Cell organization & movement

Anusara Aranarochana, PhD.
Department of Anatomy, Faculty of Medicine,
Khon Kaen University anusar@kku.ac.th
Cell organization & movement

- cell membrane
- cytoskeleton
- cell adhesion
- cell junction
Objectives

After studying this topic you should be able to:

1. Explain the major structures & components of the cell membrane
2. Explain the molecular structures, organizations & functions of the cytoskeleton
3. Classify & explain the function of adhesion molecules presented in the cell
4. Explain the junctions of the cell, particularly in molecular structures
Cell membrane (plasma) membrane

- All cells have a cell membrane
- Cell membrane separates living cell from nonliving surroundings

**Functions**

- Determines the **structural boundary**
- Provides **protection & support** for the cell
- Controls **traffic in & out** of the cell to maintain an **internal balance** of the cells

7.5 nm thick
Molecular structure of cell membrane

→ Composes of

1. Lipids (bilayer)
   - phospholipids
   - sphingolipids
   - cholesterol

2. Proteins
   - integral (transmembrane)
   - & peripheral proteins

3. Carbohydrates:
   - glycolipids
   - glycoproteins
The most abundant of lipid molecules in the cell membrane are phospholipids.

- **Phospholipid is “amphipathic molecule”**
  1. Head group is polar $\rightarrow$ hydrophilic
  2. Two hydrocarbon tail is non polar $\rightarrow$ hydrophobic **fatty acids**
     (length & saturation of fatty acid tails determines the “fluidity”)

Phospholipid Bilayer structure of cell membrane: 

- **Hydrophilic Head (Polar)**
- **Hydrophobic Tails (Non Polar)**
- **Phospholipid Bilayer**
- **Hydrophilic** (water-loving)
- **Hydrophobic** (water-hating)
Unit membrane model (Trilaminar membrane)

Robertson (1958)

Ultrastructure (TEM) of the cell membrane (aka plasma membrane or cytomembrane)

TEM image of an animal cell

Cell membrane

1st cell membrane

2nd cell membrane

"Trilaminar unit"

1 light layer: Hydrophobic tail

2 dark layers: Hydrophilic head

Fixed by osmium tetroxide (OsO₄)
3 classes of membrane lipids

1. Phosphoglycerides (phospholipids)
   - Phosphatidylethanolamine (PE)
   - Phosphatidylcholine (PC)*****
   - Phosphatidylserine (PS)
   - Phosphatidylinositol (PI)

2. Sphingolipids
   - Sphingomyelin (SM)
   - Glucosylcerebroside (glycolipid)

3. Sterols
   - Cholesterol
Structure of membranous lipid bilayer

- **Outer leaflet**
  - Phosphatidylcholine (PC)
  - Sphingomyelin (SM)
  - Phosphatidylethanolamine (PE)
  - **Glycolipids** are found only in the outer leaflet

- **Inner leaflet**
  - Phosphatidylserine (PS)
  - Phosphatidylethanolamine (PE)
  - Phosphatidylinositol (cell signaling)

[Image of membrane structure with labels for extracellular space, intracellular space, and leaflets with lipid components]
How is the membrane organized?

1972, Singer J. & G. Nicolson “Fluid mosaic model”

- The model describes biologic membranes as “protein icebergs in a lipid sea”
- A membrane is a mosaic: proteins & other molecules are embedded in a framework of phospholipids
- A membrane is fluid: most proteins & phospholipid molecules can move laterally
**Fluidity of lipid bilayer**

"Refers to the viscosity of the lipid bilayers of cell membrane"

"Fluidity" - molecules can move about within the membrane

- lateral movement, flip-flop (exchange), rotation

Fluidity depends on membrane composition & temperature

- ↑ no. of double bonds in the tail → ↑fluidity
- ↑ temperature → ↑fluidity

Cholesterol contained in plasma membrane helps to enhance membrane integrity
Cholesterol in cell membrane

- Located in both leaflets of the plasma membrane
- Helps to stabilize membrane structure

Cholesterol gives the layer greater strength, more flexibility, less fluid & less permeable to ions & monosaccharide

- Fluidity decrease as membrane cholesterol increases
  - fluidity - permeability of membranes to small molecules e.g. water
Lipid molecules form bilayer spontaneously in aqueous solution.

