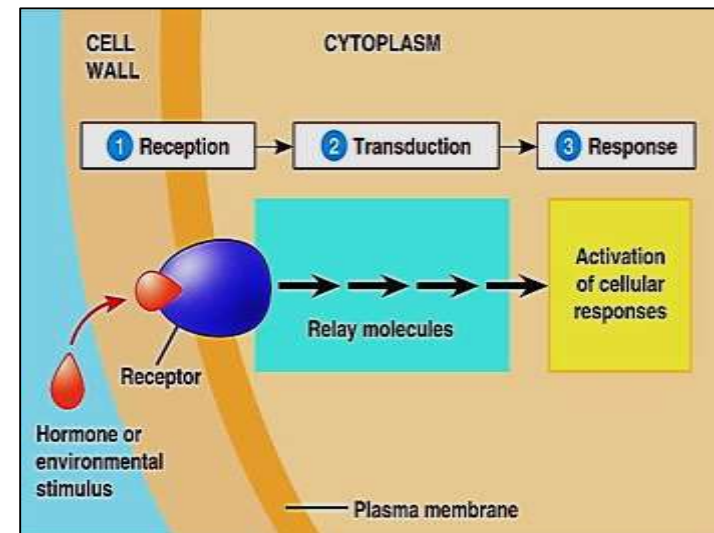
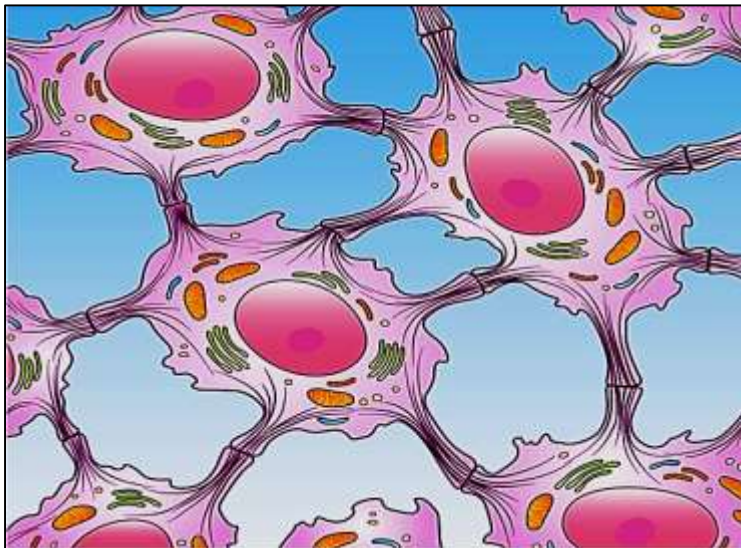
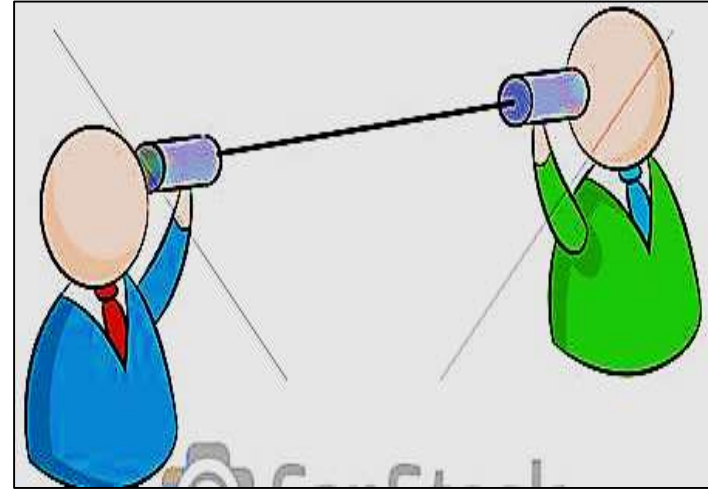
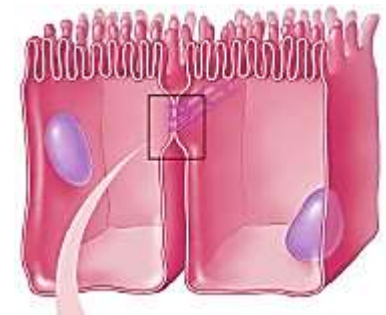


Cell Junctions & Cell Communication



Cell Junctions

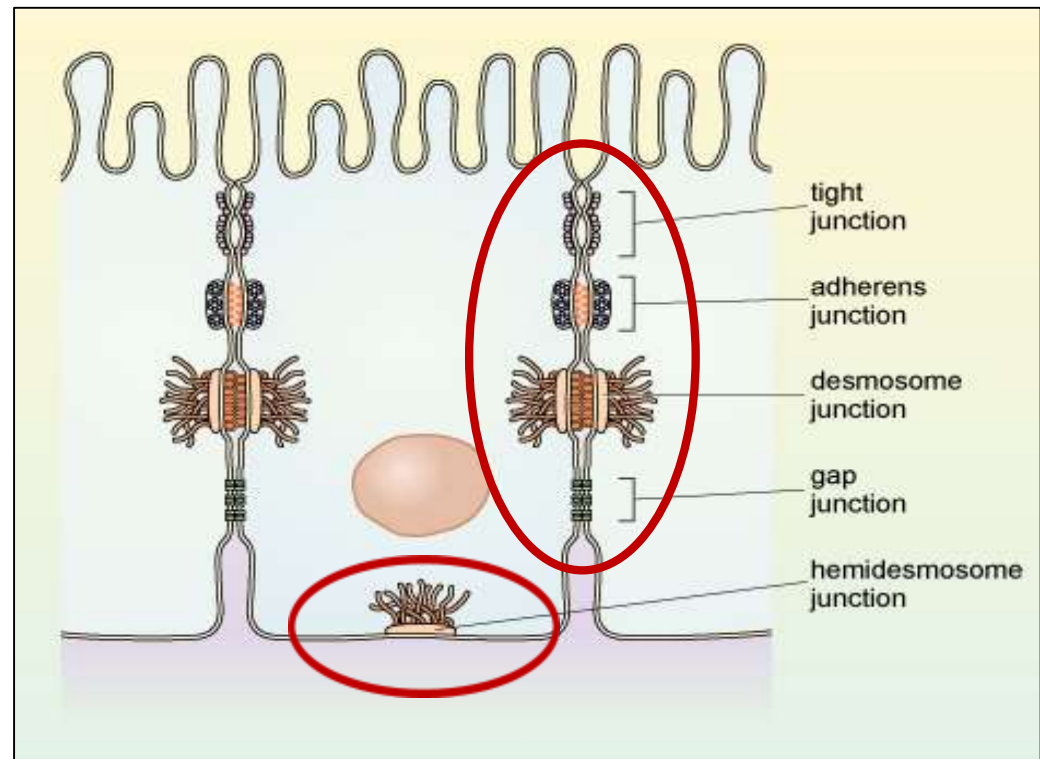


Definition & classification:

- Cell junction is the connection between **adjacent cells** or between the cell and extracellular matrix (**basement membrane**)

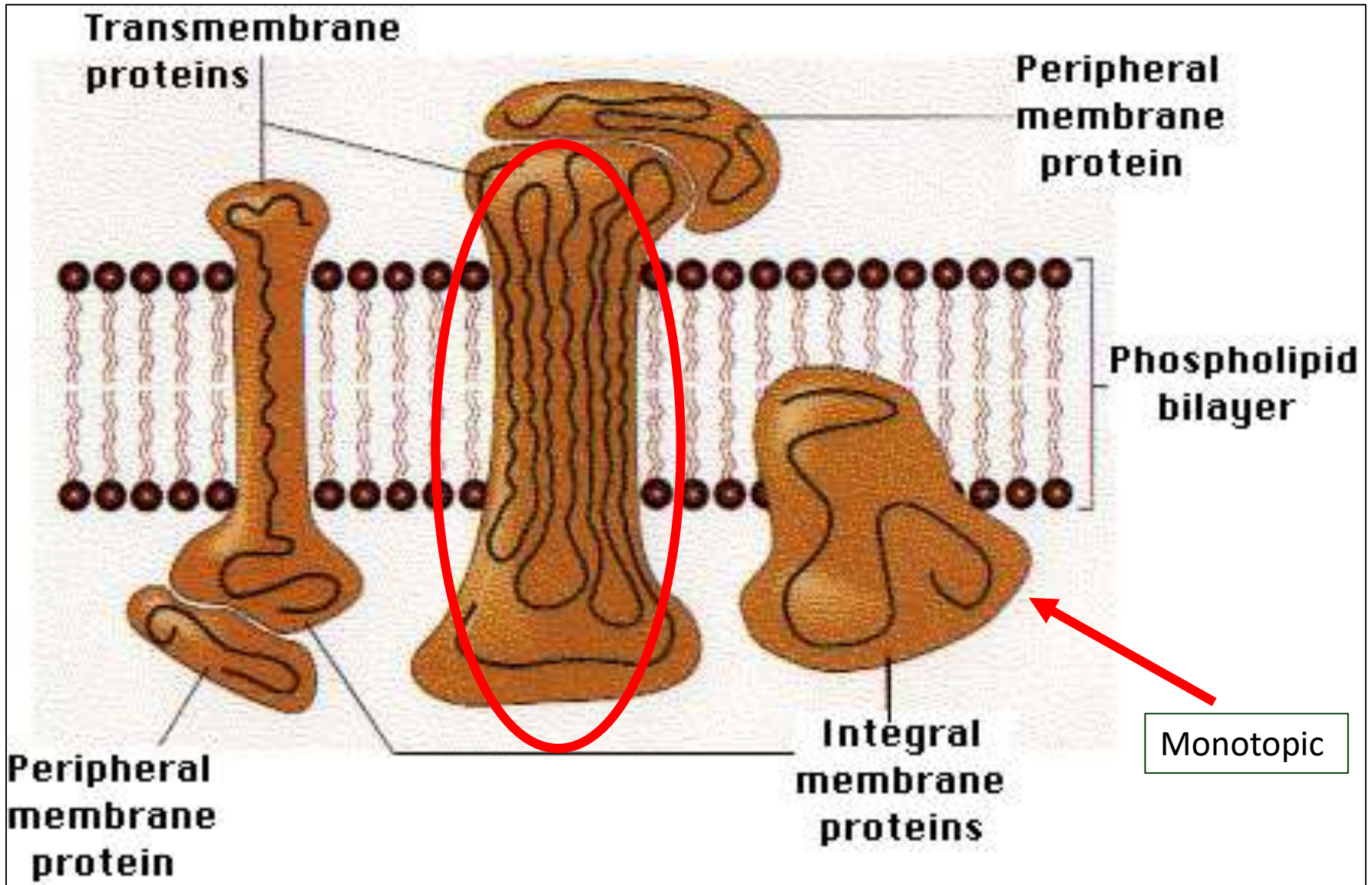
1- cell- cell adhesion

2- cell- matrix adhesion



Cell membrane proteins

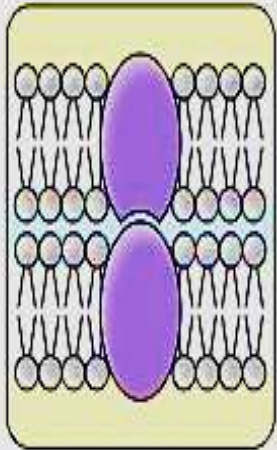
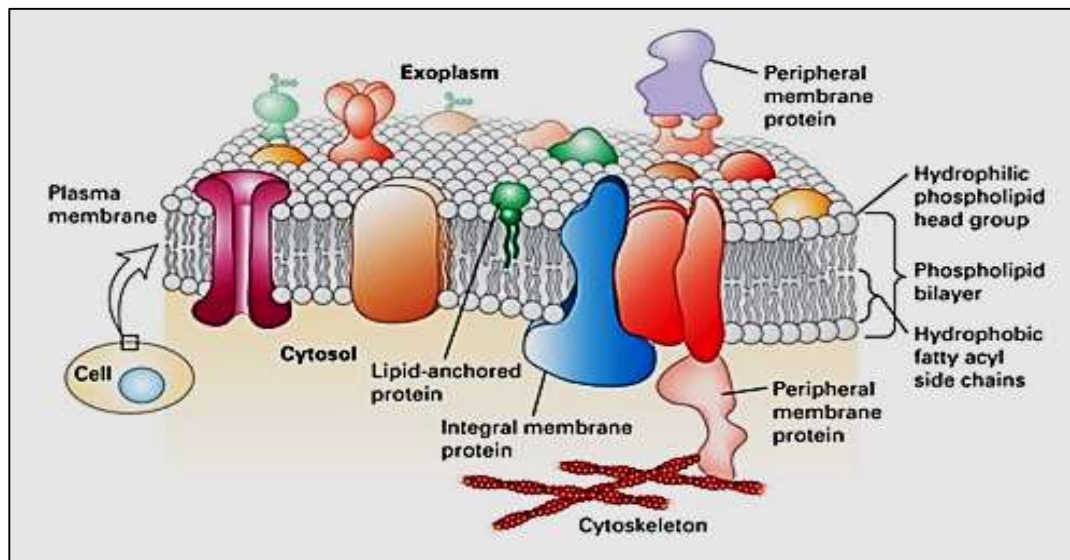
- They are of two types either **peripheral** or **integral**
- **Peripheral**: are **temporary attached** to the cell membrane. Found either on the outside or the inside surfaces of the cell membrane.
- **Integral** : are **permanently attached** to the membrane. They are of two types :
 - **Transmembrane** proteins that span **across** the cell membrane
 - **Monotopic** : proteins **attached to only one side** of the membrane and do not span across the cell membrane .



