



**Cihan University/ Sulaymaniyah**

**College of Health Science**

**Medical Laboratory Analysis**

**4<sup>th</sup> Stage- 1<sup>st</sup> Semester**

**Clinical Immunology**

**Lecture- 5: Specific Immunity**

**Antibodies and Cytokines**

**2024- 2025**

Lecturer: Mohammed T. Salih



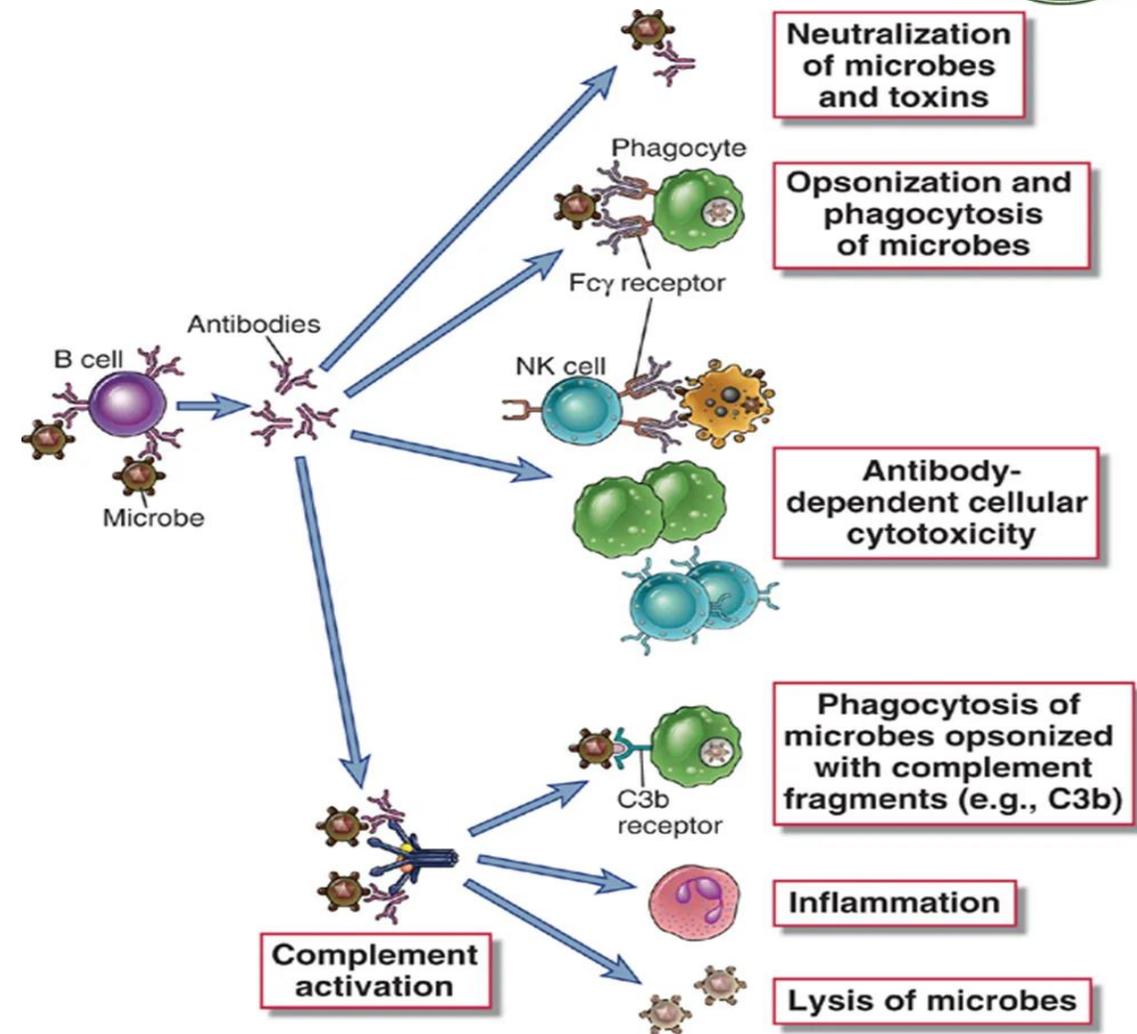
# Antibodies or Immunoglobulins

- They are **globular proteins** present in the **serum** and **tissue fluids**.
- They are produced by the **plasma cells (B-cells)** and are used in the **immune system** of the body to neutralize pathogenic microbes or other toxic foreign components.
- **Antibodies** are the antigen binding proteins found on the **B-cell membrane** and **Body secretions which are secreted by the plasma cells** of the immune system.
- Antibodies are commonly called as '**IMMUNOGLOBULINS**' = IG.

# Functions of Antibody

They can:

1. Prevent the attachment of microbes to the mucosal surface of the host.
2. Reduce the virulence of the pathogen by neutralizing the toxins and viruses.
3. Facilitate phagocytosis by opsonization of microbes.
4. Activate the complement system.



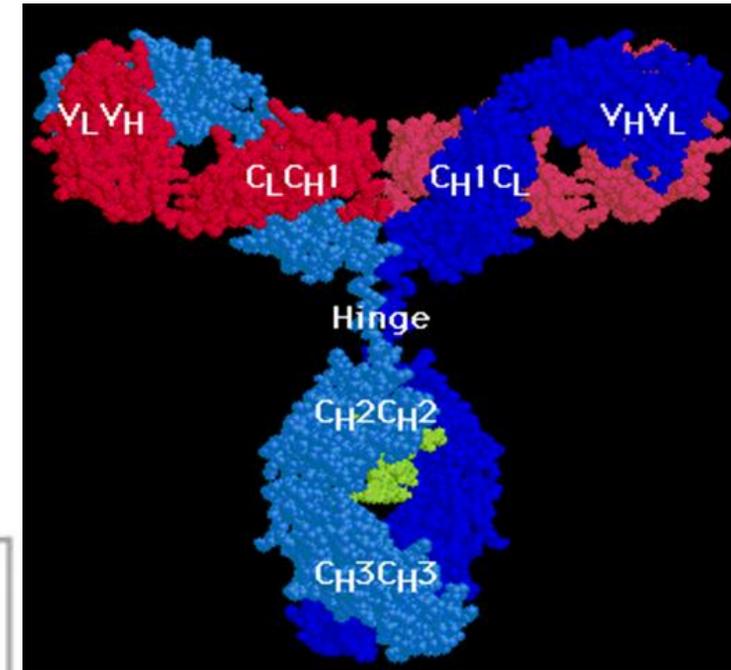
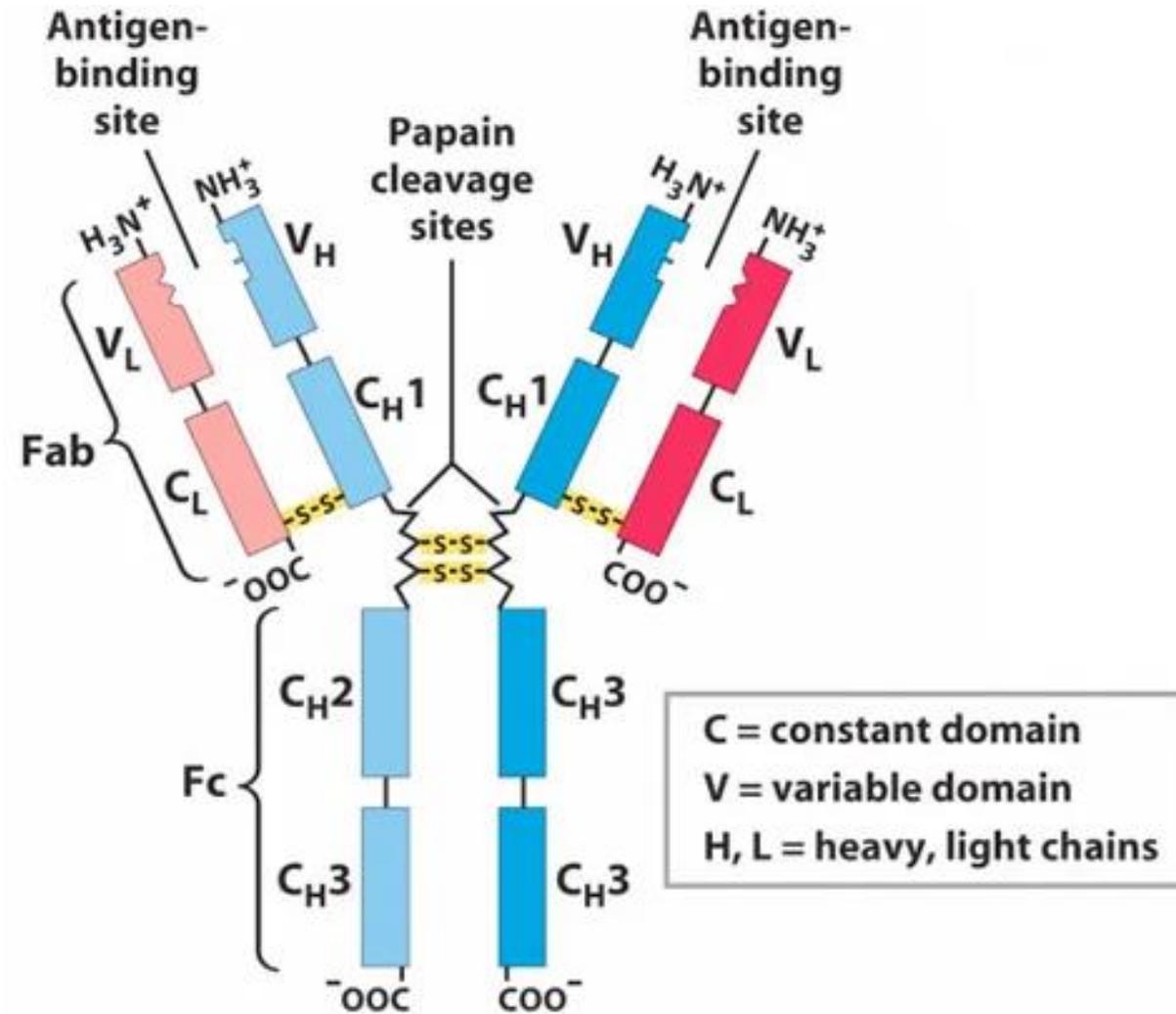
Abbas et al: Cellular and Molecular Immunology, 7e.  
Copyright © 2012, 2007, 2005, 2003, 2000, 1997, 1994, 1991 by Saunders, an imprint of Elsevier Inc.



