University of Jordan
Faculty of Medicine

2018 2012
Medical Committee
The University of Jordan

Biochemistry

● Sheet ○ Slides

Lecture #: 5 Date: 23/9/2013

Title: *Classes of Immunoglobulins*

Professor: Dr. Nafith Abu Tarboush

Done by: *Khaled Al Jbour*

Price: .....

DESIGNED BY
WASEEM KAMAL

University of Jordan
MD Class of 2018

groups/Doctor2012
http://medstudygroup.weebly.com

Classes of Immunoglobulins

IgM Class

Location:

- Intravascular mainly (Blood/Lymph) (Pentamer or Hexamer)
- B-cell surface (Monomer IgM only)

Forms:

- Mono
- Penta, the most common form
- Hexa, the rarest

Functions:

- Primary Immune Response, the 1st immunoglobulin to face the antigen in the circulation.
- primary role in antigen agglutination (eg: ABO):

When giving a patient a different blood group, blood agglutination would occur, IgM would link different blood groups (Cells from different groups) by binding to them & dealing with them as antigens and eventually agglutinate & precipitate them from the circulation.

-IgM has a very **low affinity** for antigens, because it is the first antibody that will bind the antigens thus it's not specific for it. Low binding affinity means less complementarity between the antigen & the antibody.

Multimerization:

- A chain of amino-acids called **A J chain** (joining chain) is involved in the formation of the pentamer and hexamer form -Multimerization-
- During **Multimerization** we'll have more than one joining chain involved in the process, but only one will remain in the final product.. (One joining chain in each multimer at the end)
- IgMs are connected together by the constant chains, mainly CH4 & less contribution by CH3

How does Multimerization occur?

1-IgM & another IgM, come together by the joining chain bringing them closer, then two **cysteine** molecules will be close enough to make a **disulfide bridge** (covalent bond) between the CH4 of the 2 adjacent antibodies.

2- Another antibody comes by the joining chain bringing it closer & 2 cysteine molecules will come & do the disulfide bridge & so on till we get the multimer we want (with only ONE Jchain)

Why we don't get more disulfide bridges in other parts of the IgM?

1- Large space between them, unlike the close one where the disulfide bridge is usually formed

2- No cystiene molecule to initiate the disulfide bridge

IgG Class

Location:

- Blood & Lymph (filters outside the blood to most tissues)
- Intestine

Function:

- Secondary Immune Response, Provide defense against different pathogens
- Major defense line of fetus & new born, **Because:**
    1) It is the only immunoglobulin that can cross the placenta (Immunity for fetus)
    2) For new born by circulating in the circulation till the lymphocytes of the new born are mature & then they will secrete their own immunoglobulins
- Responsible for the process of opsonization (coating of a foreign body by IgG molecules

from their Fab portions.. **How?**

1) The Fab portion of the antibody will recognize the epitopes of the foreign body

2) The FC portion will be left available to connect to immune cells (Macrophages, Natural killer cells..etc)

3) Recognization of that foreign body ended by phagocytosis of that foreign body

IgA Class

Structure:

Mono, Di or Tri

-The main Ig present in the **secretions**, always a **dimer** in secretions

-In the blood (plasma) it can be found as a mono, di or tri.

-Structure of it's Dimer form:

One antibody (IgA) connected to another IgA through a joining chain => This complex is wrapped up by a **secretory component ,** The secretory complex's function:

1) Enable it (dimer) to be secreted

2) Protects the IgA dimer from proteolysis by proteolytic enzymes (Proteolytic enzymes of our body's secretions)

Functions of IgA :

* Immunity for new born, By mother's milk… (Localized immunity), in the new born's GI tract

So: - In the circulation of the new born => IgG

- In the GI tract of the new born => IgA

*dimerization process, 2 IgA connected by A J-chain with a disulfide bridge

-How the IgA is secreted? By:

IgA Transcytosis

Most secretions occur in spaces lined up by epithelial tissue.

" IgA (mainly the secretory dimer) is produced by plasma cells (B cells) in the submucosa underneath the epithelium. It binds to the polymeric immunoglobulin receptor on the basolateral surface of epithelial cells, and is taken up into the cell via **endocytosis**(internalized through epithelial cells) The **receptor-IgA complex** passes through the cellular compartments before being secreted on the luminal surface of the epithelial cells, still attached to the receptor. Proteolysis (digestion) of the receptor occurs (because it is not protected via the secretory component), and the dimeric IgA molecule, along with a portion of the receptor known as the secretory component, are free to diffuse throughout the lumen."

