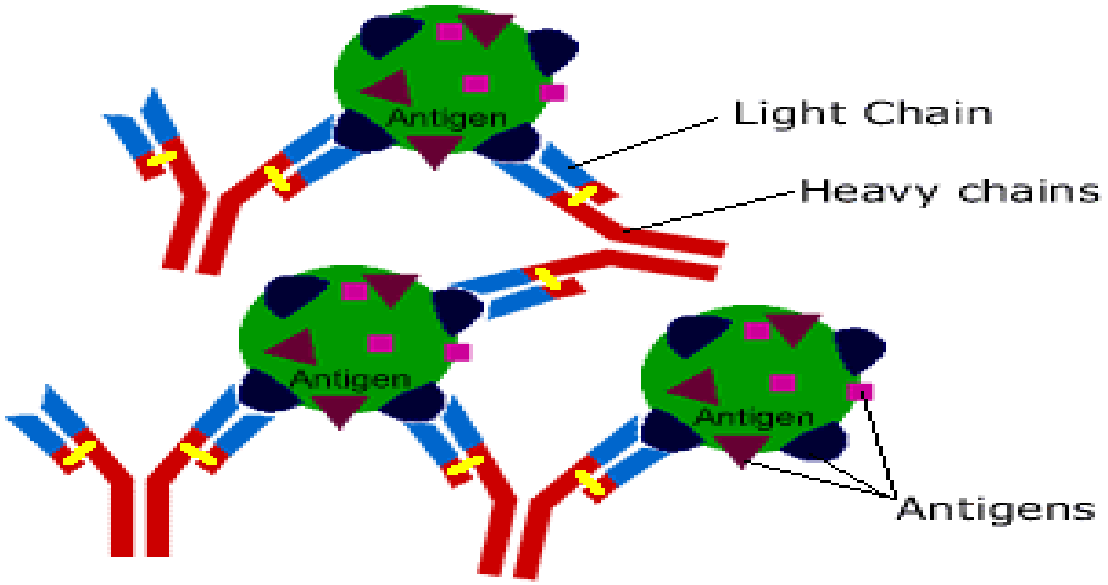
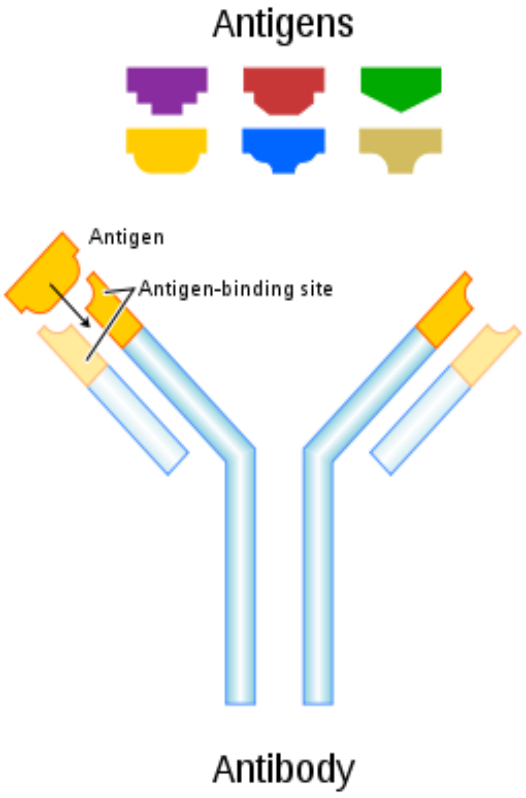
Antigen and Antibody



By: **Dr. Suzan Y.**

Antigen:

- It s a substance that may be specifically bound by an antibody (Ab) molecule or T cell receptors (TCR). When this binding lead to the activation of B cells or T cells ,this substance is known as immunogen. There are some Ag do not induce immune response. So all immunogens are antigens, but not all antigens are immunogen .
- Antigens can be proteins, polysaccharides, conjugates of lipids with : proteins (lipoproteins) and polysaccharides (glycolipids)



- The body recognizes antigens by the three-dimensional shapes or regions called antigenic determinants or epitopes.
- Antigenic determinants may be mutivalent,or monovalent
- Mutivalent antigens elicit a stronger immune response than monovalent antigens.
- Multivalent antigen, variously called a hetrophil antigen, hetrologus antigen, or forssman antigen, can react with antibodies produced in response to different antigen

- **Properties of immunogens:**

The ability of a substance to induce immune response is referred to as immunogenicity ,and the substance which induces the immune response is said to be immunogenic. the immune responses induced by an immunogen depend on many factors:

1- Foreingnness

2- Chemical composition

3- Molecular size

4- Chemical complexity

5- Genetic constitutes of the host

6- Route of entry of immunogen into the host

7- Dose of immunogen

Origin of Antigens

Antigens can be classified in order of their class

- **Exogenous antigens**

  are antigens that have entered the body from the outside , for example by inhalation, ingestion, or injection.

- **Endogenous antigens**

are antigens that have been generated within cells as a result of normal cell metabolism, or because of viral or intracellular bacterial infection.

- **Autoantigens**

- An autoantigen is usually a normal protein or complex of proteins (and sometimes DNA or RNA) that is recognized by the immune system of patients suffering from a specific autoimmune disease.

- These antigens under normal conditions, not be targeted of the immune system, but due to mainly genetic and environmental factors, the normal immunological tolerance for such an antigen has been lost in these patients.

Haptens

- very small compounds can elicit immune response only when coupled to largermolecule called a carrier.
- Hapten is a greek word meaning to fasten. These are partial antigens. These are not immunogenic.
- Hapten needs carrier proteins like albumin, globulin and synthetic polypeptide to become immunogenic.
- Hapten (Hp)+Carrier Protein (Cp) →Hp+Cp-→Ab formation against hapten
- Antibiotics, analgesics, penicilin and alpha-methyldopa
- Therefore haptens are antigenic and not immunogenic

Adjuvant: Injecting an immunogen along with certain substances can increase the intensity of the immune responses to the immunogen. The substances, which enhances the immune response to immunogen are called **adjuvant.**

The mechanisms by which adjuvant can enhance the immune response include:

1- prolonging retention i.e, increase the time of exposure of host to immunogen.
2- increasing the effective size.
3- promoting immunological activities of immune cells.
4- stimulating the influx of immune cells to the site of administration.

