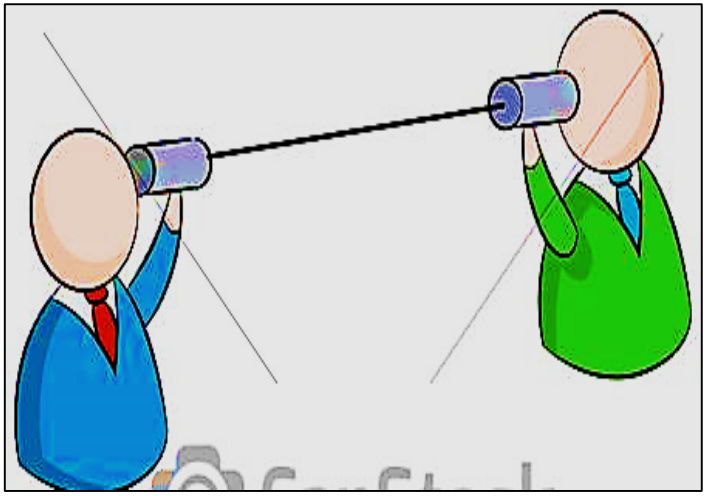
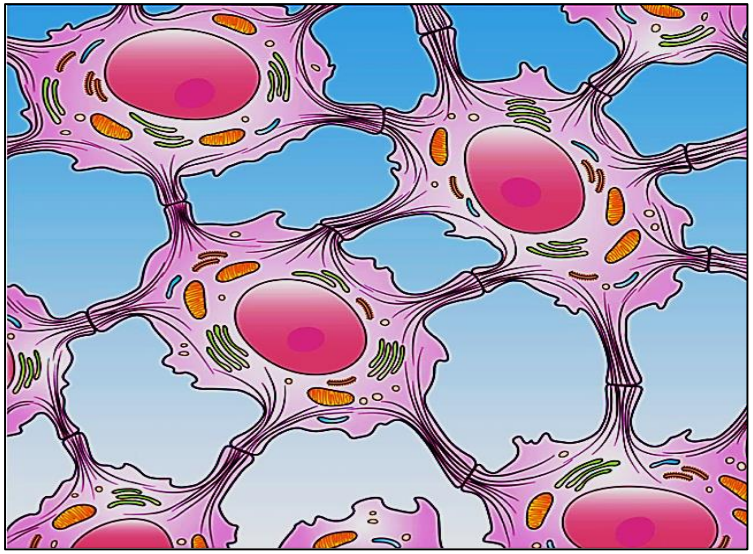
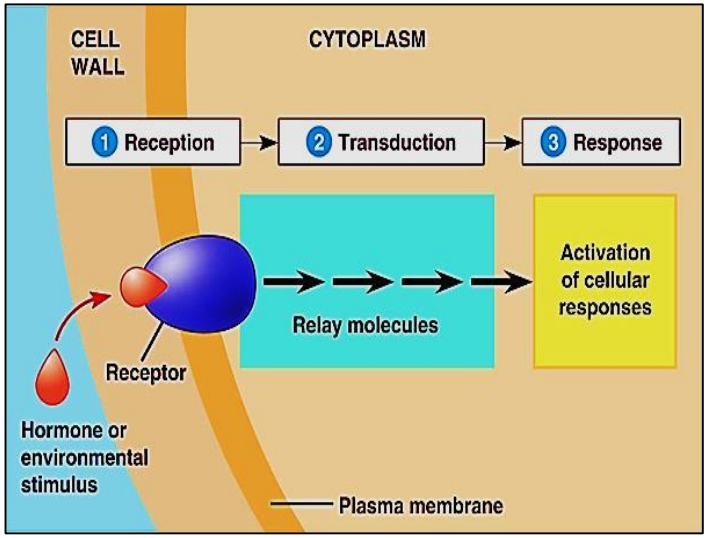
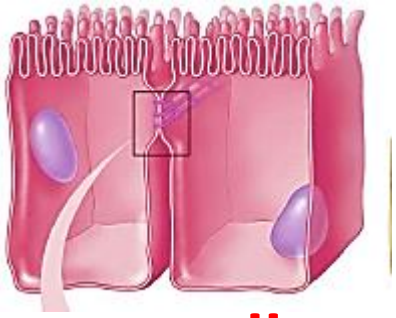
# Cell Junctions & Cell Communication





# Cell Junctions

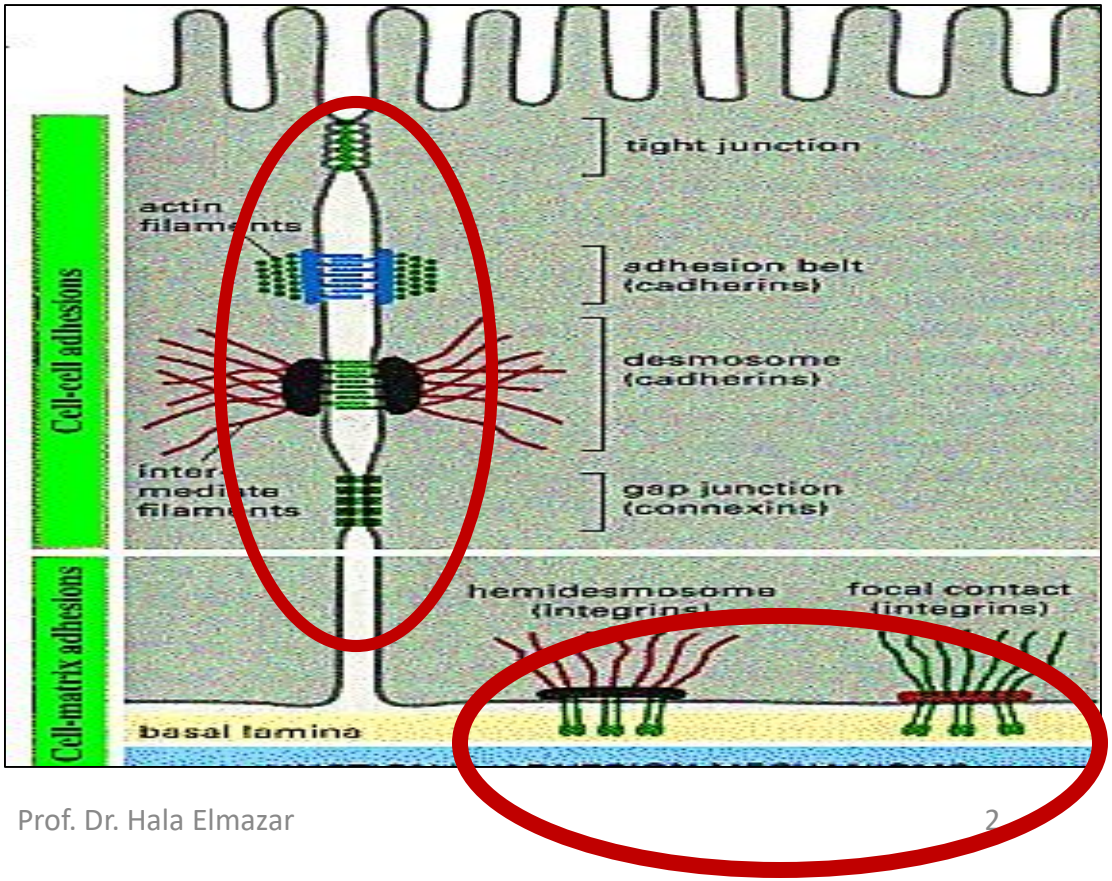


## Definition & classification:

- 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**



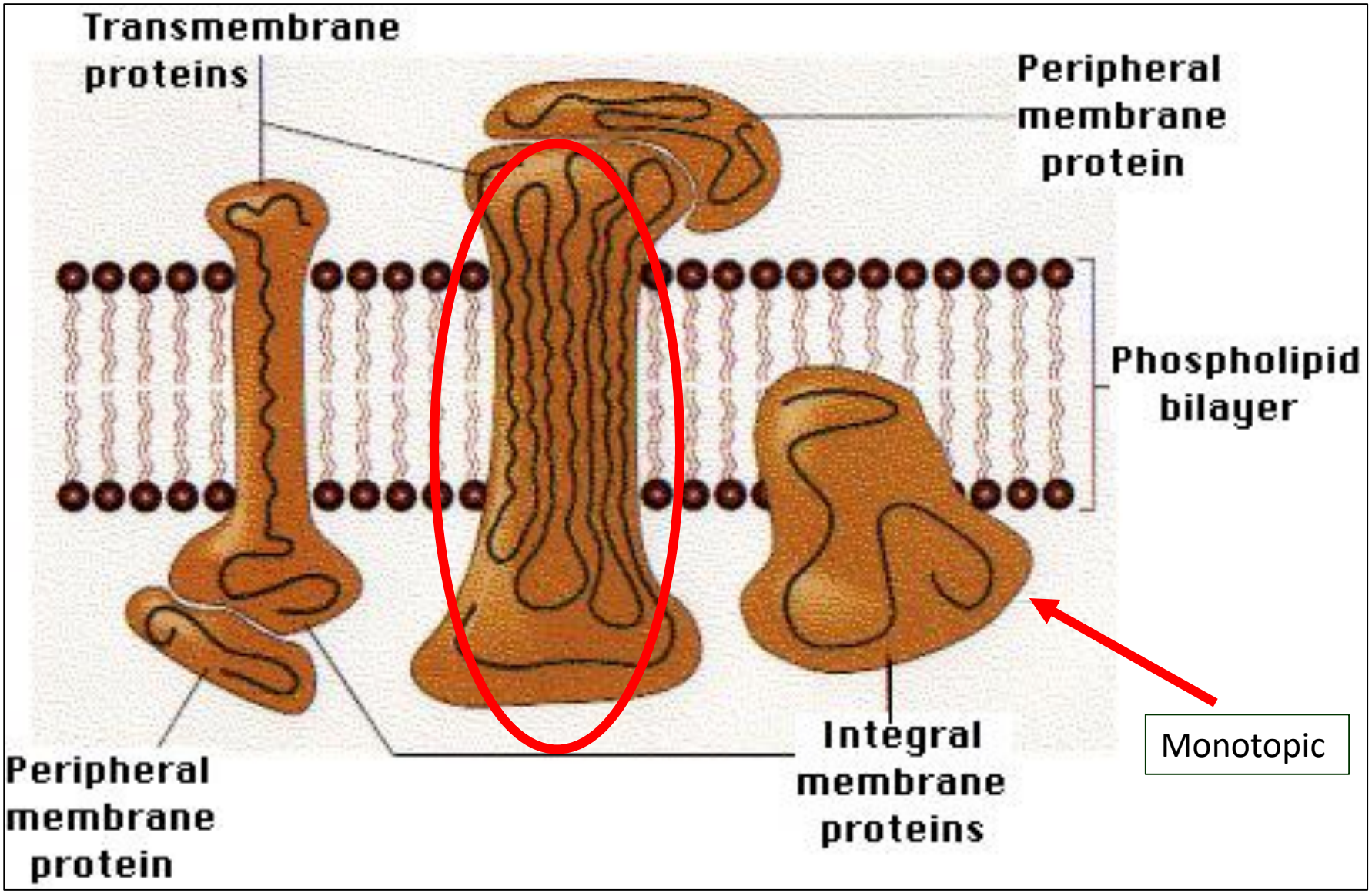
# Cell membrane proteins

- They are of two types either peripheral or integral

- Peripheral: are temporary attached to the cell membrane. Found on the outside & inside surfaces of the cell membrane.

- Integral : are permanently attached to the membrane. They are of two types :

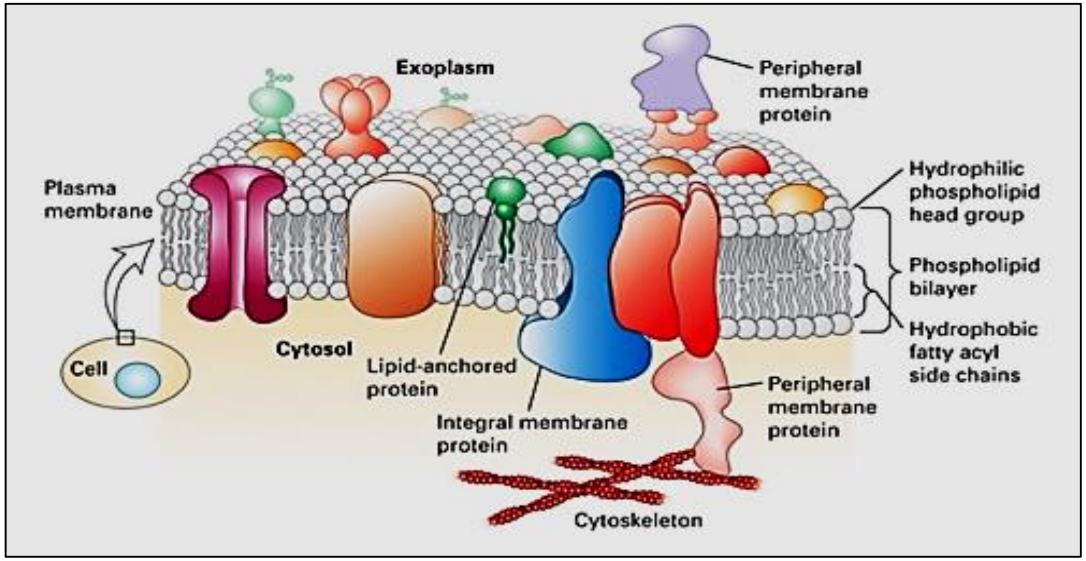
- *Transmembrane* proteins that span **across** the cell membrane
- *Monotopic* : proteins **attached to only one side** of the membrane and do not span across the cell membrane .

