Antigens

A. Immunogen
A substance that induces a specific immune response.
B. Antigen (Ag)
A substance that reacts with the products of a specific immune response.
C. Hapten
A substance that is non-immunogenic but which can react with the products of a specific immune response. Haptens are small molecules which could never induce an immune response when administered by themselves but which can when coupled to a carrier molecule. Free haptens, however, can react with products of the immune response after such products have been elicited. Haptens have the property of antigenicity but not immunogenicity.
D. Epitope or Antigenic Determinant
That portion of an antigen that combines with the products of a specific immune response.
E. Antibody (Ab)
A specific protein which is produced in response to an immunogen and which reacts with an antigen.

FACTORS INFLUENCING IMMUNOGENICITY

A. Contribution of the Immunogen

1. Foreignness
The immune system normally discriminates between self and non-self such that only foreign molecules are immunogenic.
2. Size
There is not absolute size above which a substance will be immunogenic. However, in general, the larger the molecule the more immunogenic it is likely to be.
3. Chemical Composition
In general, the more complex the substance is chemically the more immunogenic it will be. The antigenic determinants are created by the primary sequence of residues in the polymer and/or by the secondary, tertiary or quaternary structure of the molecule.
4. Physical form
In general particulate antigens are more immunogenic than soluble ones and denatured antigens more immunogenic than the native form.

5. Degradability

Antigens that are easily phagocytosed are generally more immunogenic. This is because for most antigens (T-dependant antigens, see below) the development of an immune response requires that the antigen be phagocytosed, processed and presented to helper T cells by an antigen presenting cell (APC).

B. Contribution of the Biological System

1. Genetic Factors

Some substances are immunogenic in one species but not in another. Similarly, some substances are immunogenic in one individual but not in others (*i.e.* responders and non-responders). The species or individuals may lack or have altered genes that code for the receptors for antigen on B cells and T cells or they may not have the appropriate genes needed for the APC to present antigen to the helper T cells.

2. Age

Age can also influence immunogenicity. Usually the very young and the very old have a diminished ability to mount and immune response in response to an immunogen.

C. Method of Administration

1. Dose

The dose of administration of an immunogen can influence its immunogenicity. There is a dose of antigen above or below which the immune response will not be optimal.

2. Route

Generally the subcutaneous route is better than the intravenous or intragastric routes. The route of antigen administration can also alter the nature of the response

3. Adjuvants

Substances that can enhance the immune response to an immunogen are called adjuvants. The use of adjuvants, however, is often hampered by undesirable side effects such as fever and inflammation.

CHEMICAL NATURE OF IMMUNOGENS

A. Proteins

The vast majority of immunogens are proteins. These may be pure proteins or they may be glycoproteins or lipoproteins. In general, proteins are usually very good immunogens.

B. Polysaccharides
Pure polysaccharides and lipopolysaccharides are good immunogens.
C. Nucleic Acids
Nucleic acids are usually poorly immunogenic. However, they may become immunogenic when single stranded or when complexed with proteins.
D. Lipids
In general lipids are non-immunogenic, although they may be haptens.

TYPES OF ANTIGENS

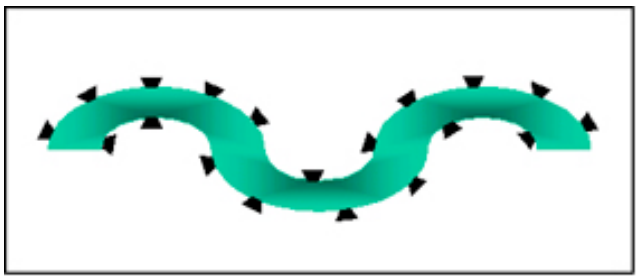
A. T-independent Antigens

T-independent antigens are antigens which can directly stimulate the B cells to produce antibody without the requirement for T cell help In general, polysaccharides are T-independent antigens. The responses to these antigens differ from the responses to other antigens.

Properties of T-independent antigens

1. **Polymeric structure**

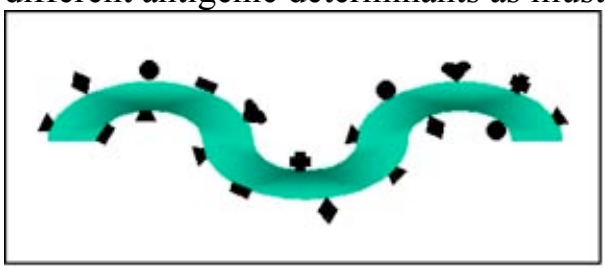
These antigens are characterized by the same antigenic determinant repeated many times as illustrated in Figure .



