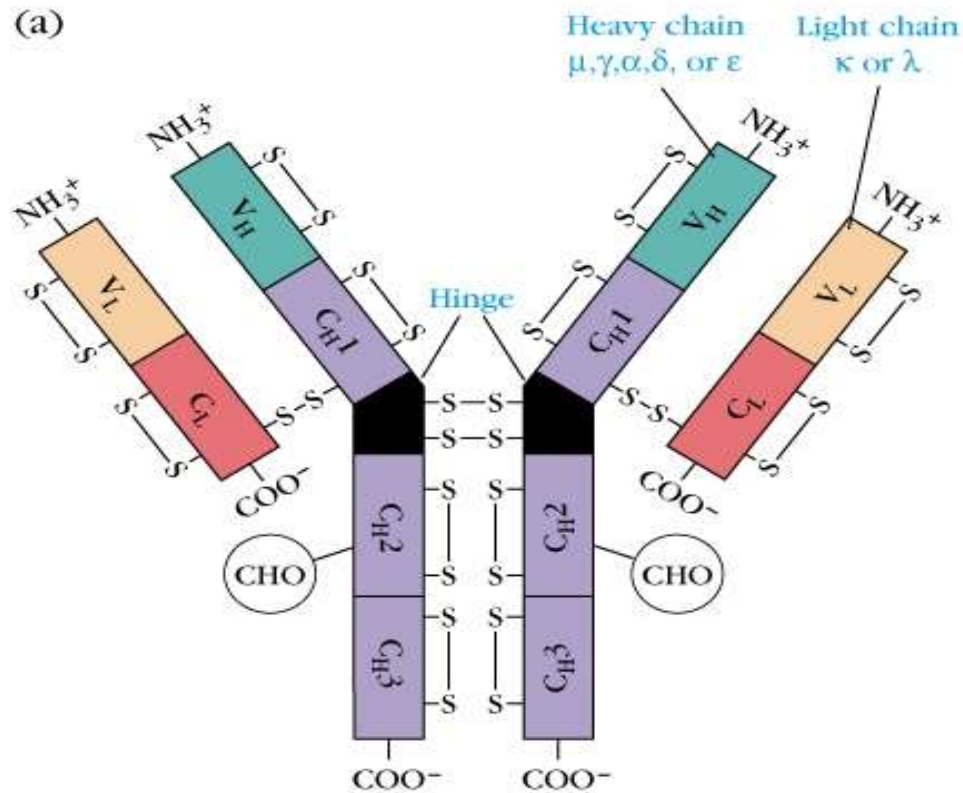
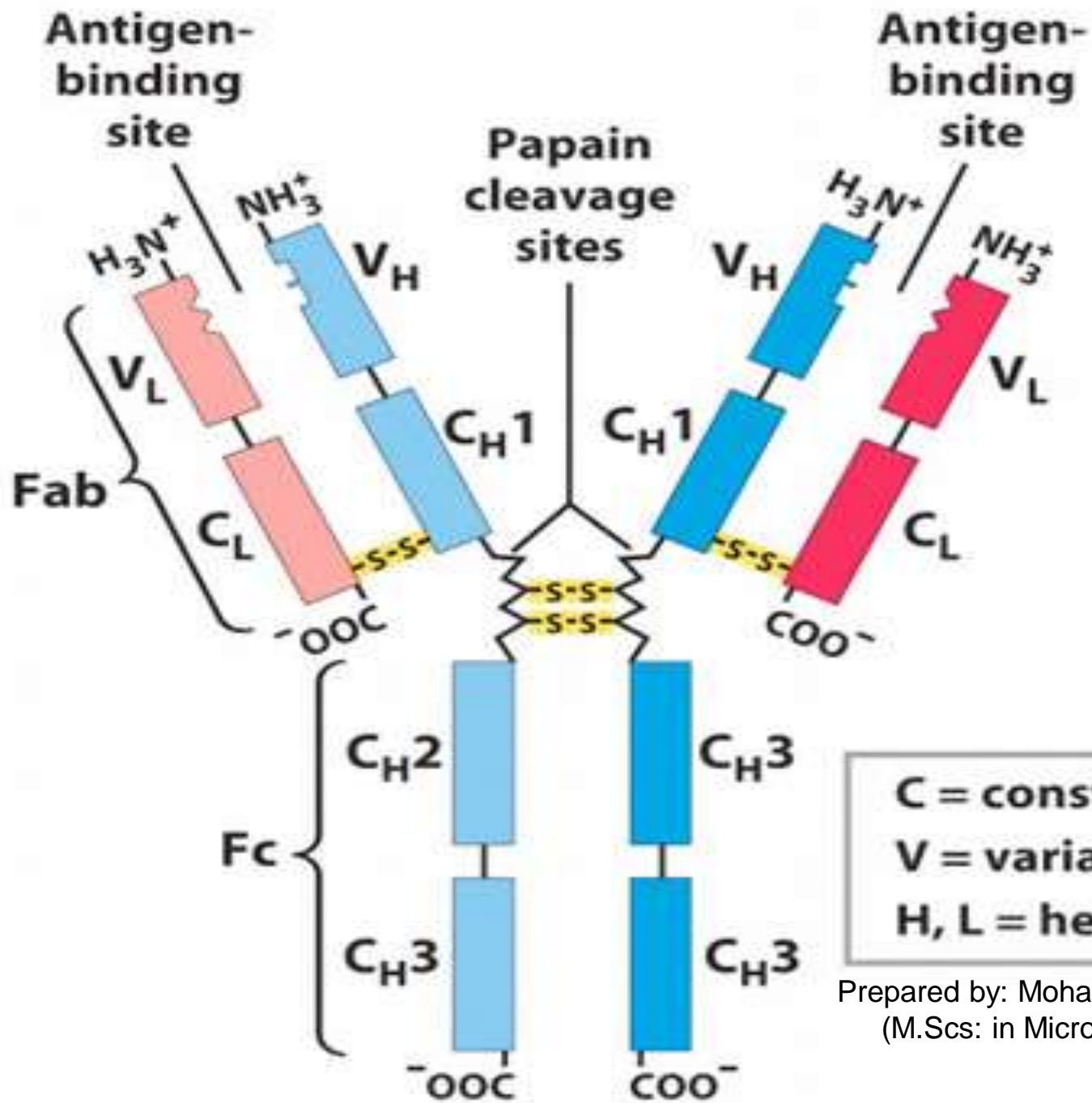


# Immunoglobulin Structure and Function Antibody (Abs)



Prepared by: Mohamed Mohamed Tarik Bashir  
M.Sc.s: in Microbiology and Immunology

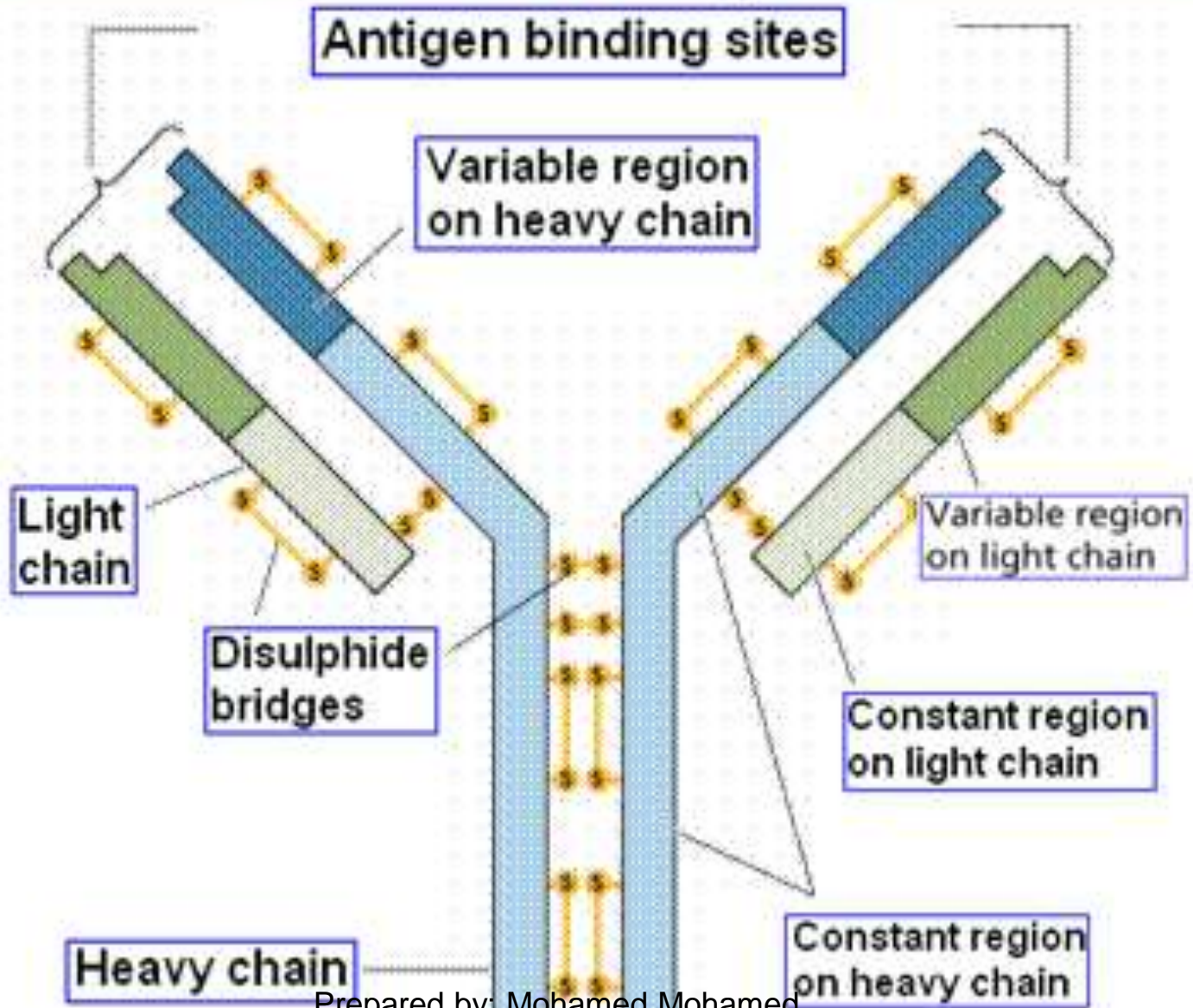
Prepared by: Mohamed  
Mohamed Tarik Bashir (M.Sc.s: in  
Microbiology and Immunology)



**C = constant domain**  
**V = variable domain**  
**H, L = heavy, light chain**

Prepared by: Mohamed Mohamed Tarik E.  
 (M.Sc.s: in Microbiology and Immunology)

