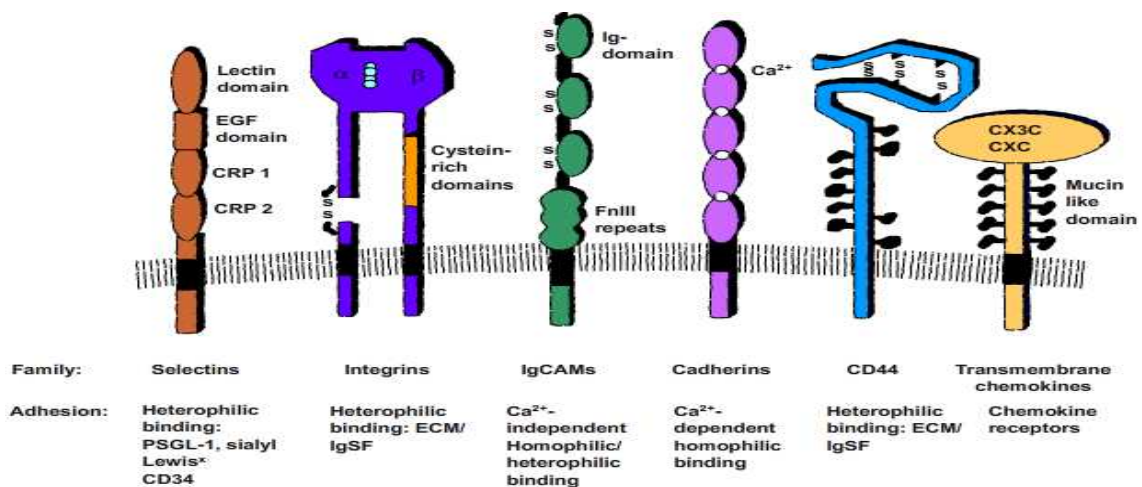


Molecular Cell Biology
Prof. D. Karunakaran
Department of Biotechnology
Indian Institute of Technology Madras

Module 8
Cell-Cell Recognition and Adhesion

Lecture 1
Cell-Cell Interaction

- The assembly of distinct tissues and their organization into organs are determined by molecular interactions between the adhesive molecules present on the plasma membrane of the cells.
- Cells in tissue adhere with each other through specialized membrane proteins called cell-adhesion molecules (CAMs).
- Cell adhesion molecules bind to one another and to intracellular proteins as well as extracellular matrix proteins.
- All the cell adhesion molecules (CAM) can be classified into four major groups-
 - Cadherins
 - Immunoglobulin superfamily
 - Integrins
 - Selectins