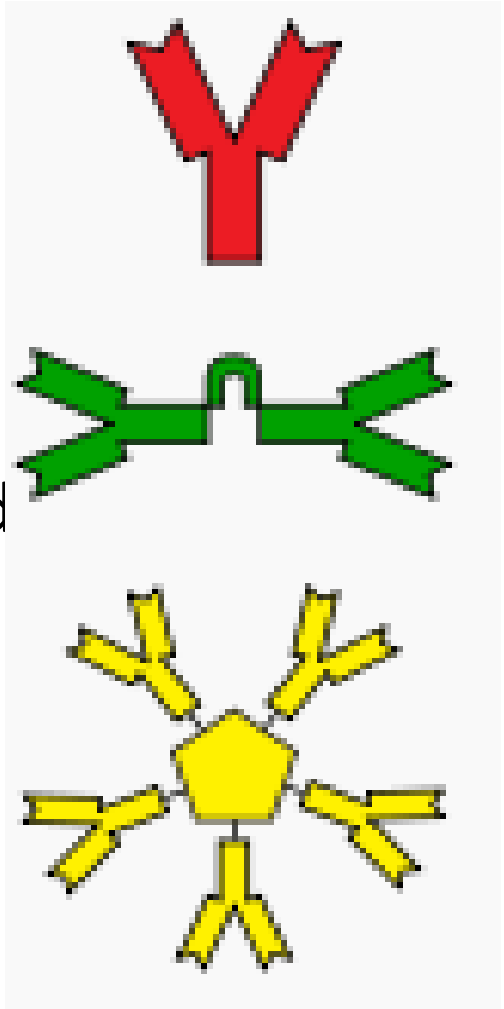
Examples of commonly used adjuvant:

a- Complete Freund's adjuvant: A water –oil emulsion used in BCG vaccine ,act by mechanisms(1,3,4).
b- Aluminum –salts: fine particles of aluminum phosphate or aluminum hydroxyl ,act by mechanism(2)

Antibody:

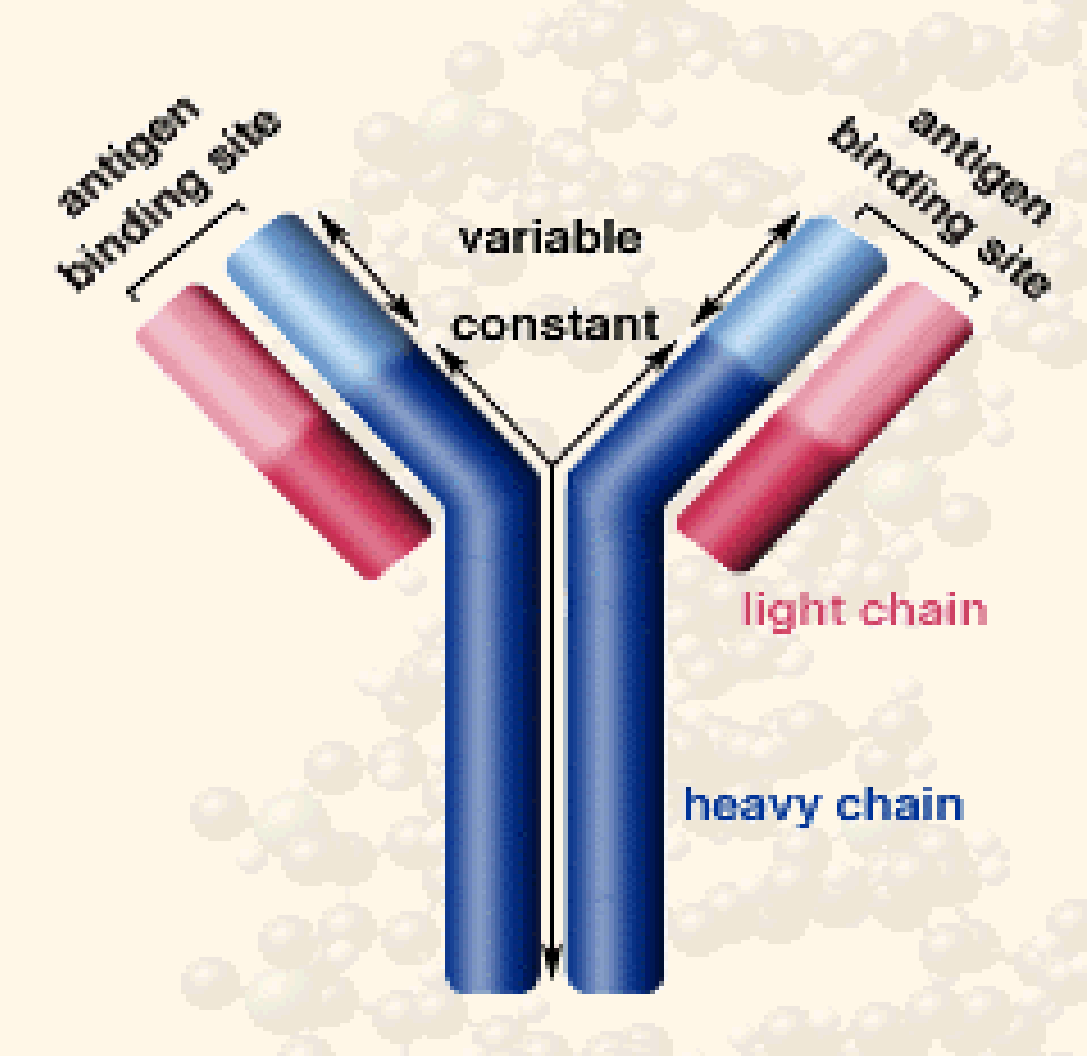
Antibody Structure

- Antibodies are glycoprotein
- Produced by B-cell
- Are antigen-specific
- Bind and inactivate foreign particles
- The basic functional unit of each antibod
  an immunoglobulin



Y-shaped molecule

Each antibody consists of four polypeptides - two heavy chains and two light chains connected by disulfide bonds, joined to form a "Y" shaped molecule.



Heavy Chain

- Each heavy chain has two regions, the *constant region* and the *variable region*
- The constant region is identical in all antibodies of the same isotype, but differs in antibodies of different isotypes.

