Antigens (Ags) and antigenic determinants

Lec. 3.

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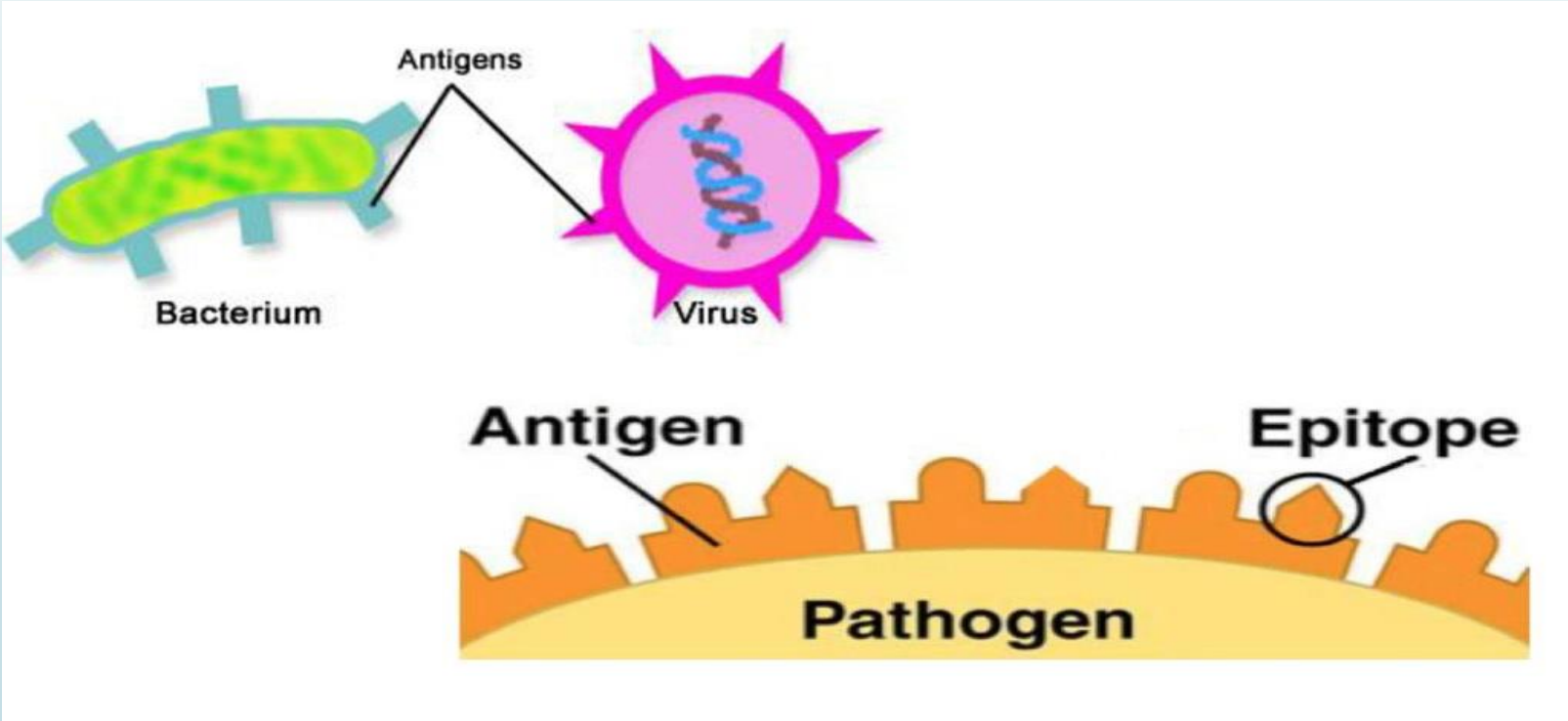
Introduction

- **The antigen** is any substance capable of provoking the immune system of an animal or a person to generating an immune reaction either by producing specific antibody from B-cell or by producing specifically sensitized T-cells or both.
- Any foreign substance may act as an antigen, such as:

- Dead or living microorganisms
- Vegetable proteins
- Egg albumin & milk
- Plant or animal tissue
- Bacterial toxins
- Serum & Red blood cells
- Snake venom

Antigenic determinants

- **Antigenic determinant** is the smallest unit of antigenicity represented by a small area on the antigen molecule possessing a specific chemical structure and steric configuration, which determines the specific immune response and reacts specifically with antibody also called **epitopes.**



