Lecture 18 Integrating cells into tissues I

Outline

I. Overview of cell-cell and cell-ECM junction and adhesion

II. Cadherins and cell- cell adhesion

III. Integrins in cell-ECM adhesion

- Cells are the basic building blocks of an organism.
- How do the cells arrange into a 3-D “architecture”?

Let us first take a look at how a building is made up

- Steel-concrete-skeleton
- Room-room connection
- Pipelines
- Cords
- Specialized rooms

etc.

From cells to tissues

- Cytoskeleton resides inside the cells to maintain inner structural support
- Cell and cell link together through either direct cell-cell contact or extracellular matrix (ECM)
- ECM maintains extracellular support.
- ECM is secreted by cells. Different type of cells secret different types of ECM based on their function.
- Cells aggregate into “tissue” which can coordinate together.

Plant cells have strong cell wall to support its structure

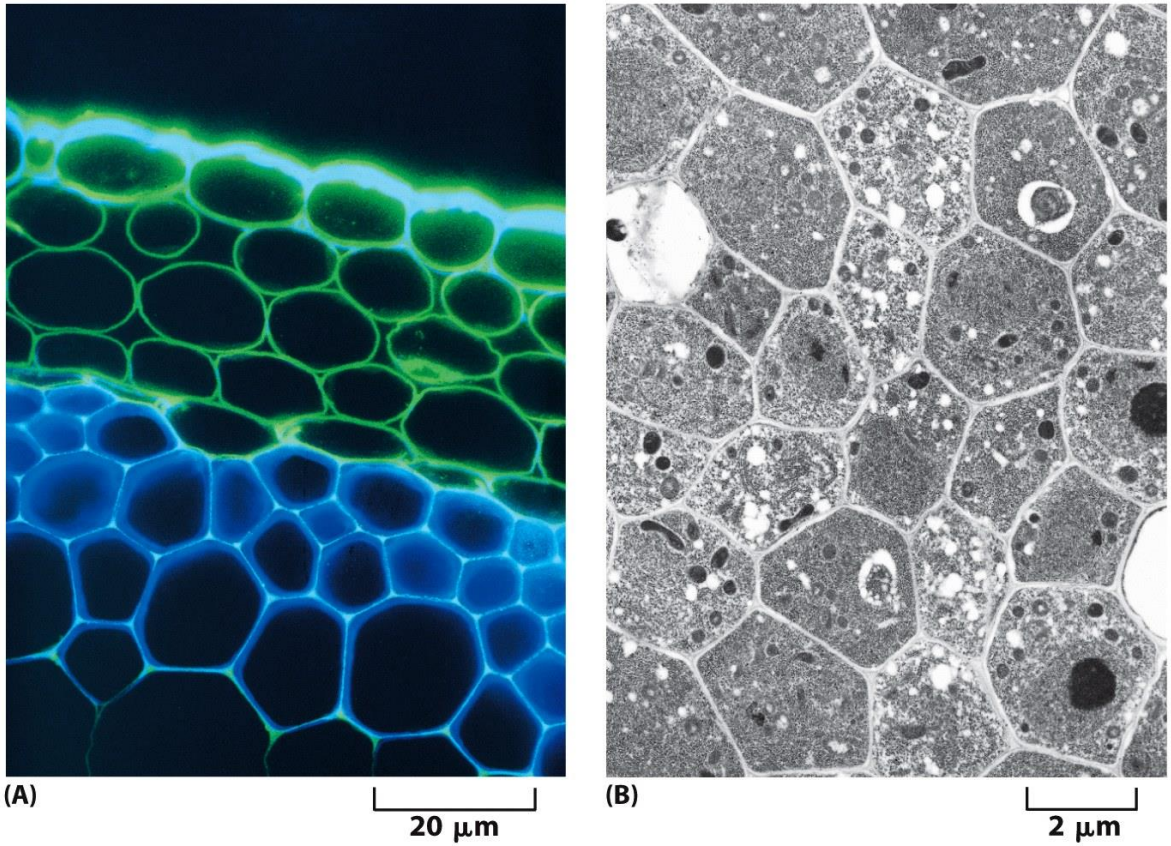


Figure 20-3 Essential Cell Biology 3/e (© Garland Science 2010)

Cell wall is made of cell matrix
Secreted by plant cells.

Green: polysaccharide(outer root cross-section)
Blue: cellulose(inner root cross-section)

Four major types of tissues

- Epithelial tissue
- Connective tissue (plenty amount of ECM)
- Neuron tissue
- Muscle tissue

