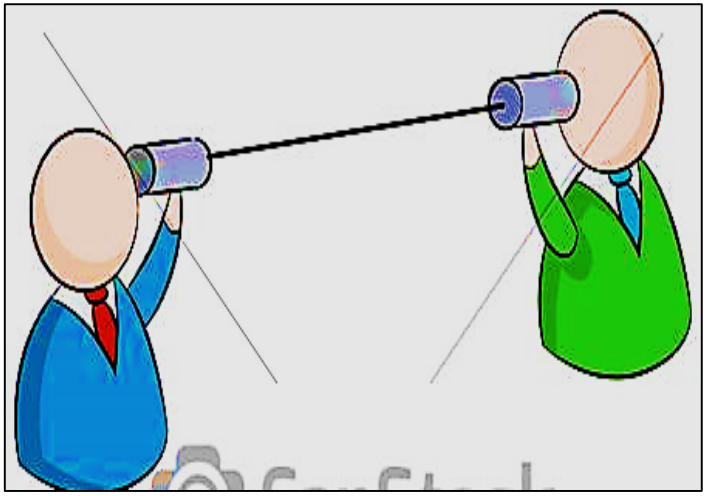
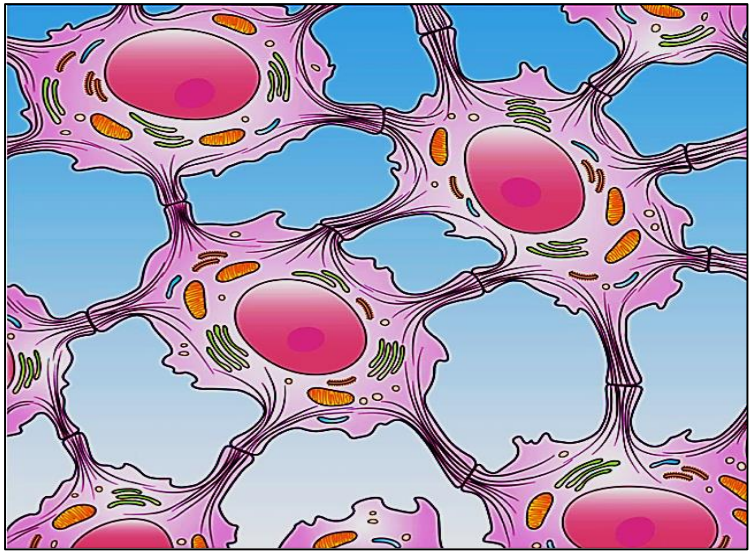
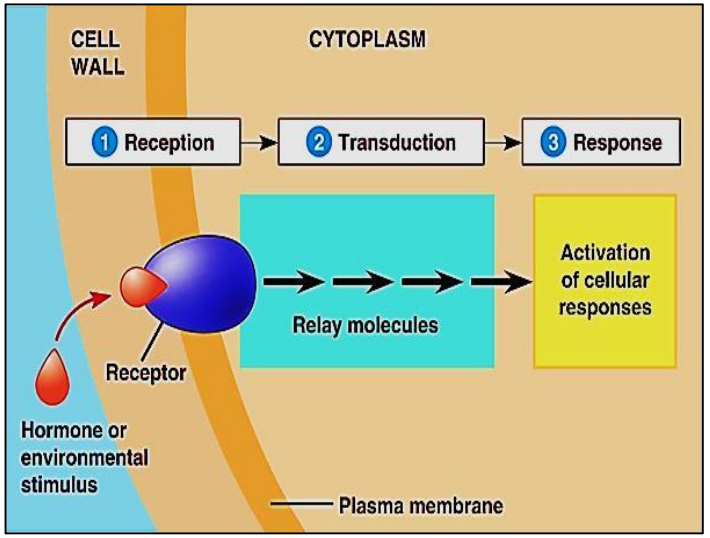
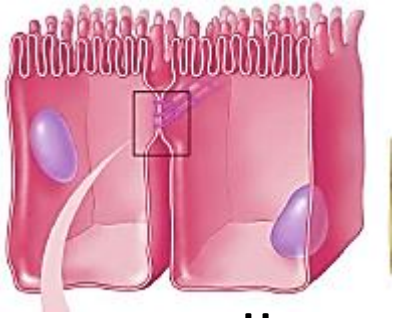
Cell Junctions & Cell Communication







Cell Junctions

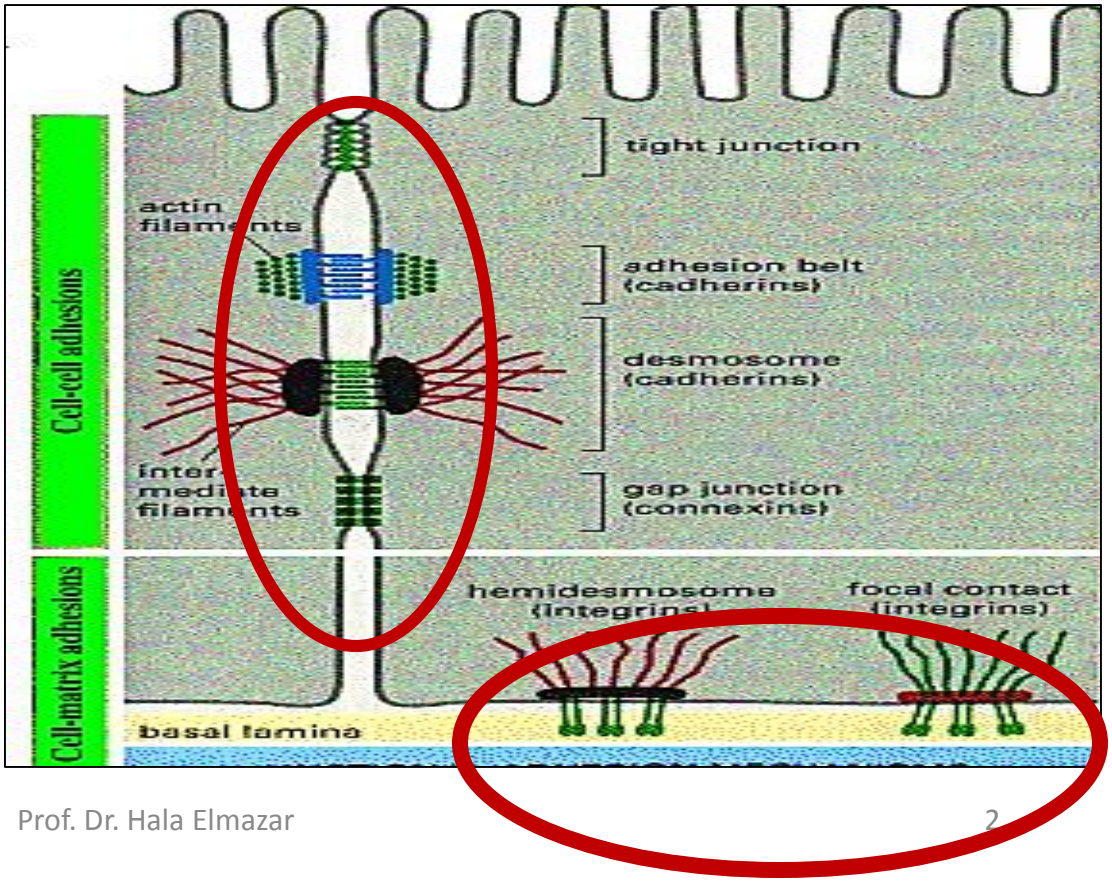


Definition & classification:

- Cell junction is the connection between adjacent cells or between the cell and extracellular matrix

1- cell- cell adhesion

2- cell- matrix adhesion



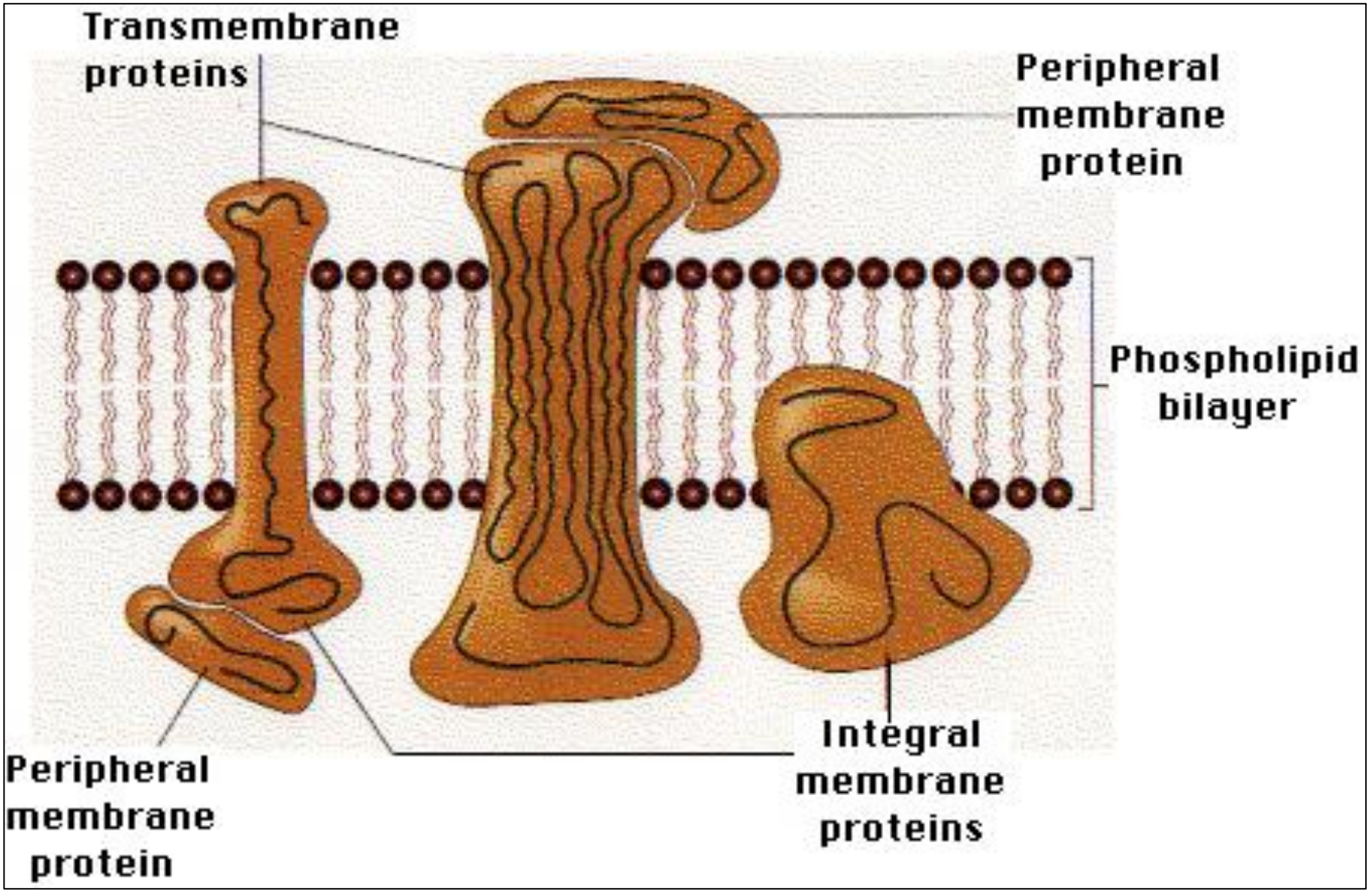
Cell membrane proteins

- 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. Can be dissociate from membrane following treatment with a polar reagent, such as a solution with an elevated pH or high salt concentrations.

