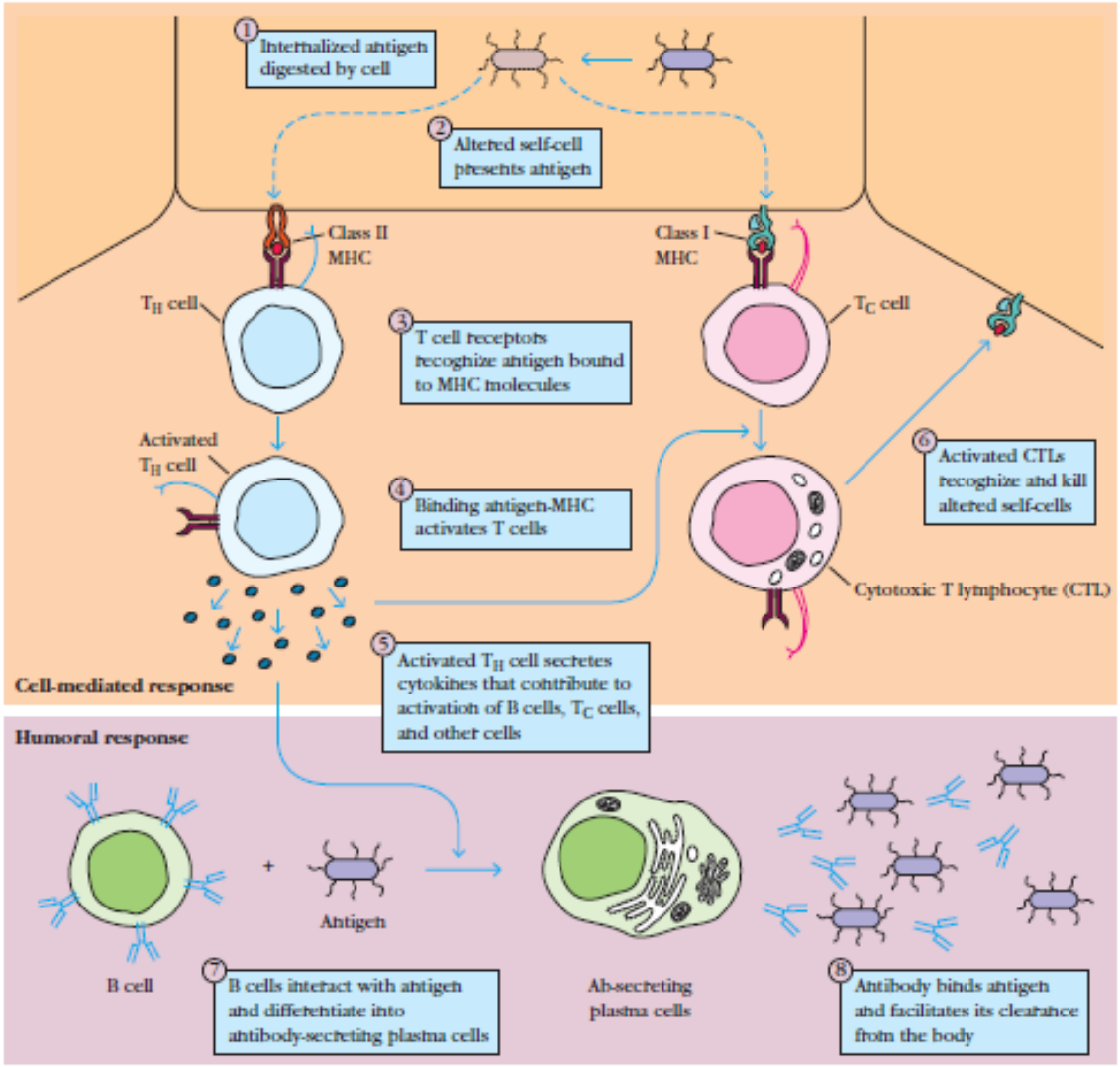
  - Body's own proteins, expressed in an inappropriate manner like tumor cells, autoantigens, transfused blood or the cells of transplanted organs.





