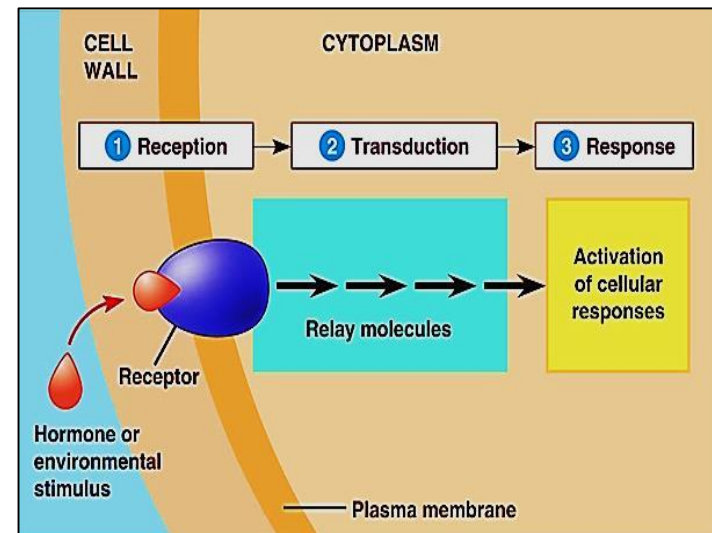
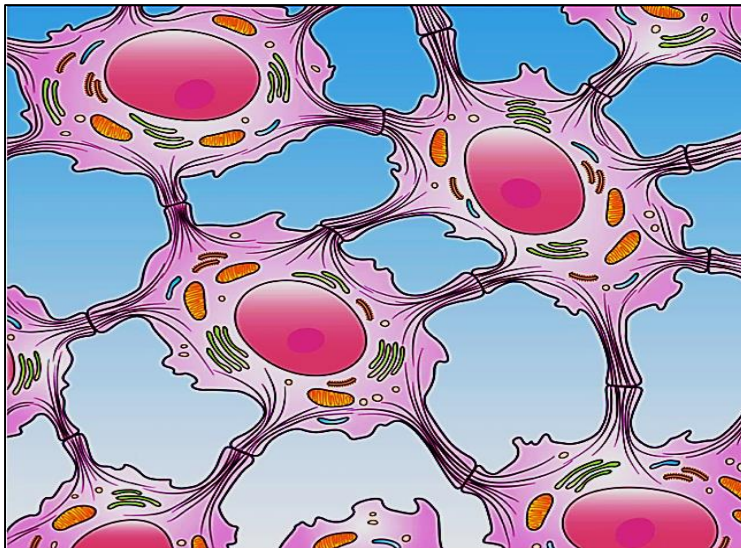
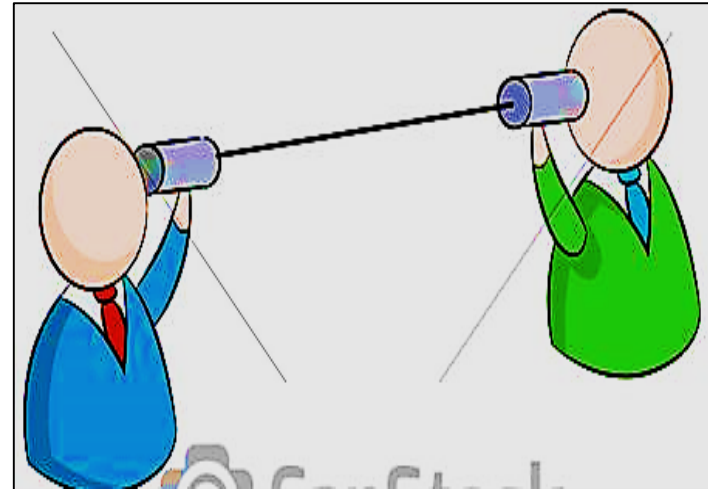
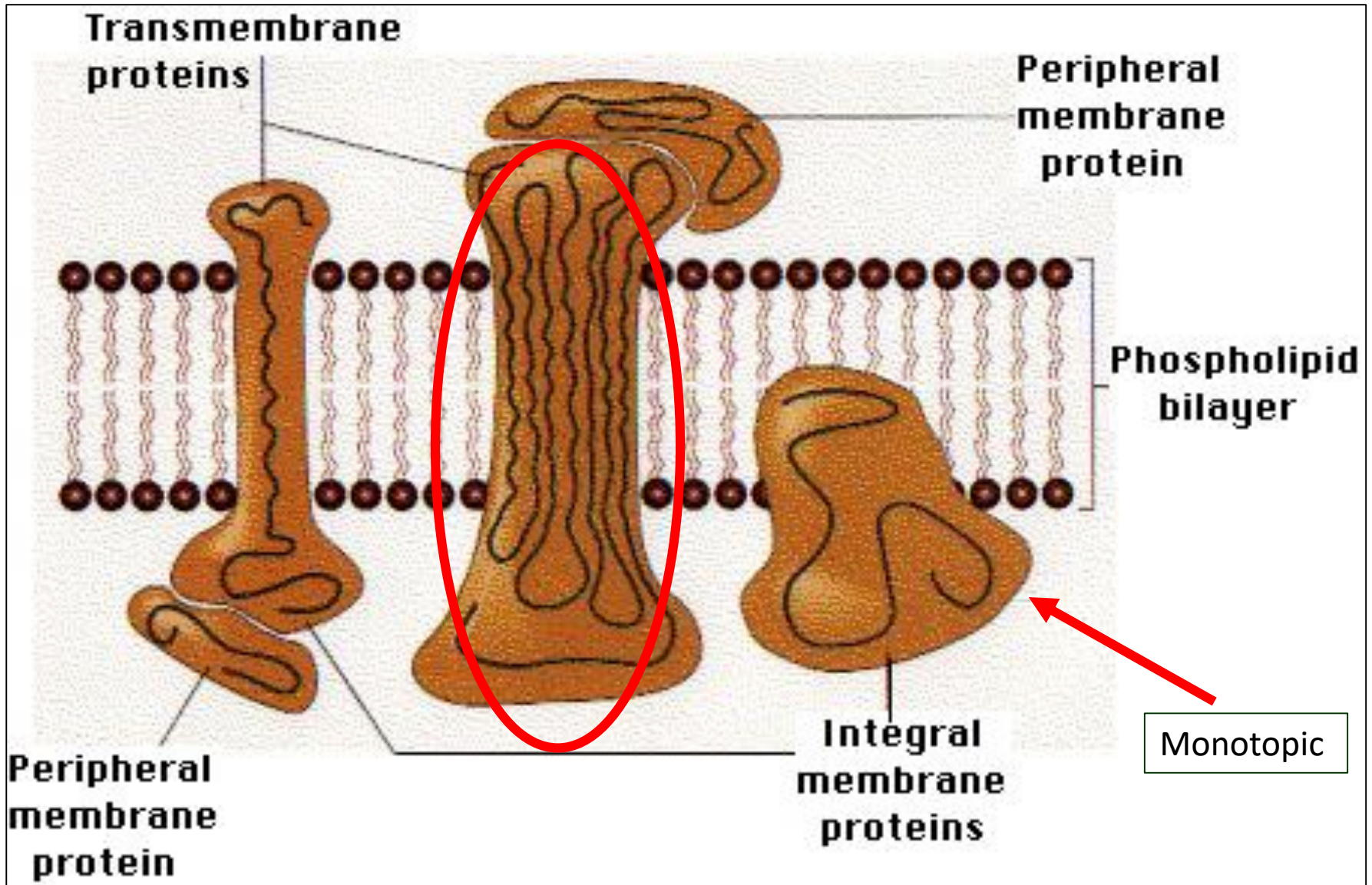


Cell Junctions & Cell Communication



Cell membrane proteins

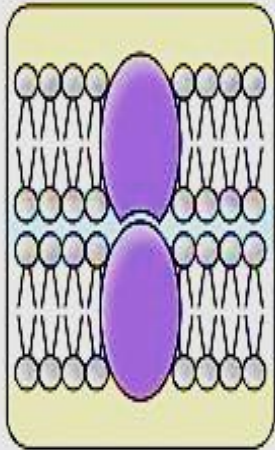
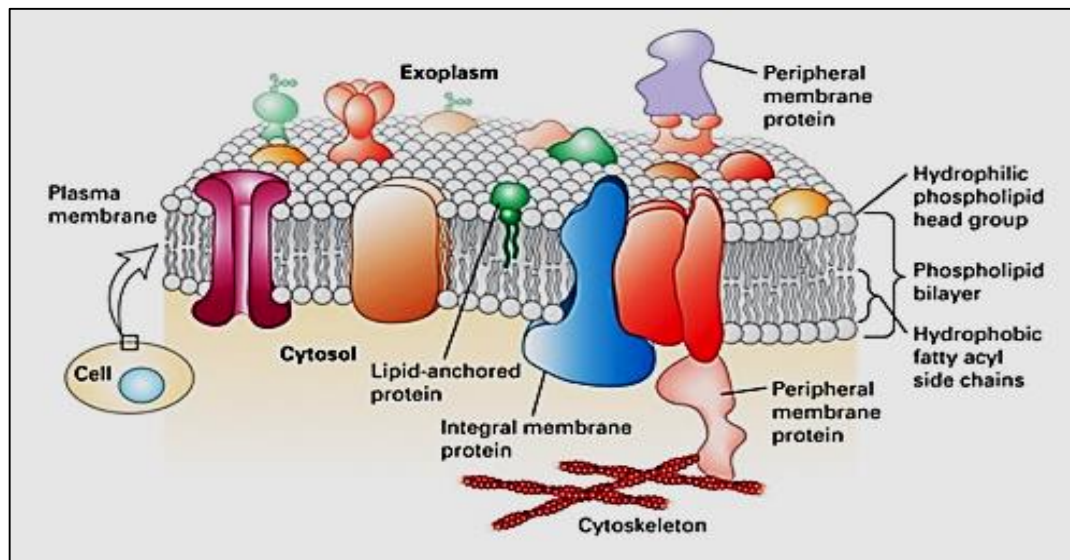
- They are of two types either **peripheral** or **integral**
- **Peripheral**: are temporary attached to the cell membrane. Found either on the outside or the inside surfaces of the cell membrane.
- **Integral** : are permanently attached to the membrane. They are of two types :
 - **Transmembrane** 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 .



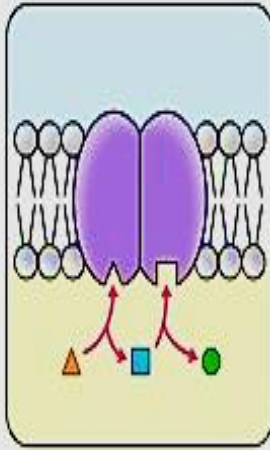
Types of cell membrane proteins

Function of integral membrane proteins

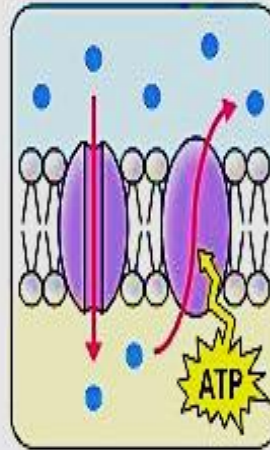
- **Junctions** – Serve to **connect and join** the cells together
- **Transport** – Responsible for **facilitated diffusion** and active transport
- **Anchorage** – **Attachment** points for cytoskeleton and extracellular matrix
- **Enzymes** – Fixing to membranes to **perform a localized metabolic**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



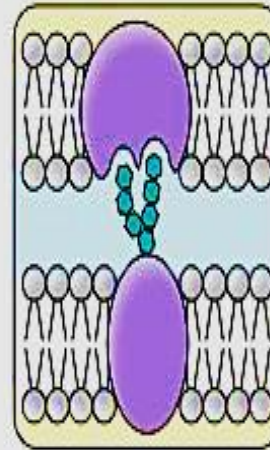
**Intercellular
Joinings**



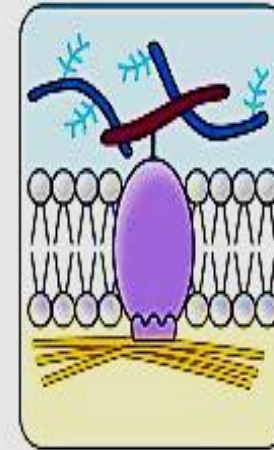
**Enzymatic
Activity**



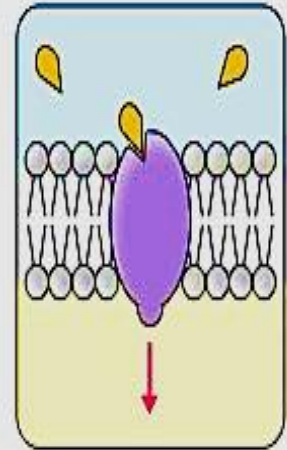
**Transport
(Active / Passive)**



**Cell-Cell
Recognition**



**Anchorage /
Attachment**

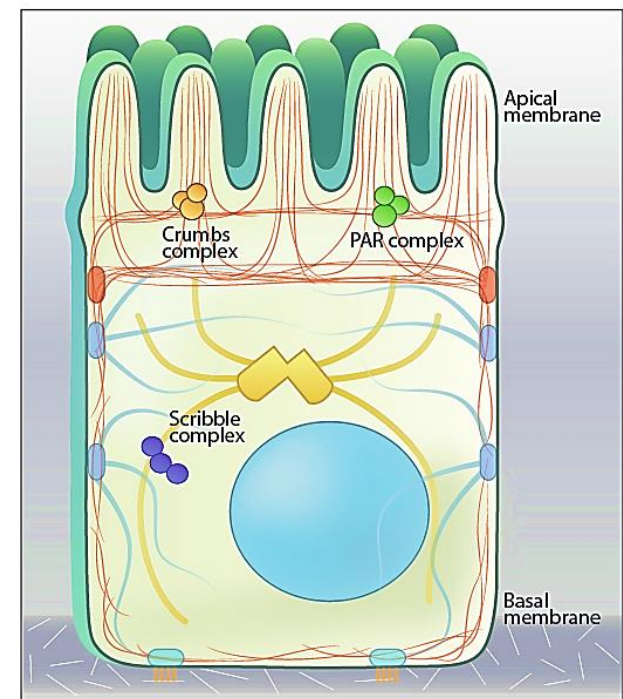
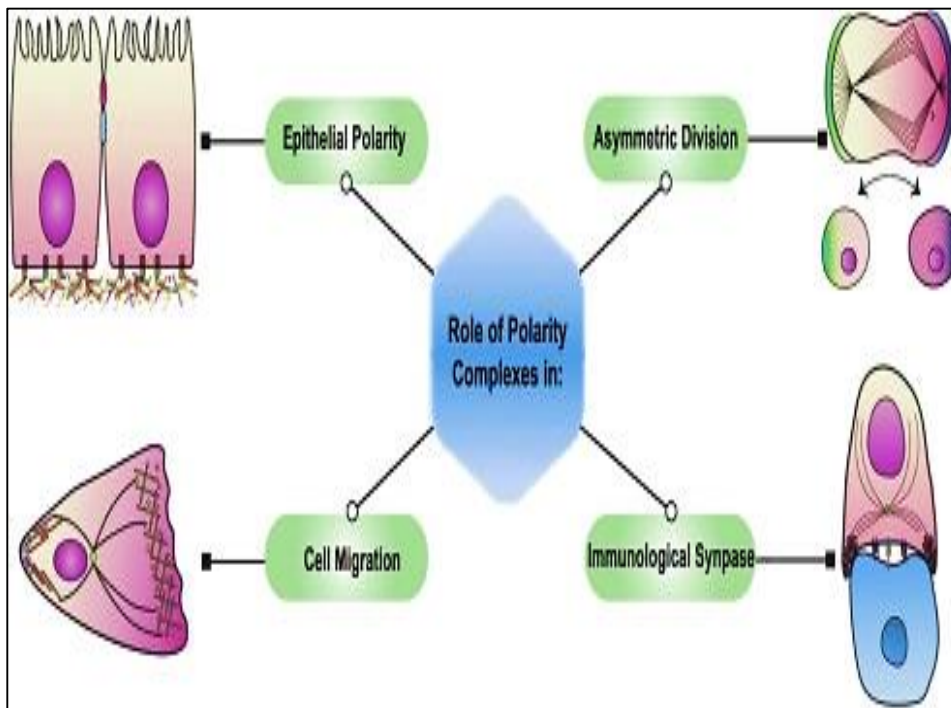


**Signal
Transduction**

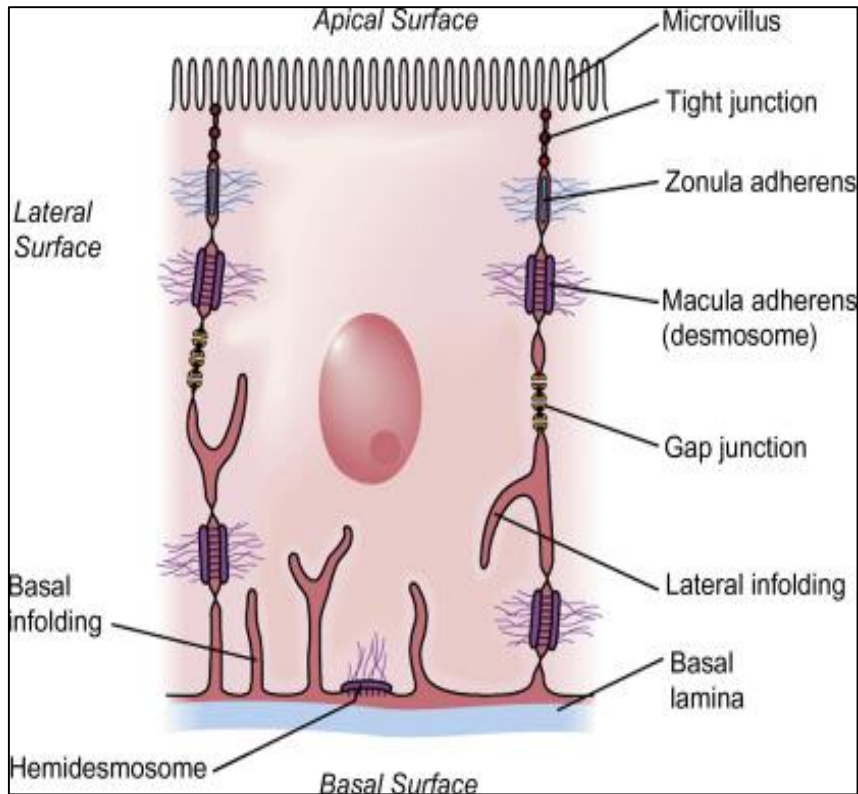
Function of cell membrane integral proteins

Cell polarity :Asymmetry in the structure, function & organization of cells allowing them to carry out specialized functions this is crucial for the process of cell division, signaling & movement.