- When phospholipids are mechanically dispersed in aqueous solution, phospholipids aggregate into one of three forms:
  1. Spherical micelles
  2. Spherical liposomes
  3. Sheet-like phospholipid bilayer
Micelle

- Single layer of phospholipid with polar head facing out, nonpolar tail facing inward
- Micelles are formed if one / two fatty acid chains is removed from phospholipid by hydrolysis
- Common detergents & soaps form micelles that act as tiny ball bearings, thus giving soap solutions lubricating properties

Liposome

- Is an artificially-prepared spherical vesicle composed of a lamellar phase lipid bilayer
- Can be used as a vehicle for administration of nutrients & pharmaceutical drugs
Sheet-like phospholipid bilayer

- Under suitable conditions, phospholipids of the composition present in cells spontaneously form "symmetric phospholipid bilayers"

- Fatty acid chains minimize contact with water by aligning themselves tightly together in the center of bilayer, forming a hydrophobic core

- Close packing of nonpolar tails is stabilized by van der Waals interactions
Membrane proteins

**Glyco**proteins—cell recognition—between cells, antibodies, hormones and viruses

**Glycolipids** also have a role in helping cells to aggregate in the formation of tissues.

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**Cholesterol** in the membrane disturbs the close packing of the phospholipids and keeps the membrane more fluid. Provides rigidity and water resistance. Membranes would break down without it. Plants have phytosterol.

Some substances, particularly ions and carbohydrates, are transported across the membrane via the proteins.

Some substances, including water, are transported directly through the **phospholipid bilayer**. But mostly impermeable to water soluble (polar) molecules—most movement via proteins.

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**Consist of**

1) Integral (transmembrane) protein
2) Peripheral protein

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1) Integral (transmembrane) proteins

- Span the entire thickness of a phospholipid bilayer
- Comprise 3 segments

- Cytosolic & exoplasmic domains (1&2) have hydrophilic exterior surfaces that interact with aqueous solutions

- Membrane-spanning segments contain hydrophobic amino acids that interact with hydrophobic hydrocarbon core of phospholipid bilayer
**Different functions of integral membrane proteins**

- **Pumps** serve to transport certain ions, such as Na\(^+\), actively across membranes.

- **Channels** allow the passage of small molecules, ions, & water across membranes (i.e., passive diffusion).

- **Receptors** allow recognition & localized binding of ligands in processes such as hormonal stimulation, coated-vesicle endocytosis, & antibody reactions.

- **Linkers** anchor the intracellular cytoskeleton to extracellular matrix (i.e., **Integrins** link cytoplasmic actin filaments to extracellular matrix protein; fibronectin).

- **Structural proteins** form junctions with neighboring cells (i.e., in epithelial cells).
2) Peripheral/extrinsic proteins

- Do not extend into the lipid bilayer
- Can be removed by high/low ionic strength or extreme pH
- Are attached by covalently attached lipid in the cytoplasmic layer
- Are attached to membrane only by noncovalent interaction with other proteins
Cell Cytoskeleton (โครงร่างเซลล์)

- Is a three-dimensional network of proteins distributed throughout the cytoplasm → provide a structural framework for cellular organization

- The cytoskeleton has roles in
  - Cell movement
  - Support & strength for the cell
  - Phagocytosis
  - Cytokinesis
  - Cell-cell & cell-extracellular matrix adherence
  - Changes in cell shape
3 types of fibers make up the cytoskeleton

- Microfilament (actin filament) 7 nm
- Intermediate filament 8–12 nm
- Microtubule 25 nm

Bacteria: no cytoskeleton
1. Microfilaments (actin filaments)

**Structure & Organization**

- The thinnest class of the cytoskeletal fibers (7 nm)
- Actin filament has polarity: plus (+) & minus (-) end

Actin filaments are composed of globular monomers (G-actin), which can polymerize to form helical & asymmetrical filamentous (F-actin)
Actin filament is a polarized structure
- Plus (barbed) end → add new monomers
- Minus (pointed) end → loss monomers
- Actin polymerization requires ATP, which is hydrolyzed to ADP after each G-actin molecule is incorporated into the filament
Actin filaments: assembly & disassembly

- **Treadmilling phenomenon**

  - Is the **dynamic balance** between the polymerizing & depolymerizing ends to maintain the length of actin filament