# Structure of Immunoglobulins

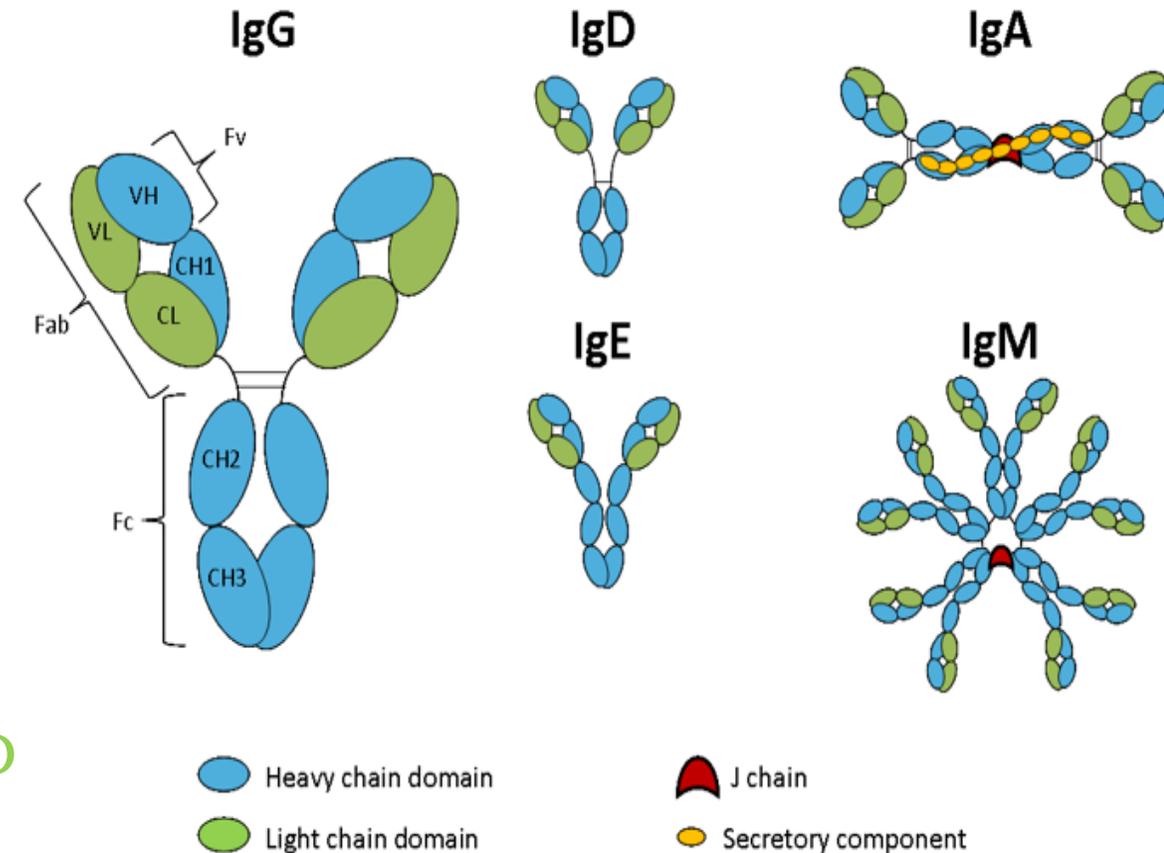
- The basic unit of a single immunoglobulin consists of **four linear polypeptide chains**.
- These peptide chains are named as two identical Heavy Chains and two identical Light Chains.
- The heavy chains are long and heavy with a molecular weight of 50 –70 kDa.
- The light chains are smaller and lighter in weight with a molecular weight of 25 kDa.
- The heavy chains are designated as ‘H’ and the light chains are designated as ‘L’
- Since an immunoglobulin contain two heavy (H) chains and two light (L) chains, they are together represented as H<sub>2</sub>L<sub>2</sub>.
- H<sub>2</sub>L<sub>2</sub> is the basic structural unit of any class (isotypes) of immunoglobulins.
- Both H chains and L chains are connected through **disulfide bonds**.
- Some antibodies are very complex as in Immunoglobulin M (IgM) which is a pentamer. In such case, the basic structural units will be H<sub>2</sub>L<sub>2</sub> and they are multiplied in ‘n’ times (H<sub>2</sub>L<sub>2</sub>)<sub>n</sub>.

# Typical Antibody Structure



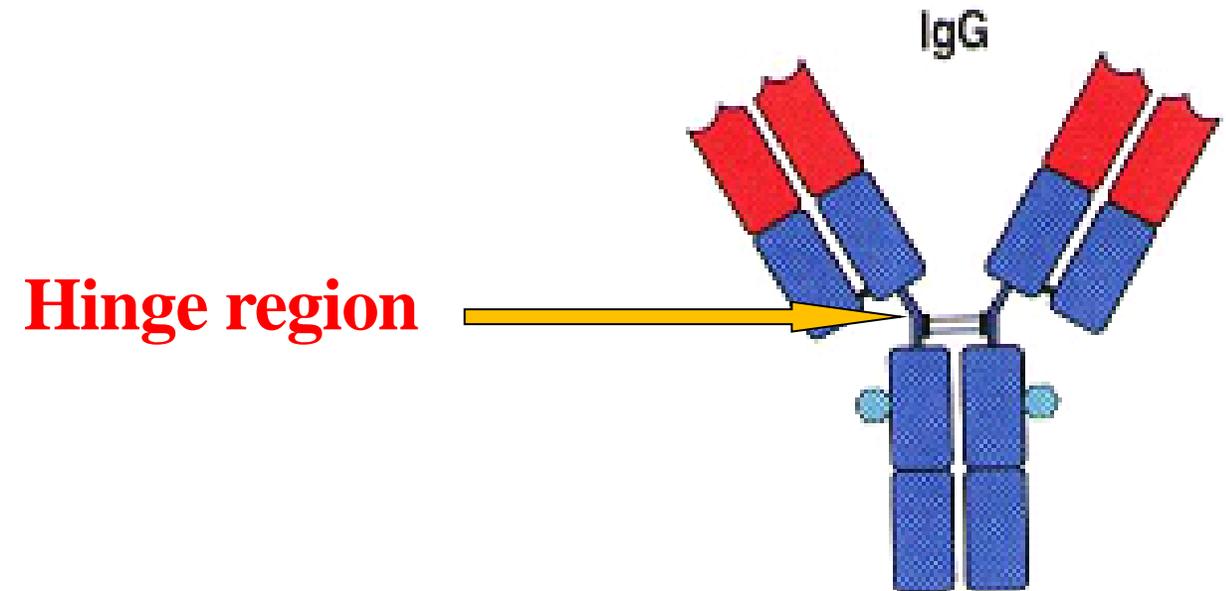
# Classes and types of Ig

- According to the differences of **H chains** (amino acid composition, sequence, H chains) can be divided into five classes of H Chain:  $\gamma$   $\alpha$   $\mu$   $\delta$   $\epsilon$  (IgG IgA IgM IgD IgE).
- The heavy chains of Immunoglobulin M (IgM) contains mu ( $\mu$ ), IgG contains gamma ( $\gamma$ ), **IgA contains alpha ( $\alpha$ )**, IgE contains epsilon ( $\epsilon$ ) and IgD contains delta ( $\delta$ ) chains.