In epithelial cells polarity allows the cell to have epical side, basal side & lateral sides

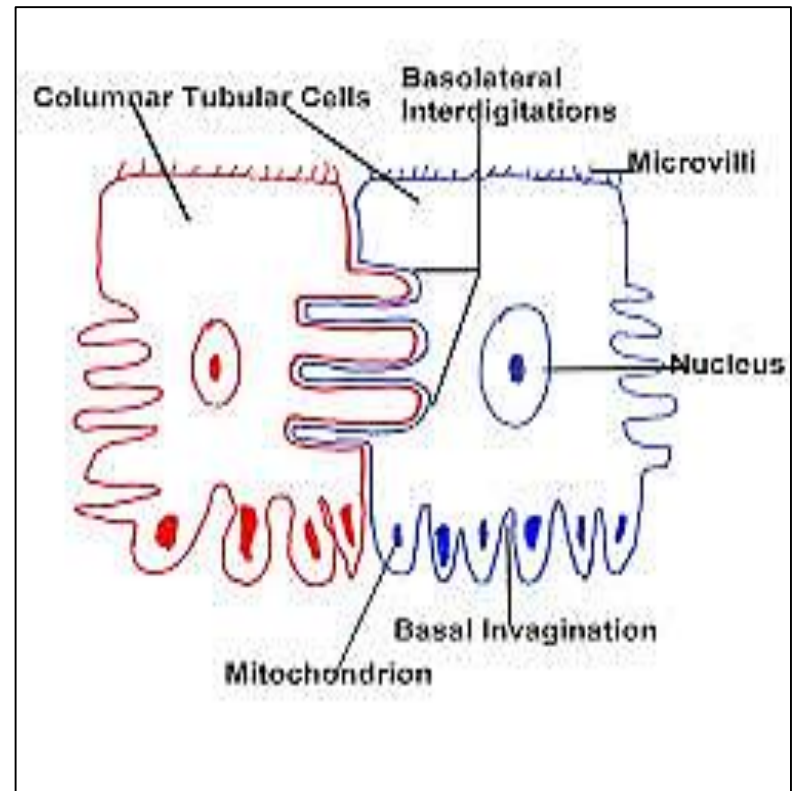


The Epithelia cells has 4 surfaces:



1- **Apical surface** projections which may be Cilia, microvilli, Stereocilia

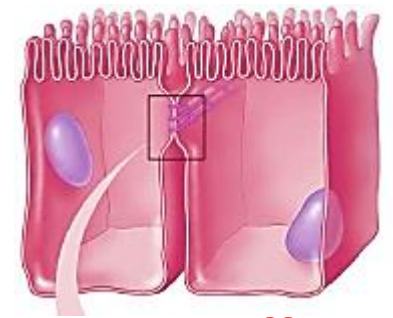
2- Intercellular junctions which link the neighboring cells together



3- Lateral interdigitating
Increase surface area for absorption
(Na-K pump)

4- Basal infodings & basement membrane

Intercellular Cell Junctions

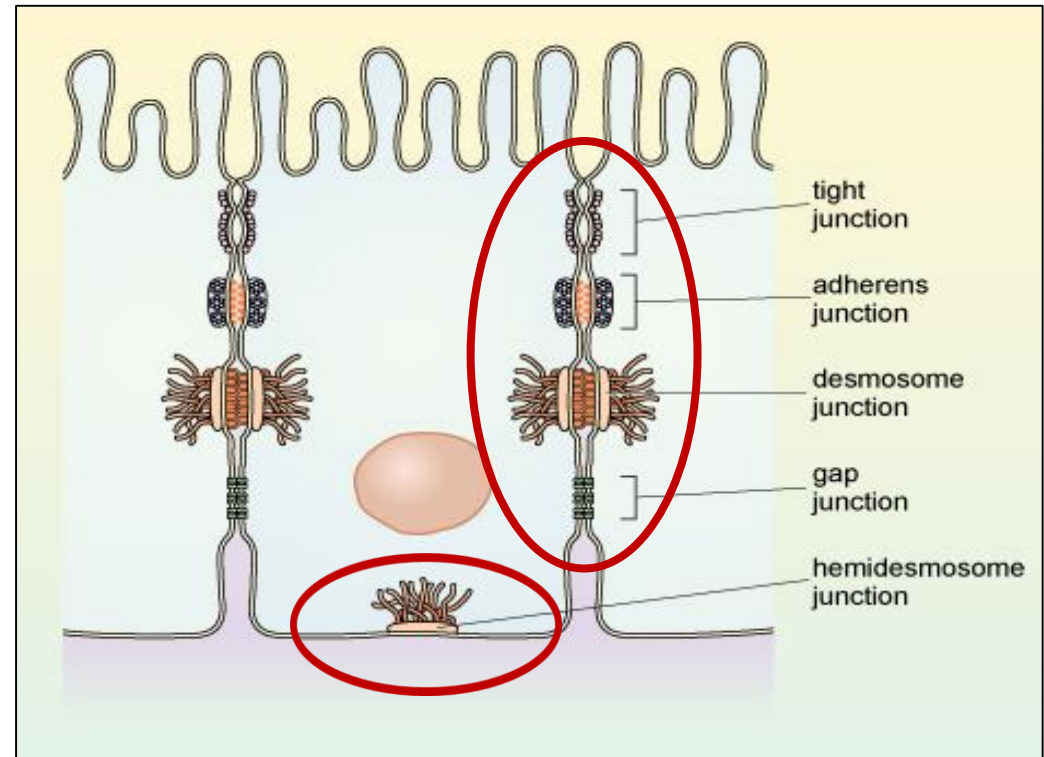


Definition & classification:

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

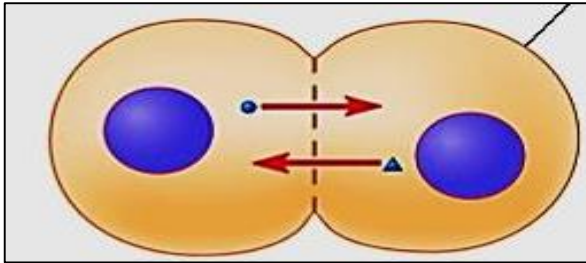
1- cell- cell adhesion

2- cell- matrix adhesion



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 :

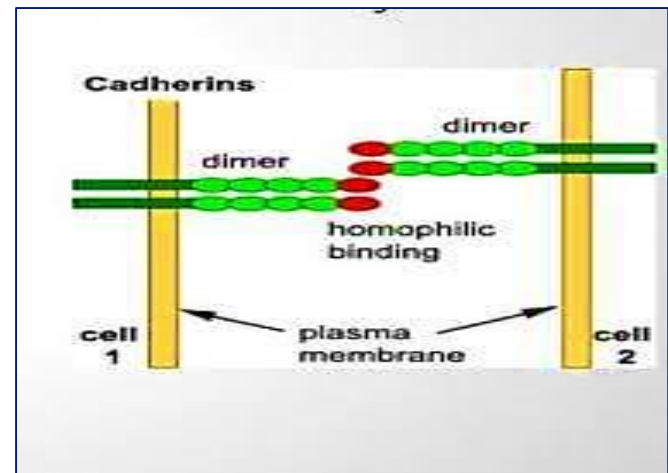
**1- Cell Adhesion
Molecules
(CAMs)**

**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

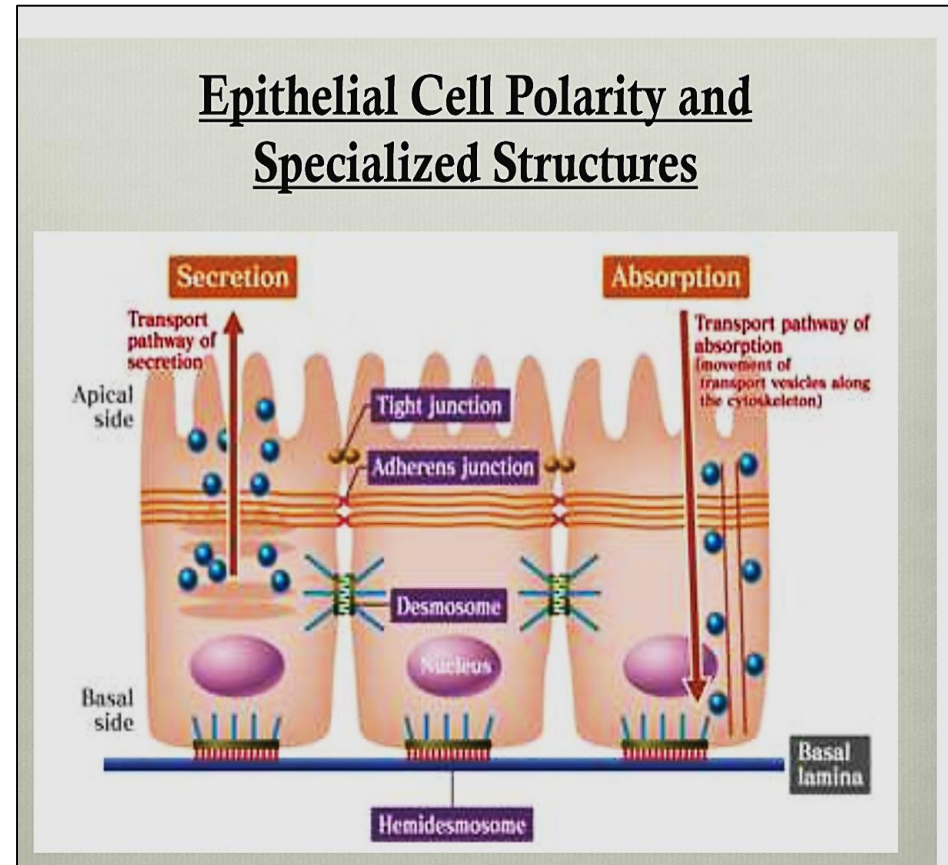
CAM Responsible
for

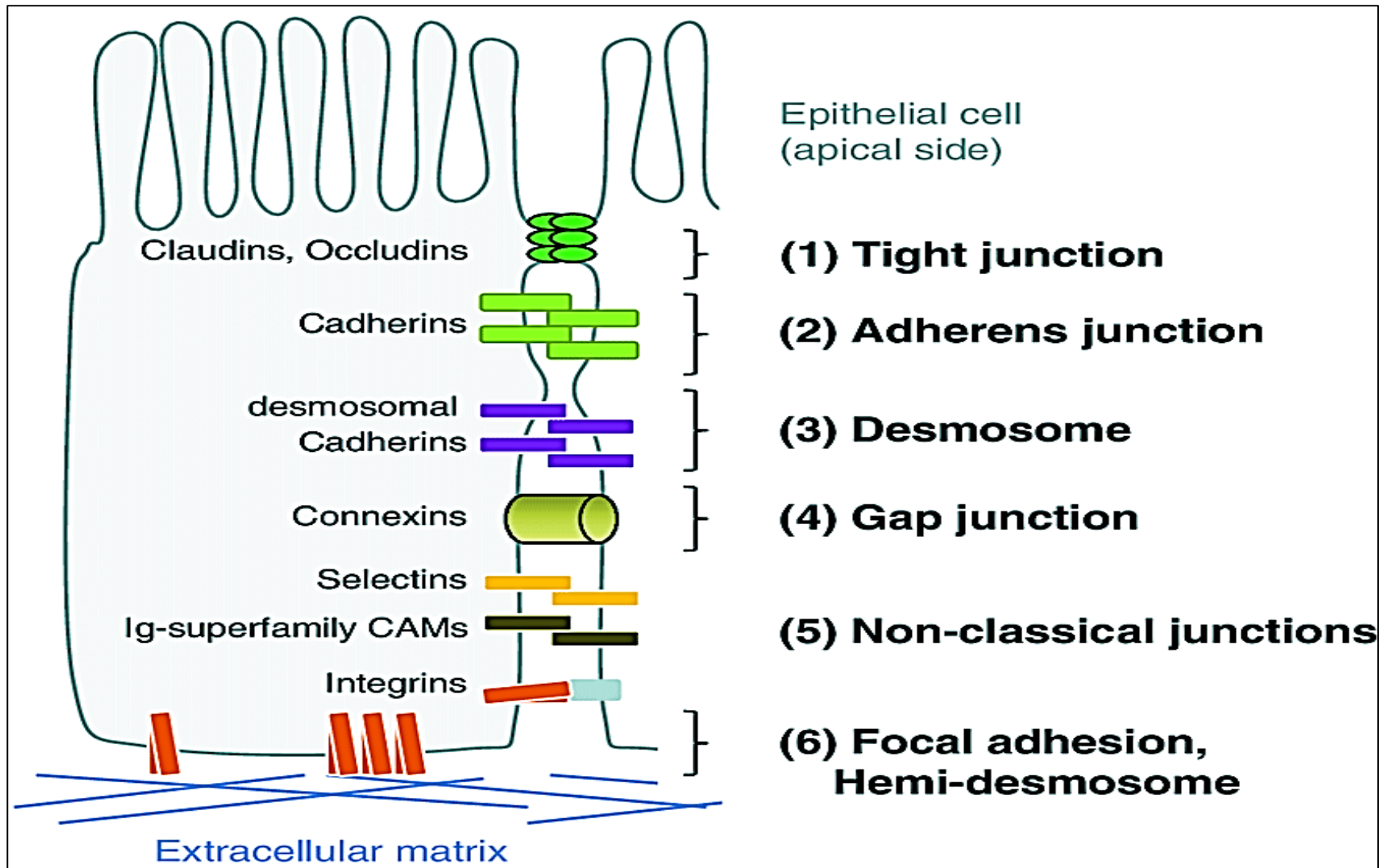


- Cell-cell junctions (Adhesions)

