ANTIGENS

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Immunogen vs. Antigen

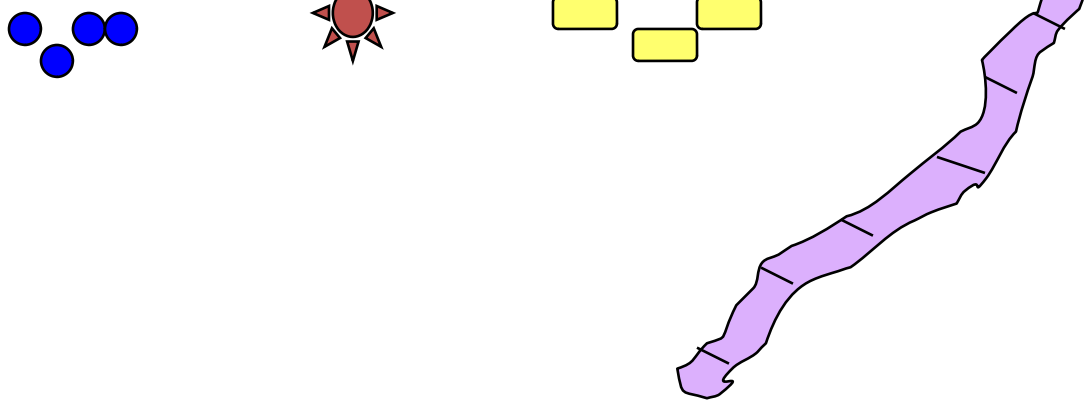
Immunogen - Agent capable of **inducing** an immune response by interactions with B cells, T cells and/or antigen-presenting cells

Antigen - Agent that **binds** with varying degrees of specificity to preformed antibodies or T cells

ANTIGENS

INFECTIOUS
(Microbial)

Bacterial Viral protozoal Helminths

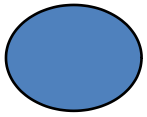


NON-INFECTIOUS

- Self antigens
- Food Antigens
- Plant products (Pollen)
- Dust
- Cell surface
- Synthetic Chemicals
- Venoms
- Insect Bites

FACTORS INFLUENCING IMMUNOGENICITY

1. **SIZE:**

Size	Strength of Immune response
 **Large:**	**Strong** (e.g. bacterial toxins, Vrial capsids, protozoal membranes, hormones, venoms) minmal size of 8000-10000 daltons
 **Small:**	**Poor**
 **Very small:**	**None**

2. **COMPLEXITY:** Complex antigens are good antigens (i.e can induce a good immune response)
   e.g. Proteins are good antigens or immunogens.

   Simple substances are poor antigens (i.e do not induce a strong immune response) e.g. pure lipids, polymers

3. **STABILITY:** Flexible structures are poor antigens, e.g. Flagellin

4. **DEGRADABILITY:** Highly degradable (poor antigen)
   Non-degradable (poor antigen)

5. **FOREIGNNESS:** Foreign antigen evoke a strong immune response.
   Self antigens in normal individuals do not induce immune response

FACTORS INFLUENCING IMMUNOGENICITY

6. Physical Form

- Particulate > Soluble
- Denatured > Native

7. Chemical Composition

- Primary Structure — **Sequential determinants**
- Secondary Structure
- Tertiary Structure
- Quarternary Structure

} **Conformational determinants**

FACTORS INFLUENCING IMMUNOGENICITY

Contribution of the Biological System

- **Genetics**
  - Species
  - Individual
    - **Responders vs Non-responders**
- **Age**
- **Hormonal status**

FACTORS INFLUENCING IMMUNOGENICITY
Method of Administration

- **Dose**
- **Route**
  - **Subcutaneous > Intravenous > Intragastric**
- **Adjuvant**
  - **Substances that enhance an immune response to an Ag**