# Hinge region

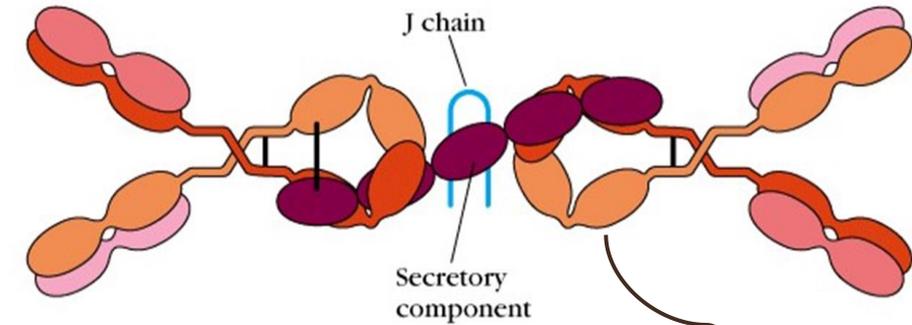
- The **hinge region** is segment of heavy chain between the CH1 and CH2 domains.
- **Flexibility** in this area permits the **two antigen-binding sites** to **operate independently**.



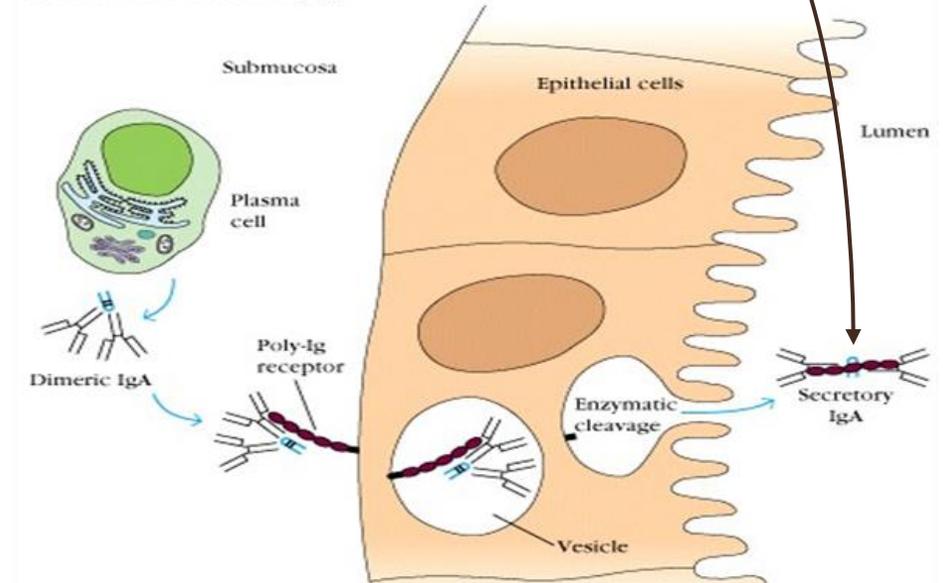
# Other components of Ig

- **Joining chain(J):** Produced by plasma cells.
  - ✓ **Functions:** linker: Join monomer of Ig to form dimer ( Ig A, IgM).
- **Secretory piece ( SP):** is an epithelial-derived glycoprotein that facilitates transfer of Igs from subepithelial sites into epithelial-lined lumina by transepithelial transport and secretion.

Structure of secretory IgA



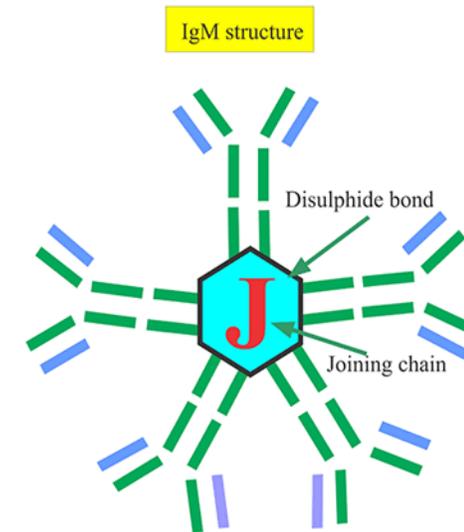
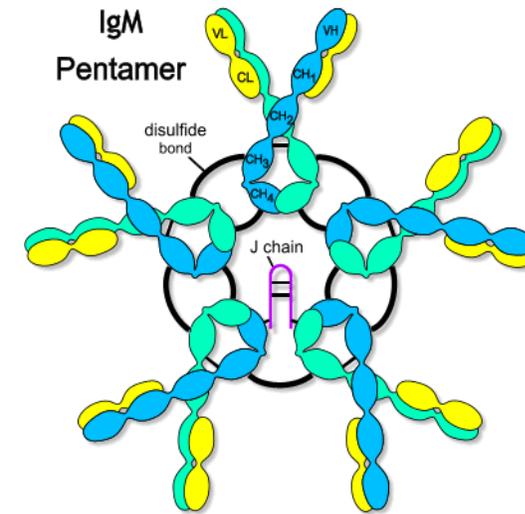
(b) Formation of secretory IgA



# Types of Antibody (Immunoglobulin)

## 1. IgM

- Largest of all the antibody molecules, consists of five of the basic units (**pentamer**) mu heavy chains joined together by a structure known as **J-chain**.
- Expressed on **membrane of mature B cells** as monomer
- **MW is highest: pentamer (90KD).**
- **life is shorter (4~5 days).**
- **IgM is more efficient in anti-infection and anti-bacterium.**
- Restricted almost entirely to the intravascular space due to its large size.
- 5-10% of serum immunoglobulin.
- Membrane (mIgM) expressed on B-cells as BCR.
- First Ig of primary immune response.
- More efficient than IgG in **complement activation**
- **Does not cross the placenta.**



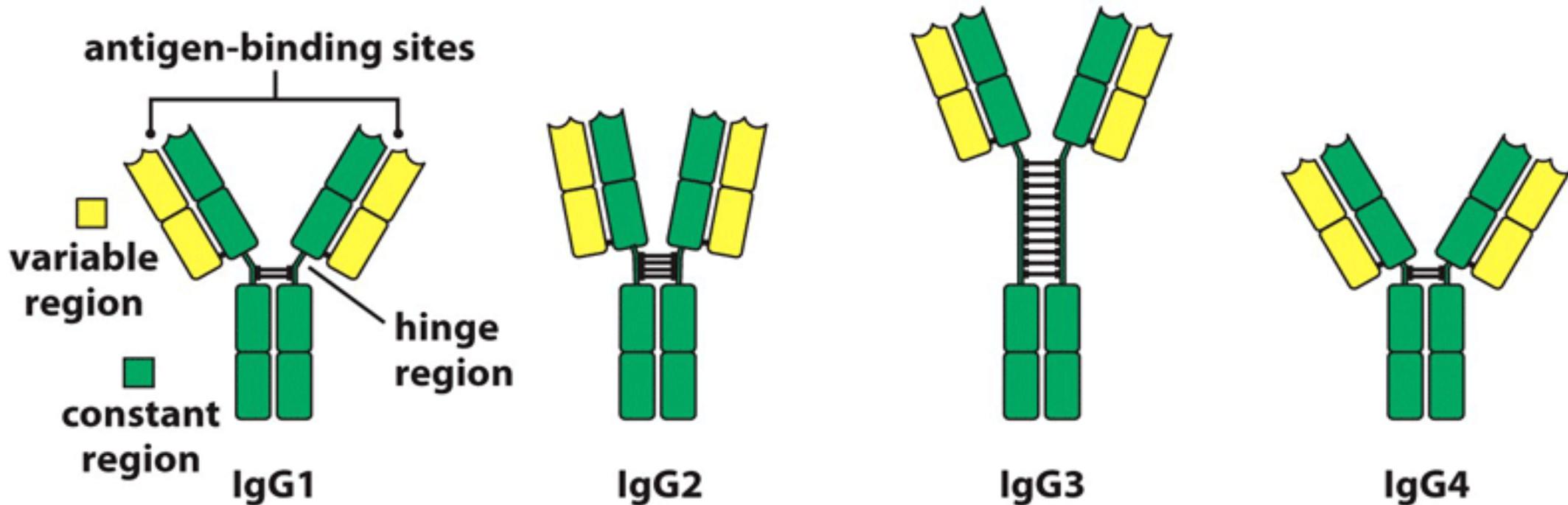


## 2. IgG

- Most abundant immunoglobulin 80% of serum Ig.
- ~10 mg/mL
- One basic structural unit, i.e. Y-shaped molecule having 2 light chains and 2 Gamma heavy chains.
- Produced in response to a wide variety of antigens, including bacteria, viruses,
- Coats organisms to enhance phagocytosis by neutrophils and macrophages.
- Through its **ability to cross the placenta**, maternal IgG provides the **major line of defense against infection for the first few weeks of a baby's life.**
- Four subclasses which differ in their heavy chain composition and in some of their characteristics such as biologic activities. IgG1, IgG2, IgG3 and IgG4.
- Partial activator of the Complement System.