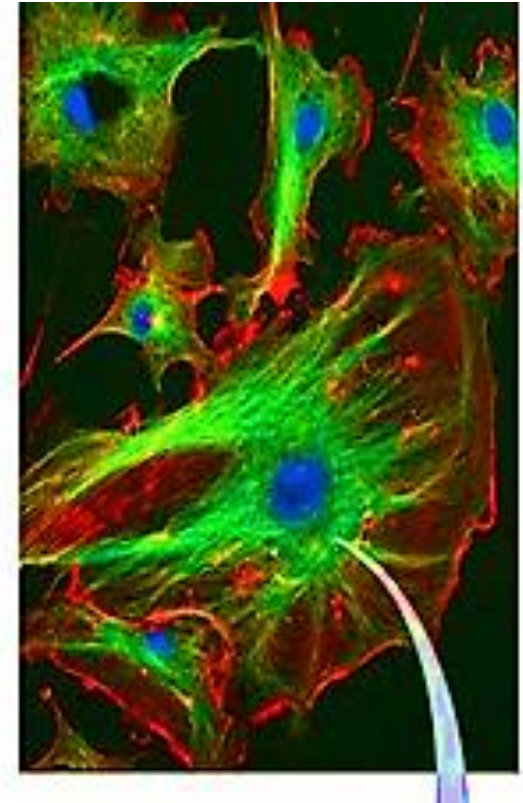
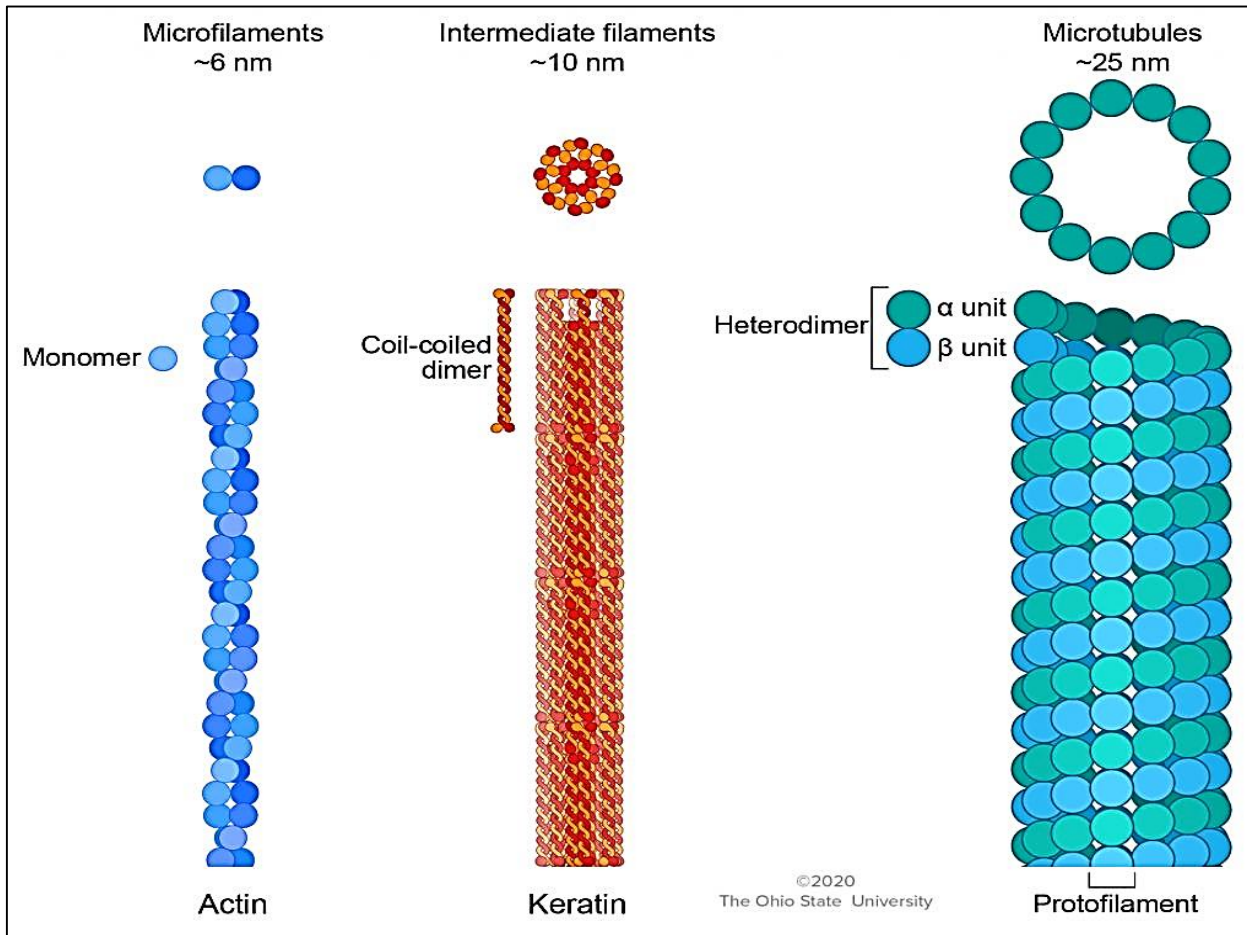
This is achieved by CAMs molecules present at the surface of both cells . Cell junctions is vital for multicellular structural maintenance

- 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





Cell adhesion molecules & cell junctions

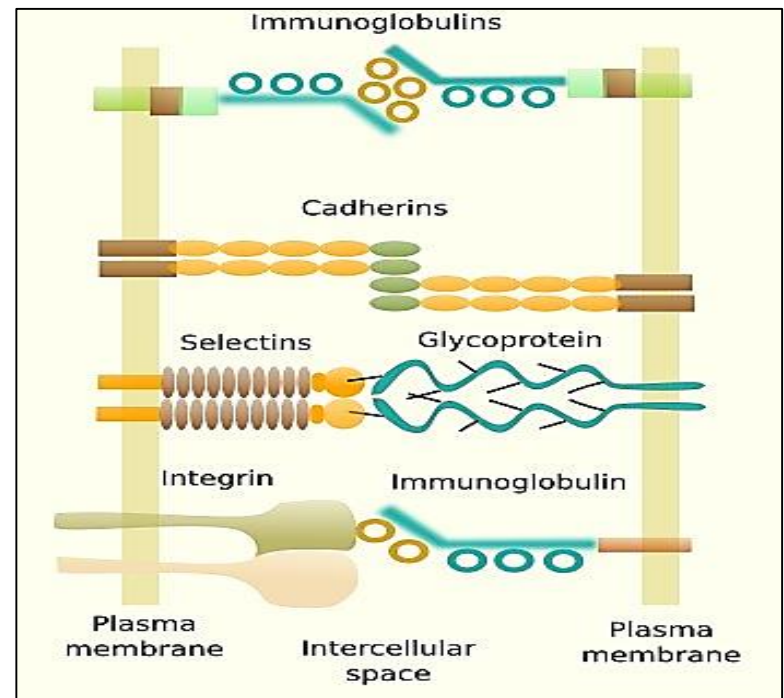
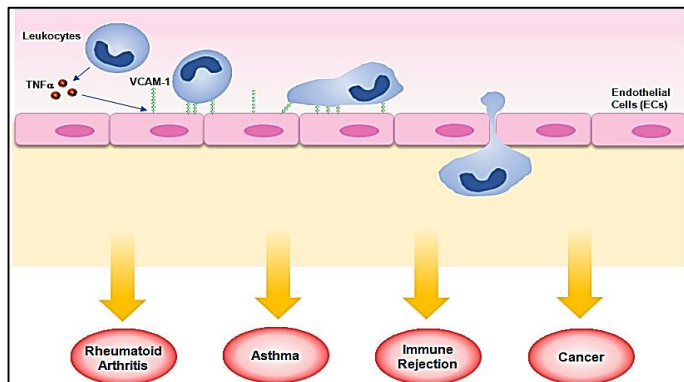
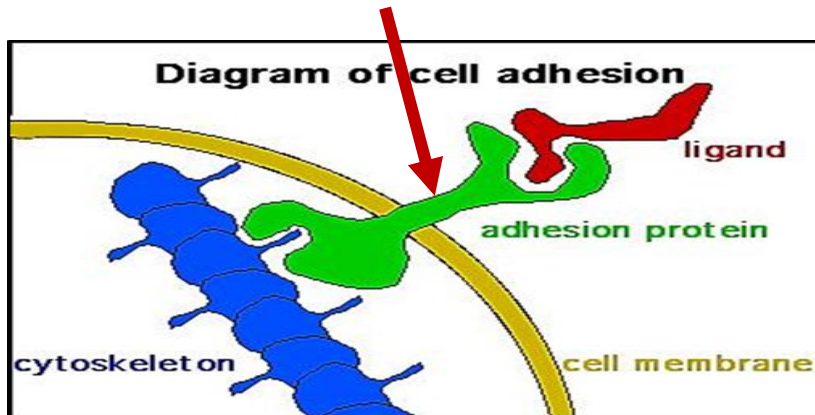


Inside the cell there are 3 types of **cytoskeletons** : actin filament , intermediate filament & Microtubules

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

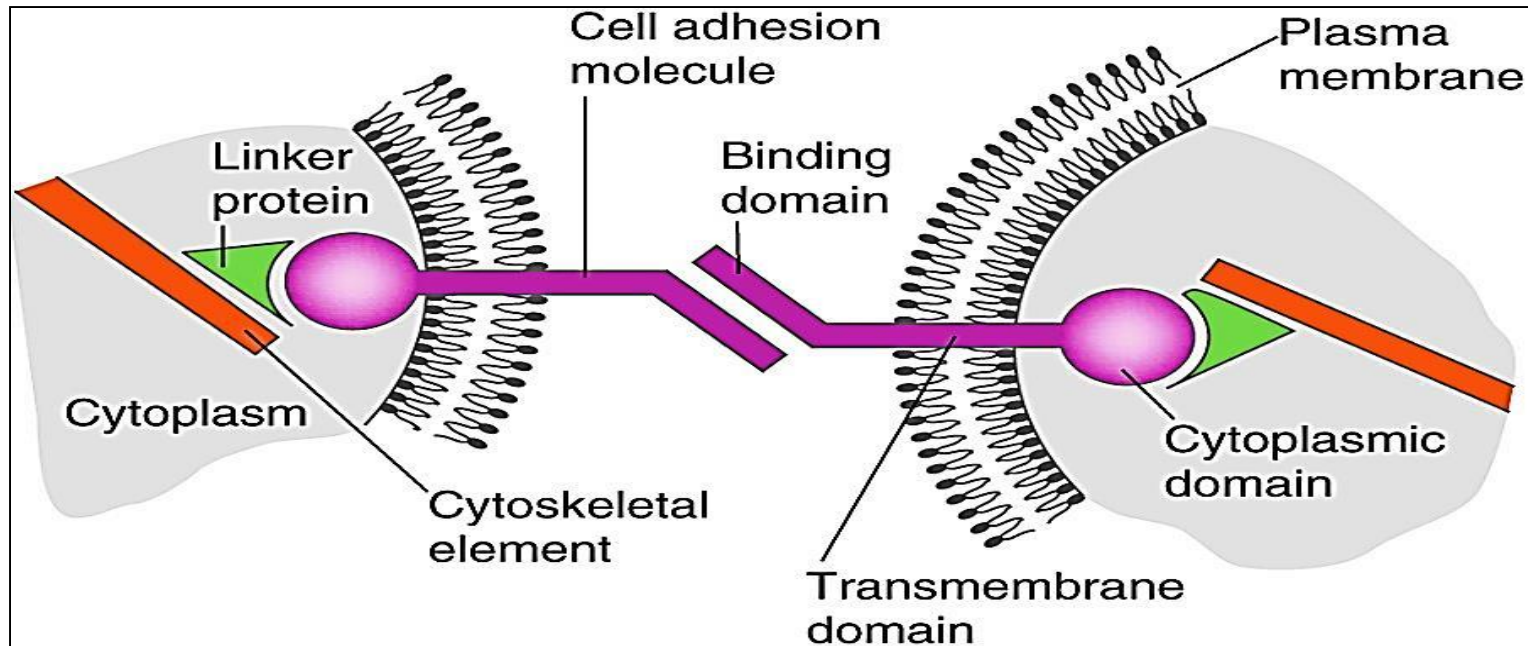
Cell Adhesion Molecules (CAMs)

- **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:

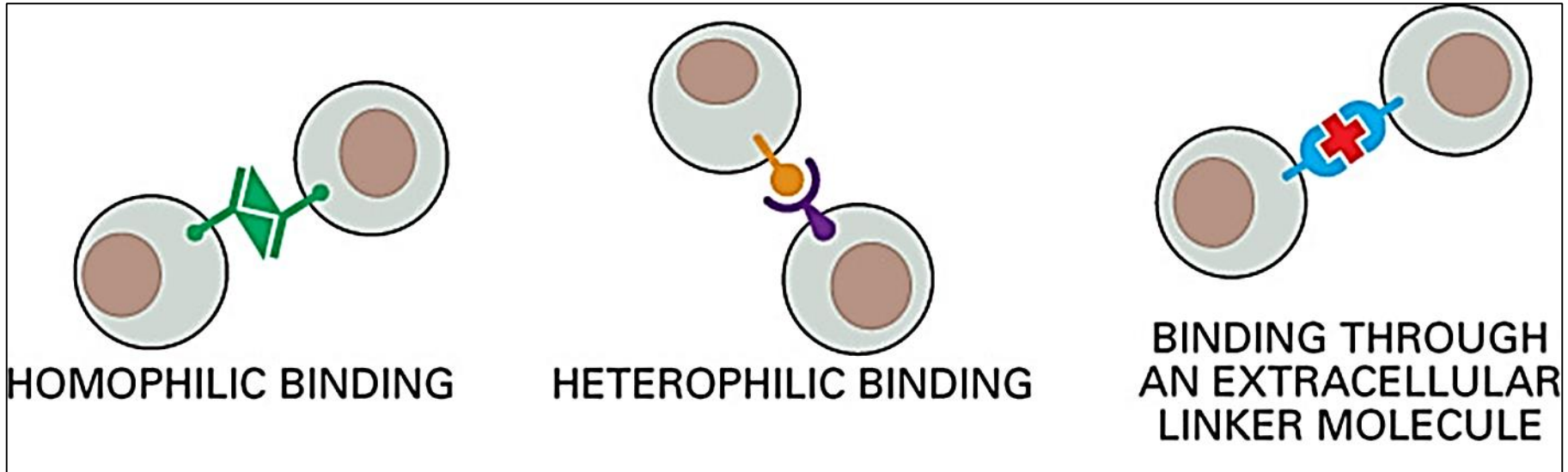
- The extracellular (ecto) domain: allows one CAM to bind with another CAM on an adjacent cell.
- The transmembrane domain: links the CAM to the plasma membrane through hydrophobic forces.
- The cytoplasmic (endo) domain: is directly connected to the cytoskeleton by linker proteins.



How CAM molecules bind with each other?

- When CAMs of the **same type** 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 similar .Laminin (linker molecule) is a family of large cross shaped molecules with multiple receptor domains.

Interactions between CAMs can be mediated by :



HOMOPHILIC BINDING

HETEROPHILIC BINDING

BINDING THROUGH AN EXTRACELLULAR LINKER MOLECULE

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

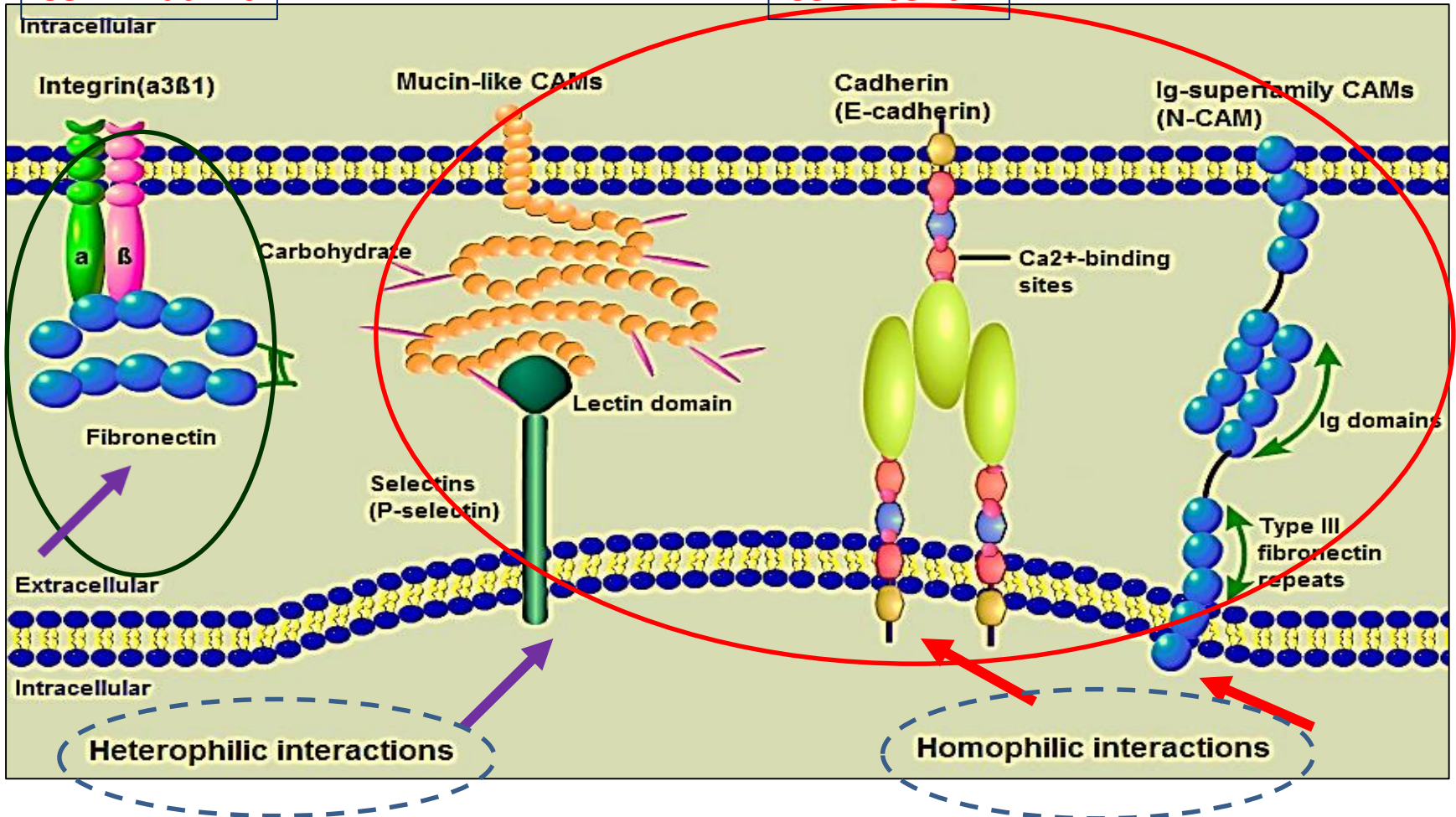
selectins

**Immunoglobulin
superfamily**

Integrins

Cell – matrix J

Cell – cell J



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

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

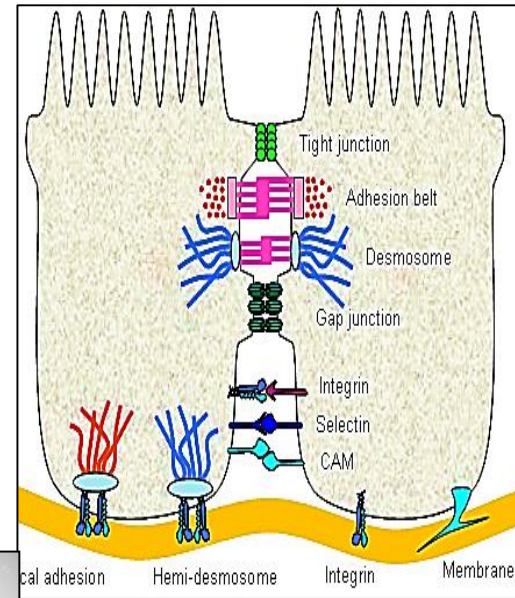
2- Anchoring junctions: attach cells & their