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

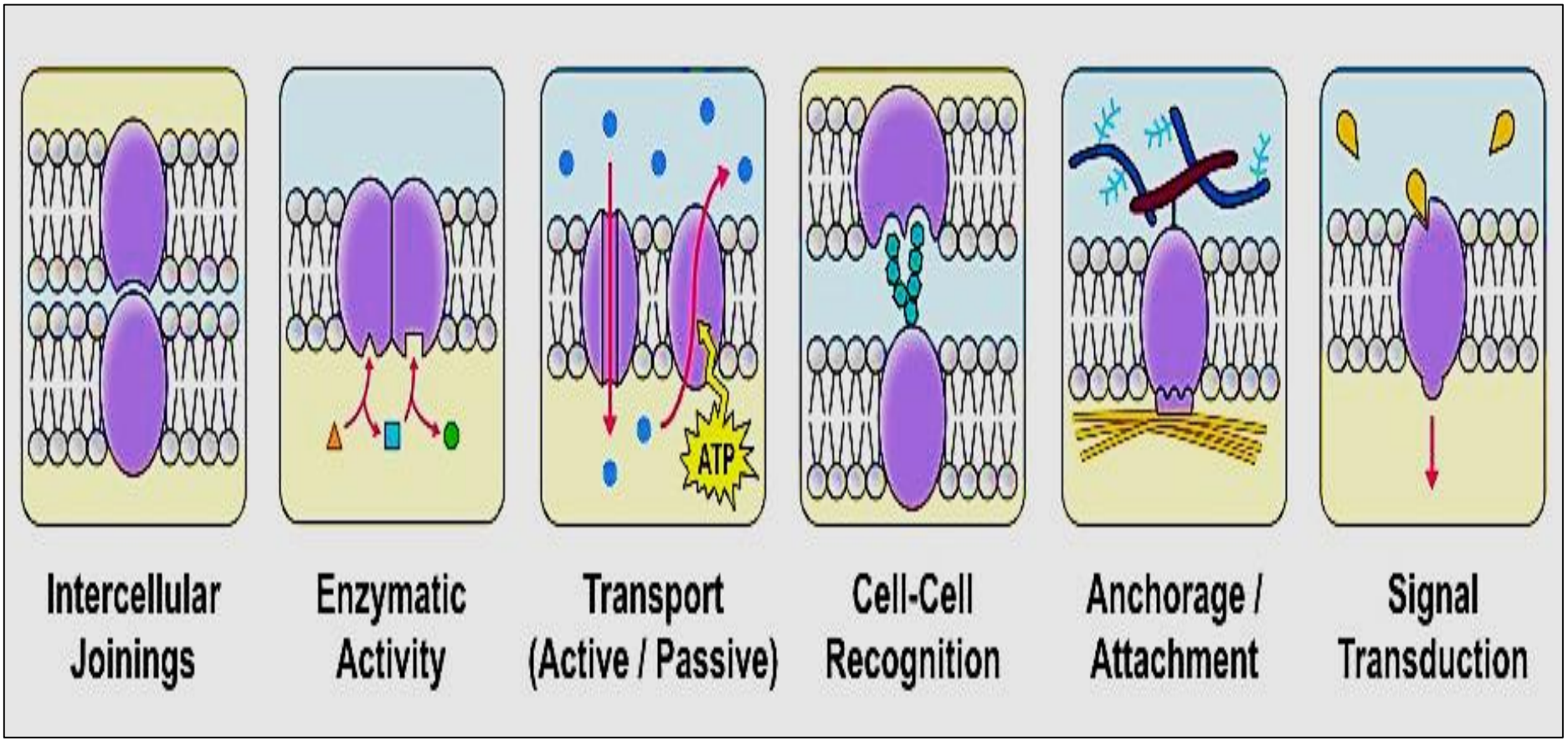
➢ *Transmembrane* proteins that span across the cell membrane
➢ *Monotopic* : proteins attached to only one side of the membrane and do not span the whole way across.



Types of cell membrane proteins

Function of integral membrane proteins

- **Junctions** – Serve to connect and join two cells together
- **Enzymes** – Fixing to membranes localizes 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

- **Cell adhesion molecules (CAMs)**

A group of cell proteins located on the cell surface & involved in binding of the cell with other cells or with the extracellular matrix in a process called cell adhesion

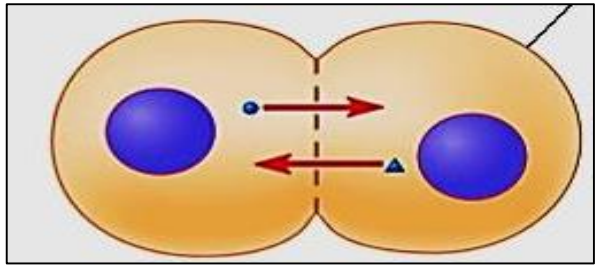
(CAMs play a complex role in immunity & in cancer)

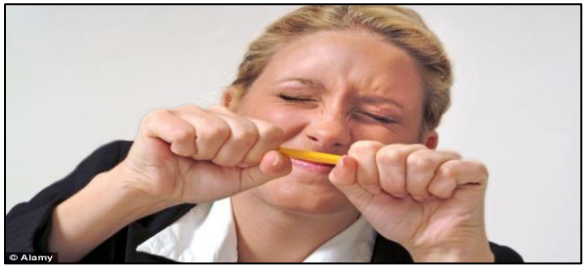
- **Cell-cell junctions (Adhesions)**

Represent the mechanism behind how cells interact with each other, this is achieved by molecules present at the surface of both cells. It is crucial of multicellular structural maintenance

Function of cell- cell junctions (adhesions)

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





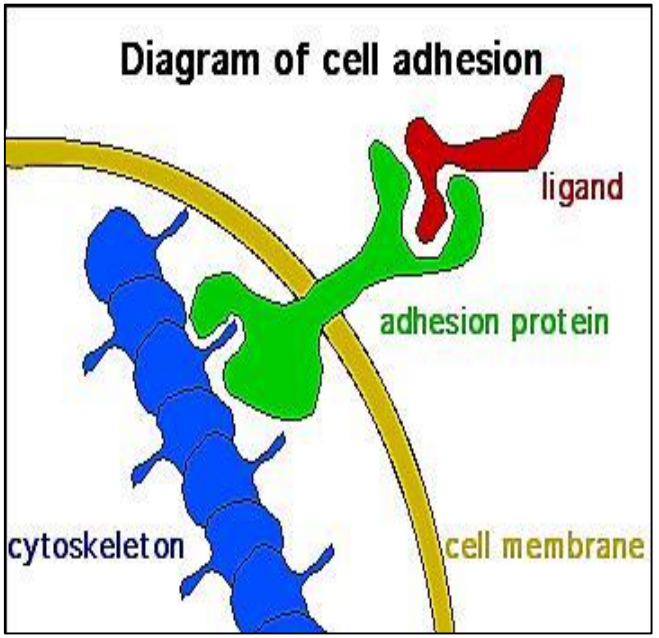
Cell adhesion (junction) is due to the action of :

1- Cell Adhesion Molecules (CAMs)

2- Intercellular junctions (Adhesions)

Cell Adhesion Molecules (CAMs)

- 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
- composed of **3 domains**:

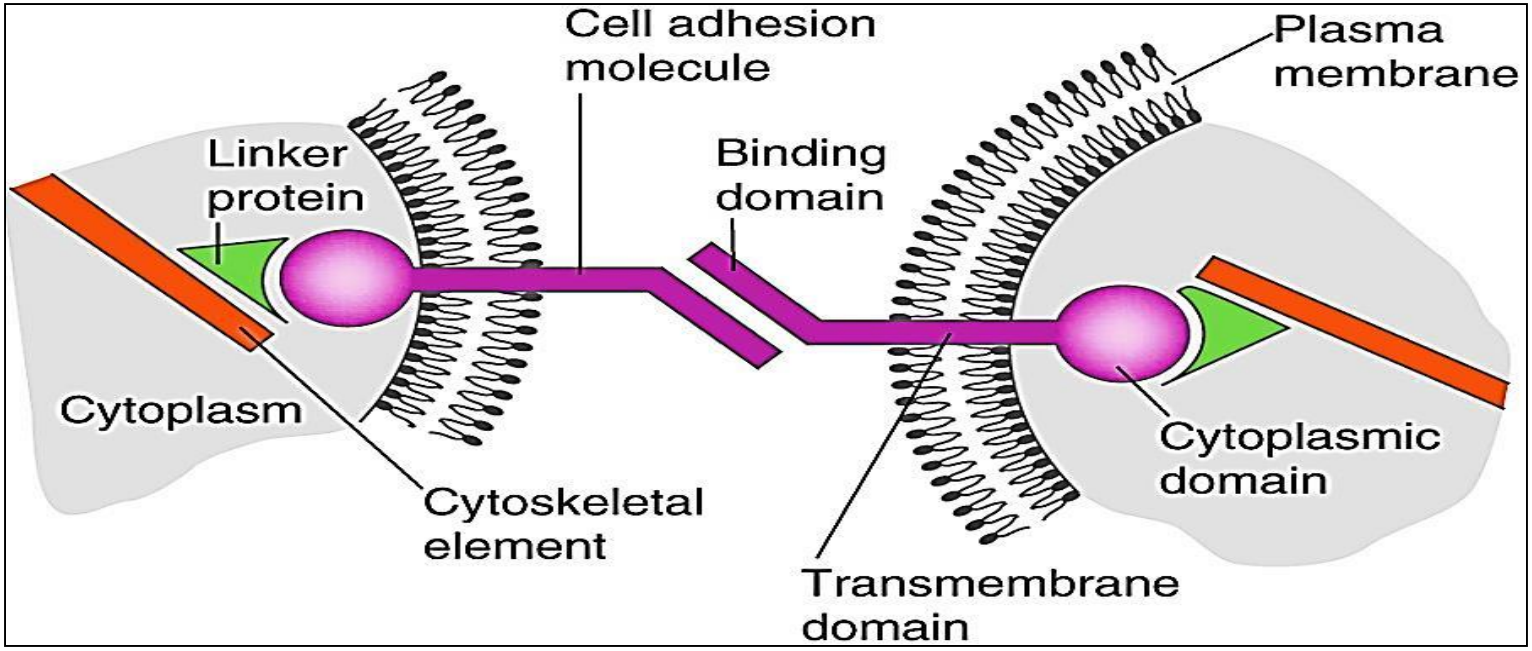
✓ Intracellular domain that interacts with the cytoskeleton

✓ Transmembrane domain : span across the membrane

✓ Extracellular domain that interacts either with other CAMs of the same kind (***homophilic binding***) or e different CAMs or the extracellular matrix (***heterophilic binding***).