# Structural Regions

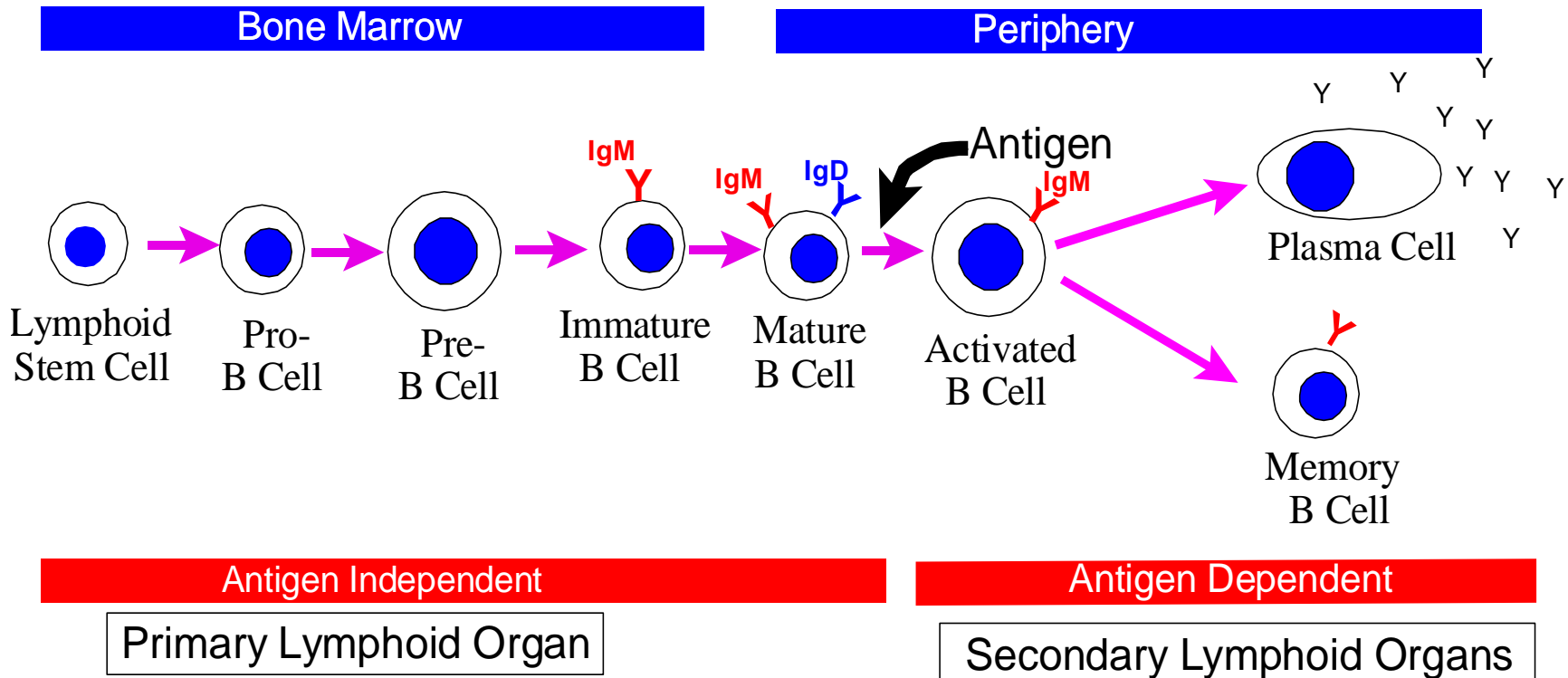


# Humoral Immunity

- Humoral immunity is mediated by antigen-specific proteins called **Antibodies(Abs)**.
- **Antibody (Abs)** also known as **Immunoglobulin (Ig)** is the **large Y shaped protein** produced by the body's immune system when it detects harmful substances, called antigens like (bacteria and viruses). The **production of antibodies** is a major function of the immune system and is carried out by a type of white blood cell called a **B cell (B lymphocyte)**, when B cells release **Antibodies** called **plasma cells**.

- The **humoral immune** response is uniquely adapted for elimination of **extracellular pathogens**.
- B-cell involved in **humoral immunity** when B-cell released **antibodies** called **plasma cell**.

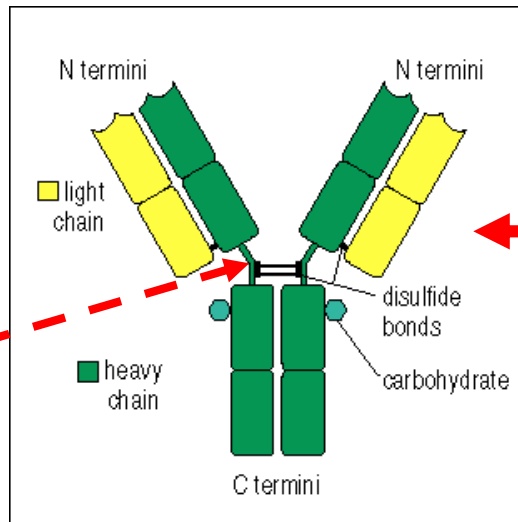
# Overview of B-Cell Development



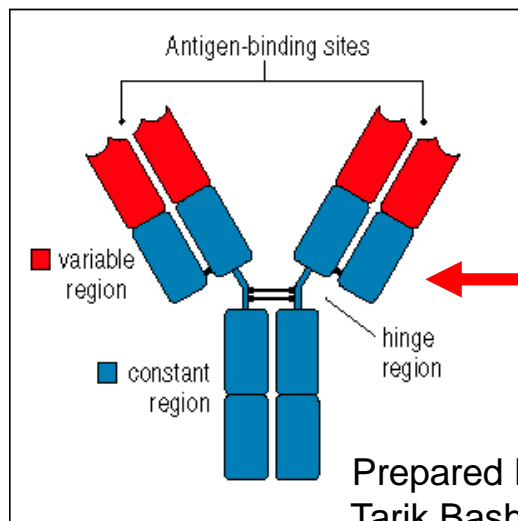
**Concept:** Antibodies are composed of polypeptides with variable and constant regions.

### THE IMMUNOGLOBULIN G MOLECULE

Hinge



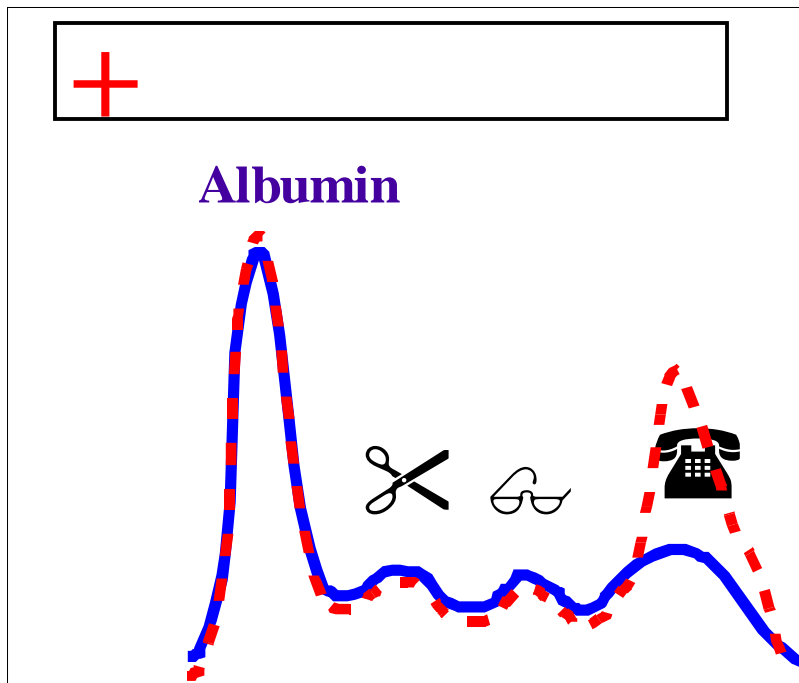
Made up of : 2 identical heavy chains (green) 25 KDa and 2 identical light chains (yellow) 50 KDa.



Note: Location of the **variable** (red) and **constant** (blue) regions in the antibody molecule.

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and Immunology)

# Antibodies are Found in the Gammaglobulin Fraction of Serum



— **Antibodies**: it portion of gamma globulin

**The B cells are activated and undergo two important changes.**

**Antibody affinity**: refers to the tendency of an **antibody** to bind to a specific epitope at the surface of an antigen.

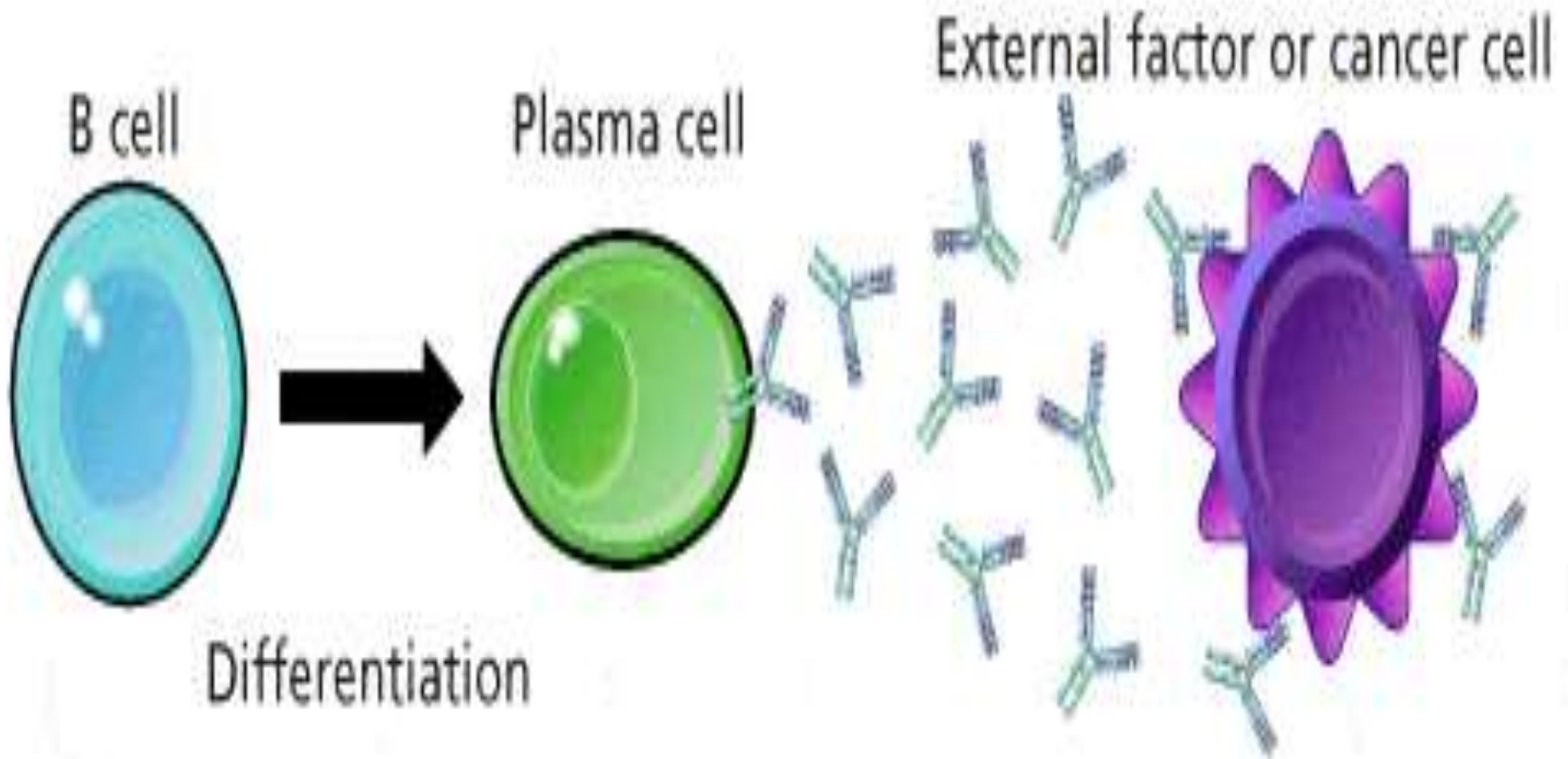
**(is the strength of the interaction).**

**Antibody avidity**: Is the measurement of the total binding strength of an **antibody** at every binding site is termed **avidity**.