Light Chain

- A light chain has two domains one constant domain and one variable domain
- Each antibody contains two light chains that are always identical

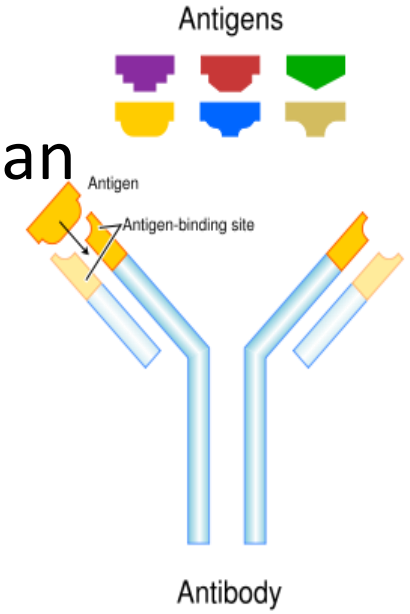
Fab and Fc Regions

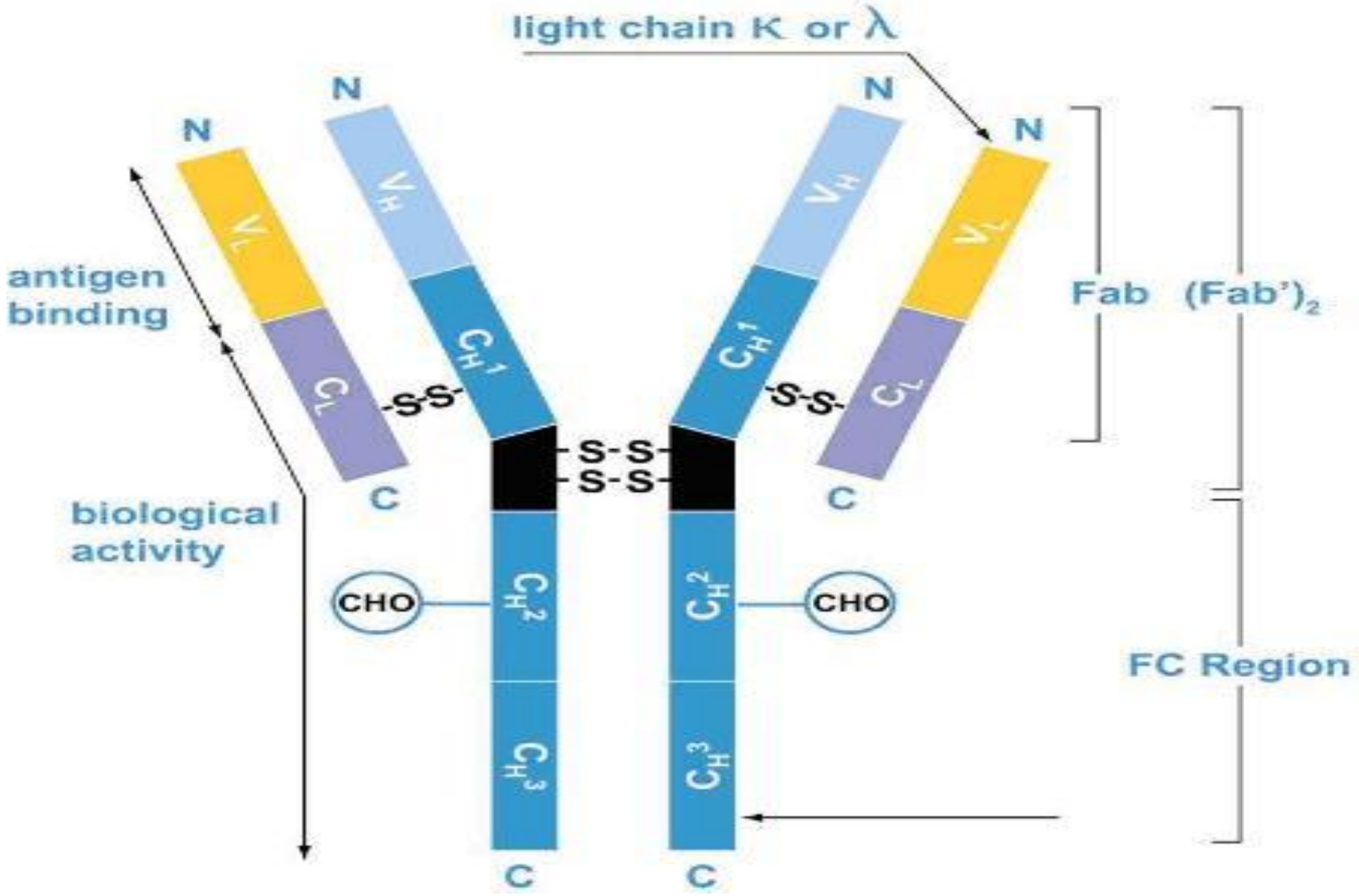
- Some parts of an antibody have unique functions. The tips of the Y contain the site that bind antigen and, therefore. This region of the antibody is called the **Fab (fragment, antigen binding).**

- The base of the Y plays a role in modulating immune cell activity. This region is called the **Fc (Fragment, crystallizable) region**, and is composed of two heavy chains.
- Fc regions contain amino acid sequences that anchor the immunoglobulin to the cytoplasmic membranes of cells by binds to various cell receptors.

- By binding to specific proteins the Fc region ensures that each antibody generates an appropriate immune response for a given antigen.

- Although the general structure of all antibodies is very similar, a small region at the tip of the “Y” varies greatly among different antibodies
- This variable region, composed of 110-130 amino acids, allowing millions of antibodies with slightly different tip structures, or antigen binding sites
- The variable region includes the ends of the light and heavy chains.
- Each antibody binds to a specific antigen; an interaction similar to a lock and key




light chain κ or λ
N
N
N
N
antigen binding
biological activity
V_L
V_H
C_L
C_H1
V_H
V_L
C_H1
C_L
-S-S-
-S-S-
S-S
S-S
C
C
CHO
CHO
C_H2
C_H2
C_H3
C_H3
C
C
Fab
$(Fab')_2$
FC Region

Antibody Isotypes

Name	Types	Description
IgA	2	Found in mucosal areas, such as the gut, respiratory tract and urogenital tract, and prevents colonization by pathogens. Also found in saliva, tears, and breast milk
IgD	1	Functions mainly as an antigen receptor on B cells that have not been exposed to antigens. Its function is less defined than other isotopes.
IgE	1	Binds to allergens and triggers histamine release from mast cells and basophile, and is involved in allergy. Also protects against parasitic worms
IgG	4	In its four forms, provides the majority of antibody-based immunity against invading pathogens. The only antibody capable of crossing the placenta to give passive immunity to fetus.
IgM	1	Expressed on the surface of B cells and in a secreted form with very high avidity. Eliminates pathogens in the early stages of B cell mediated (humoral) immunity before there is sufficient IgG