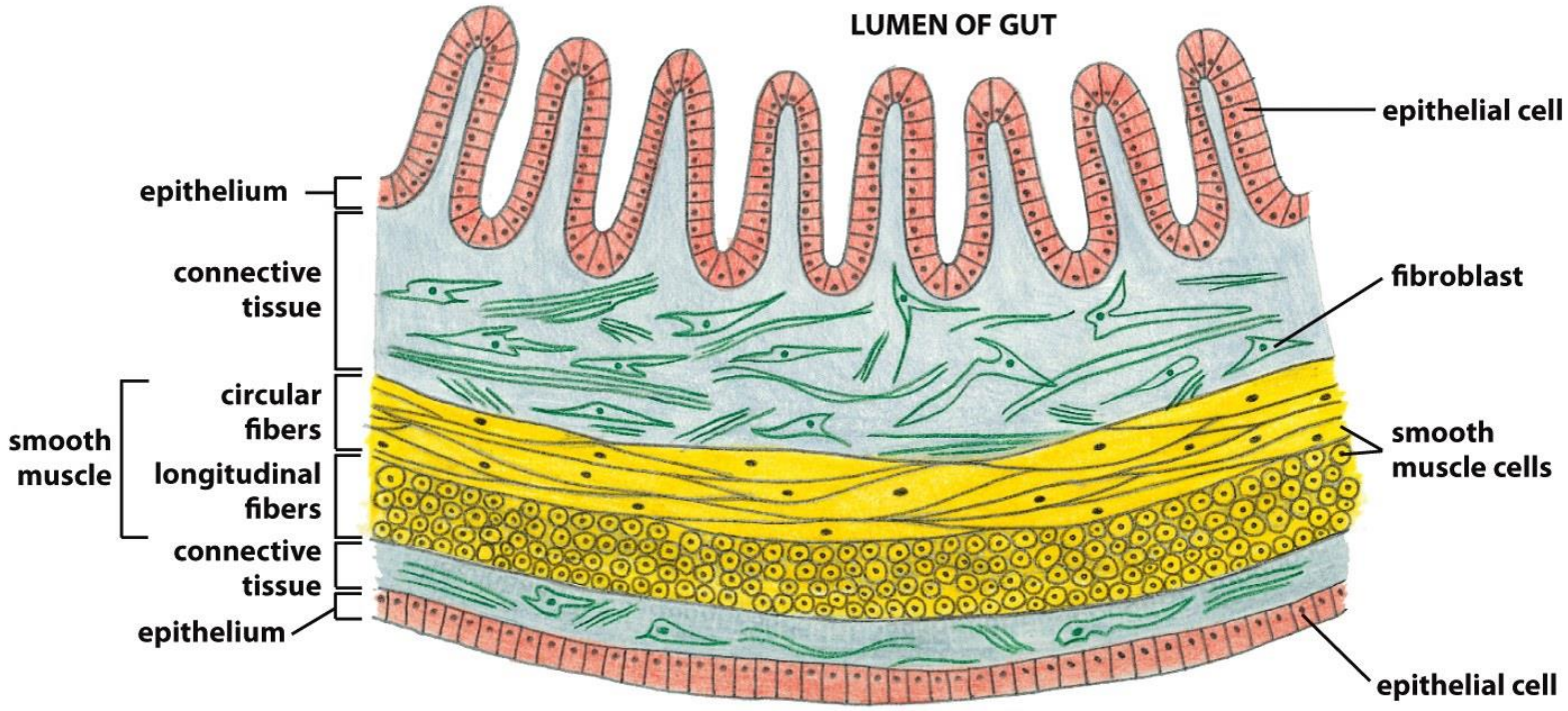


Figure 20-2 Essential Cell Biology 3/e (© Garland Science 2010)

- Normally fibroblast secret proteins to make up ECM

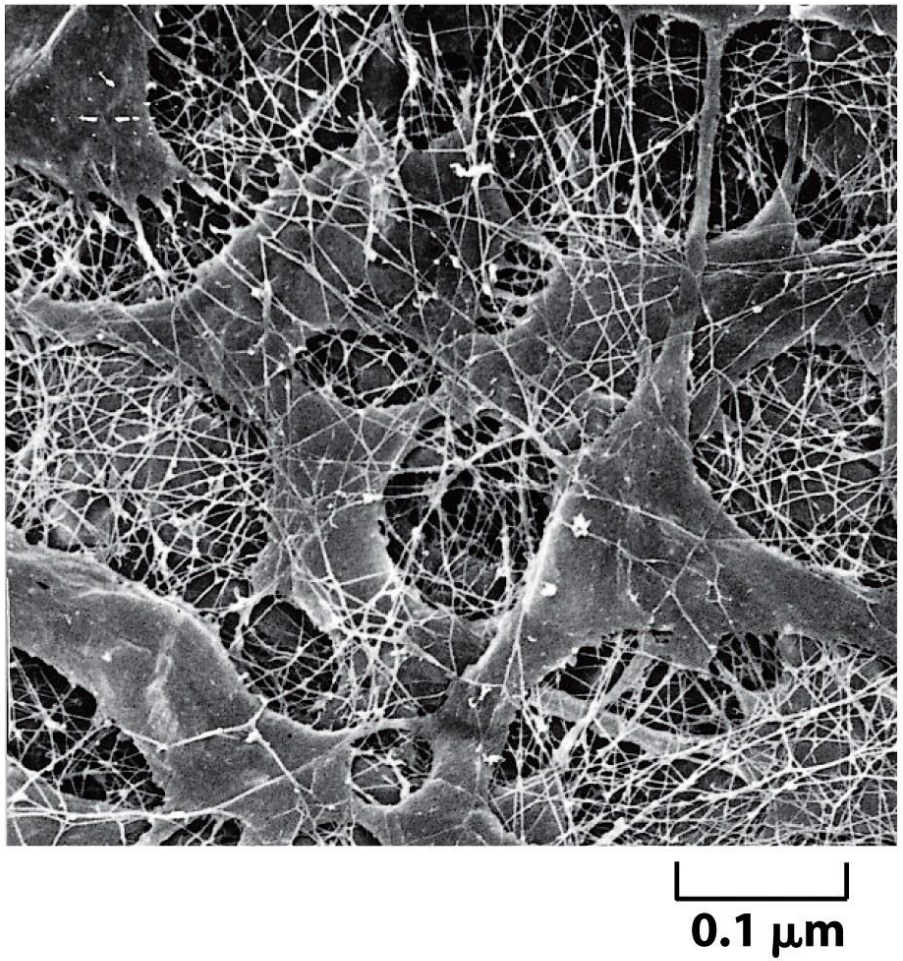
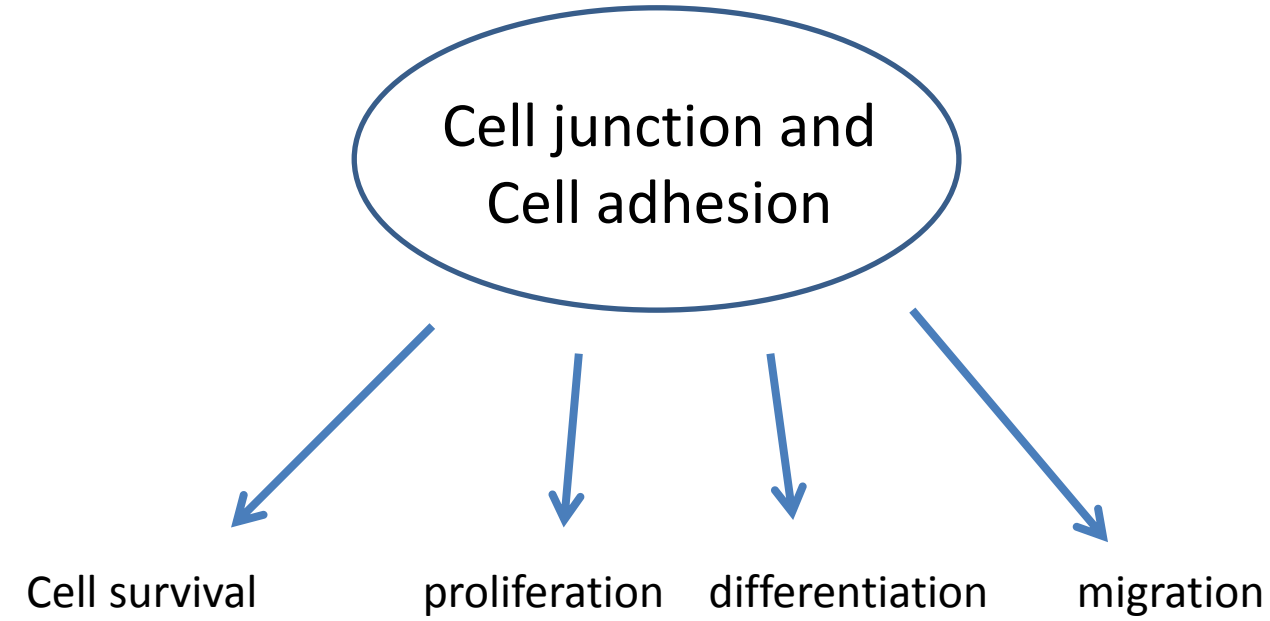


Figure 20-10 Essential Cell Biology 3/e (© Garland Science 2010)