# Where else are antibodies found in the body?

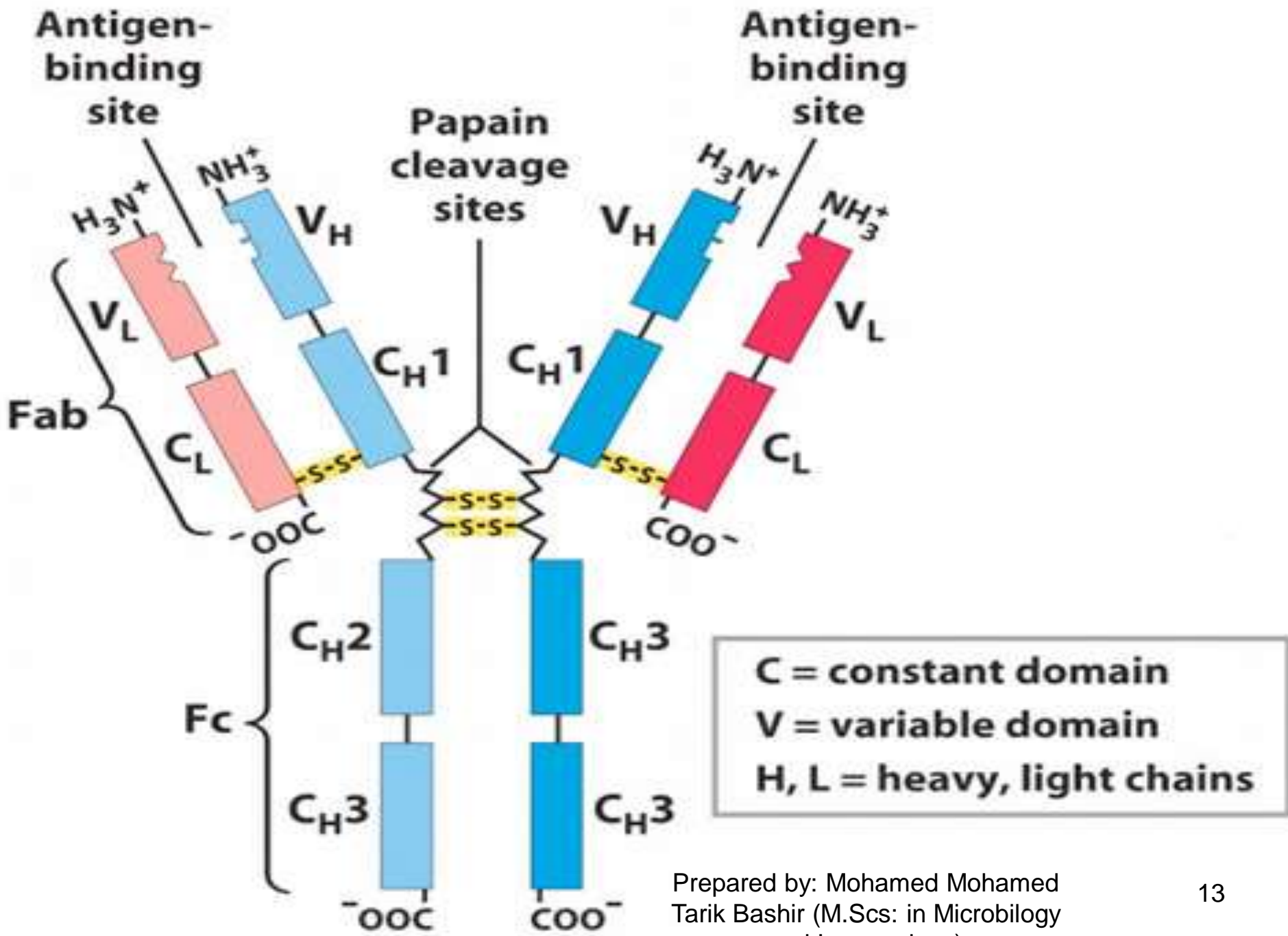
- The **antibodies** found in the fluid part of blood, In addition the **anti-bodies** are found in several anatomic locations.
  - **Cytoplasm and cell surface of B lymphocytes**
  - **Interstitial spaces**
  - **Secretory fluids (mucous, tears, milk) (IgA)**
  - **Surface of certain immune effectors cells** which do not synthesize **antibody** but have specific receptors Fc receptors that bind antibody molecules.



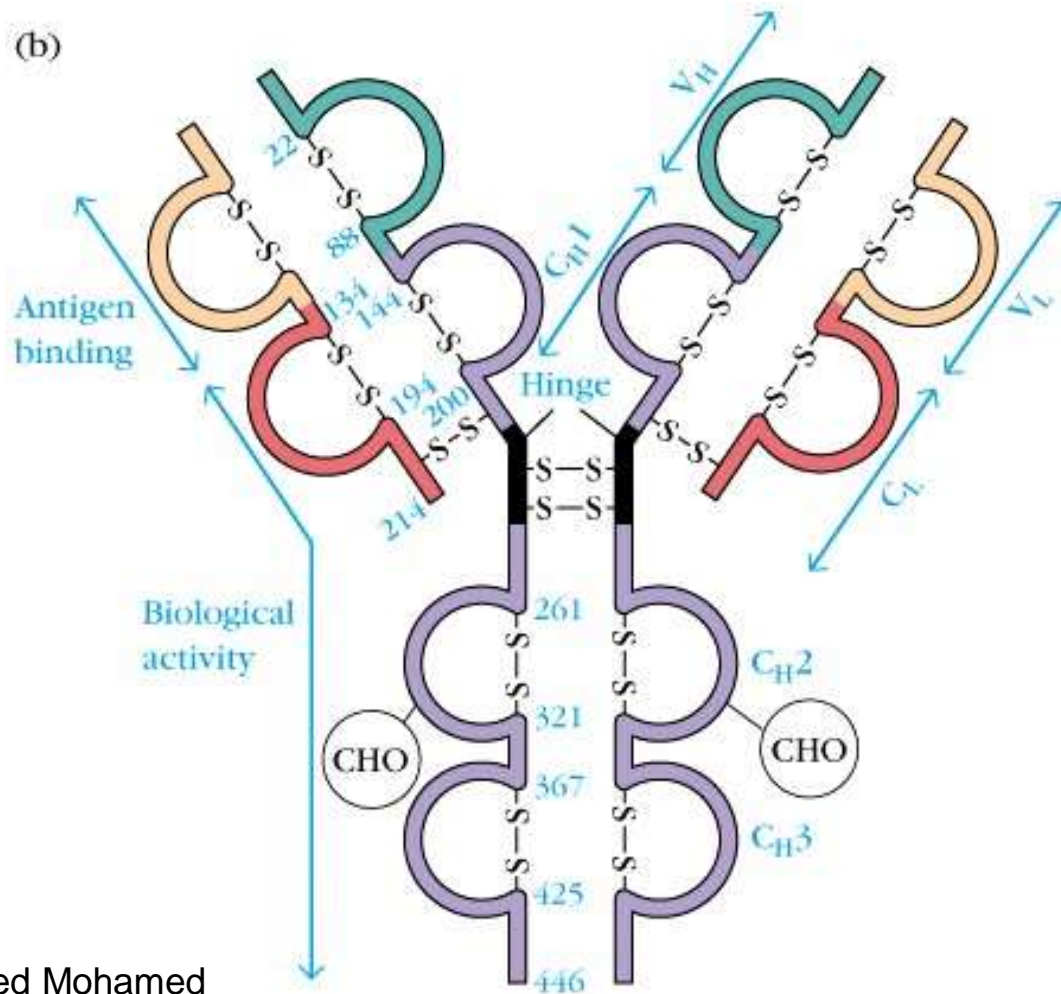
# STRUCTURAL BASIS OF ANTIBODY DIVERSITY

- The **antibody** molecule has two separate functions: one is to **bind specifically to molecules from the pathogen** that elicited the immune response(**Fab region**); the other is to **interact with various cells and molecules to destroy the pathogen** once the antibody is bound to it(**Fc region**).

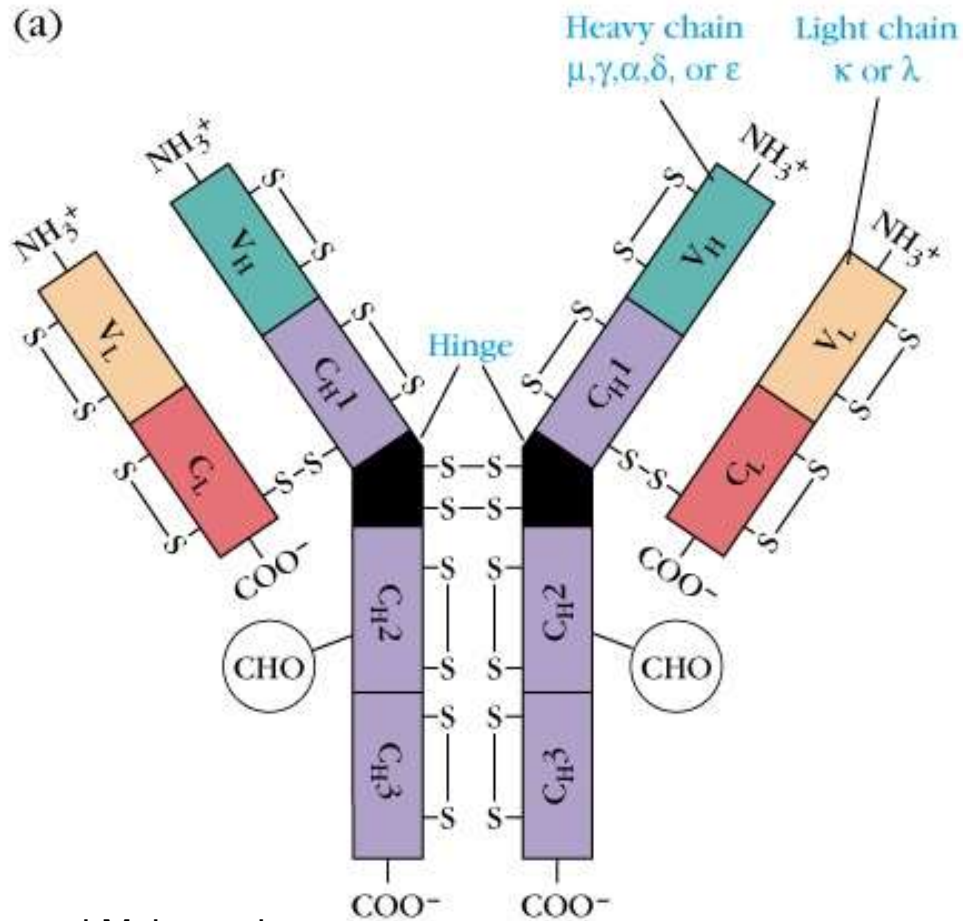
- These functions are **structurally separated** in the **antibody** molecule, one part of which specifically **recognizes antigen** and the **other engages effectors mechanisms that dispose of it.**
- The antigen-binding region varies extensively between **antibody** molecules and thus is known as the **variable region** or **V region.(Fab)**
- The region of the antibody molecule that engages the effector functions of the immune system does not vary in the same way and is thus called the **constant region** or **C region.**



# H and L chains are comprised of discrete domains



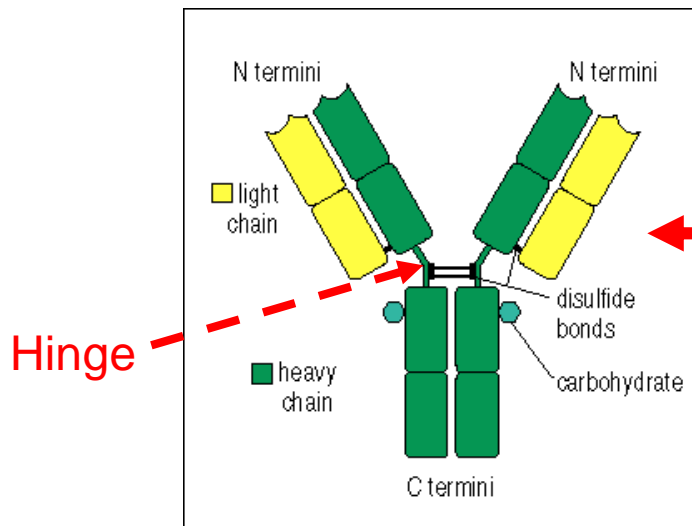
# Schematic of Immunoglobulins



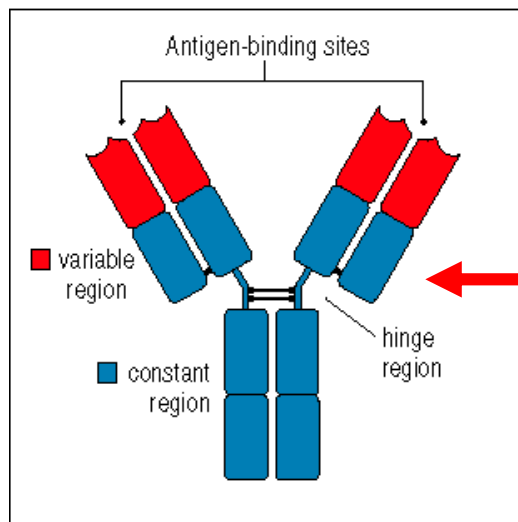
Prepared by: Mohamed Mohamed  
Tarik Bashir (M.Sc.s: in Microbiology  
and Immunology)

**Concept:** Antibodies are composed of polypeptides with variable and constant regions.

## THE IMMUNOGLOBULIN G (IgG) MOLECULE



Note: 2 identical heavy chains (green) and 2 identical light chains (yellow).