CAMs express 3 major domains:

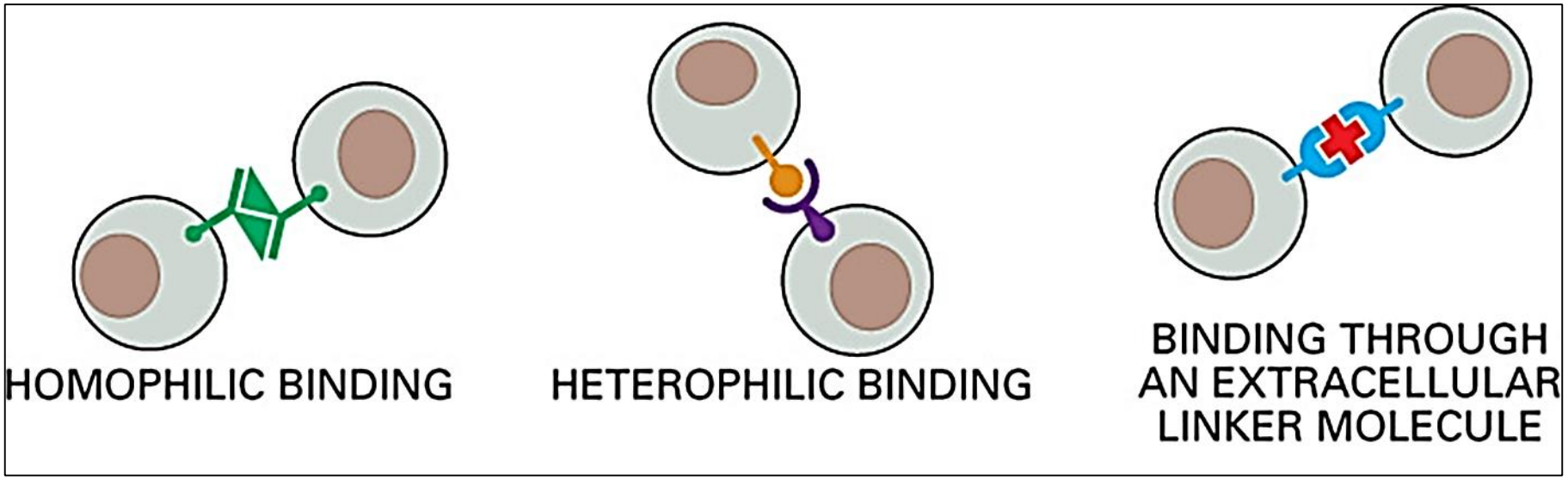
- The extracellular domain: allows one CAM to bind with another CAM on an adjacent cell.
- The transmembrane domain: links the CAM to the plasma membrane through **hydrophobic forces**.
- The cytoplasmic domain: is directly connected to the cytoskeleton by linker proteins.



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

cadherin	selectins
Immunoglobulin superfamily	Integrins

Interactions between CAMs can be mediated by :

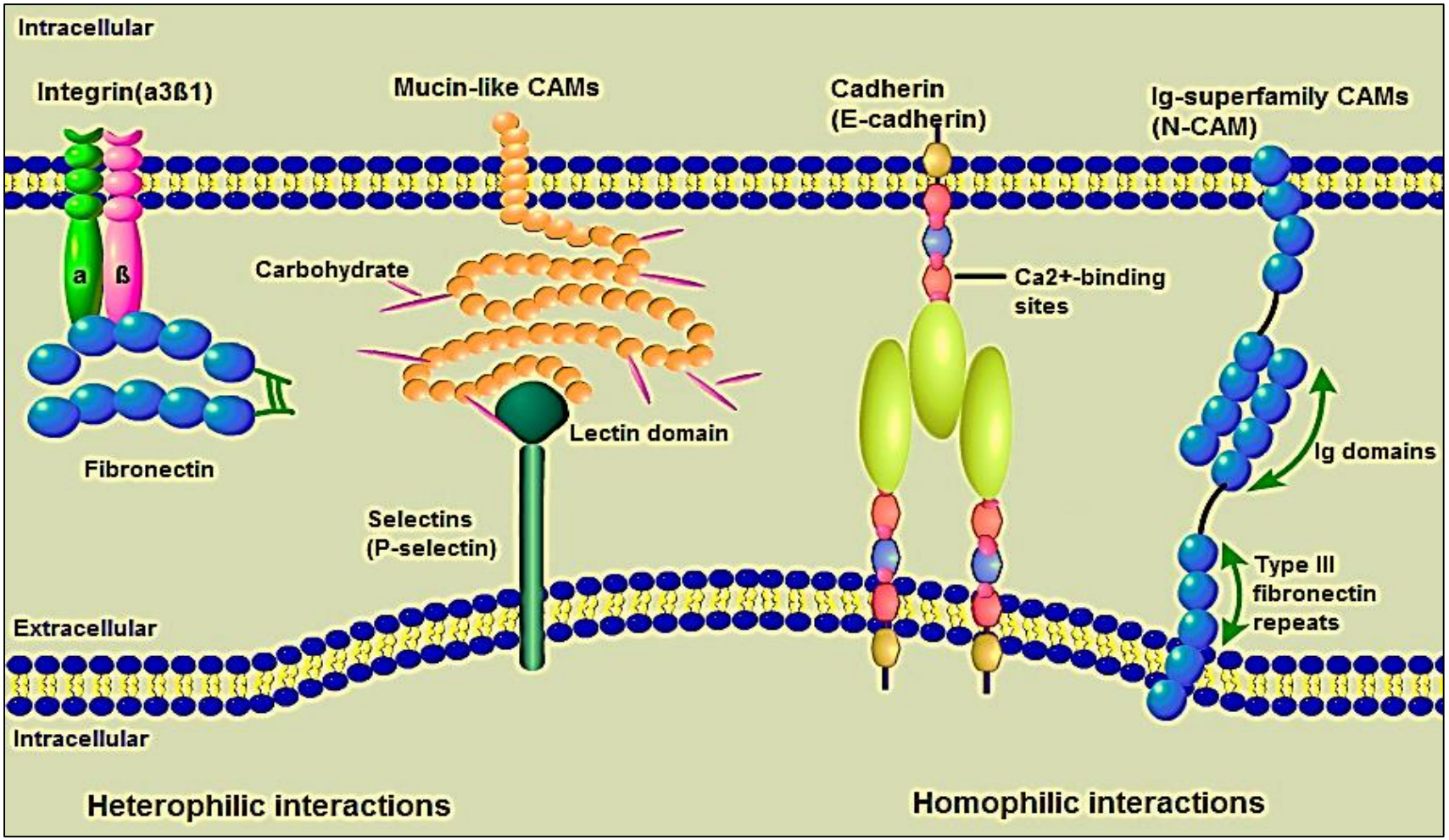


Binding of CAM on one cell to the same CAM on a second cell
Cadherin - cadherin

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

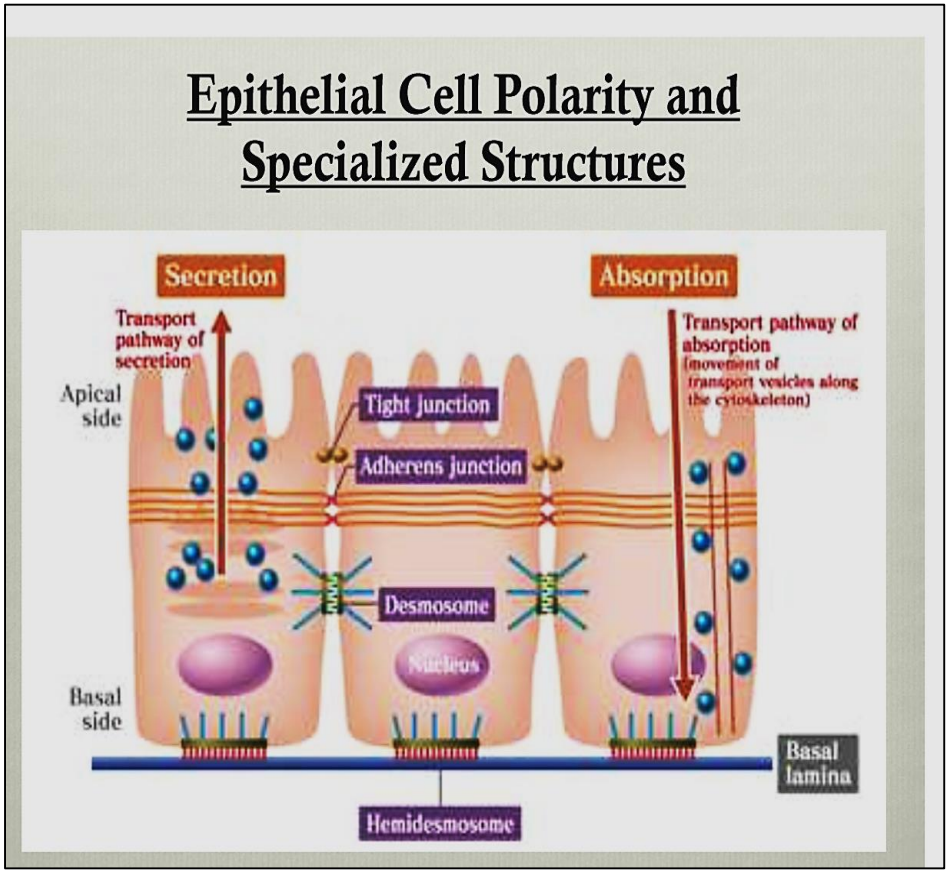
CAM binds to EC matrix is also a heterophilic binding

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



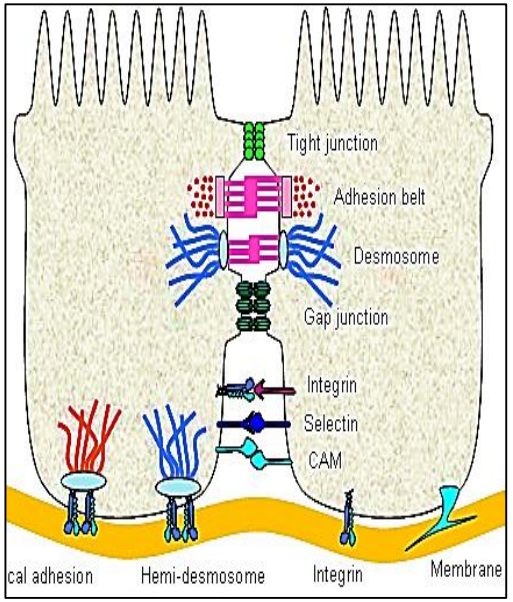
CAMs Families: Integrins typically binds to the extracellular matrix, while selectins, cadherins , and IgSF members are associated with cell- cell adhesion