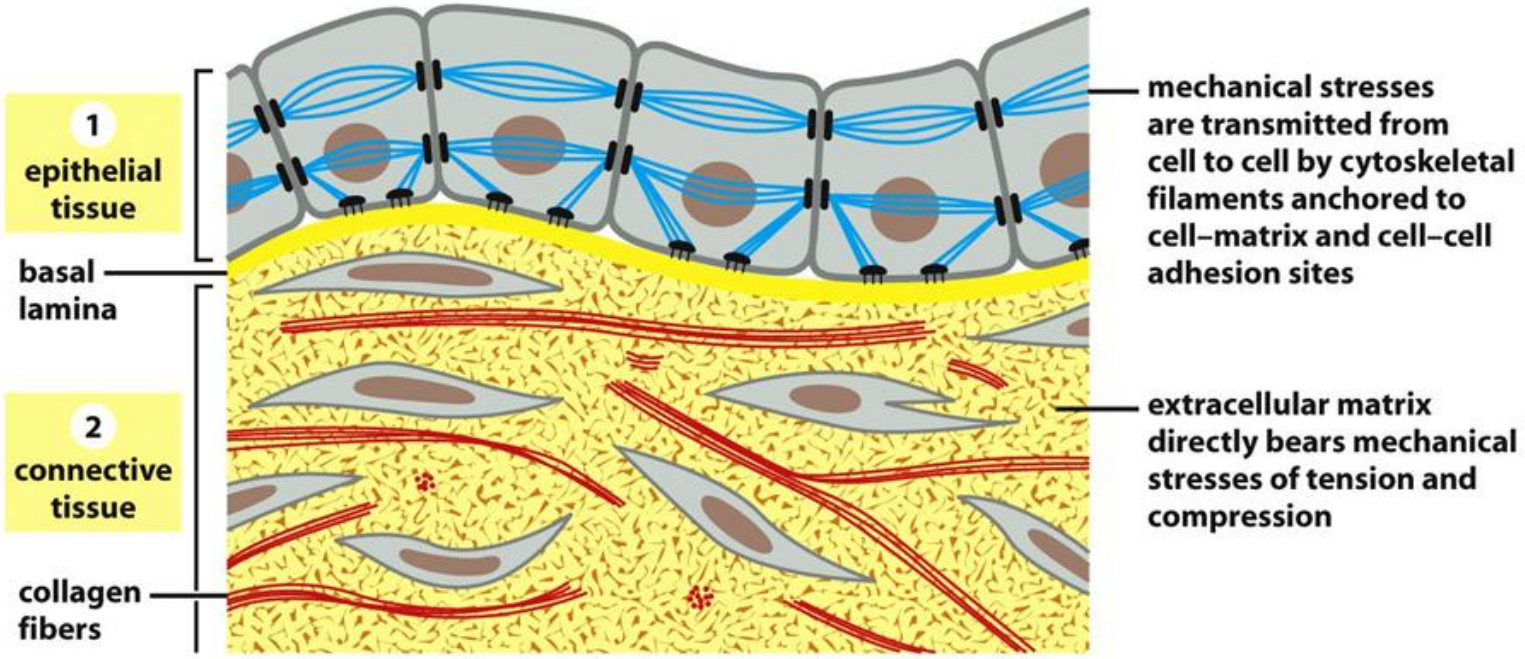
- Cell junction and adhesion are very important for multicellular organisms