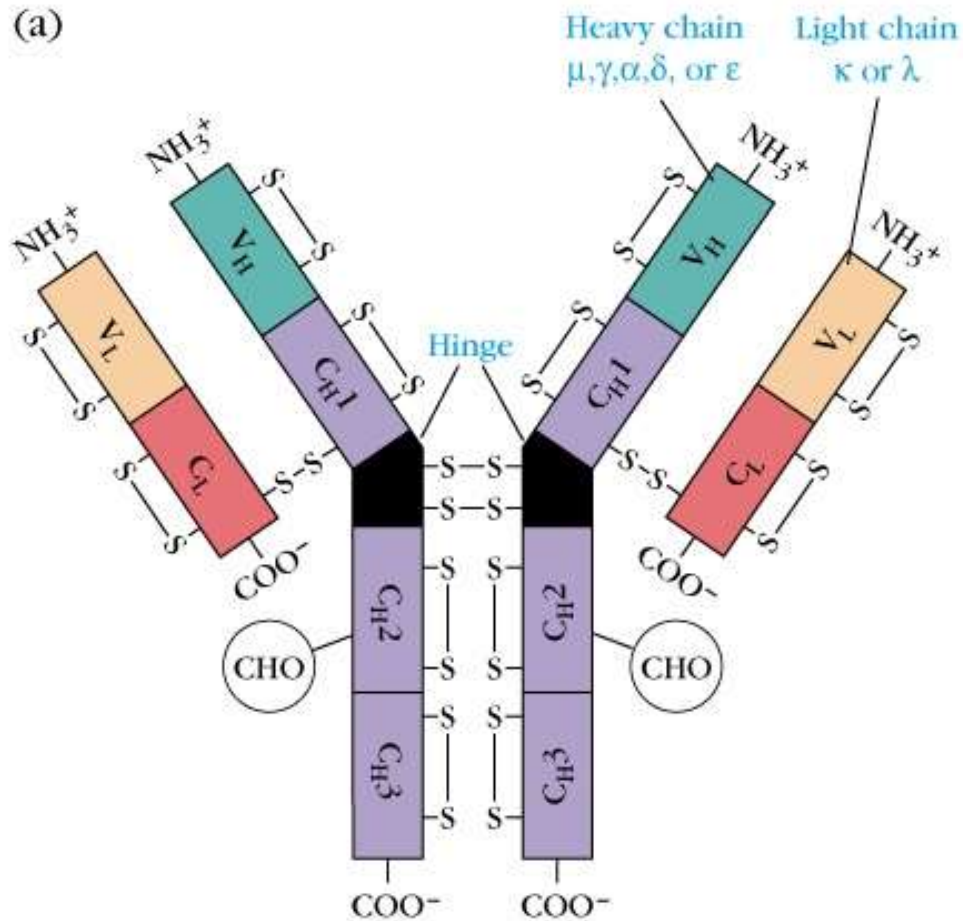
Note: Location of the variable (red) and constant (blue) regions in the antibody molecule.



# Immunoglobulin Structures

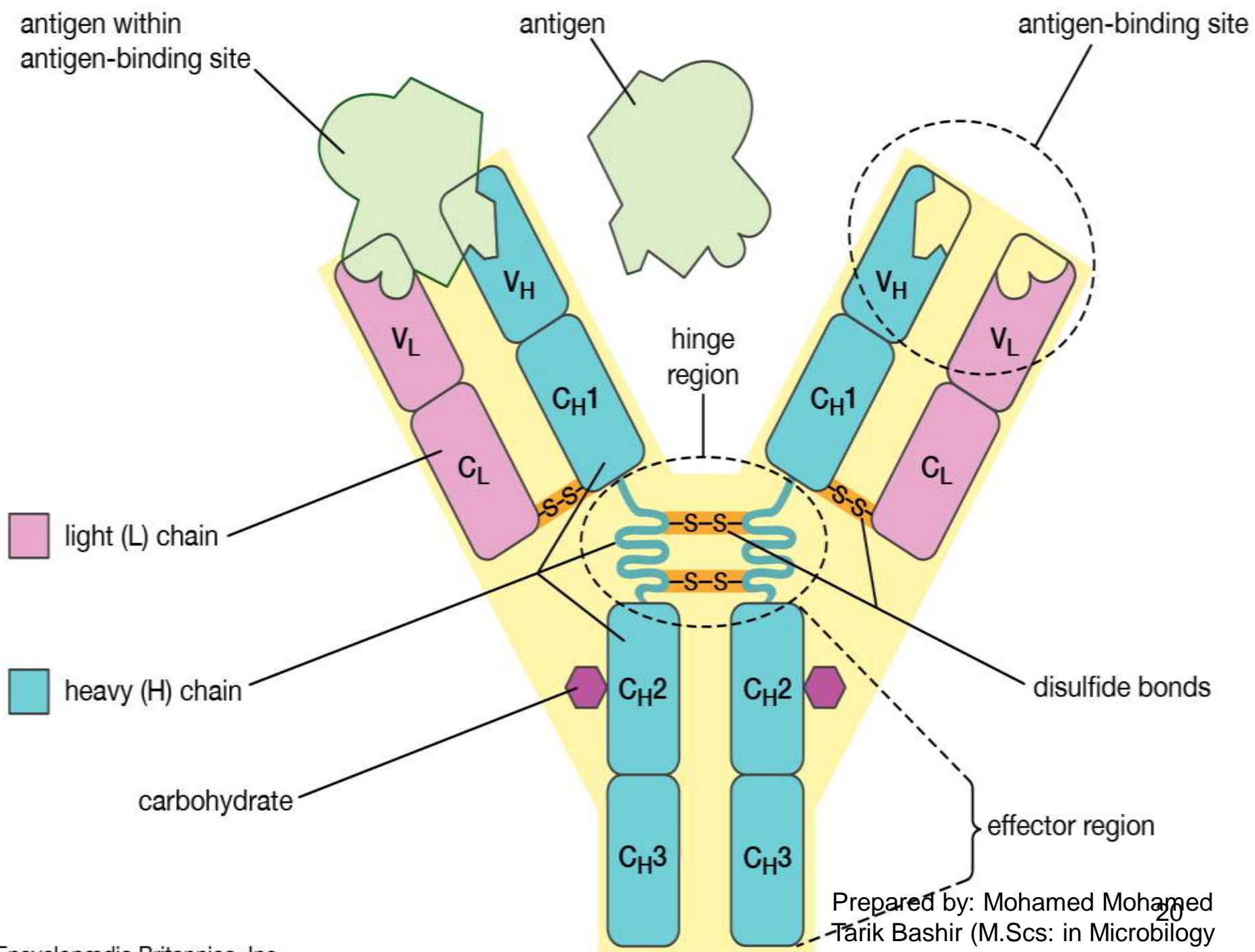
- **Light chain sequencing:**
  - The amino terminal half of the L chains varied considerably between different isolates – termed the **variable (V) region**
  - The carboxyl terminal half of the L chain – called the **constant (C) region**. – had two basic amino acid sequences – i.e. two types of light chains – **kappa ( $\kappa$ )** and **lambda ( $\lambda$ )**. Subsequently it was shown that there are three – four subtypes of lambda chains –  $\lambda_1$ ,  $\lambda_2$ , etc
- **IMPORTANT NOTE:** A single **antibody** molecule contains only one light chain type – never both.

# Schematic of Immunoglobulins



# Immunoglobulin Structures

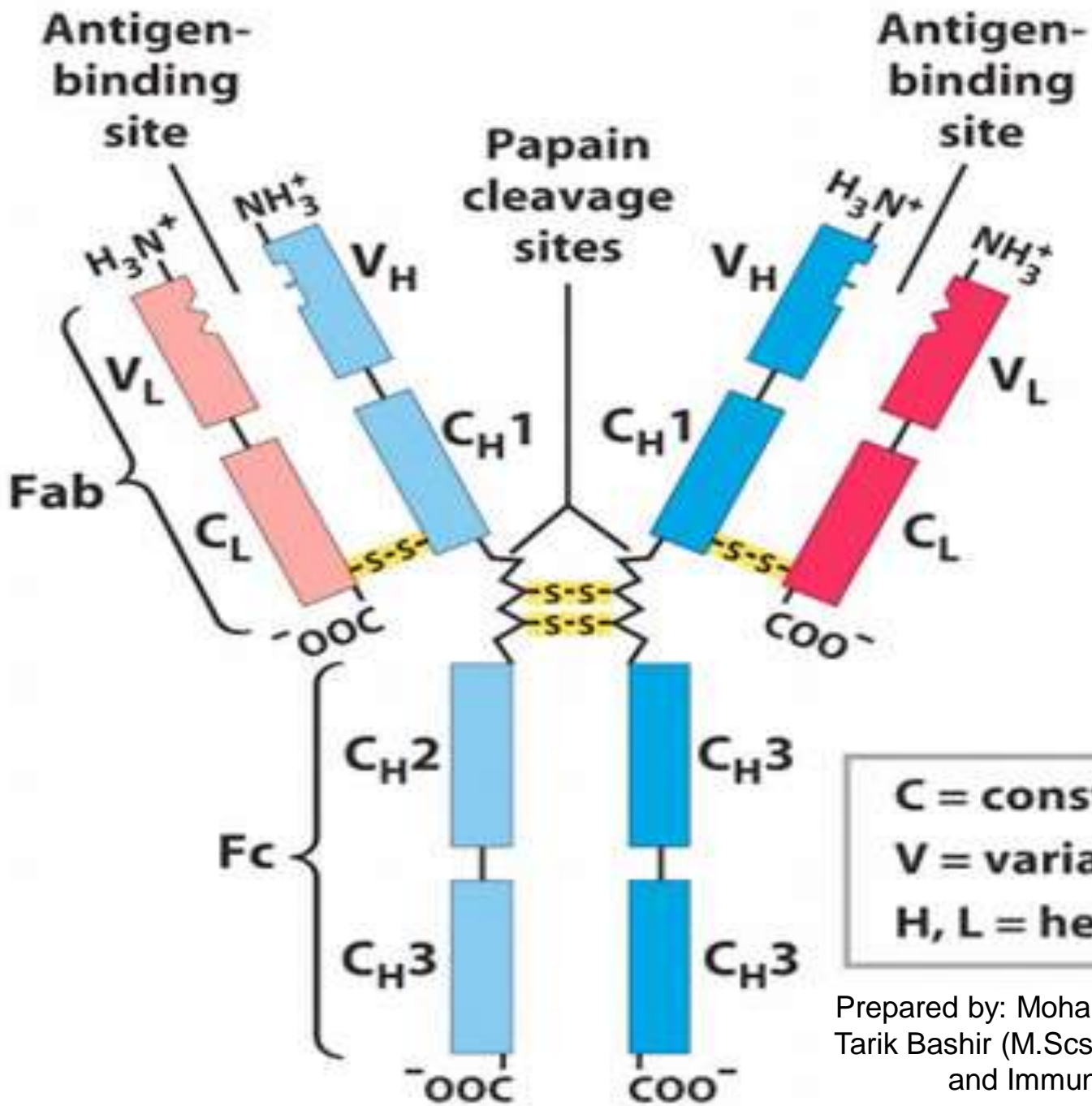
- **Heavy chain sequencing:**
  - The amino terminal 110 amino acids make up the variable region
  - The remaining part of the H chains showed five basic sequence patterns corresponding to five different heavy-chain constant (C) regions ( $\gamma$ ,  $\alpha$ ,  $\mu$ ,  $\delta$ ,  $\epsilon$ )
  - Each of these five different heavy-chains is called and **isotype**.
  - The constant regions of  $\mu$  and  $\epsilon$  are larger than the constant regions of  $\gamma$ ,  $\alpha$ , and  $\delta$  due to the presence of an extra constant domain.
- A single **antibody** molecule contains a single type of heavy-chain.