VISUALIZING CONCEPTS

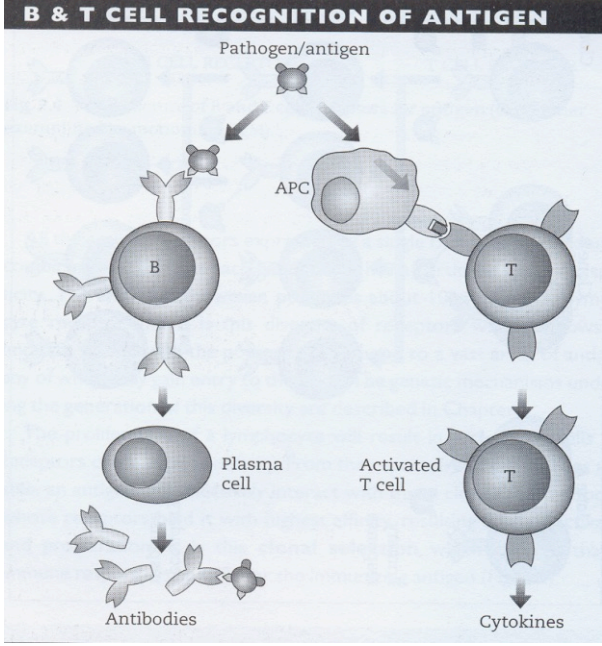




Properties of Antigen

- 2 properties of antigen:
  - Immunogenicity – Induction of immune response
  - Immunological reactivity - Specific reaction with Abs or with T cells.
- * Based on these 2 attributes, functional classification of Ags has been made.

Recognition of an Antigen



- Bacteria or viruses are not Ags by themselves but they contain Ags both on their surface and inside the cell.

- Ags are recognized by
  - B cells and their surface Igs (sIgM)
    - Abs recognize the tertiary structure of a protein (i.e. the way it folds)
  - the T cell receptor on T cells.
    - The T cells require the protein to be ingested, degraded and presented on the surface of a special cell called Antigen Presenting Cell (APC). The processed Ags are presented along with MHC/ HLA molecules by APCs

Classification of Antigens

- Based on
  - Immunogenicity (functional classification)
  - Origin of Ag
  - Source of Ag
  - Biological classification

Classification of antigen….

1. Functional classification of antigen (immunogenicity)

- Complete Ag - Able to induce Ab formation. Hence called as IMMUNOGENS.

  - Produce a specific & observable reaction with the Abs so produced.

- Haptens / Incomplete Ag - Substances which can not induce Ab formation by themselves but can react specifically with Abs.

- Hapten + Carrier ⟶ Complete antigen (Immunogen)

Classification of antigen….

2. Classification on origin of antigens

- Ags can be classified on the basis of their origin:
  - Exogenous Ags – from outside
    - enter the body by inhalation, ingestion or injection.
    - these are taken by the APCs and degraded into small peptides. APCs then present them to helper T cells by using MHC type II molecules (Fig A).
  - Endogenous Ags – generated within the cell as a
    - result of normal cell metabolism, or
    - because of viral or intracellular pathogenic infection.
    - The fragments are presented along with MHC type I molecules to cytotoxic T cells (Fig B).