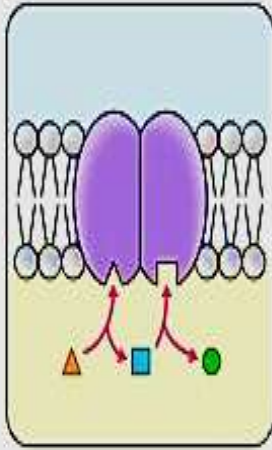
Types of cell membrane proteins

Function of integral membrane proteins

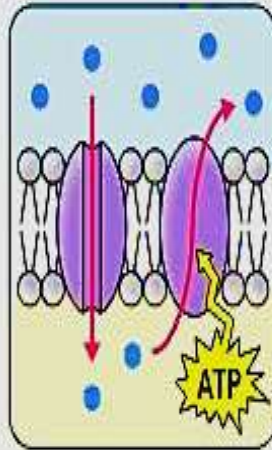
- **Junctions** – Serve to connect and join the cells together
- **Enzymes** – Fixing to membranes to perform a localized metabolic pathways
- **Transport** – Responsible for facilitated diffusion and active transport
- **Recognition** – May function as markers for cellular identification
- **Anchorage** – Attachment points for cytoskeleton and extracellular matrix
- **Transduction** – Function as receptors for peptide hormones



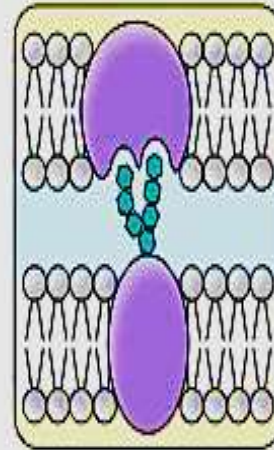
Intercellular Joinings



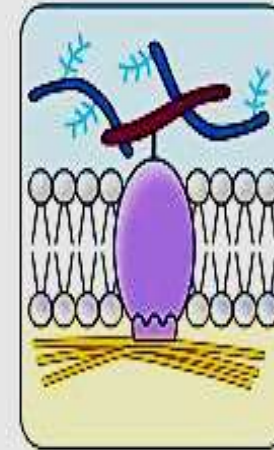
Enzymatic Activity



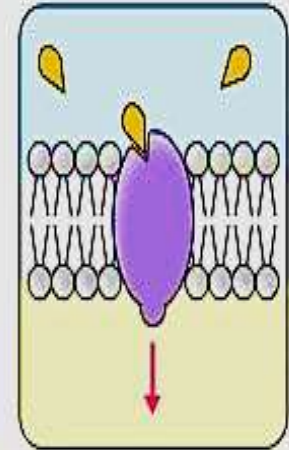
Transport (Active / Passive)



Cell-Cell Recognition



Anchorage / Attachment

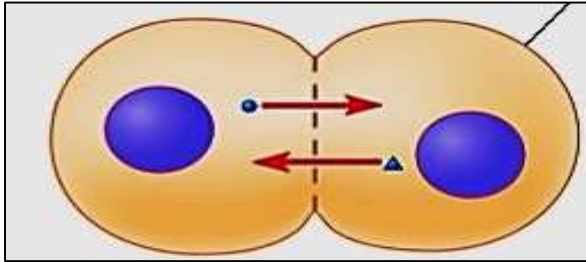


Signal Transduction

Function of cell membrane integral proteins

Function of cell- cell junctions (adhesions)

1. Communication between adjacent cells.
2. Support & reduce stress placed upon cells.



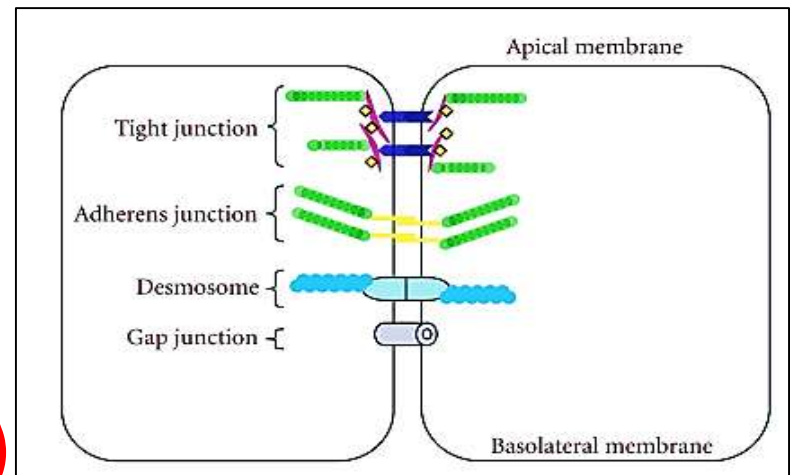
Cell adhesion (junction) is due to the action of :

**1- Cell Adhesion
Molecules
(CAMs)**

**2- Intercellular
junctions
(Adhesions)**

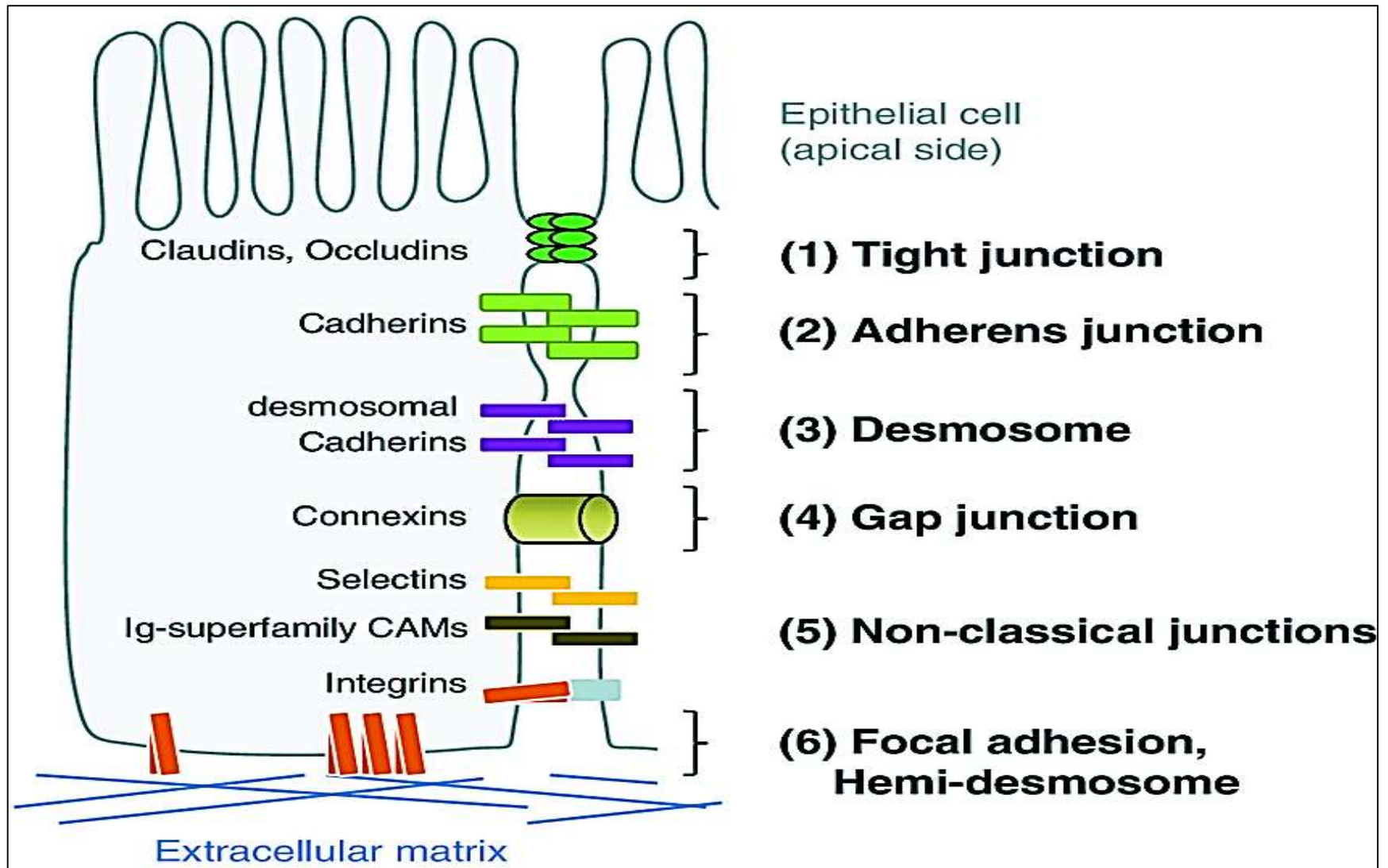
- Cell adhesion molecules (CAMs)

A group of cell proteins (glycoproteins) located on the cell surface (transmembrane) & involved in binding of the cell with neighbor cells or with the extracellular matrix in a process called cell adhesion

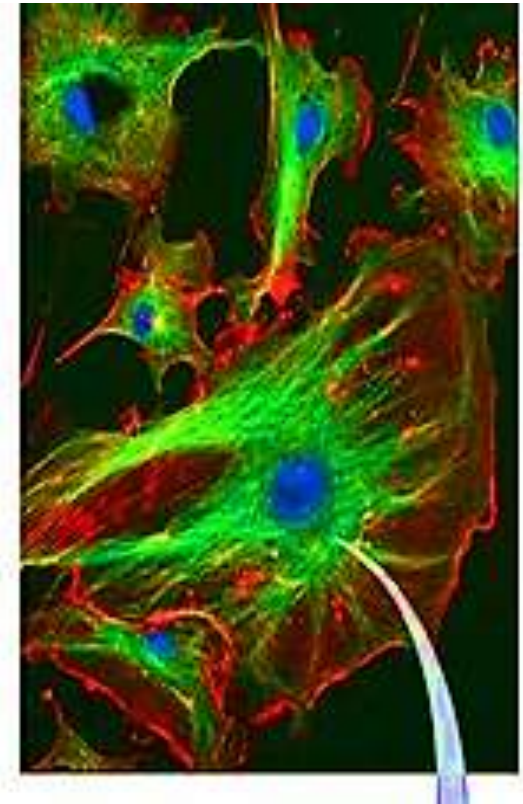
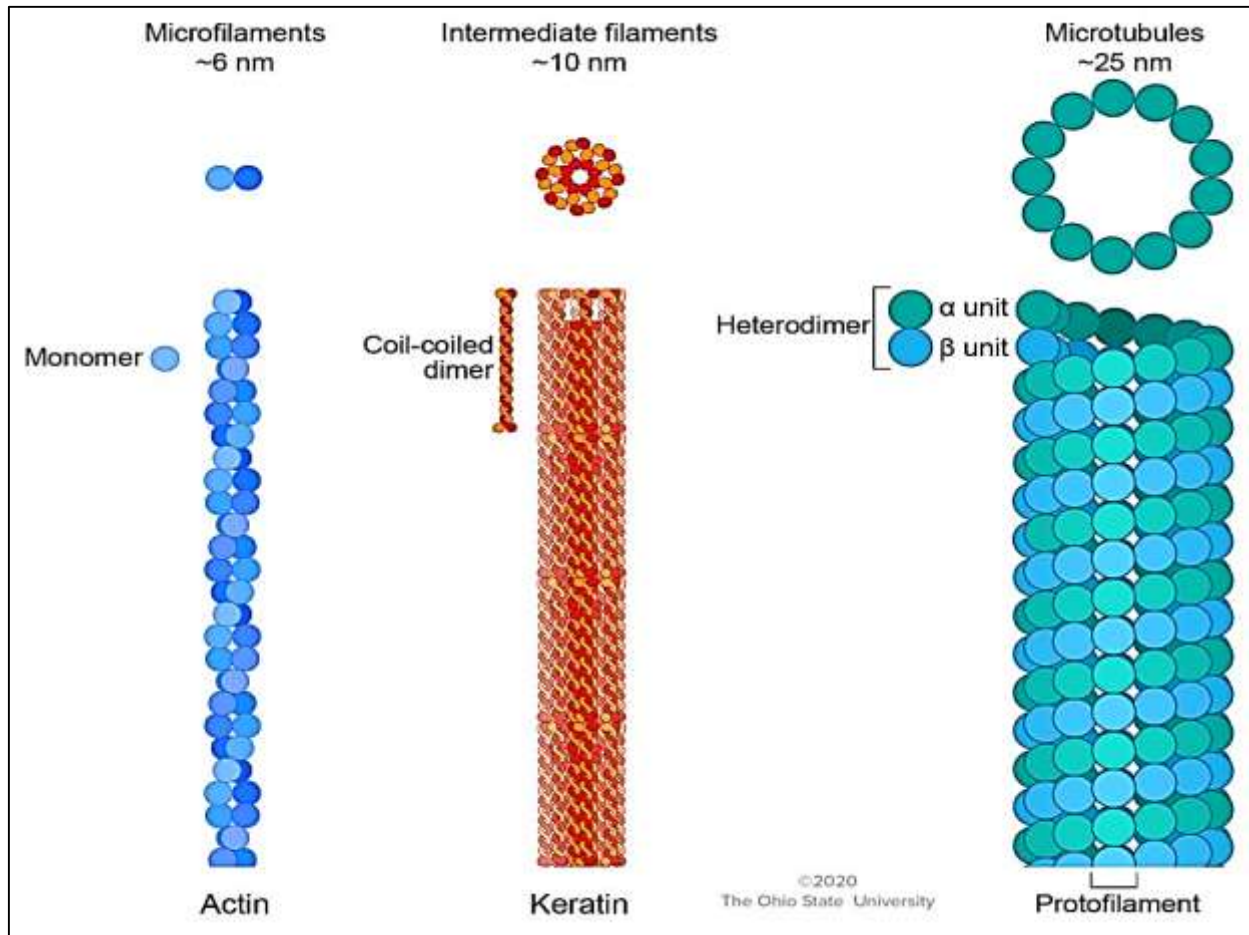


- Cell-cell junctions (Adhesions)

Represent the mechanism behind how cells connect & interact with each other, this is achieved by molecules of CAMs present at the surface of both cells. Cell junctions is vital for multicellular structural maintenance