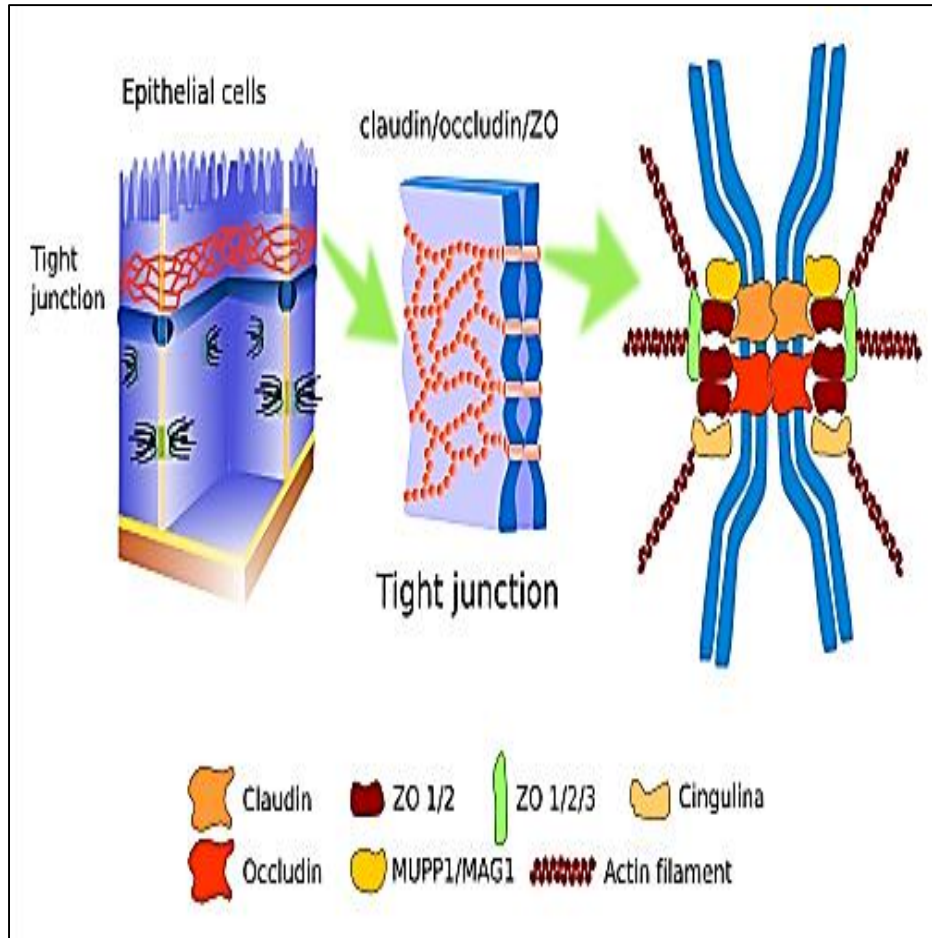
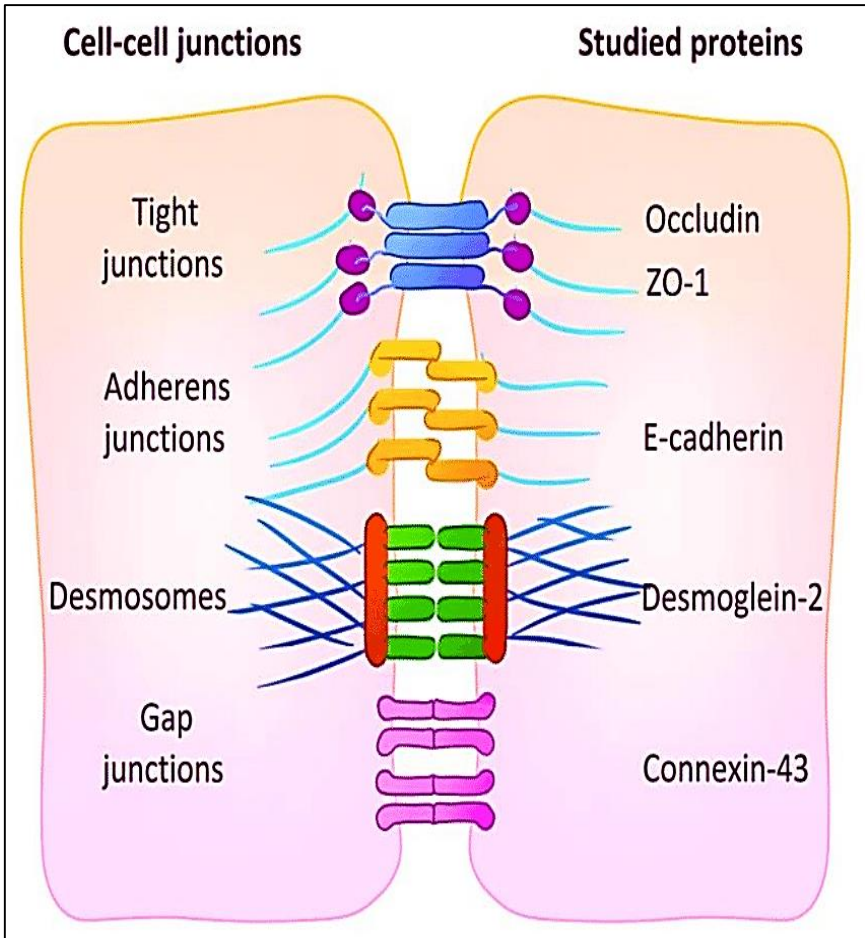
cytoskeleton to other cells or to ECM

provide mechanical support

3- Gap junctions: allow exchange of chemical / electrical

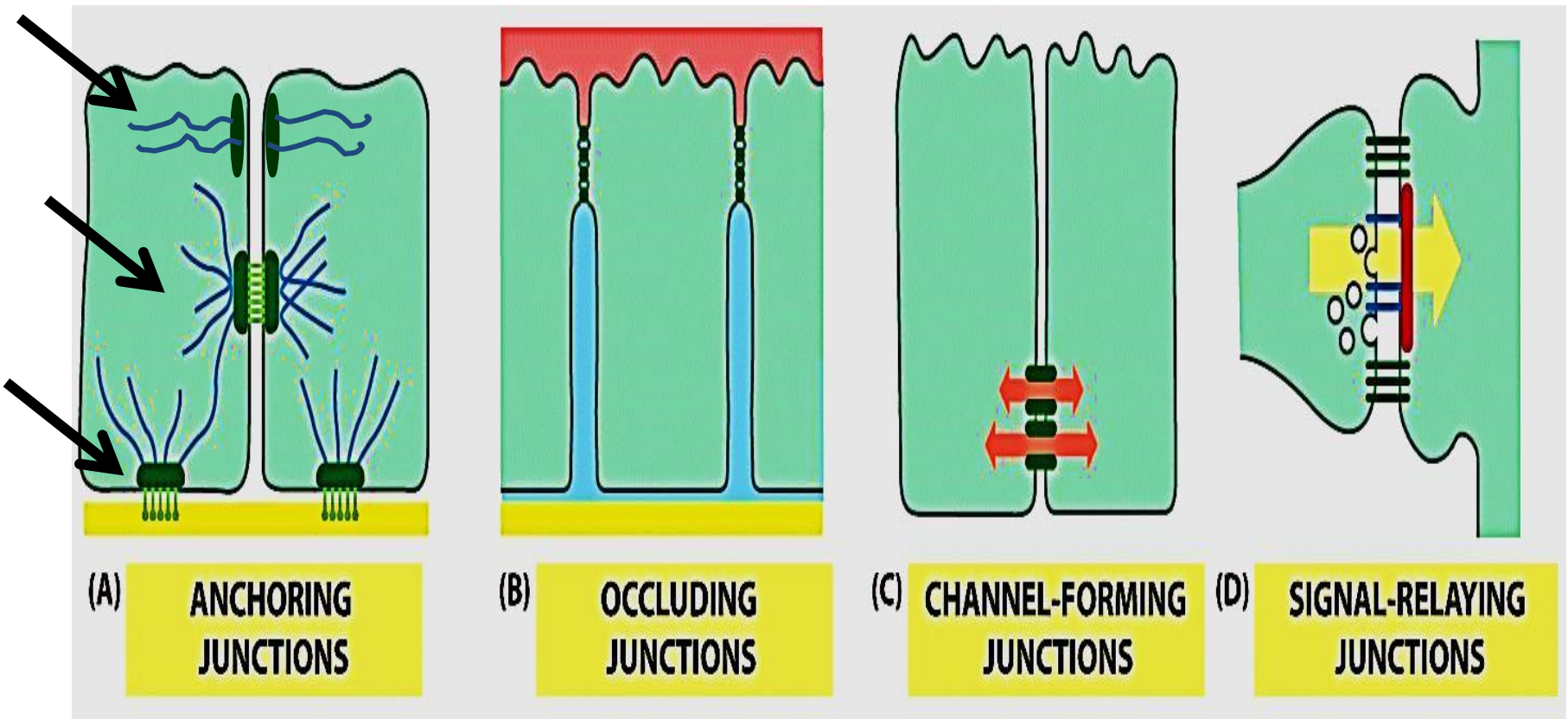
information between adjacent cells





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

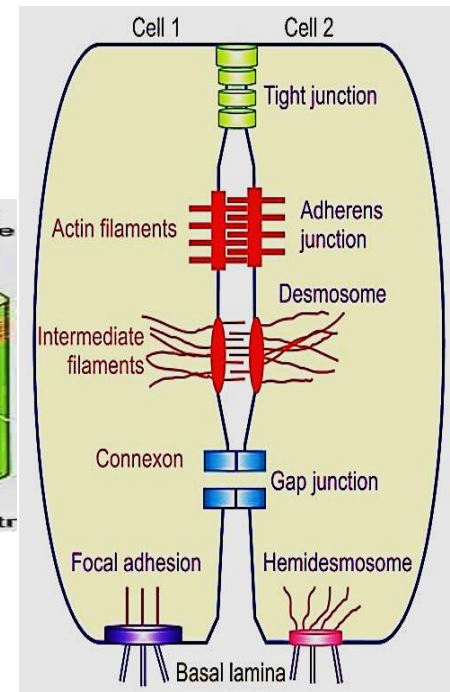
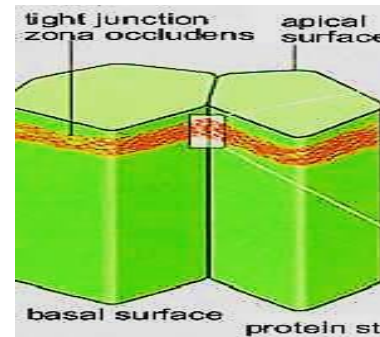
Synapse

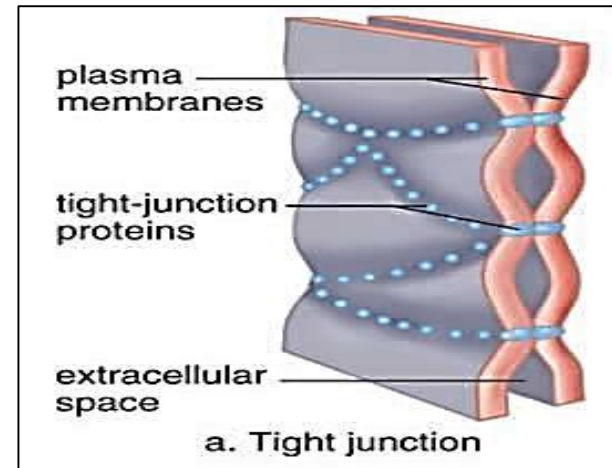
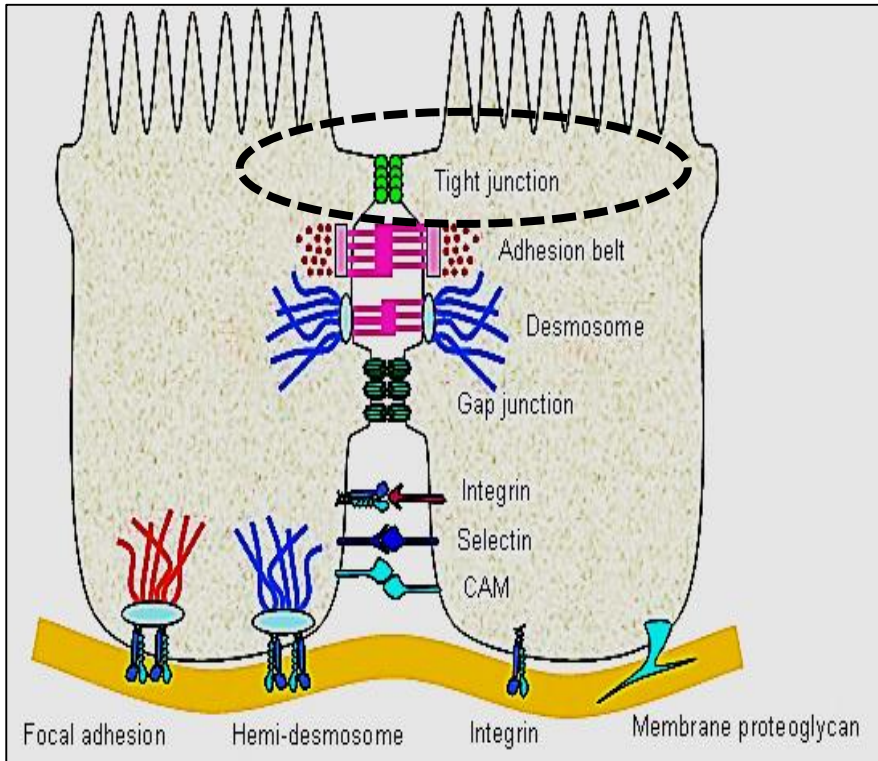


Cells are 3-D in the human body

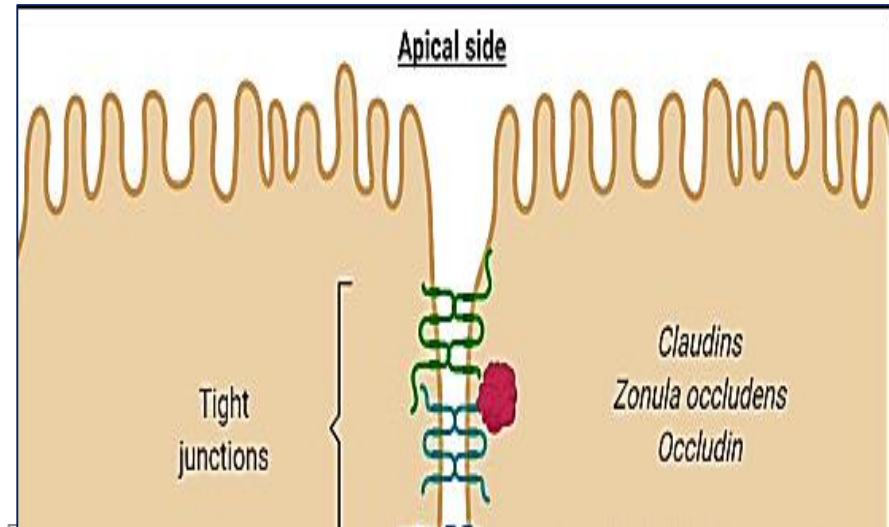
1- Occluding junctions

- Also called **Tight** Junctions / **Zonula Occludens**
- Seal adjacent epithelial cells & is the most apical type of junctions
- Belt-like structure completely encircle 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**





