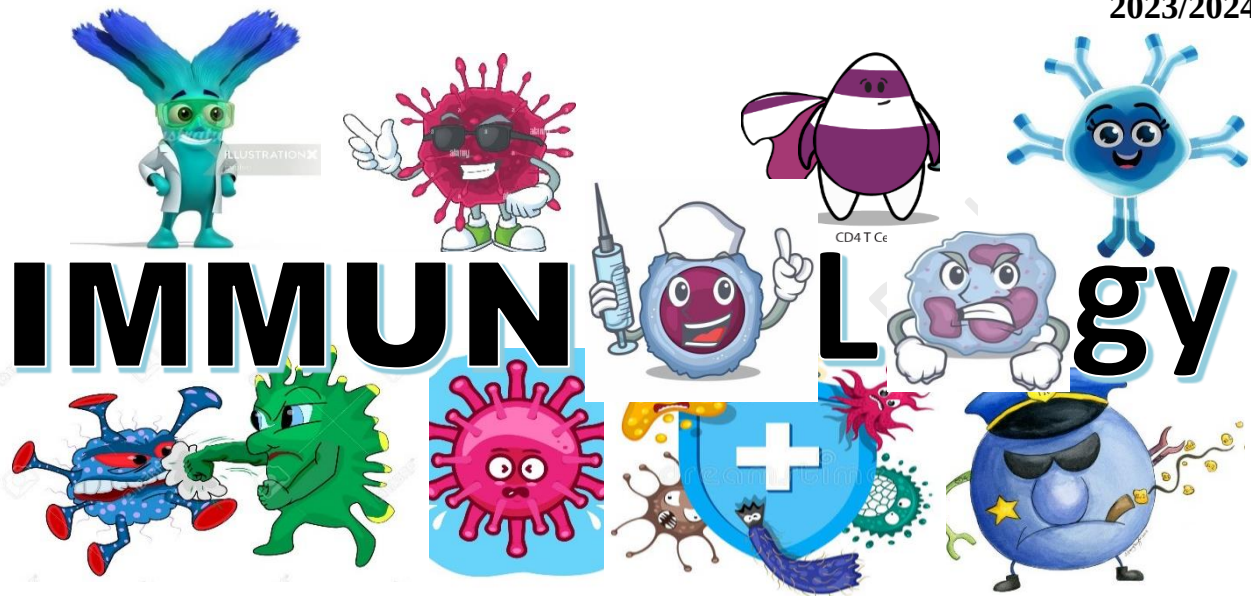




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Lecture 4

Antigens and Immunogens

Antigen (Ag.)

Antigen is a substance/molecule has the ability to react with the products of immune response after activation such as the production of the antibodies by the immune system.

المستضد هو مادة /جزيئة لها القدرة على التفاعل مع نواتج الاستجابة المناعية بعد التنشيط مثل إنتاج الأجسام المضادة من قبل الجهاز المناعي.

Immunogen

Immunogen is a specific type of antigen; it is capable to induce an immune response and binds to the products of the immune response, while an antigen is able to combine with the products of the immune response once they are made.

Immunogen هو نوع معين من المستضدات وهي قادرة على حث الاستجابة المناعية والتفاعل مع نواتج الاستجابة المناعية.

The foreign substances that induce an immune response possess two properties:-

1- Immunogenicity is the ability of a substance (immunogen) to induce a specific immune response, resulting in the formation of antibodies or cell-mediated immune response.

2- Antigenicity is the property of a substance (**antigen**) that causes it to react specifically with the final products of the immune response (i.e. secreted antibodies and/or surface receptors on T-cells).

ان الاجسام الغريبة التي تحث الاستجابة المناعية لها خاصيتان هما:

1- القدرة على حث الاستجابة المناعية

2- التفاعل مع نواتج الاستجابة المناعية

- Although, All immunogens are antigens but not all antigens are immunogens because all immunogens can stimulate and binds to the components of immune system but not all antigens can induce the immune response.