Cell adhesion molecules & cell junctions

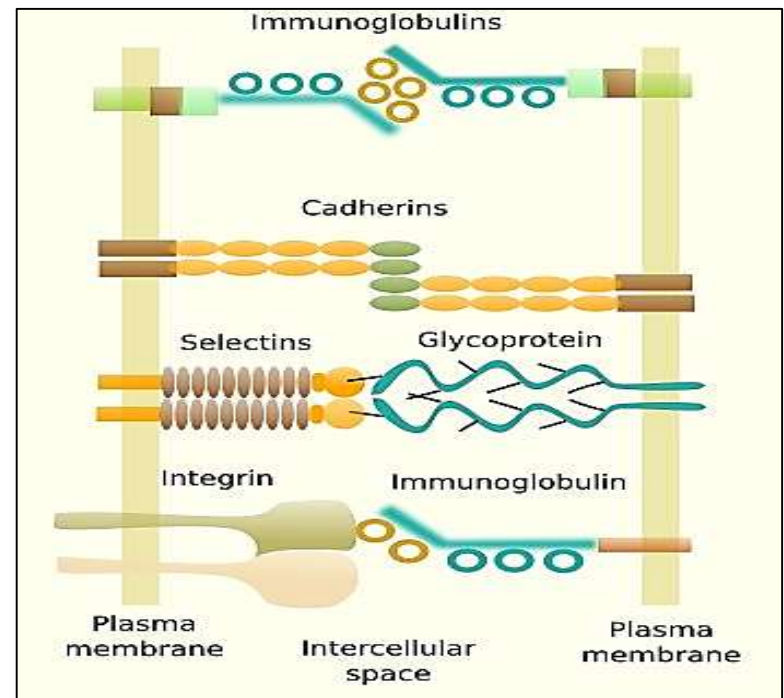
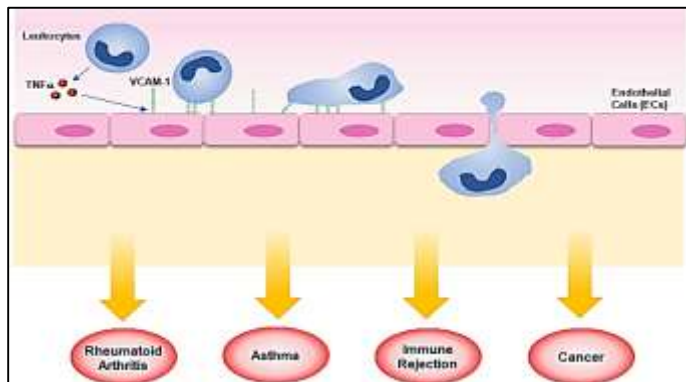
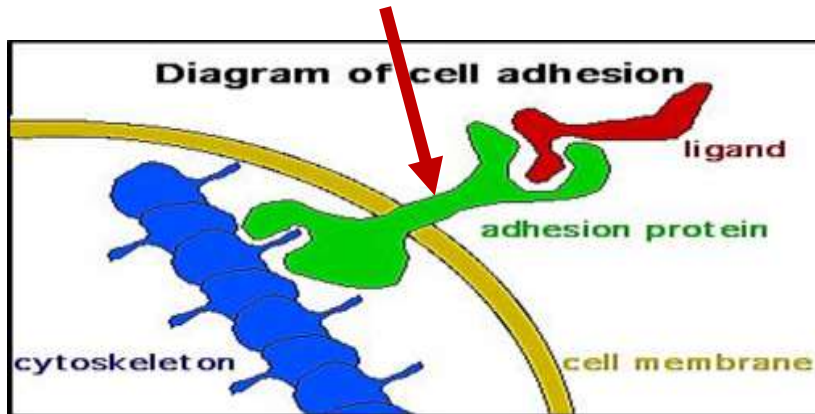


Inside the cell there are 3 types of **cytoskeletons** : actin filament , intermediate filament & Microtubules

Theses cytoskeleton is responsible for support, contraction, motility ,movement of organelles, organization of the cytoplasm & polarity of the cell

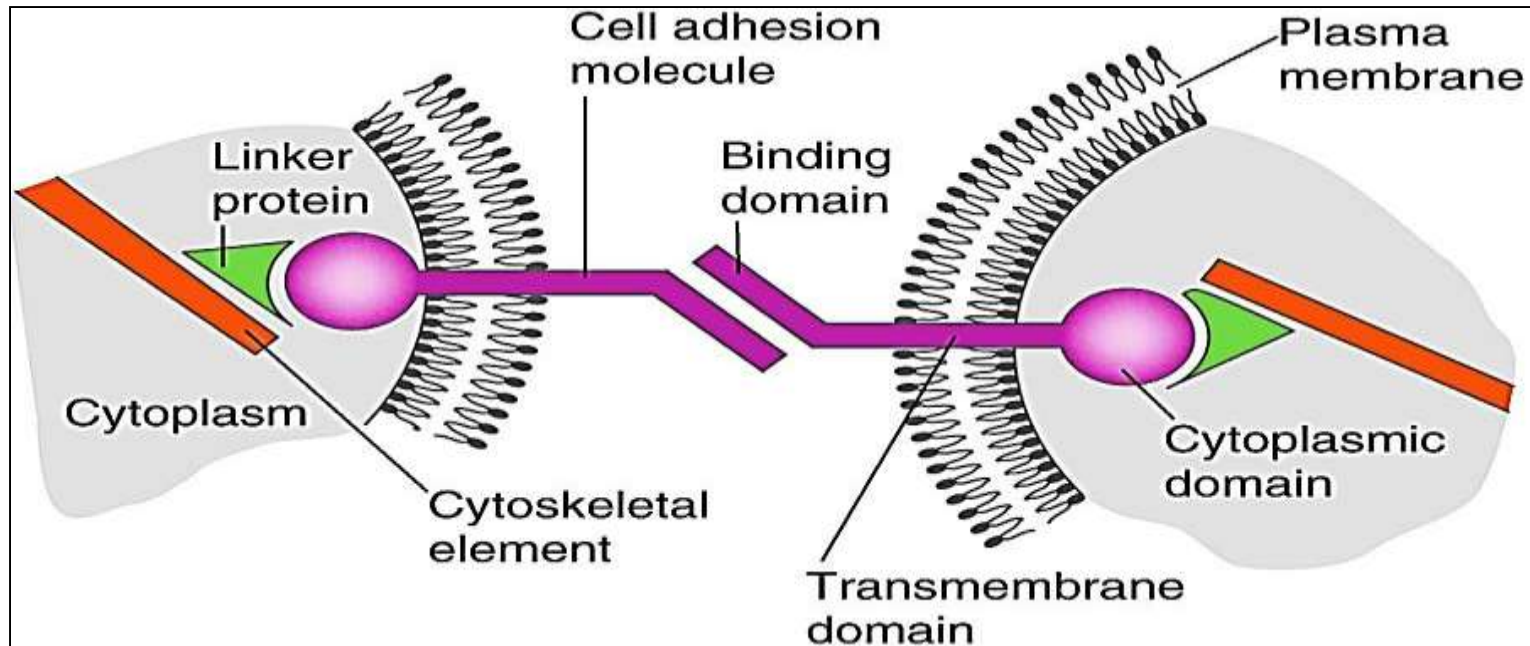
Cell Adhesion Molecules (CAMs)

- **Are Proteins** located on the cell surface (*Trans-membrane proteins*)
- They **help in attaching cells** e each other & e their EC matrix also **Play a role in immunity ,cancer metastasis, wound healing, and cell- tissue -organ development**



CAM molecule composed of 3 major domains:

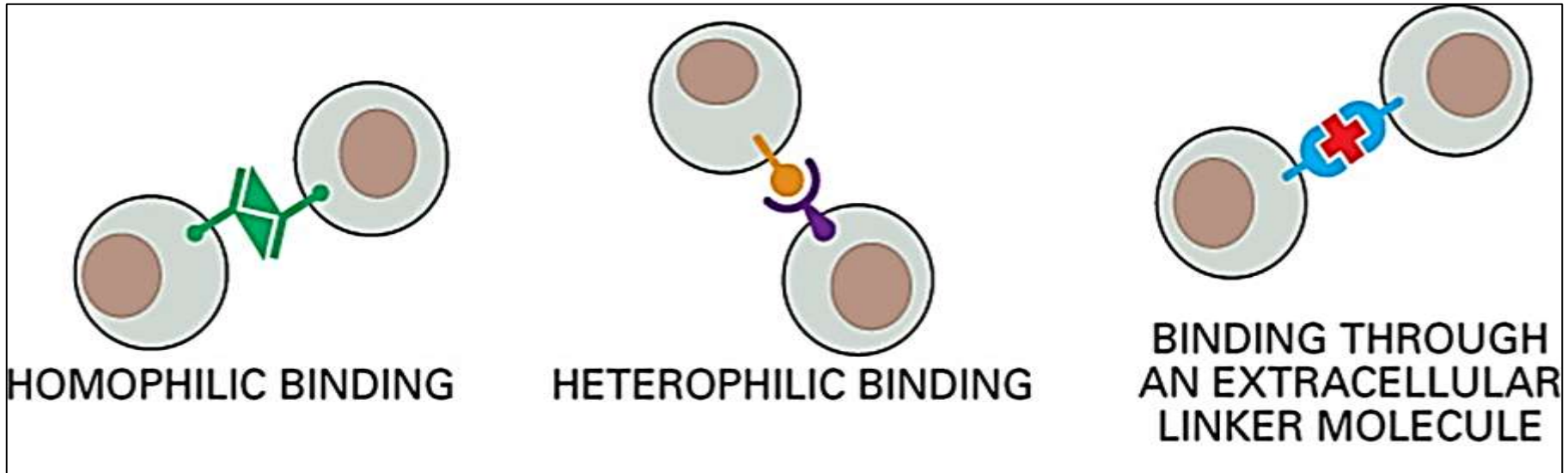
- The extracellular (ecto) domain: allows one CAM to bind with another CAM on an adjacent cell.
- The transmembrane domain: links the CAM to the plasma membrane through hydrophobic forces.
- The cytoplasmic (endo) domain: is directly connected to the cytoskeleton by linker proteins.



How CAM molecules bind with each other?

- When CAMs of the same kind bind together is called (***homophilic binding***)
- When CAMs of different types bind together or with the extracellular matrix is called (***heterophilic binding***).
- Through ***The linker molecule*** when the two CAMS are different .Laminin (linker molecule) is a family of large cross shaped molecules with multiple receptor domains.

Interactions between CAMs can be mediated by :



Binding of CAM on one cell to the same CAM on a second cell
Cadherin - cadherin

CAM on one cell type binds to a different type of CAM on a second cell
Selectins - mucins

CAM binds to EC matrix is also a heterophilic binding

The linker molecule in most cases is *Laminin*, a family of large cross shaped molecules with multiple receptor domains.

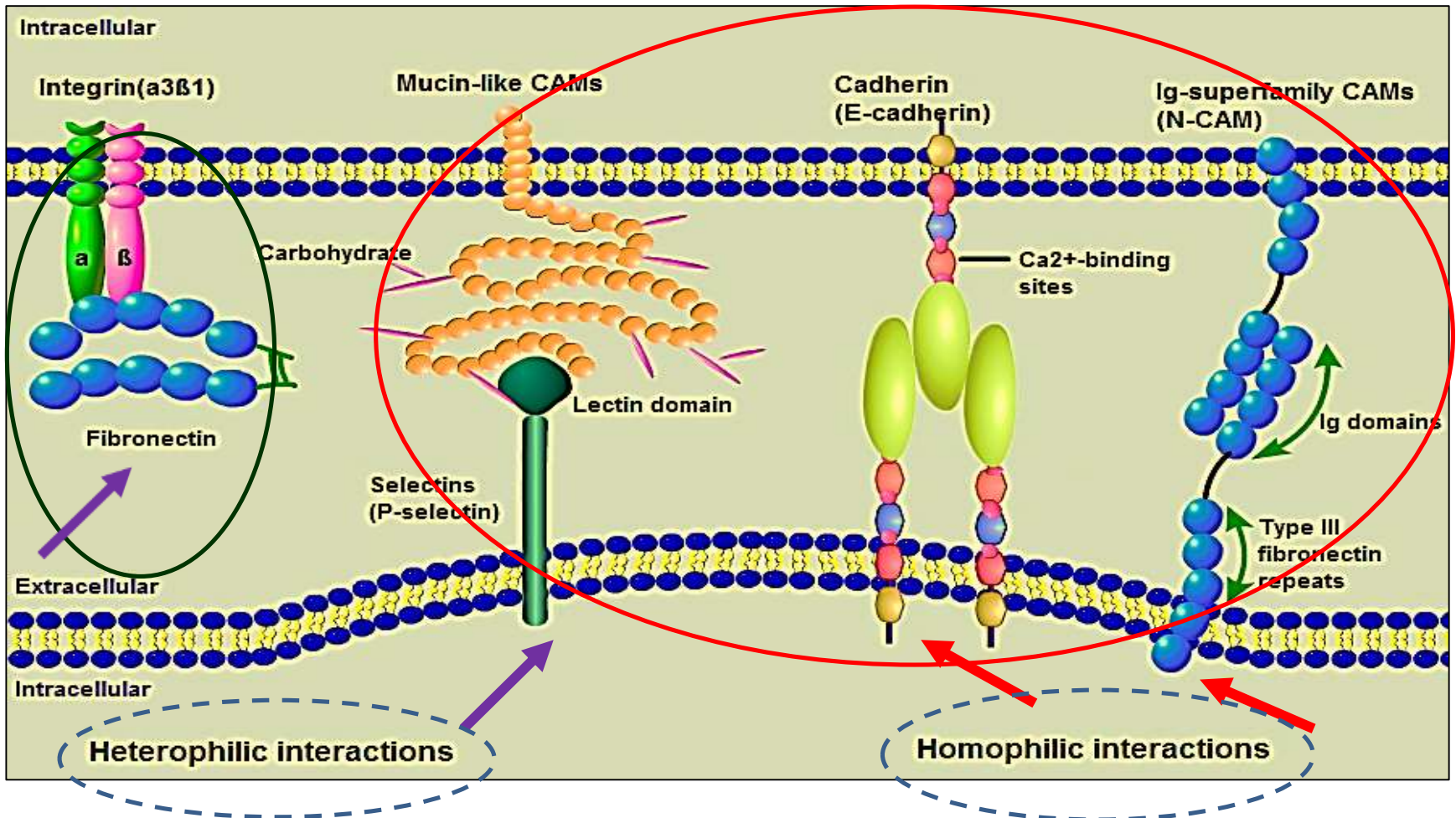
- **CAMs can be divided into 4 major protein families:**

cadherin

selectins

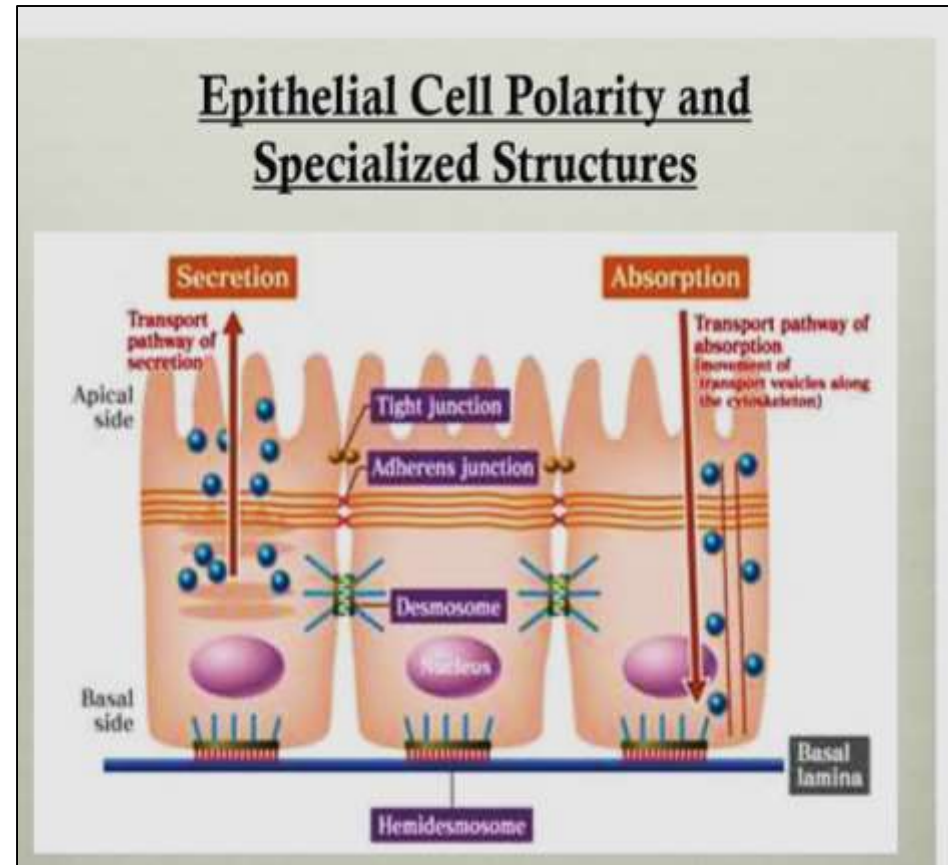
**Immunoglobulin
superfamily**

Integrins



CAMs Families: Only **Integrins** binds cell to the extracellular matrix (basement membrane), while **selectins**, **cadherins** , and **IgSF** members are associated with cell- cell adhesion