- Epithelial Cells are polar in nature
- Epithelial Cells rest on basal lamina
- Adjacent cells attach with CAMs & intercellular junctions
- CAMs have greater role in CNS development at embryonic life
- CAMs Protect & 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 :

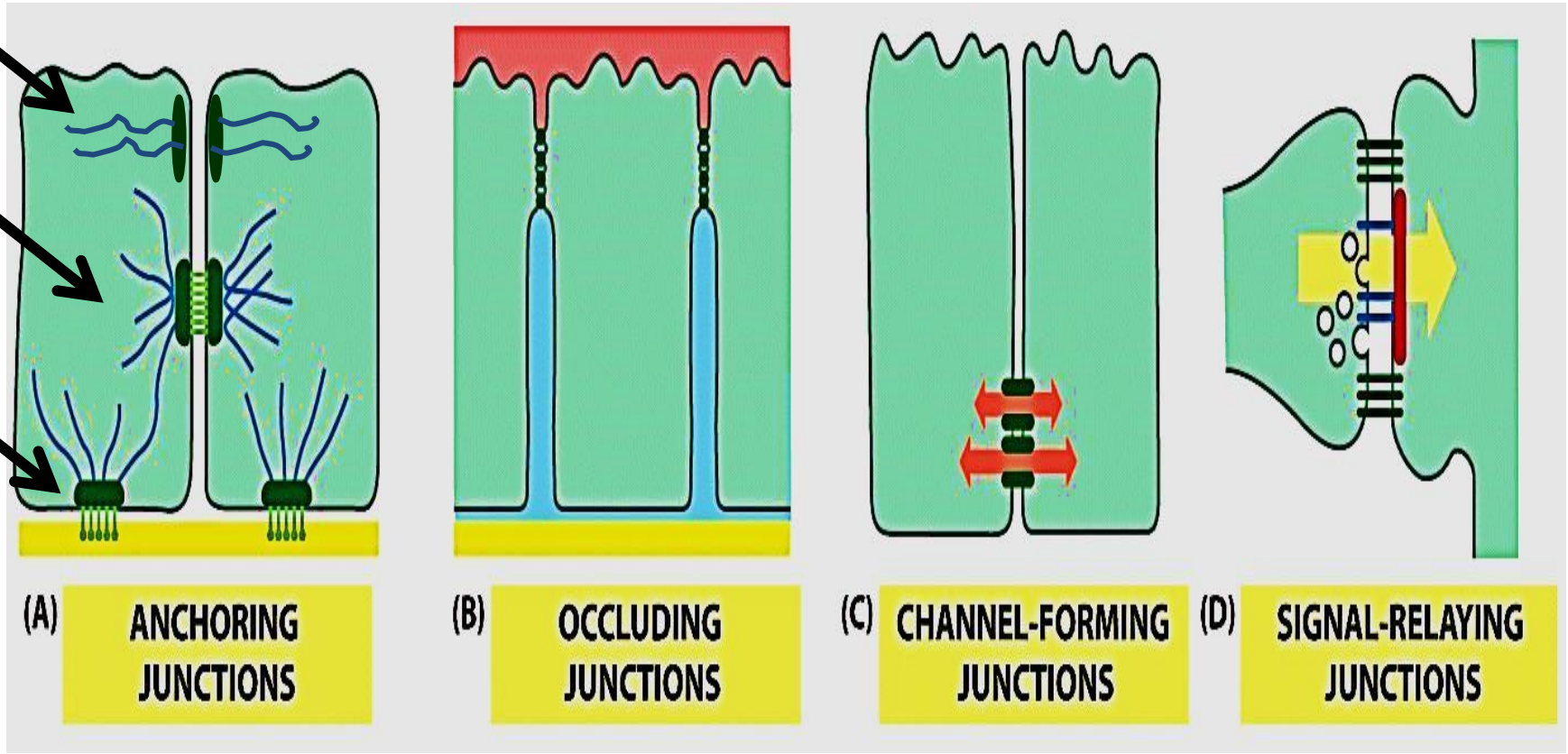


1- Occluding/Tight junctions: Seal cells Together like sheet to prevent flow of molecules even water or ions between cells

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

Types of cell junctions in multicellular organism



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

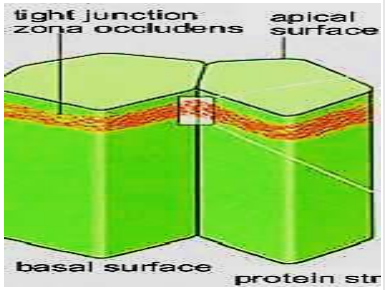
Tight junctions (zonula occludens)

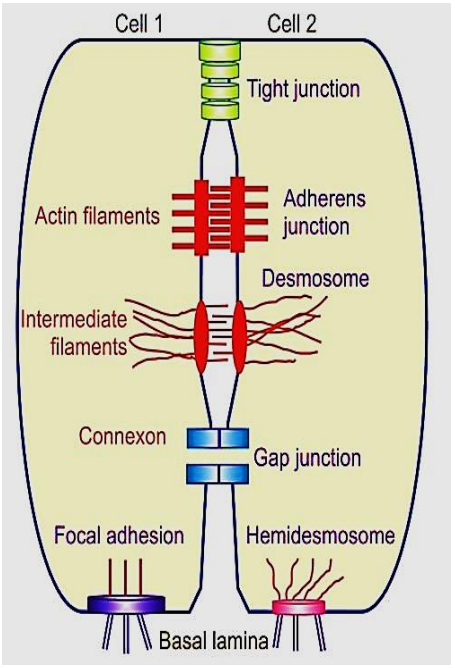
Gap junctions

Synapse

1- Occluding junctions

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



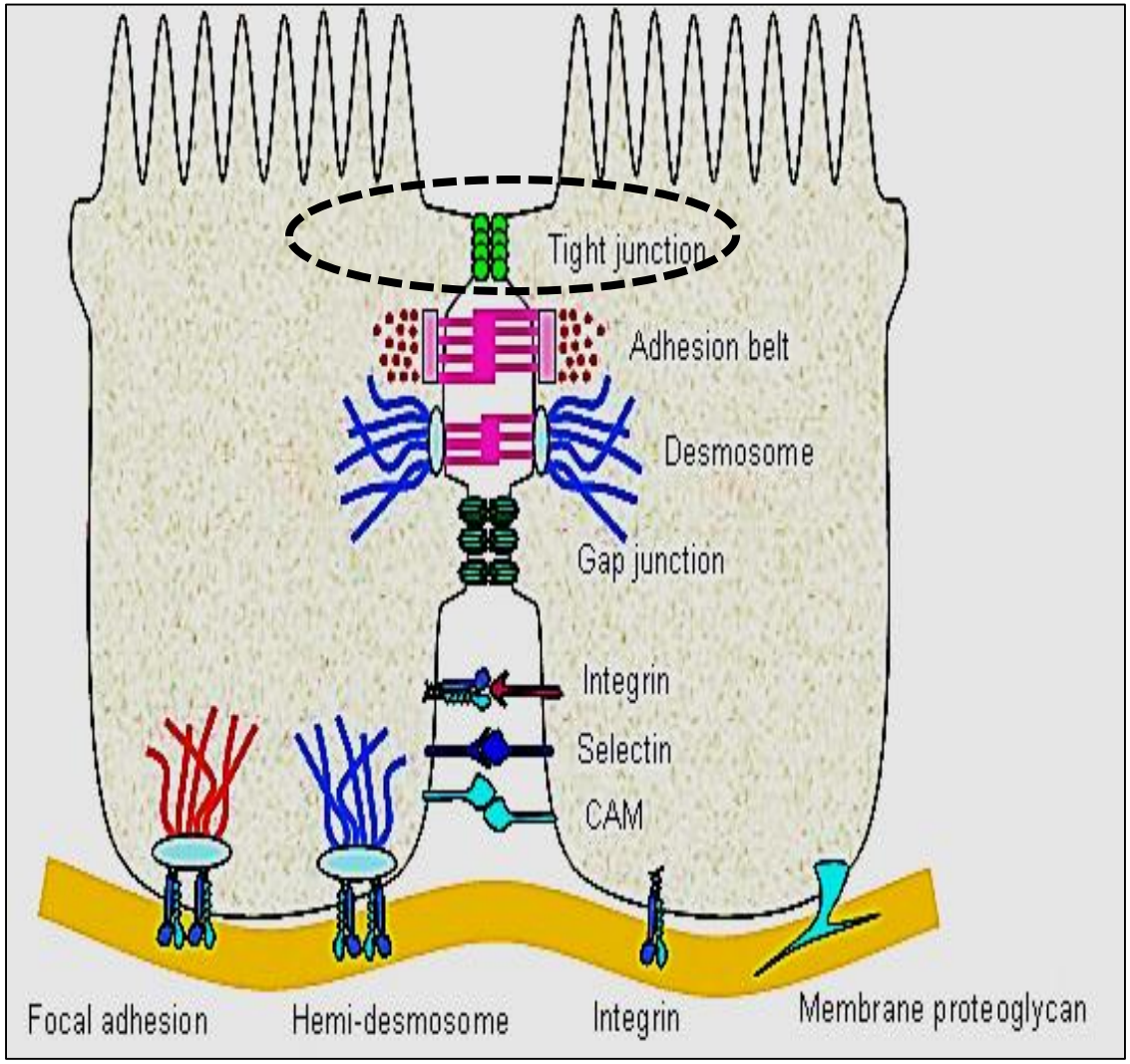


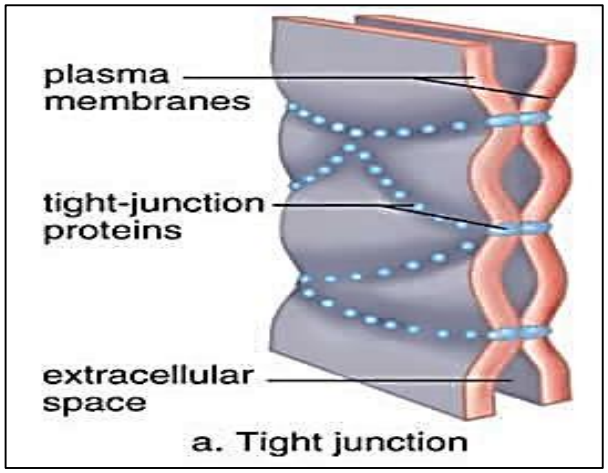
- Seal adjacent epithelial cells & is the most apical type of junctions

