Cell Adhesion Molecules

Cell adhesion molecules (CAMs) are a subset of cell adhesion proteins located on the cell surface involved in binding with other cells or with the extracellular matrix (ECM) in the process called cell adhesion. In essence, cell adhesion molecules help cells stick to each other and to their surroundings. Cell adhesion is a crucial component in maintaining tissue structure and function. In fully developed animals, these molecules play an integral role in creating force and movement and consequently ensure that organs are able to execute their functions. In addition to serving as "molecular glue", cell adhesion is important in affecting cellular mechanisms of growth, contact inhibition, and apoptosis. Oftentimes aberrant expression of CAMs will result in pathologies ranging from frostbite to cancer. Combined with cell junctions and ECM, CAMs help hold animal cells together.

Structure

CAMs are typically transmembrane receptors and are composed of three conserved domains:

i. An intracellular domain that interacts with the cytoskeleton,
ii. a transmembrane domain, and
iii. an extracellular domain.

Functions

1. Structural Integrity
2. External Sensing
3. Migration
4. Regulation of Transport
5. Communication

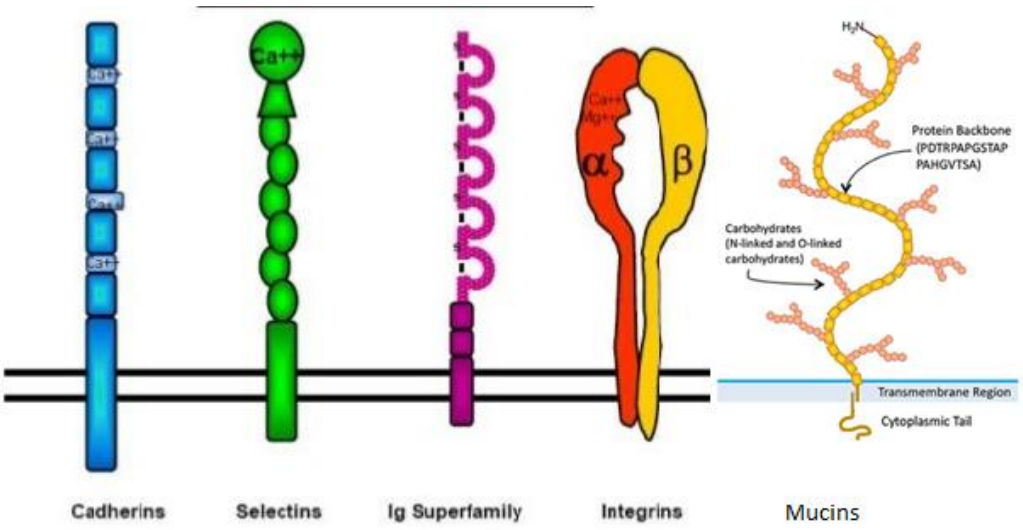
Cell Adhesion complexes

The CAM proteins can interact in several different ways to form Cell Adhesion complexes

1. **Homophilic** binding: The first method is through **homophilic** binding, where CAMs bind with the same CAMs.
2. **Heterophilic** binding: They are also capable of binding of one CAM on one cell with different CAMs on another cell.
3. **An** extracellular ligand may bind two different CAMs between cells and substrate.

Families of (Types) CAMs

There are four major superfamilies or groups of CAMs:

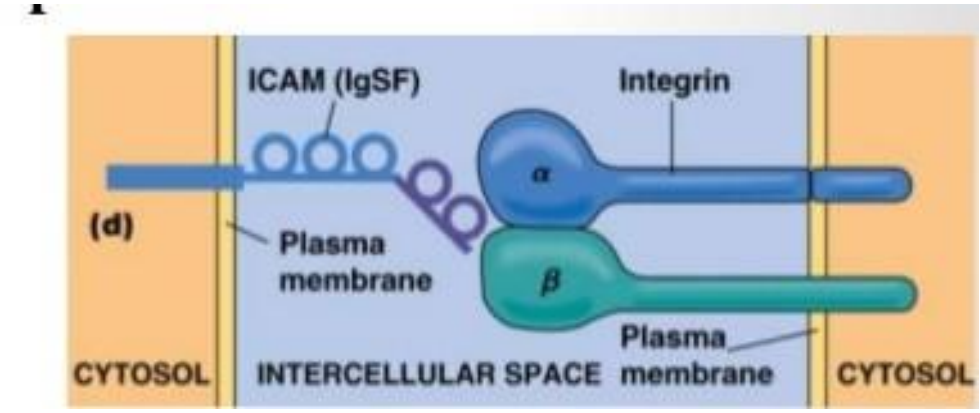


i. Integrins,
ii. the immunoglobulin super family of cell adhesion molecules (IgCAMs),
iii. Cadherins,
iv. Mucins
v. Selctins