- Epithelial Cells are polar in nature because :
- Epithelial Cells rest on basal lamina & have apical & lateral borders
- Adjacent cells attach with CAMs & intercellular junctions
- CAMs Support & hold the tissues together



A. Cell- Cell junctions

- Cell junctions consist of multi-protein complexes
- They are particularly plentiful in epithelial tissue
- Types of cell junctions :

1- Occluding/Tight junctions: Seal cells

Together like a sheet to prevent flow of molecules even water or ions between cells

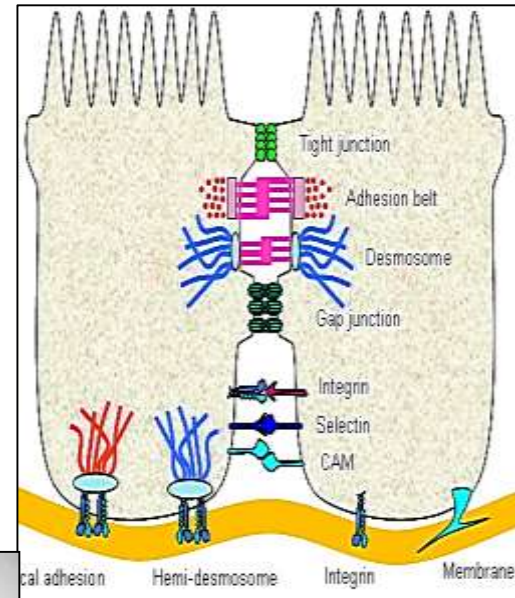
2- Anchoring junctions: attach cells & their

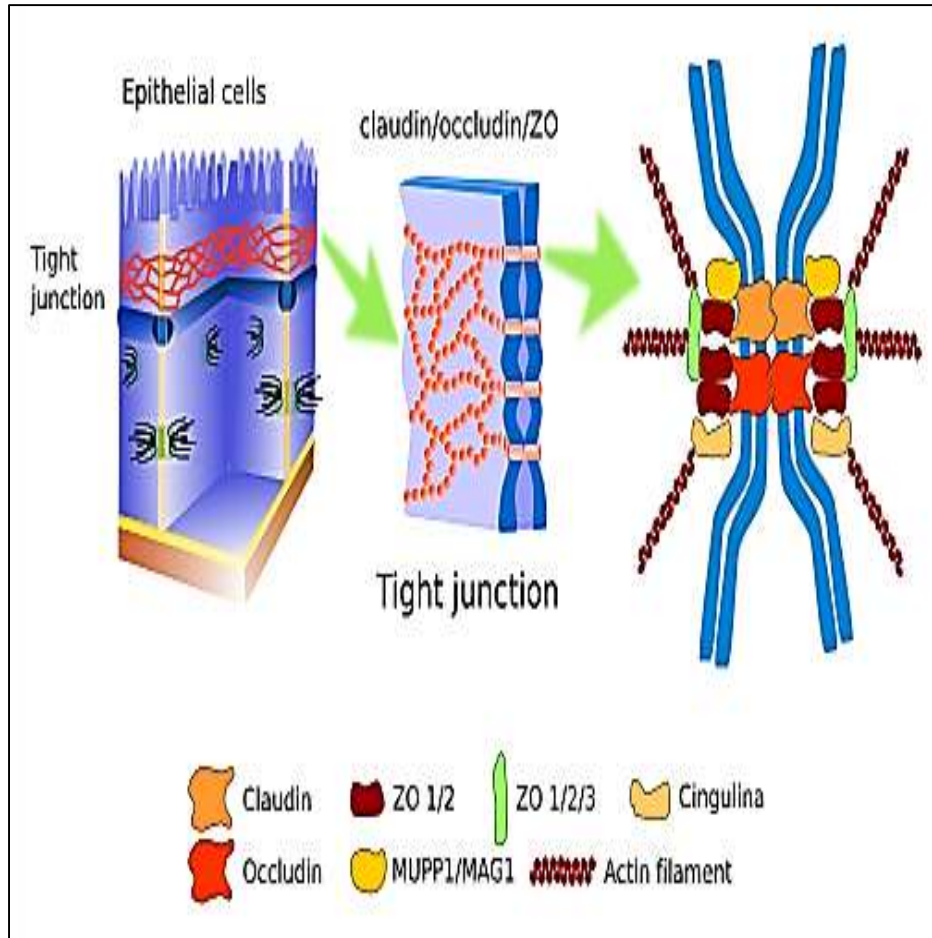
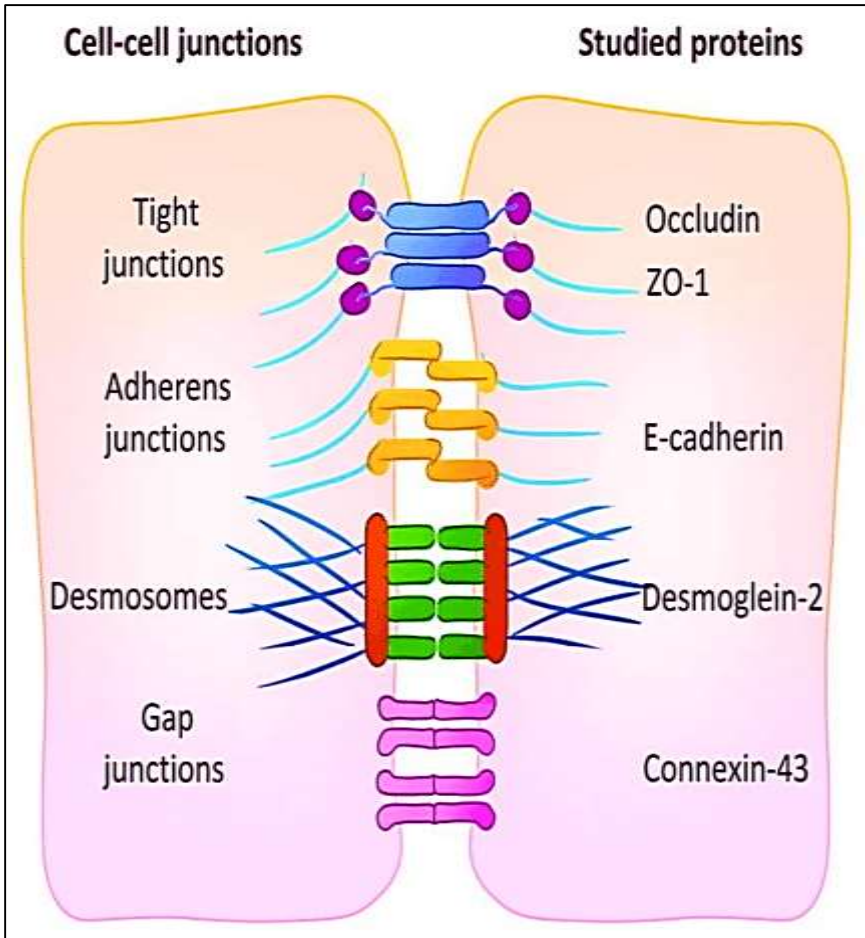
cytoskeleton to other cells or to ECM

provide mechanical support

3- Gap junctions: allow exchange of chemical / electrical

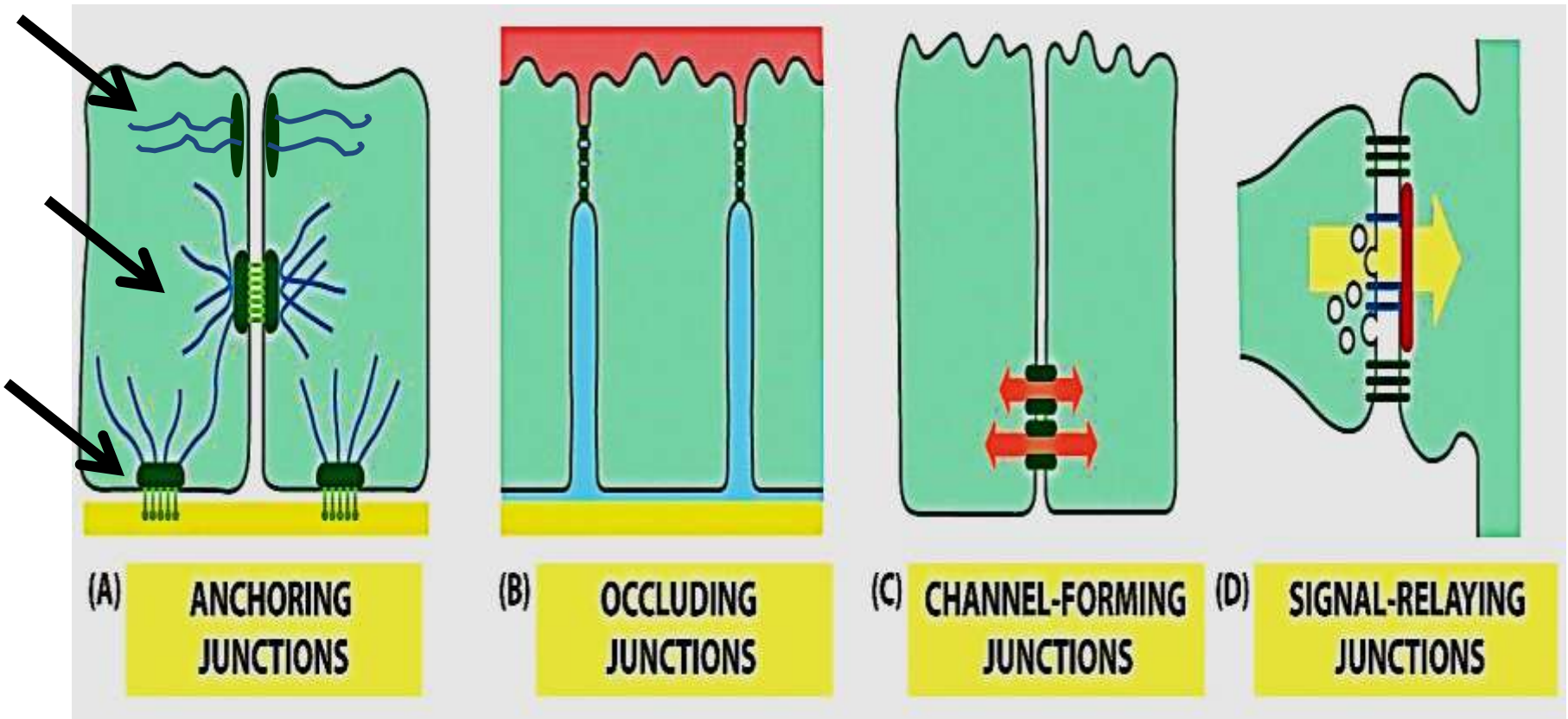
information between adjacent cells





Cell junctions are multi-protein complexes

Types of cell junctions in multicellular organism



1- Adherens junction,
2- Desmosome,
3- Hemidesmosome

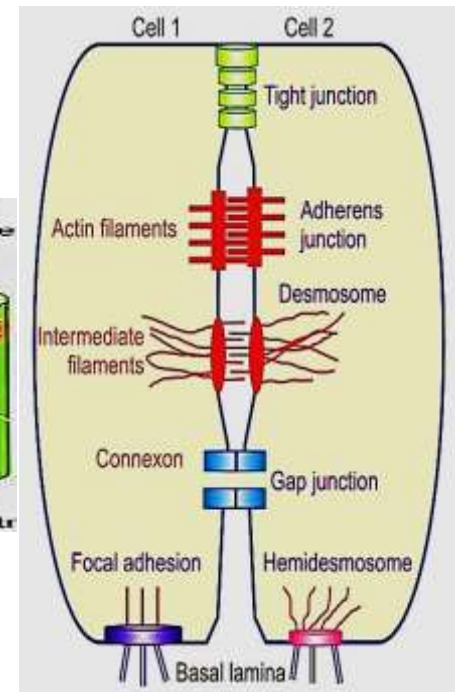
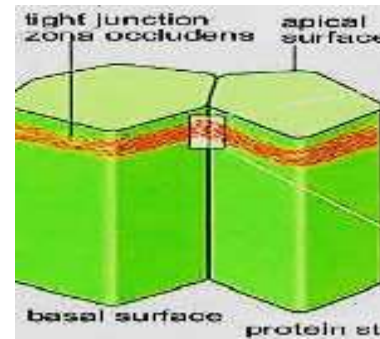
Tight junctions
(zonula occludens)

