

Lecture :antigen

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Slides are included.

Sheet correction link :bit.ly/odimmuno

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Phagocytosis

- Special areas in the phagocyte membrane are called: clathrin-coated pits...these contain different receptors (PRRs, complement receptors...etc.)

- Phagocyte activation:

-Lysosomal destruction of microbe: -acid hydrolases (proteases,

lipases, nucleases..etc)

-oxygen free radicals

..this process is called:

-nitrous oxide (NO)

-acidity

-...etc

**Remember the enzymes:
1- NADPH oxidase
2- Myeloperoxidase

Sheet note :these are killing mechanisms or anti microbial mechanisms

- ✓ Phagocytosis is one of the reaction in innate immune system
- ✓ The part of phagocyte that from it the phagocyte engulfs the microbes is **clathrin- coated pits**
- ✓ Extra picture;



✓ Clathrin-coated pits

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Receptors that are found in the clathrin pits :

- PRRs
- complement receptors (complement receptor : receptors circulate in the blood)
- FC receptors (receptor of the immunoglobulin in the surface of phagocyte is receptor for PRR)

Immunoglobulin has many function :

1-fight antigen (the main function)>>here it is BCR >>adaptive

2-opsinon >>>here it is PRR>>innate

- ✓ After the phagocyte engulfs the microbes, it kills him (lysosomal destruction by using enzymes)
- ✓ Oxidative burst :producing oxygen free radicals
- ✓ The phagocyte membrane contains enzyme that converts $O_2 \longrightarrow O_2^-$ this enzyme called phagocyte oxidase or NADPH oxidase
- ✓ Inside the phagocyte, there is enzyme called Myeloperoxidase ($Cl + H_2O_2 \longrightarrow OCl$ (strong free radical)
- ✓ When the phagocyte is active ,it will secrete cytokines , activate inflammation and the adaptive immune system .
- ✓ There is another process that resembles phagocytosis called macropinocytosis
- ✓ Macropinocytosis is a method used by dendritic cell ,the dendritic cell has dendrites uses them to encircle large area of(fluid and what it contains) and pulls it to inside the cell .
- ✓ Although ,the main function of dendritic cell is antigen presenting, it does phagocytosis (to do antigen presentation)

Some cytokine actions

- IL-1 and IL-6: fever, also vascular permeability
- TNF-alpha: vascular permeability, also fever
- IL-8 and IL-12: chemotaxis of neutrophils and NK cells, respectively

Antigens

= Specific structures in microbes/foreign materials that the body responds to by adaptive responses

*3 receptors for antigens:

1-On B cells...or secreted from B cells

*Antibody (soluble receptor for antigen)

2-On T cells (sheet note :TCR is the receptor in T Cell)

3-Major histocompatibility complex (MHC)...= human leukocyte antigen (HLA)...encoded by a cluster of genes

function: presentation of antigenic peptides to T cells

- ✓ The receptor in B cell is immunoglobulin (the soluble form of it is antibody that is secreted by plasma cell)
- ✓ The role of MHC is offering the antigen to the T cell
- ✓ The T cell needs antigen presentation ,it cannot catch the antigen by it self

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- ✓ There are some conditions to enable the T cell to connect with the antigen :
 1. The antigen should be found on the surface(membrane) of cell
 2. The antigen is carried by MHC
 3. The antigen should be peptide antigen
- ✓ However ,the B cell can connect to the antigen without needing another presenting cell or MHC(in some cases ,B cell needs presentation the antigen to the BCR by follicular dendritic cell not by the usual MHC)

More about receptors for antigens...

- B cell: binds the antigen directly without the need of a MHC molecule

...but T cell bind both: antigen + MHC bound to the antigen

*in this case the Ag is cell-associated (virus...etc)

- ✓ There are two methods to present the antigen on the surface of cell :
 1. Extracellular antigen: the cell that will present the antigen phagocytosed the microbe and processed it ,giving peptides are carried by MHC on the membrane of it .
In this case ,the MHC is MHC type 2
 2. Intracellular antigen :Another scenario for presenting antigen on cell membrane is that one cell is invaded by virus or a cancer cell so inside theses cells there are products of its antigen and those antigens are then presented on MHC for TCR
بمعنى آخر هذا النوع من تقديم مولدات ضد على سطح الخلية مصدره الخلية نفسها نتيجة لغزوها بواسطة فيروس او انما اصبحه متحولة سرطانيا ..وليس عملية بلعمة له من خارج الخلية