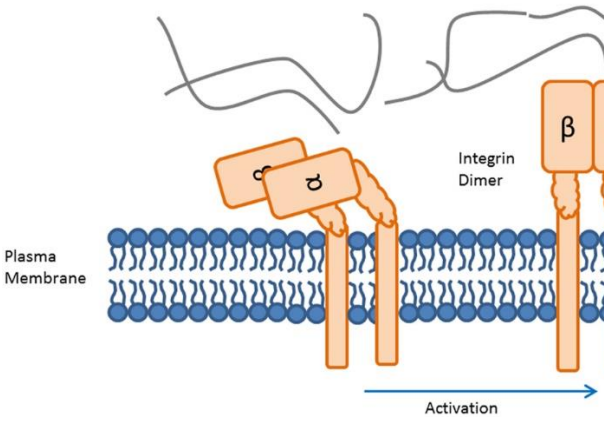
(i) Integrins

Integrins, are one of the major classes of receptors within the ECM that mediates cell to Extra Cellular Matrix interactions with collagen, fibrinogen, fibronectin, and vitronectin. Integrins provide essential links between the extracellular environment and the intracellular signalling pathways, which can play roles in cell behaviours such as apoptosis, differentiation, survival, and transcription.

Integrins are heterodimeric, which consist of an alpha and beta subunit. There are 18 alpha subunits and 8 beta subunits, which combine to make up 24 different integrin combinations. Within each of the alpha and beta subunits there is a large extracellular domain, a transmembrane domain and a short cytoplasmic domain. The extracellular domain is where the ligand binds.through the use of divalent cations. In general, Mn^{2+} increases affinity, Mg^{2+} promotes adhesion to cells, and Ca^{2+} decreases cell adhesion. Integrins regulate their activity within the body by changing conformation.



Integrins exist at rest in a low affinity state. When an external agonist binds to it, it is stimulated and causes a conformational change within the integrin, and altered to high affinity state.

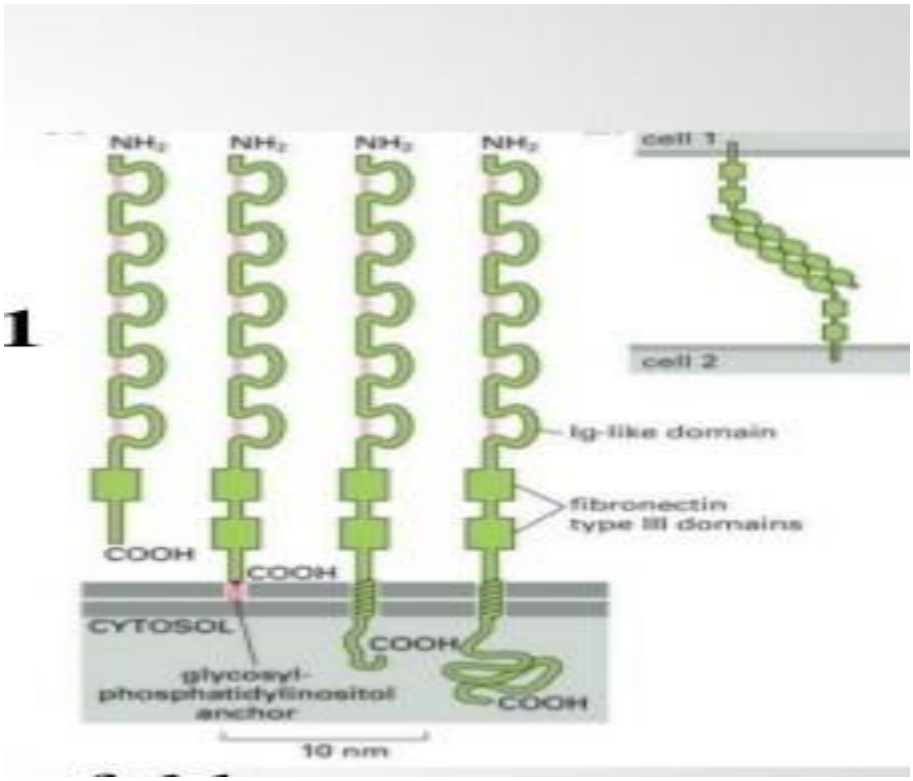


An example of this is the aggregation of platelets. Agonists such as thrombin or collagen trigger the integrin into its high affinity state, which causes increased fibrinogen binding, causing platelet aggregation.