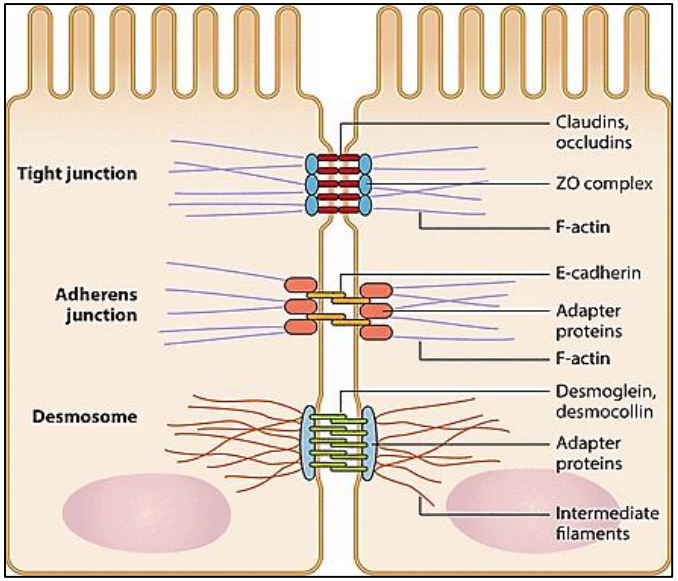
- Belt-like structure encircle each cell completely just below the free surface
  Water & ion molecules cant pass through that junction (passaging either through active transport or facilitated diffusion

- The membranes of adjacent cells **fuse** at the tight junction completely forming **impermeable barrier**

- Proteins forming this junction are **occludins** and **claudins** & **members of IG superfamily**


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

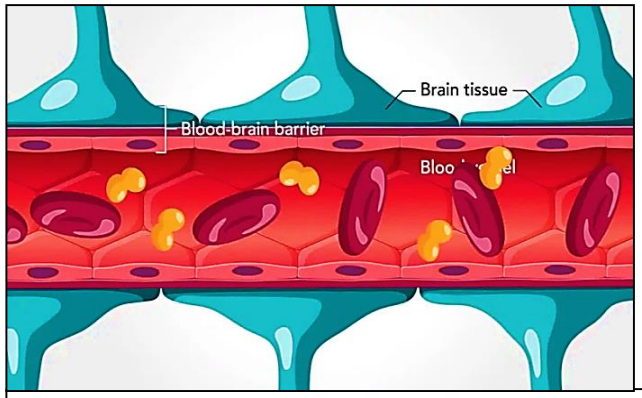

plasma membranes
tight-junction proteins
extracellular space
a. Tight junction


Tight junction
Claudins, occludins
ZO complex
F-actin
Adherens junction
E-cadherin
Adapter proteins
F-actin
Desmosome
Desmoglein, desmocollin
Adapter proteins
Intermediate filaments

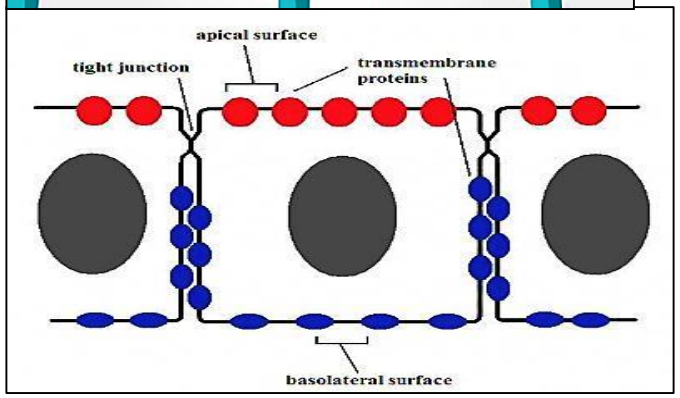
Functions of Tight Junction

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

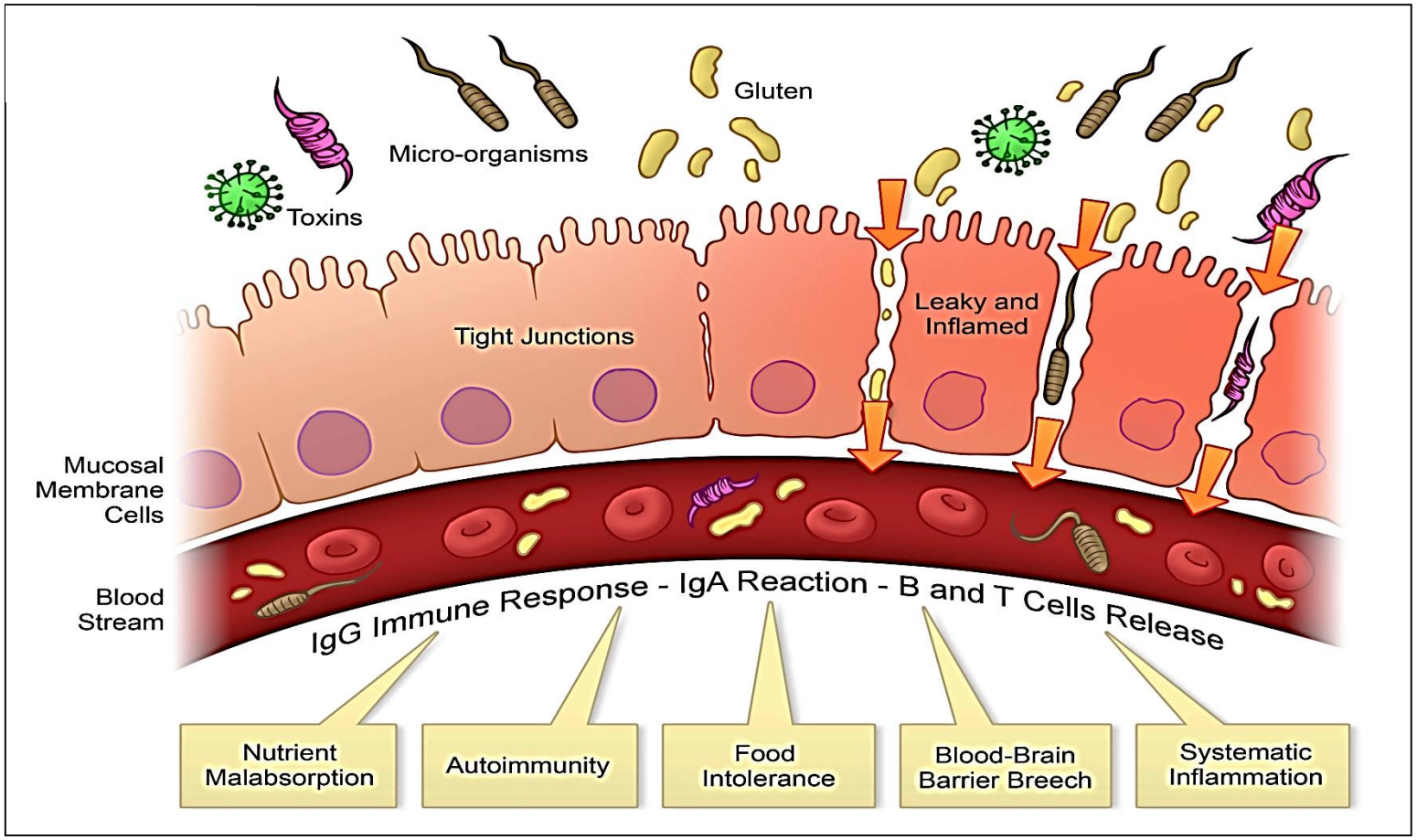
- **Blood-brain barrier & other barriers in the body**



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

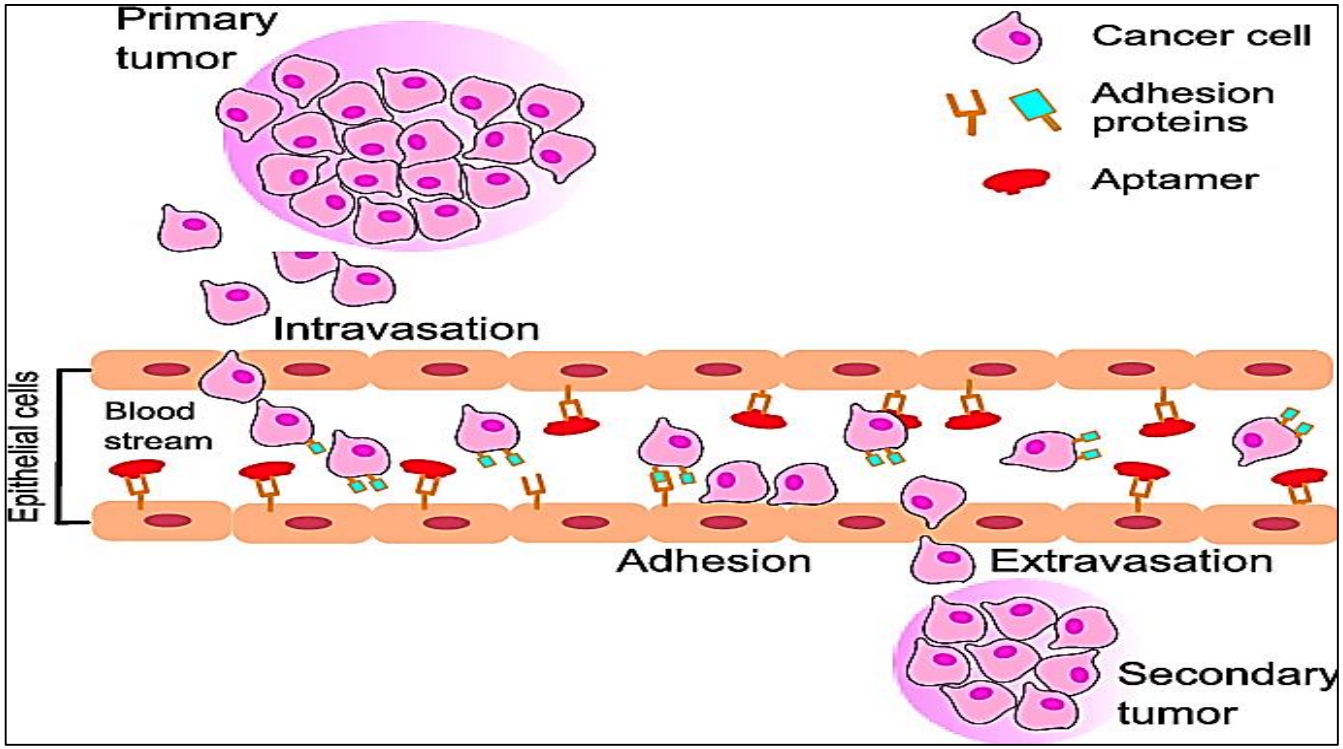


- **Ensure unidirectional transport, the apical set of transport proteins must not be allowed to migrate to the basolateral surface & vice versa**