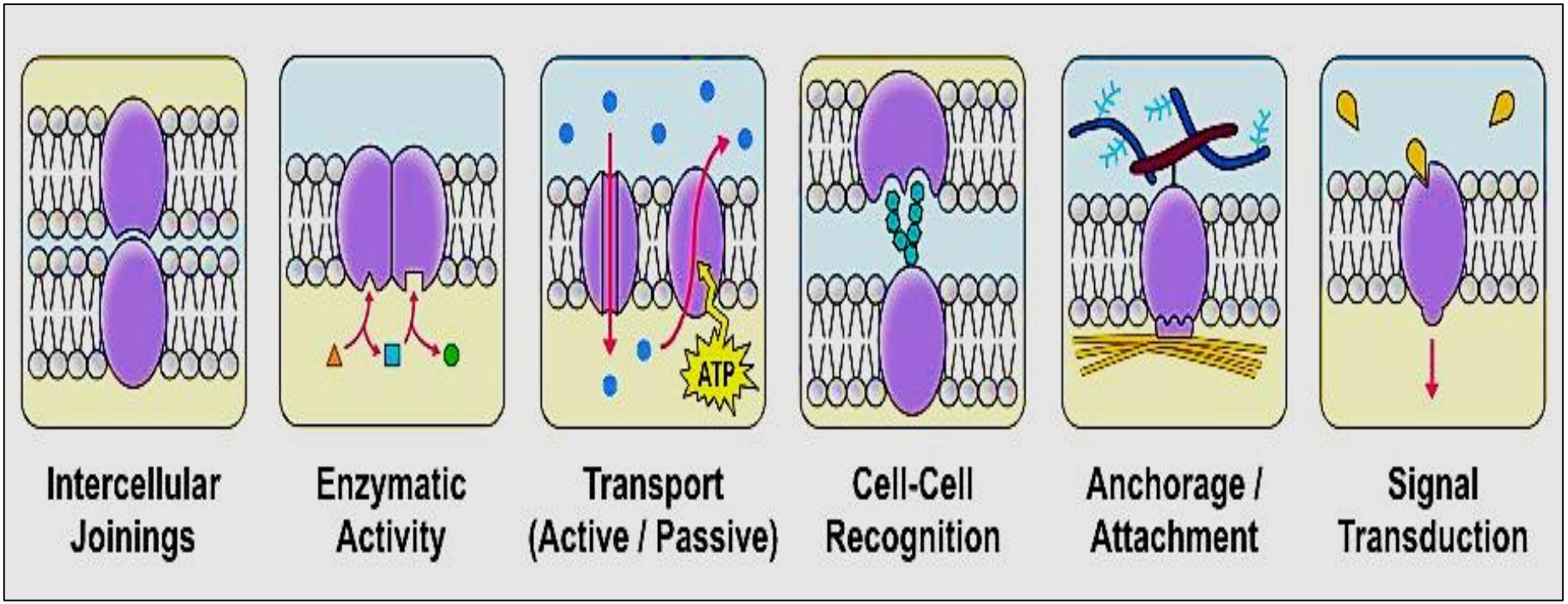



**Types of cell membrane proteins**

# 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

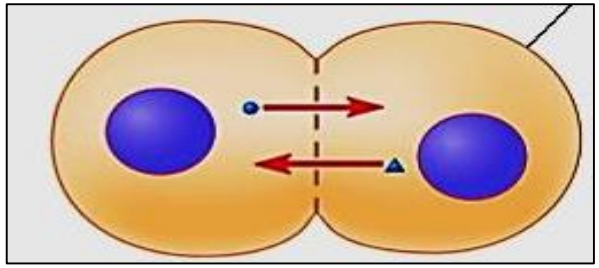


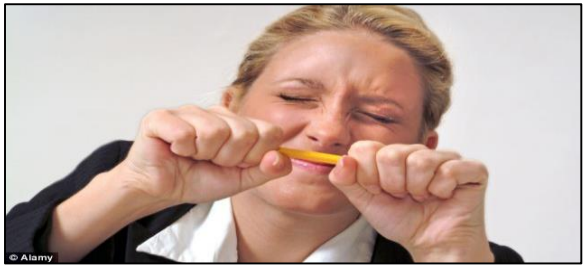




**Function of cell membrane integral proteins**

# Function of cell- cell junctions (adhesions)

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





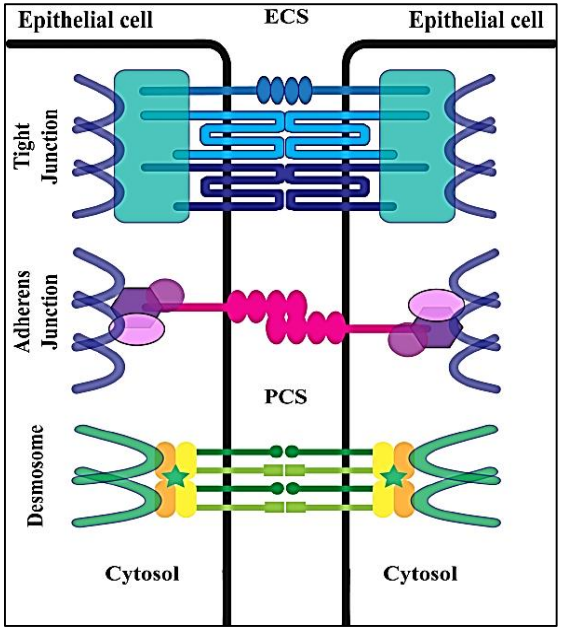

**Cell adhesion (junction) is due to the action of :**

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

**2- Intercellular junctions (Adhesions)**

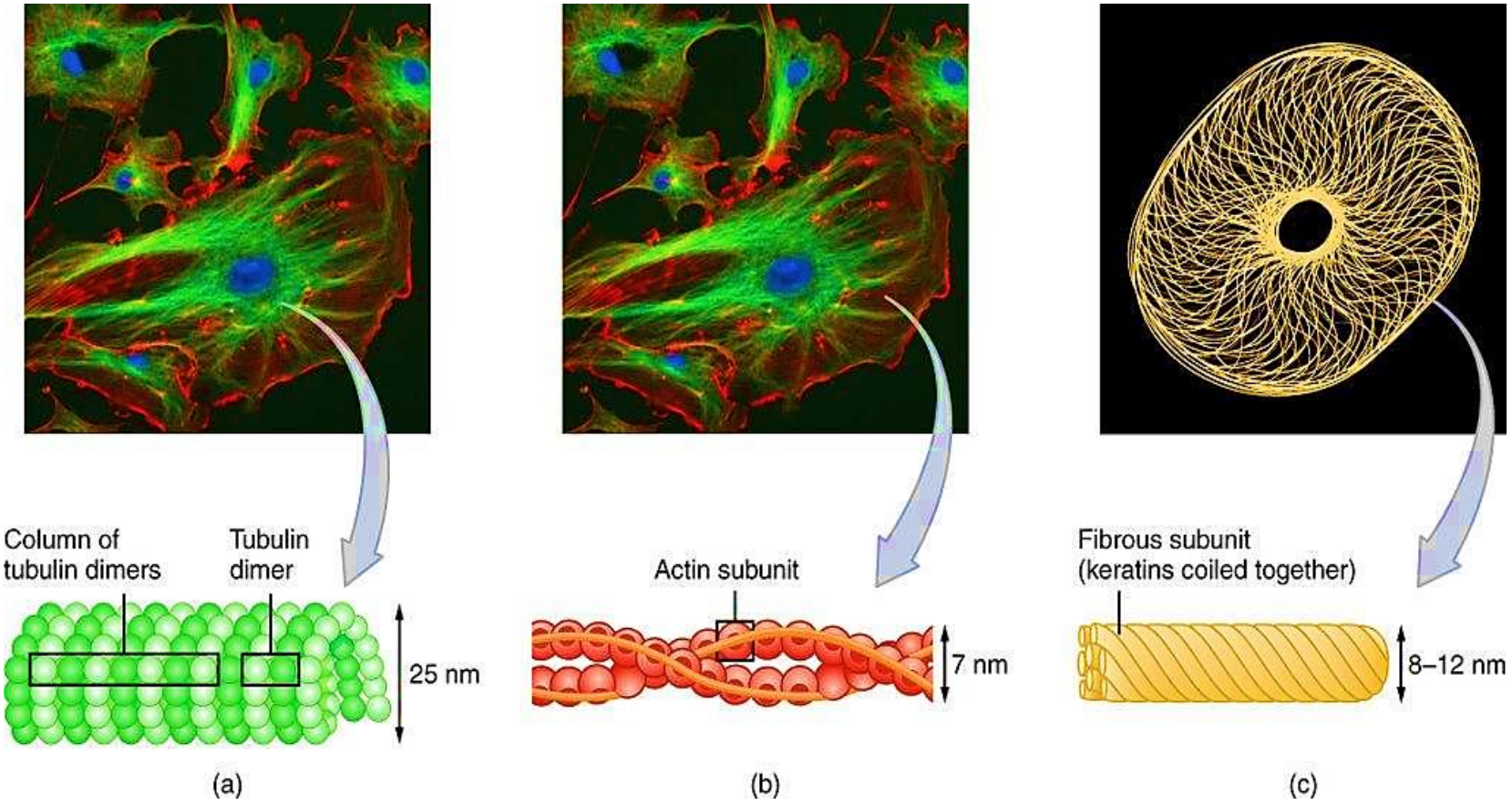
- **Cell adhesion molecules (CAMs)**

A group of cell proteins located on the cell surface & 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