FACTORS INFLUENCING IMMUNOGENICITY

Chemical Nature of Immunogens

- **Proteins**
- **Polysaccharides**
- **Lipids**
  - Some glycolipids and phosopholipids can be immunogenic for T cells and elicit a cell mediated immune response
- **Nucleic Acids**

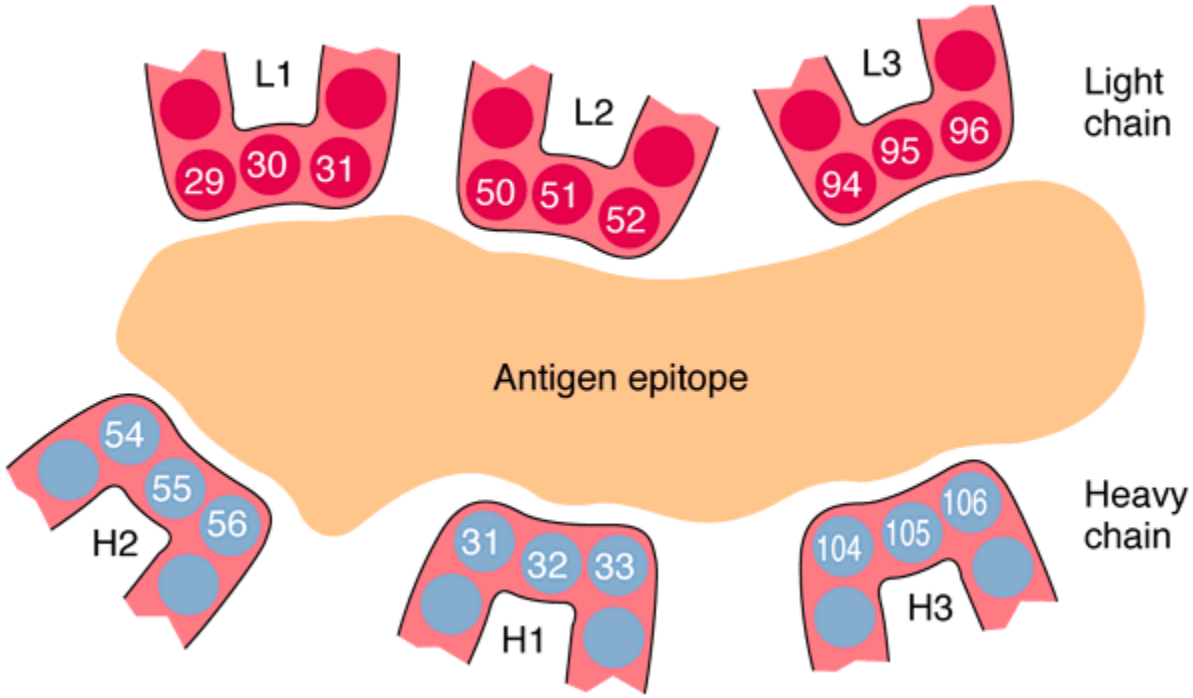
Factors that influence the immunogenicity of proteins

Parameter	Increased immunogenicity	Decreased immunogenicity
Size	Large	Small (MW<2500)
Dose	Intermediate	High or low
Route	Subcutaneous > intraperitoneal > intravenous or intragastric	
Composition	Complex	Simple
Form	Particulate	Soluble
	Denatured	Native
Similarity to self protein	Multiple differences	Few differences
Adjuvants	Slow release	Rapid release
	Bacteria	No bacteria
Interaction with host MHC	Effective	Ineffective

Figure A-2 Immunobiology, 6/e. (© Garland Science 2005)