2. Polyclonal activation of B cells
Many of these antigens can activate B cell clones specific for other antigens (polyclonal activation). T-independent antigens can be subdivided into Type 1 and Type 2 based on their ability to polyclonally activate B cells. Type 1 T-independent antigens are polyclonal activators while Type 2 are not.
3. Resistance to degradation
T-independent antigens are generally more resistant to degradation and thus they persist for longer periods of time and continue to stimulate the immune system.

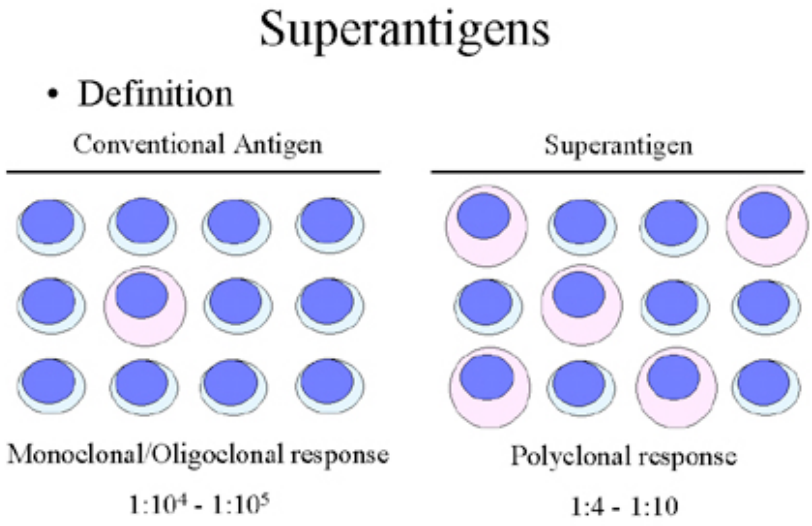
B. T-dependent Antigens

T-dependent antigens are those that do not directly stimulate the production of antibody without the help of T cells. Proteins are T-dependent antigens. Structurally these antigens are characterized by a few copies of many different antigenic determinants as illustrated in the Figure



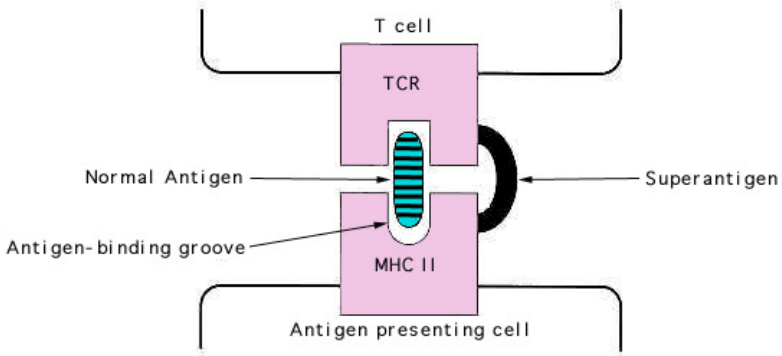
SUPERANTIGENS

When the immune system encounters a conventional T-dependent antigen, only a small fraction (1 in 10000 -100000) of the T cell population is able to recognize the antigen and become activated (monoclonal/oligoclonal response). However, there are some antigens which polyclonally activate a large fraction of the T cells (up to 25%). These antigens are called **superantigens** .



Examples of superantigens include: Staphylococcal enterotoxins (food poisoning), Staphylococcal toxic shock toxin (toxic shock syndrome), Staphylococcal exfoliating toxins (scalded skin syndrome) and Streptococcal pyrogenic exotoxins (shock). Although the bacterial superantigens are the

best studied there are superantigens associated with viruses and other microorganisms as well.
The diseases associated with exposure to superantigens are, in part, due to hyper activation of the immune system and subsequent release of biologically active cytokines by activated T cells.