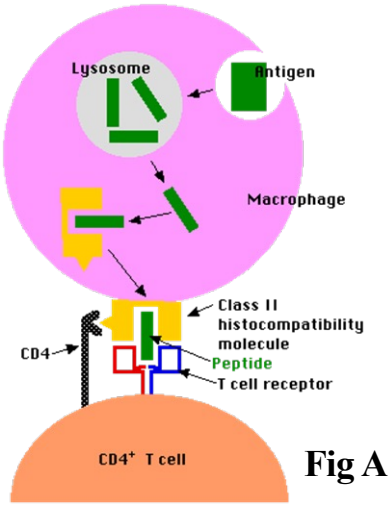


Fig A

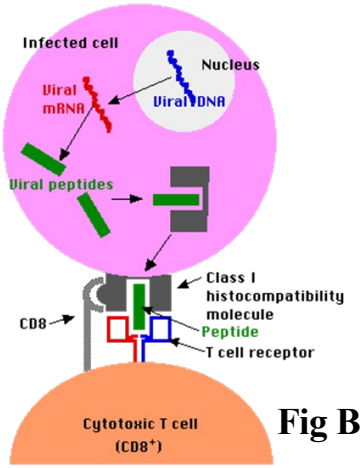


Fig B

3. Classification of antigen based on its source

- Xenoantigen – foreign Ag, from different species e.g. bacteria, viruses
- Alloantigen – different individual from same species e.g. blood group Ag
- Autoantigen – same individual e.g. lens protein, tumor cells
- Heterophile antigen – Common/ related Ags shared by different species

  e.g. M protein of *Streptococcus* spp. bears common antigen determinant with basement membrane of kidney

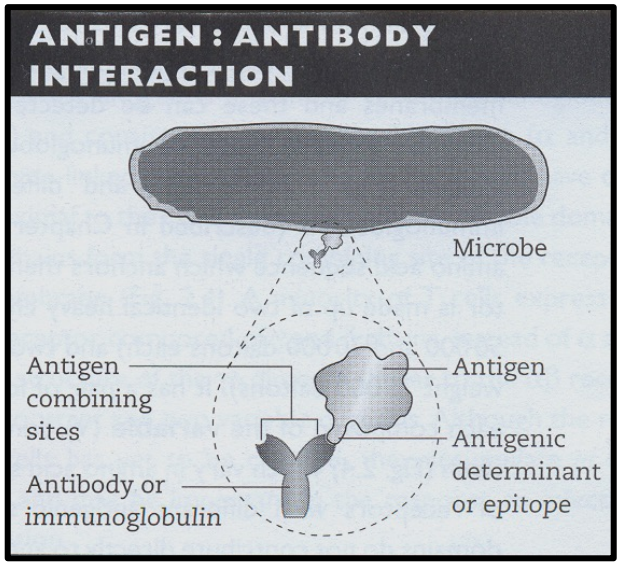
Lecture 12
24 Aug 2023

Classification of antigen….

- **T cell independent (TI) Ags**
  - Directly stimulate Ab production by B cells, **WITHOUT** the participation of T cells.
  - Structurally simple, being composed of a limited no. of repeating epitopes.
    e.g. Pneumococcal capsular polysaccharide, bacterial LPS, flagellar protein
  - Immune response is dose dependent.
    - Too little - non immunogenic
    - Too much - tolerance
  - Do not produce immunological memory.
  - Do not require processing by APCs.
  - Remain in the body for long periods

Epitope or Antigenic determinant

- Smallest unit of antigenicity.
- Small area/ part on the Ag which combines with its complementary site either on the specific Ab or T cell receptor.



Features of Epitopes

- Made up of 4 or 5 amino acid or monosaccharide residues.

- An Ag may have one or many epitopes on the same molecule.

- This helps body to have a better response against the Ag as many T & B cells can be activated to a single target.