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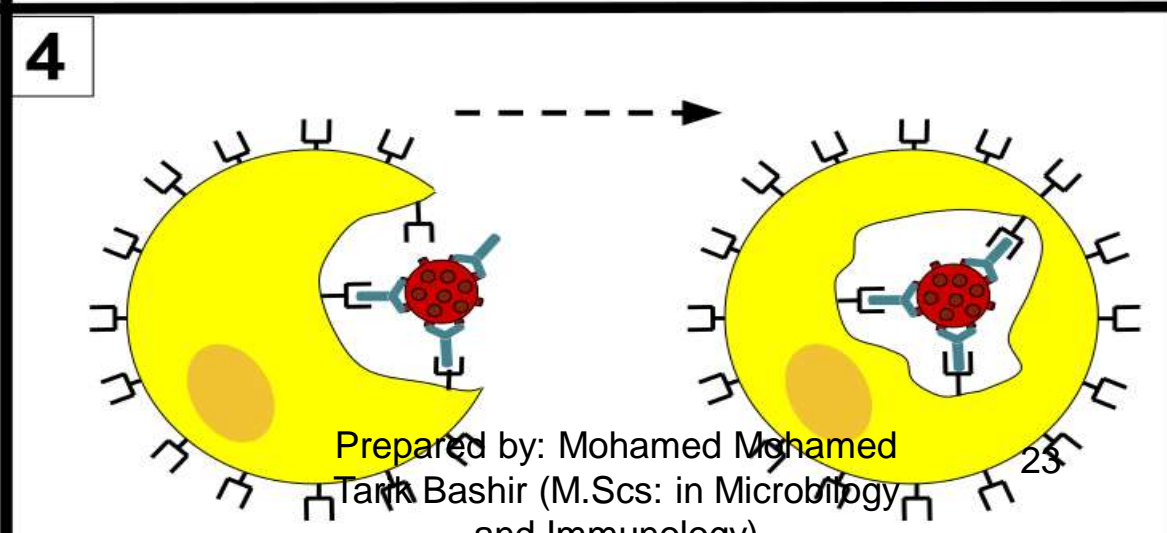
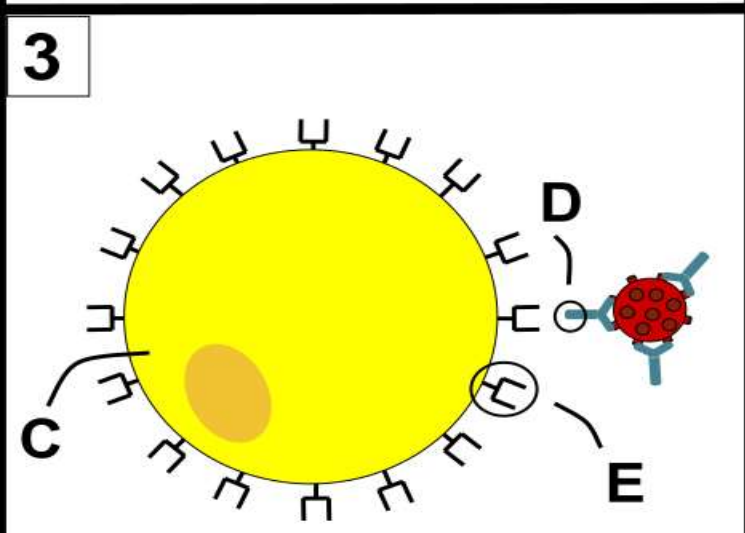
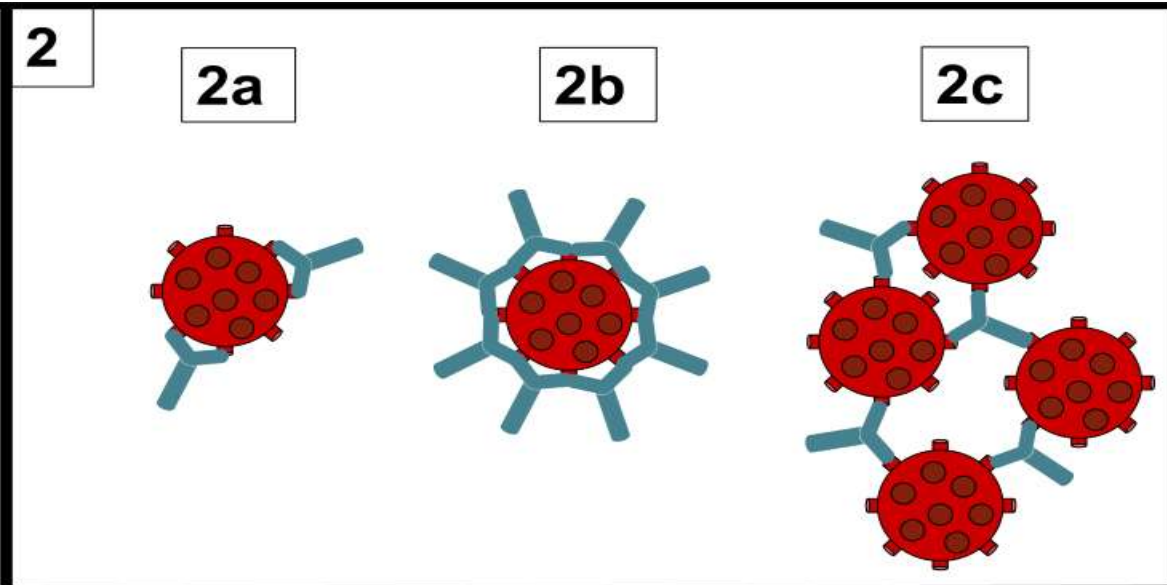
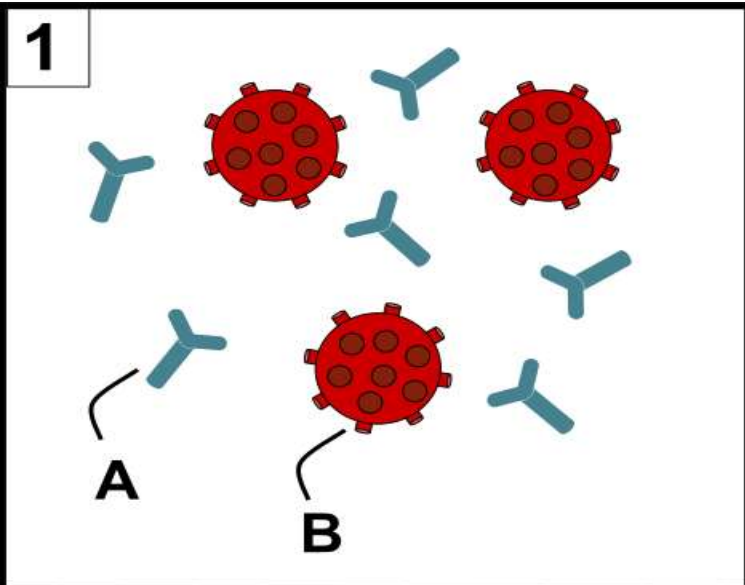
**TABLE 4-1 CHAIN COMPOSITION OF THE FIVE IMMUNOGLOBULIN CLASSES IN HUMANS**

Class	Heavy chain	Subclasses	Light chain	Molecular formula
IgG	$\gamma$	$\gamma 1, \gamma 2, \gamma 3, \gamma 4$	$\kappa$ or $\lambda$	$\gamma_2\kappa_2$ $\gamma_2\lambda_2$
IgM	$\mu$	None	$\kappa$ or $\lambda$	$(\mu_2\kappa_2)_n$ $(\mu_2\lambda_2)_n$ $n = 1$ or $5$
IgA	$\alpha$	$\alpha 1, \alpha 2$	$\kappa$ or $\lambda$	$(\alpha_2\kappa_2)_n$ $(\alpha_2\lambda_2)_n$ $n = 1, 2, 3,$ or $4$
IgE	$\epsilon$	None	$\kappa$ or $\lambda$	$\epsilon_2\kappa_2$ $\epsilon_2\lambda_2$
IgD	$\delta$	None	$\kappa$ or $\lambda$	$\delta_2\kappa_2$ $\delta_2\lambda_2$



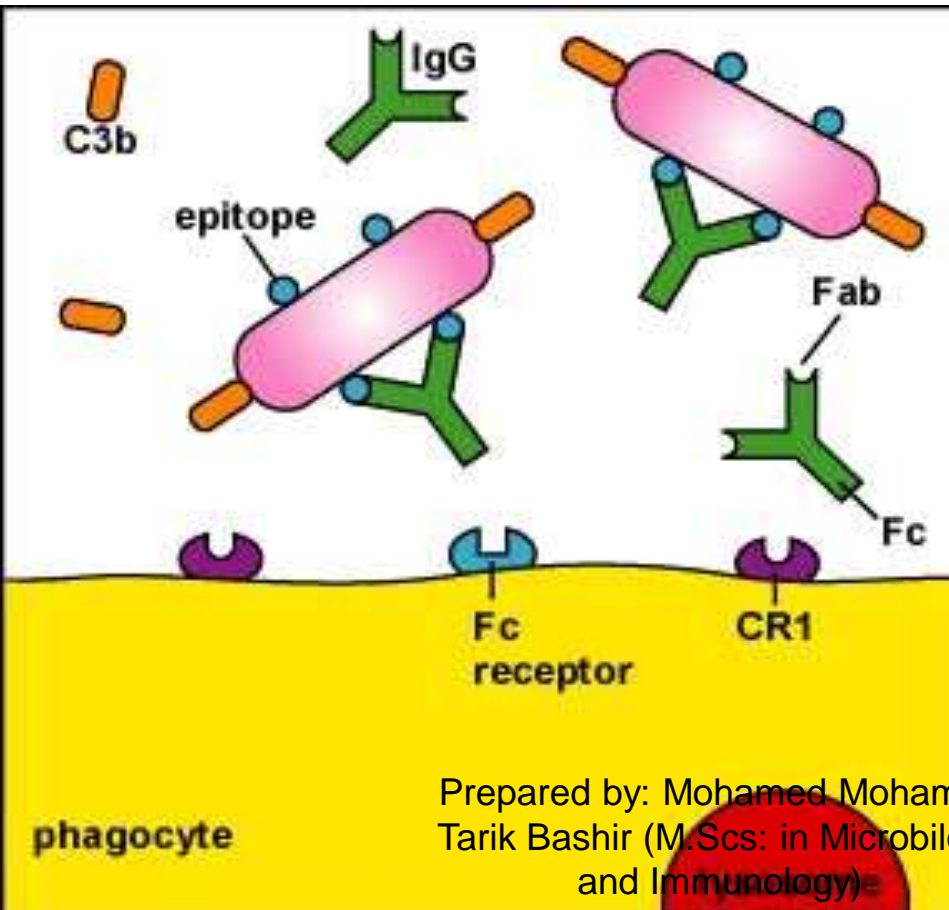
Prepared by: Mohamed Mohamed  
 Tarik Bashir (M.Sc.s: in Microbiology  
 and Immunology)

# Opsonization by **Antibodies**

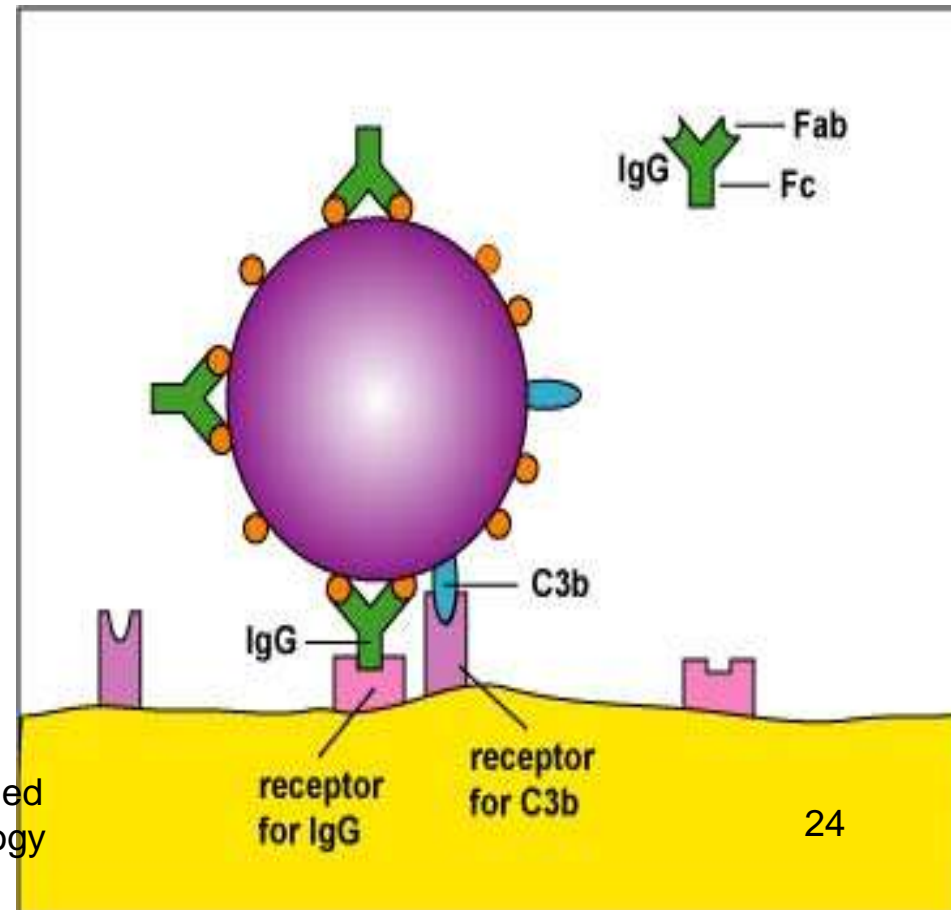


# Antibodies dispose from Antigens

1) **Antibodies** bind to Antigens by Fab region



2) **Antibodies** attach to FC receptor on phagocytic cell.