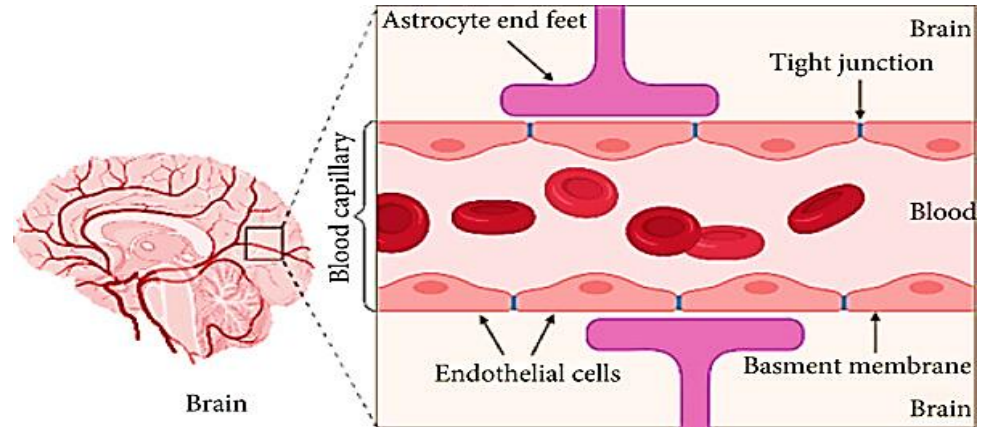
Tight junction **stitches** cells together



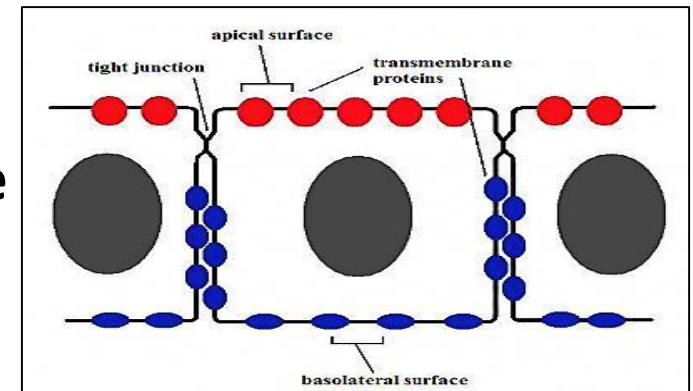
Functions of Tight Junction

- Protection: Seals cells so it creates barriers to prevent leaks

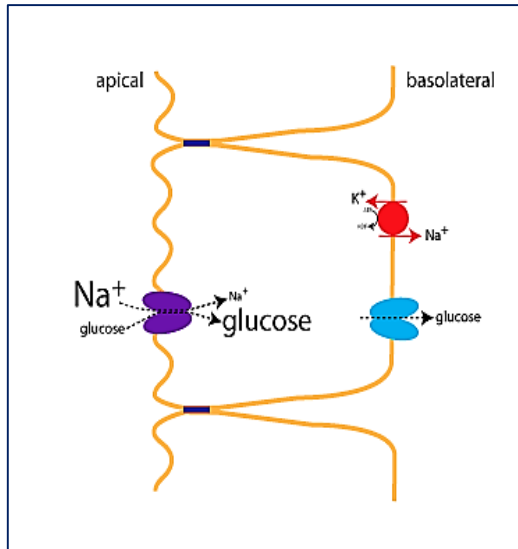
- Form Blood-brain barrier
- & other barriers in the body especially in GIT (GIT barrier)



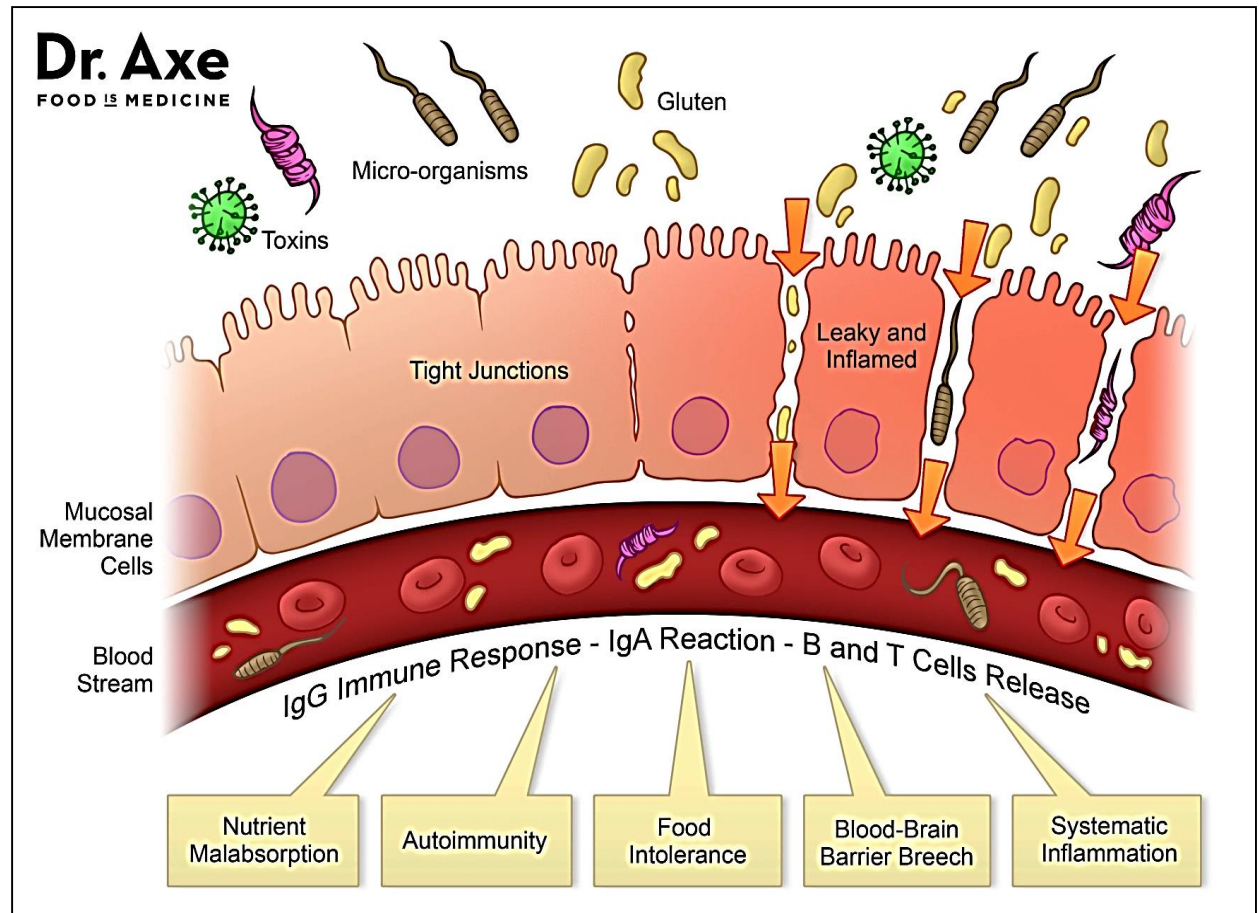
- Maintain cell polarity: prevent membrane proteins of apical surface from being moved to basolateral surface to maintain cell receptors & function



- Ensure unidirectional transport, the apical set of transport proteins **must not** be allowed to migrate to the basolateral surface & vice versa

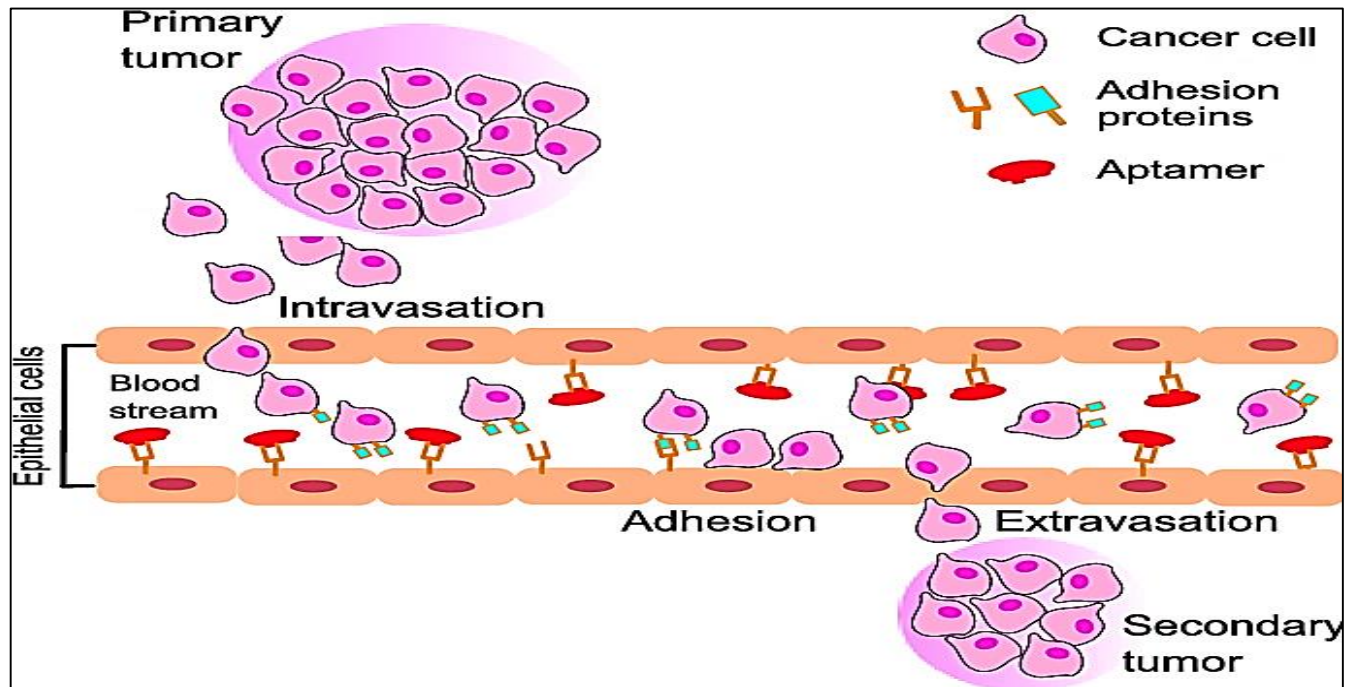


Ensure unidirectional transport of molecules



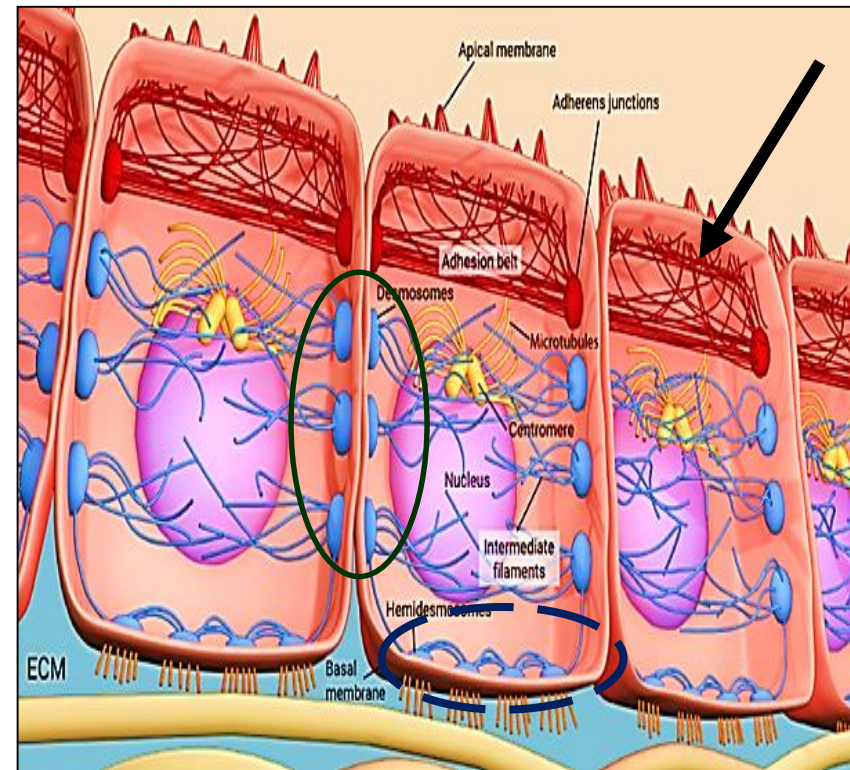
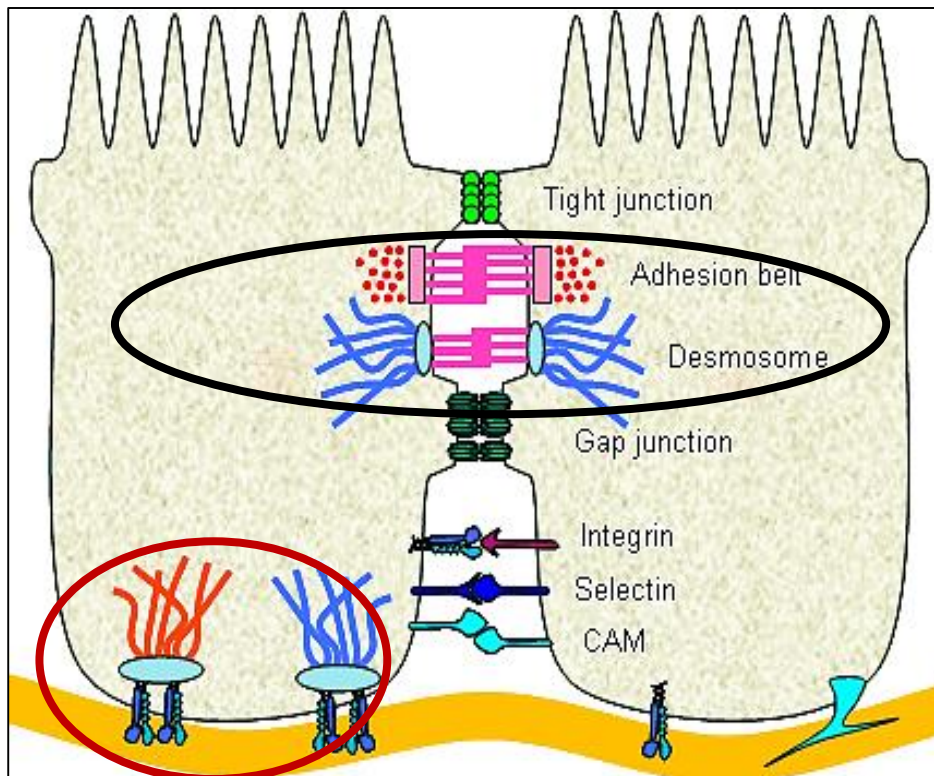
Leaky gut syndrome : is a disease happen when tight junctions between intestinal epithelial cells (**intestinal barrier**) become defective → abnormal increases in the intestinal permeability → leaking of a undigested food particles, toxins & microbes from the lumen into the bloodstream → diarrhea and 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: $\left\{ \begin{array}{l} \text{Adherens junction} \\ \text{Desmosome} \end{array} \right.$
- Cell – matrix: $\left\{ \text{Hemi-desmosome} \right.$



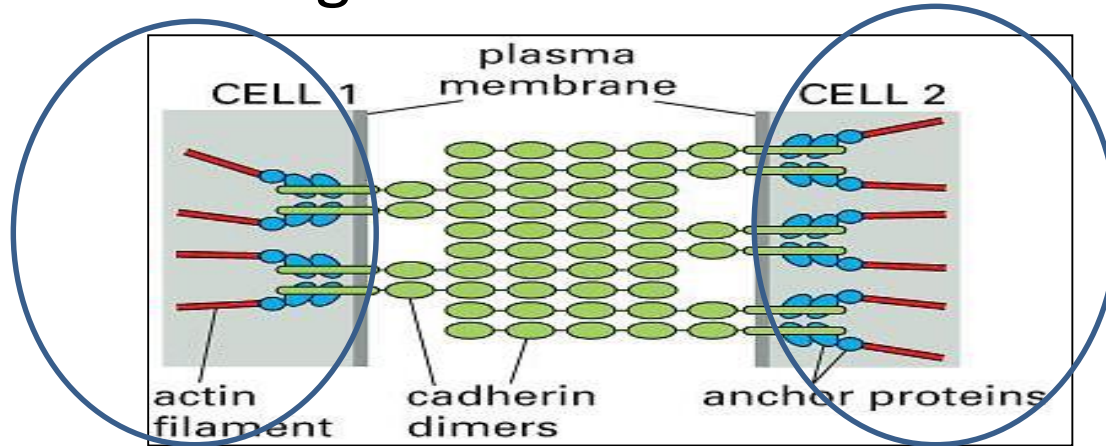
2- A- Adherens junction/Zonula adherens

- Integral membrane proteins, connect the cell cytoskeleton to the cytoskeleton of 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**), & is Ca⁺ dependent junction
- The opposing plasma membranes has a narrow space in-between (30nm)
- The cytoplasmic surfaces of adjacent cell membranes at the junction have electron dense plaques (glycoprotein)