1). Allow cells to aggregate into distinct tissues

2). Bidirectional communication between interior and exterior of cells



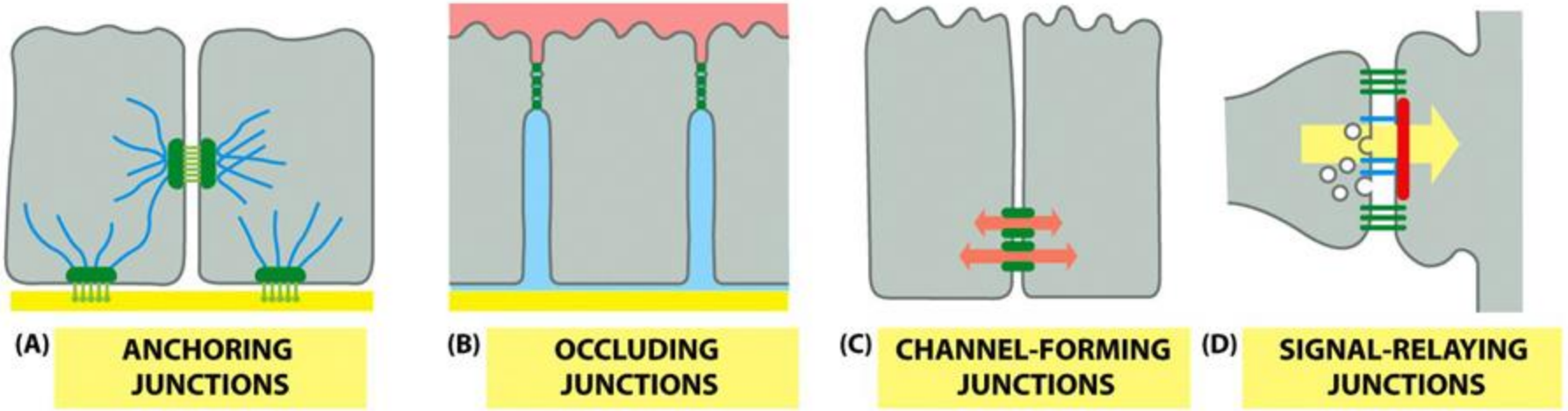
Epithelial and connective tissues



Epithelial tissue: cell- cell junctions

Connective tissue: Cell- ECM adhesions

Four major types of junctions

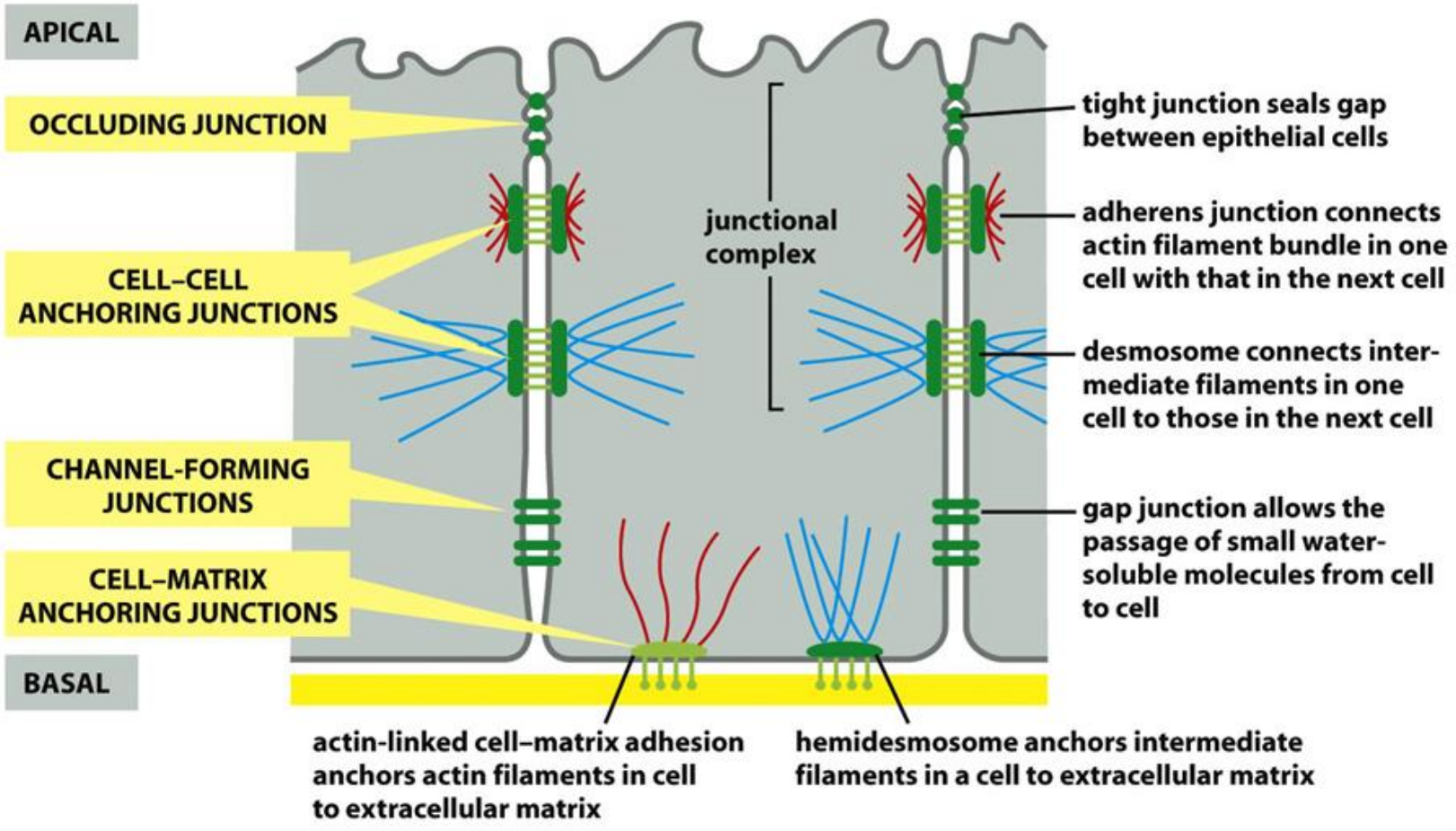


1. Anchoring junctions
2. Occluding junctions
3. Channel-forming junctions
4. Signal relaying junctions

Table 19–1 A Functional Classification of Cell Junctions

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)
OCCLUDING JUNCTIONS
1. tight junctions (in vertebrates)
2. septate junctions (in invertebrates)
CHANNEL-FORMING JUNCTIONS
1. gap junctions (in animals)
2. plasmodesmata (in plants)
SIGNAL-RELAYING JUNCTIONS
1. chemical synapses (in the nervous system)
2. immunological synapses (in the immune system)
3. transmembrane ligand–receptor cell–cell signaling contacts (Delta-Notch, ephrin-Eph, etc.). Anchoring, occluding, and channel-forming junctions can all have signaling functions in addition to their structural roles

Summary of the cell junctions



- Transmembrane adhesion proteins mediate anchoring junctions
  - Cadherins: cell-cell attachment (link actin filaments or intermediate filaments)
  - Integrins: cell-matrix attachment (link actin filaments or intermeidate filaments

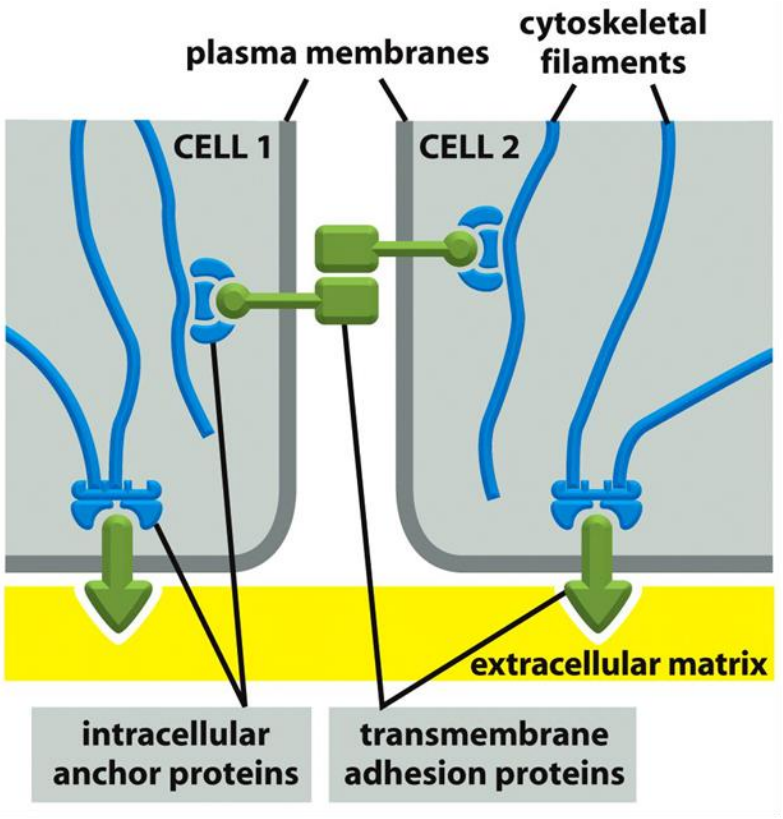


Table 19–2 Anchoring Junctions

JUNCTION	TRANSMEMBRANE ADHESION PROTEIN	EXTRACELLULAR LIGAND	INTRACELLULAR CYTOSKELETAL ATTACHMENT	INTRACELLULAR ANCHOR PROTEINS
Cell–Cell				
adherens junction	cadherin (classical cadherin)	cadherin in neighboring cell	actin filaments	α-catenin, β-catenin, plakoglobin (γ-catenin), p120-catenin, vinculin, α-actinin
desmosome	cadherin (desmoglein, desmocollin)	desmoglein and desmocollin in neighboring cell	intermediate filaments	plakoglobin (γ-catenin), plakophilin, desmoplakin
Cell–Matrix				
actin-linked cell–matrix adhesion	integrin	extracellular matrix proteins	actin filaments	talin, vinculin, α-actinin, filamin, paxillin, focal adhesion kinase (FAK)
hemidesmosome	integrin α6β4, type XVII collagen (BP180)	extracellular matrix proteins	intermediate filaments	plectin, dystonin (BP230)

II. Cadherins and cell-cell adhesion

- 1. cadherins family
- 2. homophilic binding for cadherins
- 3. adheren junctions
- 4. desmosome junctions
- 5. selectins in blood cells adhesion
- 6. immunoglobulin proteins mediate Ca2+-independent adhesion
-