# Immunoglobulin Domains

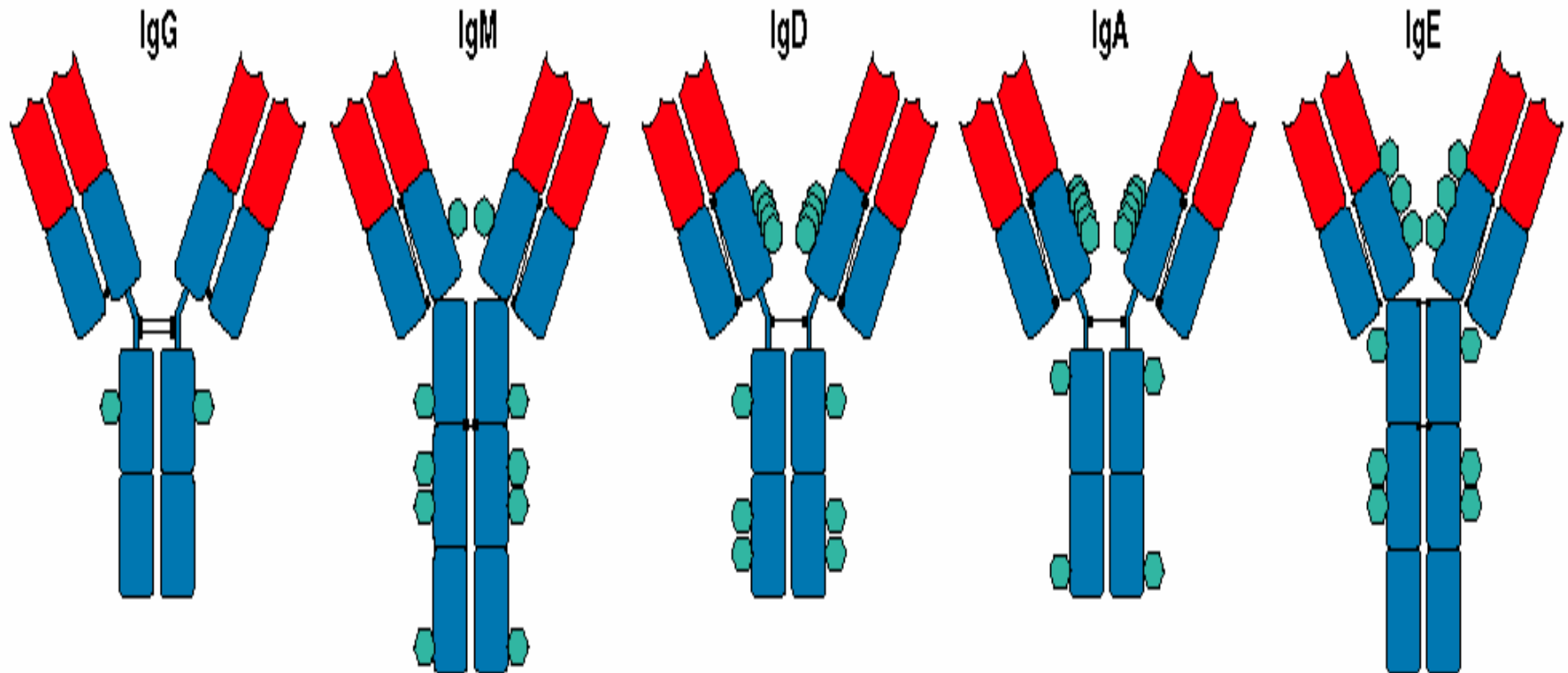
- **Both H and L chains** contain several homologous units of about 110 amino acids termed .
- **L chains** contain one **variable** domain ( $V_L$ ), and one **constant** domain ( $C_L$ )
- **H chains** contain one **variable** domain – ( $V_H$ ) – and **either three** or **four constant** domains – ( $C_{H1}$ ,  $C_{H2}$ ,  $C_{H3}$ , and  $C_{H4}$ ) **depending** on the **antibody** types.

# Constant-Region Domains

- The carboxyl-terminal domains of **immunoglobulins** display considerably less sequence variability within a given isotype than observed for **V-region domains**. These domains are referred to as **constant (C) regions**.
- **H-chain C regions** are numbered (**C<sub>H</sub>1, C<sub>H</sub>2, C<sub>H</sub>3, and C<sub>H</sub>4**).
- The **C region** domains of the **H-chain** have been shown to be responsible for many aspects of **antibody** function, including **interaction with Fc receptors, complement fixation, transplacental transfer**, the ability to form multimer, and the capacity to be **secreted across mucosal surfaces**.

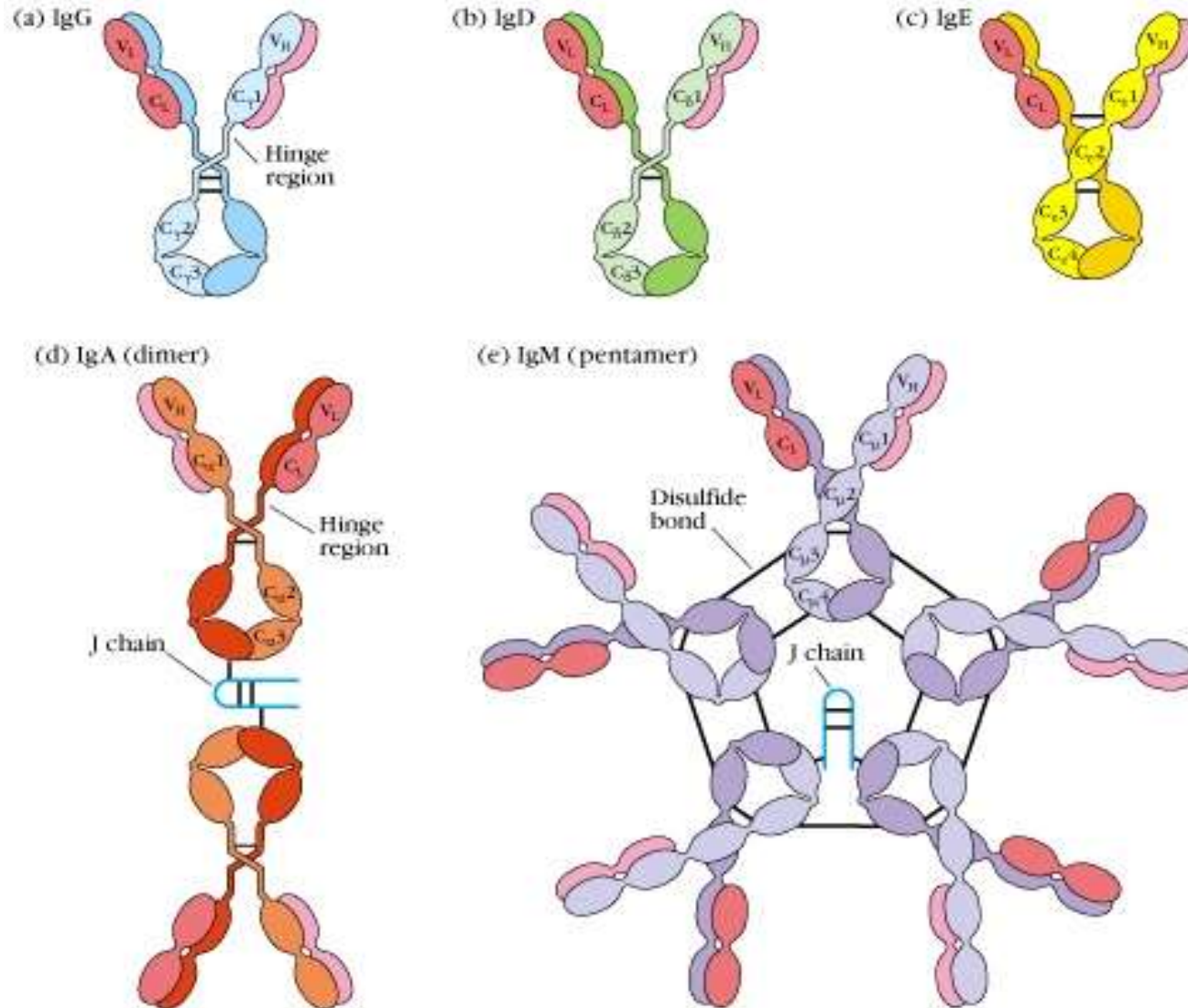
- Because different H-chain isotypes have different **Constant region** domains, these capabilities vary with the class of the particular **antibody**.
- **Five major classes** of **H-chain C regions** exist: ( $\gamma$ ,  $\alpha$ ,  $\mu$ ,  $\delta$ ,  $\epsilon$ ). As a direct consequence of the correlation between the H-chain class of an antibody and its resultant effector functions, **immunoglobulins** have been **named according to their heavy chain**, i.e., IgG, IgA, IgM, IgD and IgE.

**Concept:** All classes of **antibody** have the same basic structure. Two identical heavy chains and two identical light chains: each of which contributes to antigen binding.



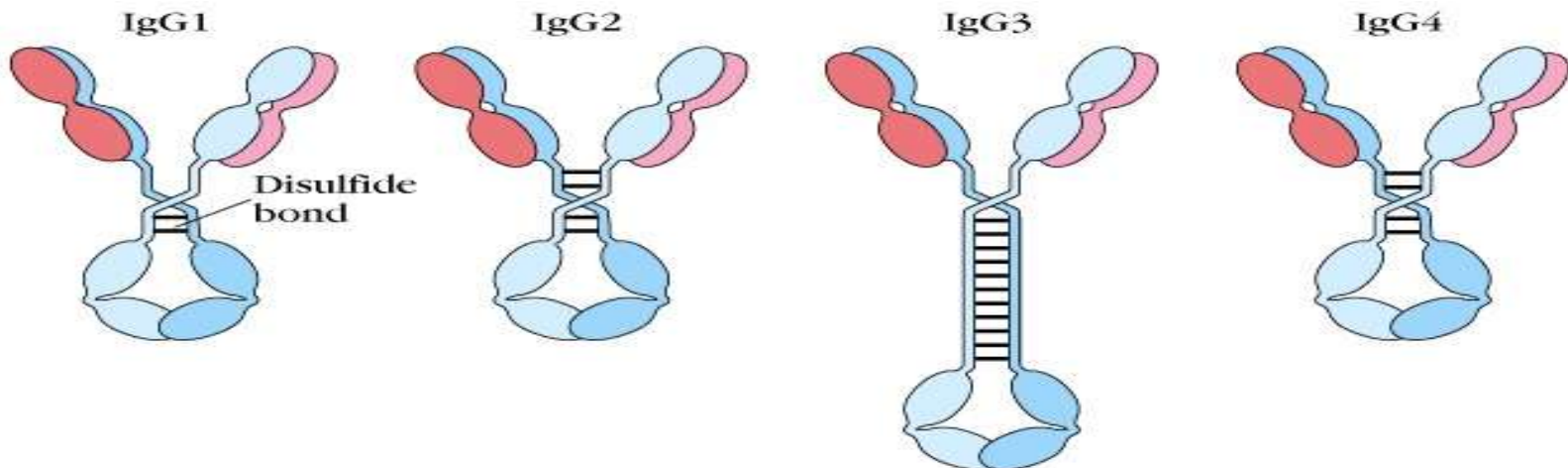
### The Structural Organization of the Human Immunoglobulin Isotypes.