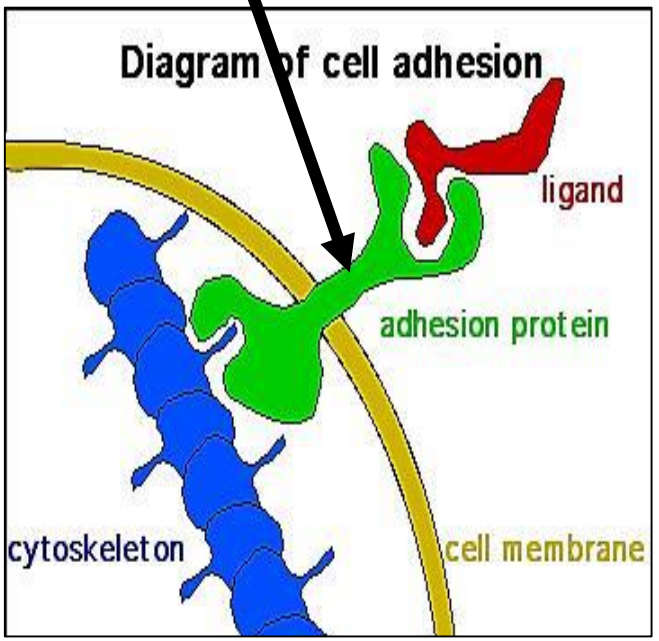



**Inside the cell there are 3 types of cytoskeletons : actin filament , intermediate filament & Microtubules**

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

# Cell Adhesion Molecules (CAMs)

- Proteins located on the cell surface *(typically trans-membrane proteins)*



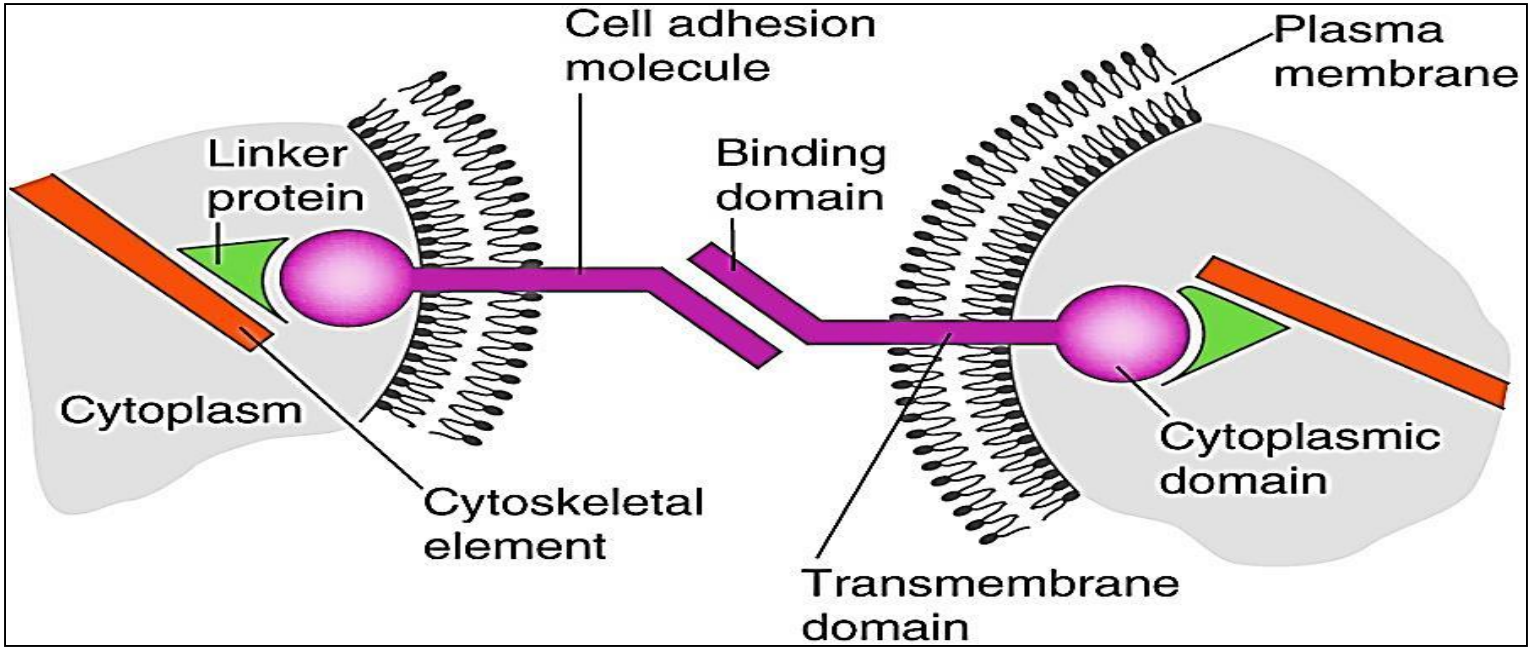

- They help in attaching cells e each other & e their EC matrix

  also Play a role in immunity & cancer

- When CAMs of the same kind bine together is called (***homophilic binding***)
- When CAMs of different types bind together or with the extracellular matrix is called (***heterophilic binding***).

## CAM molecule composed of 3 major domains:

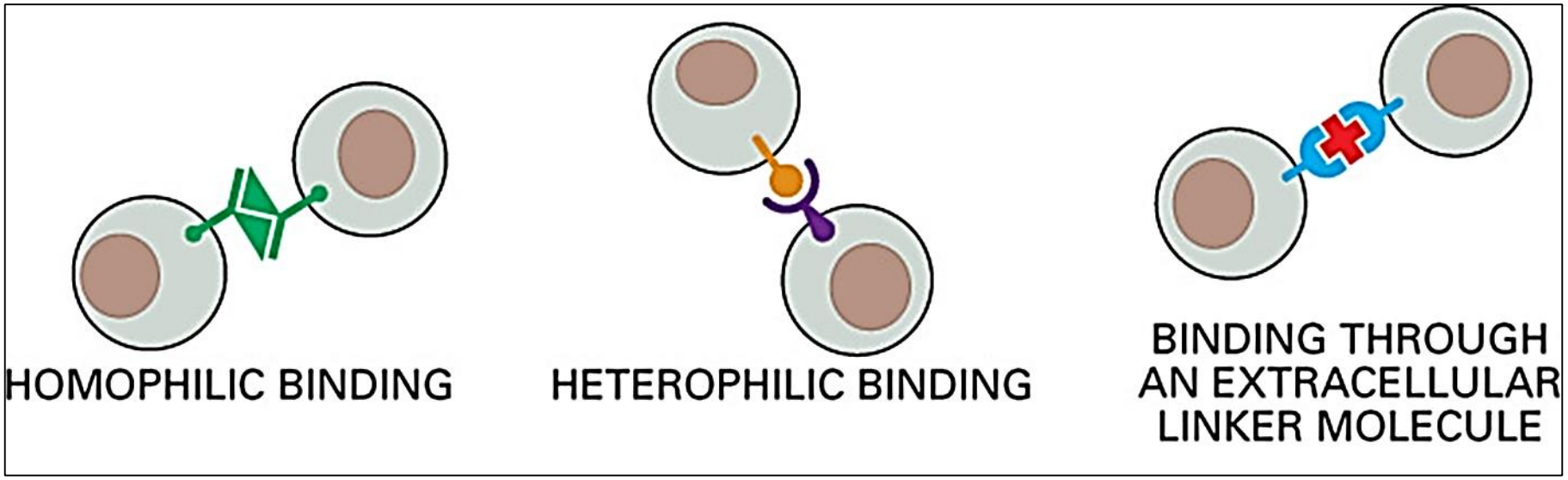
- The extracellular domain: allows one CAM to bind with another CAM on an adjacent cell.
- The transmembrane domain: links the CAM to the plasma membrane through **hydrophobic forces**.
- The cytoplasmic domain: is directly connected to the cytoskeleton by linker proteins.



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

| | |
|---|---|
| cadherin | selectins |
| Immunoglobulin superfamily | Integrins |

# Interactions between CAMs can be mediated by :

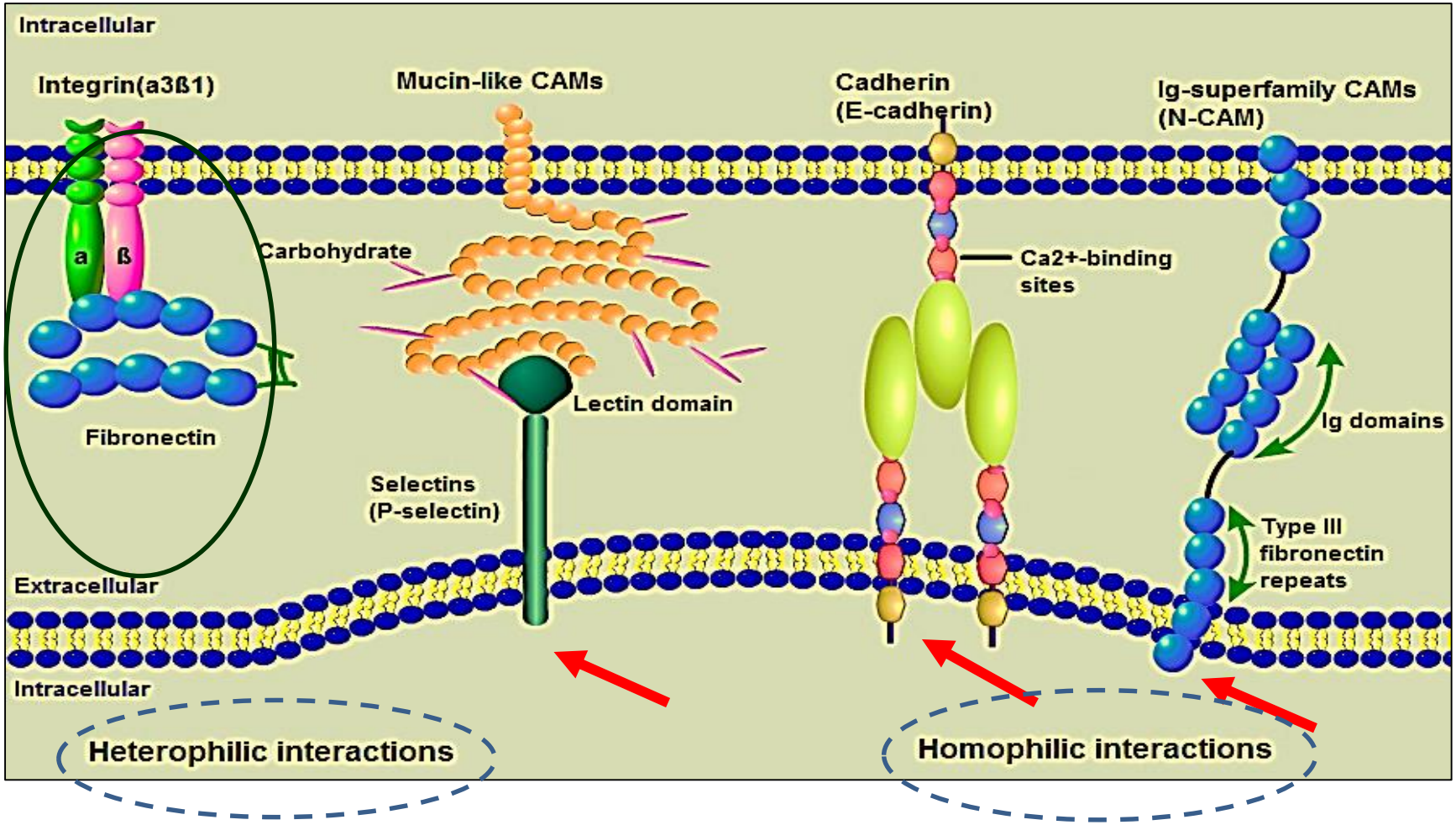



**Binding of CAM on one cell to the same CAM on a second cell**
***Cadherin - cadherin***

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

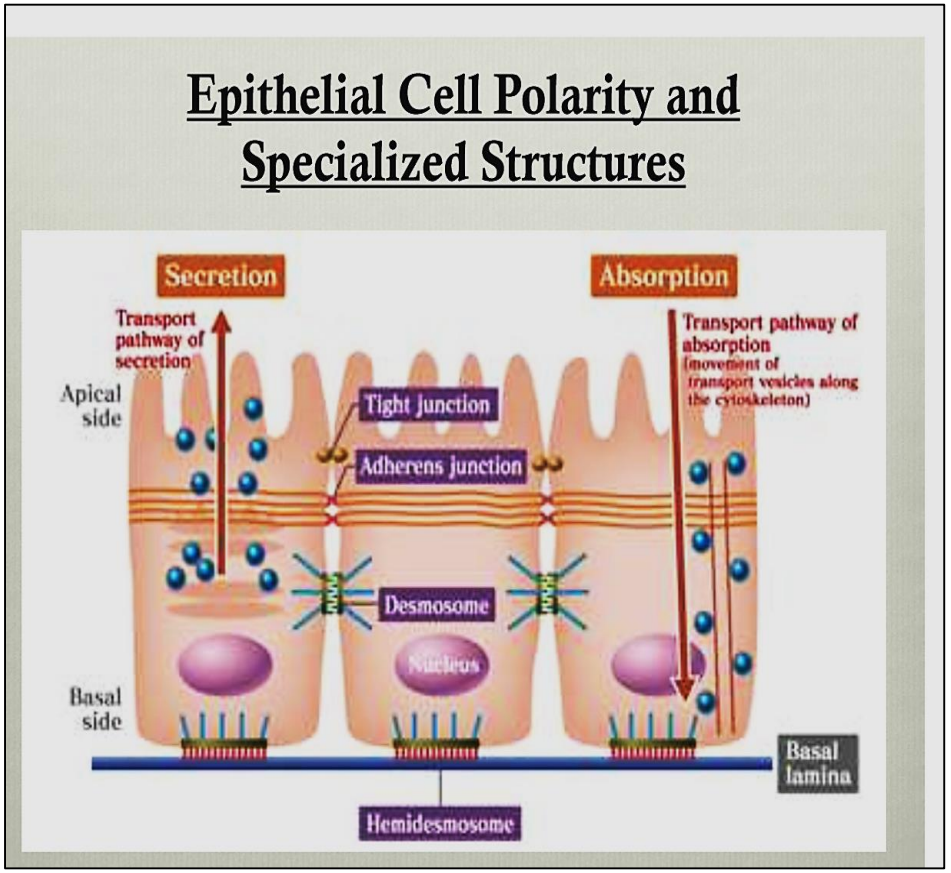
**CAM binds to EC matrix is also a heterophilic binding**

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



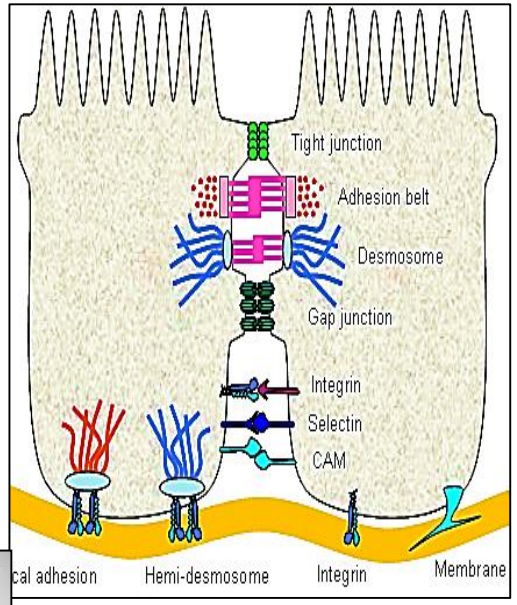

**CAMs Families: Only Integrins binds cell to the extracellular matrix ( basement membrane), while selectins, cadherins , and IgSF members are associated with cell- cell adhesion**