Epitopes

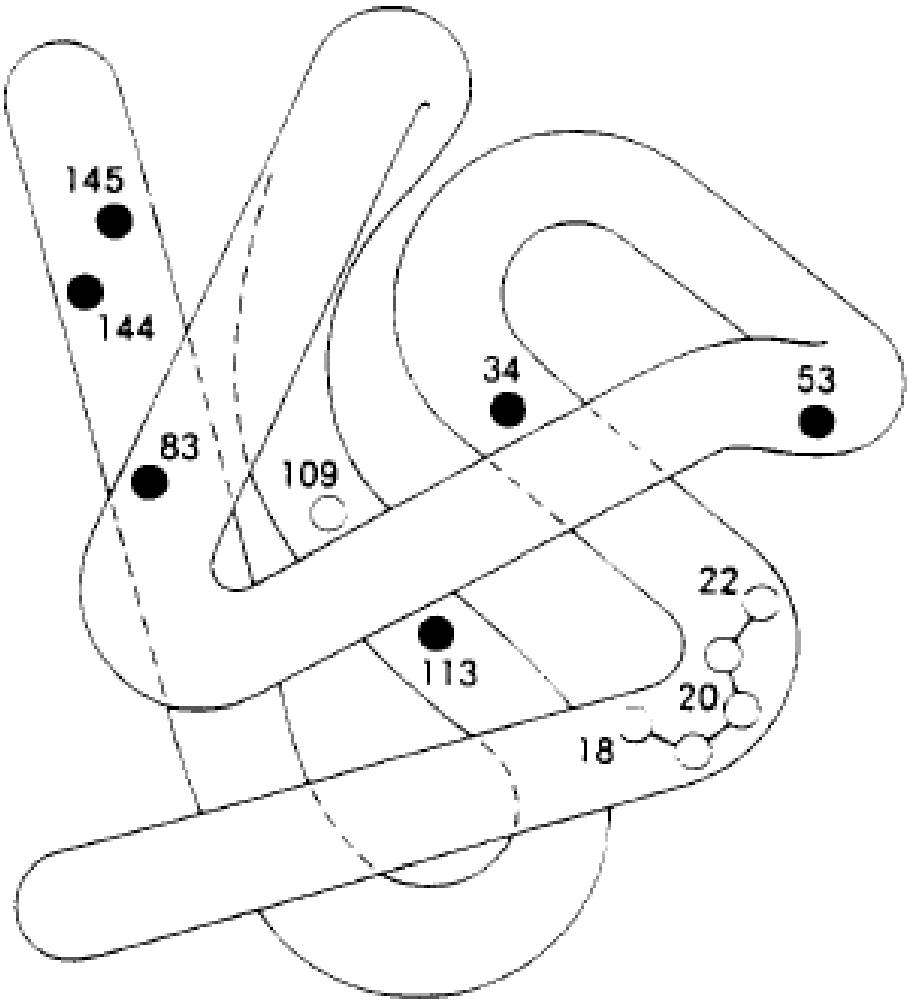
- Site on antigen surface recognized by antibody paratope.
- Upper size is 7 x 12 x 35 Angstroms.
- Lower size is undefined

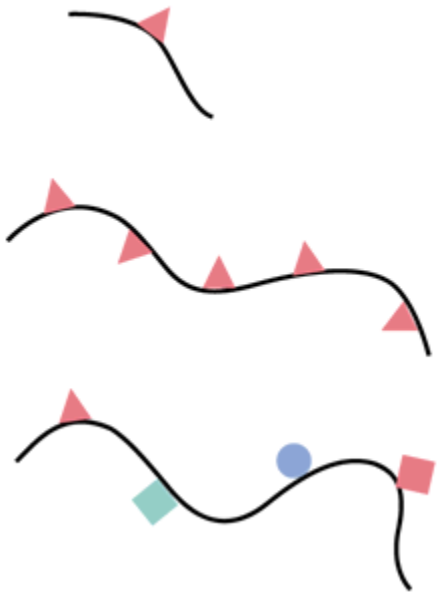

L1
29
30
31
L2
50
51
52
L3
94
95
96
Light chain
Antigen epitope
54
55
56
H2
31
32
33
H1
104
105
106
H3
Heavy chain

Sequential and Conformational Epitopes

- **Sequential Epitopes** - Short stretches of amino acids (4-7) recognized by Ab when free in solution, Ag is denatured, or native. Only form of T cell epitope.
- **Conformational Epitopes** - Require the unaltered, native 3-D shape of Ag for recognition by Ab.