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- The antigens/epitopes are divided into four broad functional categories:
- **1. Immunogens.** (Complete Antigens) antigens/epitopes that induce immune response either by producing antibody or sensitized lymphocytes, which in turn react specifically with immunogens, which produced them. Although all molecules that have the property of immunogenicity also have the property of antigenicity, the reverse is not true.
- **2. Haptens.** (Partial Antigens) is a molecule too small to stimulate antibody formation by itself. When combined with a larger carrier molecule, together function as an antigen and can stimulate an immune response
- **3. Tolerogens.** antigens (usually self), which induce in normal condition when the tolerance to self-molecules is removed in autoimmune disorders
- **4. Allergen.** are foreign and apparently harmless molecules that induce an abnormal immunological response **allergic reaction** involving IgE antibodies

Classification OF Antigens

- **Based on Origin**
- • Microbial
- • Fimbrial
- • Somatic
- • Flagellar
- • Capsular
- **Based on Immune Response**

1- T-independent Antigen

- • immunoglobulin production without the help of T lymphocytes, e.g. large molecular weight antigens such (pneumococcal polysaccharide, bacterial lipopolysaccharide, fimbrial and flagellar antigen) produce IgM is the main antibody and be Short memory.

2- T-dependent Antigens

- • Do not stimulate antibody production without the help of T lymphocytes, e.g. serum proteins, erythrocytes, haptens, etc. produce IgM, IgG, IgA and IgE and be Long memory.

Superantigens (SAgs)

- SAgs are a class of antigens that result in **excessive activation of the immune system**. Specifically it **causes non-specific activation of T-cells resulting in polyclonal T cell activation and massive cytokine release**. SAgs are produced by some pathogenic viruses and bacteria most likely as a defense mechanism against the immune system.
- Diseases associated with superantigen production: Diabetes mellitus, Eczema, Kawasaki disease, Rheumatic fever, Rheumatoid arthritis, Scarlet fever and **Toxic shock syndrome**
- Treatment: **eliminate the microbe that is producing the SAgs**. This is accomplished through the use of vasopressors, fluid resuscitation and antibiotics, The body naturally produces antibodies to some SAgs, and this effect can be augmented by stimulating B-cell production of these antibodies.