- 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

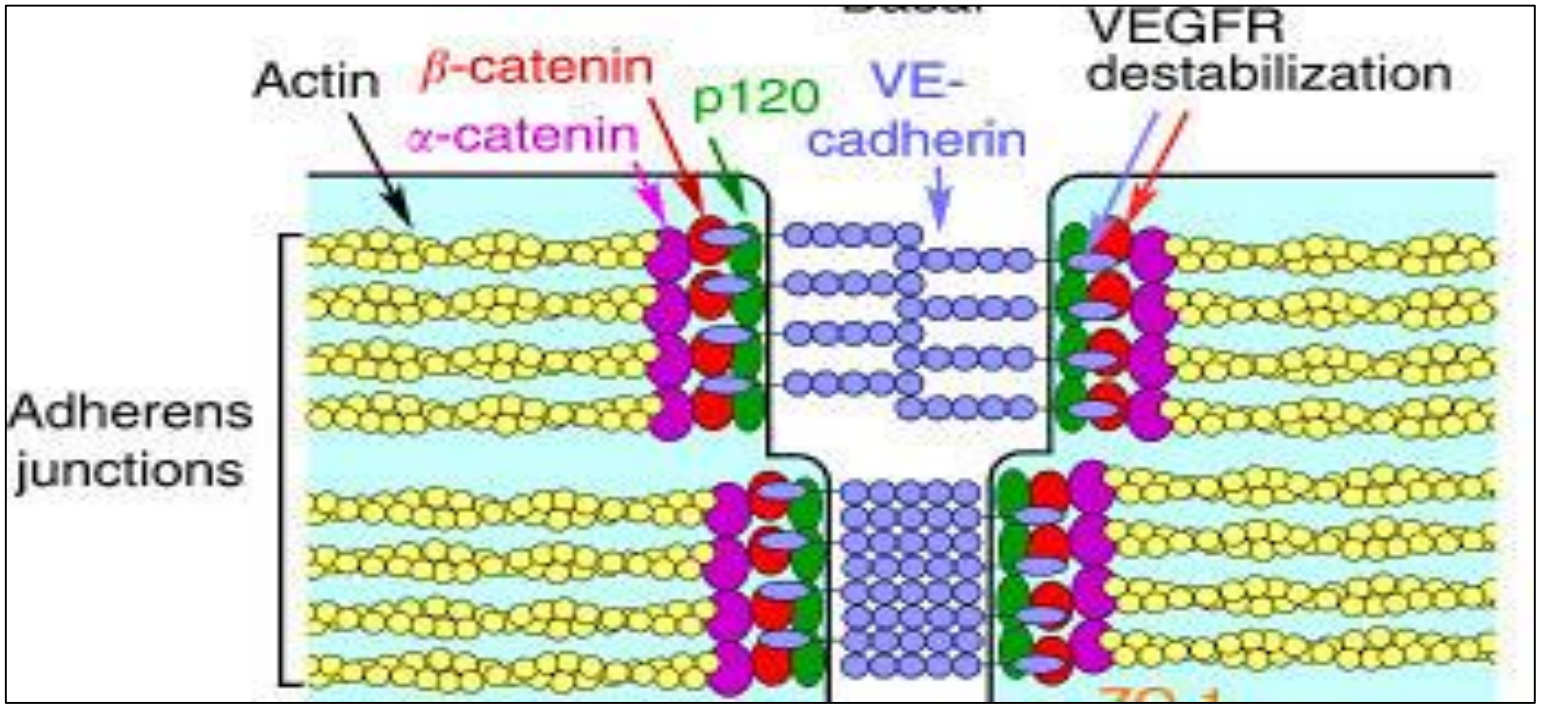
- Cell junctions consist of multi-protein complexes
- They are particularly plentiful in epithelial tissue
- Types of cell junctions :



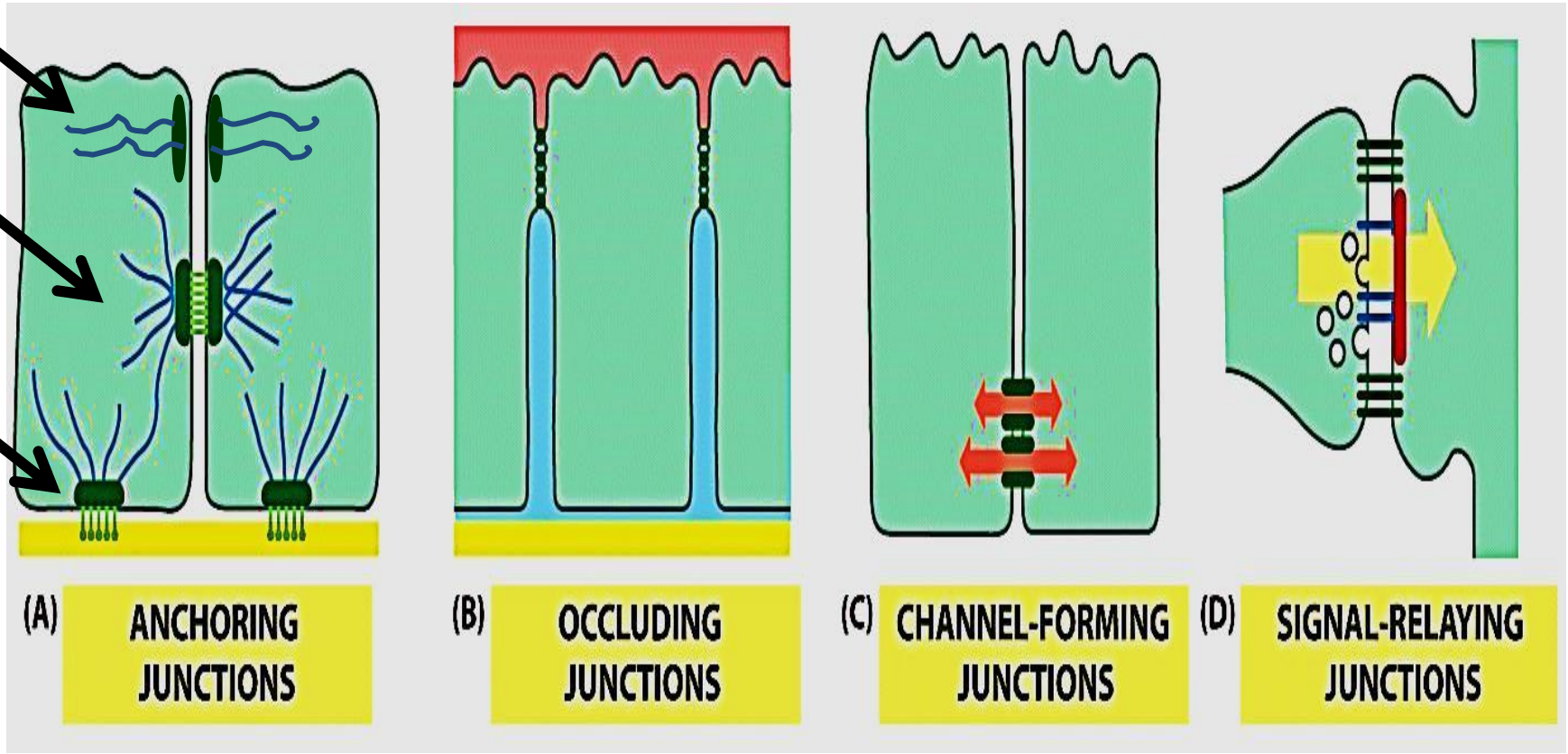

**1-** Occluding/Tight junctions: Seal cells Together like a sheet to prevent flow of molecules even water or ions between cells

**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


Actin
β-catenin
α-catenin
p120
VE-
cadherin
VEGFR
destabilization
Adherens
junctions

# Types of cell junctions in multicellular organism




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

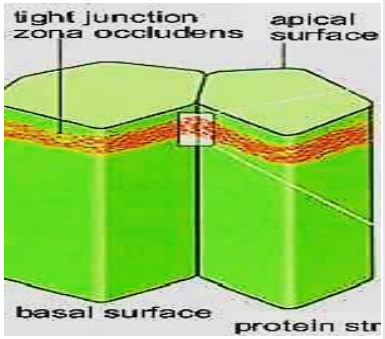
**Tight junctions (zonula occludens)**

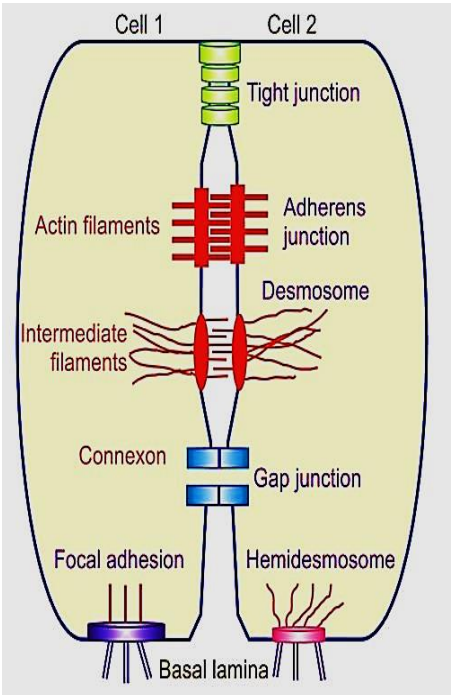
**Gap junctions**

**Synapse**

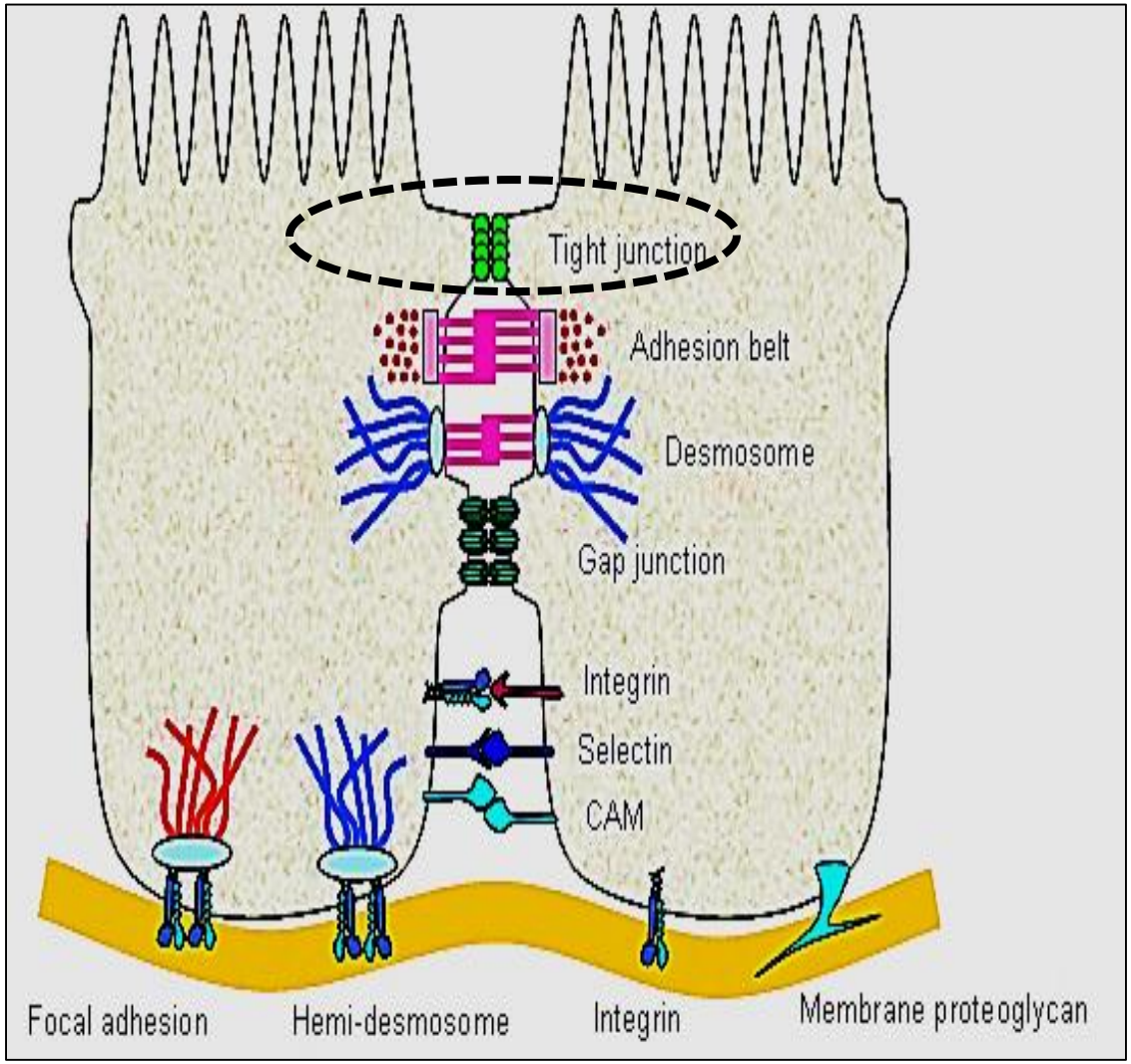
# 1- Occluding junctions

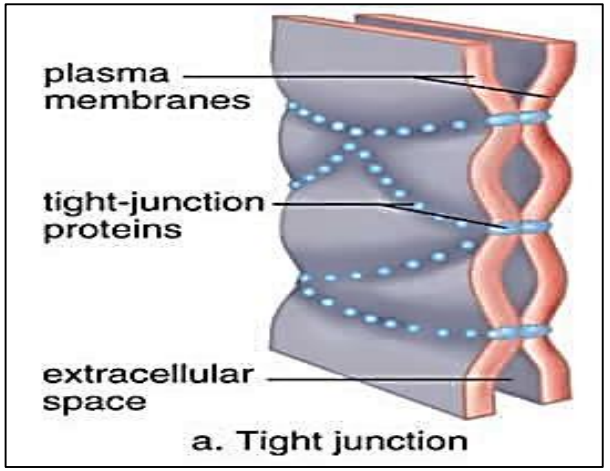
- Also called **tight** Junctions / zonula occludens