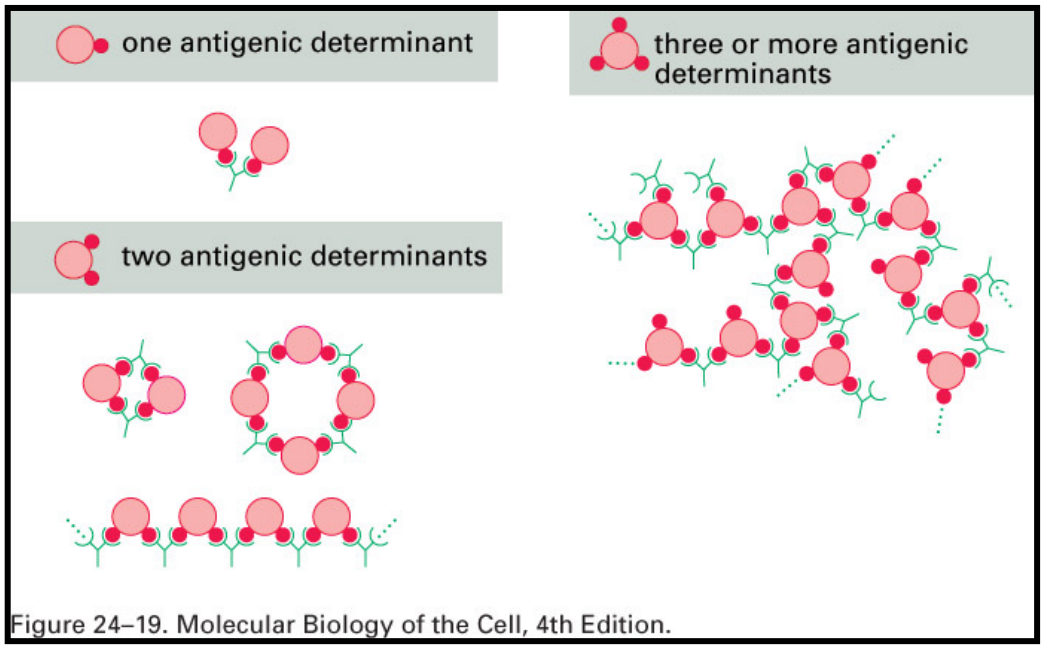
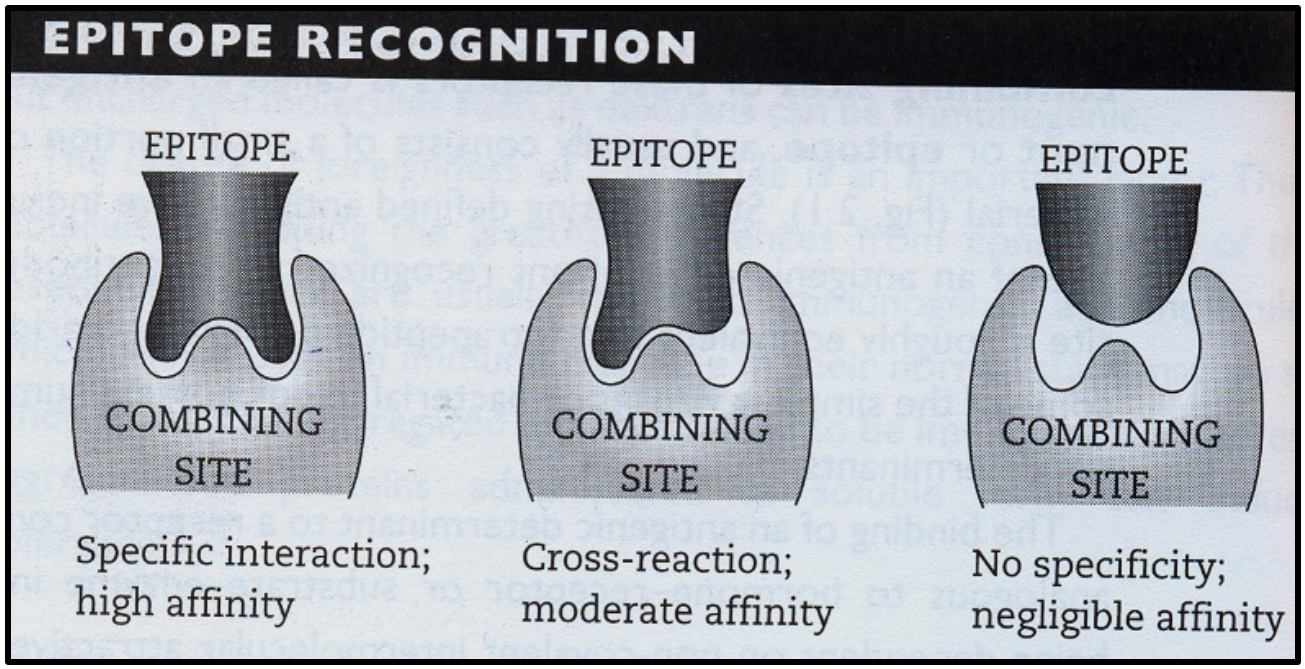