  - **4 types** of proteins control treadmilling:
    1. Thymosin
    2. Profilin
    3. Cofilin
    4. Gelsolin

"actin associated protein"
Actin associated proteins

- **Thymosin** (actin monomer sequestering protein)
  - sequesters G-actin from polymerization

- **Profilin**
  - enhances polymerization of ATP-bound actin to (+) end
Actin associated proteins

- **Cofilin**: removes ADP-bound actins from (-) end
- **Gelsolin** has a dual role:
  - a severing & capping protein
Higher organized structure: bundle & network

**FIGURE 12.8** Actin bundles and networks  
(A) Electron micrograph of actin bundles (arrowheads) projecting from the actin network (arrows) underlying the plasma membrane of a macrophage. The bundles support cell surface projections called filopodia (see Figure 12.19).  
(B) Schematic organization of a bundle and a network. Actin filaments in bundles are cross-linked into parallel arrays by small proteins that align the filaments closely with one another. In contrast, networks are formed by large flexible proteins that cross-link orthogonal filaments.  
(A, courtesy of John H. Hartwig, Brigham & Women’s Hospital.)

- **Actin bundle** in microvilli of the intestinal epithelium
- **Filopodia** (pointed protrusions), **lamellipodia** (flatted protrusions), ameboid movement
- **Actin stress fibers**
- **Actin contractile ring** in cytokinesis of animal & fungal cells
Actin-associated motor system: Cell Movement

***Muscle contraction involves the relative movements of actin-myosin, which bring the Z lines closer together***
ATP-Ca\textsuperscript{2+} dependent actin-myosin movement

(a) Tropomyosin and troponin work together to block the myosin binding sites on actin.

(b) When a calcium ion binds to troponin, the troponin-tropomyosin complex moves, exposing myosin binding sites.
Actin–myosin movement in cell division

- Actin–myosin contraction in non-muscle cells
- Another contractile process → cytokinesis, is the contraction of a ring of actin/myosin resulting in formation of two daughter cells

**EXPERIMENTAL FIGURE 17-34** Fluorescent antibodies reveal the localization of myosin I and myosin II during cytokinesis.
(a) Diagram of a cell going through cytokinesis, showing the mitotic spindle (microtubules green, chromosomes blue) and the contractile ring with actin filaments (red). (b) Fluorescence micrograph of a Dictyostelium ameba during cytokinesis reveals that myosin II (red) is concentrated in the cleavage furrow, whereas myosin I (green) is localized at the poles of the cell. The cell was stained with antibodies specific for myosin I and myosin II, with each antibody preparation linked to a different fluorescent dye. [Courtesy of Y. Fukui.]
2. Intermediate filament

- The intermediate filament (8–12 nm) is specialized for bearing tension

- Form a rope-like structure

- Very stable structures in the cell & provides mechanical strength to cells

- Reinforce cell shape & fix organelle location
2. Intermediate filament

***** Tensile strength
→ cell enable to withstand the mechanical stress (stretched)

Stretching a sheet of cells with intermediate filaments

Cells remain intact & together

Stretching a sheet of cells without intermediate filaments

Cell rupture
Intermediate filaments form strong rope-like multi-protein assemblies

- 2 monomers → dimer
- 2 dimers → tetramer
- 2 tetramers → protofilament
- 2 protofilaments → protofibril
- 4 protofibrils → rope-like
Classes of proteins form the intermediate filament

**CYTOPLASMIC**
- Type 1, 2
- Acidic & basic keratins
  - : epithelial cells

- Type 3
- Vimentin, desmin, glial fibrillary acidic protein
  - : fibroblast, WBC, muscle, glial cells

- Type 4
- Neurofilaments
  - : neurons

**NUCLEAR**
- Type 5
- Nuclear lamins
  - : all animal cells
Intracellular organization of the intermediate filaments

“Intermediate filaments & Cell Junctions”

- Desmosome
- Hemidesmosome
3. Microtubule

- Is hollow cylinder tube (25 nm in diameter)
- Consists of tubulin dimers (α & β), which polymerize in the presence of GTP & joint end-to-end to form protofilaments
- Each protofilament: β-tubulin at plus end & α-tubulin at minus end
- 13 protofilaments are assemble to form the microtubule

Functions:
- Microtubules move chromosomes during cell division
- Function as the tracks for guiding motor proteins carrying organelles / vesicles to their destinations
Microtubules-Dynamic Instability

Tubulin dimers polymerize in the **presence of GTP at the plus (+) end** to grow the filaments.