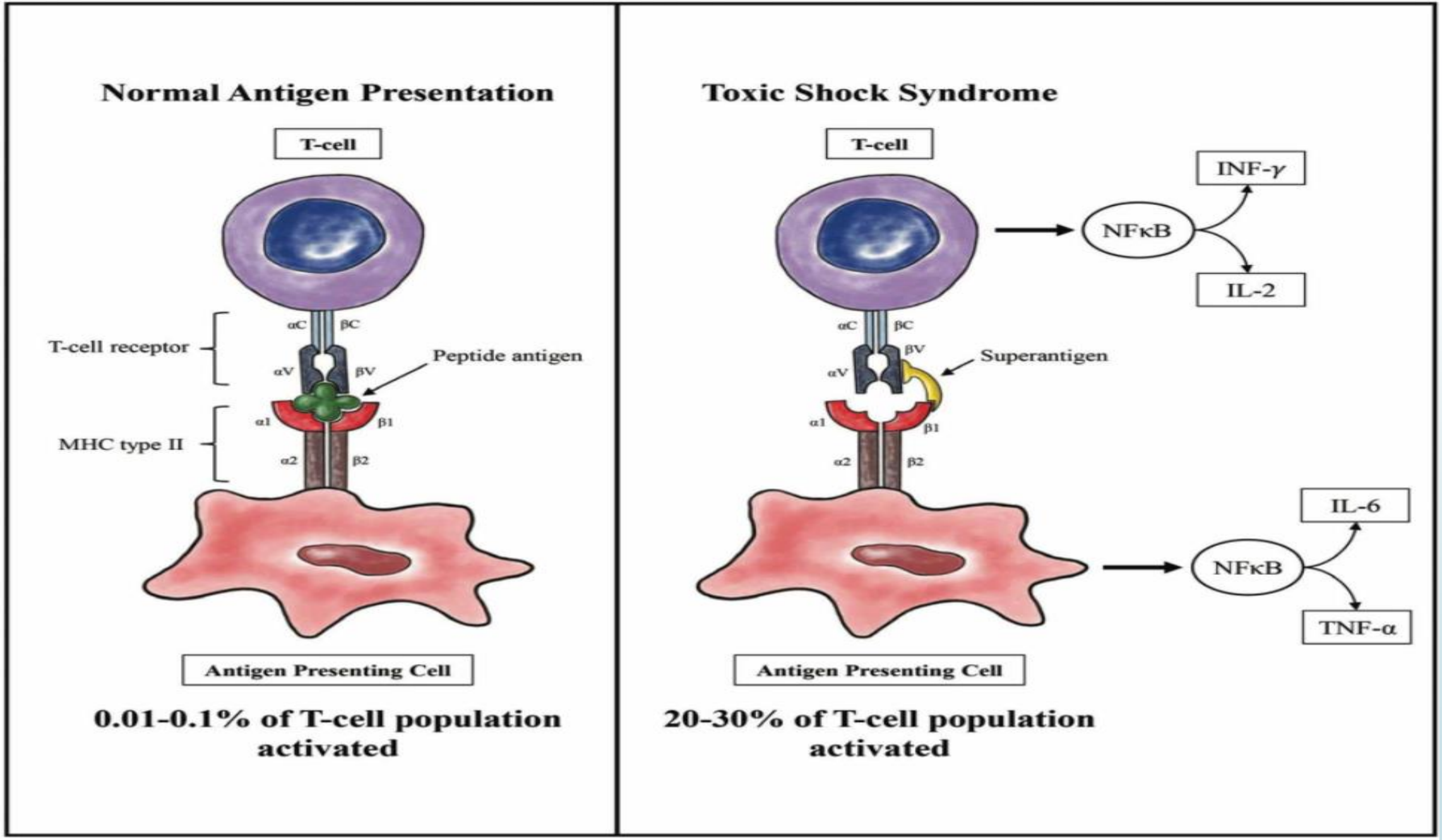

Fig. 4. Schematic of normal T-cell activation and abnormal T-cell activation induced by superantigen. Note that more inflammatory markers are secreted downstream than are shown in the figure.

Determinants of immunogenicity

- **Foreignness→** The first and the most important factor for immunogenicity is the foreignness of antigen. As recognition of self and non-self is an essential function of immune system, Therefore, the more dissimilar molecule from host molecules have greater immunogenicity.
- **Size (Molecular Weight)→** The most potent immunogens are usually large proteins. Large molecules (hemocyanins, molecular weight 6.75 million) are highly antigenic. Molecular weight less than 10,000 are weakly immunogenic. They become immunogenic only when linked to carrier protein.
- **Chemical Complexity→** Protein Ags are more effective than polysaccharide Ags, Lipids and nucleic acids are less antigenic and their antigenicity can be enhanced by coupling them with proteins, Not all proteins are however antigenic A well known exception is **gelatin**.
- **Susceptibility to Tissue Enzymes→** Substances, which are metabolized and are susceptible to enzymic action, are antigenic or immunogenic.

Antigen receptors

- The receptors, which recognize antigen and allow the antigen to bind are different in innate or adaptive immune system.
- **pattern recognition receptors (PRRs)** found on the cell membrane of macrophages, neutrophils and dendritic cells, and present in bloodstream and tissue fluid as soluble circulating proteins bind pathogen-associated molecular pattern **(PAMP)**
- **B-cell receptors BCR** antibodies recognize soluble antigen
- **T-cell receptors TCR** recognize peptides (antigen) when combined with major histocompatibility complex (**MHC**) molecules on the surface of antigen presenting cells (**APC**).

Antigenic specificity

- The specificity of natural tissue antigens of animals may be of various types:
- 1. **Species specificity→** Tissues of all members in a species possess species-specific antigen. Some degree of cross-reaction may exist between antigens from related species.
- 2. **Isospecificity→** Isoantigens are found in some, but not in all members of a species, Such human erythrocyte antigens in different individuals are classified into different blood groups
- 3. **Autospecificity→** self-antigens are ordinarily non-antigenic, but behave as foreign antigens. Lens protein and sperm when released into the circulation (by injury to lens or damage to the testis) antibodies are produced against them.
- 4. **Organ specificity→** Some organs such as brain, kidney, lens protein of different species share a common antigen. For example, brain tissue antigen of man, shares antigenicity with brain tissue antigen of sheep.
- 5. **Heterogenetic specificity→** The same or closely related antigens present in different biological species, such Proteus strains (OX-19, OX-2, OX-K) used as antigens in the diagnosis of typhus fever caused by Rickettsiae in (Weil-Felix) test.

Questions

- Q 1\ define the antigen and antigenic determinants
- Q 2\ numerate the types of antigens\epitops
- Q 3\ what is the determinants of immunogenicity
- Q 4\ numerate the antigenic specificity and mention one example for each one