Imagine the structure of adherens junction

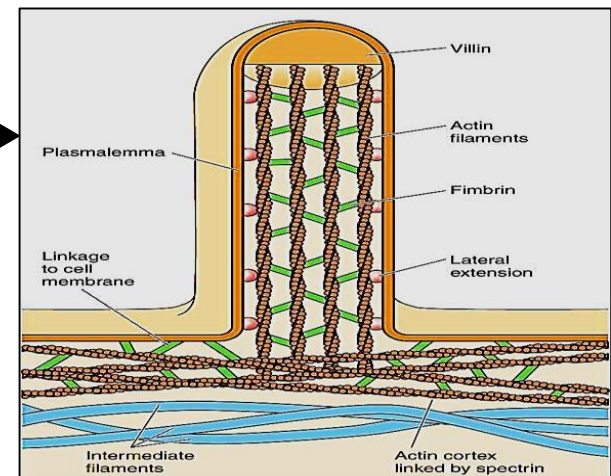
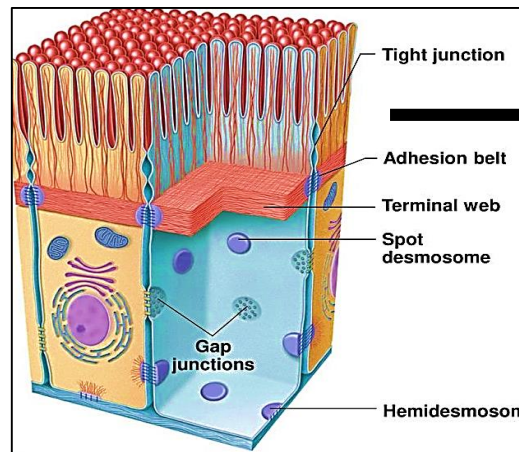
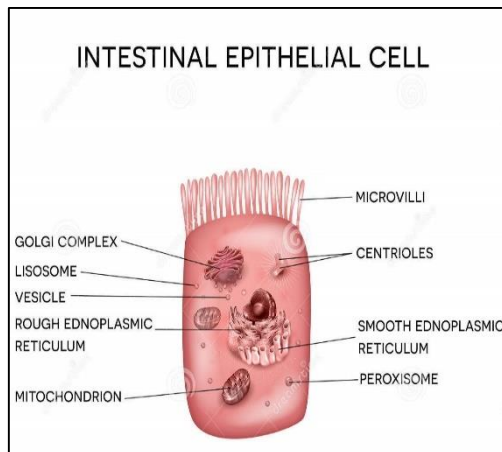
- Proteins forming the Junction are **Cadherins, Catenin**



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

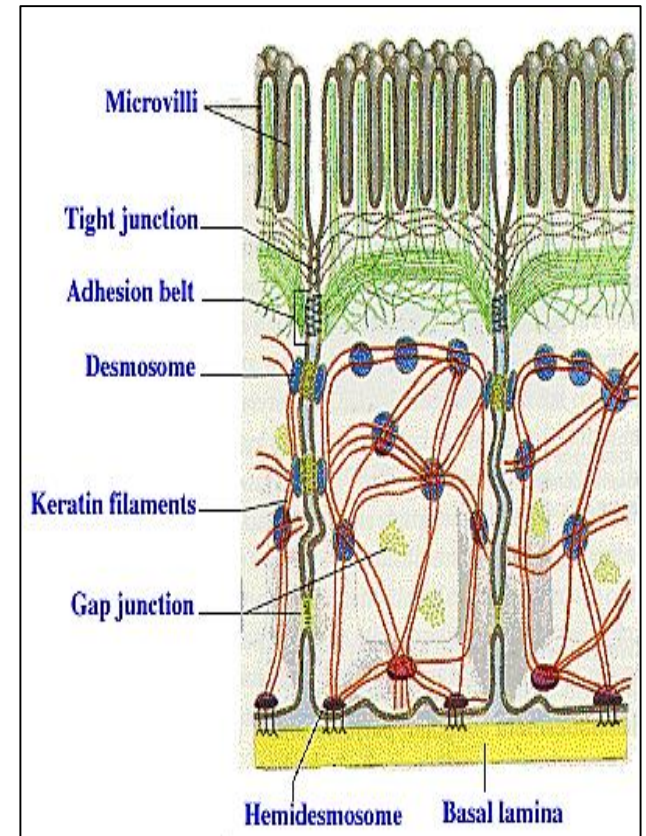
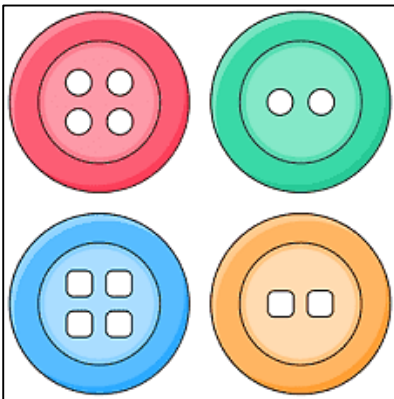
Actin filaments.

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



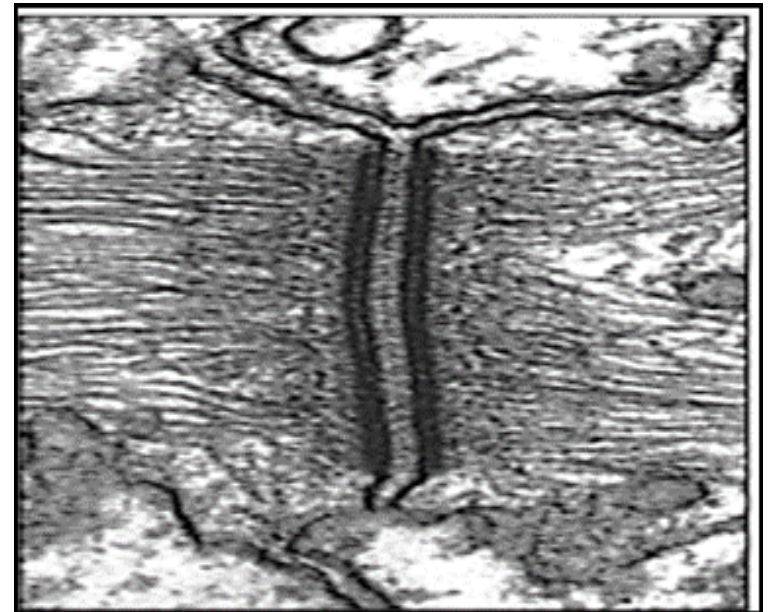
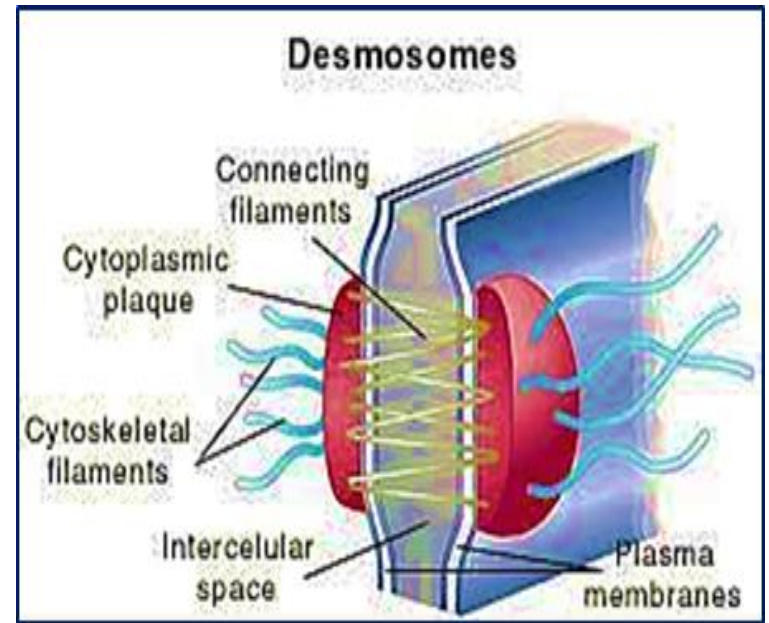
2- B- Desmosomes/Macula adherens

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



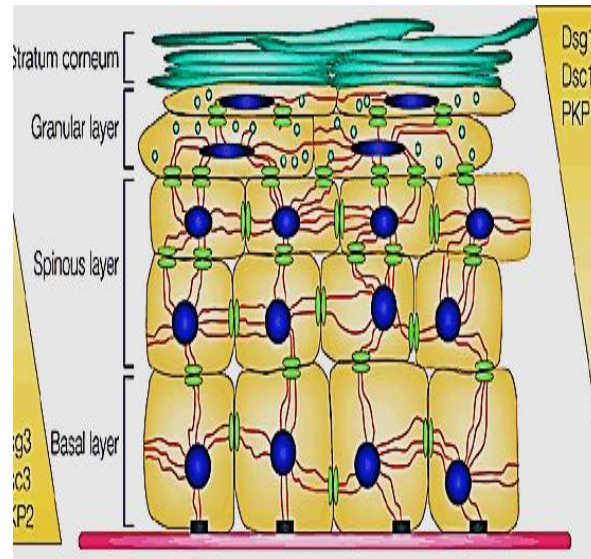
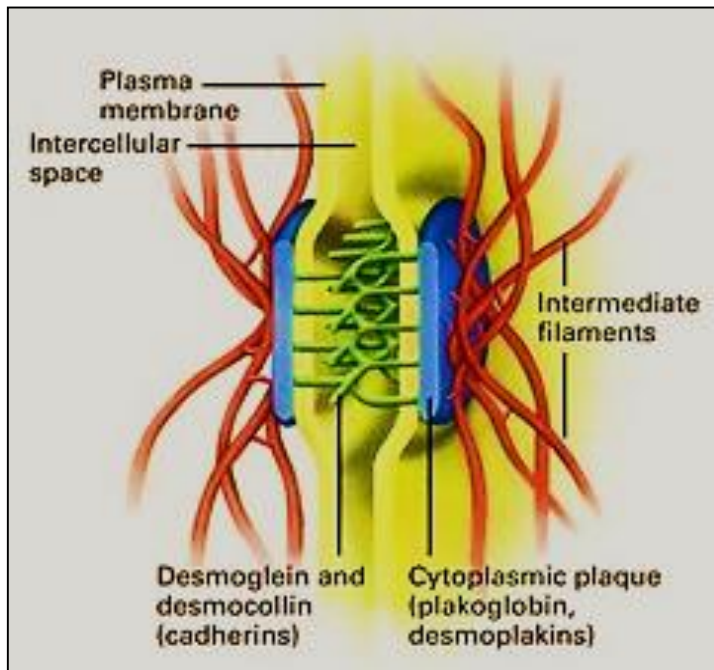
Proteins forming the junction of the desmosome are called **desmoglein & desmocoline** transmembrane proteins (members of the cadherin family) & it is Ca^+ dependent

They are connected on the cytoplasmic surface of each cell membrane to a protein plaque called **desmoplakin**

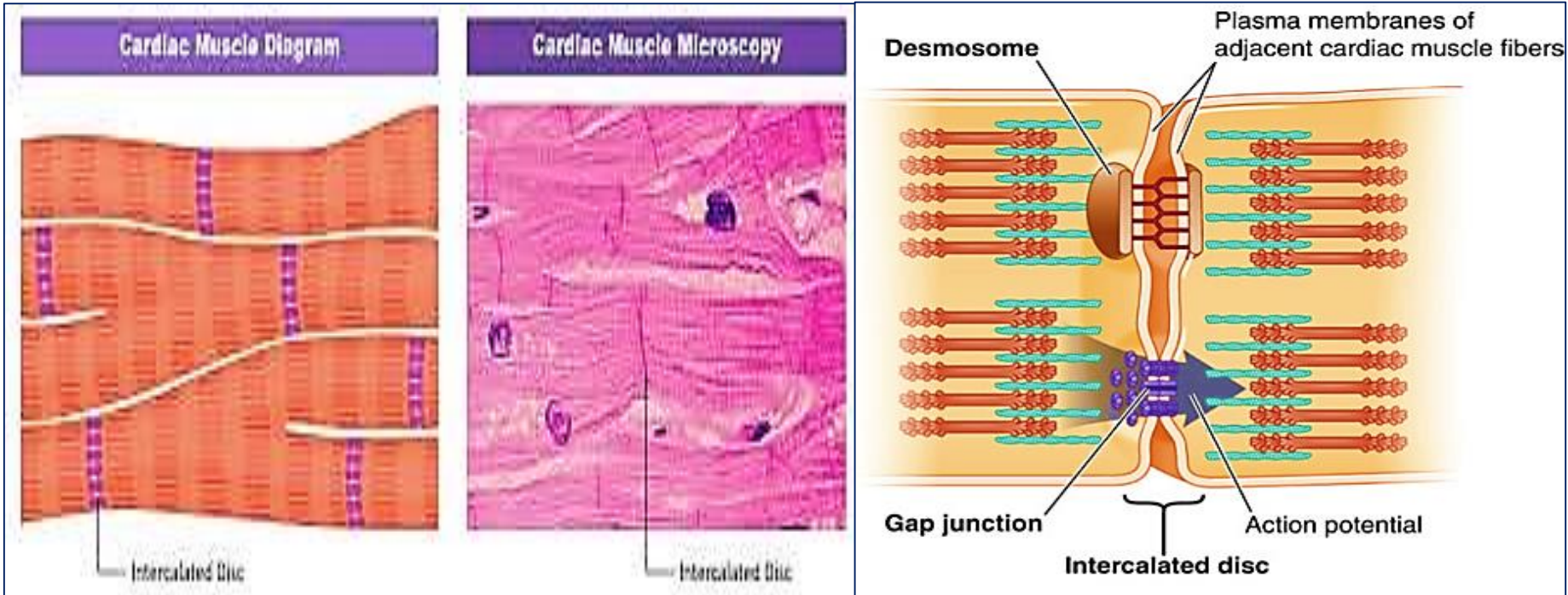


TEM of desmosome

- Within the cell, the desmoplakin provide attachment 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 the **strongest** of the cell junctions



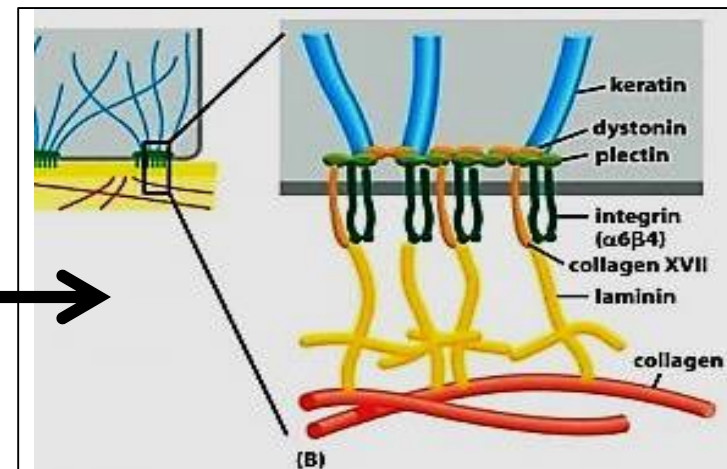
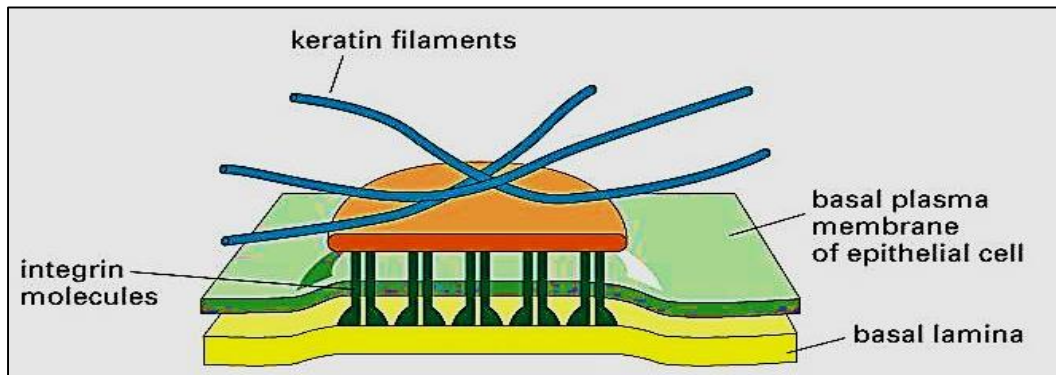
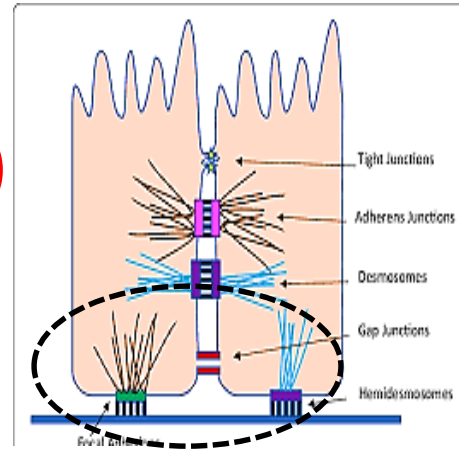
Pemphigus vulgaris
Due defect in desmoglein of Epidermis of skin



Intercalated discs between the cardiac muscles

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 which in turn connect to collagen in ECM → cell-matrix adhesion