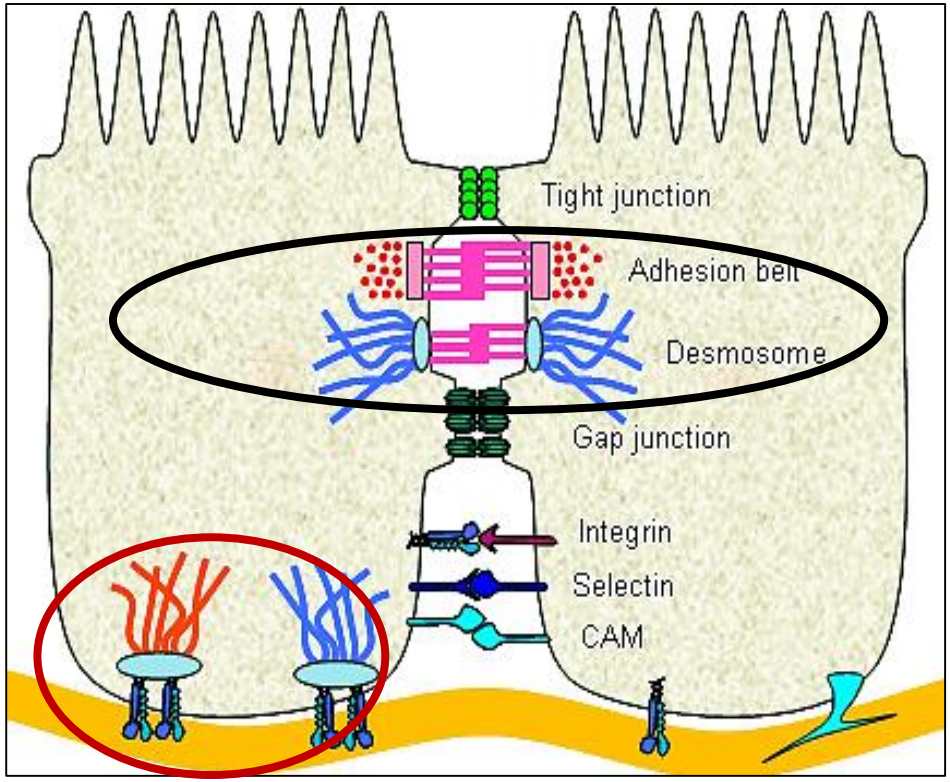
Leaky gut syndrome : **is a disease happen when tight junctions between intestinal epithelial cells become defective → abnormal increases in the intestinal permeability → releasing of a large number of molecules & microbes from the lumen into the bloodstream**

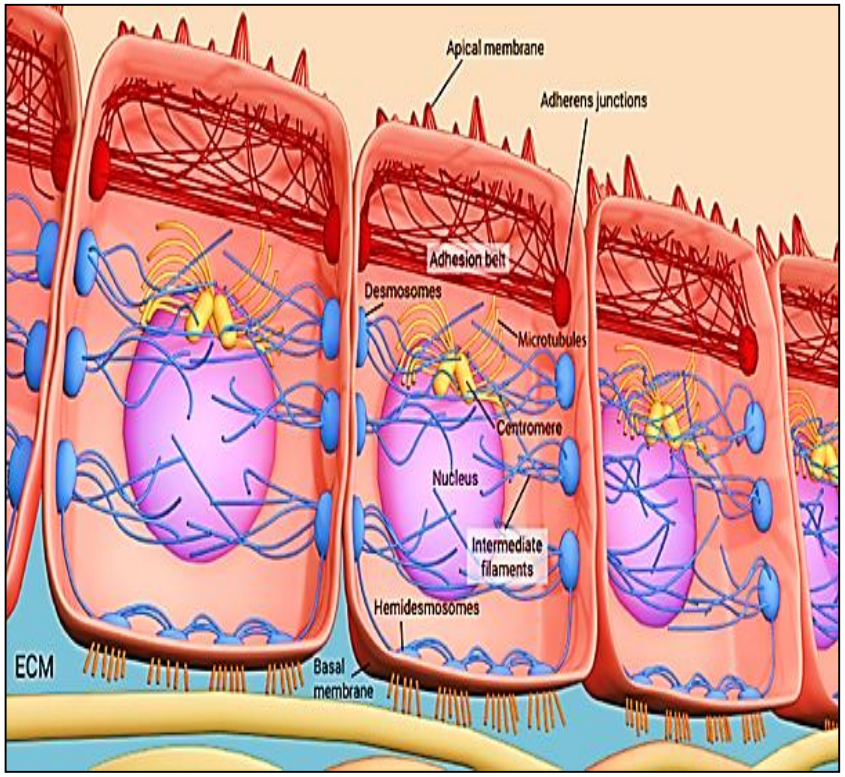
- Most cancers originate from epithelial cells.
- Down regulation of Tight junctions adhesion proteins lead to tumor dissociation and subsequent metastasis.
- Researchers observed low expression of TJ among highly metastatic cancer cells



2- Anchoring junctions

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

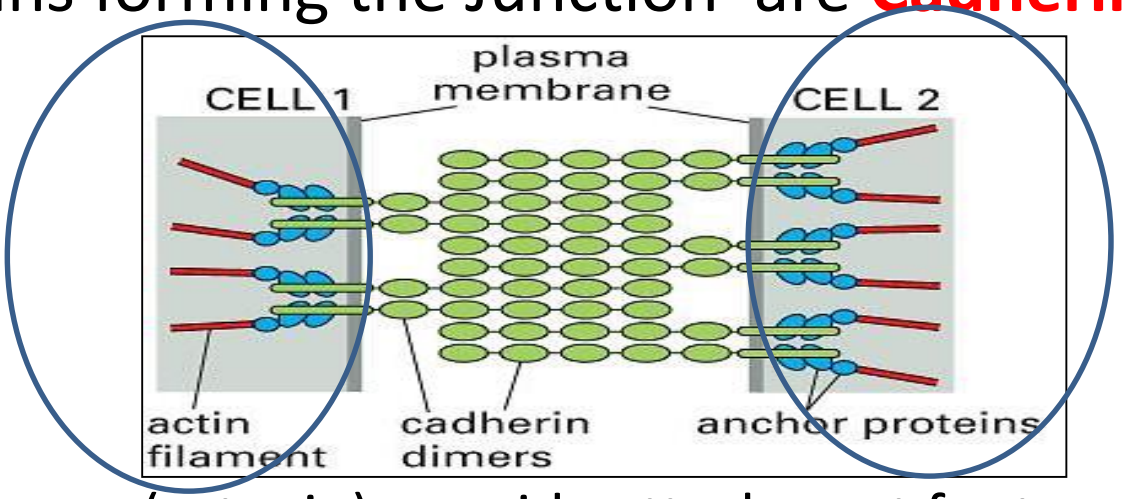




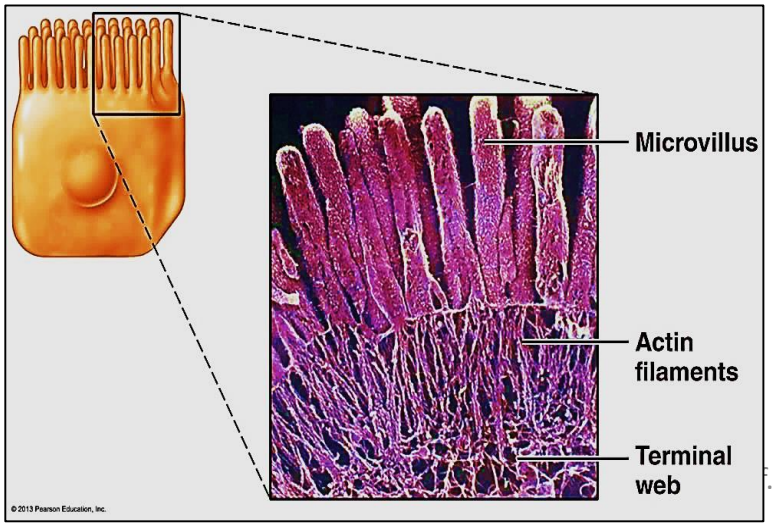
2- A- Adherens junction/Zonula adherens

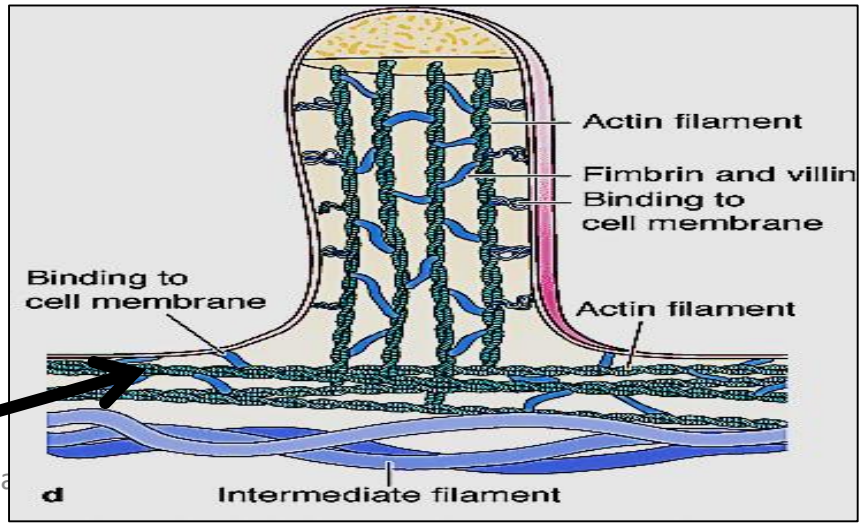
- Integral membrane proteins, connect the cells cytoskeleton to another cell or ECM
- Encircle the cell, just **below ZO,** but don't seal
- Found in tissues subject to **Stretch t**o resist separation during contraction (bladder, uterus, skin).
- The opposing plasma membranes has a narrow space in-between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

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



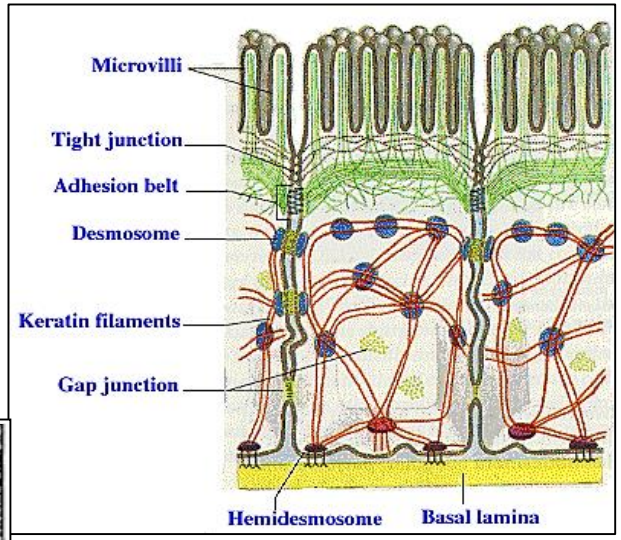
- The plaques(catenin) provide attachment for transmembrane protein (cadherins) and for the fine cytoskeleton filaments (**actin filaments).** This junction makes the **Terminal Web** at the apical part of epithelial cells having microvilli