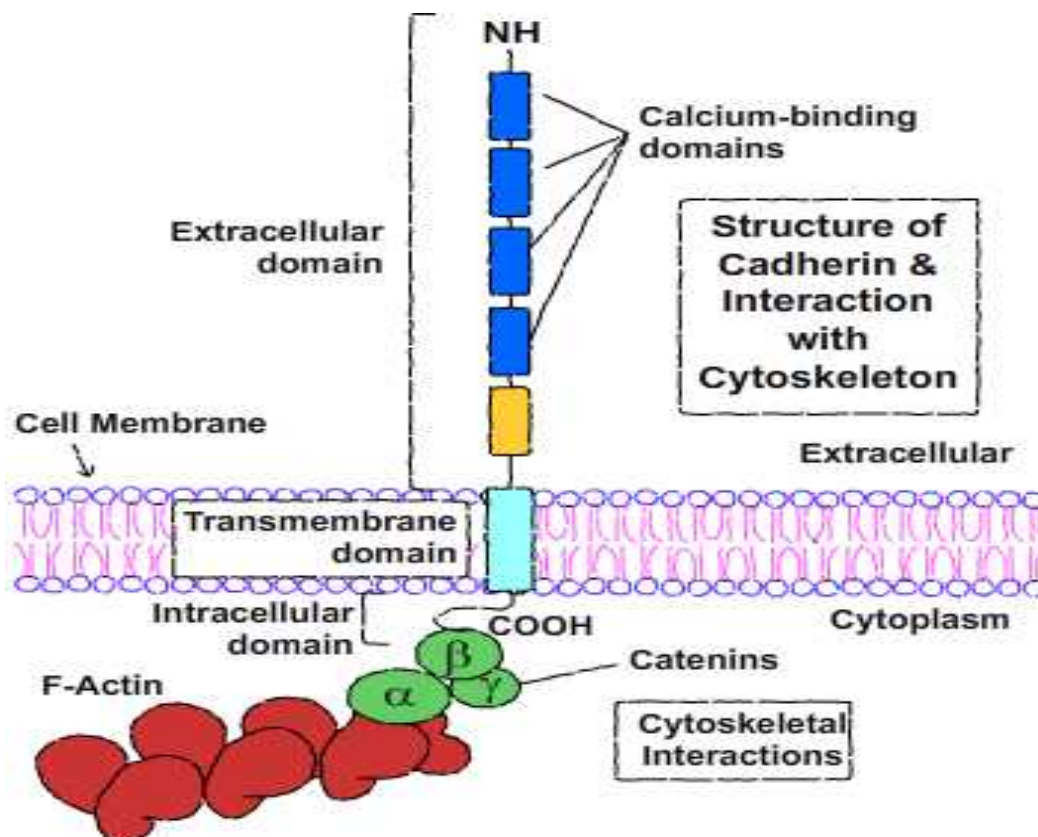
- CAMs can mediate the interaction between two same types of cells (homotypic adhesion) or two different types of cells (heterotypic adhesion).
- CAMs on one cell can bind to the same kind of CAMs on an adjacent cell (homophilic binding) or different kinds of CAM (heterophilic binding).

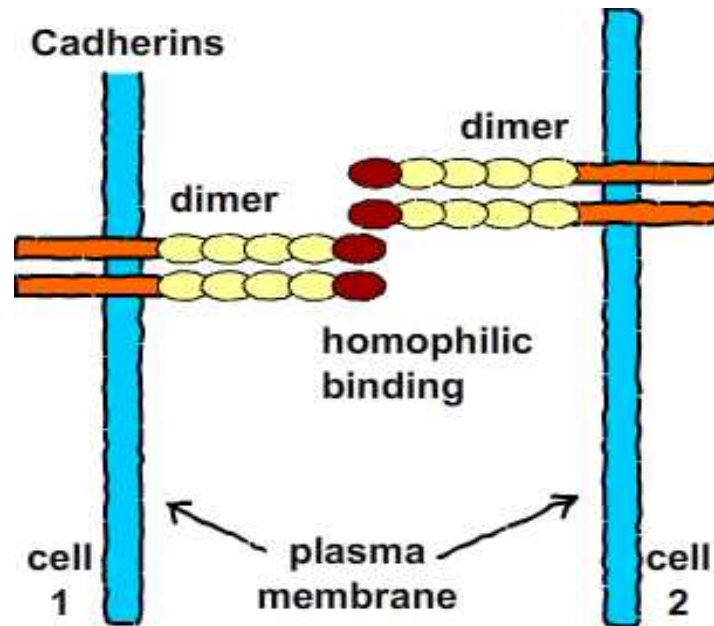
CADHERINS

- Contain 100 members in the family that can be grouped into subfamilies namely cadherin, desmocollins, desmogleins, flamingo and protocadherins.
- The diversity of cadherins is formed by alternative RNA splicing and multiple cadherin genes.

Classical cadherins

- It includes E-cadherins, N-cadherins and P-cadherins. E and N cadherins are expressed during the early stages of differentiation. Cadherin is concentrated in adheren junction and present on lateral surface of each cell to connect the adjacent cell membranes.
- E- cadherins mediate homophilic interaction.