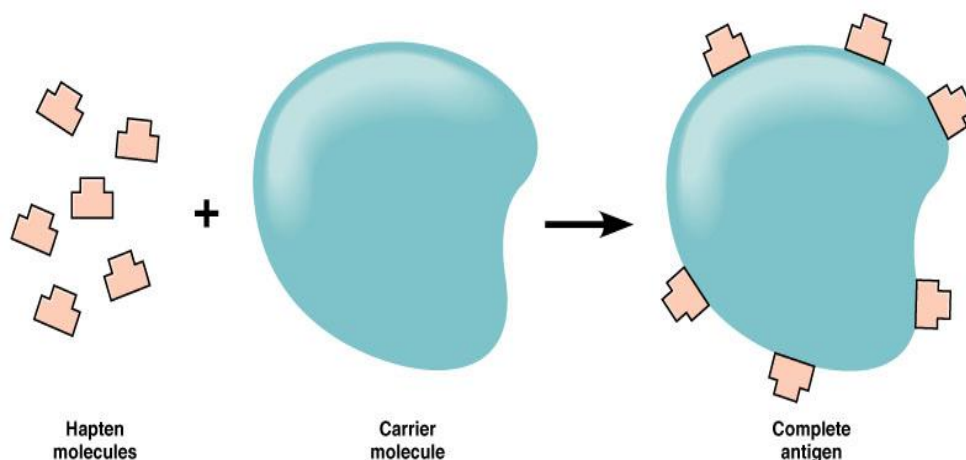
- All molecules that have the property of immunogenicity also have the property of antigenicity.

Hapten (Incomplete antigen)

- Hapten is a molecule or substance with low molecular weight (Non-immunogenic) that cannot induce an immune response on its own.
- However, if a hapten is combined with larger macromolecules (usually proteins) which serve as **carriers** then a response can be induced.

Hapten + carrier $\longrightarrow$ complete antigen (immunogen)

- Examples of haptens are antibiotics, analgesics, penicillin and other low-molecular weight compounds
- The carrier molecules may be **albumins, globulins, or synthetic polypeptides**.



الهابتن (الانتجين الغير مكتمل)

- هابتن هو جزيء أو مادة ذات وزن جزيئي منخفض (غير مناعية) لا يمكن أن تحفز الاستجابة المناعية من تلقاء نفسها.

- ومع ذلك، إذا تم الارتباط بين الهابتن مع الجزيئات الكبيرة الأكبر (البروتينات عادة) التي تكون بمثابة ناقلات ثم يمكن أن يكون قادرا على حث الاستجابة المناعية.

Epitopes (antigenic determinants)

- Epitopes (also called **determinant groups or antigenic determinants**) are the sites either on or within the antigen with which antibodies react.
- Antibodies are specific for epitopes.
- A particular antigen molecule may have many different epitopes or determinant, each of which can be a target for antibody binding.
- The epitopes on an antigen can be linear or conformational (Figure 1).

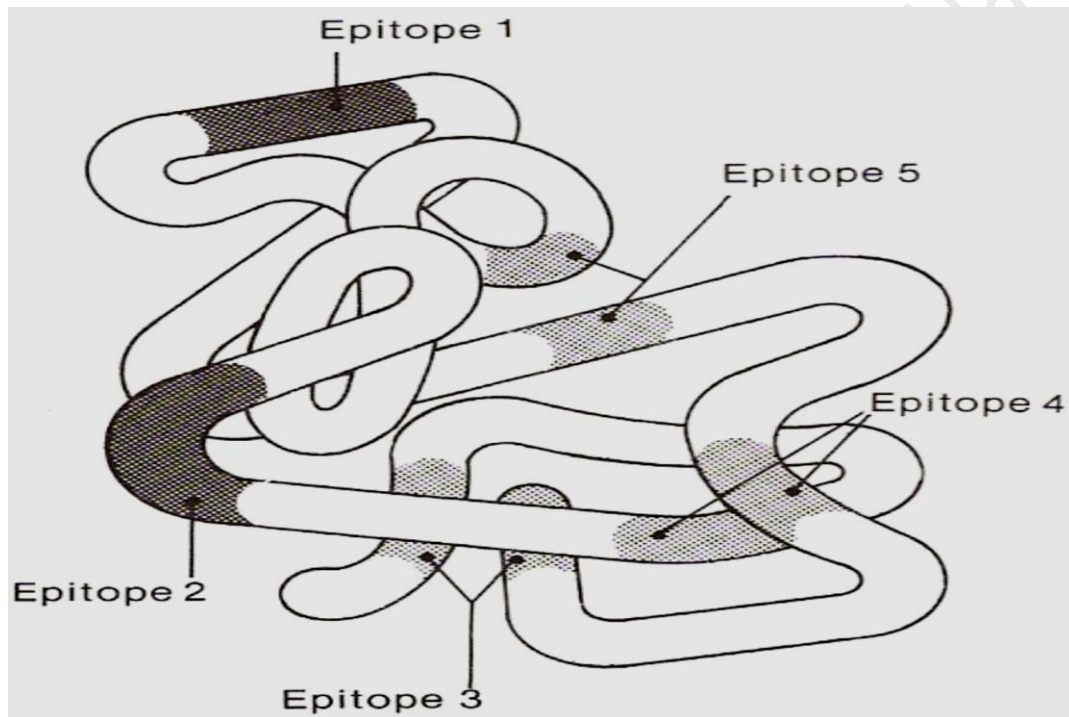


Figure 1. Model of epitopes on lysozyme, the shaded areas is the specific epitopes. They are composed of chain segments that are either linear (epitopes 1 and 2) or conformational (epitopes 3-5).