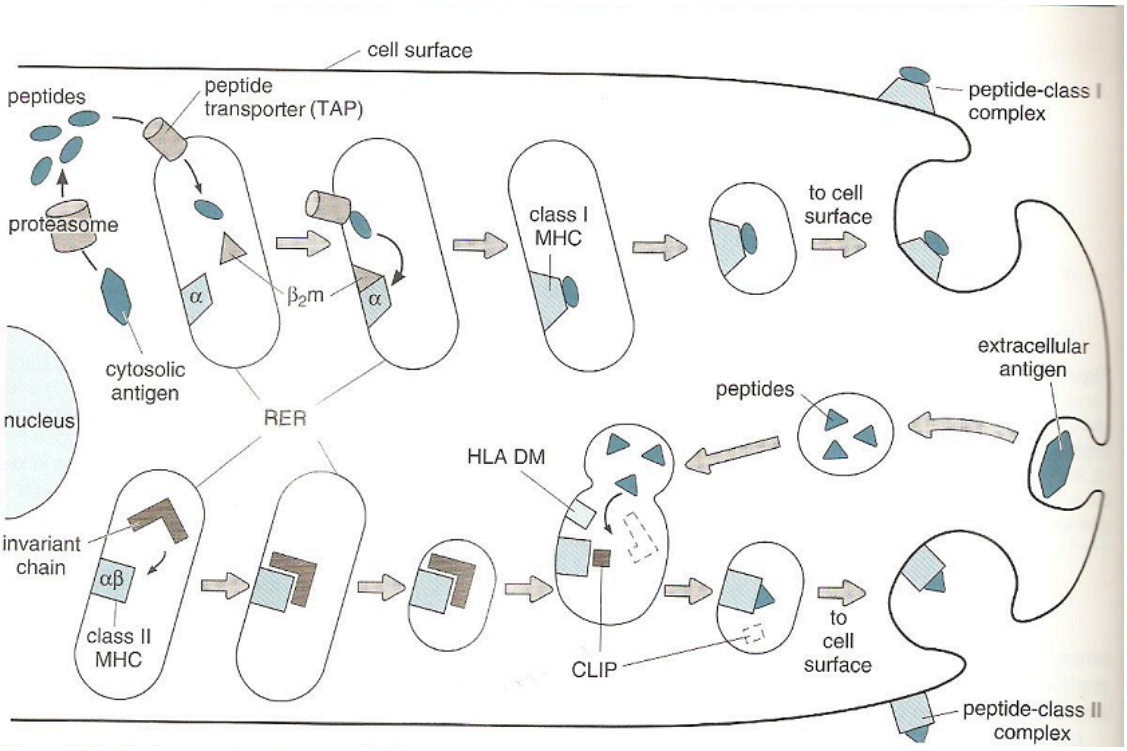


Antigen Processing and Presentation

Antigens are captured and taken from external environment in to a cell through engulfment by:
A- phagocytosis: for micriorganism, part of microorganism and large partical of protein.
B- endocytosis: small particles or individual proteins captured by receptors
C- pinocytosis: for free, soluble proteins.
Antigen-presenting cells(APC): refers to cell that express class II MHC molecules so can present Ag to helper T-cells. Three major class of cells function as APCs (Dendritic cells, Macrophage, and B-cells).
Mature dendritic cell most potent APCs because of their efficiency in capturing, transporting, presentation of Ag and attracting and activation of specific T-cells. Single dendritic cell can activate up to 3000 T-cells.
The antigen-processing pathways.
A- Endocytic pathway:
Protein captured through any of engulfment pathway and taken into endosomal vesicles and gradually broken down by exposure to an acidic ph and cellular proteolytic enzymes. Protein is destroyed to short peptides which cleaveage by proteinase then the peptides transported to the cell surface for presentation to T cells. This pathway delivers peptides to MHC classII molecules, which are expressed by macrophage and other APCs that present Ag to CD4 Th lymphocytes.

B- Cytosolic pathway:

This way include pathogen that live inside infected host cells (e.g. Viruses, intracellular bacteria (shigella), richettsia, chlamydia, listeria and intracellular parasites (Toxoplasma).



Intracellular pathogen processed through a sequence of event: cytosolic antigenes cleavage within proteasome enzyme to short peptides then pumped to lumen of rough-endoplasmic reticulum (RER) through a channal called transporter of antigenic peptides then associated with class I MHC proteins and are delivered to the cell surface for presentation to CD8 T-lymphocytes.

This pathway expressed by every nucleated human cell ensuring that any cell that becomes infected can present Ag to cytotoxic T-cells which lead to killing of infected cell and help to limit spread of the pathogen while endocytic pathway expressed only by APCs.

The Ag-processing occure in all normal cells even in the absence of infection e.g. Unstable cellular protein from the cytosol cleaved in to peptide and then processed by cytosolic pathway thus human cell normally presents a great peptides as MHC Class I complex on its surface.