If the rate of polymerization is faster than the rate of GTP hydrolysis, the microtubule will **grow**.

If the rate of GTP hydrolysis is faster than the rate of polymerization, the microtubule will **disassemble**.

Alternate phases of slow growth & rapid depolymerization, a process known as **“dynamic instability”** resulted from hydrolysis of GTP-tubulin dimers releasing of GDP-tubulin subunits.
Microtubules are assembled from microtubule organizing center (MTOC) to generate diverse organizations

- The distribution of microtubules in cells & structures are assembled from distinct MTOCs
  - (c) In interphase cell: MTOC is called a “centrosome”
  - (d) In mitotic cells: the 2 MTOCs are called “spindle poles”
  - (e) In neuron: microtubules in both axons & dendrites are assembled from MTOC in the cell body
  - (f) To make up the shaft of cilium / flagellum: MTOC is called a “basal body”
**Centrosome** (microtubule-organizing centers: MTOCs)

- Consist of a pair of centrioles surrounded by pericentriolar material

→ **3 major functions**

1. Nucleates the polymerization of tubulin subunits into microtubules
2. Organizes microtubules into functional units
3. Duplicates once every cell cycle

**Centrioles align mitotic spindle during cell division**

![Image of centrioles and microtubules](image)

**Figures 2.54 & 18-6**

- **Fig. 2.54** Mitotic spindle during normal cell division and in cells lacking centrioles. This schematic drawing shows the orientation of the mitotic spindle in a normal cell undergoing mitosis. Note the positions of the centrioles and the distribution of the spindle microtubules.
- **Fig. 18-6** Structure of centrosomes. (a) Thin section of an animal-cell centrosome showing the two centrioles at right angles to each other surrounded by pericentriolar material (arrows). (b) Diagram of a centrosome showing the two centrioles, each of which consists of nine linked outer triplet microtubules embedded in pericentriolar material that contains γ-TURC nucleating structures.
Motile cilia & flagella contain a core of microtubules called the axoneme.

Both cilia & flagella are microtubule-based structures with a central pair of singlet microtubules & 9 sets of outer doublet microtubules “(9+2)”

Cilia & flagella grow from basal bodies, structures with 9 sets of outer triplet microtubules.
Microtubule Motor Proteins

- 2 main classes (ATP-dependent)
  - **Kinesin**: walks along microtubules **toward the plus end**
  - **Dynein**: walks along microtubules **toward the minus end**

*Kinesin & cytoplasmic dynein, 2 molecular motor proteins, use microtubules as tracks for the transport of vesicle & non-vesicle cargos to their destinations*

“Use energy from ATP hydrolysis”
Microtubule-based transport systems

1) Axonemal transport (intraciliary & intraflagellar transport)

→ It is essential for delivery of tubulin dimers to the distal end of microtubules of cilia & flagella

→ The particles are mobilized by kinesin & dynein alone the microtubule

→ Defective axonemal transport results in the abnormal assembly of cilia & flagella
Microtubule-based transport systems

2. Axonal transport, along the axon of neuron

→ It is crucial for the traffic of neurotransmitter-containing vesicles to neuronal synapses

→ It conducts of nerve impulse

→ The vesicles are transported by kinesin & dynein
### Summary of components of cytoskeletal & functions

#### Microtubules
- **Polymer**: Heterodimers of αβ-tubulin
- **Subunit**: α and β tubulin (54 kDa)
- **Overall structure**: Hollow tube with a wall of 13 parallel protofilaments
- **Diameter**: 25 nm
- **Monomeric proteins**: α and β tubulin (54 kDa)
- **Polarity**: + and – ends
- **Relative stability**: Dynamic in cytoplasm; stable in axonemes
- **General locations**: Radiating through cytoplasm from concentration at centrosomes; axonemes
- **Key functions**: Maintain cell’s shape and polarity; provide tracks for organelle and chromosome movement; move cilia and flagella