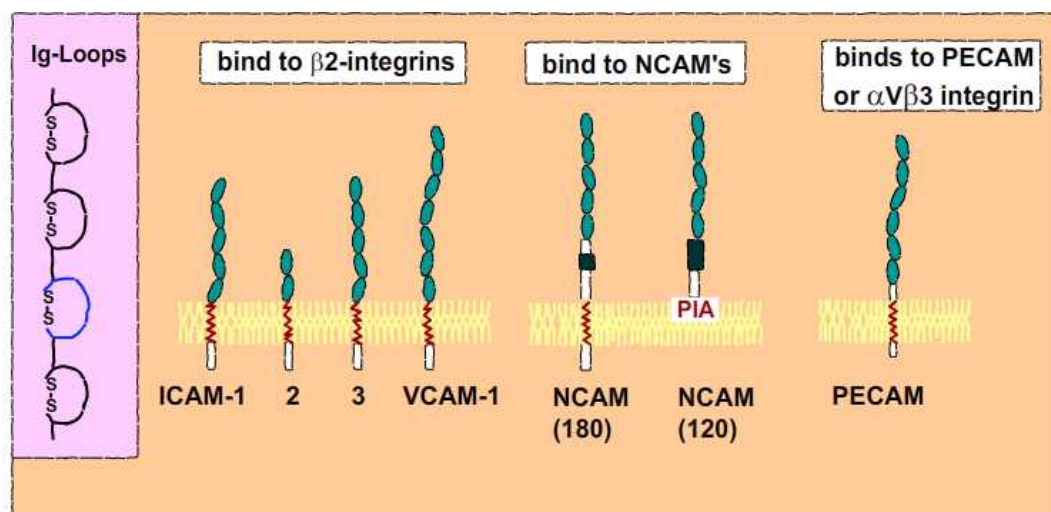




- The adhesiveness of cadherin depends on the of calcium concentration and hence it was known as calcium adherin or cadherin.
- Classical cadherins contain following domains
 - A transmembrane domain
 - A relatively short C-terminal cytosolic domain and
 - Five extracellular cadherin domains
- Cadherin mediated adhesion occurs by lateral interaction during intracellular interaction and trans interaction during intercellular interaction
- C terminal of cadherins are linked to actin cytoskeleton by adaptor proteins.
- Cytosolic part of cadherin also interacts with intracellular signaling molecules as beta catenin, and p20 catenin.
- Epithelial-mesenchymaltransitions are mediated by reduction in E-cadherin expression
- A loss of function of E-cadherin has been also observed during the development of certain types of cancer and metastasis.

Desmosomal cadherins

- Includes desmoglein and desmocollins.
- Cytosolic part of desmosomal cadherins interact with adaptor proteins as plakoglobin, plakophilins and desmoplakin.
- Immunoglobulin super family adhesion molecule (IgCAM)
- These are the transmembrane proteins having multiple immunoglobulin domain in their extracellular region.
- IgCAMs include neural CAM N-CAM, intercellular CAMs that are involved in movement of leukocytes into tissues and junction adhesion molecule JAMs present in tight junction.
- N-CAMs play a very important role in differentiation of muscle, glial and nerve cells.