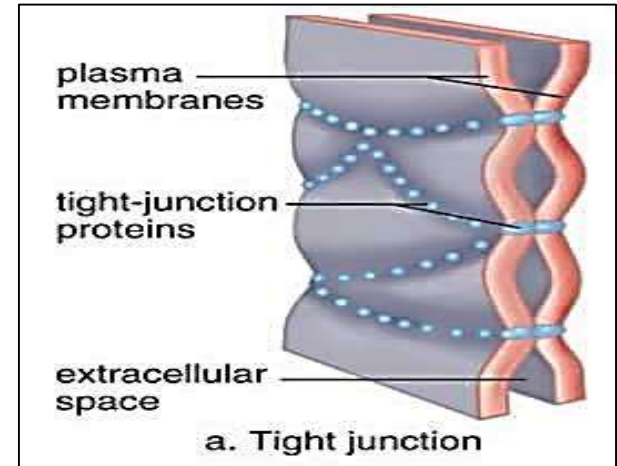
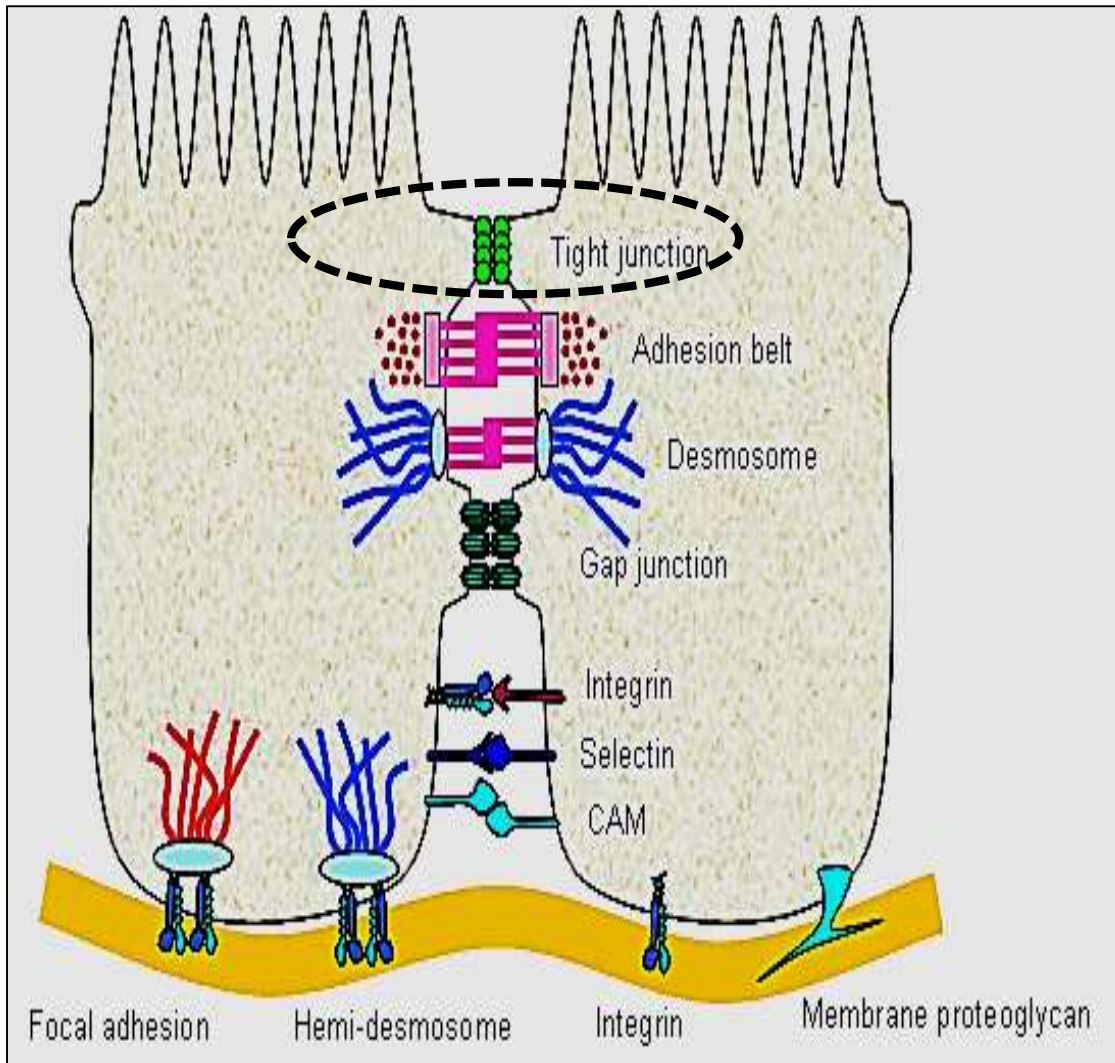
Gap junctions

Synapse

1- Occluding junctions

- Also called **tight** Junctions / **zonula occludens**
- Seal adjacent epithelial cells & is the most apical type of junctions
- Belt-like structure encircle completely the apical cell surface of the epithelial cells
Water & ion molecules cannot pass through that junction (passaging either through active transport or facilitated diffusion)
- The membranes of adjacent cells **fuse** at the tight junction completely forming **impermeable barrier/diffusion barrier**
- Proteins forming this junction are **occludins** and **claudins**

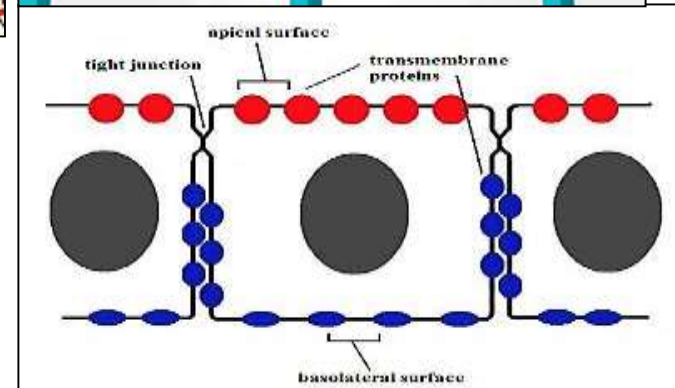
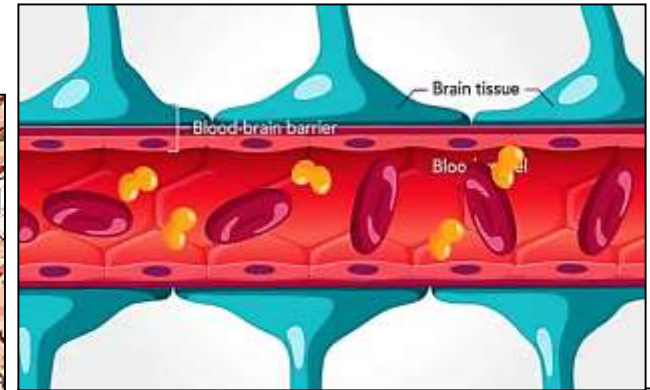
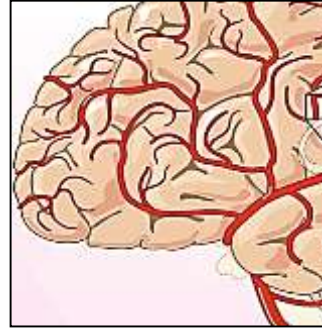


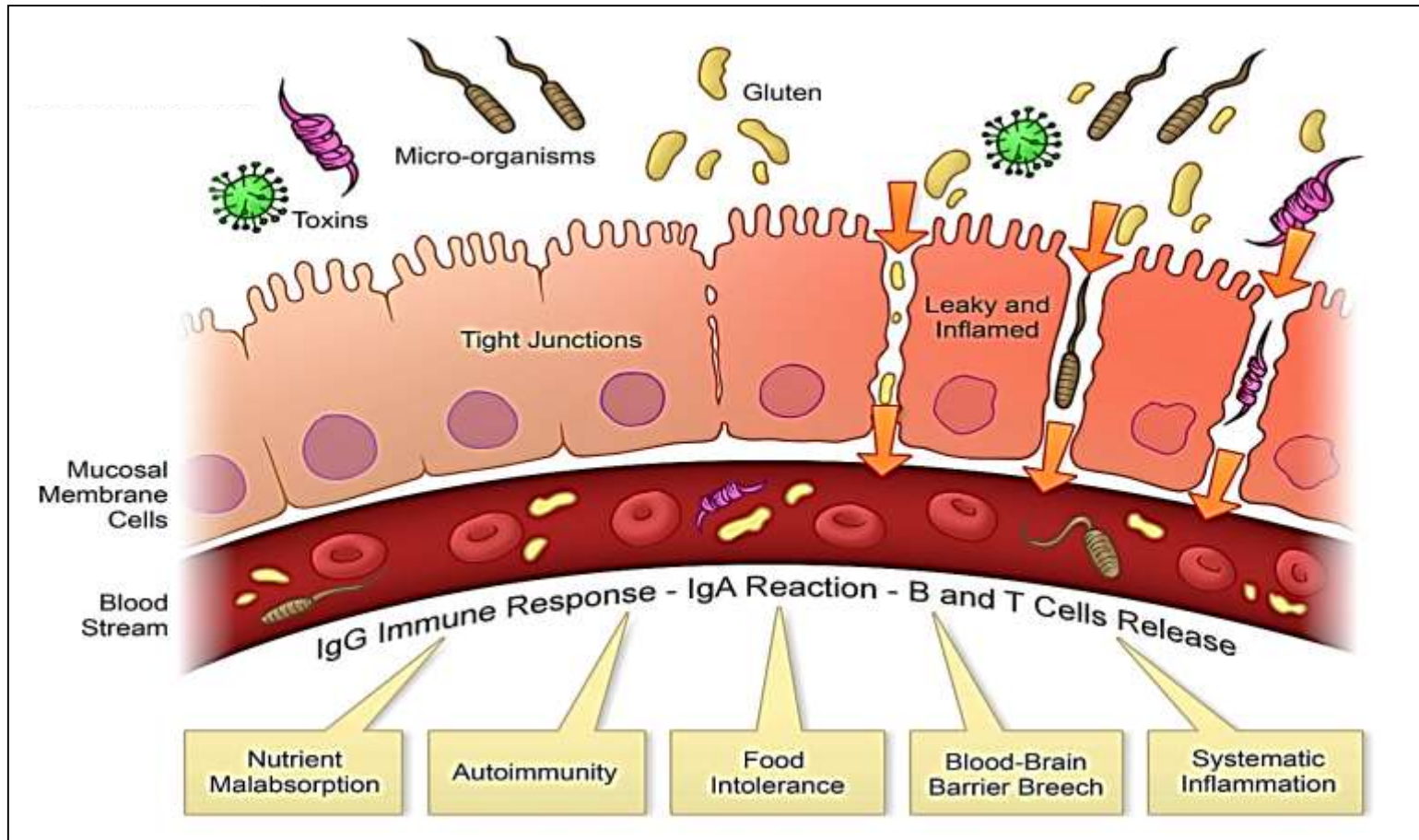


Tight junction **stitches** cells together

Functions of Tight Junction

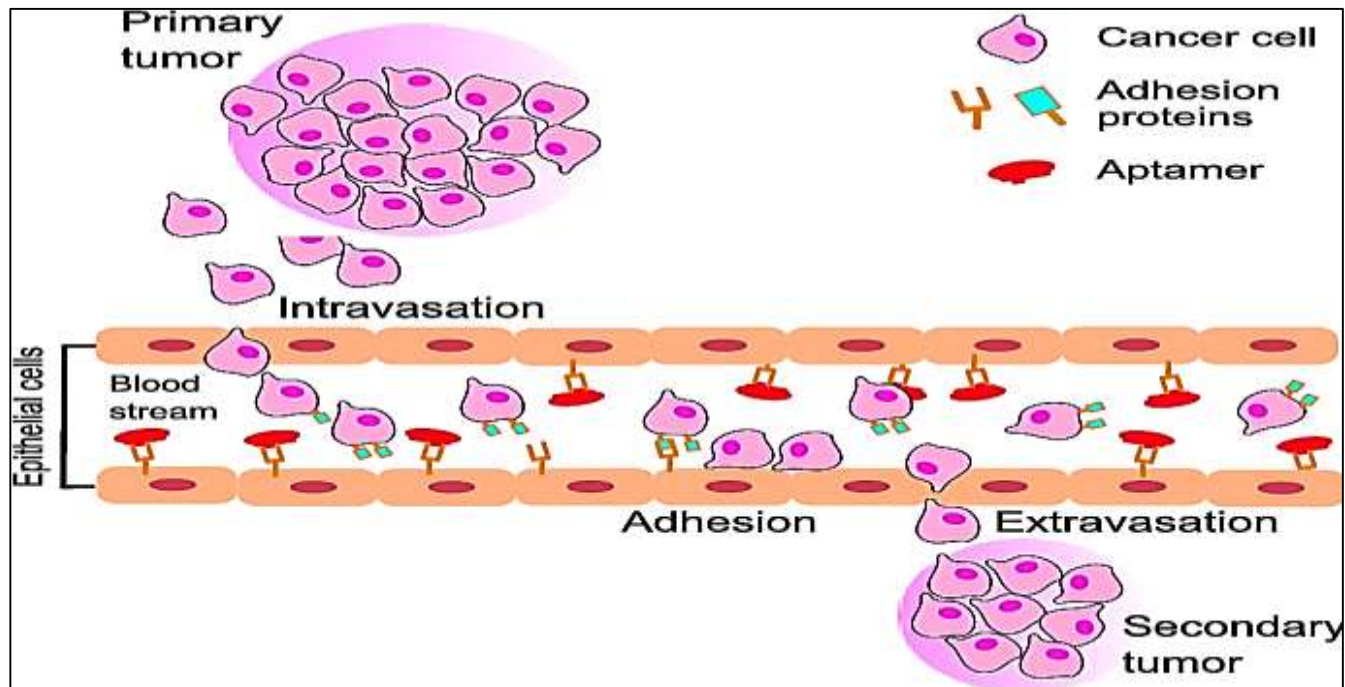
- **Protection: Seals cells so it creates barriers to prevent leaks**
- **Blood-brain barrier & other barriers in the body especially in GIT**
- **Maintain cell polarity: prevent membrane proteins of apical surface from being moved to basolateral surface to maintain cell receptors & function**
- **Ensure unidirectional transport, the apical set of transport proteins must not be allowed to migrate to the basolateral surface & vice versa**