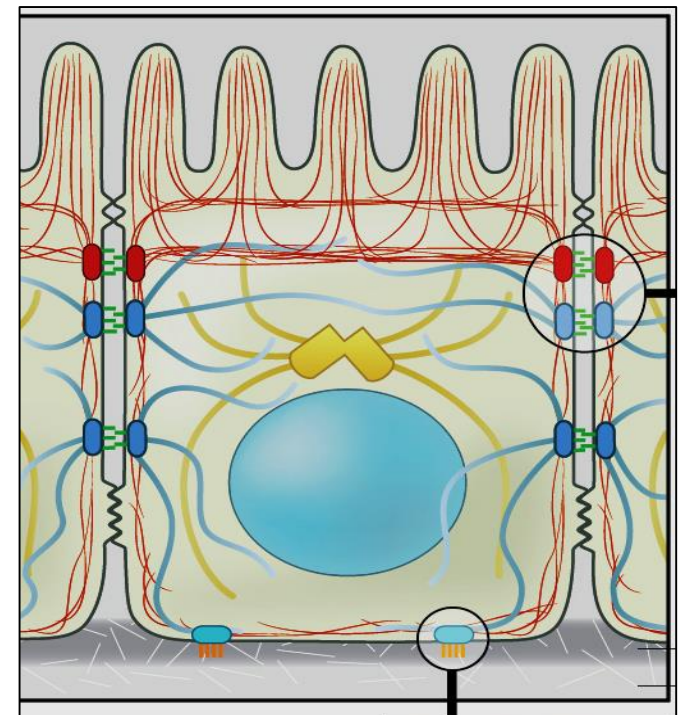
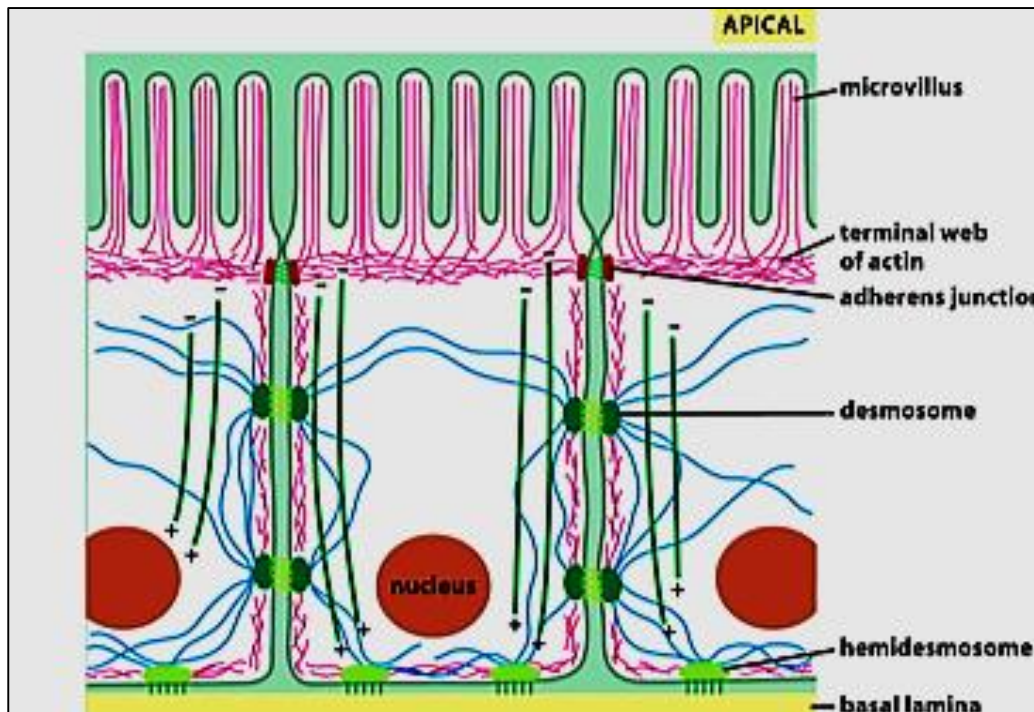


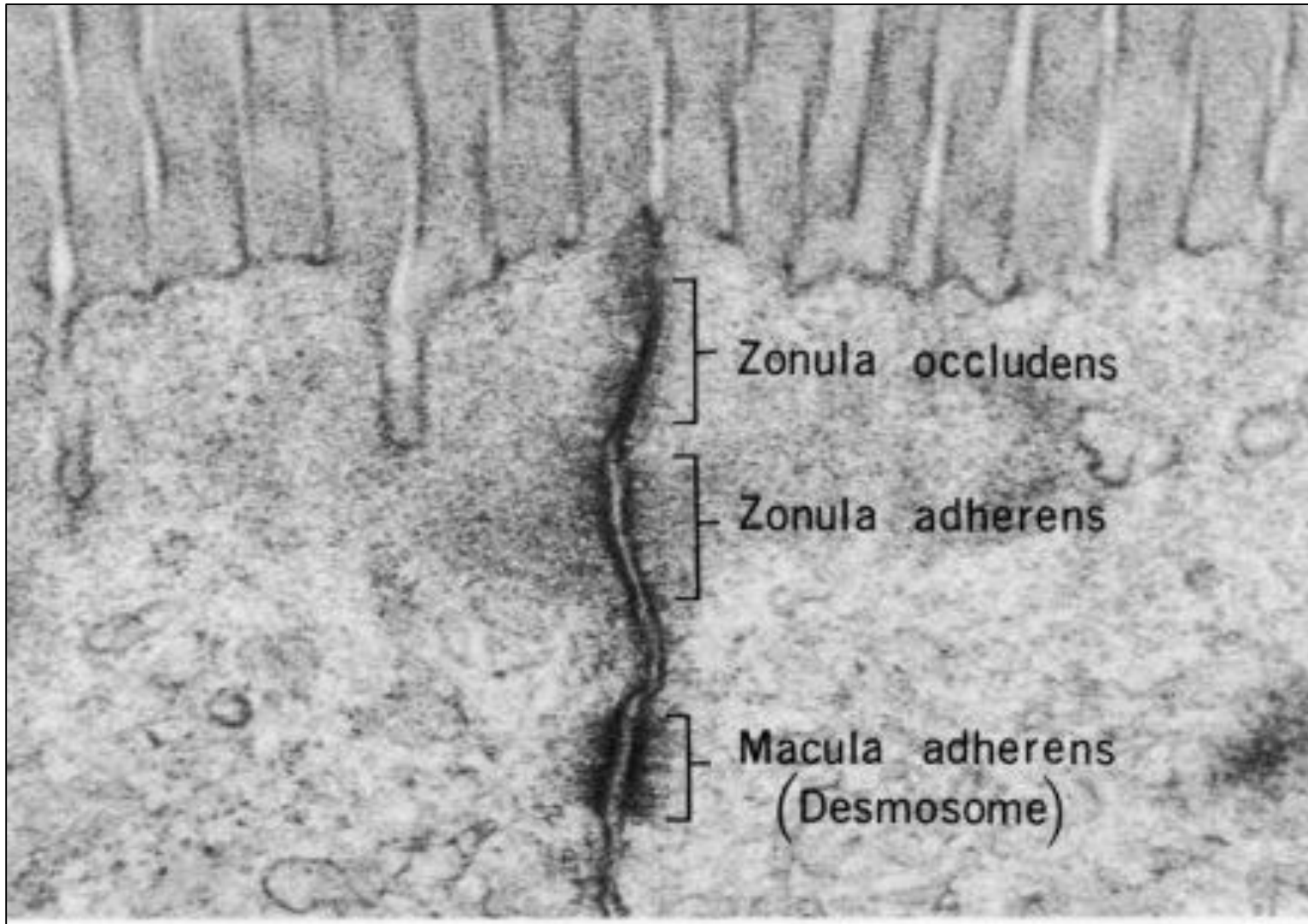
Bullous pemphigoid (BP)

is a chronic blistering of the skin. It ranges from mildly itchy swellings 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.

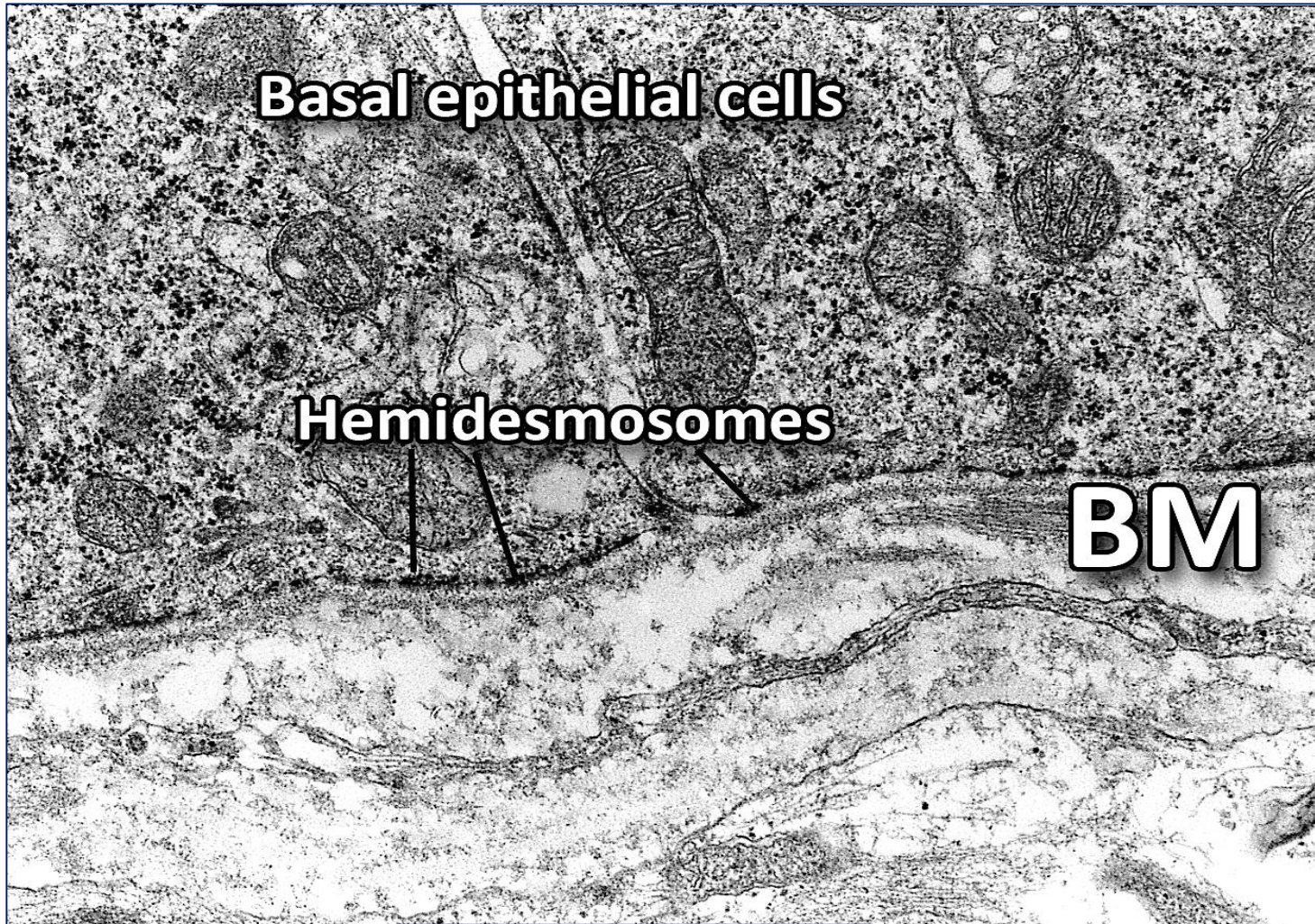
Function of anchoring junctions

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





TEM for arrangement of the intercellular junctions on the lateral border of the epithelial cells



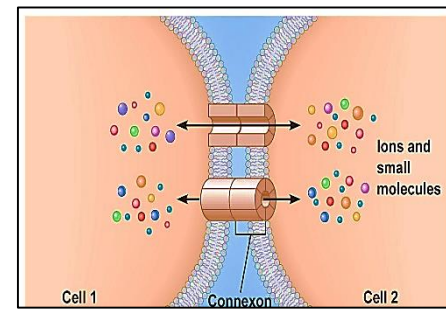
Basal epithelial cells

Hemidesmosomes

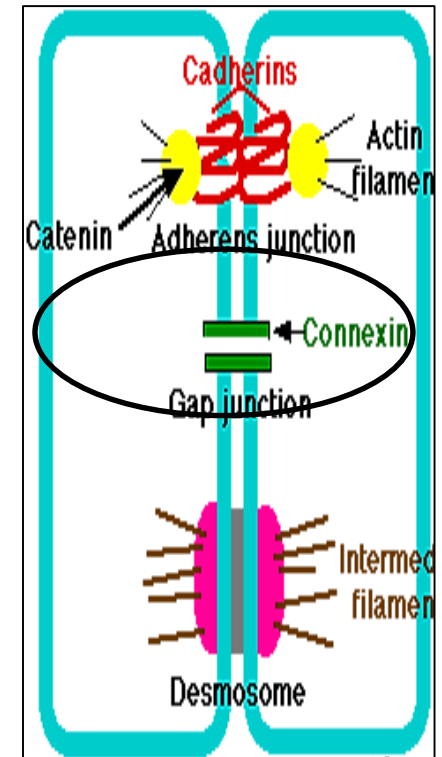
BM

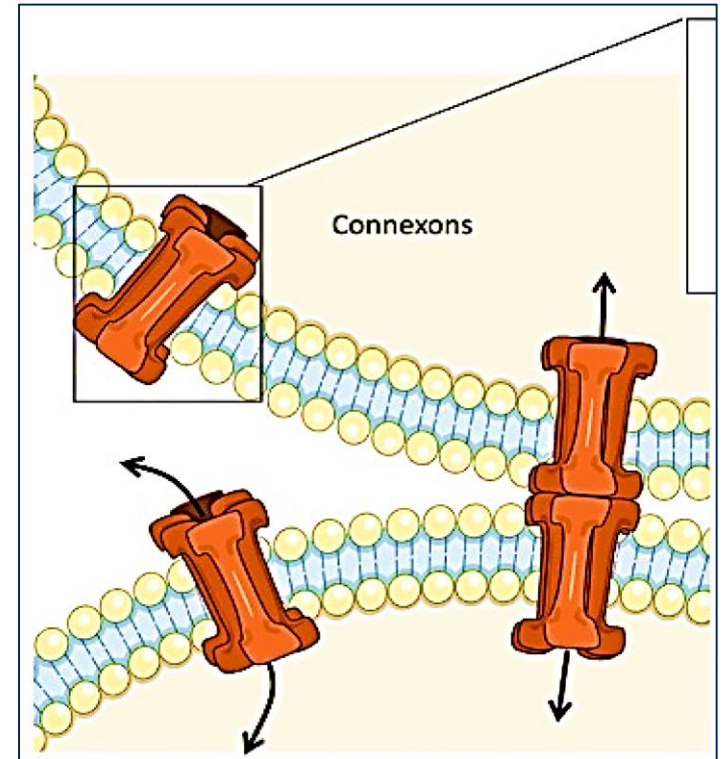
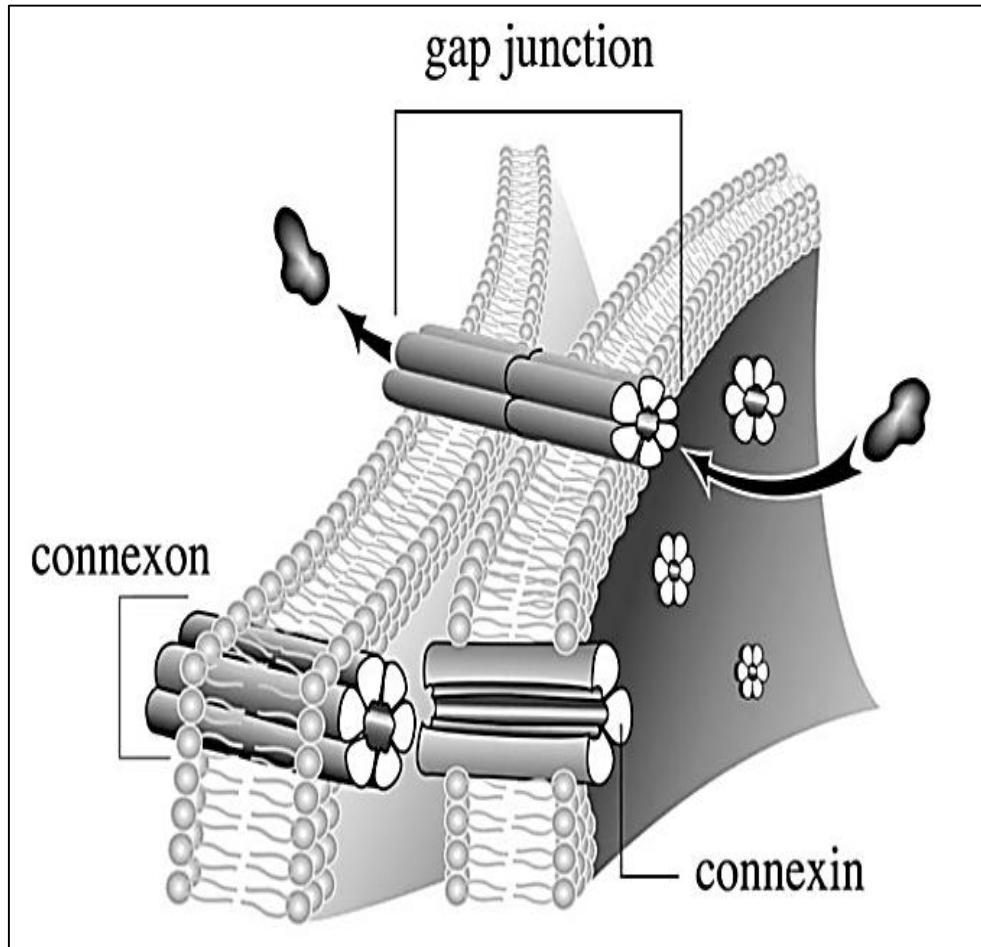
TEM of Hemidsmosome