# Immunoglobulin G (IgG)

- *Structure, Subclasses and Functions*

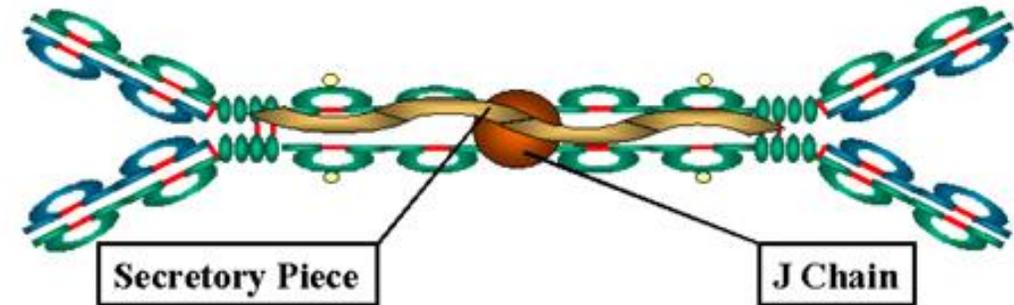


# 3. IgA

## IgA

### Structure

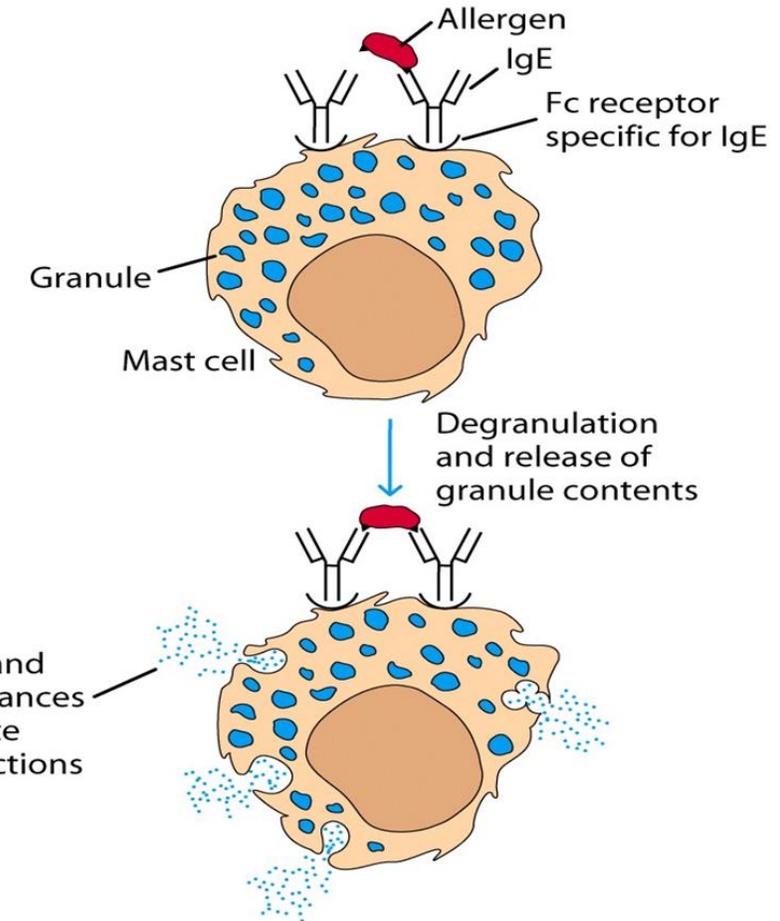
- Serum - monomer
- Secretions (sIgA)
  - Dimer (11S)
  - J chain
  - Secretory component



- 10-15% of serum IgG
- Predominant Ig in secretions
  - ✓ Milk, saliva, tears, mucus and in nasal, bronchial and intestinal secretions.
- Secretions, as dimer or tetramer+J-chain polypeptide + secretory component (Poly IgR)
- The IgA present in secretions exists as two basic units (a dimer) attached to another molecule known as secretory component.
- IgA does not cross the placenta and does not bind complement.

## 4. IgE

- **Clinical effects** of IgE mediated reactions include increased vascular permeability, skin rashes, respiratory tract constriction (wheezing), and increased secretions from epithelium (watery eyes, runny nose).
- Not much else is known about its biologic role.
  - ✓ Very low serum concentration,  $0.3\mu\text{g/mL}$
  - ✓ Participate in immediate hypersensitivities reactions. Ex. Asthma, anaphylaxis,
  - ✓ responsible for an individual's immunity to invading parasites.
- Fc regions bind very well to high affinity IgE receptors on Mast Cells (tissue) and basophils (blood) through FcεR
- Binding causes degranulation (Histamine Release)
- IgE does not fix complement and does not cross the placenta.





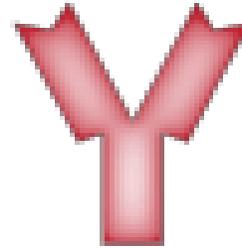
## 5. IgD

- Accounts for less than 1% of the total immunoglobulin pool.
- This is primarily a **cell membrane** immunoglobulin found on the surface of B lymphocytes.
- *IgD does not fix complement and does not cross the placenta.*
- Little is known about the function of this class of antibody.

# Structural differences among Ig isotypes

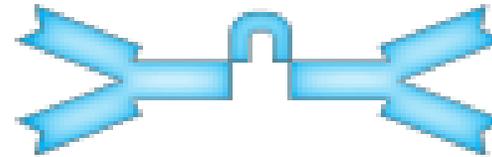


1. Monomer



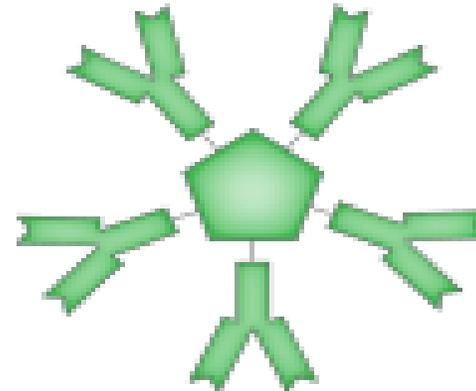
Monomer  
IgD, IgE, IgG

2. Dimer



Dimer  
IgA

3. Pentamer

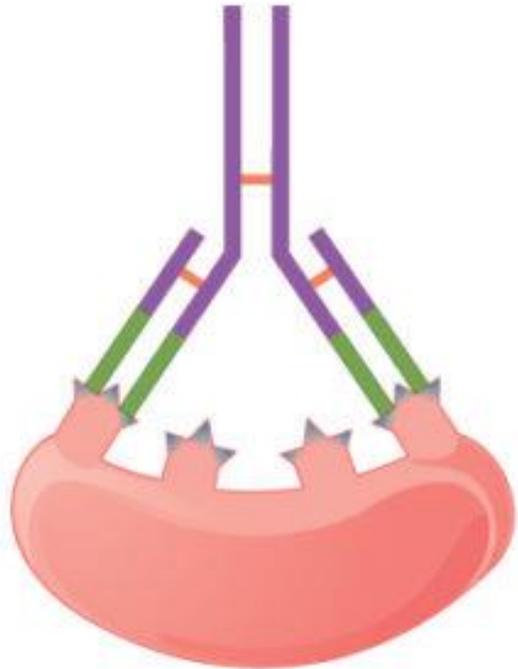


Pentamer  
IgM

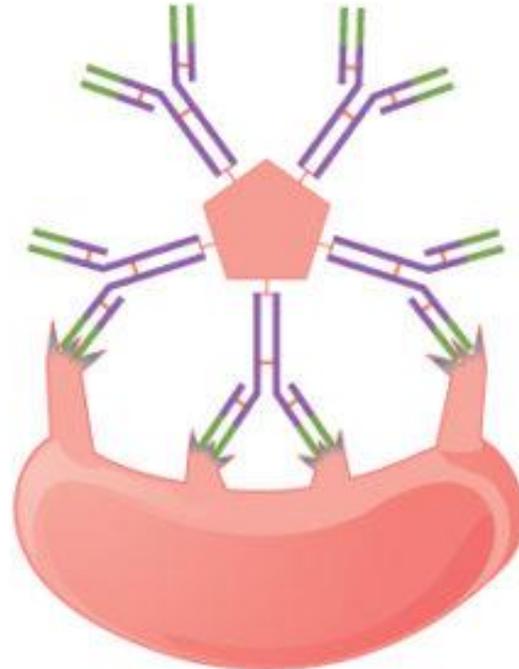
# Affinity, Avidity and Cross Reactivity