- 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/diffusin barrier**
- Proteins forming this junction are **occludins** and **claudins**

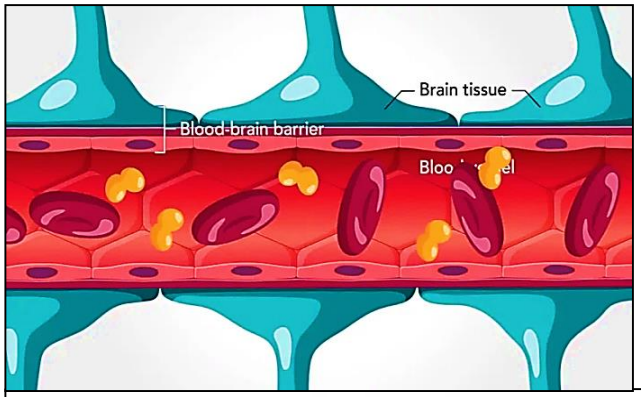

Tight junction
Adhesion belt
Desmosome
Gap junction
Integrin
Selectin
CAM
Focal adhesion
Hemi-desmosome
Integrin
Membrane proteoglycan

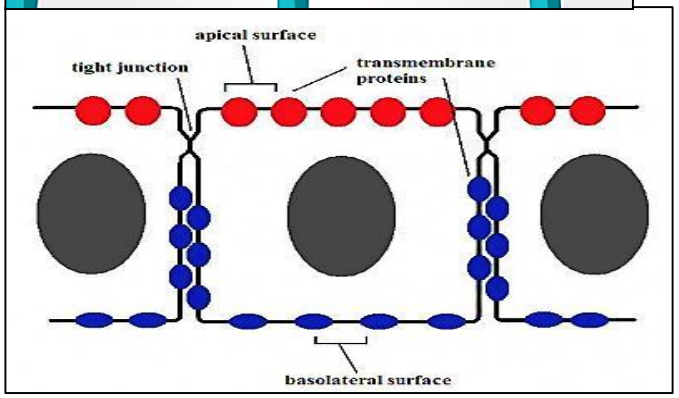

plasma membranes
tight-junction proteins
extracellular space
a. Tight junction

# Functions of Tight Junction

- **Protection: Seals cells thus it creates barriers to prevent leaks**

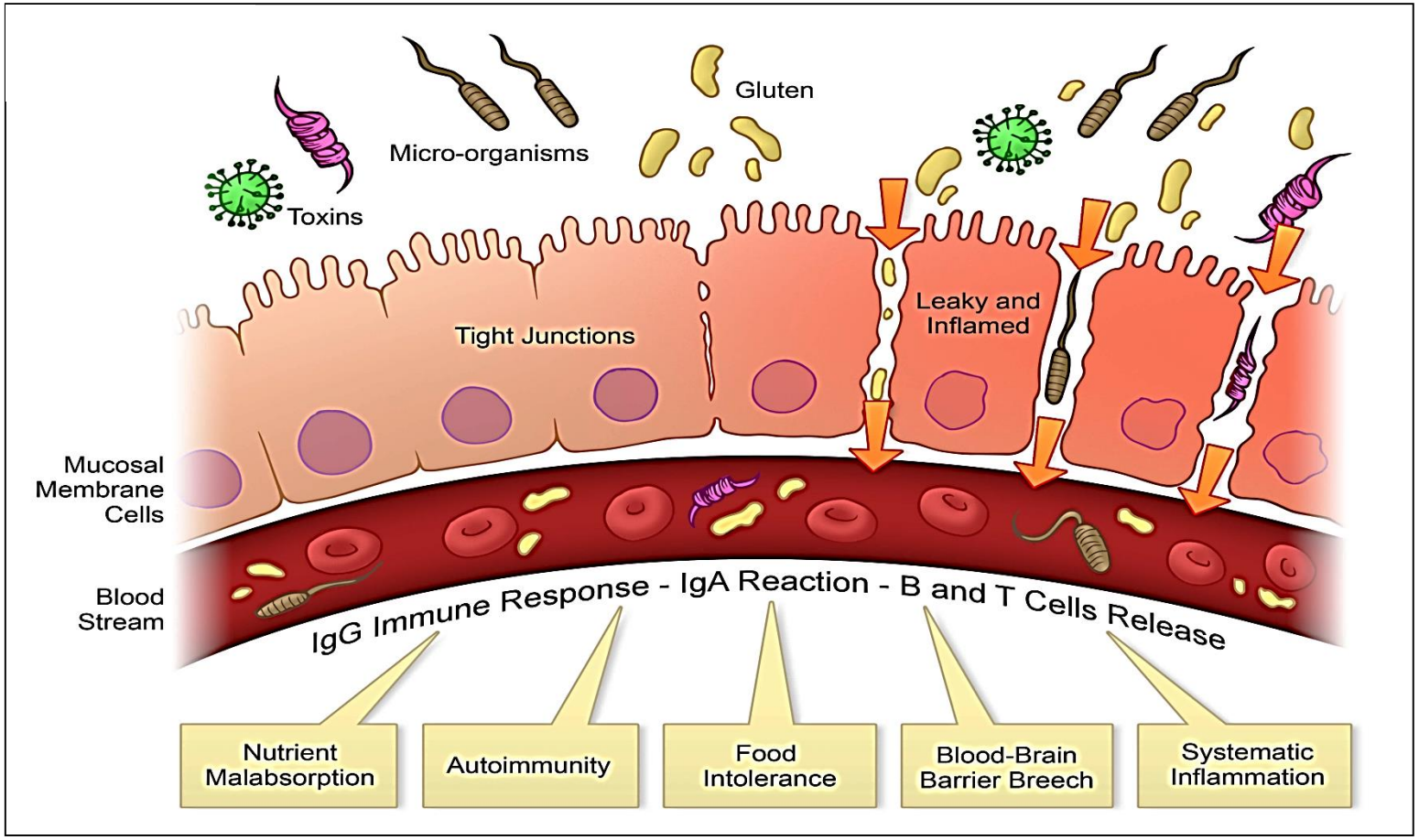
- **Blood-brain barrier & other barriers in the body especially in GIT**



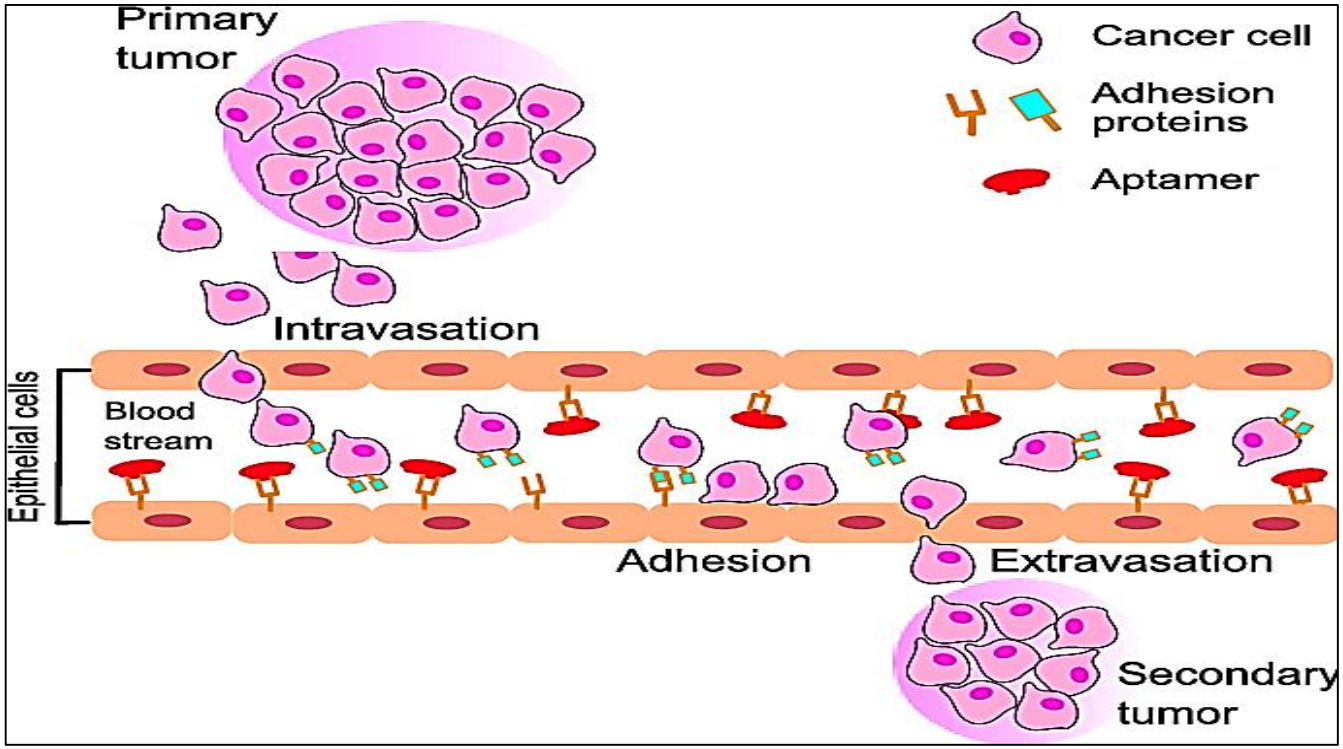

- **Maintain cell polarity: prevent membrane proteins of apical surface from being moved to basolateral surface to maintain cell receptors & function**

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



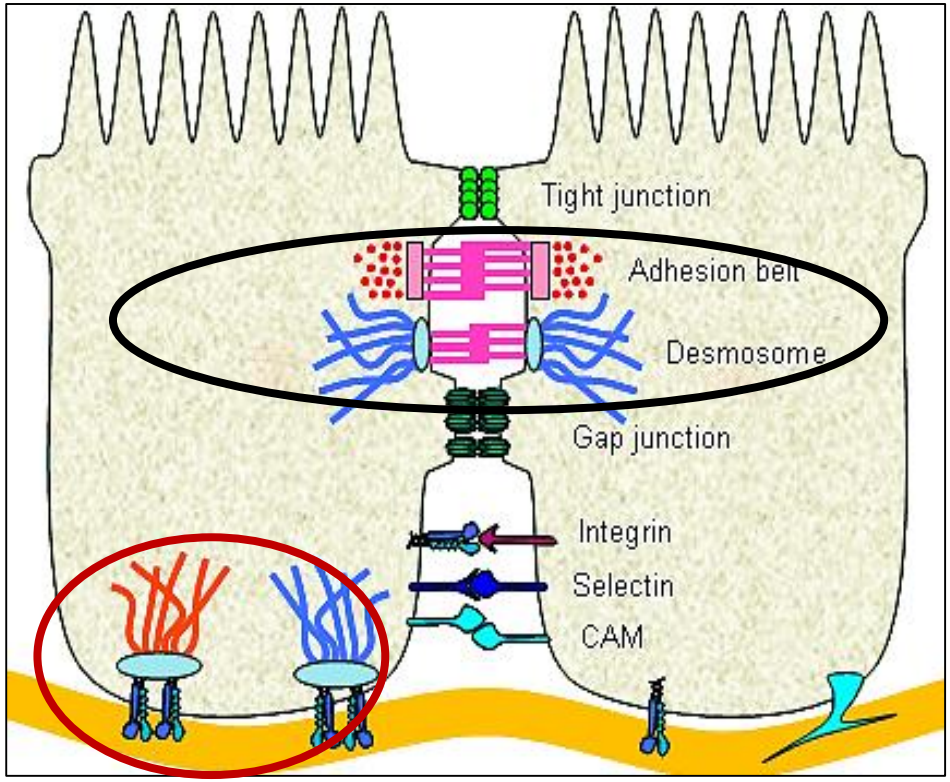

**Leaky gut syndrome :** **is a disease happen when tight junctions between intestinal epithelial cells (intestinal barrier) become defective → abnormal increases in the intestinal permeability → leaking of a undigested food particles, toxins & microbes from the lumen into the bloodstream → digestive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