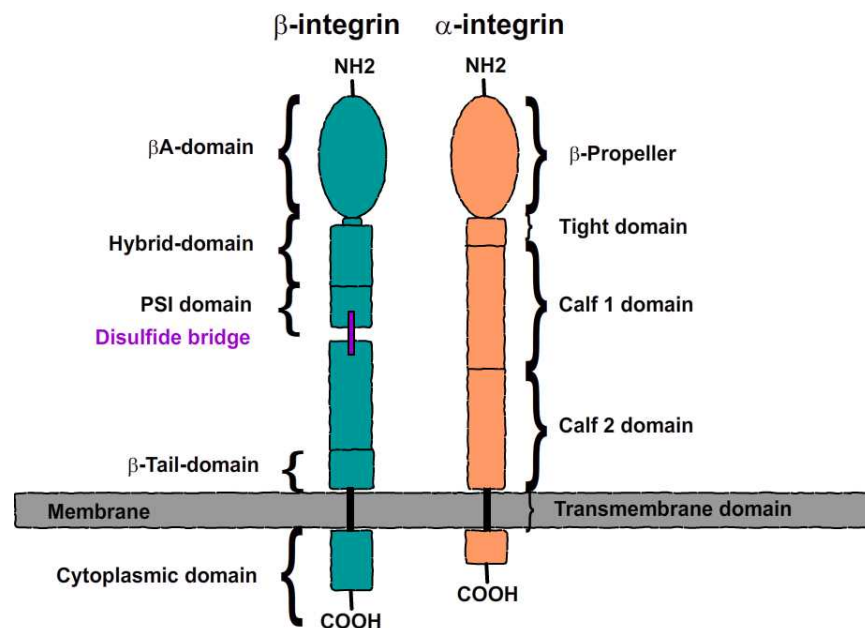


Cellular adhesion molecules belonging to the immunoglobulin superfamily. These adhesion molecules are characterized by the presence of repeated loop-like structures that are homologous to those present in immunoglobulins (Ig-loops). There are several members of this family, all having a single membrane-spanning domain. They interact with different ligands (or counter-receptors). PIA, phosphatidy inositol anchor.

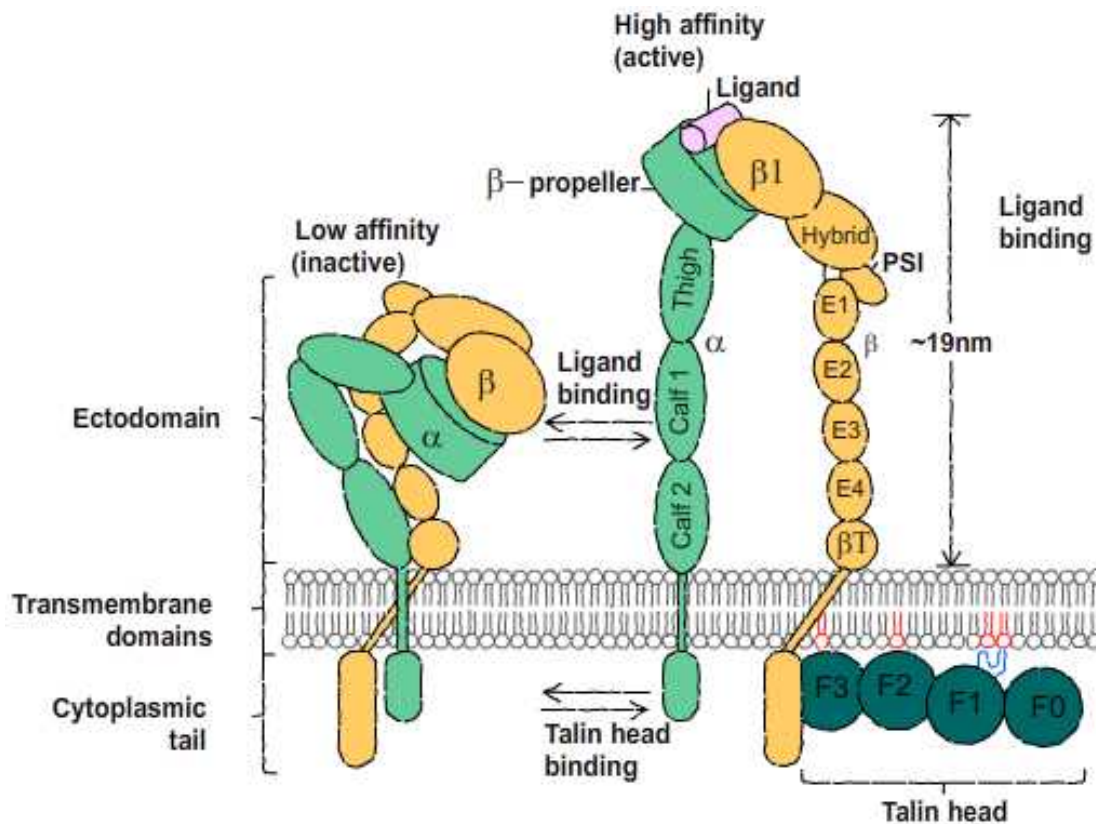
- N- CAM consists of an extracellular region with five Ig repeats, and two fibronectin type III repeats, a single membrane spanning segment and a cytosolic segment interacting with cytoskeletons.
- Adhesions mediated by IgCAMs are calcium independent.