1. Cadherins family

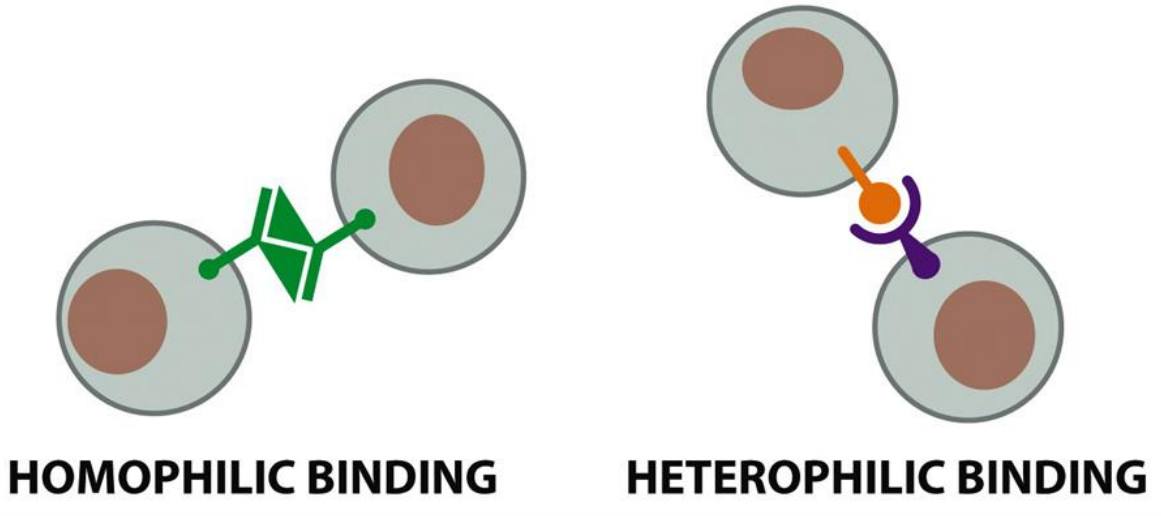
- Derived from (“Ca2+” + “adherin”), meaning Ca2+-dependent.
- To dissociate cells from tissue, need EDTA/trypsin, EDTA can chelate Ca2+ to deactivate cadherins.
- Plants, fungi, bacteria and archaea have no cadherins.
- Classical cadherins and non-classical cadherins, over 180 family members in humans.

Table 19–3 Some Members of the Cadherin Superfamily

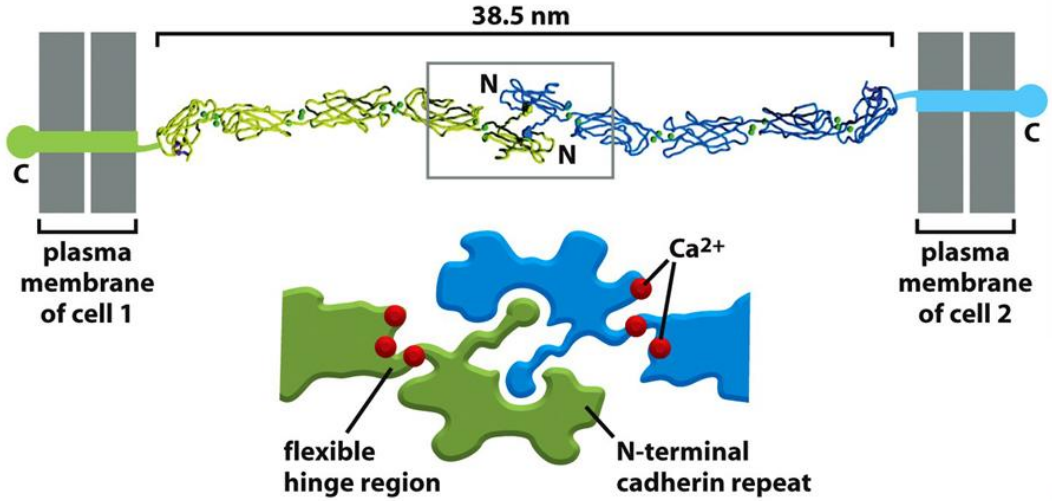
NAME	MAIN LOCATION	JUNCTION ASSOCIATION	PHENOTYPE WHEN INACTIVATED IN MICE
Classical cadherins			
E-cadherin	many epithelia	adherens junctions	death at blastocyst stage; embryos fail to undergo compaction
N-cadherin	neurons, heart, skeletal muscle, lens, and fibroblasts	adherens junctions and chemical synapses	embryos die from heart defects
P-cadherin	placenta, epidermis, breast epithelium	adherens junctions	abnormal mammary gland development
VE-cadherin	endothelial cells	adherens junctions	abnormal vascular development (apoptosis of endothelial cells)
Nonclassical cadherins			
Desmocollin	skin	desmosomes	blistering of skin
Desmoglein	skin	desmosomes	blistering skin disease due to loss of keratinocyte cell–cell adhesion
T-cadherin	neurons, muscle, heart	none	unknown
Cadherin 23	inner ear, other epithelia	links between stereocilia in sensory hair cells	deafness
Fat (in *Drosophila*)	epithelia and central nervous system	signal-relaying junction (planar cell polarity)	enlarged imaginal discs and tumors; disrupted planar cell polarity
Fat1 (in mammals)	various epithelia and central nervous system	slit diaphragm in kidney glomerulus and other cell junctions	loss of slit diaphragm; malformation of forebrain and eye
α, β, and γ-Protocadherins	neurons	chemical synapses and nonsynaptic membranes	neuronal degeneration
Flamingo	sensory and some other epithelia	cell–cell junctions	disrupted planar cell polarity; neural tube defects

2. Homophilic binding for cadherins

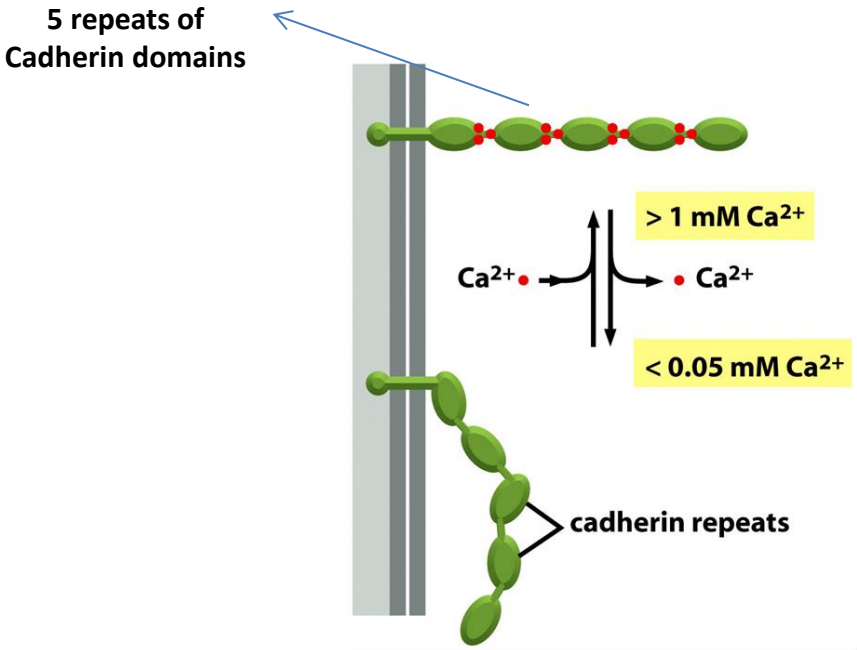
- Homophilic: the same type of cadherin binds to the same type of cadherin