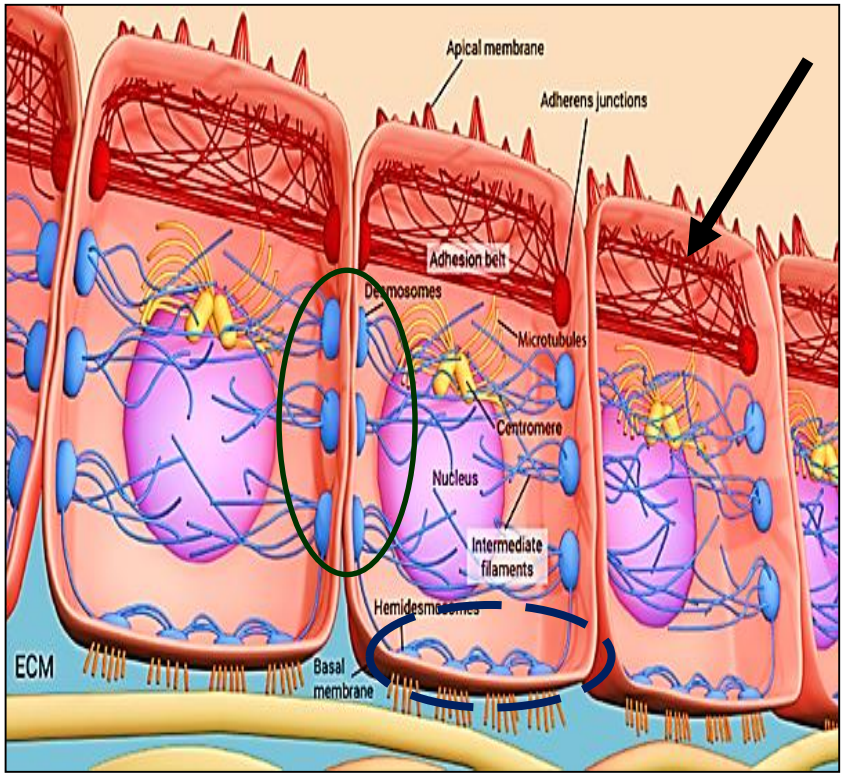
- Most cancers originate from epithelial cells.
- Down regulation of Tight junctions adhesion proteins lead to tumor dissociation and subsequent metastasis.
- Researchers observed low expression of TJ proteins among highly metastatic cancer cells



# 2- Anchoring junctions

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



# 2- A- Adherens junction/Zonula adherens

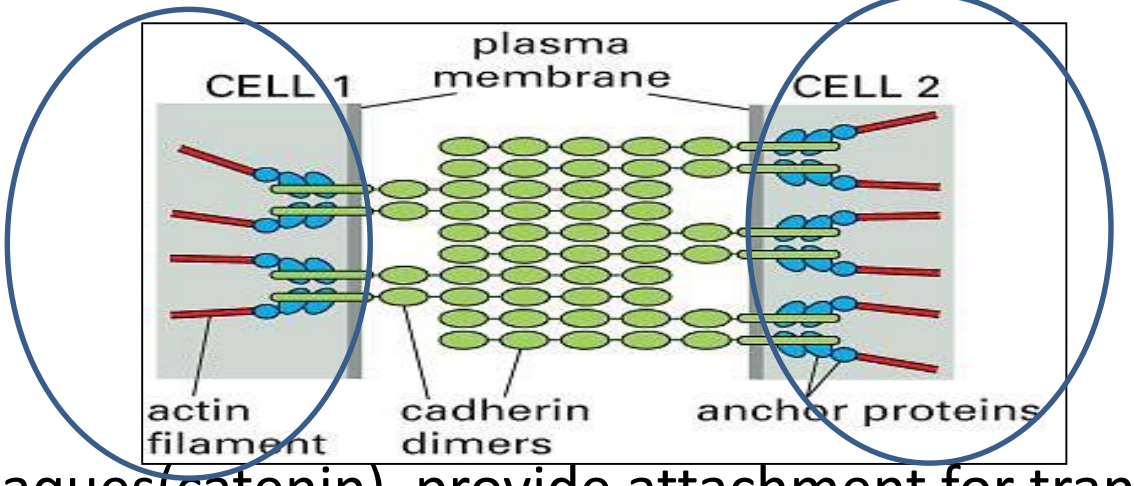
- Integral membrane proteins, connect the cell cytoskeleton to another cell
- Encircle the cell, just **below ZO,** but they don't seal

- 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

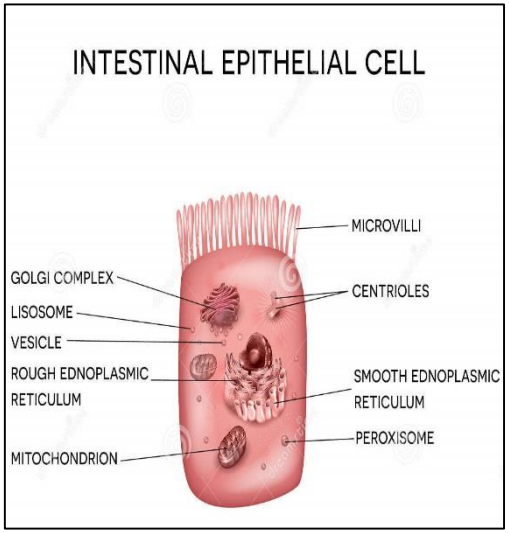
- The cytoplasmic surfaces of adjacent cell membranes at the junction have electron dense plaques (glycoprotein)

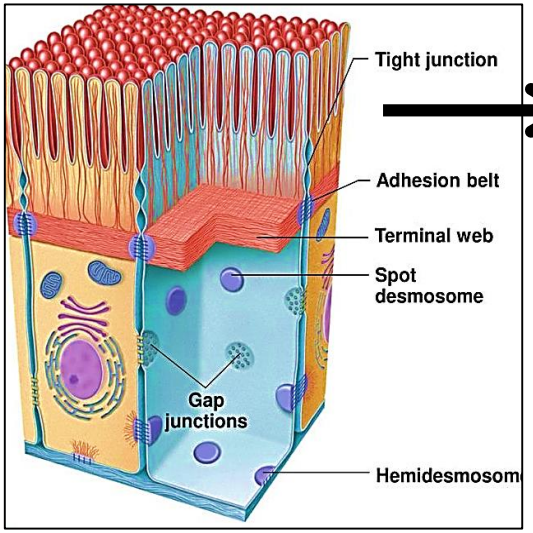
- Proteins forming the Junction are **Cadherins**, **Catenin**

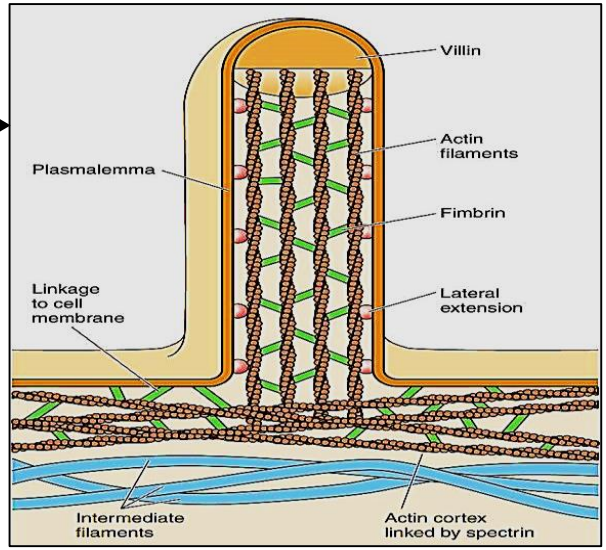



- The plaques(catenin) provide attachment for transmembrane protein (cadherins) and for the fine cytoskeleton filaments

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



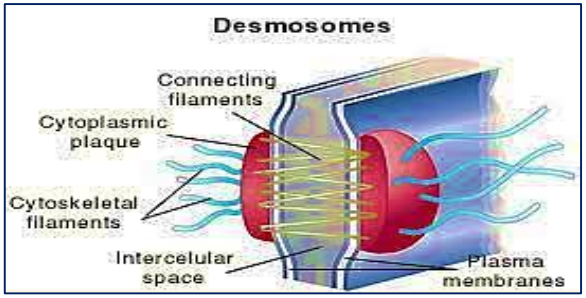



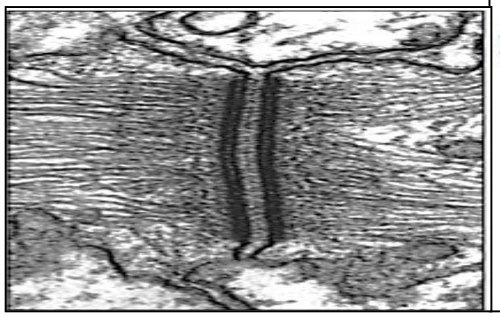



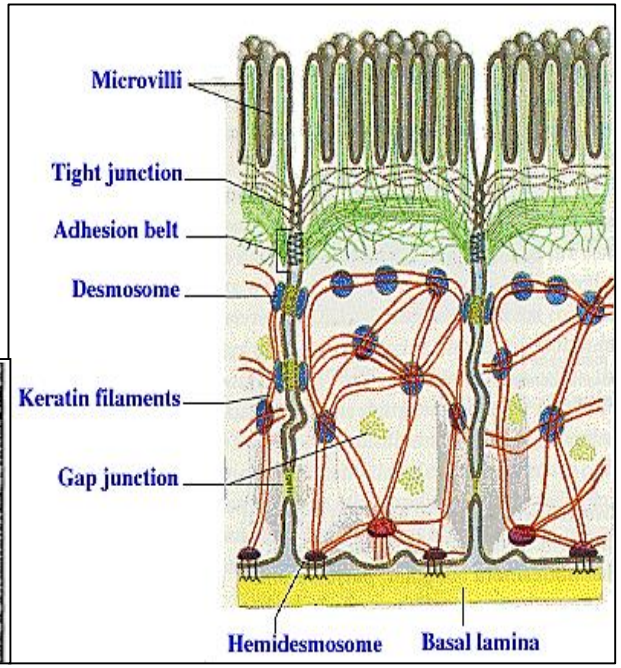
# 2- B- Desmosomes/Macula adherens

- 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

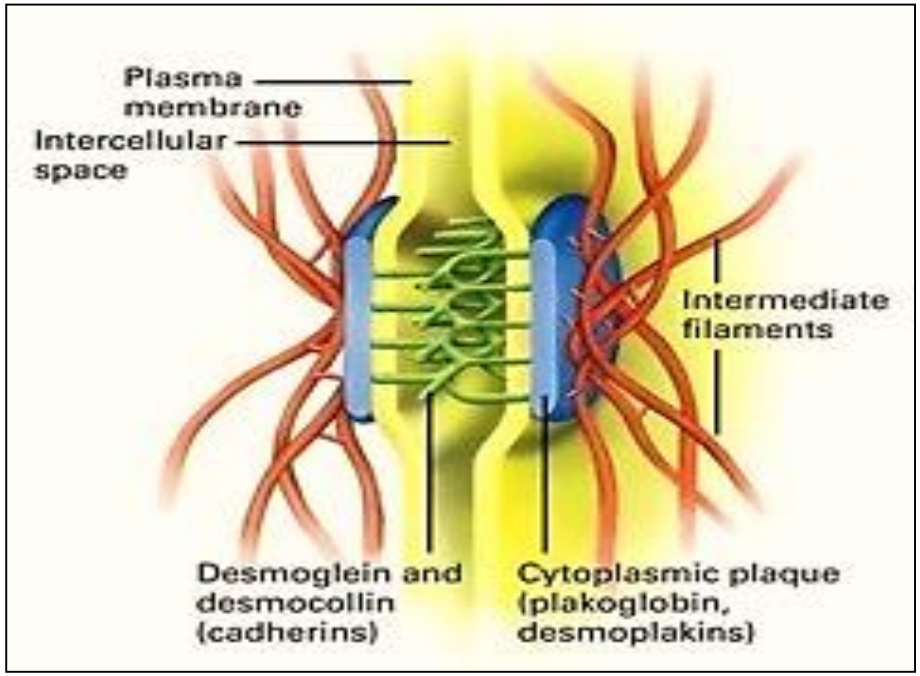




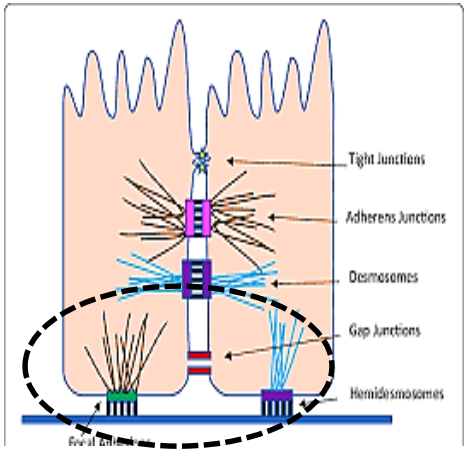

- Proteins forming the junction of the desmosome are **desmoplakin** (plaque) & **desmoglein & desmocoline** ( transmembrane proteins( members of the cadherin family)

- 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 discks),** skin, intestine. They are stronger than adherens junction