(a) Affinity versus avidity

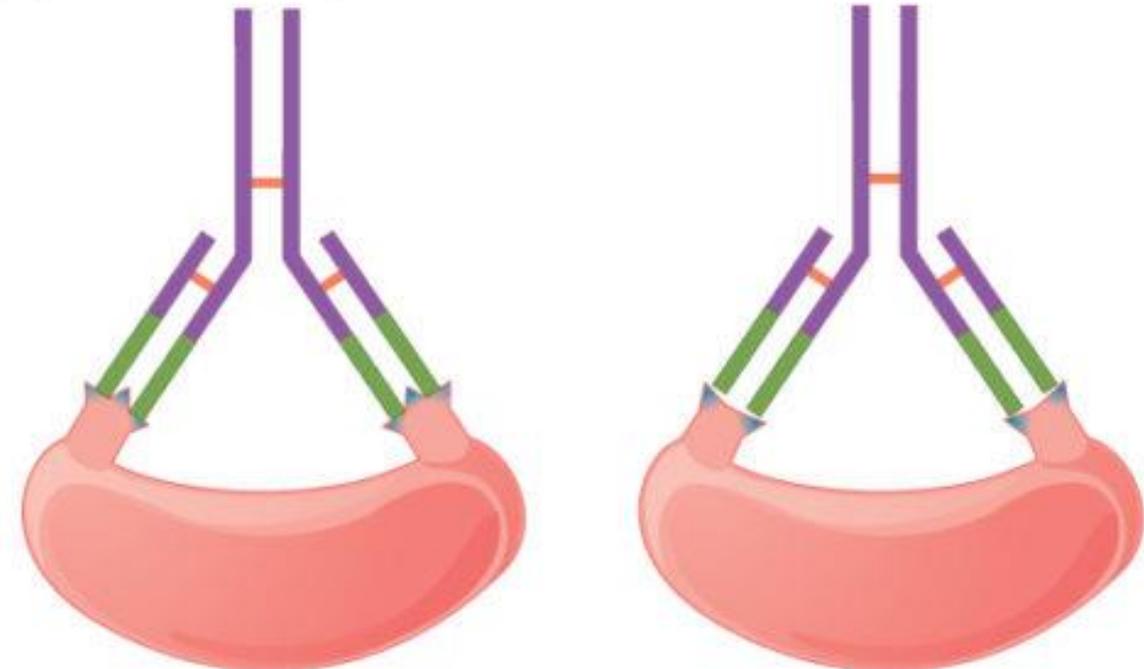


Affinity refers to the strength of a single antibody–antigen interaction. Each IgG antigen binding site typically has high affinity for its target.



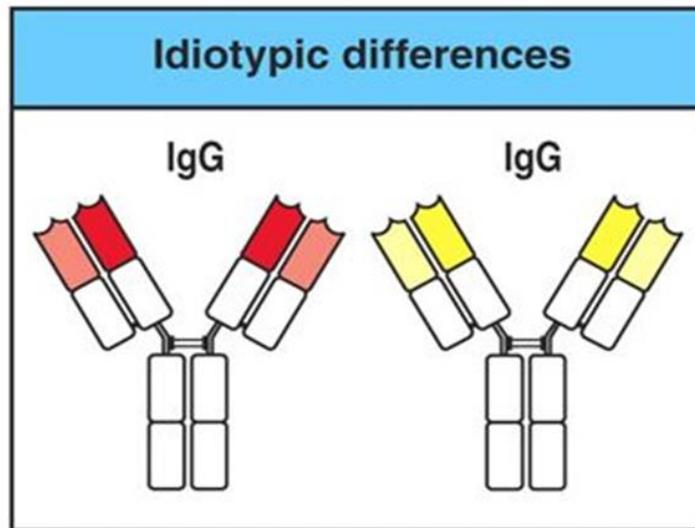
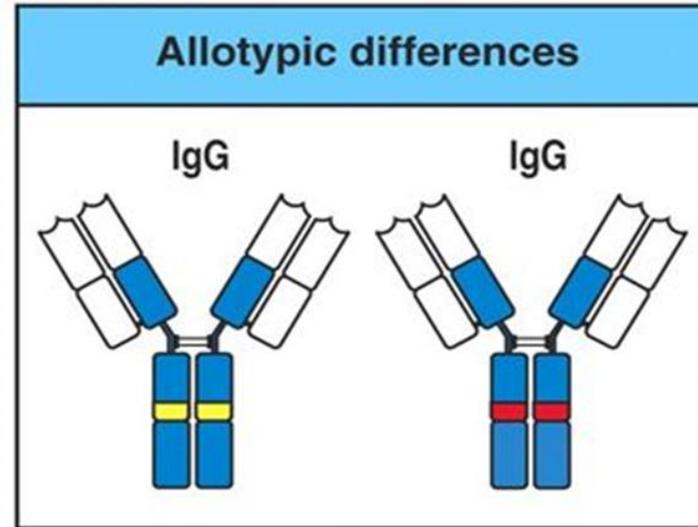
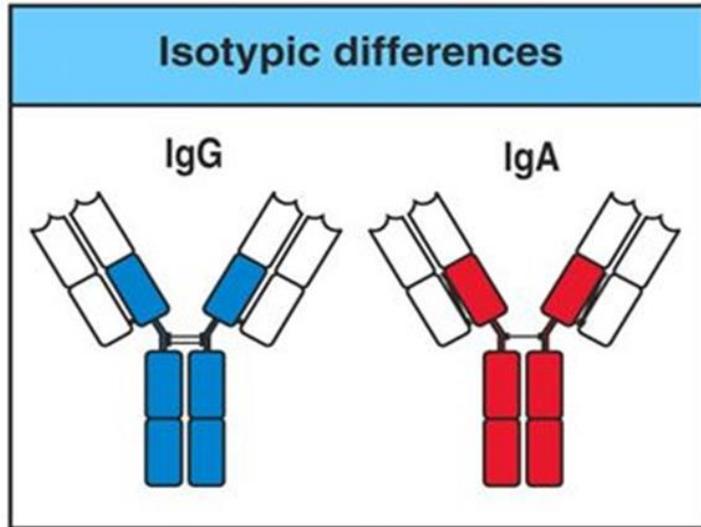
Avidity refers to the strength of all interactions combined. IgM typically has low affinity antigen binding sites, but there are ten of them, so avidity is high.

(b) Cross reactivity



An antibody may react with two different epitopes.

# Isotypes, Allotypes, and Idiotypes of Immunoglobulins



## Definitions:

### Isotype:

- Different Fc
- Different type of Ab
- IgG, IgA, IgM, IgE, IgD

### Allotype:

- Difference between species
- Most differences in Fc region.

### Idiotypes

- Different specificities of the antibody molecules.
- Eg: each idiotype recognizes a different part of or different antigen

Figure 4-24 Immunobiology, 6/e. (© Garland Science 2005)



# Cytokines

- **Cytokines**, in general, are secreted molecules involved in **cell-to-cell signaling**.
- **All cytokines** are **proteins/ glycoproteins**.
- They are usually **secreted by cells of the immune system**. Some cytokines (e.g., type I interferons [IFNs] and tumor necrosis factor [TNF]) **can be secreted by nonimmune cells (e.g., epithelial cells)**.
- **Most cytokines** are only secreted when cells become **activated as part of the response to infection**.
- **Cells of the immune system** use cytokines to **communicate and coordinate action**.



# Functional Features

## 1. Potent:

- ✓ Some function at  $10^{-15}$  molar

## 2. Local:

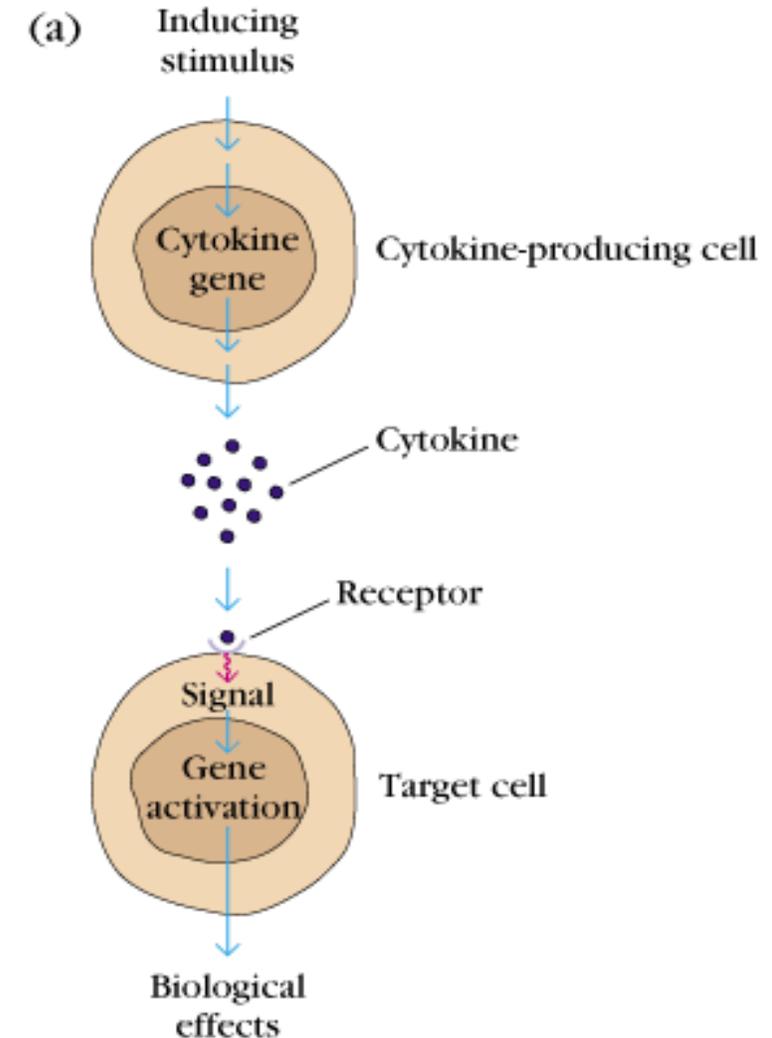
- ✓ Autocrine
- ✓ Paracrine
- ✓ (Sometimes) endocrine

