



University of Jordan
Faculty of Medicine



Medical Committee
The University of Jordan





Community Medicine



Lecture Title:	Environment				
Date:	22	9	2013	Lecture Number:	4
<input type="checkbox"/> Slides	<input checked="" type="checkbox"/> Sheet		<input type="checkbox"/> Other:		
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Immunoglobulins

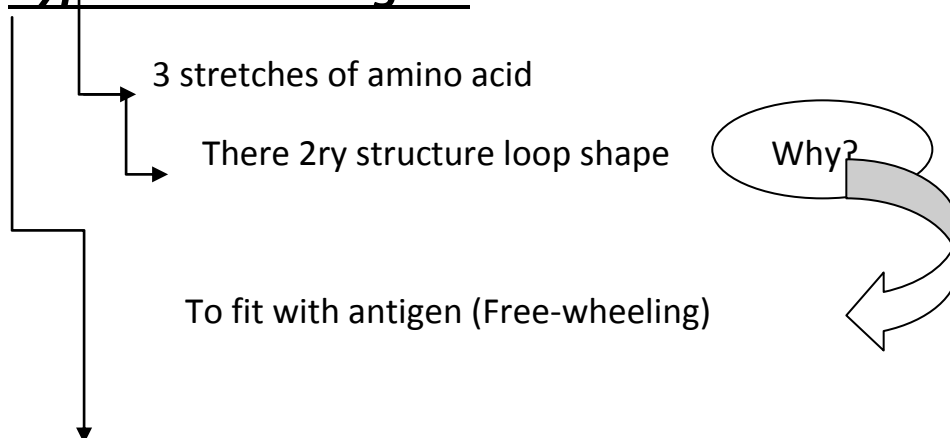
Revision:

- Immunoglobulin structure 2 light chain 25KDa and 2 heavy chain 50KDa (total=150KDa)
- Heavy chain one quarter variable three quarter constant

Even variable chain differ in variability of amino acid sequences:

The variability of amino acid in variable domain itself differ there amino acid with limited variability other with higher variability changing all the time the area with these amino acid called

hypervariable region

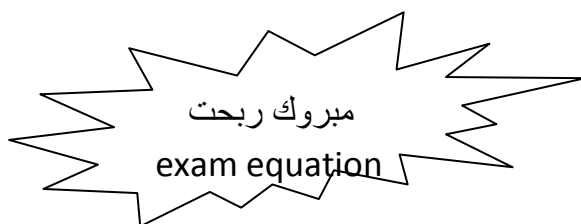


The area bind to antigen not all area it depend on the size of antigen

- The aim of binding to antigen is transmit the message that bind to the cell to produce the antibody for this antigen
- Antibody interaction with antigen through all type bond **EXCEPT** covalent bond (electrostatic,hydrophobic,...etc)
- Immunoglobulin bind with antigen in tip (fab) in variable chain exactly in hypervariable

Immunoglobulins

- The (Fab)₂ fragment CANNOT do this so it is function of (Fc) :
 - ✓ mediated Inflammatory functions associated with cells
 - ✓ mediated Inflammatory functions of complement proteins
 - ✓ mediated Intracellular cell signalling molecules
- Every antibody bind with 2 antigen



★ Igm is pentamer molecule has 5 antibody (not all but usually) how many antigen will bind with it ?

Answer: 10 antigens

- After binding (Fc) bind with another protein or cell to transmit the message
- The effect of antibody is mediated through (Fc) then through (Fab)
- When the antigen (toxin) bind with antibody it cannot bind with anything else so it stopped
- Constant domain in heavy chain either 3 or 4
- IgM and IgE → 4 constant region also an extra constant domain bind in hinge region which limit its freedom of movement
- Constant domain synthesis by constant gene
- 5 type of genes make 5 type of constant region in heavy chain

α → IgA

δ → IgD

ϵ → IgE

γ → IgG

Immunoglobulins

μ \rightarrow IgM

- Which gene is responsible for determination of antibody class?
- Answer: constant gene (like gene above) of heavy chain **NOT** light

- As we mentioned constant region of heavy chain made up by 5 constant genes the constant region in the light chain made by 2 genes (2 constant region) κ and λ

- If one of two light chains is κ the second will be λ because as we mentioned in last lecture 2 identical light chains and 2 identical heavy chains

- Disulfide bridge between:

Light chain----heavy chain

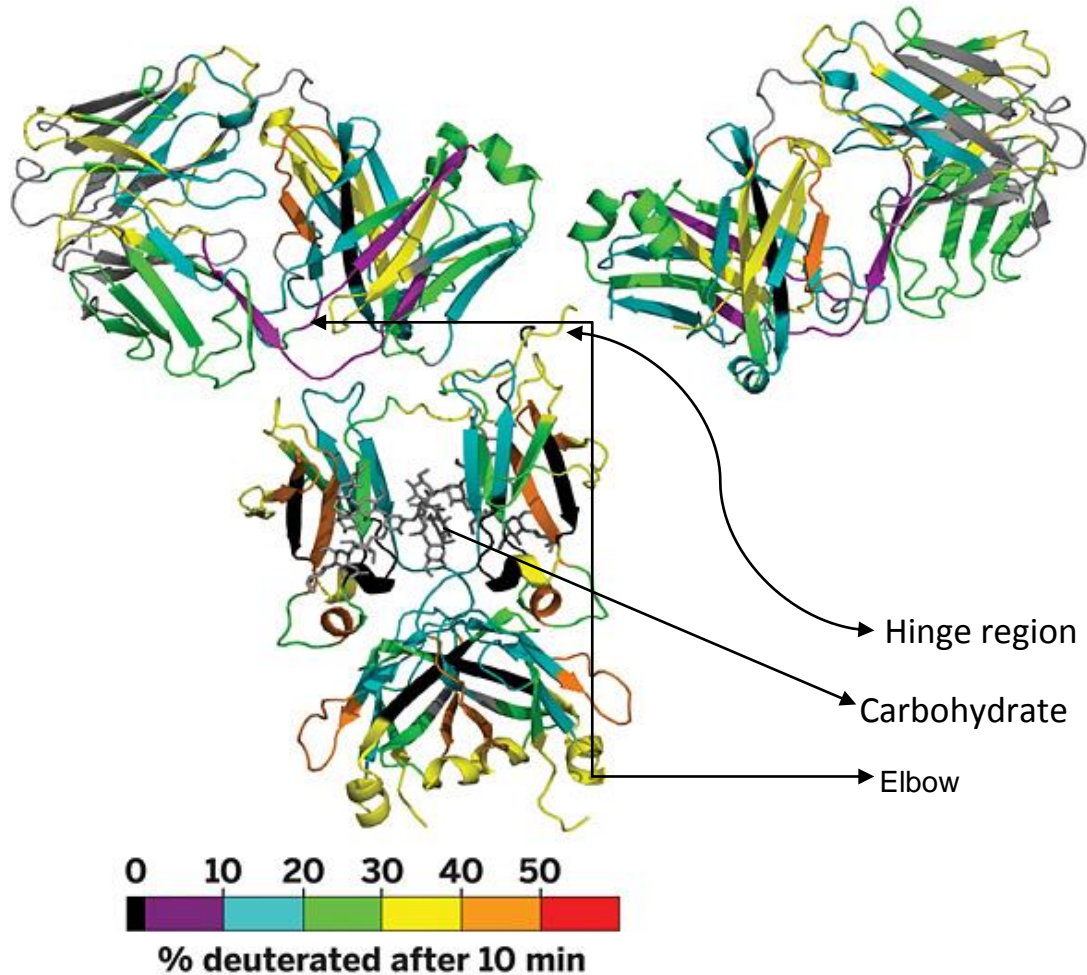
2 heavy chains in hinge region

- Pepsin cleavage sites \rightarrow 1x (Fab)₂ & 1 x Fc

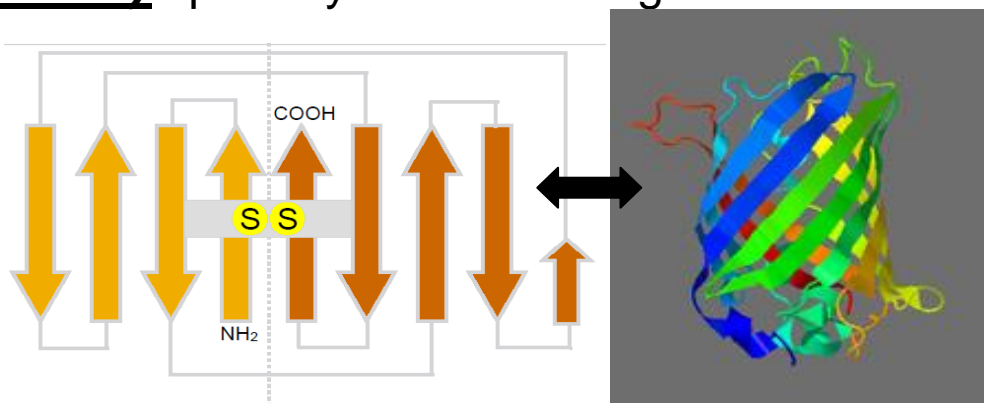
- Papain cleavage sites \rightarrow 2 x Fab 1 x Fc