#### Microfilaments
- **Polymer**: G-actin monomers
- **Subunit**: Globular G-actin (42 kDa)
- **Overall structure**: 2 intertwined filaments of F-actin
- **Diameter**: 5-7 nm
- **Monomeric proteins**: Globular G-actin (42 kDa)
- **Polarity**: + and – ends
- **Relative stability**: Dynamic
- **General locations**: Concentrated beneath cell membrane; in cell extensions like microvilli
- **Key functions**: Contract and move cells; change cell shape; cytokinesis; cytoplasmic transport and streaming

#### Intermediate filaments
- **Polymer**: Antiparallel tetramers of 2 rod-like dimers
- **Subunit**: Various α-helical rod-like proteins (~55 kDa, Table 2–5)
- **Overall structure**: Cable of 4 intertwined prototibrils, each consisting of bundled tetramers associated end to end
- **Diameter**: 8-10 nm
- **Polarity**: No apparent polarity
- **Relative stability**: Stable
- **General locations**: Arrayed throughout cytoplasm at desmosomes; inside nuclear envelop
- **Key functions**: Strengthen cell and tissue structure; maintain cell shape; maintain nuclear shape (lamins)
Cell adhesion (การยึดเกาะของเซลล์)

“Cell-Cell Adhesion”
: a selective process (cellular interaction)

- Cells adhere to other cells/extracellular matrix
- Cell adhesion is mediated by “cell adhesion molecules (CAMs)”
Cell adhesion molecules (CAMs)

- Adhesion molecules are proteins located on the cell surface.
- Are involved in binding with other cells / the extracellular matrix (ECM).

Mechanisms by which CAMs mediated cell-cell adhesion:

- Homophilic binding (the same type of CAMs)
- Heterophilic binding (different type of CAMs)
- Binding through extracellular linker molecule (less common)
The major families of Cell adhesion molecules (CAMs)

1. Ca^{2+} dependent molecules
   - Cadherin
   - Selectin
   "absent of Ca^{2+} \rightarrow break down the binding"

2. Ca^{2+} independent molecules
   - Integrin
   - Immunoglobulin (Ig) superfamily
     (structural domains similar to Immunoglobulin)
   "All molecules are mostly integral proteins"
1. Cadherin

- **Exoplasmic domain**

Four domains in the extracellular portion of cadherin bind to calcium. The function of cadherins is Ca\(^{2+}\)-dependent.

- **β-catenin binds to the intracellular tail of cadherin and the β-catenin/cadherin complex recruits α-catenin, which binds directly to actin. p120 catenin is a regulator of cadherin function.**

- **The sequence histidine-valine-alanine (HVA) facilitates the formation of cadherin cis-homophilic dimers.** Cadherin dimers of opposite cell membranes establish trans-homophilic or trans-heterophilic interaction.

- **Main adhesion protein holding epithelial cells together**

- **Play a major role in cell adhesion & morphogenesis**

- **The cytoplasmic tail interacts with actin filaments through a catenin complex (catenins & actin-binding proteins)**
Cadherin family members

- E-cadherin: found in epithelial sheets
- N-cadherin: found in the CNS, lens of eye, skeletal & cardiac muscle
- P-cadherin: found in placenta

Cadherin is main adhesion protein holding epithelial cells together

The expression of cell adhesion molecules, such as cadherins, decreases. This decrease weakens the cohesive nature of the intraepithelial tumor cells, and microinvasion starts when the basement membrane breaks down.

“A loss of cadherins is associated with cancer metastasis”
2. Selectin

There are 3 major types of selectins:

- **P-selectin** expressed by platelets & activated endothelial cells
- **E-selectin** expressed by activated endothelial cells
- **L-selectin** carries by leukocytes

Selectins have three extracellular domains:
1. A carbohydrate-recognition domain (CRD) specific for a particular sugar (galactose, mannose, N-acetylgalcosamine, and others).
2. A domain homologous to a repeat found in epidermal growth factor (EGF-like).
3. Many consensus repeats found in complement regulatory proteins.

Calcium bound at the sides of the CRD regulates the conformation of the domain and its ability to bind carbohydrates.