## 3. Highly interactive:

- ✓ Pleiotropic
- ✓ Redundant
- ✓ Synergistic / antagonistic

# Functional Features

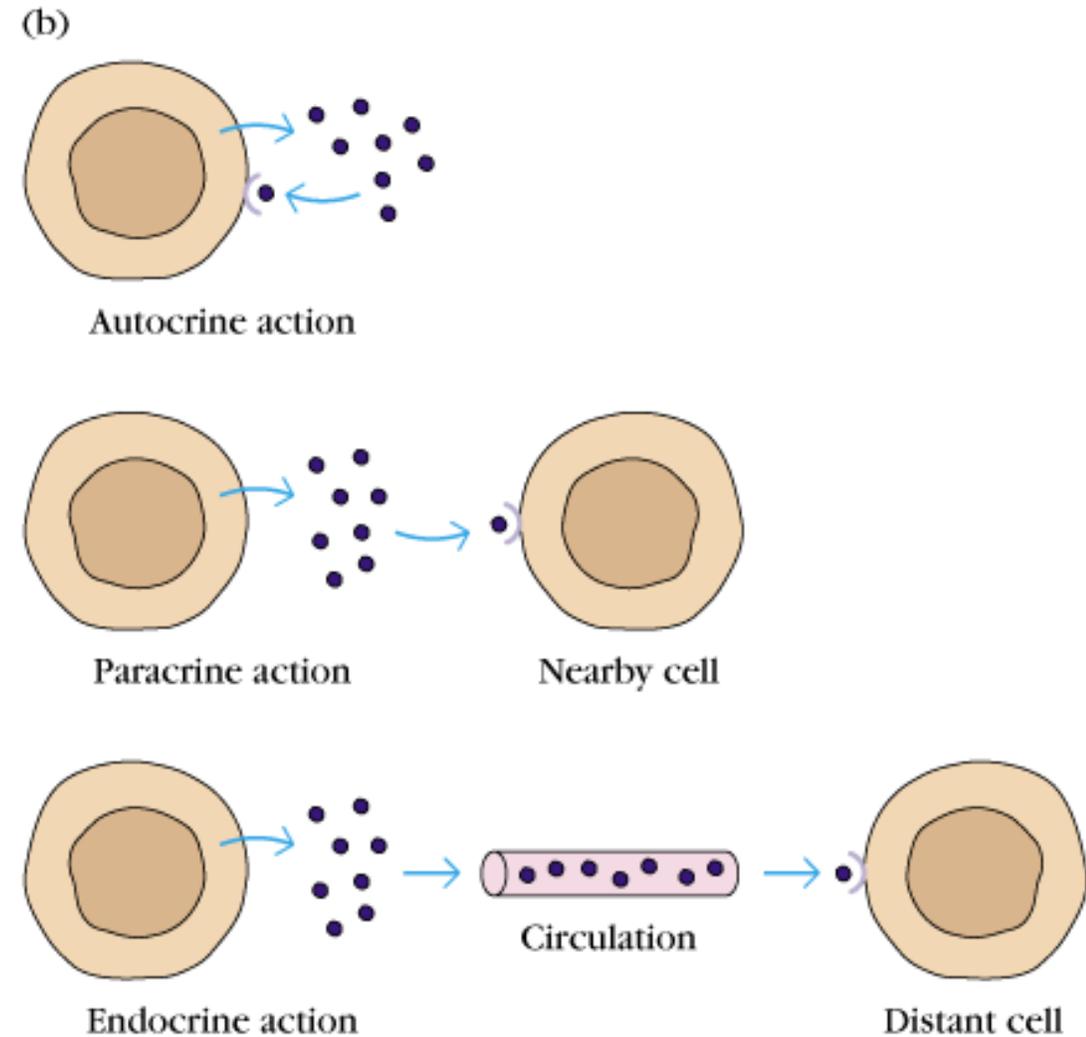
- Potent: Cytokines Mediate the Activation, Proliferation, and Differentiation of **Target Cells**:
  - ✓ Some function at  $10^{-15}$  Molar.



# Functional Features

## Local:

1. Autocrine
2. Paracrine
3. (Sometimes) Endocrine



# Functional Features



- **Highly Interactive:**

- Pleiotropic** = induces different biological effects depending on the nature of the target cell type.
- Redundant** = two or more cytokines that mediate similar functions.
- Synergy** = combined effect of two cytokines on cellular activity is greater than the additive effects of the two cytokines.
- Antagonize** = the effect of one cytokine cancels out the effect of another cytokine.
- Cascade induction** = the effect of one cytokine on a target cell leads to the production of one or more additional cytokines from that target cell.