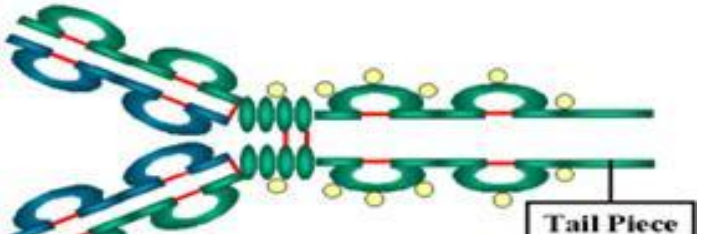
Immunoglobulin structure

IgA

- Structure
  - Serum - monomer
  - Secretions (sIgA)
    - Dimer (11S)
    - J chain
    - Secretory component

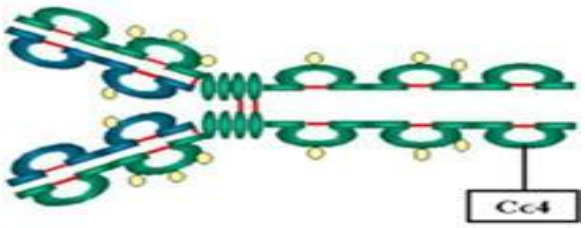
IgD

- Structure
  - Monomer
  - Tail piece



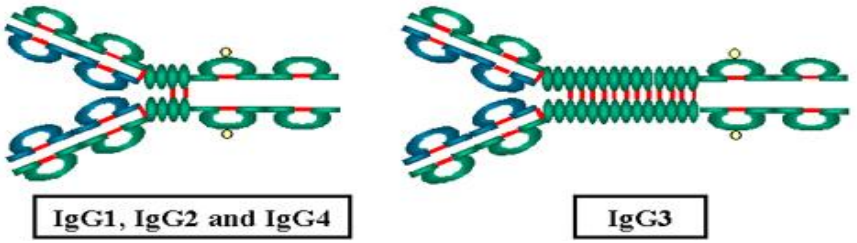
IgE

- Structure
  - Monomer
  - Extra domain (C_{H4})



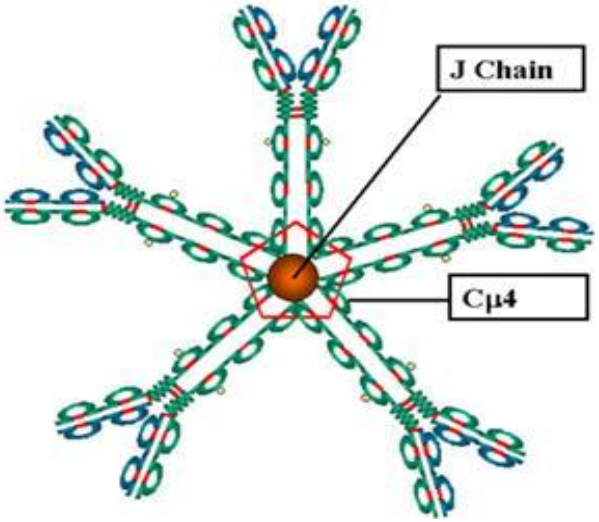
IgG

- Structure
  - Monomer (7S)