Immunoglobulins

Crystal structure of immunoglobulins

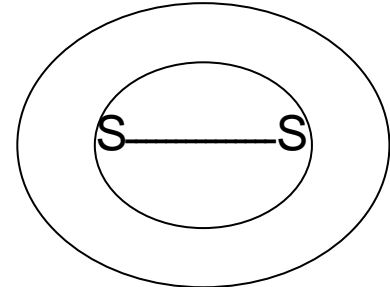


- Consist of fold (super secondary structure) **most** beta sheet which form beta barrel (برميل) **mainly** specially in variable region



Immunoglobulins

- Disulfide bridge formed between two beta sheets opposite



Top view of barrel

- Constant gen may have subclass like IgG1, igG2
- Light chain is a product of at least 3 genes:
 - Variable (VL) gene
 - Joining region (J) gene
 - Constant region (CL) gene

} responsible of variability
- Heavy chain is a product of at least 4 genes :
 - Variable region (VH) gene
 - Diversity region (D) gene
 - Joining region (J) gene
 - Constant region (CH) gene

- We have 10^8 antibody from 40,000 genes HOW?

- Light chain has 2 constant chain K and λ
 each one has the following

(V)	40	and	λ
(J)	5		30
	= 200		4
			120

By Dr. Ahmad Al-Armoti :P shaif ma a7sani

- Same thing in heavy chain
 $(V)_{51} * (D)_{27} * (J)_6 = 8262$ (without constant)
 - The total = $8262 * (120 + 200) = 2.6 * 10^6$ ((without include of constant heavy chain and mutation))
 - How diversity occur ?
 Answer: rerangment & splicing
 Splicing will increase the diversity of Ig

Immunoglobulins

transcription → pre-mRNA → splicing → mRNA →
transcription and process → 1-chain protein

- Hypervariable region is responsible of specificity of antibody to antigen

Which consist of 3 stretches consists 7-12 amino acids /stretch

- To know the variability of amino acids by remove it and see where it similar in all immunoglobulins
- What do we mean when say the variability for this protein is 30%?

That mean from 100 immunoglobulins it variable in 30 and constant in 70

- **Firmware amino acid:** that not change or its change limit
- Cytochromes C is protein has hemoglobin type C
- In other protein the variability not found or limit compare with immunoglobulins
- **Complementarity determining regions (CDRs)** are regions within antibody (hypervariable) where these proteins *complement* an antigen's shape. Thus, CDRs determine the specificity for specific antigens
- **CDRs** depend on size of antigen

Class	Heavy chain	Chains structure	% in serum	T _{1/2} (days)	Comp. fixation	Placental crossing
IgM	μ	Mono-, penta-, & hexa	5-10	5-10	++++	No
IgG	γ	Monomer	80	23	++	Yes
IgA	α	Mono-, di-, or tri	10-15	6	No	No
IgD	δ	Monomer	0.2-1	3	No	No
IgE	ε	Monomer	0.002	2	No	No

- IgG, IgD and igE only monomer
- IgM penta- five IgM bind together

Immunoglobulins

- IgE is lowest healthy people percentage but increase allergy where IgG is the highest (in serum)
- **EXAM QUESTION**: which is of the following has highest percentage???

Answer: IgG; also have highest half live

- Complement system protein: is part of the immune system

The antibody bind to cell or to (by fc) complement system
all Ig can bind?

No only IgG and IgM ; IgM has higher affinity than IgG

- Only one can crossing the placental is IgG depend in size and which give immunity to fetus even after he/she born for 6 month
- **IgA, IgD, IgG with 3 constant region**
- **IgE, IgM** has extra domain on hinge region

BEST WISHES ^ _ ^