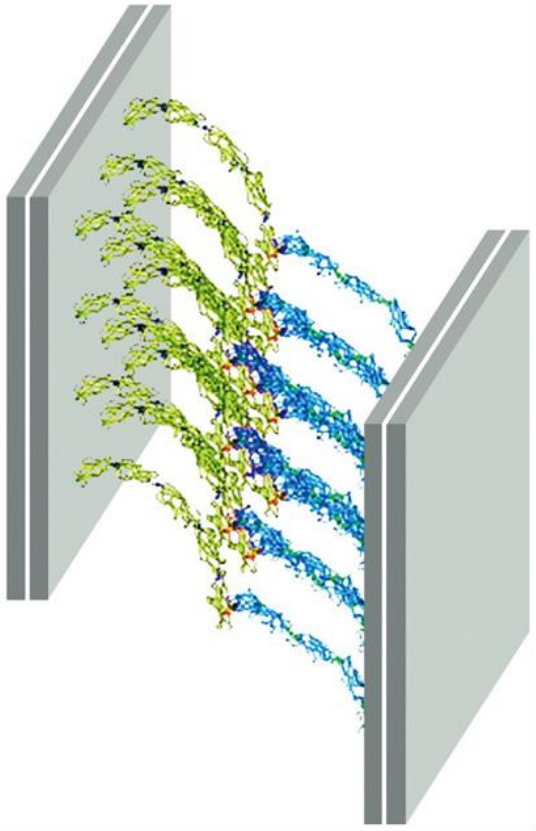


Mechanisms for cadherin function



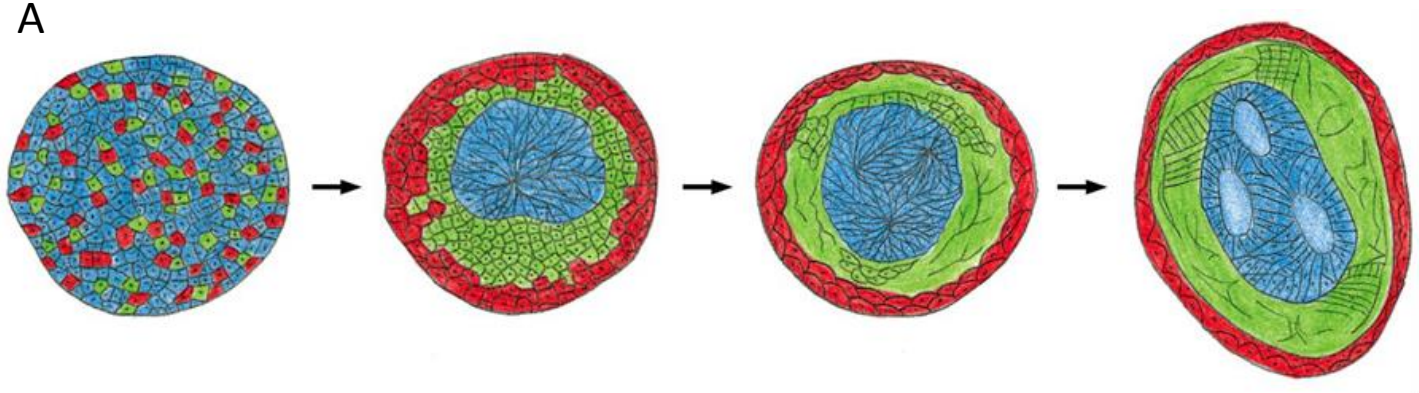
Ca2+ binding make cadherins adopt extended configuration, and bind To the other cadherins in another cell.





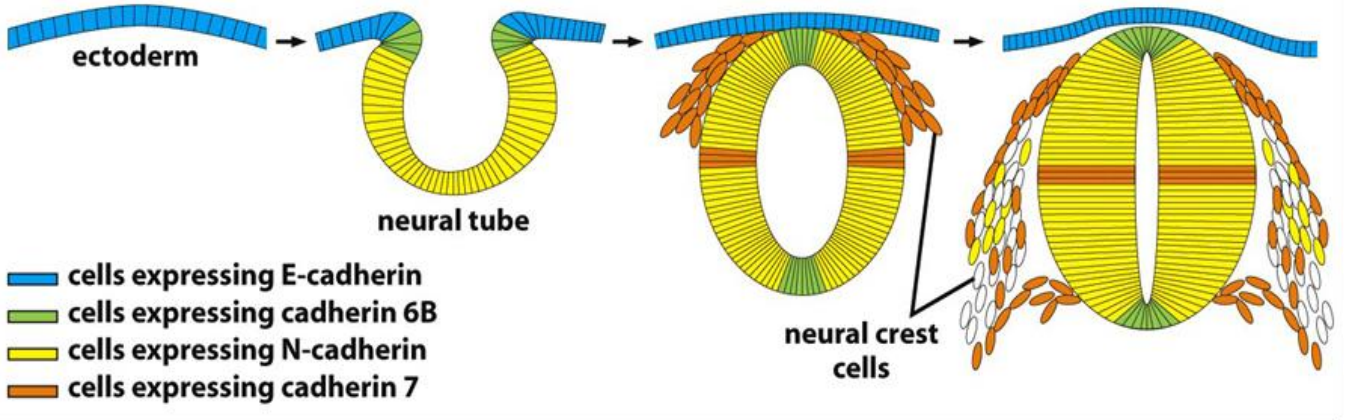
Cadherins control selective assortment of cells