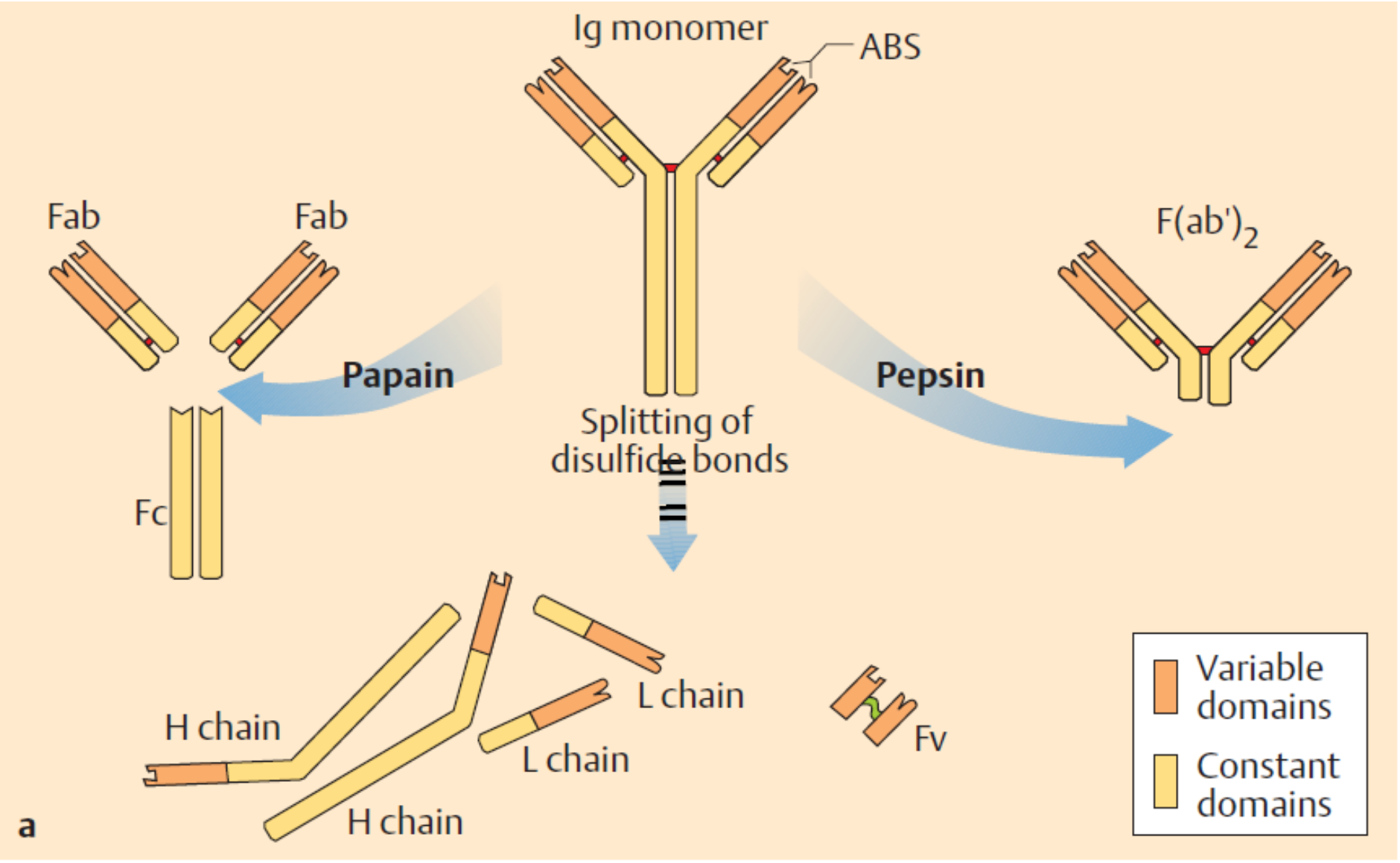
IgM

- Structure
  - Pentamer (19S)
  - Extra domain (C_{H4})
  - J chain

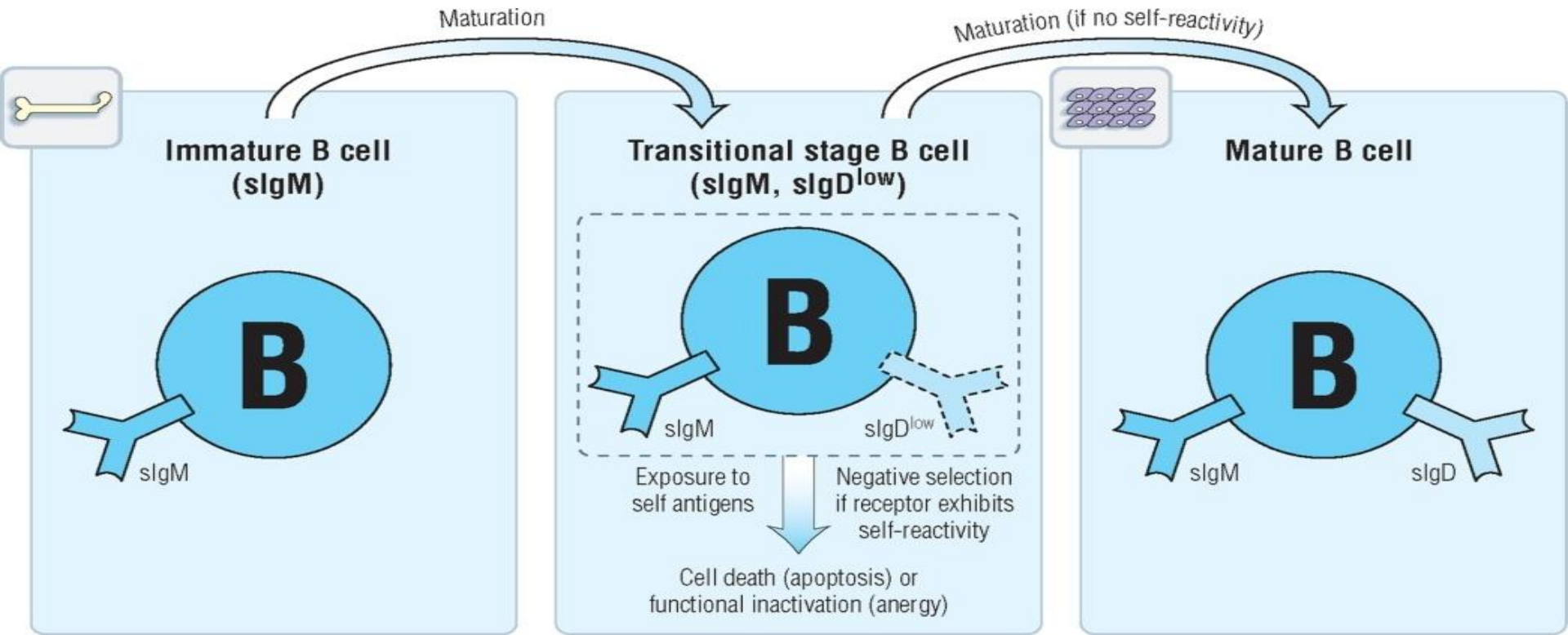


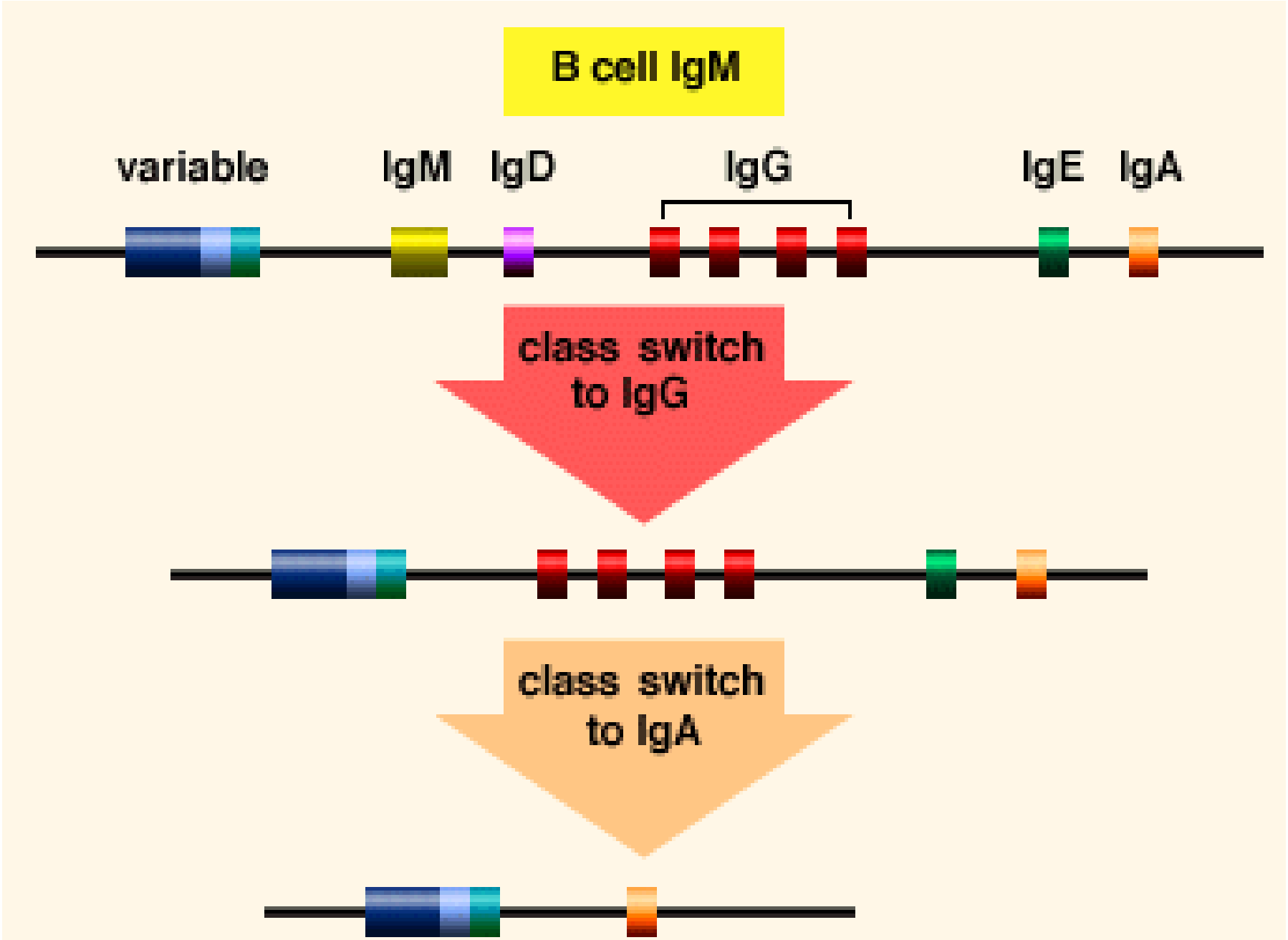
BIOLOGICAL PROPERTIES OF MAJOR IMMUNOGLOBULIN CLASSES IN THE HUMAN					
designation	**IgG**	***IgA**	**IgM**	**IgD**	**IgE**
major characteristics	most abundant internal Ig	protects external surfaces	very efficient against bacteremia	mainly lymphocyte receptor	initiates inflammation raised in parasitic infections causes allergy symptoms
antigen binding	++	++	++	++	++
complement fixation (classical)	++	—	+++	+	—
cross placenta	++	—	—	—	—
fix to homologous mast cells and basophils	—	—	—	—	++
binding to macrophages and polymorphs	+++	1	—	—	+