Sequential and Conformational Epitopes





Description	Example
One epitope	Haptens
Many epitopes of the same specificity	Many polysaccharides, homopolymers
Many epitopes of different specificities	Proteins

HAPTEN

- A small molecule (less than 1000 daltons) that by itself cannot induce an Immune response, but can combine with pre-formed specific antibodies. Thus hapten is antigenic, but non-immunogenic.
- To induce an immune response against a hapten, it has to be conjugated with a larger immunogenic molecule like BSA.

e.g. (i) Pencilloyl (a break down product of Penicllin)

(ii) Urishiol, a hapten from Poison Ivy, which binds to skin proteins.

Haptens

- Low molecular weight
- Non-immunogenic Alone
- Coupling to immunogenic compound renders it immunogenic.
- Can bind pre-formed antibodies.

Rendering haptens immunogenic

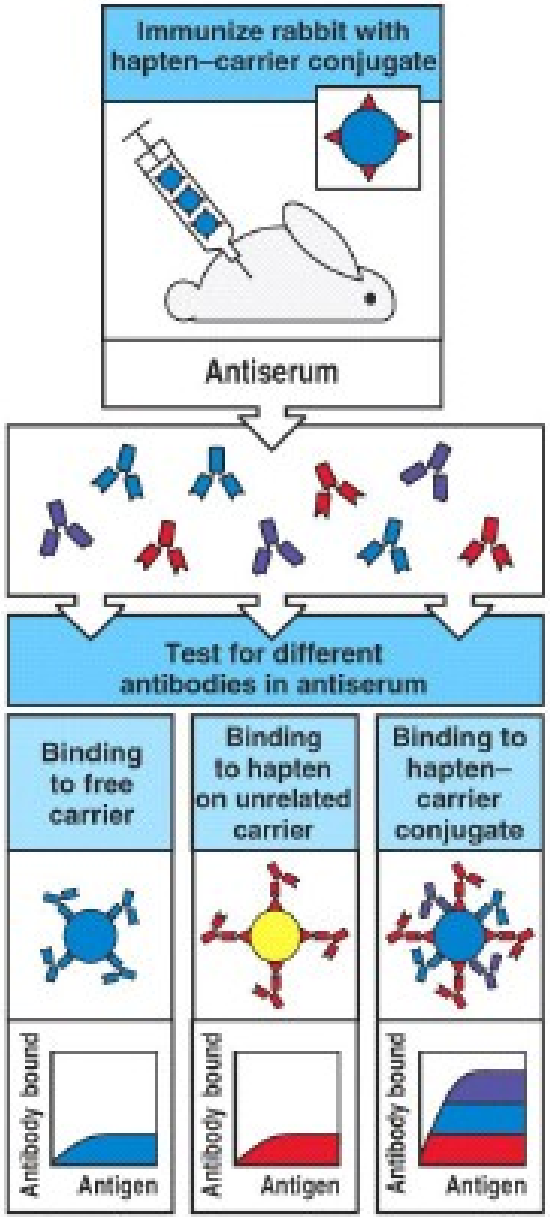
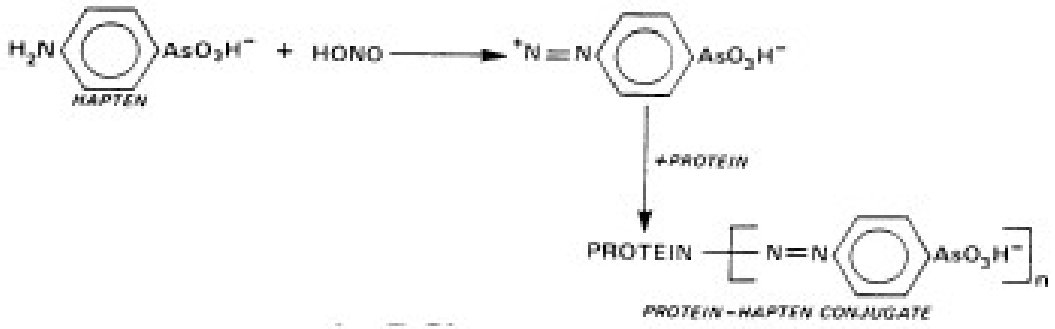