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 joined either chemically or electrically
- This type of junction is important in heart muscle cells. It provides low resistance so that **ions** cross fast through GJ allowing the cell to contract





Found in cardiac & smooth muscles only not in the skeletal muscles because Sk. muscles are voluntary

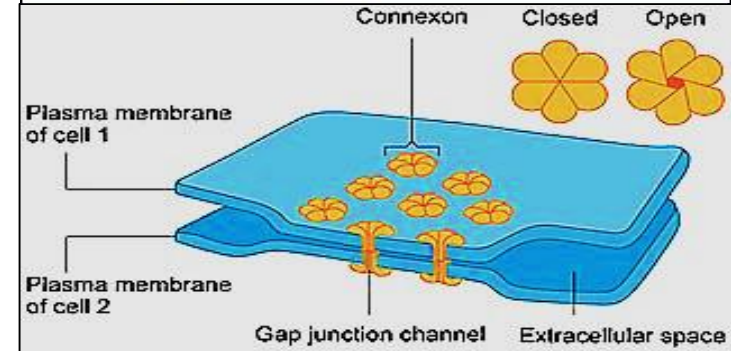
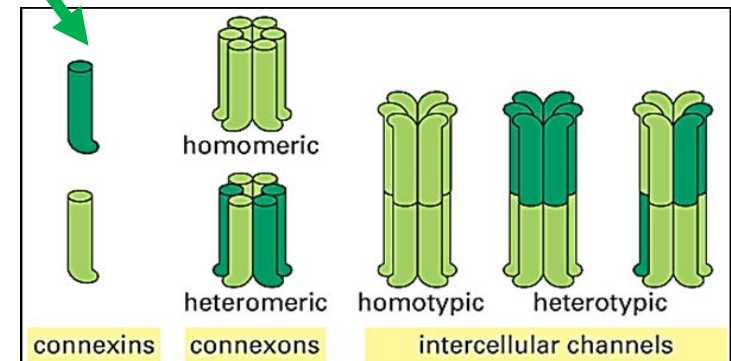
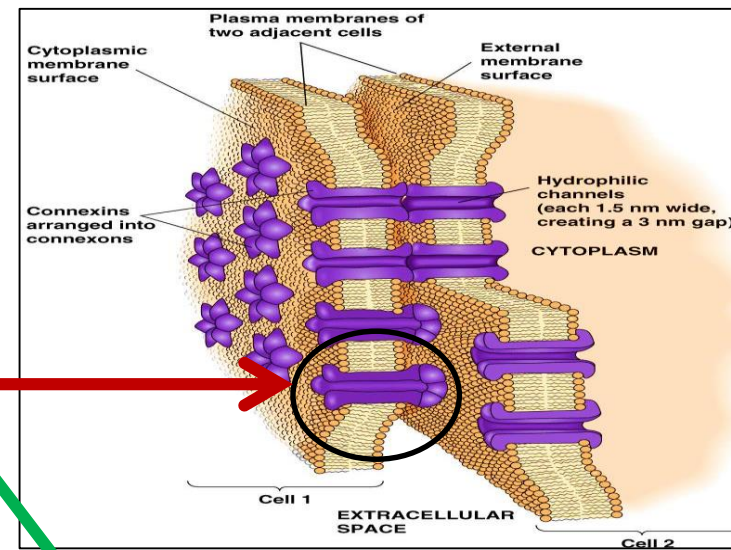
* The protein **subunit** forming the junction is called Connexin

* 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



4- Synapses

Electrical & Chemical

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

A. Electrical synapse

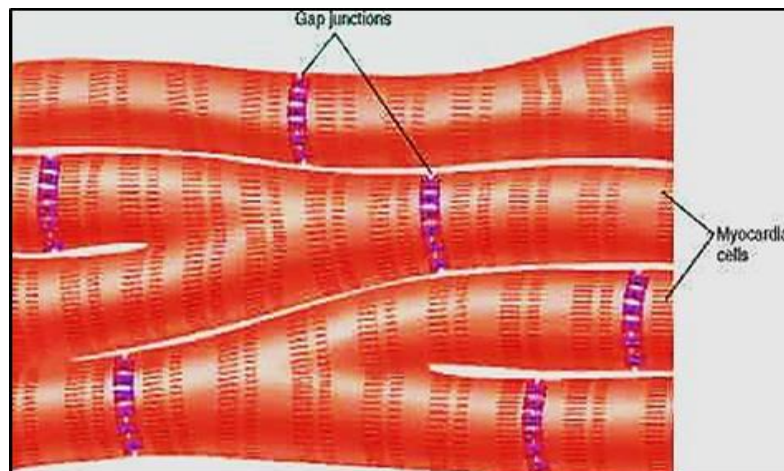
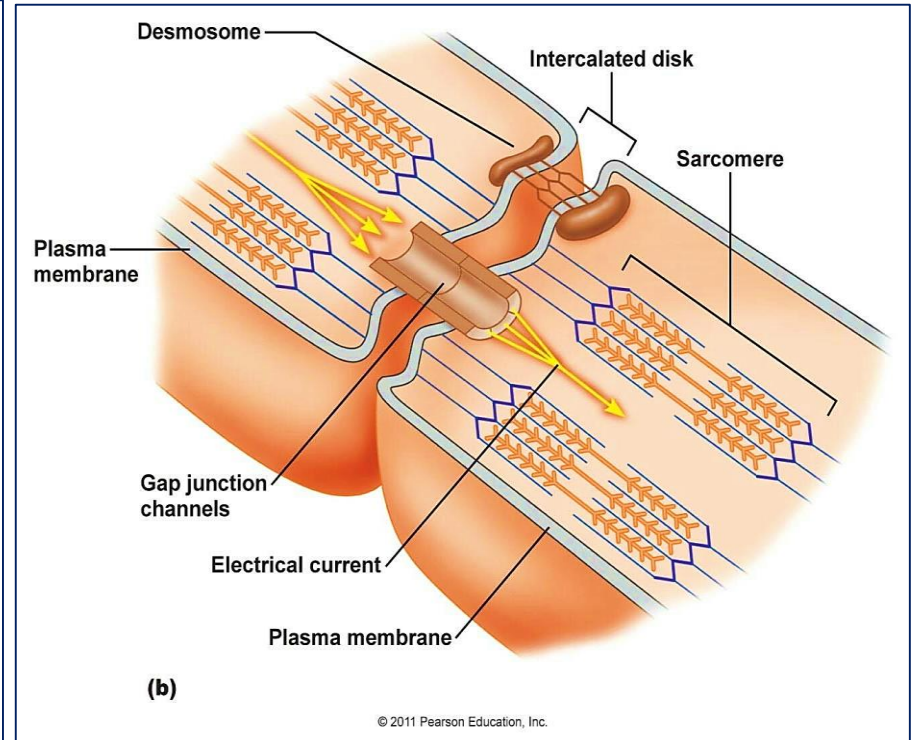
- is a GJ which has channel proteins connecting the adjacent cells.
- The signal in electric synapse can travel faster .
- Found : between: cardiac muscles (intercalated discs),
& in synapses between neurons in nervous system
& between smooth muscle cells

Intercalated discs:

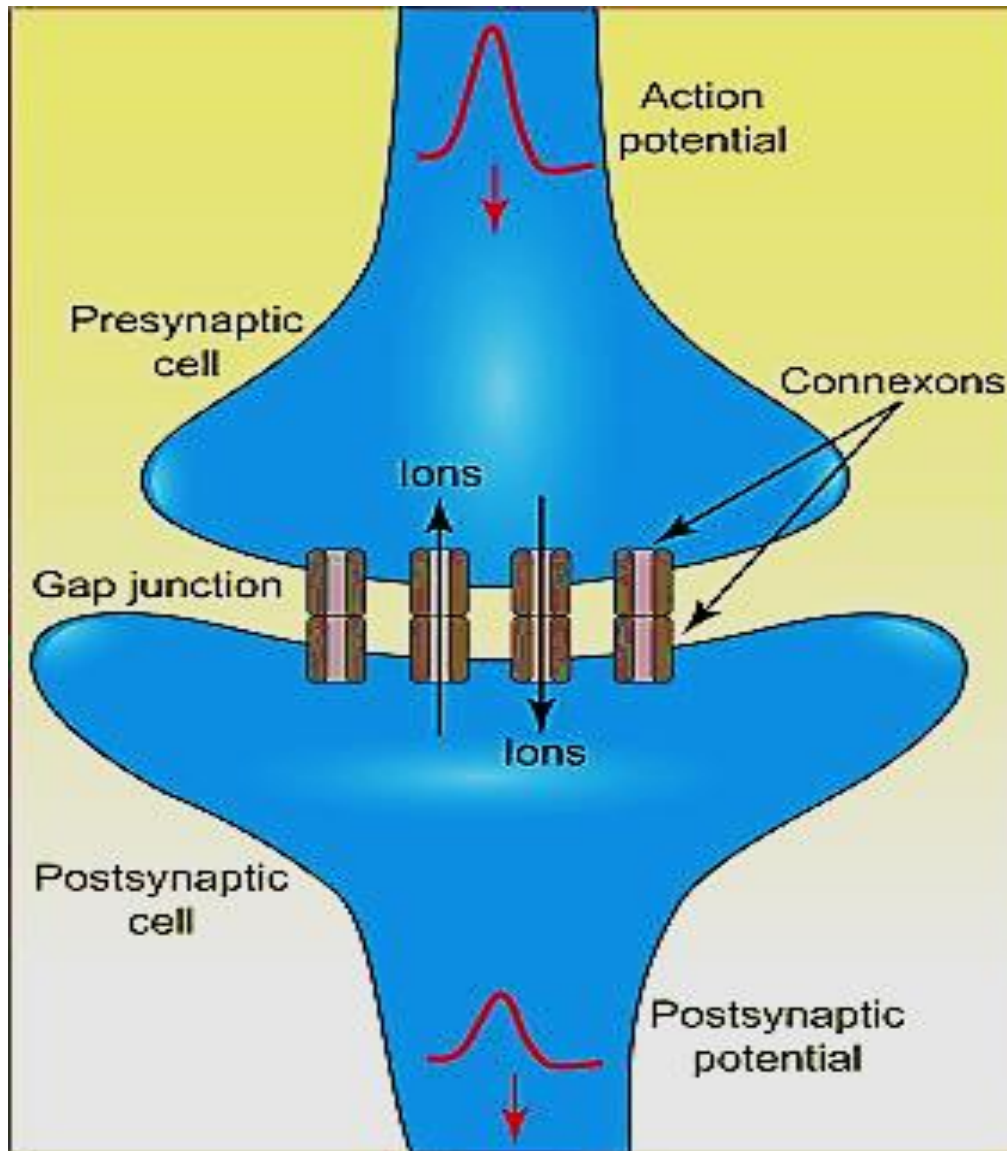
contain both

GJs & Desmosomes

to allow rapid flow of ions from one cell to another → spread of action potential & to hold the cells together i.e prevent their separate



Intercalated discs of the heart

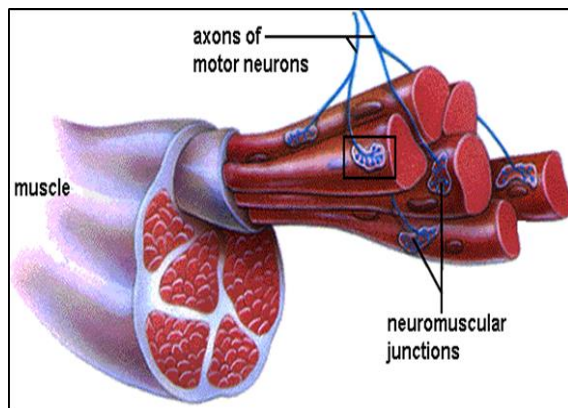


Electric synapse

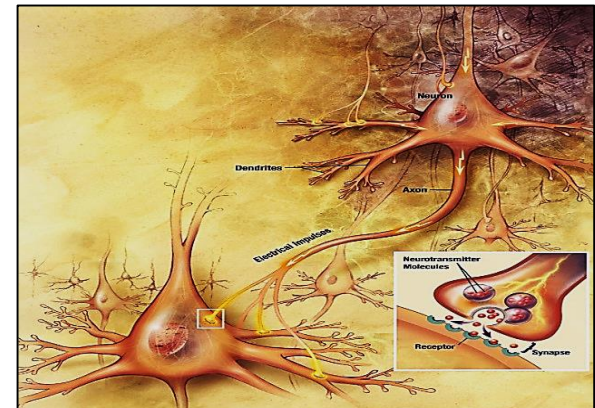
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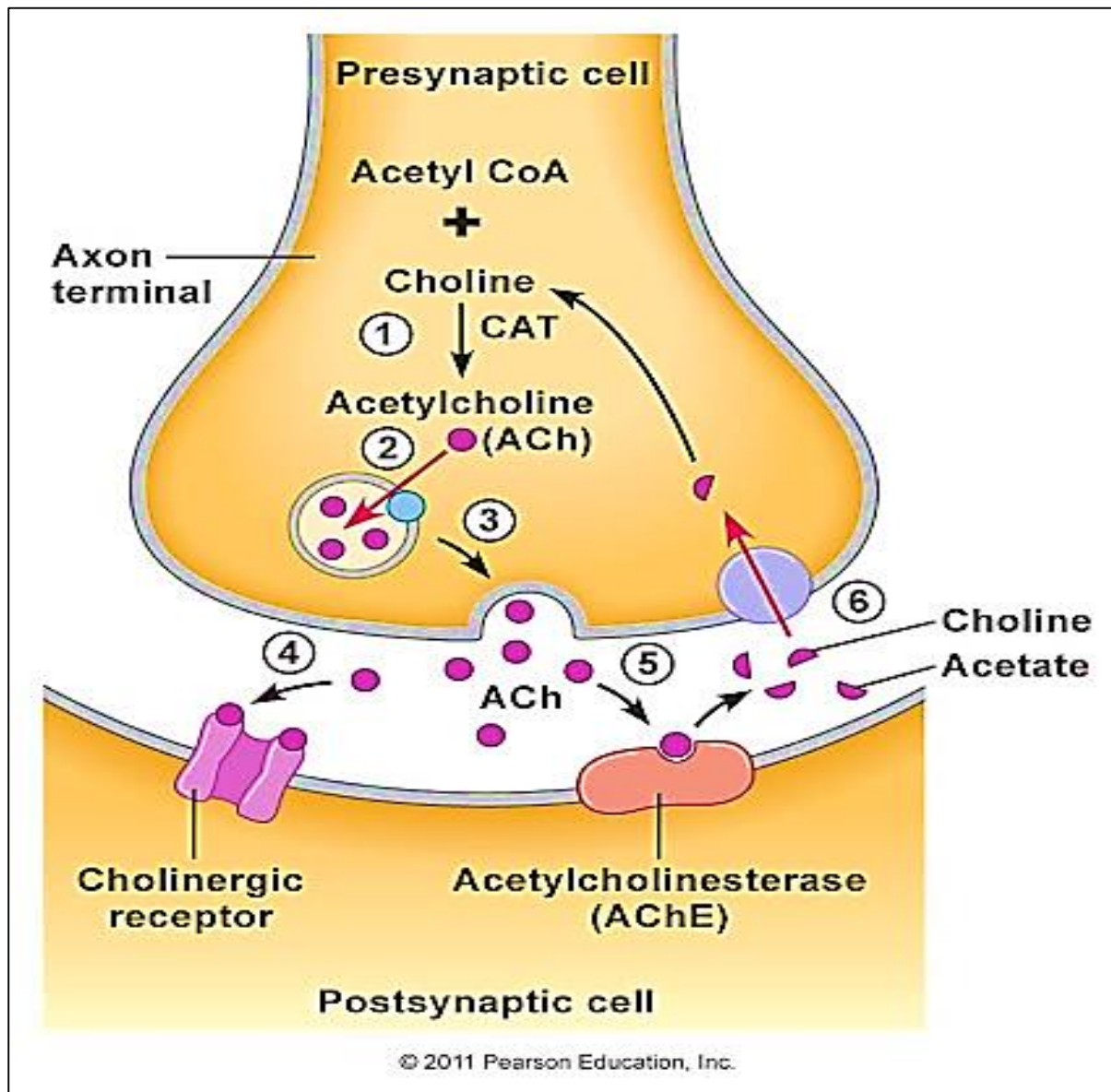
B- chemical synapse (Signal relaying junction)

- 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 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