A



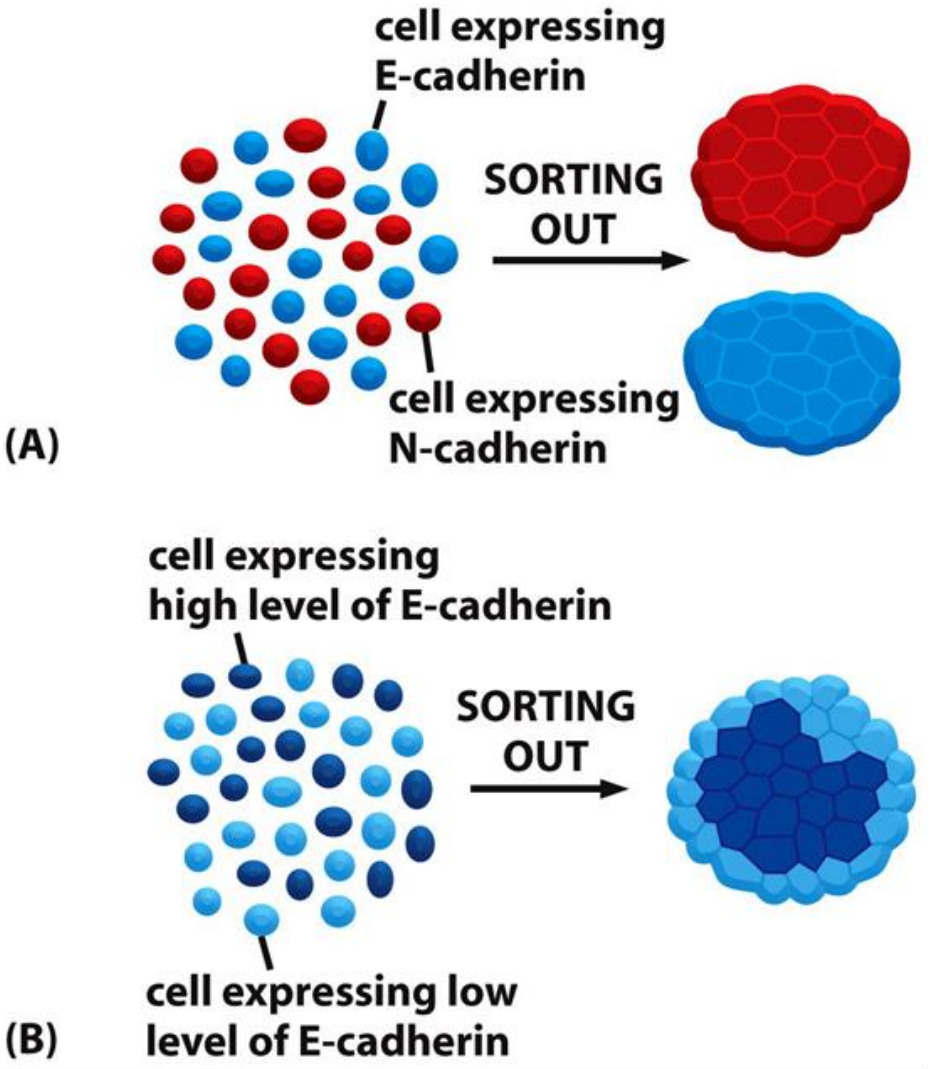
Embryo cells were dissociated and then automatically reassembled in vitro.

B

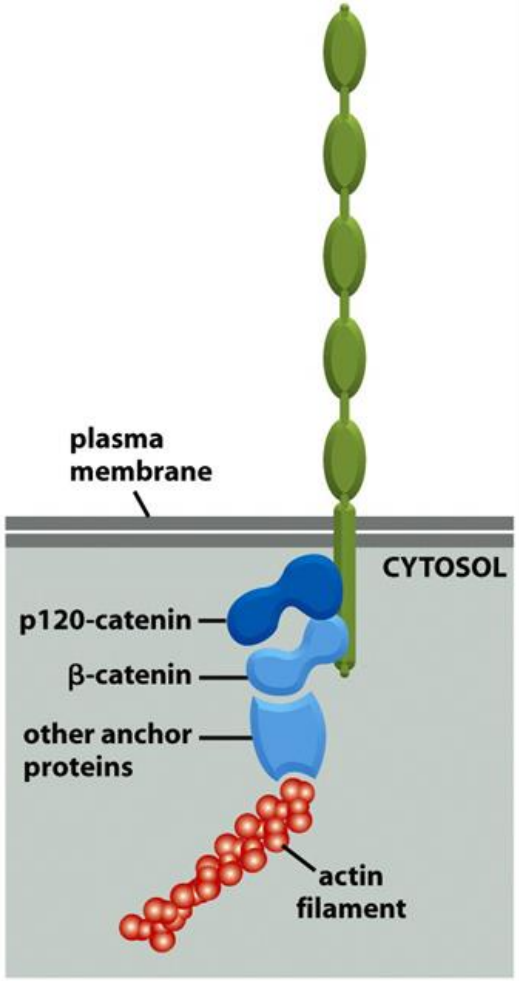


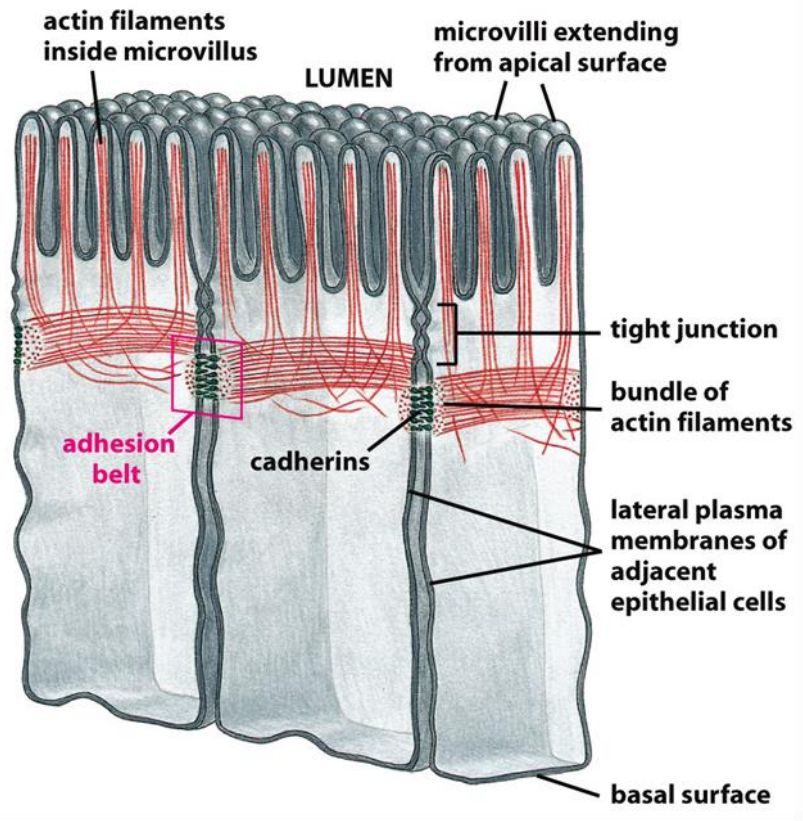
During embryonic Development, cells Expressing the same Cadherins group Together

Experiments: cells overexpression different cadherins sort out.