Integrin

- Connect the epithelial cells to the basal lamina through adaptor molecules to the cytoskeleton. Integrins form a bridge between the ECM and the cytoskeleton.
- In non-epithelial cells integrins in plasma membrane are clustered in focal adhesion and podosomes.

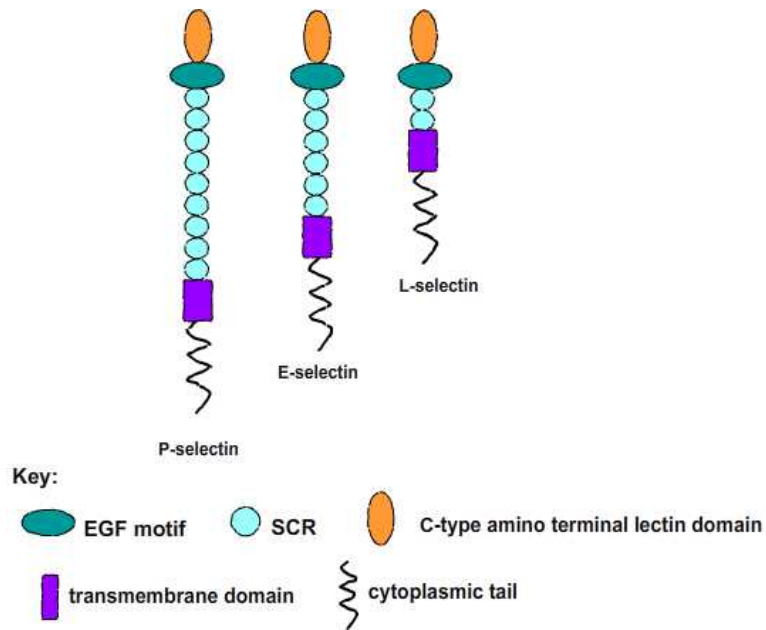


- Integrin participates in inside-out cell signaling as well as outside-in cell signaling.
- In the inactive state the heterodimer is bent and the ligand binding site allows only low affinity ligand to bind. The cytoplasmic C-terminal tails of the two subunits are closely bound together.
- In the active state the change in conformation of binding site domain permits high affinity ligand binding and the cytoplasmic tail of the integrins get separated to each other.
- Integrins play a very important role in the blood clotting by platelets.



Selectin

- Family of integral membrane glycoprotein, interacts with the specific arrangement of sugars in the oligosaccharide protruding from the surface of the other cells.
- Selectin is made up of a small cytoplasmic domain, a membrane spanning domain and a large extracellular domain having separate modules and an outermost domain made up of lectin.
- There are three types of selectins
 - P selectin-present on the surface of platelets and endothelial cells
 - E selectin- present on the surface of endothelial cells
 - L-selectin-present on the surface of leucocytes



- Binding of selectins to their carbohydrate ligand requires calcium.
- Selectins are involved during inflammation and cancer development.
- The selectin and the ligand of selectin determine the organ selectivity of the metastasis.
- Selectins are involved in lymphocyte homing.

Study Questions

1. What are different types of CAM?
2. Write a note on different types of adhesion
3. E-cadherin mediate
 - a) homophilic adhesion
 - b) heterophilic adhesion
 - c) both
 - d) none of the above
4. Match the following

P selectin	leukocytes
E selectin	Nerve cells
L-selectin	platelets
N- CAM	endothelial cells

5. Desmosomal cadherins include and