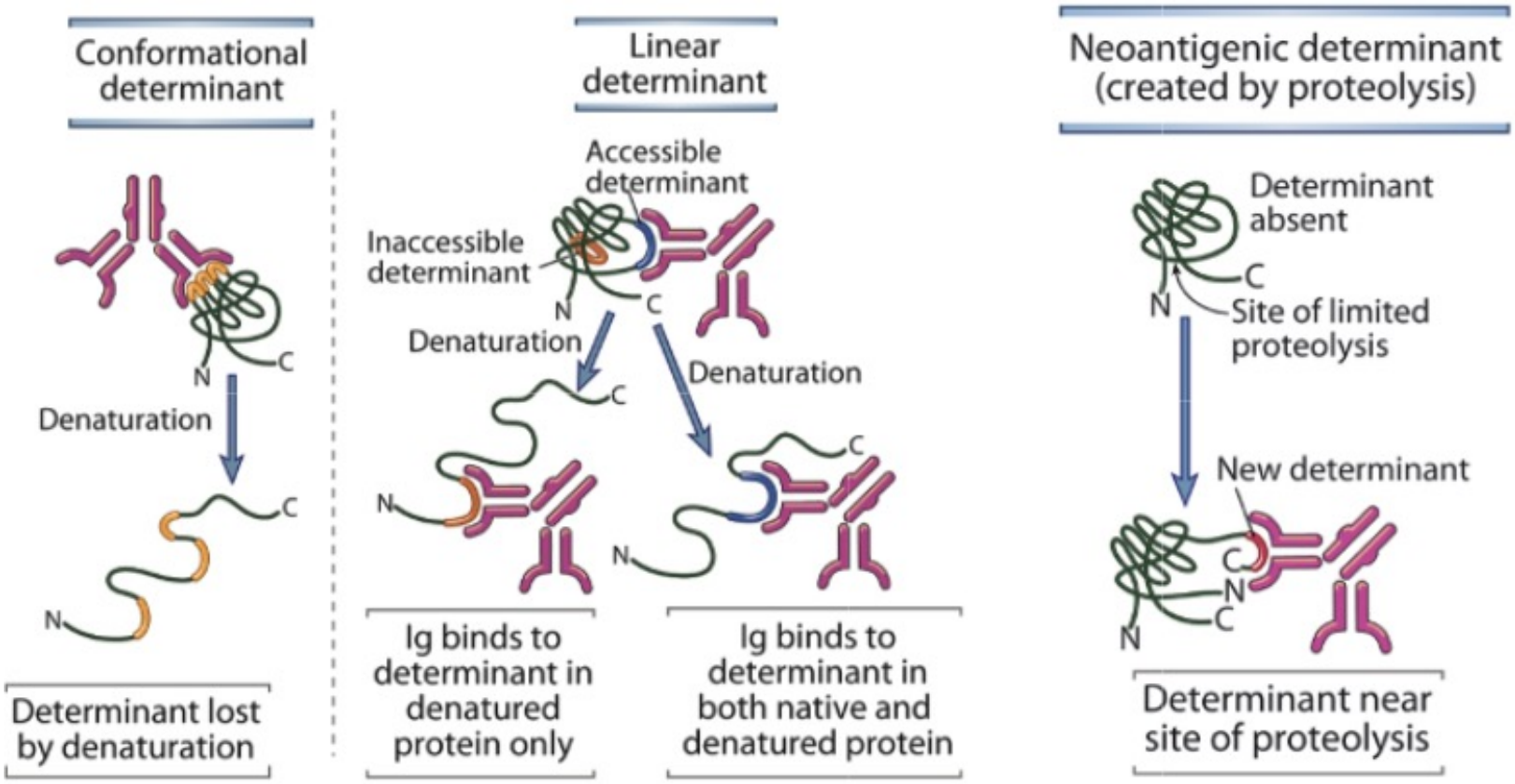