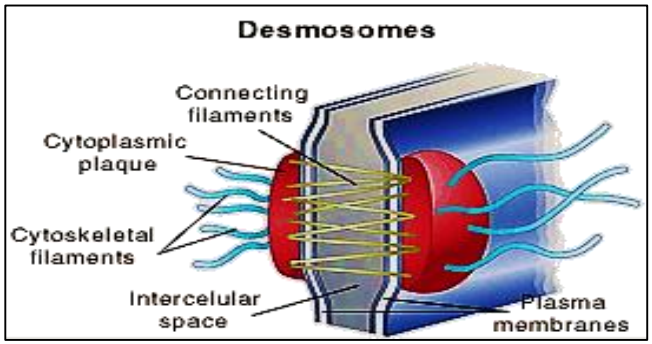


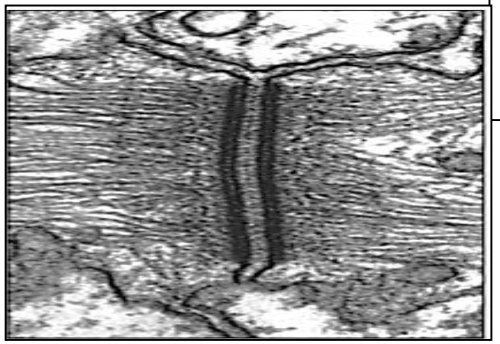
2- B- Desmosomes/Macula adherens

- Scattered disc- shaped structures, **do not form belt (spot-like)** randomly arranged on lateral sides of cells



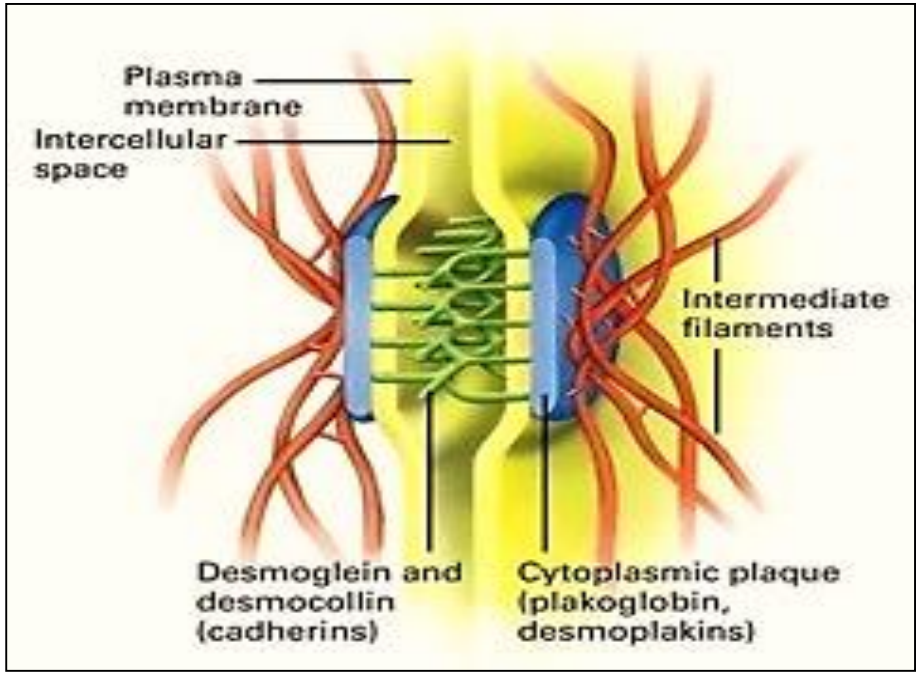
- Disc plaque at the surface of one cell connects with an identical one at the surface of the adjacent cell

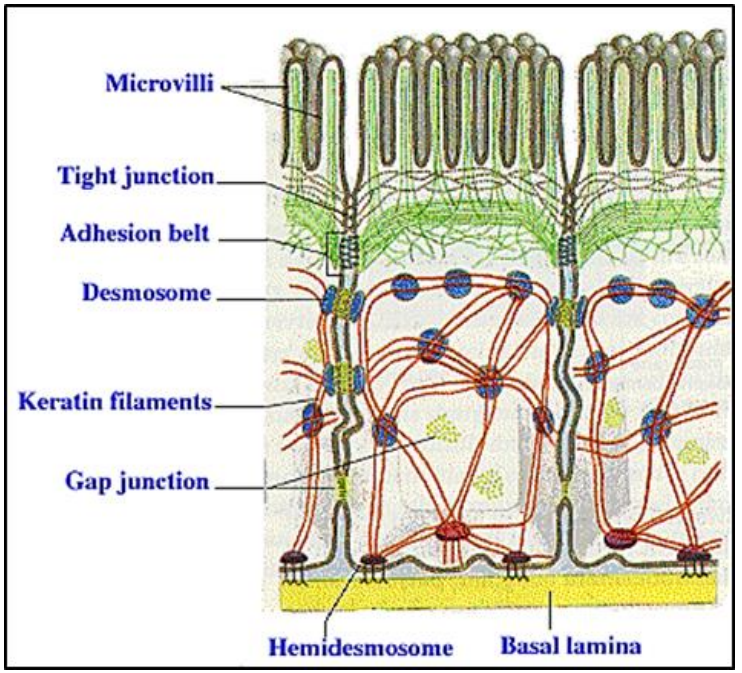




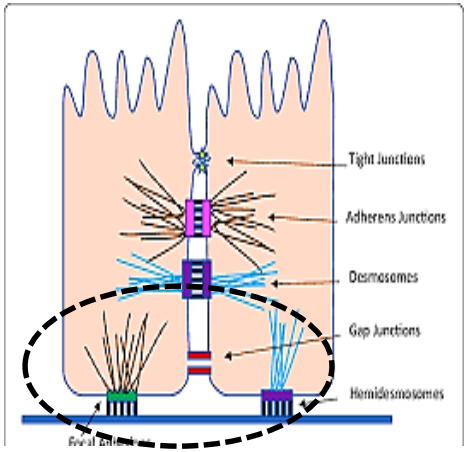
- Proteins forming the junction of the desmosome are desmoplakin (plaque) & desmoglein(transmembrane proteins, members of the cadherin family)

- Within the cell, the plaque of the desmosome provide insertion to intermediate cytoskeleton filaments **(keratin)**
- Found in tissues of constant state of stretching and stress e.g. skin, intestine, between cardiac muscles

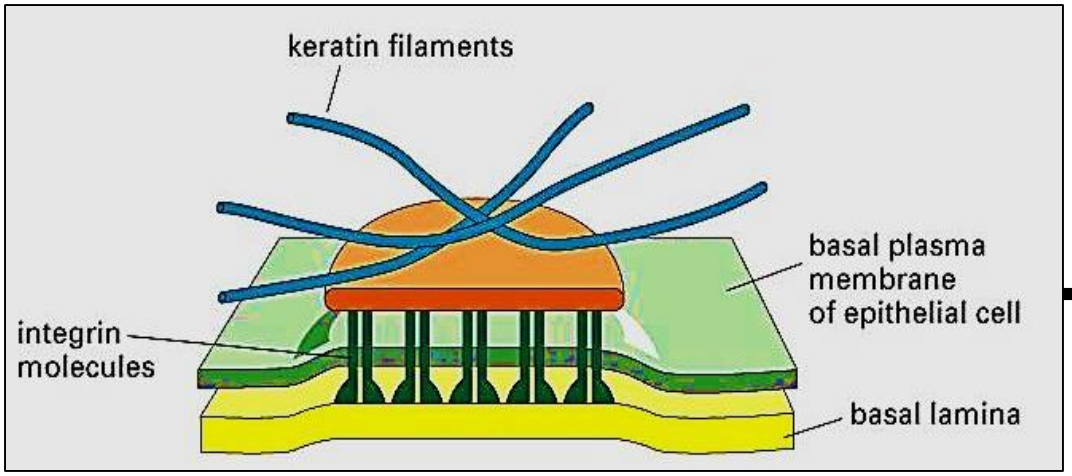


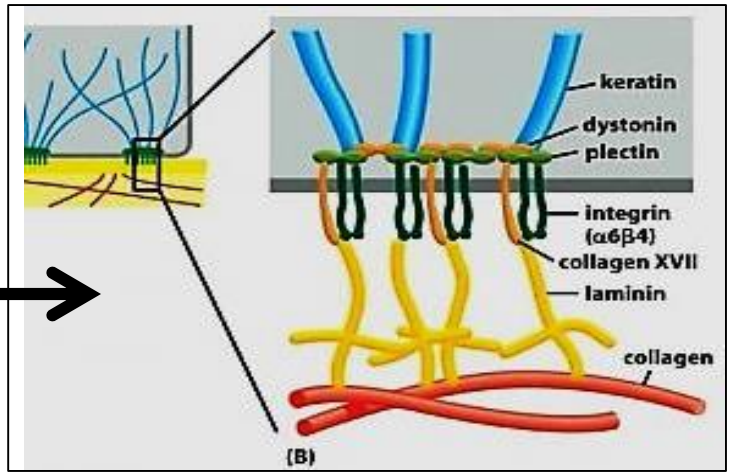


2- Hemidesmosomes



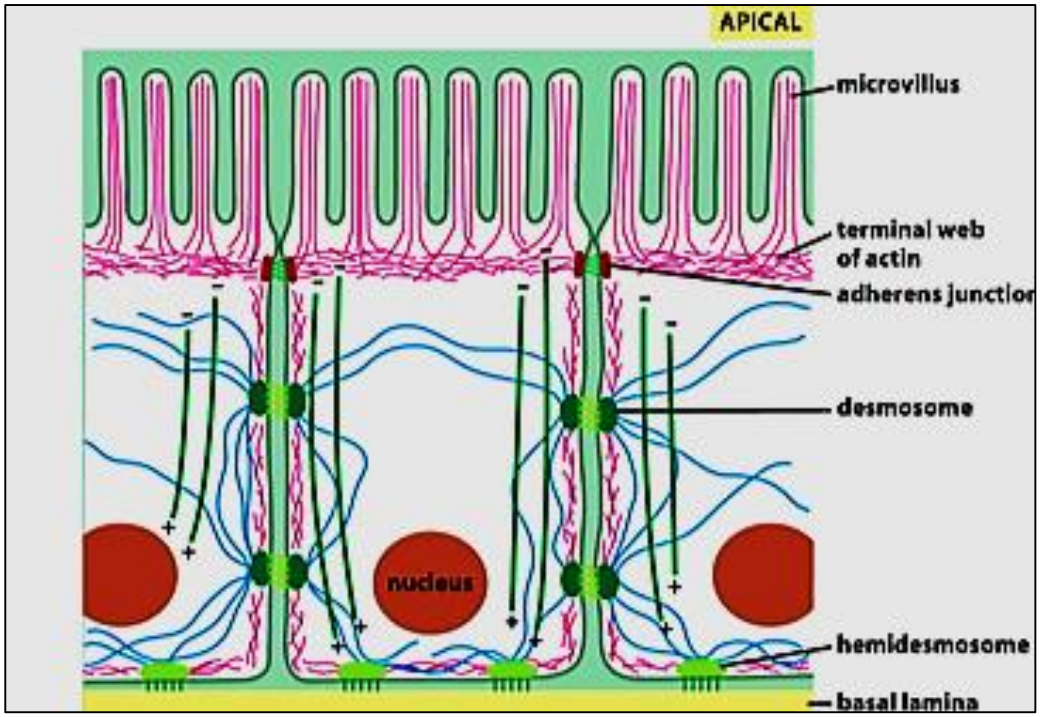
- Half desmosome (cell – basal lamina /ECM)
- At the base of epithelial cells
- Bind epithelial cells to basal lamina
- The transmembrane protein is **integrins** protein
- Plaques provide attachment for **keratin filaments**
- integrin molecules connect to **laminin** of basal lamina in turn connect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