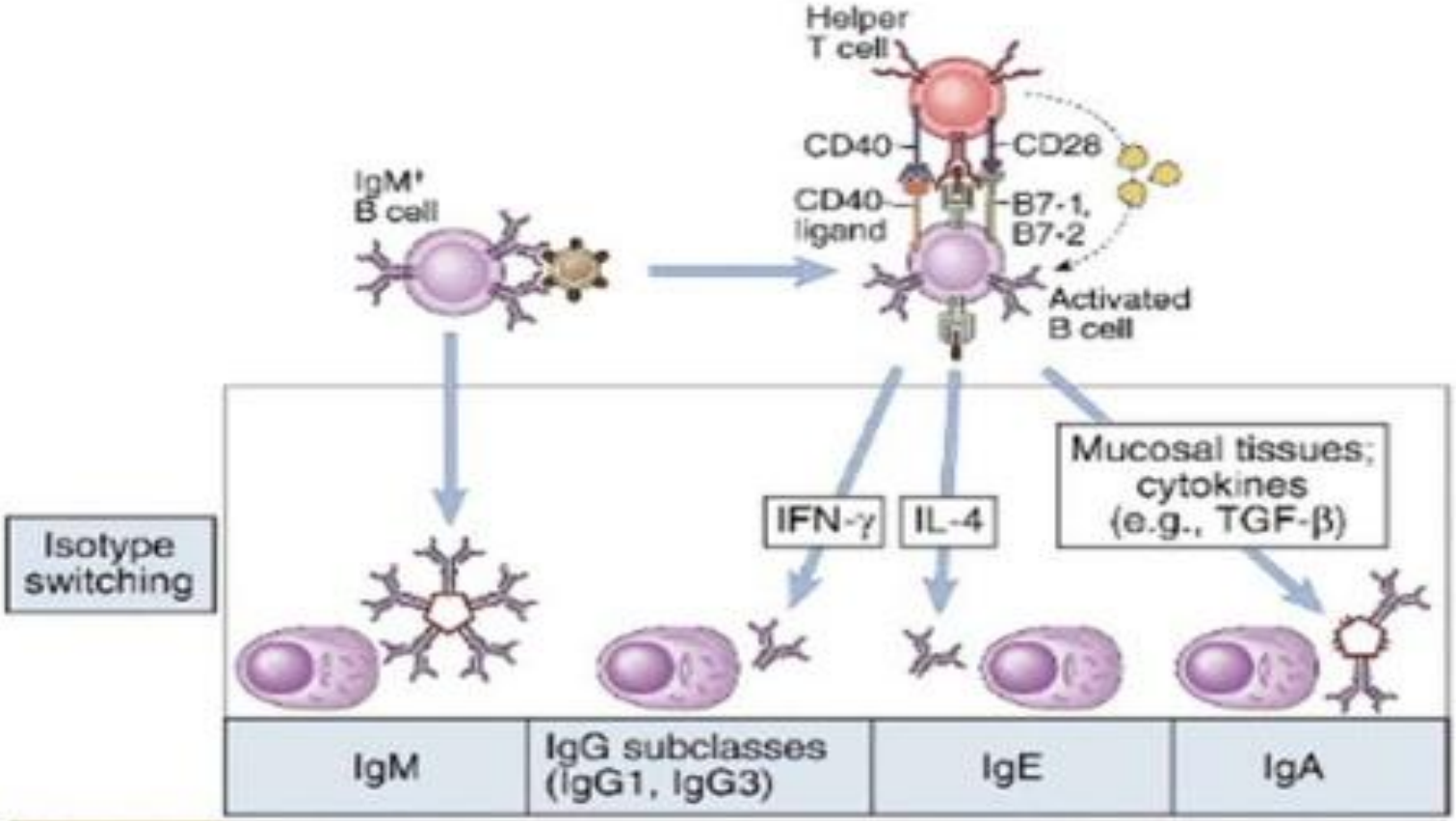
Immunoglobulin fragments



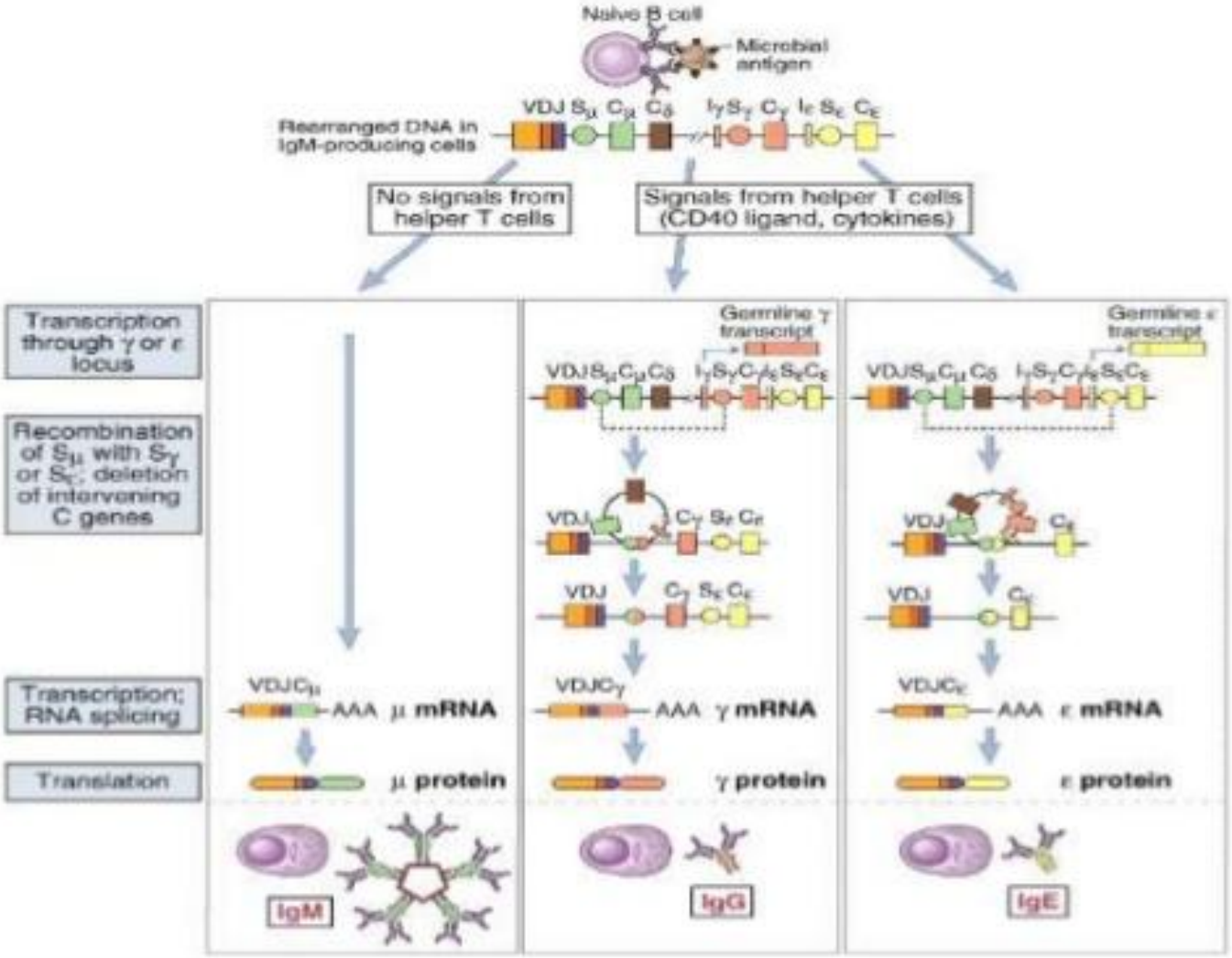
In the cours of B-cell maturation, IgD, IgM, disappear from the cell surface and instead IgM, IgG, IgE, or IgA is secreted by the cell. The process by which the function variable region appears in association with different heavy chain constant region is called heavy chain **class switching**




B cell IgM
variable
IgM
IgD
IgG
IgE
IgA
class switch
to IgG
class switch
to IgA



	IgM	IgG subclasses (IgG1, IgG3)	IgE	IgA
Principal effector functions	Complement activation	Fc receptor-dependent phagocyte responses; complement activation; neonatal immunity (placental transfer)	Immunity against helminths Mast cell degranulation (immediate hypersensitivity)	Mucosal immunity (transport of IgA through epithelia)