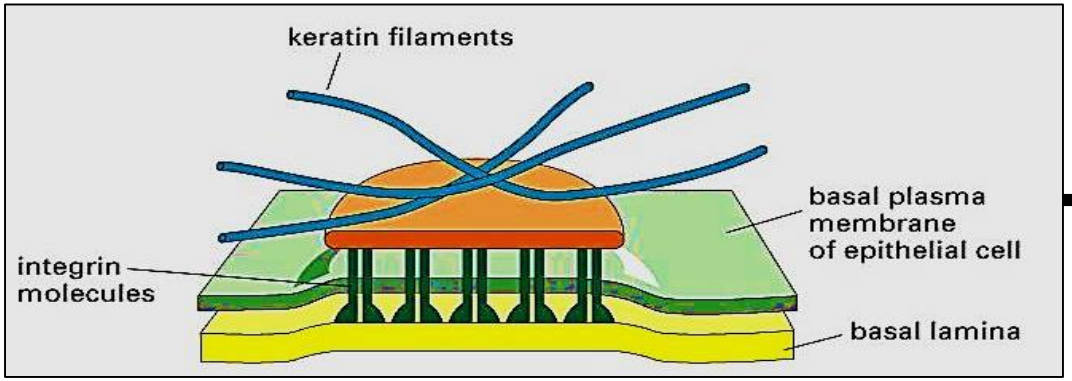


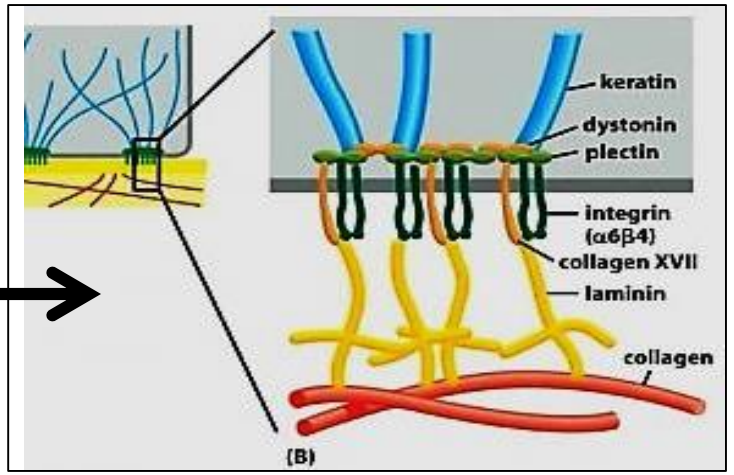

Pemphigus vulgaris
Due defect desmoglin of in
Epidermis of skin

# 2- Hemidesmosomes



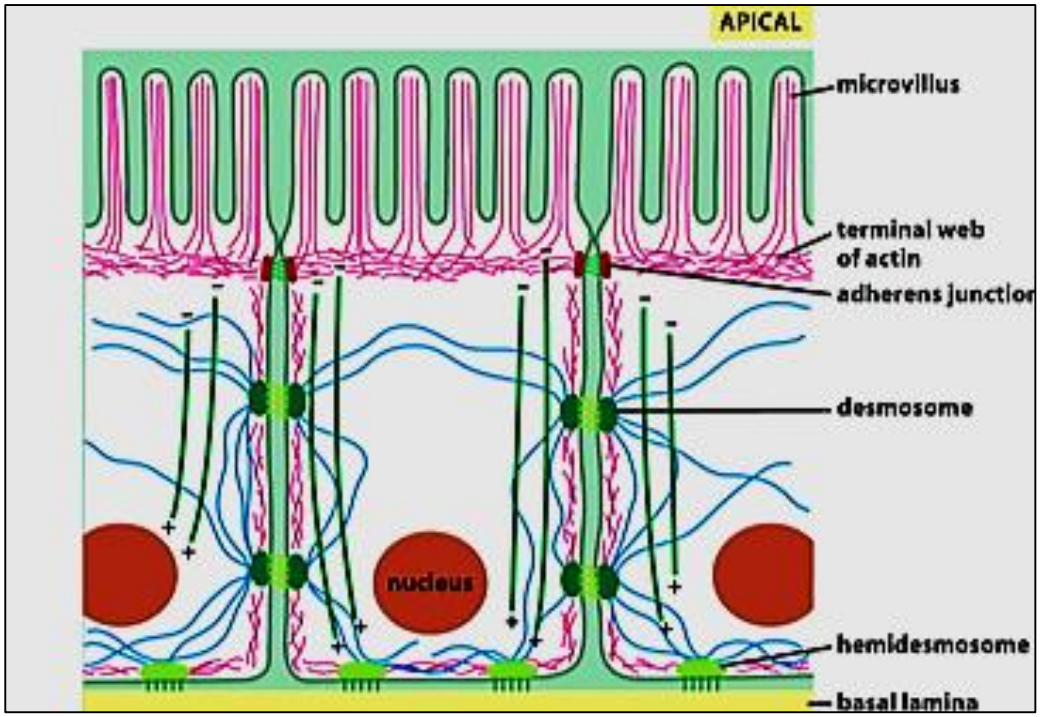

- Half desmosome (cell – basal lamina /ECM)
- At the base of epithelial cells
- Bind  epithelial cells to basal lamina
- The transmembrane protein is **integrins** protein
- Plaques  provide attachment for **keratin filaments**
- integrin molecules connect to **laminin** of basal lamina in turn connect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

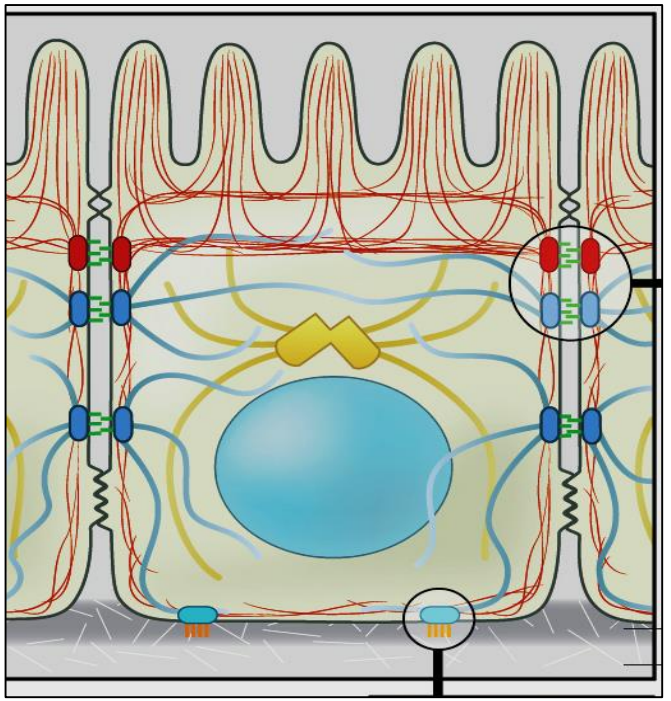


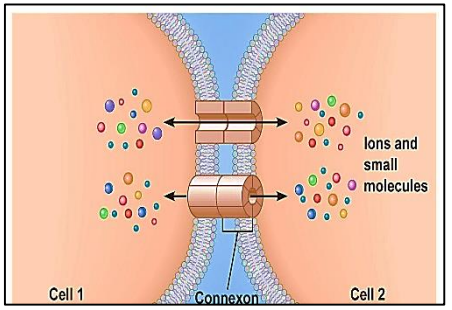
# Function of anchoring junctions

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



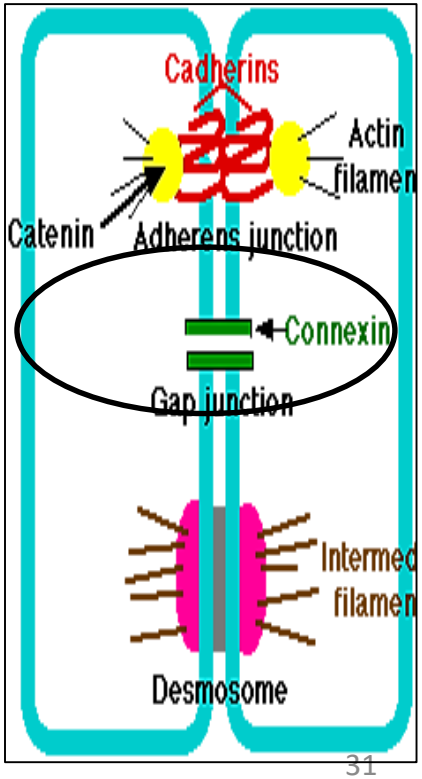
# 3- Gap junction (GJ)

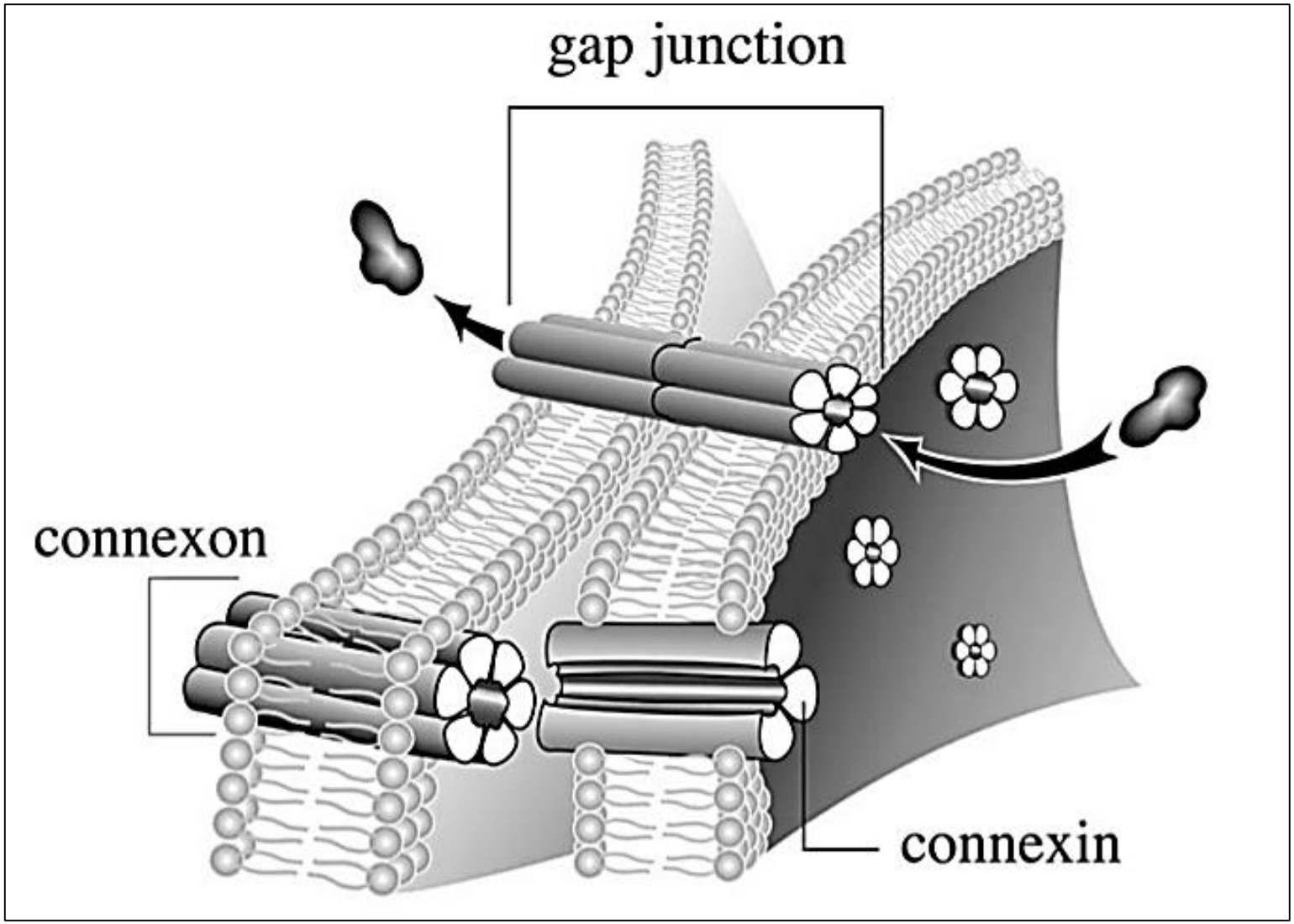



- Transmembrane proteins form intercellular channels that allow direct transfer of ions, small molecules, electric impulses between cytoplasm of adjacent cells