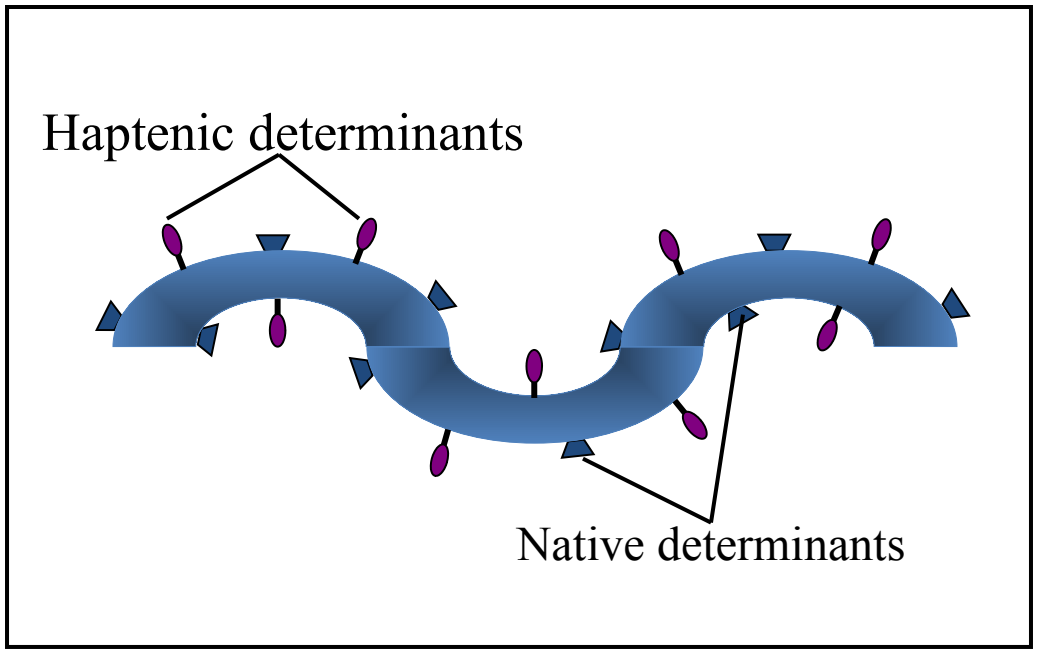
Figure A-3 Immunobiology, 6/e. (© Garland Scien



HAPTEN-CARRIER EFFECT

- **Definition**

- **Structure**
  - native determinants
  - haptenic determinants



Antigenic determinants recognized by B-cells

- **Composition**
  - Proteins, polysaccharides, nucleic acids, haptens
  - Sequence (linear) determinants
  - Conformational determinants
- **Size**
  - 4-8 residues
- **Number**
  - Limited (immunodominant epitopes)
  - Located on the external surfaces of the Ag

Antigenic determinants recognized by T-cells

- **Composition**
  - Proteins (some lipids)
  - Sequence determinants
    - Processed
    - MHC presentation (lipid presentation by MHC-like CD1)
- **Size**
  - 8 -15 residues
- **Number**
  - Limited to those that can bind to MHC

Antigen Recognition by B and T Cells

Characteristic	*B cells*	*T cells*
Mechanism	BCR binds Ag	TCR binds Ag+MHC Ag
Antigen nature	Protein/polysaccharide/lipid	Peptide
Epitopes	Surface, linear, conformational	Internal linear peptides