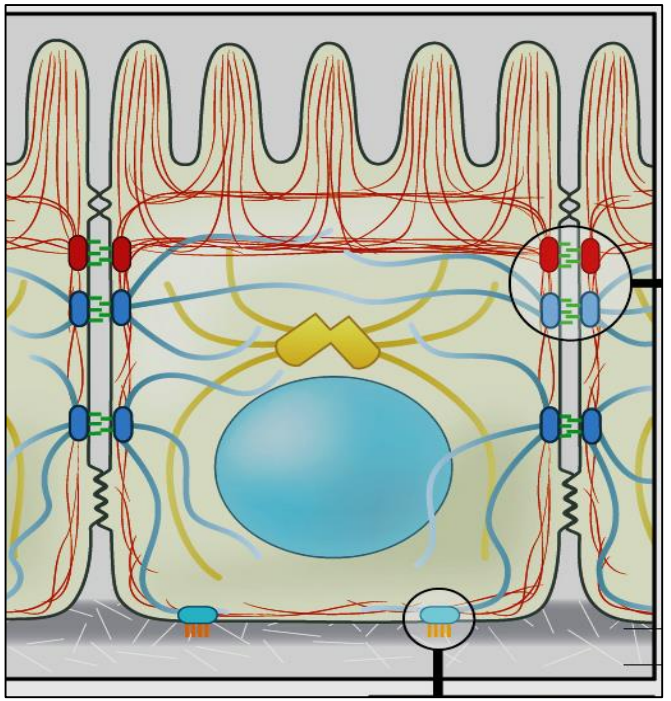




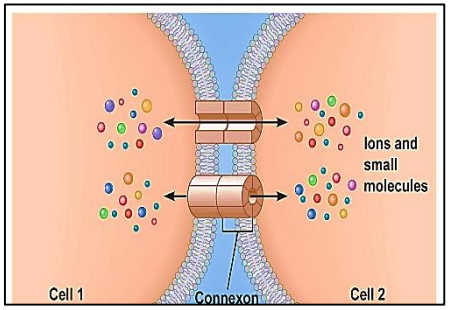
Function of anchoring junctions

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





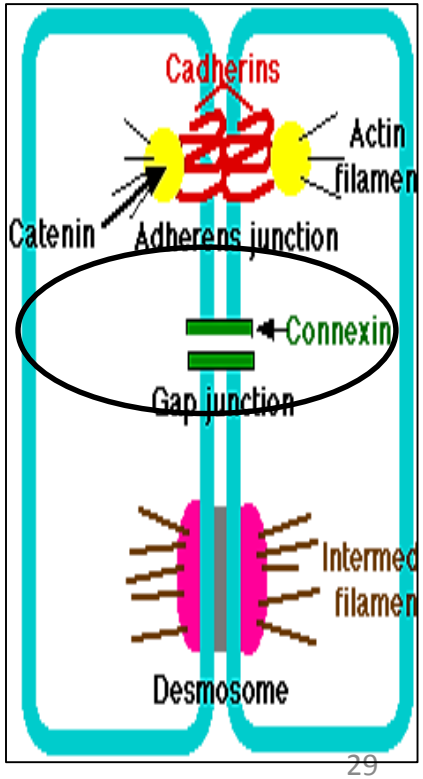
3- Gap junction (GJ)



- 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

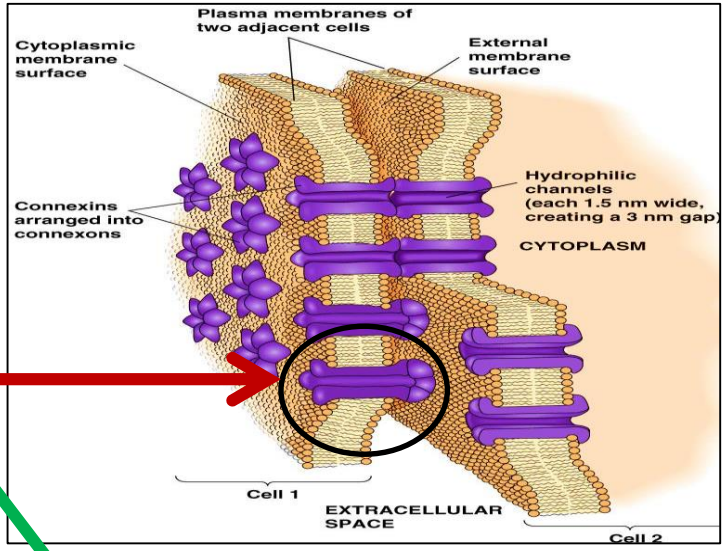


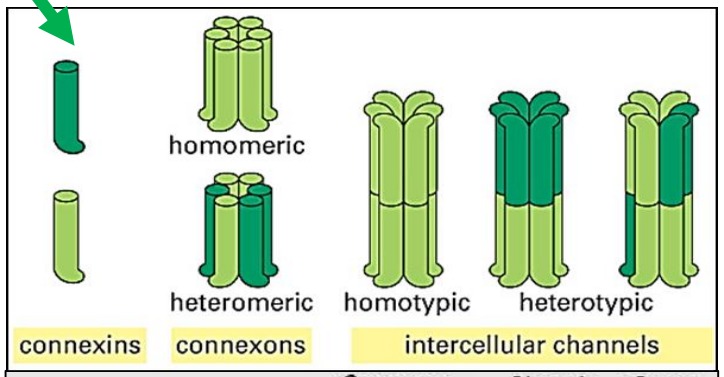
* The protein subunit forming the junction is called Connexin

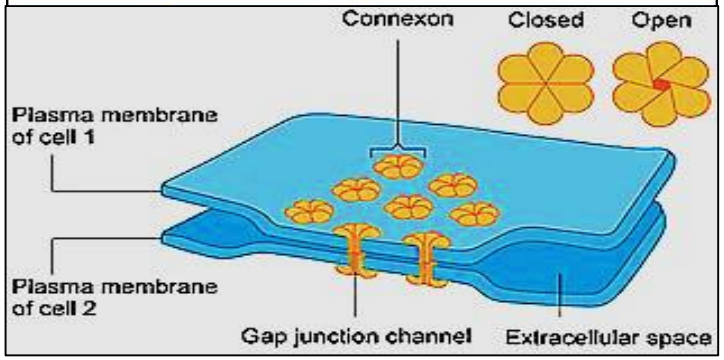
* Each channel called **Connexon** is formed by **6 Connexins** subunits which span the lipid bilayer of the cell membrane (hydrophobic)

* 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:

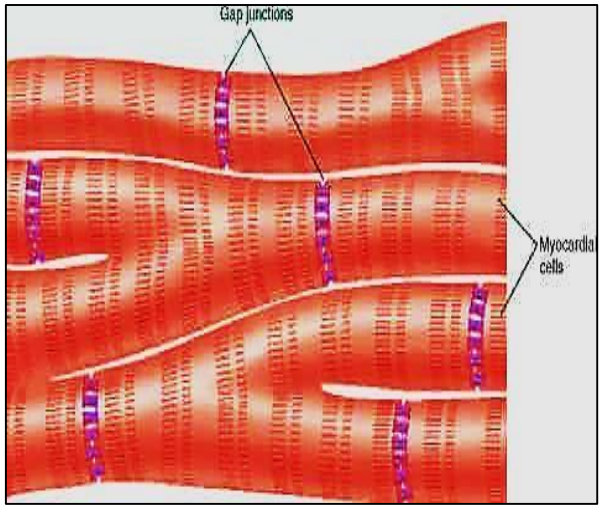
A. Electrical synapse

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) , and in synapses between neurons involved in reflexes in nervous system

*Intercalated discs: contain both **GJs**

(to allow flow of ions from one cell to another → spread of actional potential)

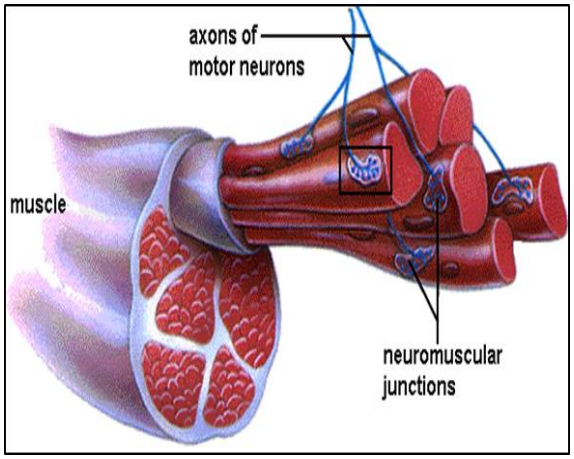
& Desmosomes(to hold cells together)*

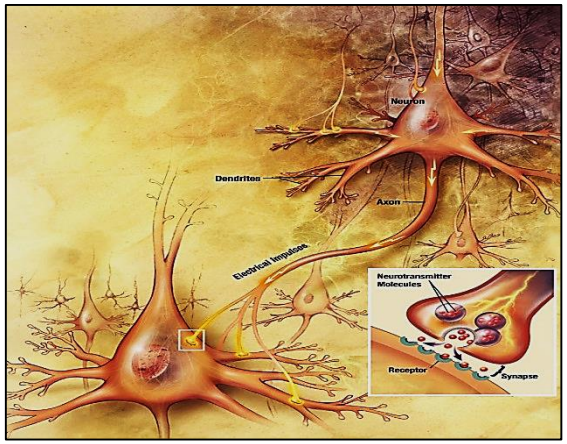


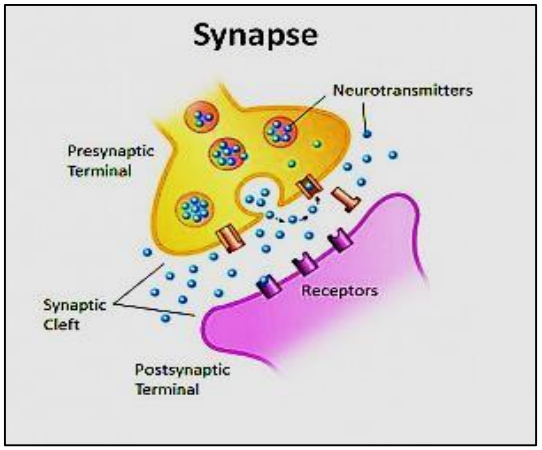
Cardiac muscles

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**







- 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