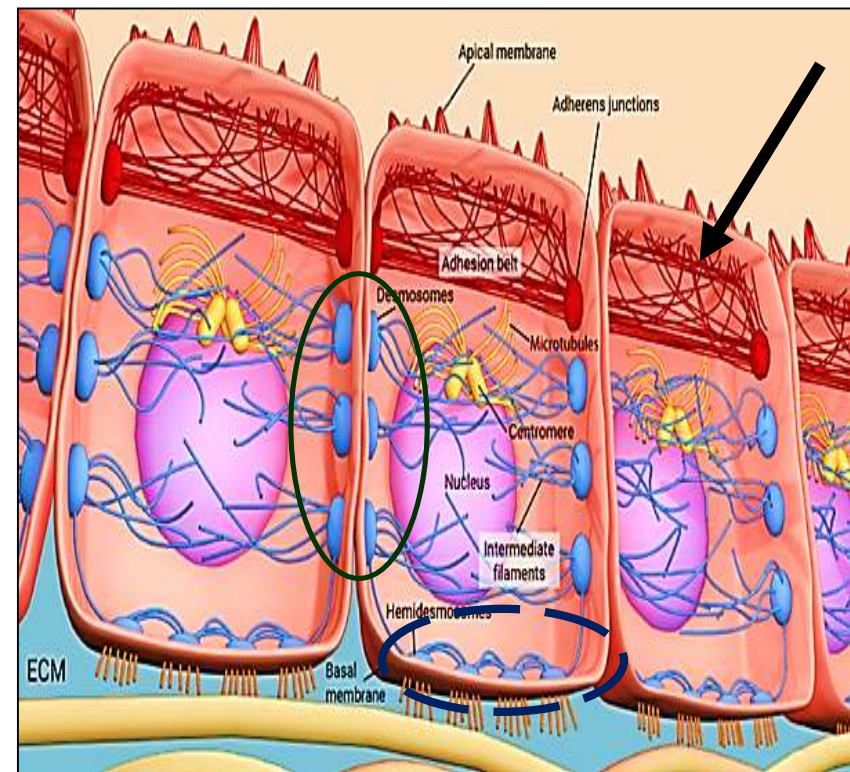
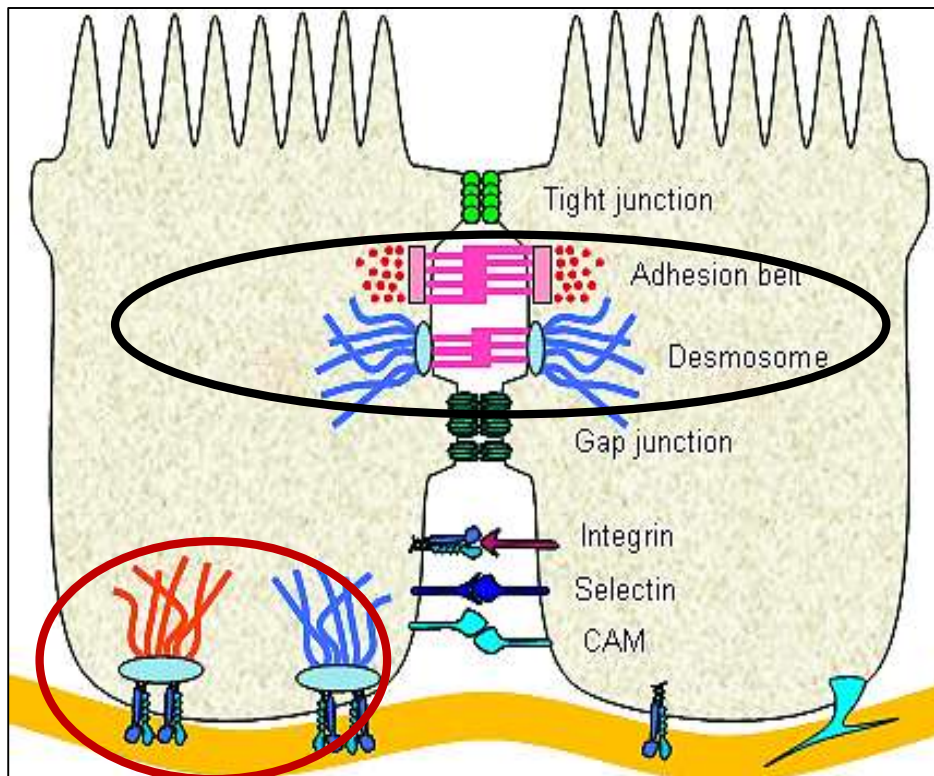
Leaky gut syndrome : is a disease happen when tight junctions between intestinal epithelial cells (**intestinal barrier**) become defective → abnormal increases in the intestinal permeability → leaking of a undigested food particles, toxins & microbes from the lumen into the bloodstream → digestive disorders and various inflammatory and immune diseases

- Most cancers originate from epithelial cells.
- Down regulation of Tight junctions adhesion proteins cause the tumor to dissociate and lead to subsequent metastasis.
- Researchers observed low expression of TJ proteins among highly metastatic cancer cells



2- Anchoring junctions

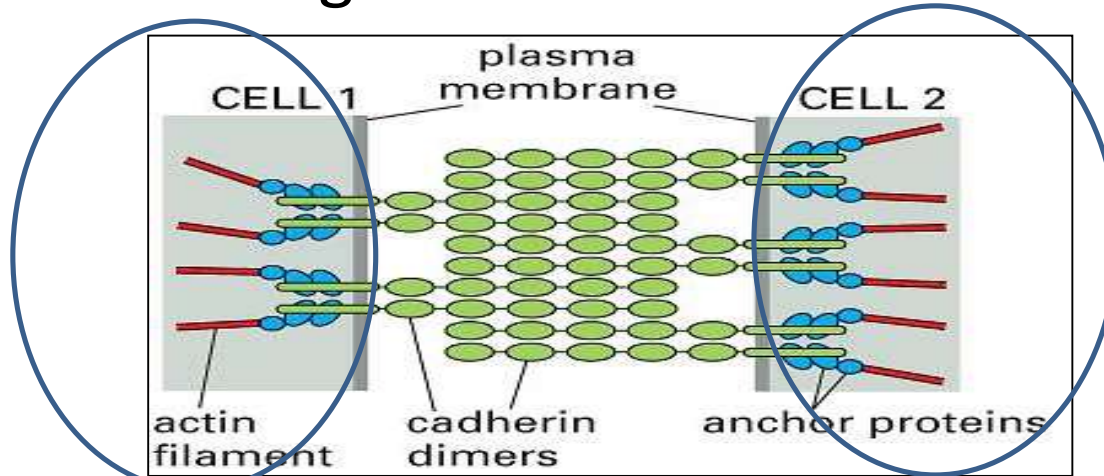
- Cell – cell: { Adherens junction
Desmosome
- Cell – matrix: { Hemi-desmosome



2- A- Adherens junction/Zonula adherens

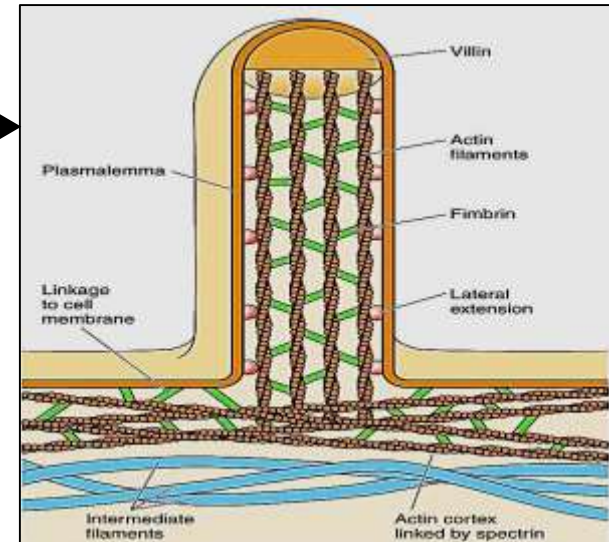
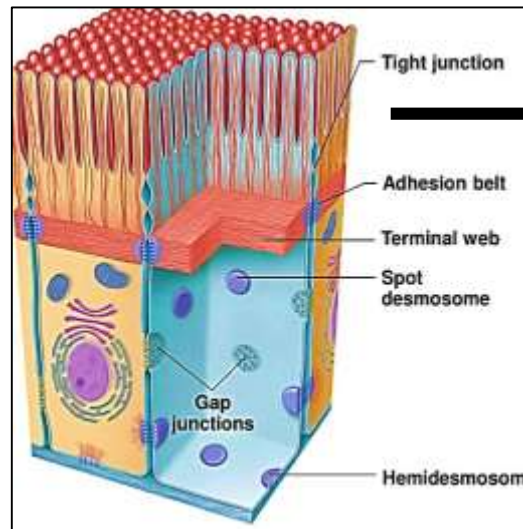
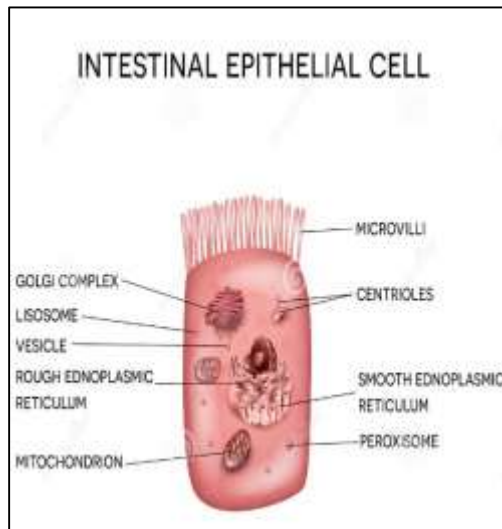
- Integral membrane proteins, connect the cell cytoskeleton to another cell
- Encircle the cell, just below ZO, but they don't seal
- Found in tissues subject to Stretch to resist separation of cells during contraction (**bladder, uterus, skin**).
- The opposing plasma membranes has a narrow space in-between
- The cytoplasmic surfaces of adjacent cell membranes at the junction have electron dense plaques (glycoprotein)

- Proteins forming the Junction are **Cadherins, Catenin**



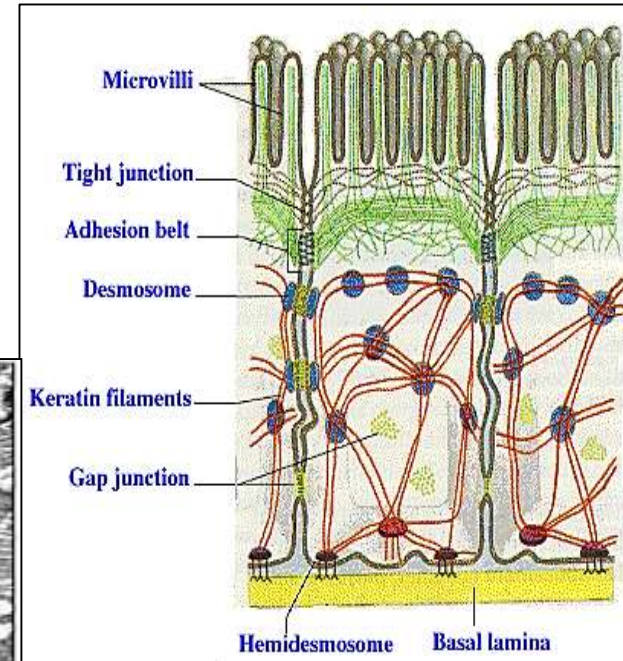
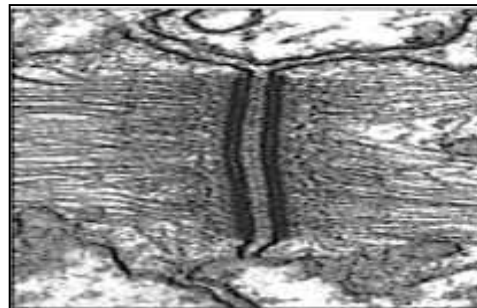
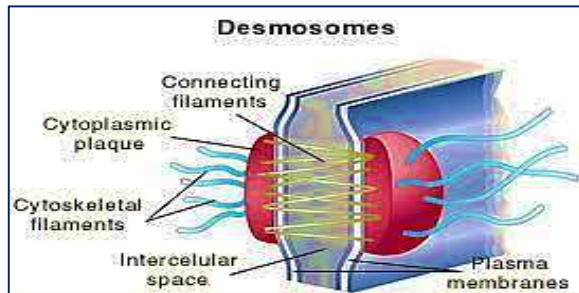
- The plaques (catenin) provide attachment for transmembrane protein (cadherins) and for the fine cytoskeleton filaments

Actin filaments. This junction makes the **Terminal Web** at the apical part of epithelial cells having microvilli



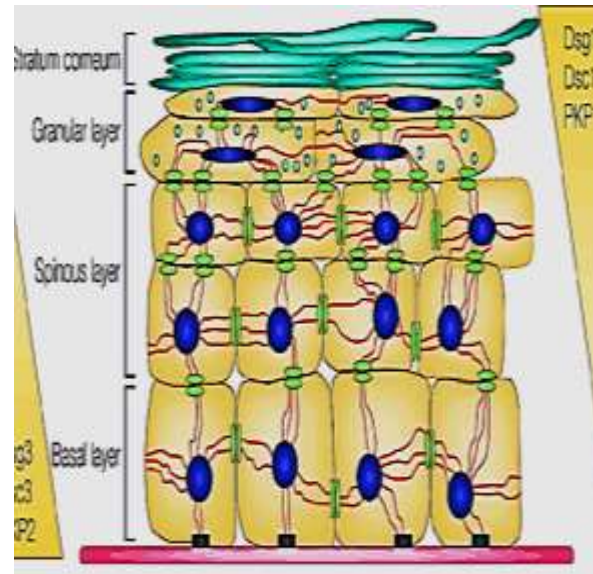
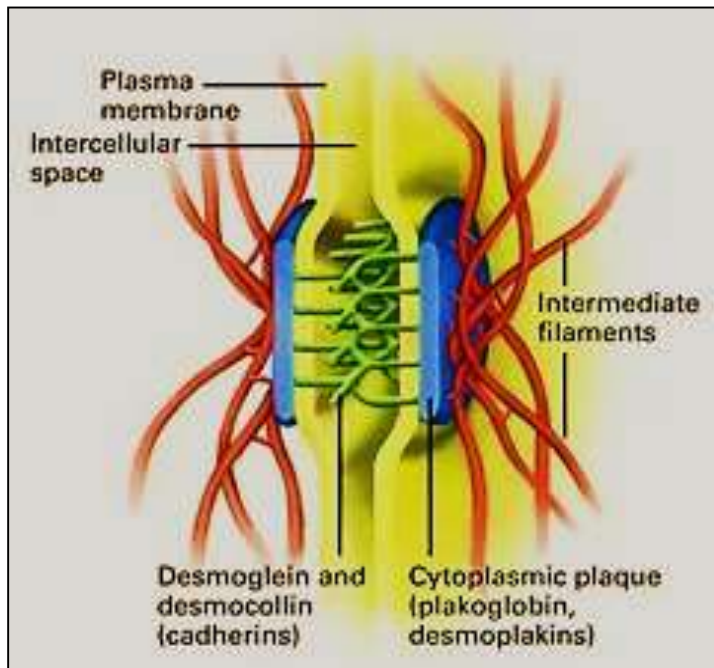
2- B- Desmosomes/Macula adherens