- 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



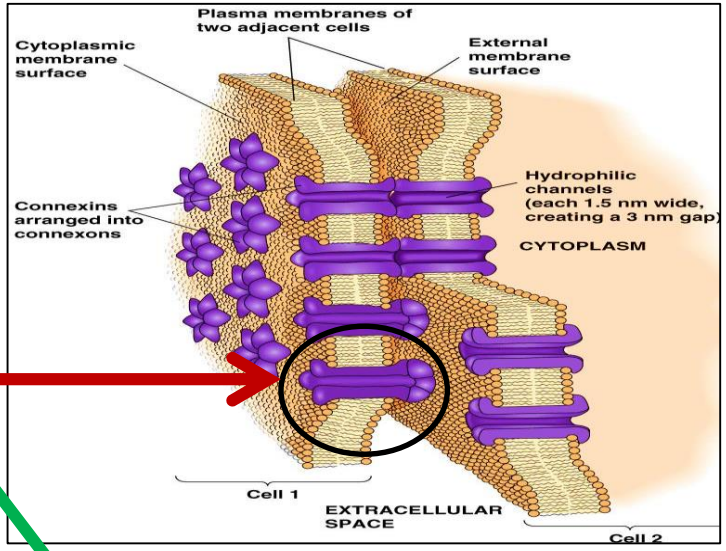

gap junction
connexon
connexin

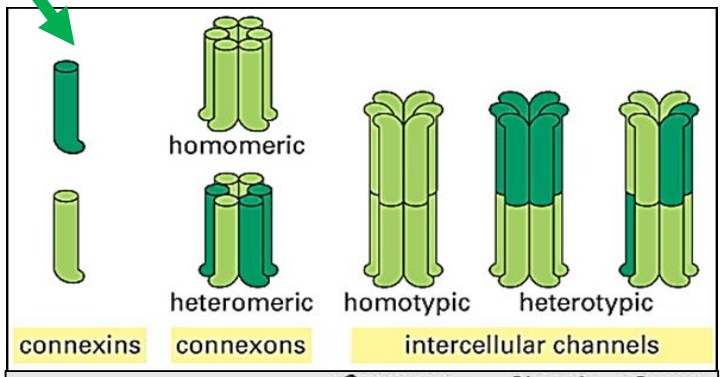
* The protein subunit forming the junction is called Connexin

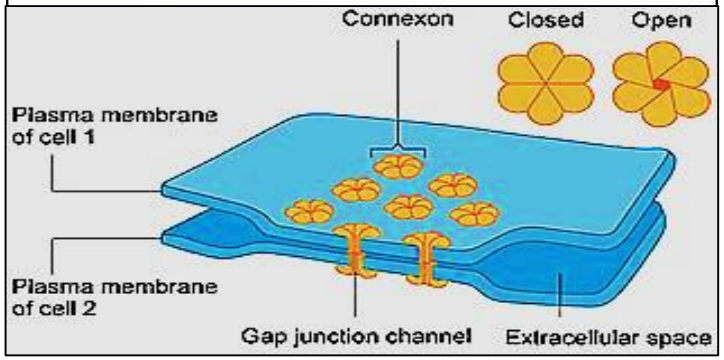
* Each channel called **Connexon** is formed by **6 Connexins** subunits which span the lipid bilayer of the cell membrane (hydrophobic)

* 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



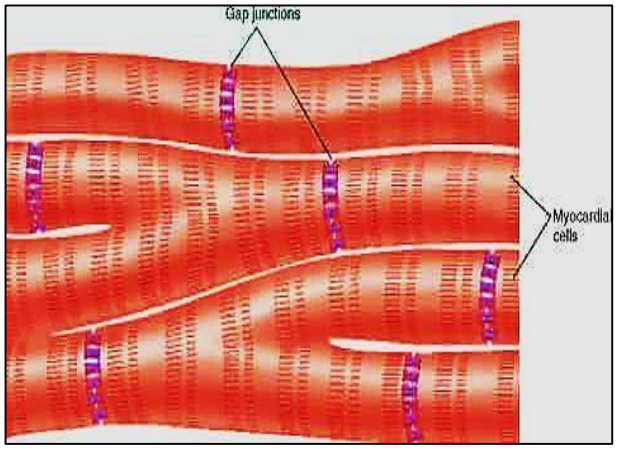
# Electrical & Chemical synapses

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

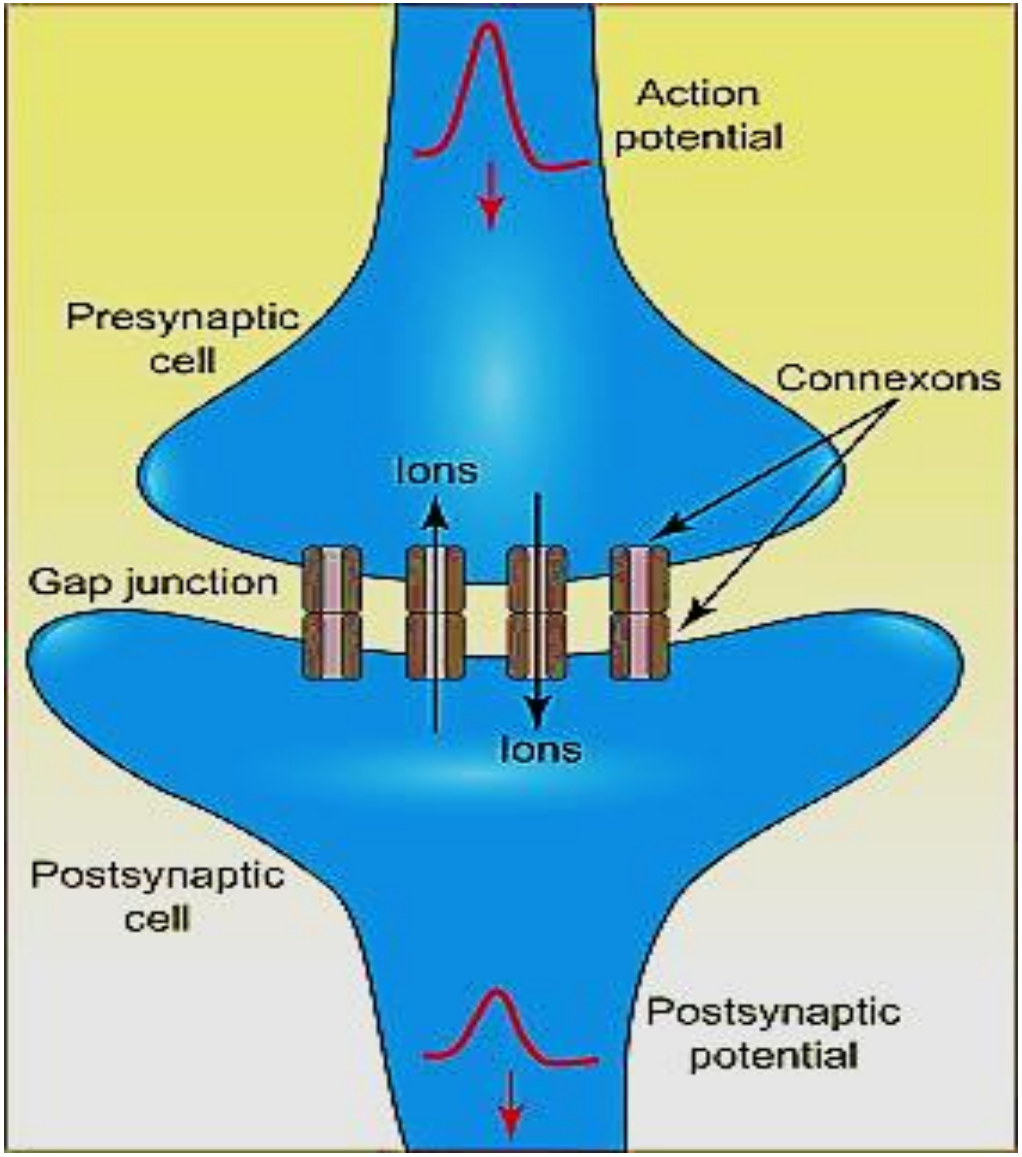
A. Electrical synapse

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) , and 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



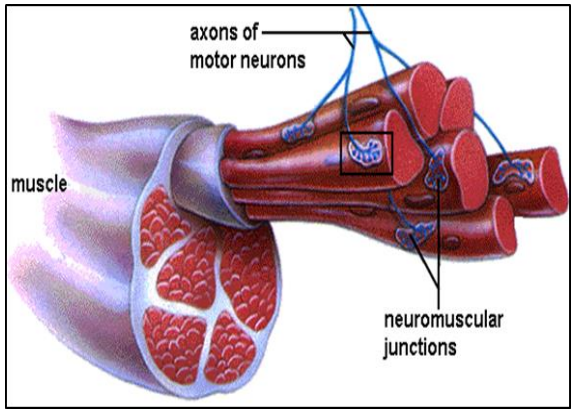
**Cardiac muscles**

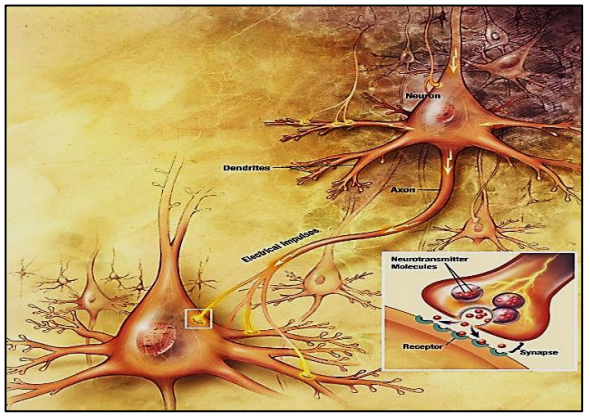


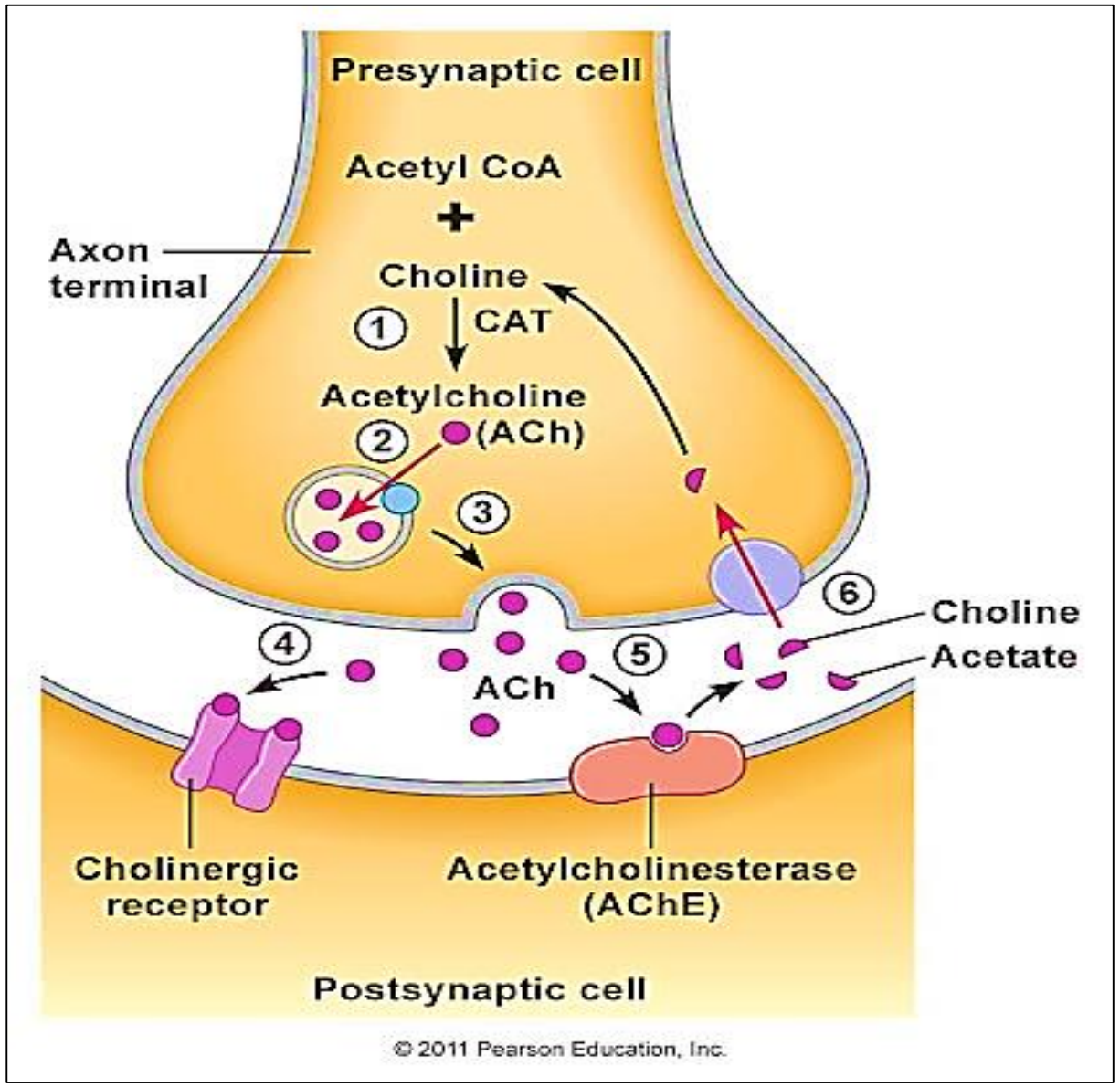

**Electric synapse**

# 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**






**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