- Epitopes هي المواقع إما على أو داخل المستضد الذي تتفاعل معه الأجسام المضادة.
- الأجسام المضادة محددة لل epitopes
- يمكن أن تكون epitopes على مستضد خطي أو تشكيلي

Types of antigens

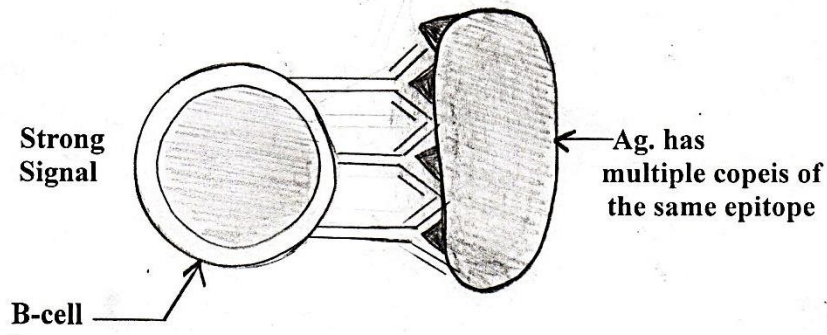
1- Thymus - Independent Antigens (TI)

T cell-independent activation occurs when antigens (that are expressed on the surface of pathogens with an organized and repetitive form) can activate specific B cells by the cross-linking of antigen receptors in a multivalent fashion. Many bacteria have repeating carbohydrate epitopes that stimulate B cells which in turn proliferate in a clonal expansion manner to produce the daughter cells and produce antibodies.

These antigens include **mitogenic antigens**, like: **lipopolysaccharides (LPS)**, **Dextrane** or **Tumor promoting agents**.

The characteristics of response to thymus independent antigens:

- 1- The type of antibodies produced is **IgM**.
- 2- There is **no class switching**.
- 3- **No memory cells**.



Thymus-independent antigens

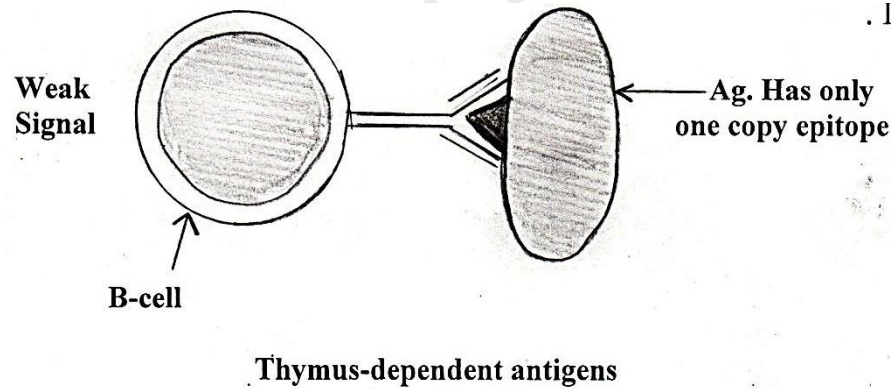
انواع الانتجينات

1- الانتجينات الغير معتمدة على خلايا T اللفاوية

يحصل التنشيط (الغير معتمد على خلايا T) عندما تنتشط خلايا B النوعية بالمستضدات (المنتظمة والمتكررة) والموجودة على سطوح الممرضات، حيث ان تلك الممرضات تظهر صفا كبيرا من المحددات المستضدية المتماثلة الى خلية B النوعية للمستضد، وهذا يساعد على حصول ارتباط قوي بينها وبين جزيئات الكلوبولين الغشائية (mIg)، وبذلك تحصل خلية B على الإشارة التنشيطية. ان هذا التنشيط يقود خلايا B الى انتاج الجسم المضاد IgM في غياب تحفيز خلايا T.

2- Thymus - Dependent Antigens (TD)

Most antigens are T-dependent, meaning T cell help is required for maximal antibody production. With a T-dependent antigen, the first signal comes from antigen cross linking the B cell receptor (BCR) and the second signal comes from co-stimulation provided by a T cell. T dependent antigens contain proteins that are presented on B cell with Class II MHC to a special subtype of T cell called a Th2 cell.