- Scattered disc- shaped structures, arranged randomly on the lateral sides of the cells **don't form belt (spot- like)**
- Disc plaque at the surface of one cell connects with an identical one at the surface of the adjacent cell



- Proteins forming the junction of the desmosome are **desmoplakin** (plaque) & **desmoglein & desmocollin** (transmembrane proteins(members of the cadherin family)

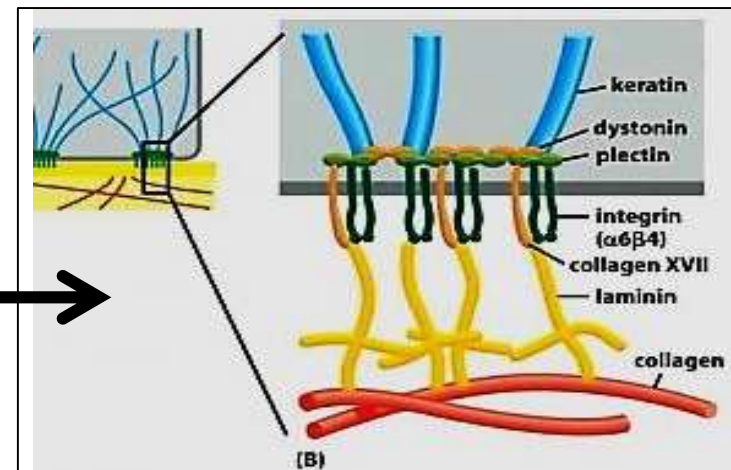
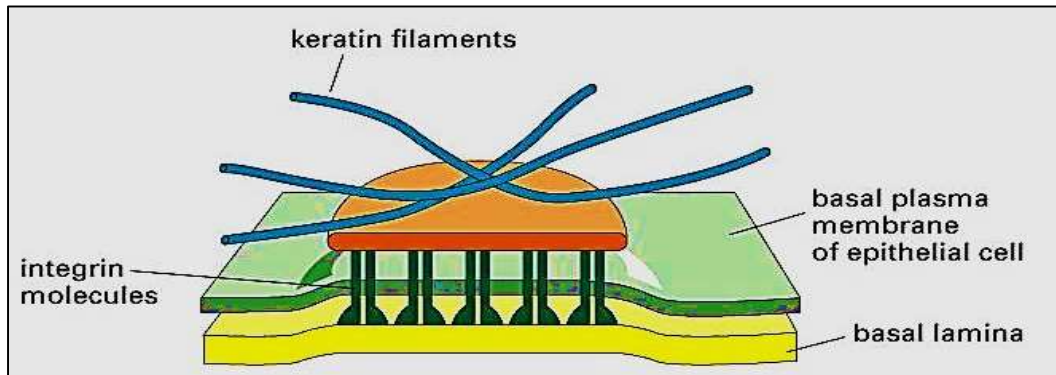
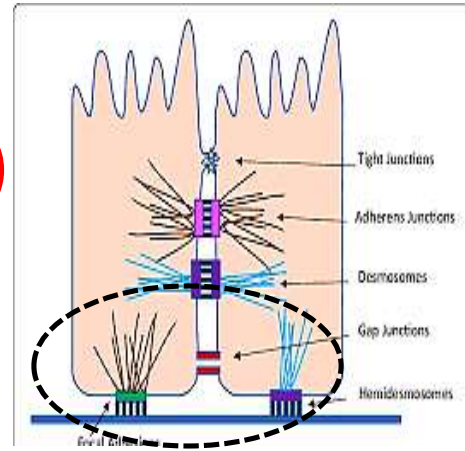
- Within the cell, the desmoplakin provide insertion to **keratin (intermediate cytoskeleton filaments)**
- Found in tissues to resist high stretch and stress e.g. **between cardiac muscles (intercalated discs)**, skin, intestine. They are stronger than adherens junction



Pemphigus vulgaris
Due defect in desmoglein of
Epidermis of skin

2- Hemidesmosomes

- Half desmosome (**cell – basal lamina /ECM**)
- At the base of epithelial cells
- Bind epithelial cells to basal lamina
- The transmembrane protein is **integrins** protein
- Plaques provide attachment for **keratin filaments**
- integrin molecules connect to **laminin** of basal lamina in turn connect e collagen in ECM → cell-matrix adhesion (**bullous pemphigoid**)



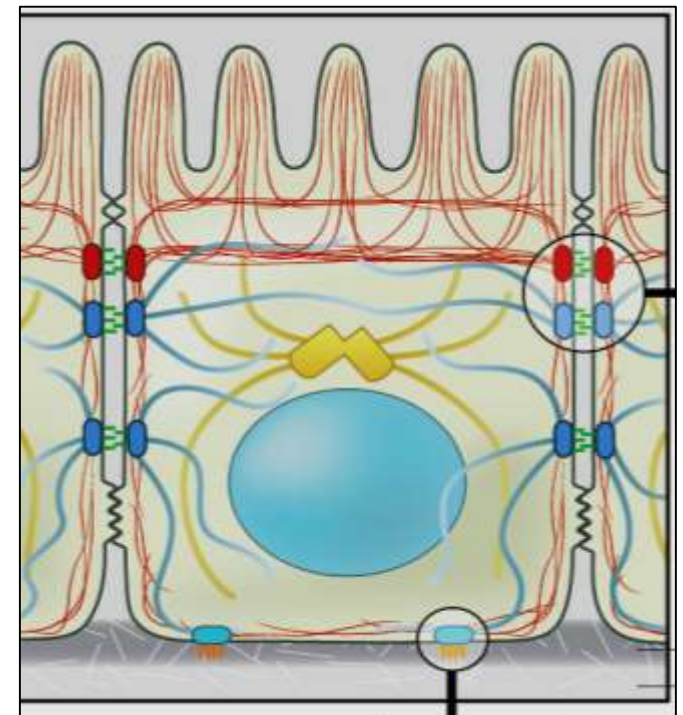
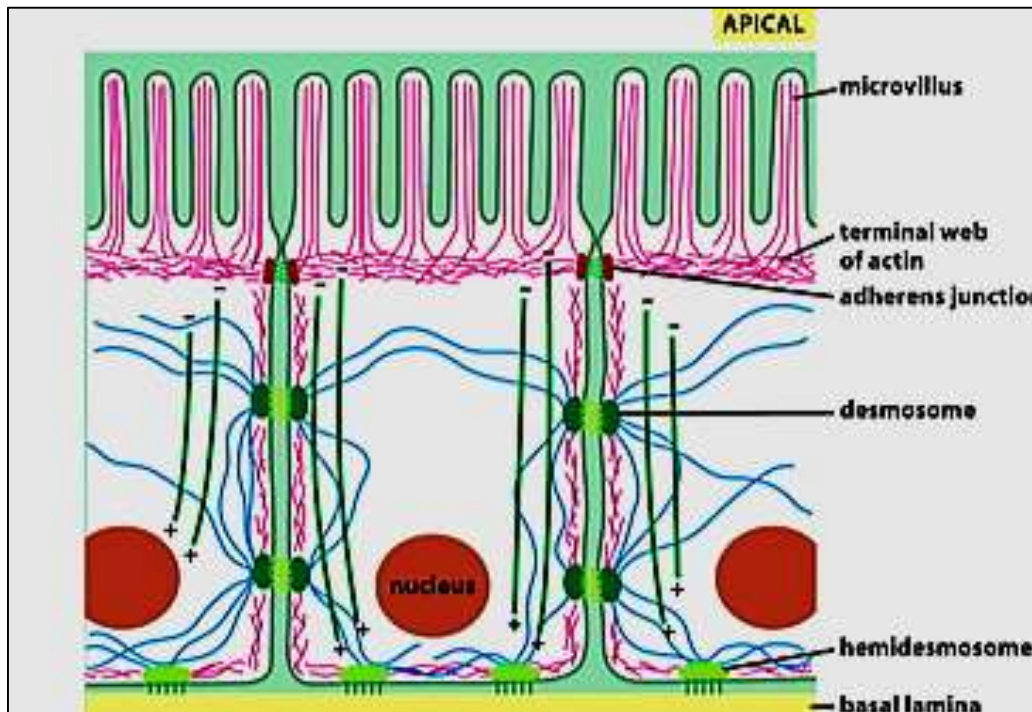


Bullous pemphigoid (BP)

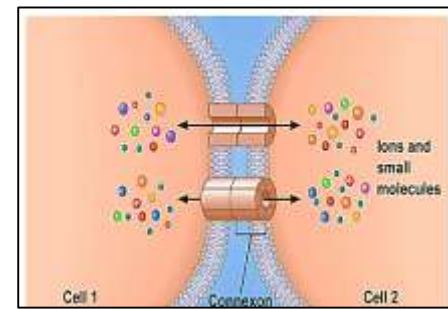
is a chronic blistering of the skin. It ranges from mildly itchy welts to severe blisters and infection, and may affect a small area of the body or be widespread. The vast majority of those affected are elderly, but it has been seen at all ages.

Function of anchoring junctions

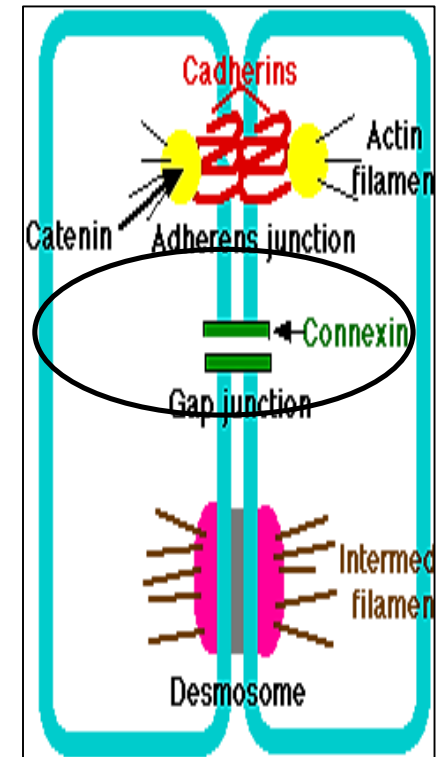
- Stabilize cells against mechanical stress
- Mechanically attach cells & their **cytoskeleton** to their **neighbor cells** or to the **extra cellular matrix**

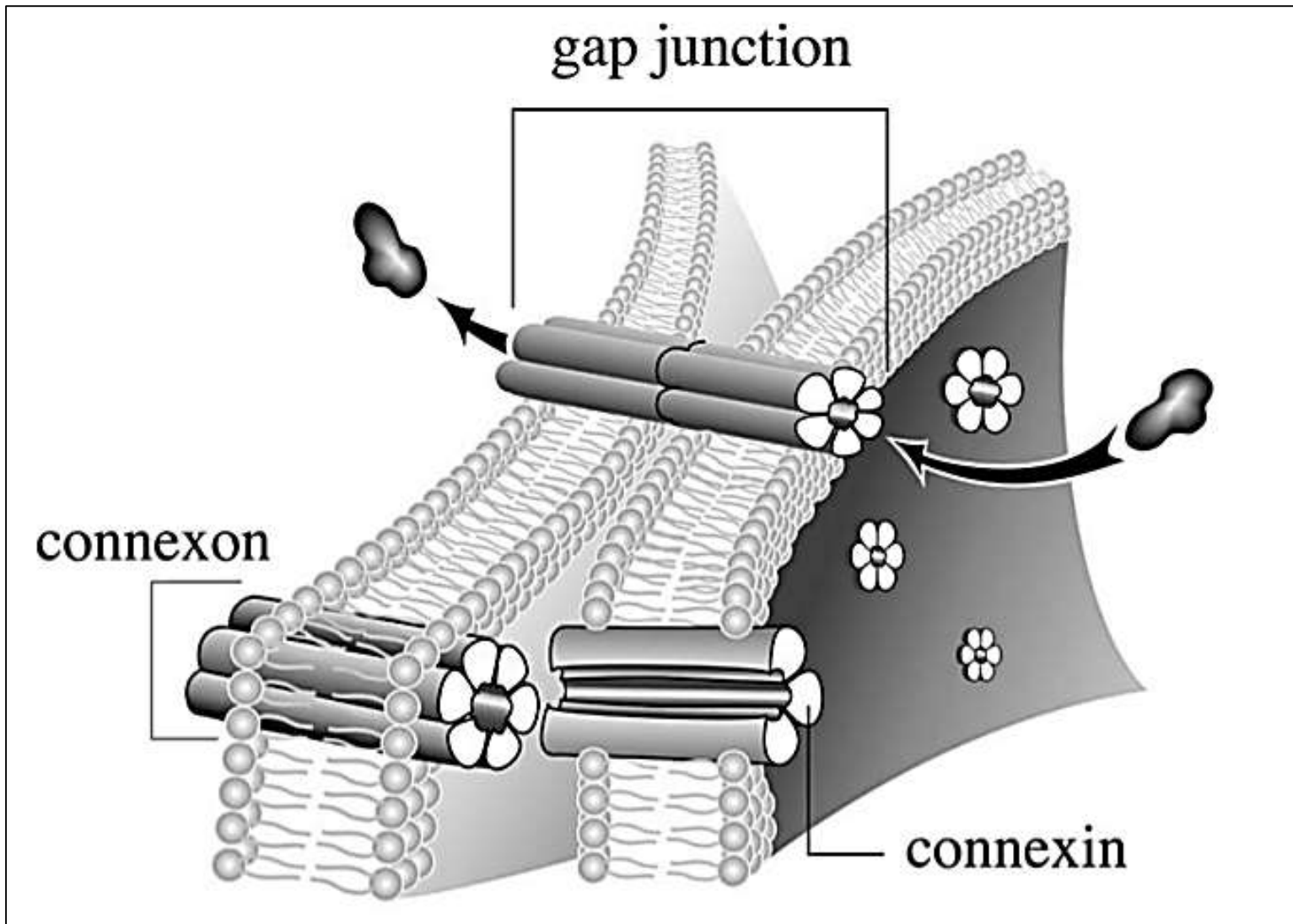


3- Gap junction (GJ)



- Transmembrane proteins form intercellular channels that allow direct transfer of ions, small molecules, electric impulses between cytoplasm of adjacent cells
- This type of junction makes the cells chemically or electrically coupled
- This type of junction is important in heart muscle cells. It provides low resistance ions pathways through GJ allowing the cell to contract