Role in inflammatory response:
- adhesion of leukocytes (white blood cells) to endothelium (vessel wall)
3. Integrin

- **Heterodimers adhesion molecule**
- Consist of 2 subunits: β & α
- Bind to the extracellular matrix (ECM) & the internal cytoskeleton
  - The cytoplasmic domain (β subunit) interacts with actin filaments
  - The extracellular domain binds to fibronectin & laminin
4. Immunoglobulin (Ig) superfamily

- The extracellular segment of Ig superfamily is folded into 2-6 immunoglobulin-like domains.

- ICAM & VCAM play an important role in T-cell interactions & binding of leukocytes to activated or resting endothelial cells in the inflammatory areas (homing process during inflammation).
Homing, a process involving selectins & integrins

“Selectins, together with integrins & intercellular cell adhesion molecules (ICAMs), play a significant role in inflammation & in the periodic migration of lymphocytes from the circulation into lymphoid organs (homing)”
The inflammatory response

The WBC-endothelial cell interaction requires

2 types of cell adhesion proteins:

selectins & integrins

Go to "Inflammatory site"
Cell junctions

Lateral surface specialization: Intercellular junctions

- Intercellular junctions are membrane-associated structures contributing to adhesion or communication between adjacent cells.

- 3 types of intercellular junctions
  1. Tight junction (zonula occludens) (a)
  2. Adherens /anchoring junction
     - Zonula adherens (belt desmosome) (b)
     - Macula adherens (spot desmosome/desmosome) (c)
  3. Communicating junction
     - Gap junction (nexus) (e)
1. Tight (occluding) junction

- A **circumferential belts** at the apical domain of epithelial cells

**Functions**

- **Determine epithelial cell polarity**
- **Seal the space between epithelial cells (paracellular barrier)** & regulate the passage of water & flux of ions between adjacent epithelial cells (paracellular pathway)

“Control the paracellular pathway of solutes, ions & water (involved in active transport)”
Molecular organization of tight junction

- Consists of transmembrane proteins; **occludin**, **claudins** & **junctional adhesion molecules** (JAMs)

- The adaptor proteins zonula occludens **ZO-1, ZO-2 & ZO-3** link **occludins**, **claudins** & **JAMs** to **actin microfilaments**

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**Afadin-nectin complex is anchored to ZO-1. Nectins form cis-homodimers, which interact with each other (trans-homo interaction) through the extracellular region.**

**Junctional adhesion molecules (JAMs) are associated to afadin and ZO-1. JAMs cis-homodimers interact with each other (trans-homo interaction) and determine the formation of cell polarity.**

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**Occludin and claudins are the molecular basis for the formation of tight junction strands seen in freeze-fracture preparations.**

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**Zonula occludens proteins (ZO-1, ZO-2, and ZO-3) facilitate the reciprocal interaction of occludin, claudins, and JAMs with F-actin.**

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**Paracellular pathway**

**Transcellular pathway**
2. Adherens junction → Provide adhesion of cells using cell adhesion molecules (CAMs) that link into cytoskeleton of adjacent cells

2.1) Zonula adherens (belt desmosome)

Anchoring cell to other cell by forming a belt around apical cell surface & associated with actin filaments
The cadherin-catenin complex regulates cell adhesion, polarity, differentiation, migration, proliferation & survival of the cell.
2.2) Macula adherens (spot desmosome, desmosomes)

- Macula adherens form links between cells & provide a connection between intermediate filaments of the cell cytoskeletons
- Keratin intermediate filaments (tonofilaments) anchor the dense plaque
- Provide strength & rigidity to epithelial cells, particularly in the stratified squamous cells
Molecular organization of macula adherens

- Two disc-like plaques connected across intercellular space
- Plaques of adjacent cells are joined by **cadherins** (no catenin)
- Intermediate filaments insert into plaque from cytoplasmic side
2.3) Hemidesmosome

- A asymmetrical structure
- Observed in basal cells of stratified squamous epithelium attaching to the basement membrane
- Hemidesmosome increases the overall stability of epithelial tissue****
Structure & composition of hemidesmosome

- Inner protein plate attaching to intermediate filaments
- Outer cellular plaque attaching to basal lamina by linking of
  - Integrin $\alpha_6\beta_4$
  - Anchoring filament (laminin 5)
- BPAG1 & BPAG2 connect to the basal lamina to keratin intermediate filaments
Clinical significant “Bullous pemphigoid”

