CELL JUNCTION

Cell-Cell and Cell-Extracellular matrix interactions are critical for assembling cell into tissues, controlling cell shape and function and determining the developmental fate of cells and tissues.

Three types of junctions mediate many Cell-Cell and Cell-Extracellular matrix interactions:

All epithelial cells in a sheet are connected to one another and to the extra cellular matrix by specialized junctions. These specialized junctions play special role in:

1. Impairing strength and rigidity to a tissue.
2. Transmitting information between the extracellular and the intracellular space.
3. Controlling the passage of ions and molecules across the cell layer.
4. Serve as conduits (a channel for conveying water or other fluid) for the movement of ions and molecules from the cytoplasm of one cell to that of its immediate neighbor.

Three major classes of animal cell junctions are prominent features of simple columnar epithelium:

1. **ANCHORING JUNCTIONS**:
   a. **Adherens Junctions (Cell-Cell)-** They connect the lateral membranes of adjacent epithelial cells and are usually located in the apical surface. Cadherin is the CAM(Cell Adhesion Molecule) ofAdherens Junctions.
   b.**Desmosomes (Cell-Cell)**-Epithelial and some other types of cells(such as smooth muscle and heart cells) are bound together tightly by desmosomes. Desmosomes are one of the stronger cell to cell adhesion types found in tissues that experience intense mechanical stress (e.g. cardiac muscle tissue). Desmoglein and Desmocollin (Desmosomal Cadherin) are CAM of Desmosomes.
   c. **Hemidesmosomes (Cell-Matrix)**- Found mainly on the basal surface of epithelial cells, anchor an epithelium to components of

underlying extracellular matrix. Adhesion Receptors of hemidesmosomes are Integrin (e.g. $\alpha_6\beta_4$)

2. **TIGHT JUNCTIONS**
3. **GAP JUNCTIONS**

Note- Anchoring junctions and tight junctions perform the key task of holding the tissue together. These junctions are organized into 3 parts:

1. Adhesive Proteins in the plasma membrane that connect one cell to another cell on the lateral surface (CAM-Cell Adhesion Molecules) or to the extracellular matrix on the basal surfaces(Adhesion Receptors)
2. Adapter Proteins- It connects CAM or Adhesion receptors to cytoskeletal filaments and signaling molecules.
3. The cytoskeletal filaments.

Bundles of intermediate filaments running parallel to the cell surface or through cell interconnect spot desmosomes and hemidesmosomes, imparting shape and rigidity to the cell. Adherens junctions and desmosomes are found in many different types of cells. Hemidesmosomes appear to be restricted to epithelial cells.

Note- 1. Tight junctions also control the flow of solutes through the extracellular spaces between the cells, forming an epithelial sheet

2.Tight junctions are found primarily in epithelial cells whereas anchoring junctions can be seen in both epithelial and non-epithelial cells.

MAIN FUNCTIONS OF JUNCTIONS

1. Anchoring Junctions- (Including both cell-cell adhesion and cell-matrix adhesions) – Transmit stresses and are tethered to
2. cytoskeletal filaments inside the cell.
3. Occluding Junctions- Seal the gaps between cell in the epithelia so as to make the cell sheet into an impermeable (or selectively permeable) barrier.
4. Channel forming junctions- Create passageways linking the cytoplasm of adjacent cells.
5. Signal-relaying junctions- Allow signals to be relayed from cell to cell across their plasma membranes at sites of cell to cell contact

(e.g.- Chemical synapses in the nervous system and immunological synapses where the T-lymphocytes interact with antigen presenting cells).

A FUNCTIONAL CLASSIFICATION OF CELL JUNCTIONS

A. ANCHORING JUNCTIONS

Actin Filament-attachment sites

1. Cell-Cell Junctions (Adherens Junctions)
2. Cell-Matrix Junctions (Actin linked Cell-Matrix Adhesions)

Intermediate Filament attachment sites

1. Cell-Cell Junctions (Desmosomes)
2. Cell-Matrix Junctions (Hemidesmosomes

B. OCCLUDING JUNCTIONS

1.Tight Junctions (In Vertebrates)
2. Septate Junctions (In Vertebrates)

C. CHANNEL FORMING JUNCTIONS

1.Gap Junctions (In animals)
2. Plasmodesmata (In plants)

D. SIGNAL RELAYING JUNCTIONS

1. Chemical Synapses (In the nervous system)
2. Immunological Synapses (In the immune system)
3. Sites of cell-cell communications via transmembrane ligand-receptor pairs such as Delta-Notch, Ephrin-Eph etc.

Note- Anchoring, occluding and channel forming junctions can all have a signaling function in addition to their structural role.

EPITHELIAL TO MESENCHYMAL TRANSITION- WITH SPECIAL ANALYSIS OF ROLE OF SLUG,SNAIL AND TWIST TRANSCRIPTIONAL FACTORS

Epithelial to mesenchymal transitions are vital for tumor growth and metastasis. Several inducers of epithelial to mesenchymal transition are transcription factors that repress E-cadherin expression such as Snail, Slug and Twist. Epithelial to mesenchymal transition (EMT) is a key step during embryonic morphogenesis and is involved in the progression of primary tumors towards metastasis. During EMT, cells undergo a developmental switch from a polarized, epithelial phenotype to a highly motile fibroblastoid or mesenchymal phenotype. Tumor cells begin to grow invasive, enter into systemic circulation, move from the circulatory system into a new host tissue and proliferate to grow to a secondary tumor. E-cadherin is required for the formation of stable adherins junctions and thus the maintenance of an epithelial phenotype. Loss of E-cadherin expression is emerging as one of the most common indicators of EMT onset, and reduced expression of E-cadherin has been reported in various cancers, being associated with tumor progression and metastasis.N-cadherin is associated with an increased invasive potentials in cancer. The transcriptional factors Snail and Slug are direct repressors of E-cadherin. Both have been suggested to be involved in the acquisition of resistance to apoptosis, thereby promoting tumor survival. A further molecule known to trigger EMT is Twist. Overexpression of Snail and Slug leads to a reduction of E-cadherin expression. An overexpression of Twist result in an increase of N-cadherin which farther leads to a decrease of E-cadherin expression.