# Structure of the 5 Major Classes of **Antibody**



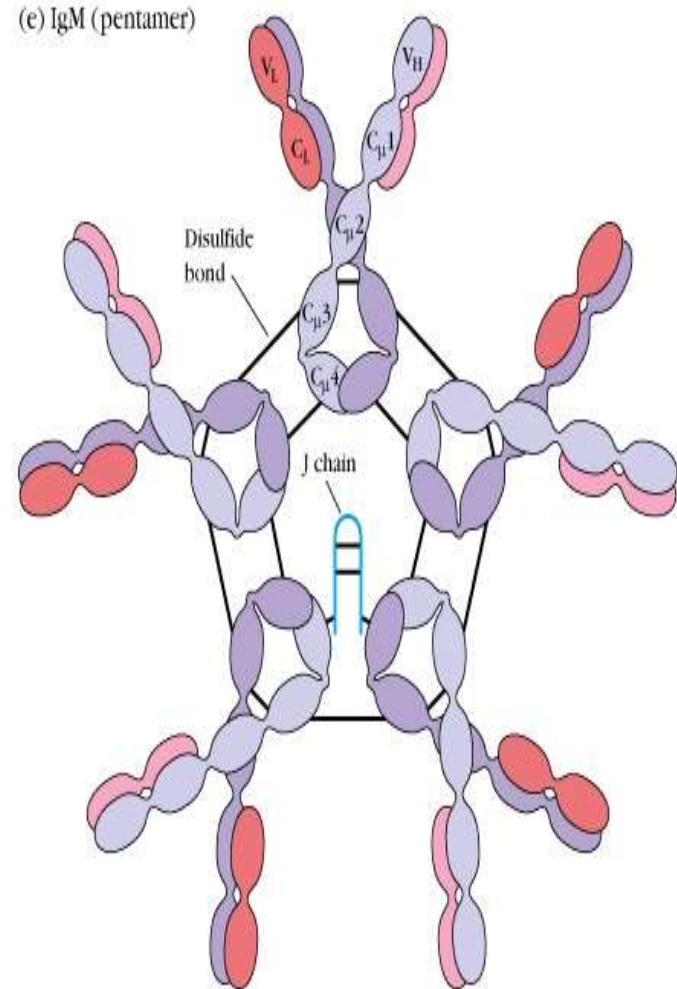
# Immunoglobulin G (IgG)

- The most abundant class in serum ~75% of the total **serum immunoglobulins**.
- **IgG** is found also in the interstitial spaces.
- In both mouse and man there are four subclasses of **IgG**.
- **IgG** can fix complement **except IgG4**.
- **IgG** is the only immunoglobulin to cross the **placenta except IgG2**.
- **IgG** reacts with **FcR's** on **phagocytic cells to promote opsonization**.



# Immunoglobulin M (IgM)

- **IgM** is the **third most abundant immunoglobulin** in the **serum**.
- IgM is secreted by plasma cells as a **pentamer** in which five monomer units are held together by disulfide bonds. Each **pentamer** contains an additional polypeptide called **J (joining) chain**.

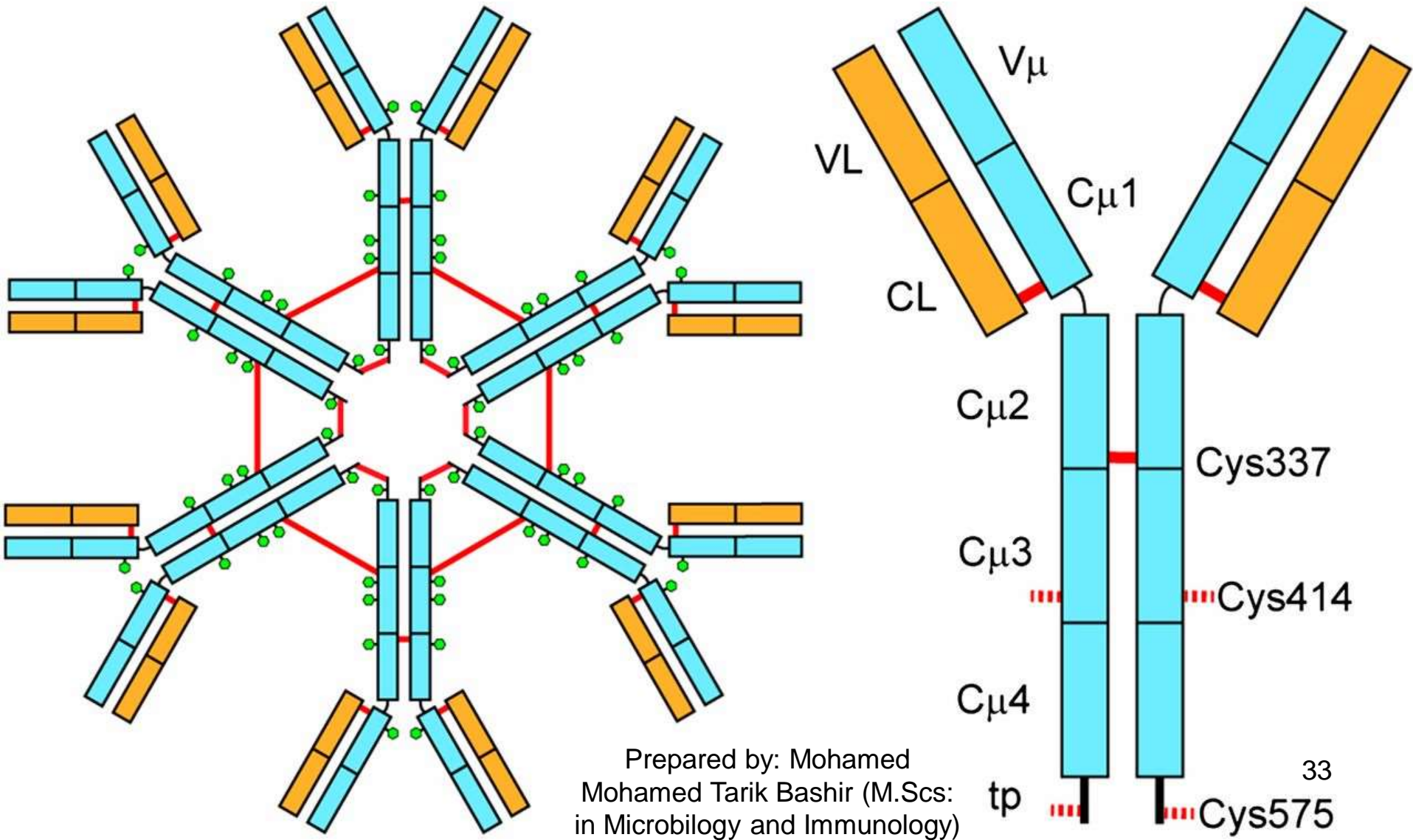


# Immunoglobulin M (IgM)

- Due to its large molecular size **IgM** is **excluded** found to in the interstitial spaces unless there is a **breaking** in the endothelium.
- **IgM** found in **monomeric** form is located on the **surface of B cells** as part of the B-cell antigen receptor.
- **IgM** is the **first** isotype to be produced **in a primary immune** response, and is also the **first** isotype to be produce by the **neonate**.
- **IgM** is very **efficient** at **fixing complement**.
- **IgM does not cross the placenta**.
- The presence of J chain allow **IgM** to bind to receptors on secretory cells, which transport it across epithelial linings to the external secretions that bathe mucosal surfaces.

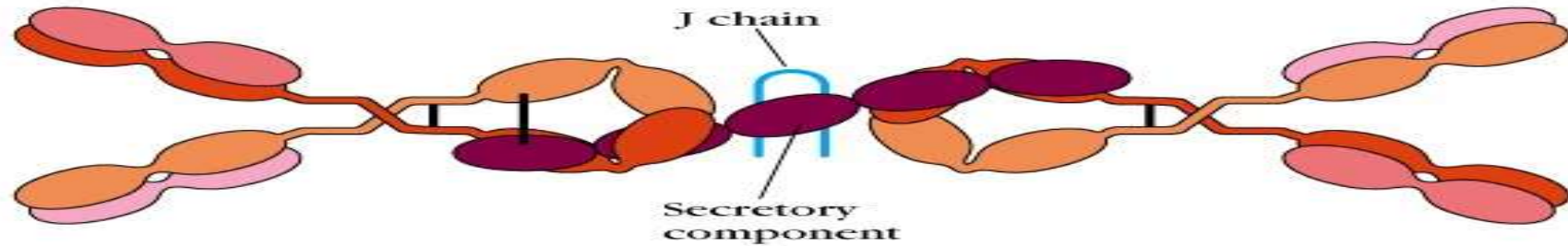


# Immunoglobulin M (IgM)



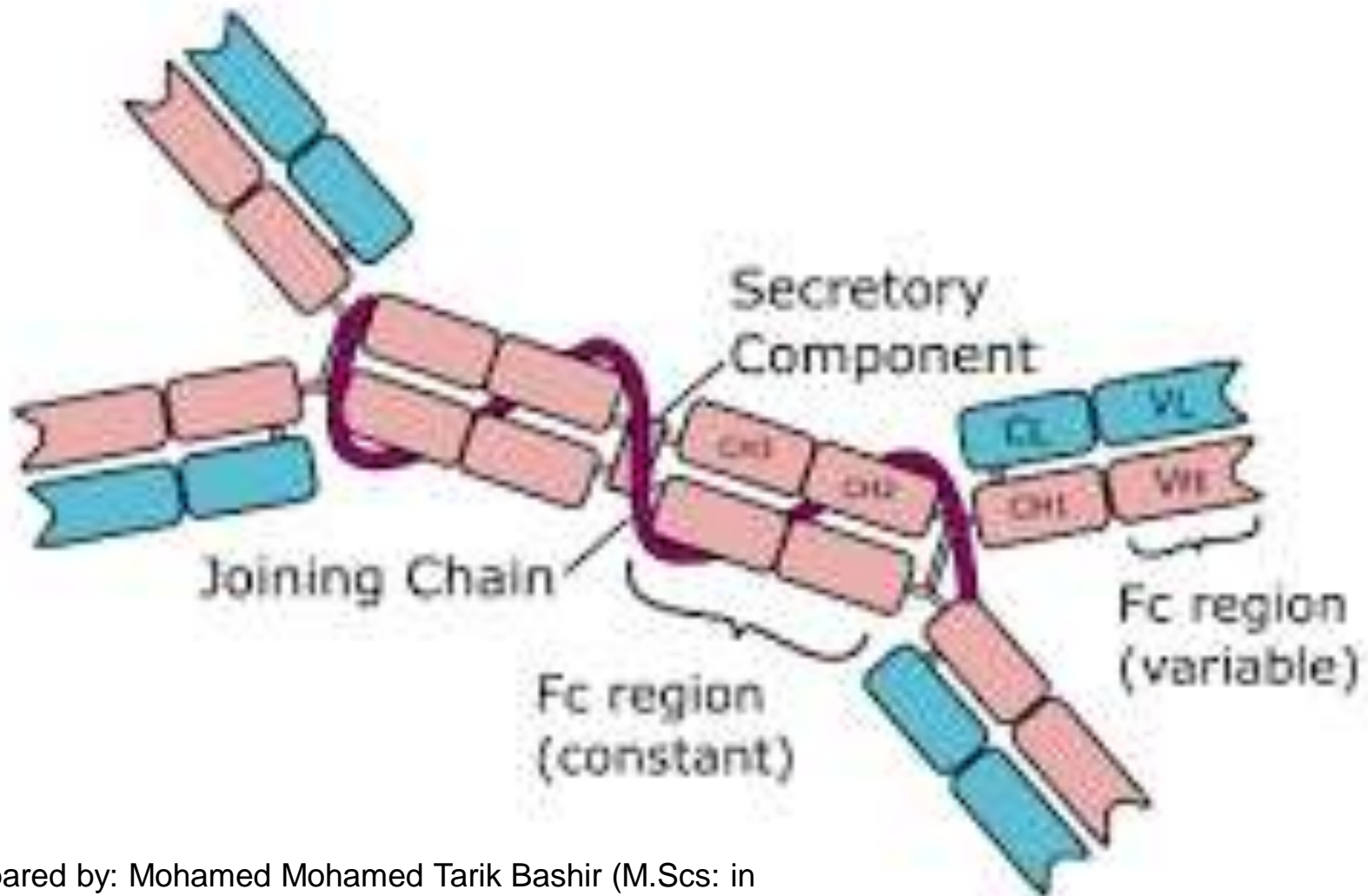
# Immunoglobulin A (IgA)