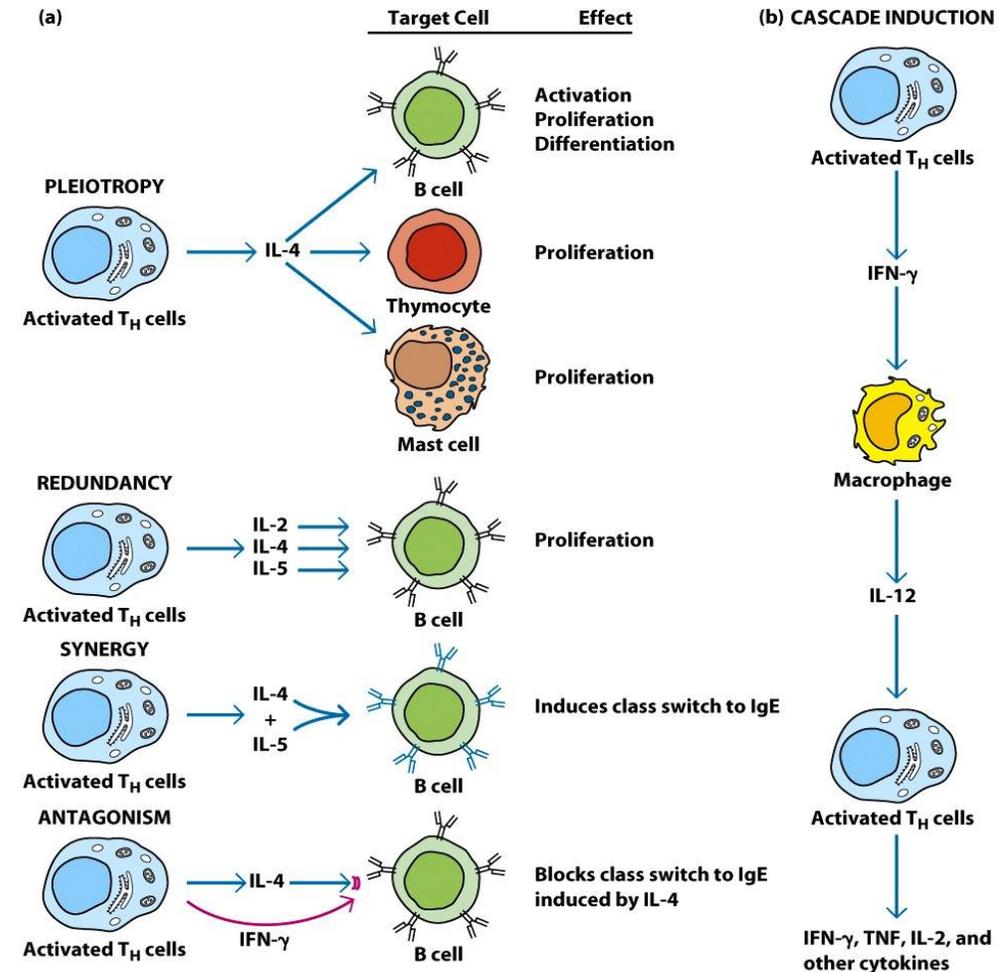


Figure 12-2  
Kuby IMMUNOLOGY, Sixth Edition  
© 2007 W.H. Freeman and Company



# Cytokine Families

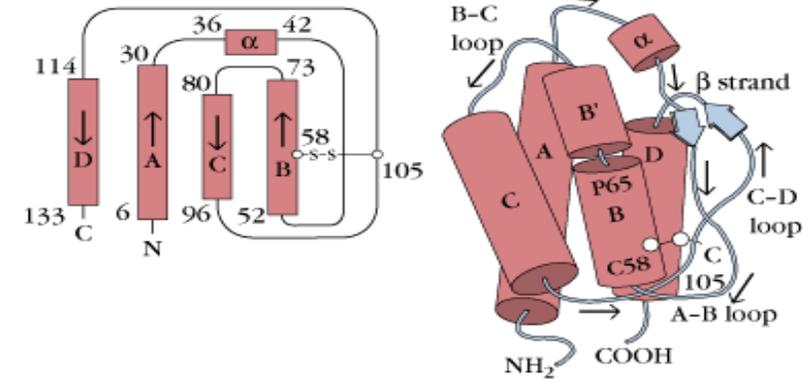
- I. Hematopoietic family
  - II. Interferon family
  - III. Tumor necrosis factor family
  - IV. Chemokine family
  - V. Interleukin 1 (IL-1)
  - VI. Interleukin 17 (IL-17)
- I, II, and III elicit physiological responses.
  - IV serves as a chemoattractant.

# Hematopoietic Cytokines

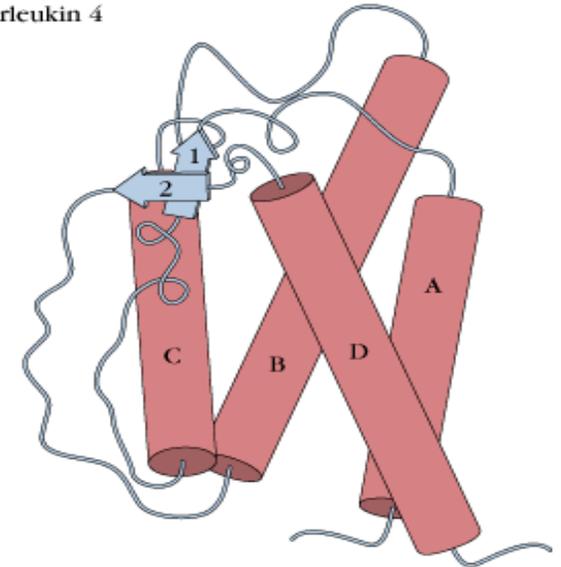


- Hematopoietic cytokines are large family of extracellular ligands that stimulate hematopoietic cells to differentiate into eight principle types of blood cells.
- Numerous cytokines are involved in the regulation of hematopoiesis within a complex network of positive and negative regulators.
- Not all involved in hematopoietic functions.

(a) Interleukin 2



(b) Interleukin 4





# Interferon (Class II) First cytokines to be discovered

**Type I** - Secreted by not only macrophages and dendritic cells but also by virus infected cells:

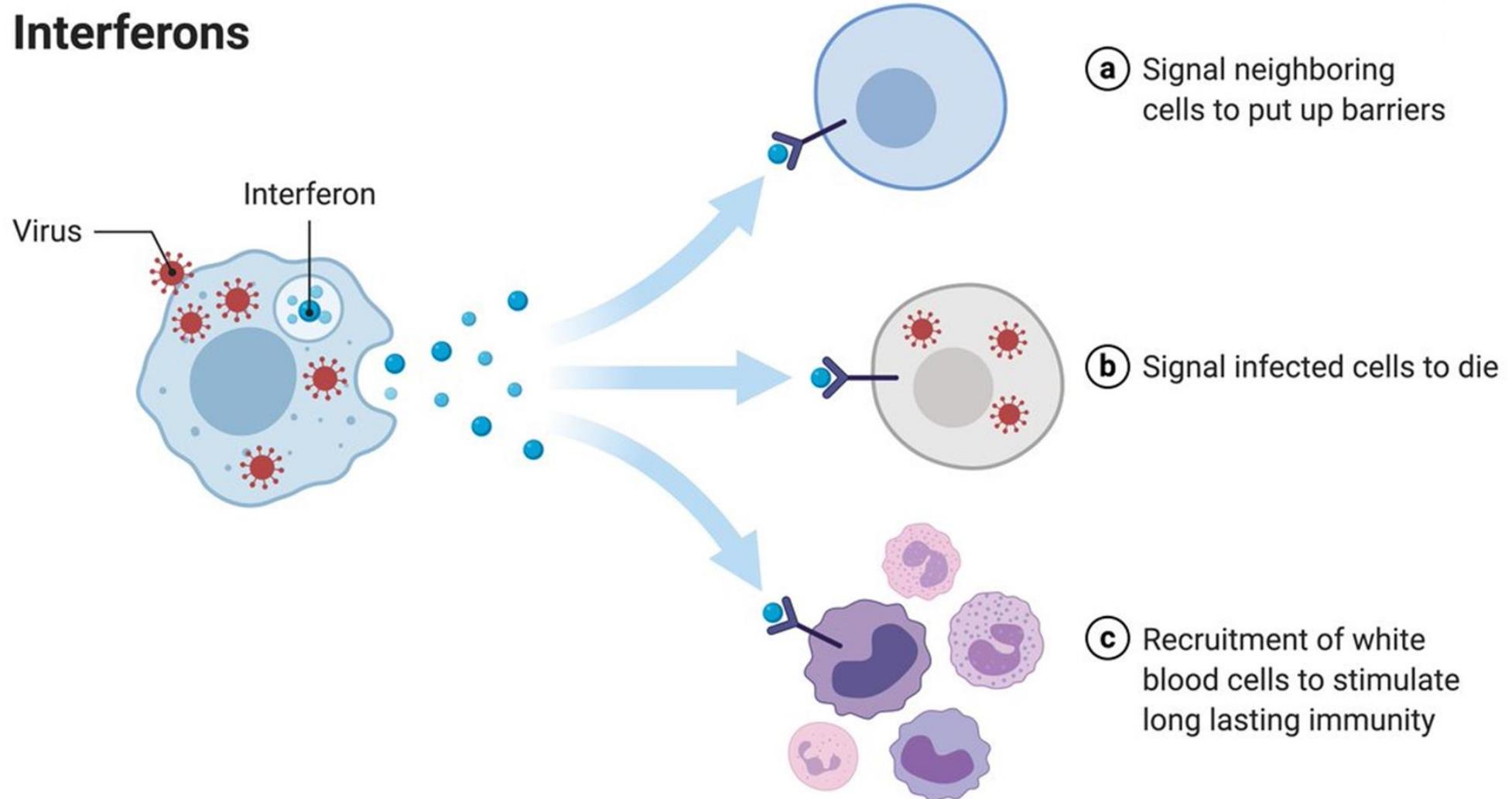
Interferons  $\alpha$ , and interferon- $\beta$ ,

**Type II** – produced by activate T and NK cells , **known as interferon- $\gamma$  & cytokines include IL-10.**

- ❖ Interferon- $\gamma$  is used medically to bias the adaptive immune system toward a cytotoxic response in diseases such as leprosy (Hansen's disease) and toxoplasmosis (intracellular pathogens), in which antibody responses are less effective.