2- الانتجينات المعتمدة على خلايا T اللمفاوية

ان أغلب المستضدات هي من نوع المستضدات المعتمدة على خلايا T، وهذا يعني ان انتاج الأجسام المضادة يحتاج الى مساعدة خلايا T، حيث ان الإشارة الأولى تأتي من ارتباط المستضد مع مستلم خلية B (BCR)، أما الإشارة الثانية فهي تأتي من إشارة التحفيز المساعدة التي يتم تجهيزها من قبل خلايا T، وتحتوي تلك

المستضدات على بروتينات تقدم من قبل خلايا B (مقترنة من معقد التوافق النسيجي من الصنف الثاني) الى خلية T المساعدة Th2.

Super antigens (SAGs)

Superantigens (SAGs) are a class of antigens that cause non-specific activation of T-cells at the T cells receptor (TCR) resulting in polyclonal T cell activation and massive secretion of cytokine (e.g. IL-2, IL-1, IL-6, TNF- α), then resulting in toxic shock syndrome. SAGs are produced by some pathogenic viruses and bacteria most likely as a defense mechanism against the immune system. SAGs including retroviral protein and bacterial toxins (e.g. staphylococcal enterotoxins, toxic shock syndrome toxin).

السوبر انتجين

هو نوع من الانتجينات التي تحفز بصورة غير نوعية خلايا T اللمفاوية من خلال مستقبلها TCR وبالتالي انتاج الحركات الخلوية (السايوكينات) مثل (IL-2, IL-1, IL-6, TNF- α) وحدوث ظاهرة الصدمة السمية. هذه الانواع من الانتجينات تنتج من البكتريا والفايروسات ومن امثلتها staphylococcal enterotoxins.

العوامل التي تؤثر في المحفزات المناعية Factors influencing Immunogenicity

1- Chemical complexity

1. **Proteins** are usually very good immunogens.
2. **Pure polysaccharides and lipopolysaccharides** are good immunogens.
3. **Nucleic acids** are usually poorly immunogenic.
4. **Lipids** are non-immunogenic, although they may be haptens.

2- Foreignness

- An antigen must be foreign to the host with which it makes contact to serve as an immunogen.
- The degree of immunogenicity is dependent upon the degree of foreignness.
- The greater the phylogenetic difference between species, the more foreign something becomes with high immunogenicity.

3- Molecular weight

- There is a correlation between molecular weight of substances and immunogenicity. High molecular weight increase immunogenicity that induces immune response.
- **The best immunogens are in the range more than 10000 Dalton (Da.)** and the most active immunogen is with 100000 Da., while **the small molecules with 5-10,000 Dalton (Da.)** are generally poor immunogens.

4- Degradability

- The molecules with the ability to biodegrade are the best immunogens to be presented by MHC molecules to activate T-cells (Ag processing by Ag-presenting cells (APC)).
- Macromolecules that cannot be degraded and presented with MHC molecules are poor immunogens.
- Example such as polystyrene

5- Rout of immunization

The rout of antigen administration plays an important role in immunogenicity. According to high immunogenicity the routs divided as following:-

- a- Intravenous (iv): into a vein (non-favorite route because it is minimize the immune response)
- b- Intradermal (id): into the skin
- c- Subcutaneous (sc): beneath the skin (best route)
- d- Intramuscular (im): into a muscle (the best route because it is prolong the period of immune response)
- e- Intraperitoneal (ip): into the peritoneal cavity (best route)

6- Stability

- The rigid structure of Ag plays an important role in the antigenicity.
- Ag with high stability acts as immunogen due to its ability to activate the immune response while the opposite is not immunogens because they are haven't a rigid structure enough to be stably bound by antibodies such as lipids and gelatin.

7- Antigen dose

- Too high or low dose of Ag will fail to activate enough immune response and cause immunologic unresponsiveness state (Tolerance)
- Appropriate dose of Ag cause optimum antigenicity.

Adjuvants

- Adjuvant is from Latin *adjuvare*, to help.
- Adjuvants are the substances enhance the immunogenicity of molecules without altering their chemical composition. This leads to a higher titer and longer lasting immune response.
- Adjuvants are non-immunogenic alone but enhance the immunogenicity of other molecules

- Freund's adjuvant is the one of the most adjuvant widely used in animals but not in humans
- Aluminum potassium sulfate (alum) is the only approved adjuvant for human use.
- There are two types of Freund's adjuvant
 - a- Complete Freund's adjuvant: contains heat-killed *Mycobacteria* and oil (highly effective)
 - b- Incomplete Freund's adjuvant: contain oils only.

Adjuvant augments the immune response through several ways:-

- 1- Prolong exposure to Ag: Adjuvants can increase the time of exposure from a few days to a few weeks.
- 2- Adjuvants also increase the size of the Ag and enhance the efficiency of macrophage processing of antigens (phagocytosis).
- 3- Increase the proliferation of T, B lymphocytes and macrophages which leads to increase the immune response.
- 4- Compensate booster doses.