T-dependent and independent Antigens

T-dependent Antigens

- Antigens for which B or Tc cells require help of Th cells for inducing an adaptive immune response
- usually proteins
- These antigens are processed and presented by APCs in association with MHC-II molecules to Th cell possessing specific TCR for further action.
- After clonal expansion of an appropriate Th cell against such antigens, a pool of memory Th cells is generated which is responsible for the ‘recall’ or ‘anamnestic’ immune response

T-independent Antigens

- antigens which can directly stimulate the B cells to produce antibody without the requirement of T cell help.
- usually polysaccharides
- MHC-restriction is not an essential pre-requisite
- These antigens do not generate pool of memory Th cells, hence ‘recall’ phenomenon is weaker.

T independent and dependent immune responses

Property	TD antigen	TI-1 antigen	TI-2 antigen
Antibody response in absence of cognate T cells	No	Yes	Yes*
Antibody production in congenital athymic individuals	No	Yes	Yes
Antibody response in infants	Yes	Yes	No
Activates T cells	Yes	No	No
Induces immunological memory	Yes	No	No
Activation of non-specific B cells	No	Yes	No
Requires repeated epitopes	No	No	Yes
	Diphtheria toxin Viral hemagglutinin Purified protein derivative (PPD) of *Mycobacterium tuberculosis*	Bacterial lipopoly-saccharide *Brucella abortus*	Pneumococcal poly-saccharide Polymerized flagellin (*Salmonella*)

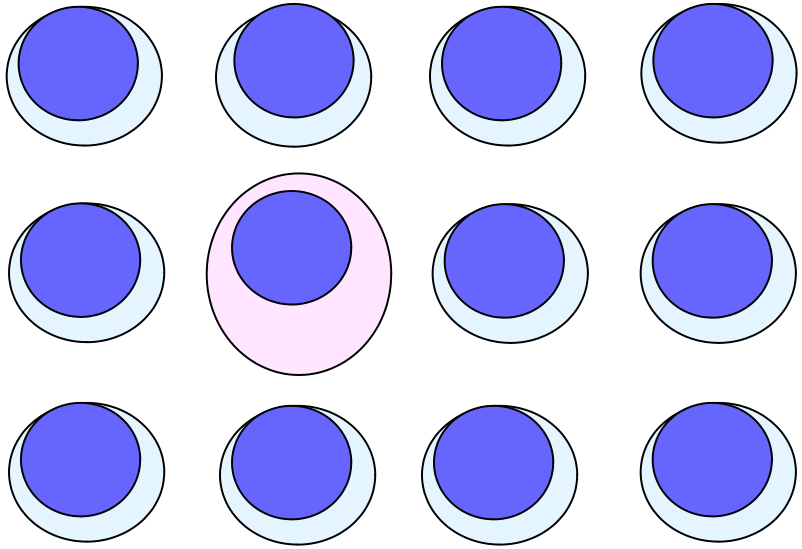
Superantigens

SUPERANTIGENS

- **bind directly to the outside of MHC-II molecules on macrophages without being processed and cross link non-specifically with many TCRs on multiple T-cells (approx. 20% T cells)**
- **cross linking causes stimulation of up to 1 in 5 T-cells in the body (normal antigens cause stimulation of 1 in 10,000).**
- **results in the secretion of excessive amounts of interleukin-2 (IL-2)**
- **high levels of IL-2 in the blood lead to symptoms such as fever, nausea, vomiting, diarrhea, and malaise.**
- **stimulation of IL-2 secretion can also lead to production of other cytokines such as TNF-alpha, IL-1, IL-8, and PAF, which can lead to SIRS (Systemic Inflammatory Response Syndrome)**