# Functions of Interferon Cytokines

## Interferons



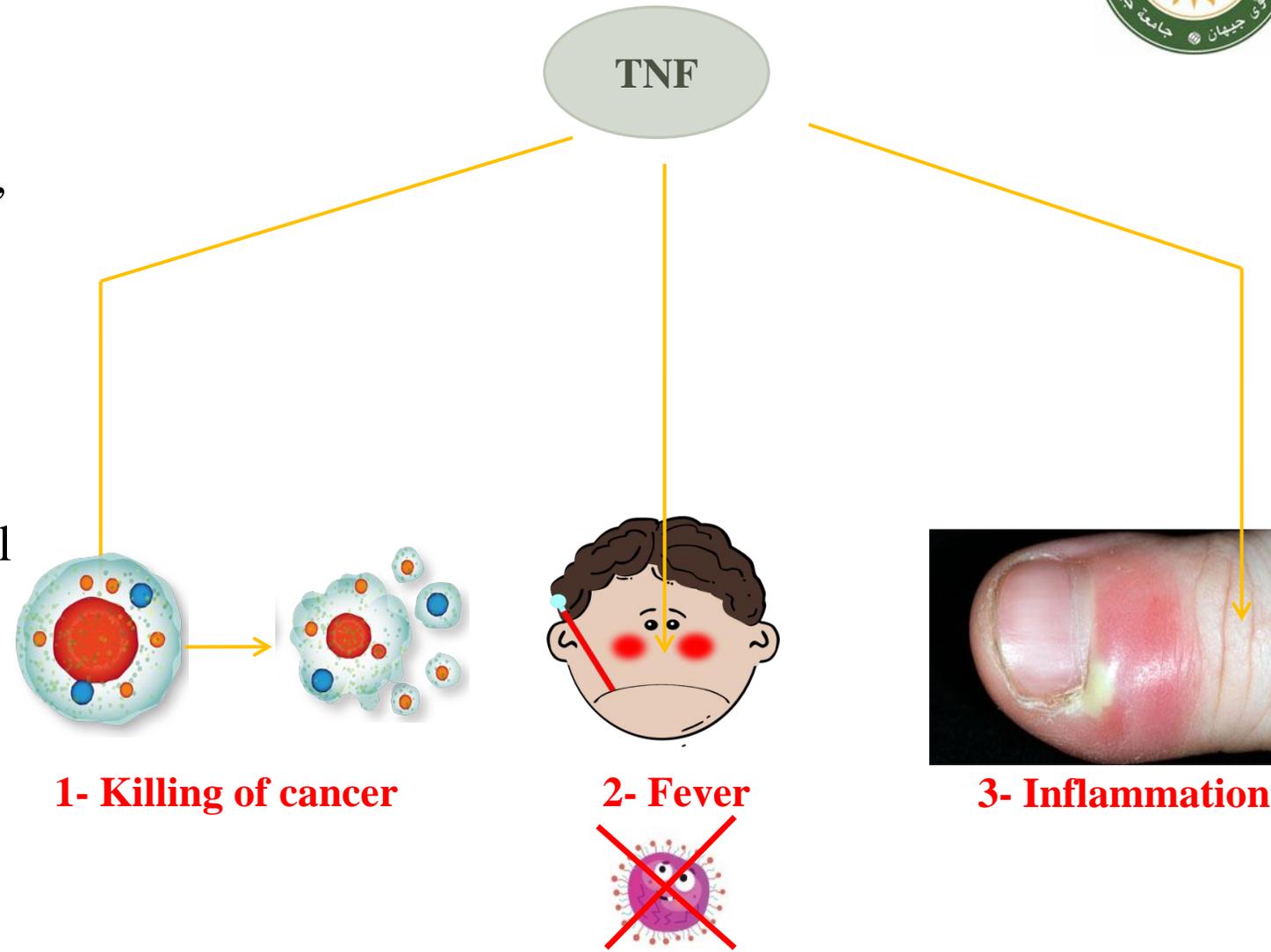


# Tumor Necrosis Factor Family

- There are two members of the TNF family:
- **TNF- $\alpha$**  and **TNF- $\beta$** . Both of these are **secreted as soluble proteins**.
  - ✓ **TNF- $\alpha$**  is a **proinflammatory cytokine**, produced primarily by activated macrophages, and lymphocytes, in response to infection, or inflammation.
  - ✓ **TNF- $\beta$**  is produced by activated lymphocytes and **can deliver a variety of signals**.
  - ✓ On binding to neutrophils, endothelial cells lead to increased expression of MHC and of adhesion molecules.
  - ✓ **Fas-ligand (FasL)**, induces apoptosis.

# Functions of Tumor Necrosis Factor (TNF)

- **TNF:** can signal development, activation, or death of certain cells (homeostasis)  
Which induce apoptosis,
- ❖ **Apoptosis** (programmed cell death), is a mechanism of cell death in which the cell dies from within and is fragmented into membrane-bound vesicles that can be rapidly phagocytosed by neighboring macrophages.



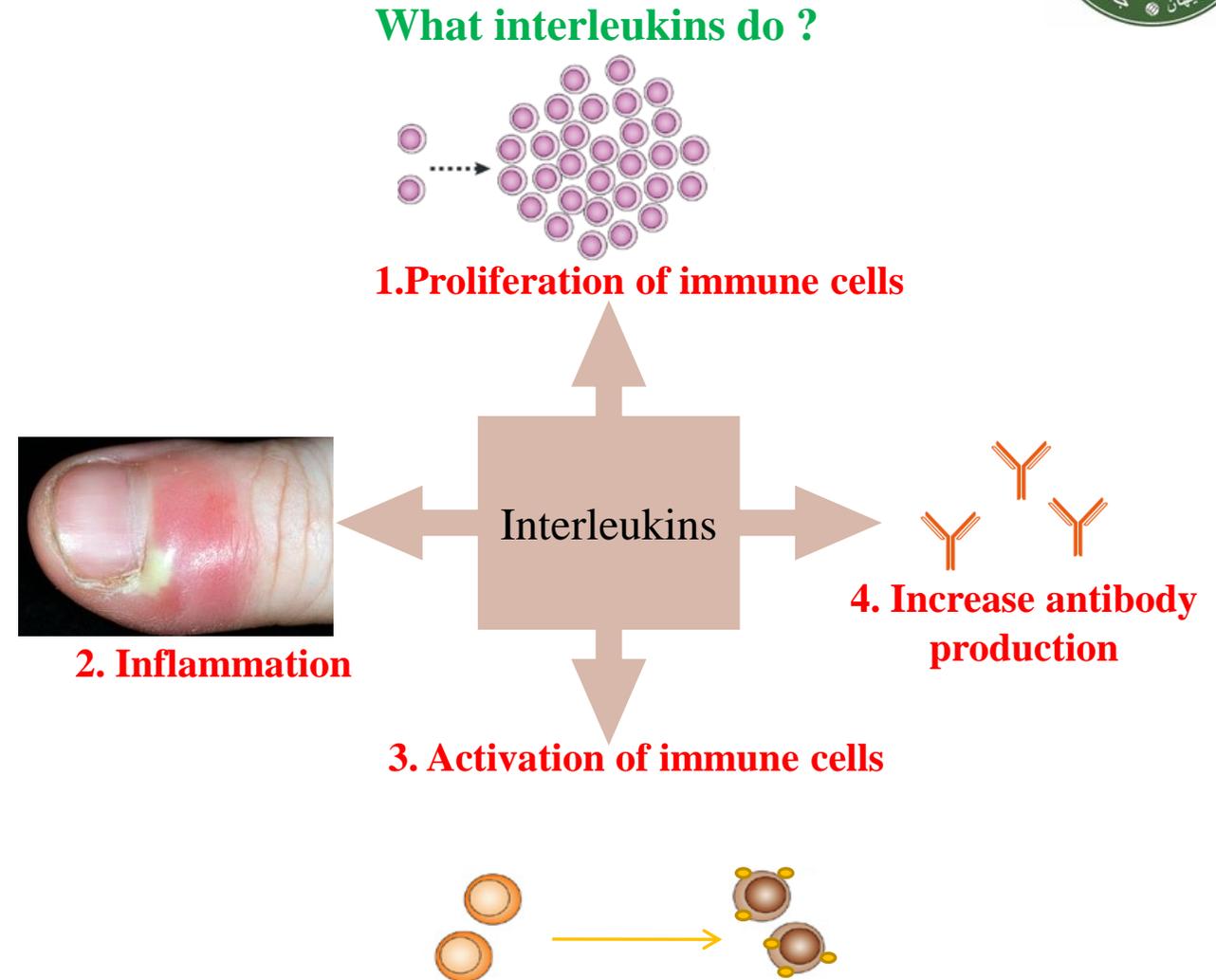


# Chemokines Family

- **Chemokines** are **chemo-attractants**: They are approximately 50 different chemokines and approximately 20 different chemokine receptors.
- **Chemoattractants** = molecules that attract cells by **influencing cellular structure** and **cell surface adhesion molecules**.
- **Chemokines** = **mobilize immune cells** from one location to another.
- They can **attract cells into inflamed tissues** and play a role in leukocyte homing.
- Chemokines in the peripheral tissues **recruit cells of the innate and adaptive immune response** to **fight off an infection**.

# Interleukin Family

- Interleukins – 1-37
- Not stored inside cells.
- Quickly synthesized and secreted in response to infection.
- Key modulators of behaviour of immune cells
- Mostly secreted by T-lymphocytes & macrophages





# References

1. Abbas, A. K., Lichtman, A. H., Pillai, S., & Baker, D. L. (. i. (2020). Basic immunology: Functions and disorders of the immune system (Sixth edition.).
2. Turgeon, M. L. (1996). Immunology & serology in laboratory medicine. St. Louis: Mosby.
3. Abul K. Abbas and Andrew H. Lichtman. Cellular And Molecular Immunology 2019, 6<sup>th</sup> edition .
4. <https://www.youtube.com/watch?v=G4jobV6-bFA>
5. <https://www.youtube.com/watch?v=ZLrIhB7GFp4>
6. [https://www.youtube.com/watch?v=\\_N1xX49AqwQ](https://www.youtube.com/watch?v=_N1xX49AqwQ)
7. <https://www.youtube.com/watch?v=gYJnZGExlws>
8. <https://www.youtube.com/watch?v=4s6IzVbyq-4>