(a) Structure of secretory IgA



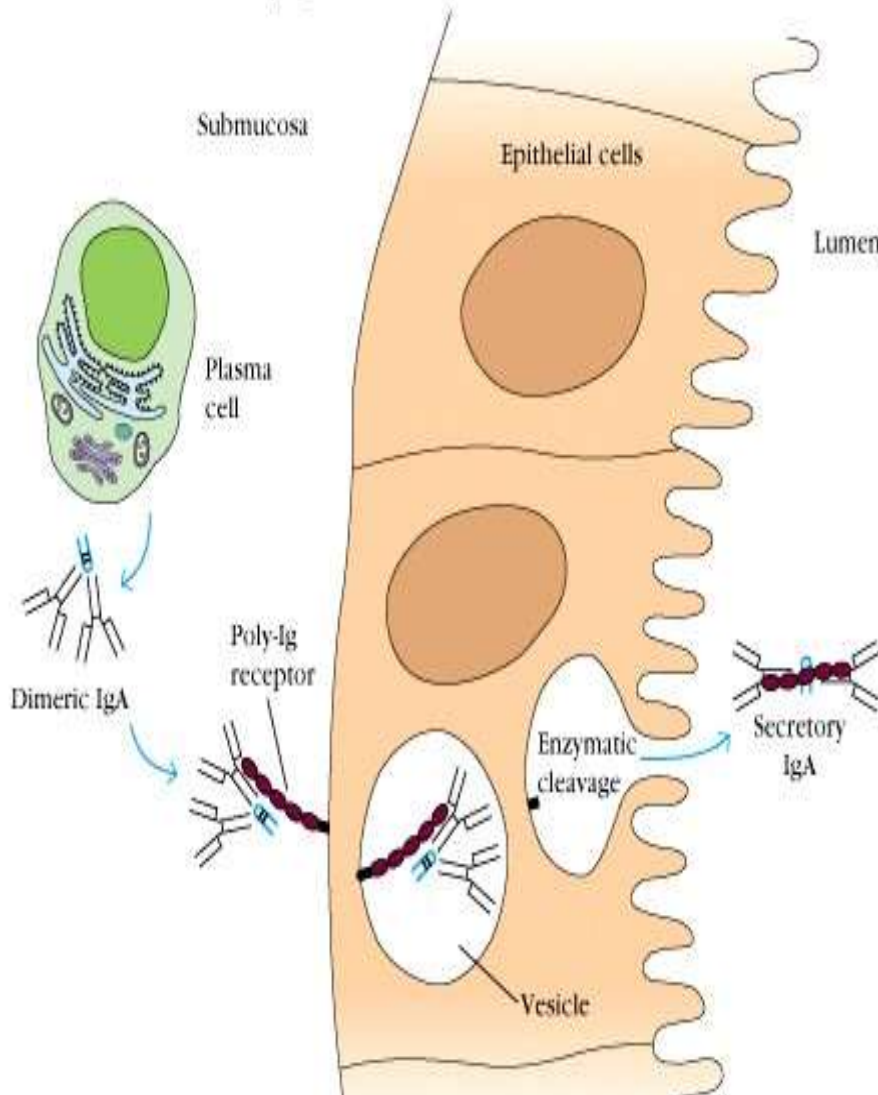
- **IgA** is the second most abundant immunoglobulin in serum.
- **IgA** is the most **abundant immunoglobulin** in **external secretions** such as **breast milk**, **saliva**, **tears**, and **mucus** of the **bronchial**, **genitourinary** and **gastrointestinal tracts**.
- In serum **IgA** is primarily a monomer.
- In secretions **IgA** (termed **secretory IgA**) is predominately a dimer but higher multimers do exist.
- Secretory **IgA** has an associated J chain and a polypeptide chain called **secretory component** which is derived from the receptor that is responsible for transporting polymeric **IgA** across membranes.

# Immunoglobulin A (IgA)



# Formation of Secretory Ig A

(b) Formation of secretory IgA



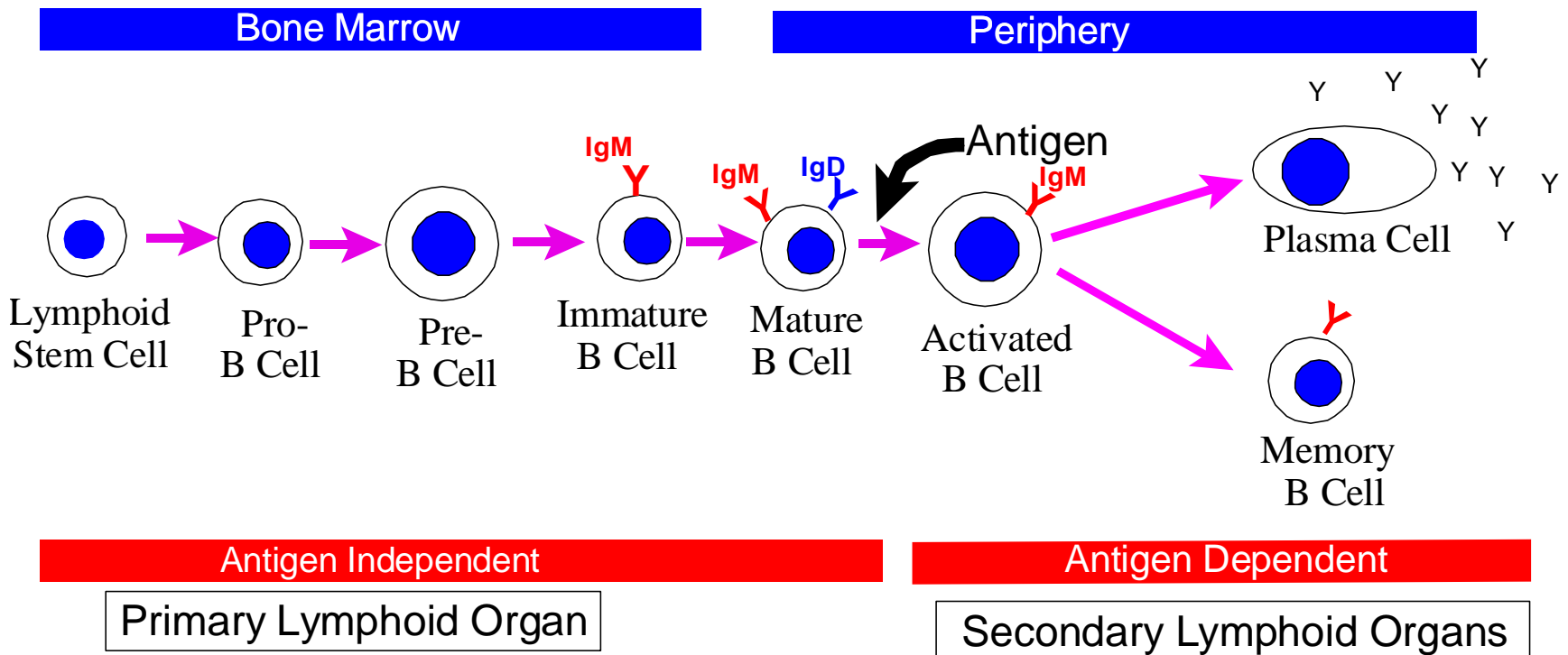
- **Secretory IgA** consists of at least two **IgA** molecules covalently linked by J chain and with the secretory component.
- Polymeric **IgA** produced by plasma cells located in the submucosa binds to the **poly-Ig receptor** on epithelial cells, and the complex is transported to the luminal surface of the mucosa. The **poly-Ig** receptor is enzymatically cleaved during the transport process and becomes the secretory component of **secretory-IgA**

# IgE

- **IgE** binds to **mast cells** and **basophils** through a high **affinity** FcR and is involved in mediating hypersensitivity reactions.
- **IgE** can be found in parasitic infection

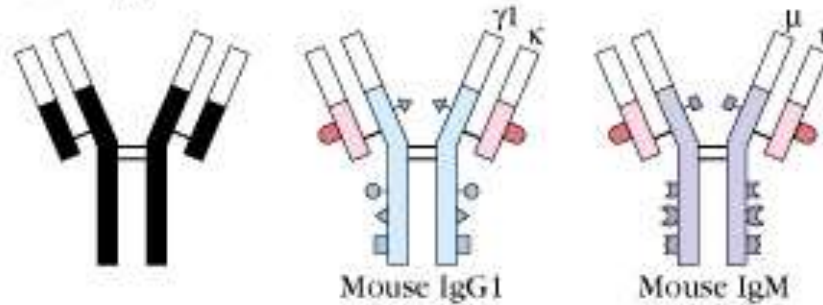
# IgD

- The principal role of **IgD**: Located on the surface of B-lymphocytes and along with **IgM** serves the function of antigen recognition by the B cell.
- There are no known effector functions of **IgD**.

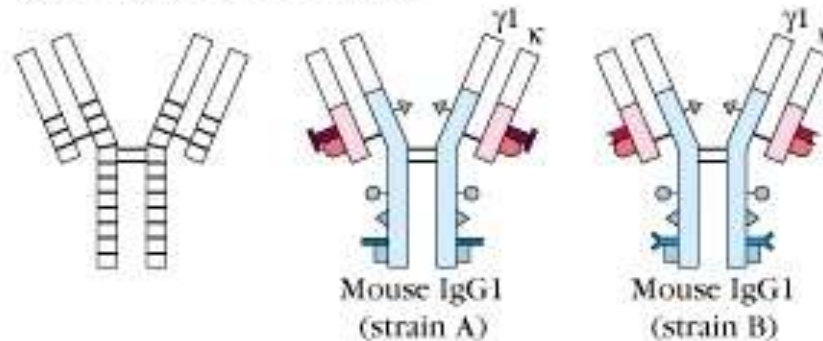


# Antigenic Determinants of Ig's

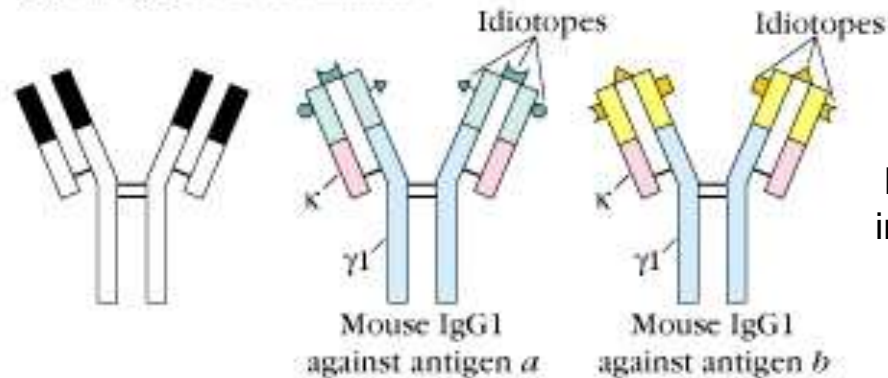
(a) Isotypic determinants



(b) Allotypic determinants



(c) Idiotypic determinants



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