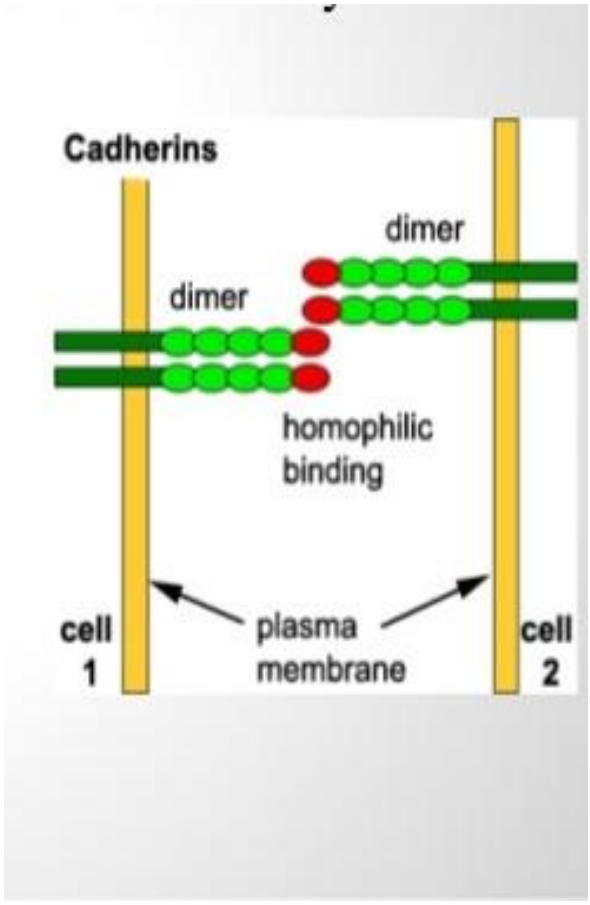
(ii) The Ig superfamily CAMs (IgSF CAMs)

Immunoglobulin superfamily CAMs (IgSF CAMs) is regarded as the most diverse superfamily of CAMs. This family is characterized by their extracellular domains containing Ig-like domains. IgSFs are anchored to the membrane by a **Glycosyl phosphatidyl inositol** (GPI) moiety. Members includes: ICAM, VCAM-1, PECAM-1, NCAM. They function by both homophilic and heterophilic binding. They involve in recognition, binding or adhesion processes o

f cells.



(iii) Cadherins

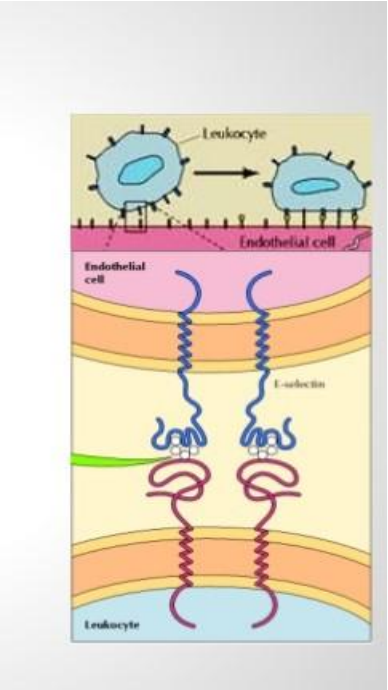


The **cadherins** are homophilic Ca^{2+}-dependent glycoproteins adhesion molecules plays important role in cell adhesion by forming desmosomes. Classic cadherins are concentrated at the intermediate cell junctions .

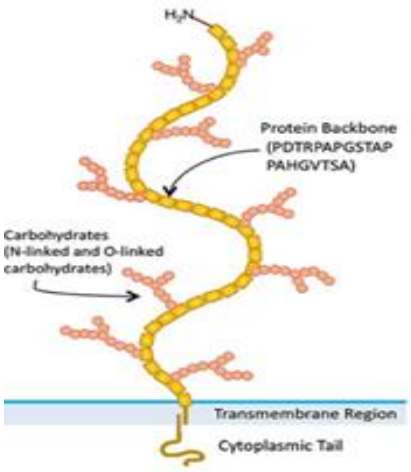
Cadherins are notable in embryonic development. For example, cadherins are crucial in gastrulation for the formation of the mesoderm, endoderm, and ectoderm. Cadherins also contribute significantly to the development of the nervous system. Each cadherin exhibits a unique pattern of tissue distribution that is carefully controlled by calcium. The failure of cadherin mediated cell-cell adhesion cascade causes breast cancer.

The diverse family of cadherins include epithelial (E-cadherins), placental (P- cadherins), neural (N-cadherins), retinal (R-cadherins), brain (B-cadherins and T-cadherins), and muscle (M-cadherins).

(iv) Selectins



The selectins are a family of divalent cation dependent glycoproteins. They are carbohydrate-binding proteins. Members includes: Endothelial (E)-selectin, Leukocyte (L)-selectin, and Platelet (P)-selectin. Selectins play an important role in many host defense mechanisms.



Mucins

(i) **Mucins**

The Mucins are the group of serine and threonine-rich protein and hydroxyproline enabling post-translational O-glycosylation. } Their extended structure allows them to present sulfated carbohydrate moieties as binding site for selectins