IgD Class

Function:

- Not well recognized In serum
- On B-cell surface, initiate the immune response

Rule:

- Most of Igs, are present in two forms.. Either **attached to a B-cell** (once the antigen is recognized it will be processed to the inside & recognized by the cell to give plasma cells to produce the secondary immune response) or **free in the circulation**

IgE Class

Location:
- Blood
- Bound to the mast cells & basophils

Function:
- Allergic reactions (by **Heparin & Histamine)**, causing: increased vascular permeability, skin rashes, respiratory tract constriction (wheezing), and increased secretions.
- Lysis of worms.

-IgE has the highest affinity (Between the IgE & its receptor on cells) among all Ig classes.

How do B-cells produce antibodies?
1- Antigen binds to the antibody on the B cell
2- Recognition of the antigen
3- Genetical rearrangement followed with a maturation of the B lymphocytes to plasma cells.
4- plasma cells will start producing antibodies
5- Another class of B lymphocytes will be kept as memory cells to remember the arrangement of the Igs (secondary immune response).
Remember:
IgM => Primary Immune response
IgG => Secondary Immune response (Higher magnitude, because it is more specific for the antigen)

Isotype (Class) switching (Inside the B lymphocyte)
-After the primary immune response by IgM, how to develop IgG for that antigen as a secondary immune response? How will the IgG recognize the same antigen?
VDJ arrangement will be kept the same, a genetic rearrangement will occur leaving the VDJ the same, splitting the genetic material at the C portion replacing the constant area alone and the variable region recognizing the antigen will be kept the same (IgM >> IgG)

Producing a different class of antibody that recognizes the same antigen

Igs' Production & Diseases:

A- Increment in the production: (occurs in cancer and inflammations)
- in which there is an increment in the production of one class of Igs , multiple classes or one polypeptide chain (light chain only) (**Bence Jones protein = light chain which was discovered by bence jones)**
- **Myeloma** => Increment in the production of a **single class** of Ig
- **Multiple Myeloma =>** increment in production of more than one class of Ig

B- Decrement in the production:
- Can affect a single class, or more than one class..
- Deficiency of B cells = no plasma cells = no Igs
- Agammlobulonemia => No Igs, because no gamma globulins (immuno-globulins).
- Gel Electrophoresis is used to figure the immunoglobulin rapidly increasing thus figuring the class of Igs with the myeloma.

Check slide #39 for further diseases acknowledgement ☺

How to make Hybridomas & monoclonal antibodies?

Benefits of Hybridomas' making:
1- Can be used to measure the amounts of many individual

proteins (eg, plasma proteins)

2- Can determine the nature of infectious agents (eg, types of bacteria)

3- Can be used to subclassify both normal (eg, lymphocytes) and

tumor cells (eg, leukemic cells)

4- Can be used to direct therapeutic agents to tumor cells

5- Can be used to accelerate removal of drugs from the circulation when they reach toxic levels

-We make a single class of antibody which can recognizes a single epitope
-For example:
1) If I want to know the amount of albumin in a blood sample I first identify the amino-acids of the albumin, dealing with it as an epitope,
2) Then I manufacture an antibody complementary to this epitope (the albumin) & can only recognize this protein
3) And now for any serum sample antibodies can be applied & the will bind to the albumin (the epitope) & the albumin concentration can be figured out easily .
- Affinity Chromatography = Antibody-Antigen reaction

Hybridomas:
-Antigen injected in a mouse or rat.
-Myeloma cells (cancer cells) can divide rapidly without stopping ..
- We take B lymphocytes with the antigen from the spleen of the mouse.
Remember: these B cells of the mouse also have produced antibodies for that antigen.
-We combine the B cells (which have antibodies specific for that antigen) with the myeloma cell in a test tube with a medium allowing the cells to unite.
-Some (not all) cells will combine together to give **Hybridoma**; Plasma cells with myeloma + B cells from the spleen with the antigen
-This Hybridoma now will start manufacturing antibodies for that antigen.
-We can either; directly get use of the antibodies or re-inject them in the mouse to get secondary immune response & get used of the antibodies produced later on.
P.S.. Check the videos the Drs showed us for this lecture.

Here are some useful links ☺

http://www.youtube.com/watch?v=c_krTc9M1WU&feature=youtube_gdata_player

http://www.youtube.com/watch?v=JMgwXx0nafw

"The snake which cannot cast its skin has to die. As well the minds which are prevented from changing their opinions; they cease to be mind."