SUPERANTIGENS

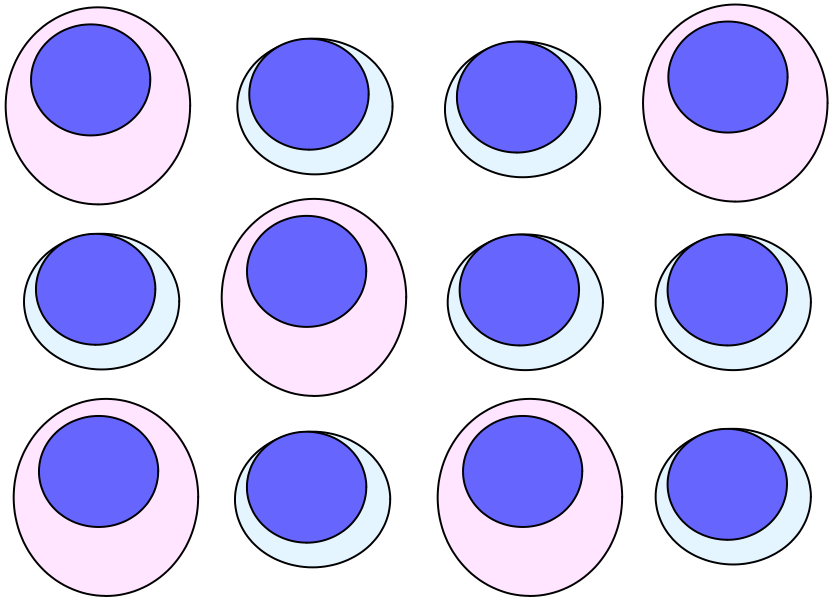
Conventional Antigen



Monoclonal/Oligoclonal
T cell response

$1:10^4$ - $1:10^5$

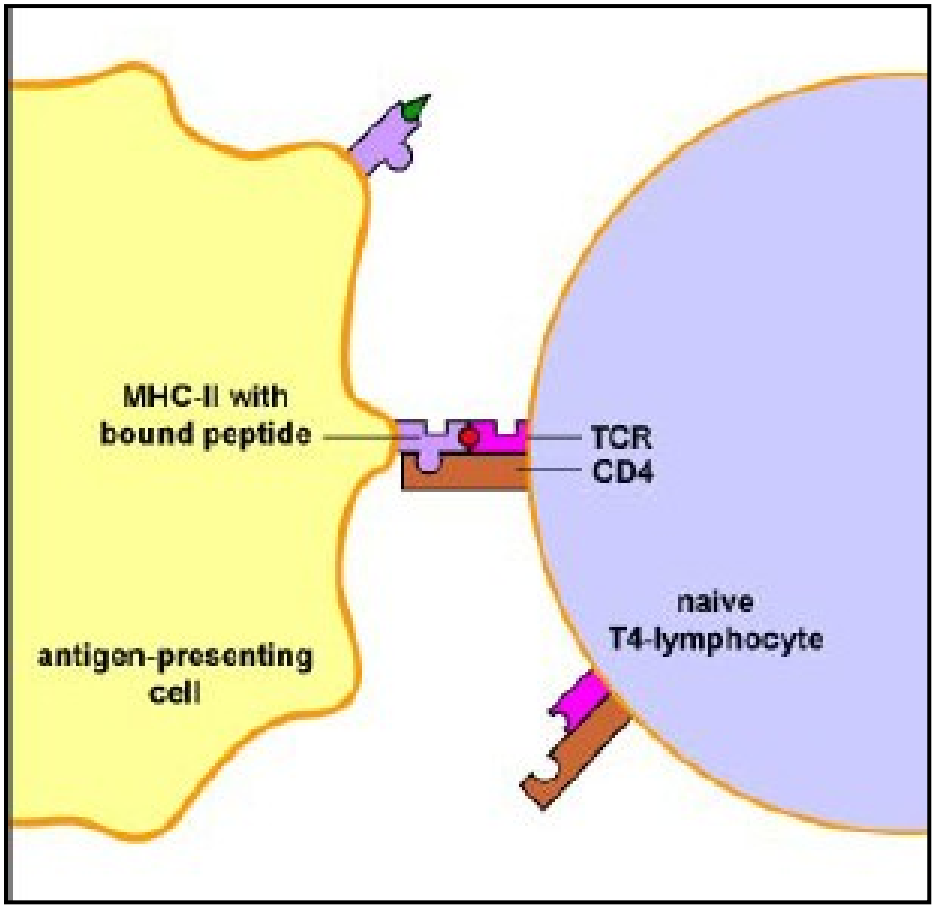
Superantigen



Polyclonal T cell response

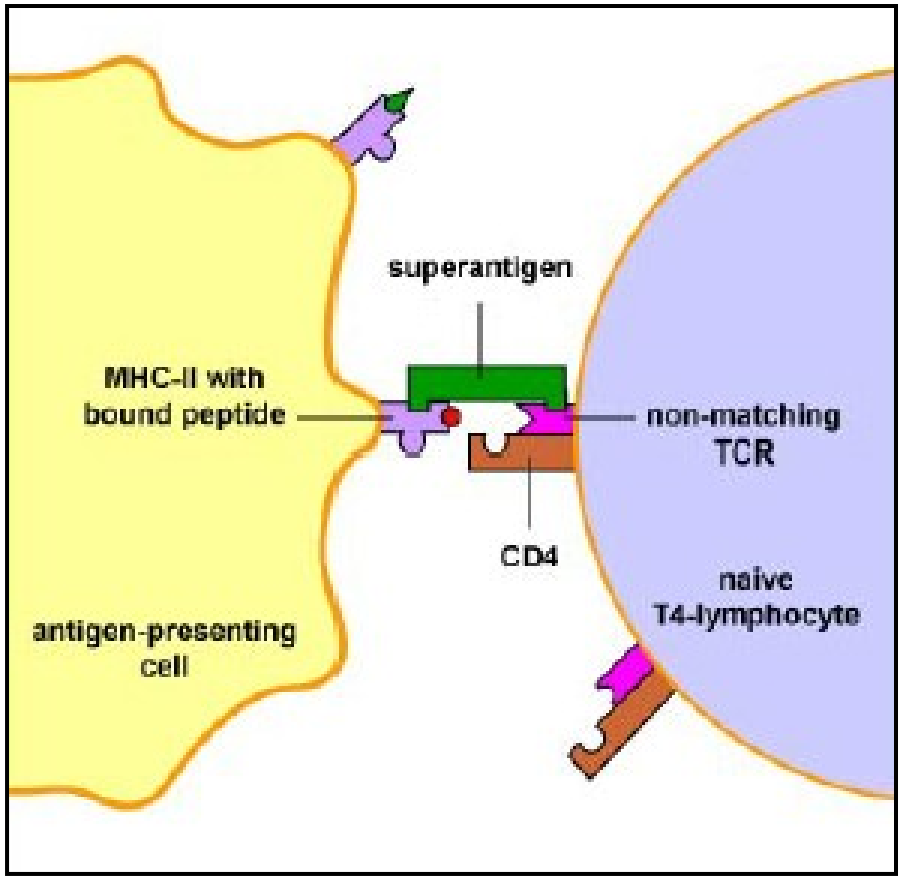
1:4 - 1:10

Binding of T4-Lymphocytes to Conventional Antigens



Conventional antigens are only recognized by specific T4-lymphocytes having a specific TCR with a shape that corresponds to a peptide of that antigen processed and presented by an antigen presenting cell and bound to MHC-II molecules.

Binding of Super antigens



Super antigens bind directly to the outside of MHC-II molecules and the TCRs and activate many T4-lymphocytes.

A specific TCR is not required for activation.

SUPERANTIGENS

- **Examples**
  - **Staphylococcal enterotoxins**
  - **Staphylococcal toxic shock toxin**
  - **Staphylococcal exfoliating toxin**
  - **Streptococcal pyrogenic exotoxins**