Figure 24–19. Molecular Biology of the Cell, 4th Edition.



Interaction between epitopes of different shapes & Ag combining site on the Ab

Types of antigenic determinants



Lecture 13
28 Aug 2023

Determinants of Antigenicity

- Properties which make a substance antigenic:
  - Size
  - Nature of Ag
  - Foreignness
  - Susceptibility to tissue enzymes.
  - Exposure to the Ag.

Determinants of antigenicity…

1. Size

- Large molecules are highly antigenic.
- Low mol.wt. (<5000 Da) substances are weakly antigenic or non antigenic.

  ✓ Can be made antigenic by conjugation to a carrier (protein or other biomacromolecule) in order to stimulate an immune response on immunisation of a host animal

2. Nature of the Ag

- Macromolecular proteins are the most potent immunogens.
- Polysaccharides, glycoproteins, synthetic polypeptides, lipids and nucleic acids are less immunogenic
- Antigenicity can be enhanced by conjugating to a protein.

Determinants of antigenicity…

3. Foreignness

- Ags which are 'foreign' to the individual induce an immune response.
- Antigenicity is related to the degree of foreignness - Ags from other individuals of the same species are less antigenic than those from other species.

4. Susceptibility to tissue enzymes

- Substances which are rapidly metabolised & are susceptible to the action of tissue enzymes behave as more potent Ags.
- Ags are degraded into fragments of appropriate size containing the epitope.
- Degradation is brought about by phagocytosis & the intracellular enzymes.

Determinants of antigenicity…

5. Exposure to the Ag

- Dose of the immunogen : optimum dose
- Lower or higher than the optimum can induce tolerance (inability to induce an immune response)
- Route of administration
- Immune response can be increased by mixing the Ag with a powerful adjuvant.

Adjuvants:

- Substances which are added to or emulsified with an Ag so as to enhance the Ab production.
- They can be - Inorganic salts : Alum; Organic: like BCG

  - Bacterial products: *Bordetella pertussis* (with Diphtheria, Tetanus toxoids)

Mechanism of adjuvants

- Ag persistence is prolonged
- Improves the Ag process and presentation ability of macrophages
- Non-specifically stimulate proliferation of lymphocytes
- Local inflammation is increased

TABLE 3-3 Postulated mode of action of some commonly used adjuvants

	POSTULATED MODE OF ACTION			
Adjuvant	Prolongs antigen persistence	Enhances co-stimulatory signal	Induces granuloma formation	Stimulates lymphocytes nonspecifically
Freund's incomplete adjuvant	+	+	+	−
Freund's complete adjuvant	+	++	++	−
Aluminum potassium sulfate (alum)	+	?	+	−
Mycobacterium tuberculosis	−	?	+	−
Bordetella pertussis	−	?	−	+
Bacterial lipopolysaccharide (LPS)	−	+	−	+
Synthetic polynucleotides (poly IC/poly AU)	−	?	−	+

Common adjuvants:

Freund's adjuvant is a solution of antigen emulsified in mineral oil and used as an immunopotentiator (booster). Two types:

-Incomplete Freund’s adjuvant

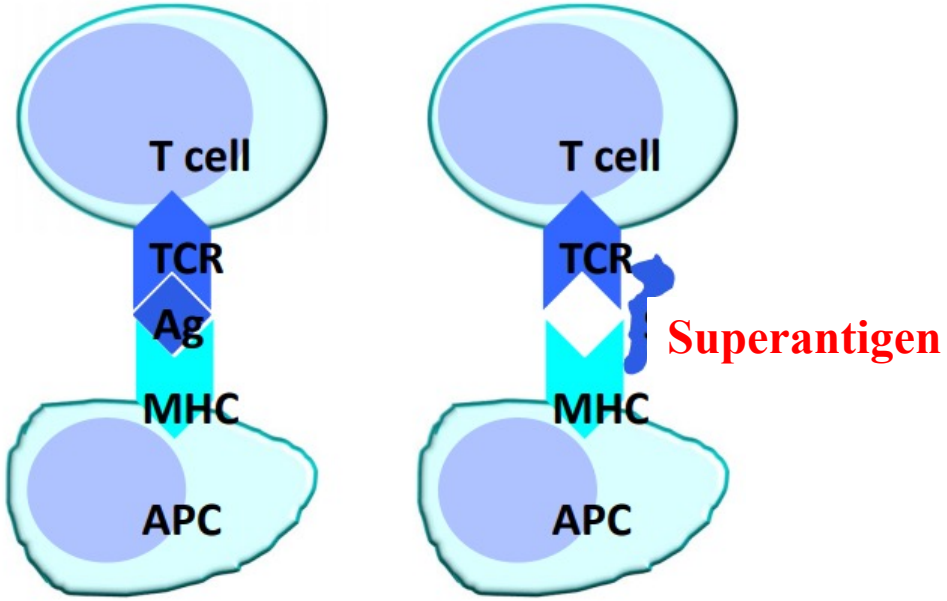
-Complete Freund’s adjuvant

- The Freund's complete adjuvant is composed of inactivated and dried mycobacteria (usually *M. tuberculosis*), whereas
- The incomplete form lacks the mycobacterial components (hence just the water in oil emulsion).
- It is named after Jules T. Freund.

Superantigens

Definition: Polyclonal T cell response

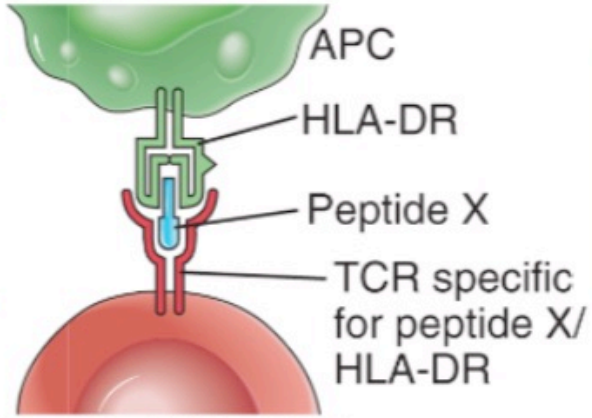
Examples *Staphylcoccal* enterotoxins and Toxic shock toxin



Superantigens mechanism

A

Conventional TCR recognition of peptide-MHC

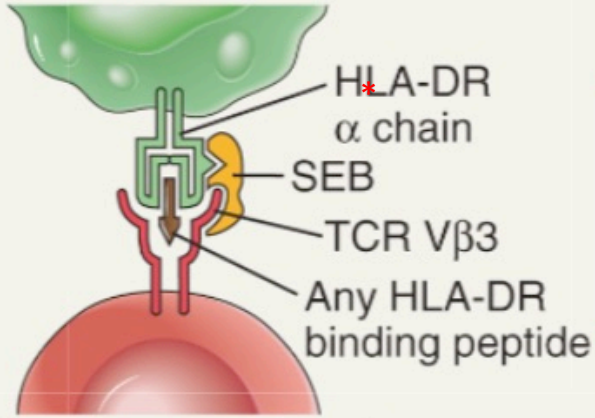


Peptide X/HLA-DR specific T cell (~.000001% of all T cells)

Activation of peptide X specific T cell clones only: protective immunity

B

Superantigen binding to Class II MHC and TCR Vβ3



Vβ3-expressing T cell (~2% of all T cells)

Polyclonal activation of Vβ3+ T cells: cytokine storm and deletion of T cells

***SEB: Staphylococcus enterotoxin B**