- **“Epitope” is the recognized part of “antigen”**

- Epitope is the real small part that is identified by the receptor

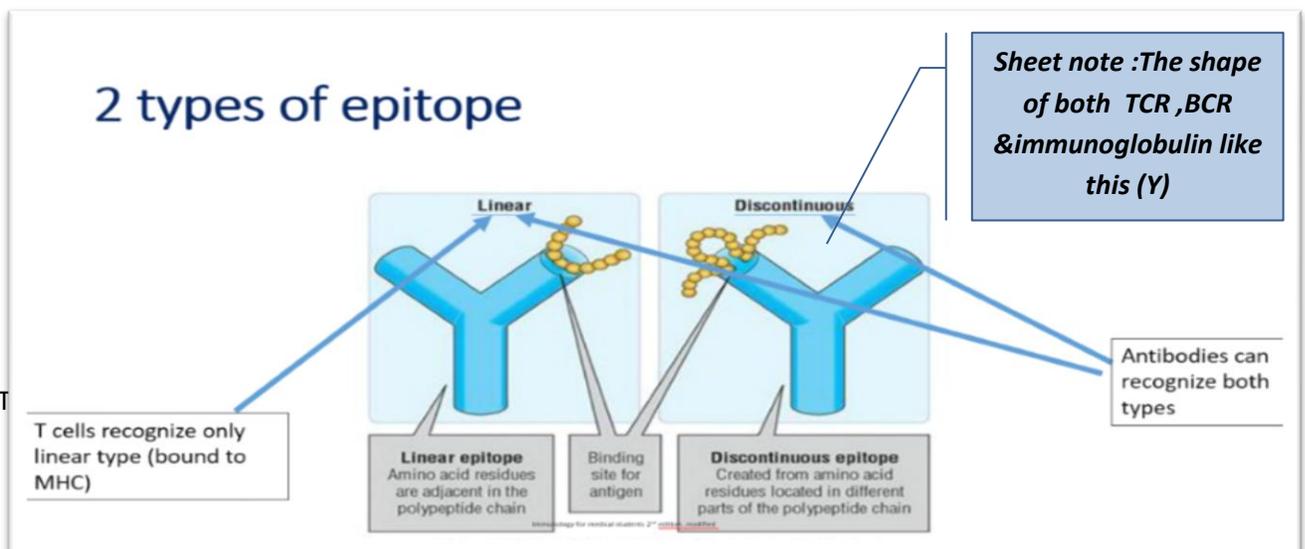
... = “Antigenic determinant”

- For example, a protein is an antigen but a small amino acid sequence of the protein is the real part that is specific for the receptor

...single molecule may have multiple epitopes

- The two terms are usually used interchangeably

- ✓ The part of antigen which actually bind receptor is called epitope or Antigenic determinant.
- ✓ Look at the image In the slide below ..the whole curved yellow peptide sequence is called antigen but the only part that have direct attachment with the antibody is called epitope.



Anyway you can use both terms interchangeably .

- ✓ So the specificity of BCRs for example that we have talked about earlier is actually the specificity for a specific epitope
- ✓ so one molecule (for example a long protein -which has many copies inside the -body) may contain multiple epitopes.. one epitope on each copy may attach specific BCR related to one B cell clone (remember that one clone of B cell is specific for one ligand) and another antigen copy OF the same protein attach to another BCR of another B cell clone by another epitope.
- ✓ The antigen that can be attached to more than one clone receptors by more than one epitope is more immunogenic than the antigen with only one epitope available for only one clone .
- ✓ More immunogenic antigen means that it has stronger immune reaction.
- ✓ So the variability of epitope of one antigen(more complexity) means more immunogenicity
- ✓ This image is for peptide epitope has two types
 1. Linear peptide epitope : a continuous linear segment attached to the receptor
 2. Discontinuous peptide epitope : 3D like appearance so attachment is by separated peptide sequences of the antigen.
 - ✓ The antibodies attach peptide antigen and non peptide either it is carried by MHC or not and either discontinuous or linear while TCR attach only to linear peptide epitope carried on MHC and attached to a cell.

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Antigen VS immunogen

- Antigen may bind to the receptor but may not effectively induce immune response (e.g., antibody production)...ineffective binding
- Immunogen is the effective antigen that elicit antibody production
- To be effective, the molecule needs to be larger and more complex and fit more to the receptor

...more complexity means greater variety of epitopes (an immune response is more

possible to occur)

- Proteins are more immunogenic than carbohydrates and lipids
- Amino acids alone are non-immunogenic
- Enzymatically-cleavable proteins are more immunogenic than non-cleavable ones

...cleavage by the phagocyte increases the accessibility to the epitopes of an antigen

- ✓ The antigen may attach receptor without inducing immune response
- ✓ How to determine if the immune response for one antigen is strong ? the body finally has to produce specific antibody for this antigen otherwise its weak immune response .
- ✓ Larger molecule is more immunogenic than smaller molecule

- ✓ Larger antigen is stronger bcz of stronger binding(fitting better).
- ✓ Cleavable protein is more immunogenic than non cleavable bcz of epitope variety.
- ✓ Vaccines are immunogenic

- **Haptens**

- They are simple molecules that are non-immunogenic...but if they are coupled to a larger molecule (an immunogen) which is called “carrier”, they bind effectively to the receptor, and now the response is directed toward both the hapten and the carrier epitope
- They are usually non-biological

- ✓ Haptens :
- ✓ Non immunogenic molecule that Need immunogenic carrier to produce response for both of them .
- ✓ They are usually non biological(synthetic)molecules for ex: penicillin
- ✓ They are small