- Is autoimmune blistering disease
- Blisters / bullae develop at the epidermis-dermis junction
- Damage the attachment of hemidesmosome & disturb the synthesis of anchoring proteins by basal cells
- The epidermis become detached from the basal lamina anchoring site
3. Gap junction (intercellular channels)

- A symmetrical “communicating junction”
- Is not anchoring junctions
- Allow direct electrical & chemical communications between cells

Membrane proteins from the adjacent cells line up to form a channel.
Molecular organization of gap junctions

- Is formed by connexin monomer
  (20 members of the family)
- 6 connexins form a connexon inserted into cell membrane
- Connexons pair with their counterparts in the cell membrane of an adjacent cells form an intercellular channel allowing the cell-cell diffusion of ions & small molecules

Forming of 6 connexin monomers surrounding a central channel → a hexametric connexon
Summary: several specialized intercellular junctions in lateral surfaces with different functions

<table>
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<tr>
<th>Junction</th>
<th>Tight Junction (Zonula Occludens)</th>
<th>Adherent Junction (Zonula Adherens)</th>
<th>Desmosome (Macula Adherens)</th>
<th>Hemidesmosome</th>
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<tr>
<td>Major transmembrane link proteins</td>
<td>Occludins, claudins, ZO proteins</td>
<td>E-cadherin, catenin complexes</td>
<td>Cadherin family proteins (desmogleins, desmocollin)</td>
<td>Integrins</td>
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<td>Cytoskeletal components</td>
<td>Actin filaments</td>
<td>Actin filaments</td>
<td>Intermediate filaments (keratins)</td>
<td>Intermediate filaments</td>
<td>None</td>
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<tr>
<td>Major functions</td>
<td>Seals adjacent cells to one another, controlling passage of molecules between them; separates apical and basolateral membrane domains</td>
<td>Provides points linking the cytoskeletons of adjacent cells; strengthens and stabilizes nearby tight junctions</td>
<td>Provides points of strong intermediate filament coupling between adjacent cells, strengthening the tissue</td>
<td>Anchors cytoskeleton to the basal lamina</td>
<td>Allows direct transfer of small molecules and ions from one cell to another</td>
</tr>
<tr>
<td>Medical significance</td>
<td>Defects in occludins may compromise the fetal blood-brain barrier, leading to severe neurologic disorders</td>
<td>Loss of E-cadherin in epithelial cell tumors (carcinomas) promotes tumor invasion and the shift to malignancy</td>
<td>Autoimmunity against desmogleins leads to dyshesive skin disorders characterized by reduced cohesion of epidermal cells</td>
<td>Mutations in the integrin-β4 gene are linked to some types of epidermolysis bullosa, a skin blistering disorder</td>
<td>Mutations in various connexin genes have been linked to certain types of deafness and peripheral neuropathy</td>
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Summary of cell junctions & cell adhesion molecules

Zonula adherens (belt desmosome)
It consists of a dense plaque associated with the catenin complex (α-catenin, β-catenin and p120), α-actinin, vinculin and fomrin-1. Actin filaments are attached to the catenin complex. The intercellular space is bridged by cadherins and the afadin-nectin complex connecting the opposite dense plaques.

Tight junctions (occluding junctions)
Consist of the transmembrane proteins occludin and claudins, associated with ZO-1, ZO-2, ZO-3, and the afadin-nectin complex at the intracellular side. Occludin and claudins seal the intercellular space.

Macula adherens (spot desmosome)
Desmosomes are symmetrical structures consisting of: (1) plaques containing desmoplakins, plakoglobin and plakophilins (2) linking cadherins (mainly desmocollins and desmogleins) and (3) keratin filaments attached to the plaques.

Hemidesmosomes
Hemidesmosomes consist of an inner plate, the anchoring site of the intermediate filament keratin and an outer plaque, attached to the basal lamina by two major components: anchoring filaments (laminin 5) and integrin α6β4.

Selectin
Selectins are Ca\(^{2+}\)-dependent molecules with binding affinity for sugars. Selectins have an important role in the homing process.

Integrins
On the extracellular side, integrins interact directly with fibronectin and laminin. On the intracellular side, the β subunits of integrin interact with actin through intermediate proteins (including α-actinin, vinculin, and talin).

Laminin
Laminin consists of three polypeptide chains (α, β, and γ) with binding sites for type IV collagen, proteoglycan perlec, integrin, and nidogen.
References