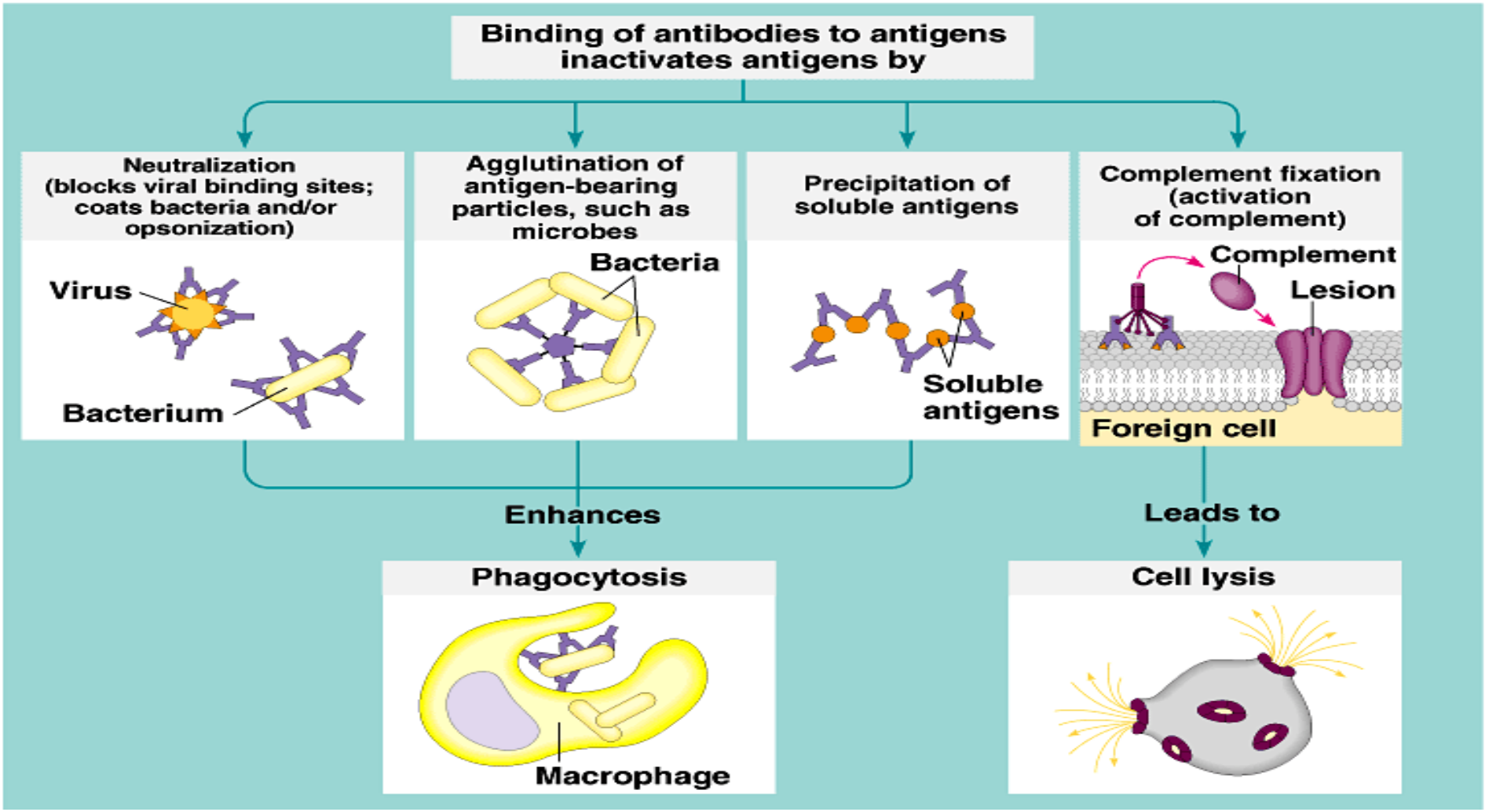
Function

- Antibodies contribute to immunity in three ways:
  - they prevent pathogens from entering or damaging cells by binding to them
  - they stimulate removal of pathogens by macrophages and other cells by coating the pathogen
  - they trigger destruction of pathogens by stimulating other immune responses such as the complement pathway

Mechanisms of Antibody Action

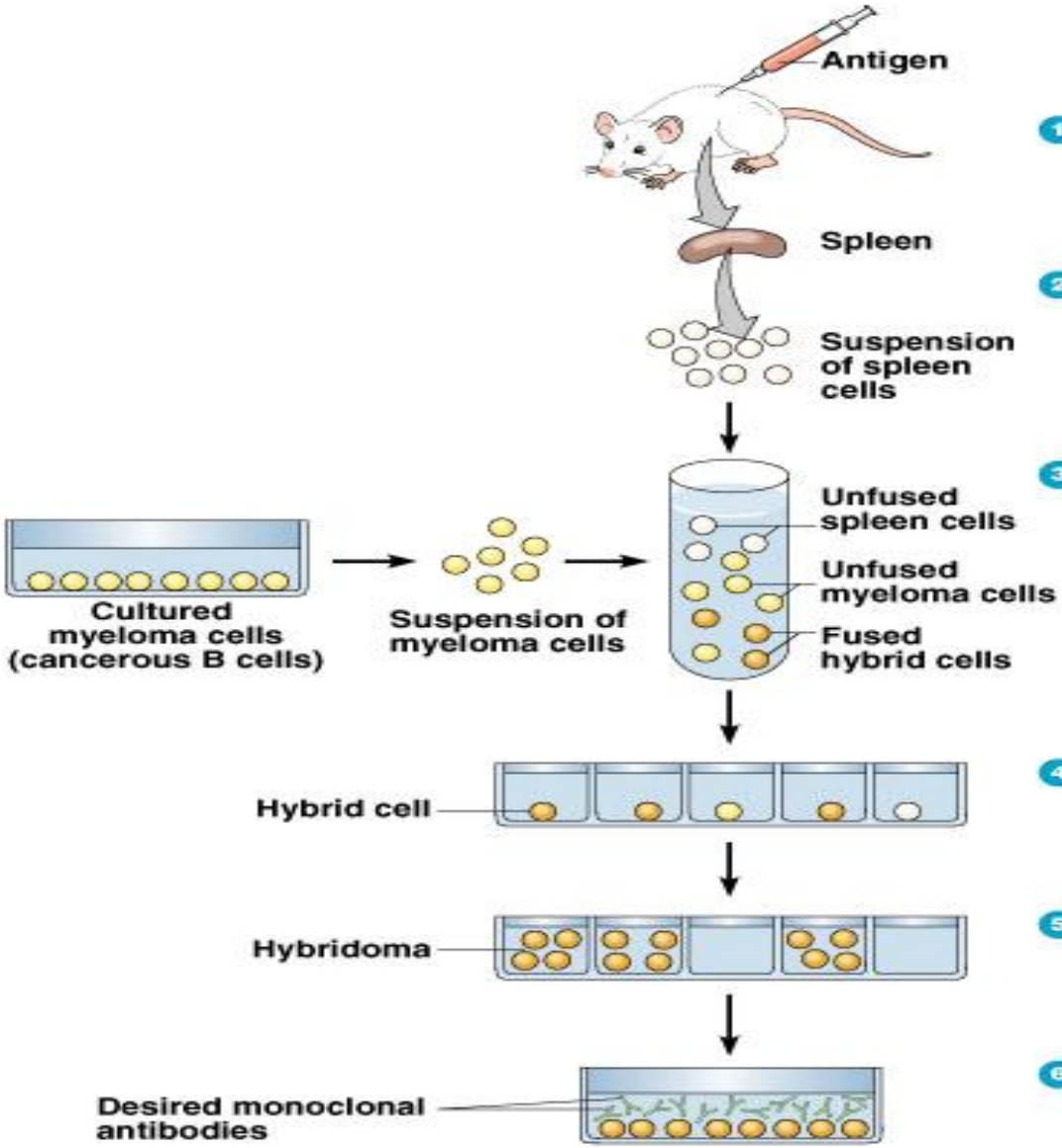
- Precipitation of soluble antigens
- Agglutination of foreign cells
- Neutralization
- Enhanced phagocytosis
- Complement activation leading to cell lysis
- Stimulates inflammation

- The binding of antibodies to antigens to form antigen-antibody complexes is the basis of several antigen disposal mechanisms.



Monoclonal antibodies

(antibdy reacts with single type of antigen)



1. A mouse is injected with a specific antigen that will produce antibodies against that antigen.
2. The spleen of the mouse is removed, and a suspension is made. The suspension includes B cells that produce antibodies against the injected antigen.
3. The spleen cells are then mixed with *myeloma cells* that are capable of continuous growth in culture but have lost the ability to produce antibodies. Some of the antibody-producing spleen cells and myeloma cells fuse to form hybrid cells. These hybrid cells are now capable of growing continuously in culture while producing antibodies.
4. The mixture of cells is placed in a selective medium that allows only hybrid cells to grow.
5. Hybrid cells proliferate into clones called *hybridomas*. The hybridomas are screened for production of the desired antibody.
6. The selected hybridomas are then cultured to produce large amounts of *monoclonal antibodies*.