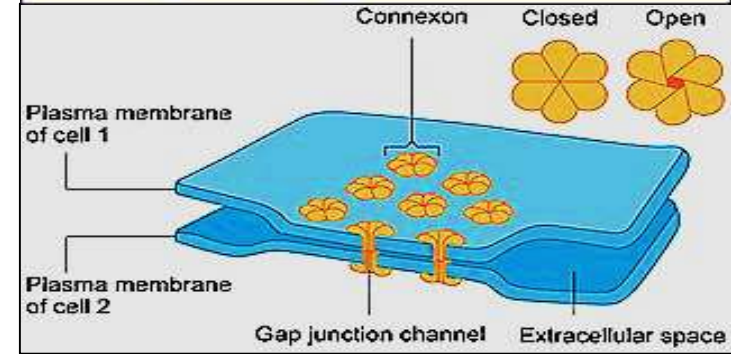
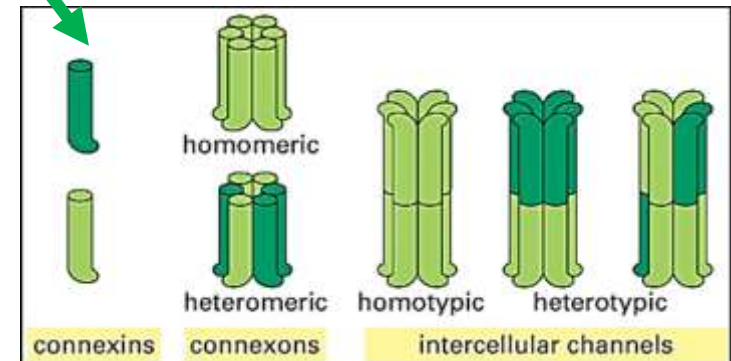
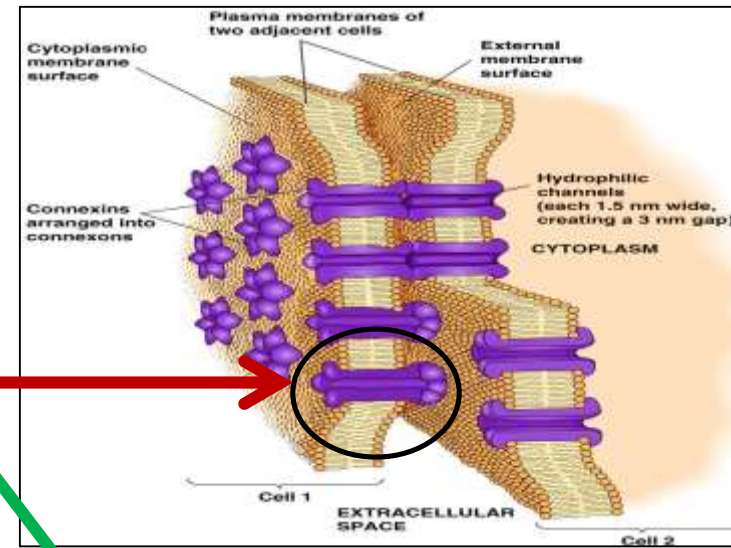
* The protein **subunit** forming the junction is called Connexin

* Each channel called **Connexon** is formed by **6 Connexins** subunits which span the lipid bilayer of the cell membrane (hydrophobic)

* The connexons tubes of 2 cells join together to make a GJ

* GJ tend to close by high concentration of Ca^+ ions or low pH. The closing of the GJ serves to

seal normal cells from traumatized or dying neighbors



Electrical & Chemical synapses

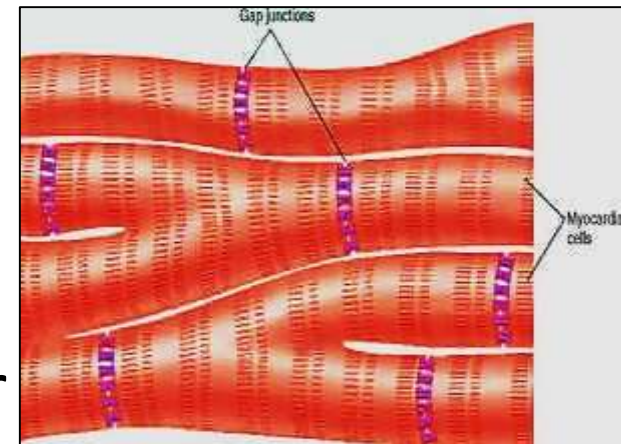
Synapse is a type of GJ where information is transmitted between adjacent cells. There are 2 types:

A. Electrical synapse

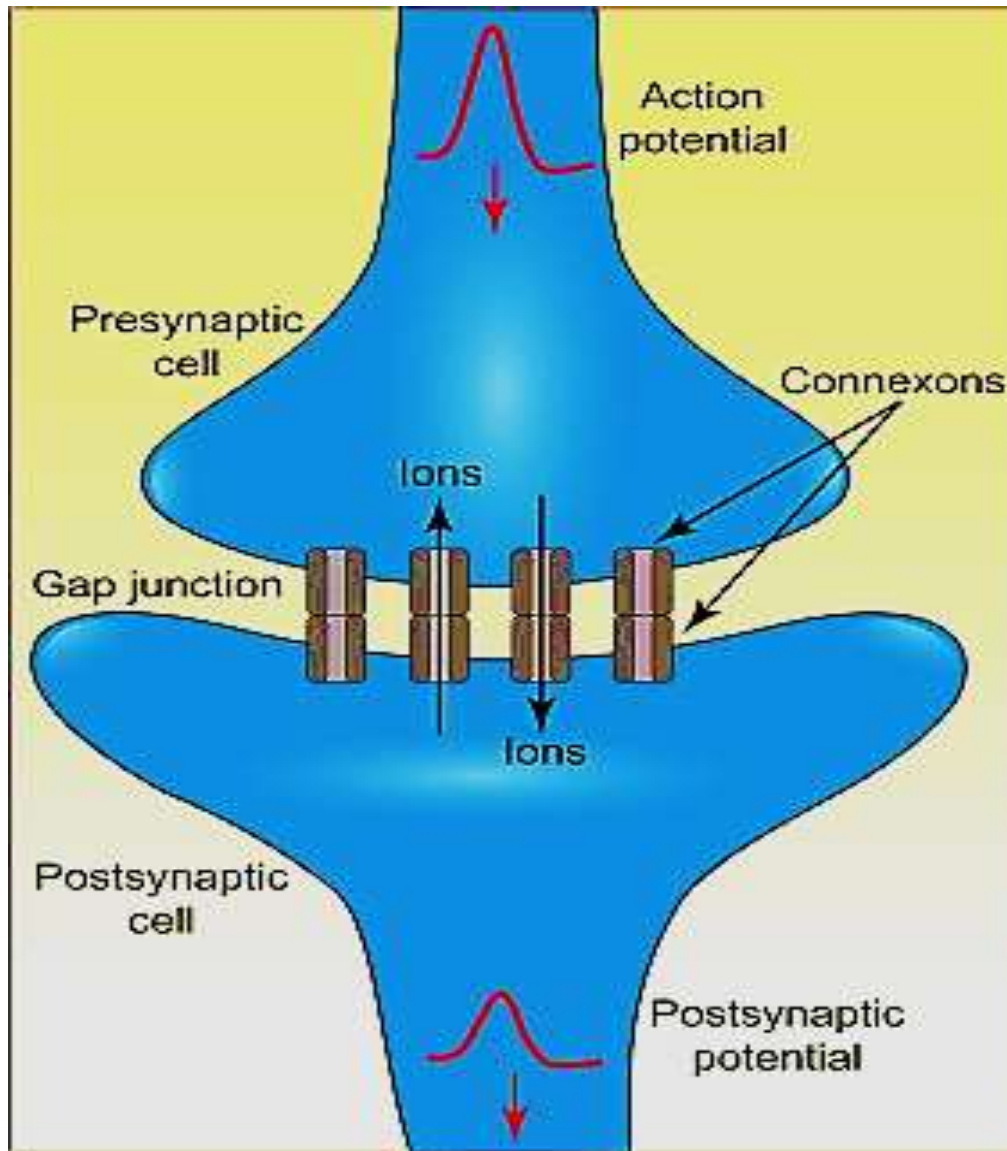
is a GJ which has channel proteins connecting the adjacent cells. The signal in electric synapse can travel faster .

Found between: **cardiac muscles (intercalated discs)**, & **in synapses between neurons involved in reflexes** in nervous system & **between smooth muscle cells**

***Intercalated discs:** contain both **GJs** & **Desmosomes** to allow flow of ions from one cell to another → spread of action potential & to hold cells together



Cardiac muscles

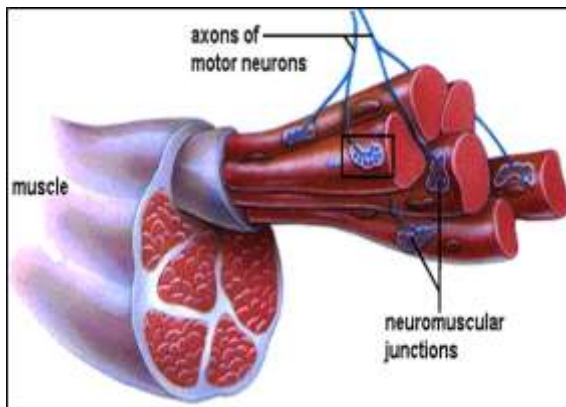


Electric synapse

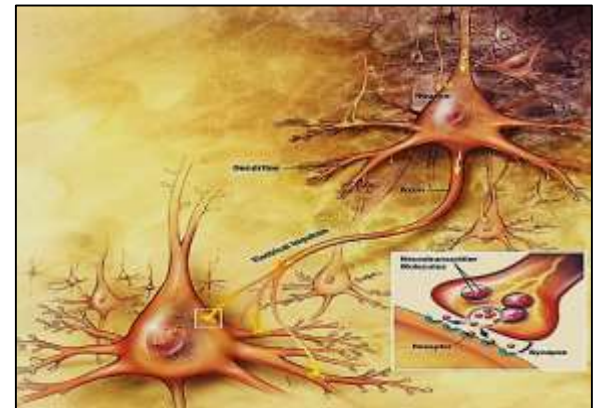
Prof. Dr. Hala Elmazar

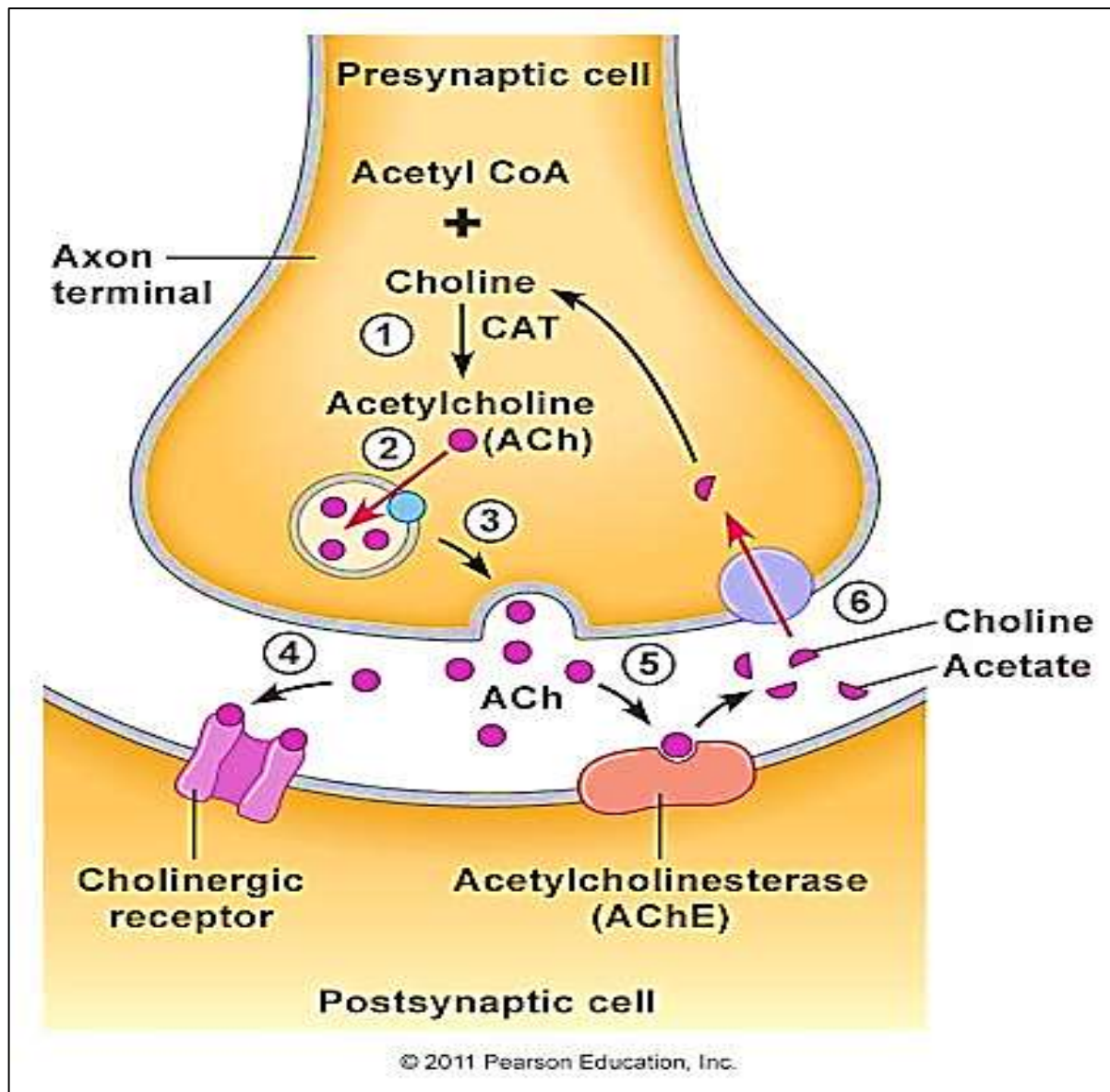
4- B- chemical synapse (Signal relaying junction)

- Junction between a nerve fiber and a muscle fiber (**motor end plate**) or between two neurons
- The neuron transmitting the signal is called **presynaptic neuron**. **Synaptic vesicles** containing neurotransmitters are found in the presynaptic neurons
- These neurotransmitters will be released into the **synaptic cleft** (space between pre & postsynaptic membranes). Neurotransmitter will bind to protein receptors on the **postsynaptic membrane**



Prof. Dr. Hala Elmazar





Chemical synapse

- Gap junctions also found between many cells e.g. osteocytes, astrocytes, endocrine cells , smooth muscles
- Cancer cells don't have gap junctions so that they fail to transfer their mitotic activity to each other which may explain their uncontrolled growth
- Changes in the number and distribution of gap junctions has been reported **in many cardiac diseases** e.g. arrhythmias

Thank you