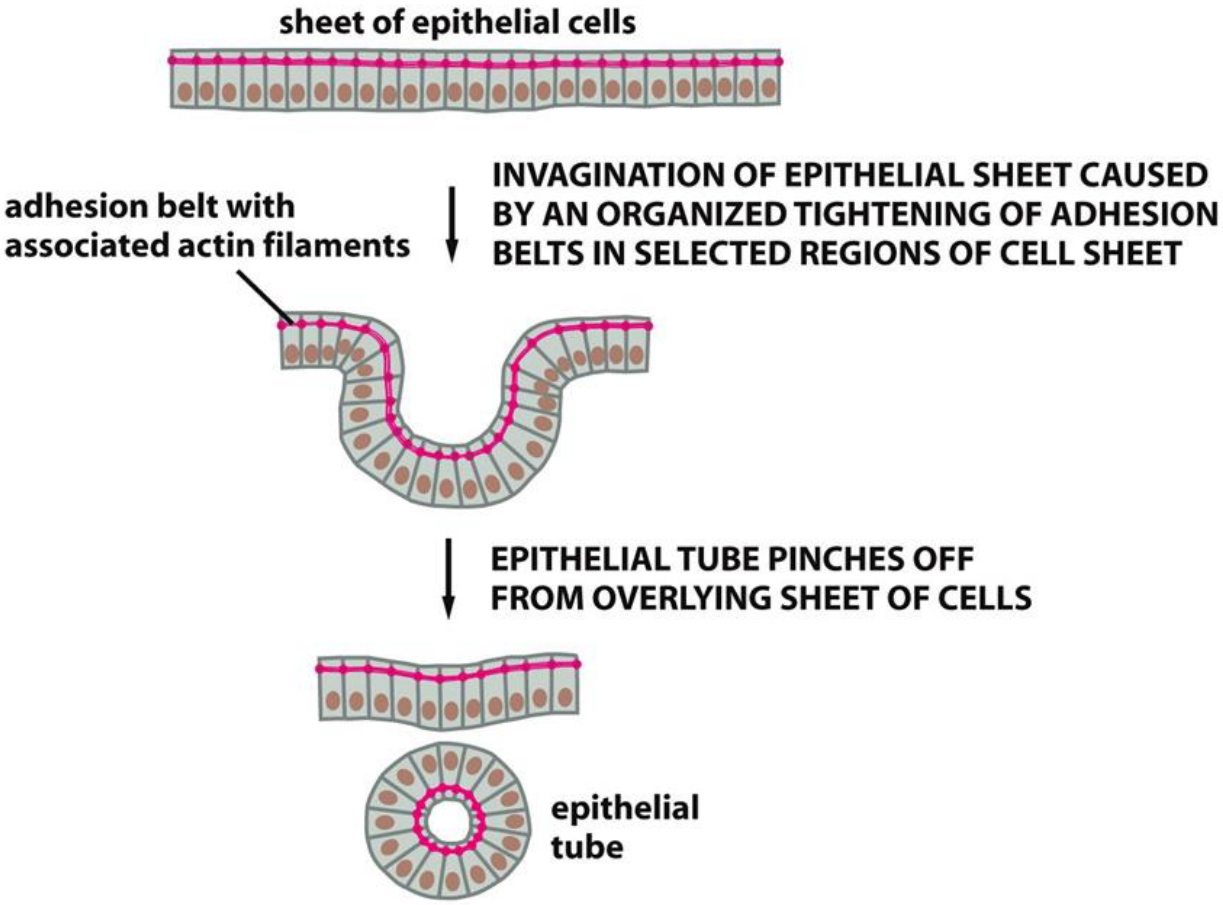


3. β-Catenin link classical cadherins to the actin cytoskeleton in adheren junctions





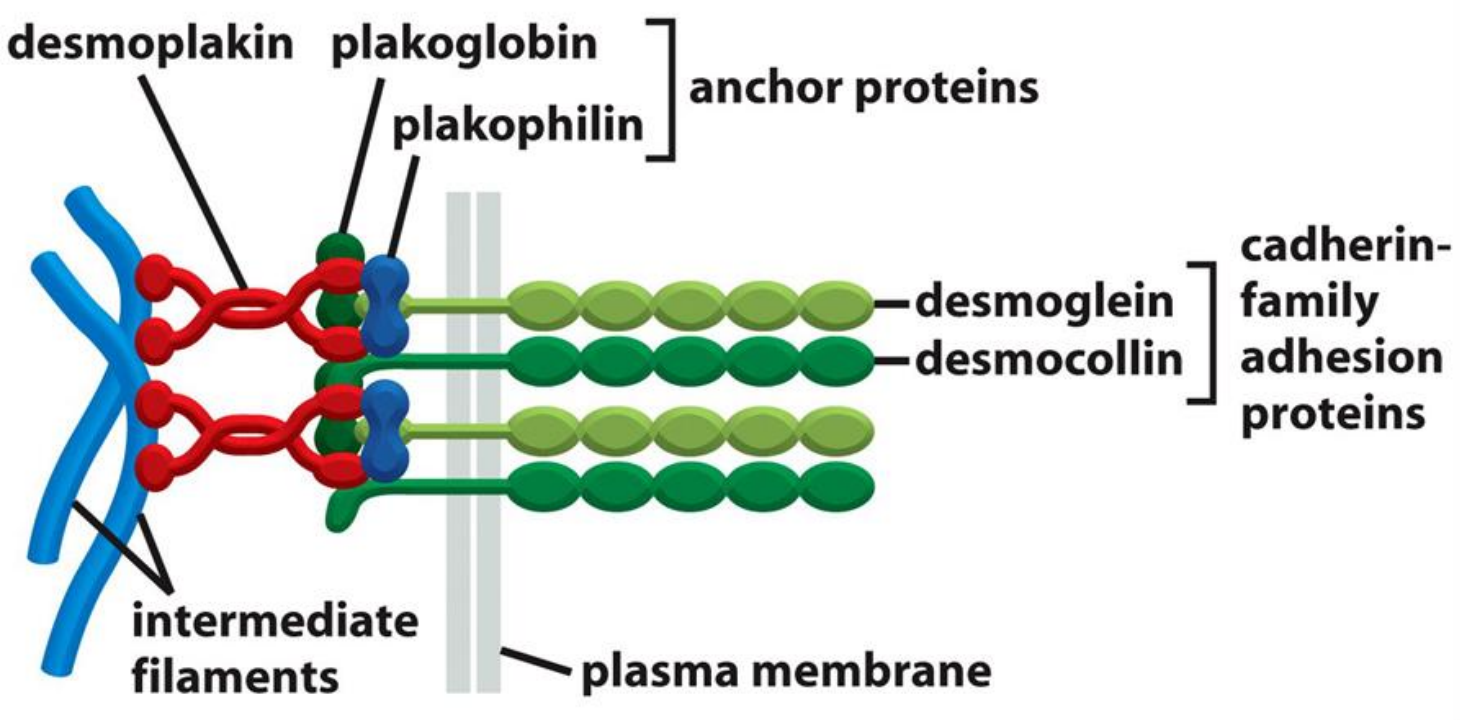
- Myosin motor can cause contraction on the adhesion belt to form epithelial tube



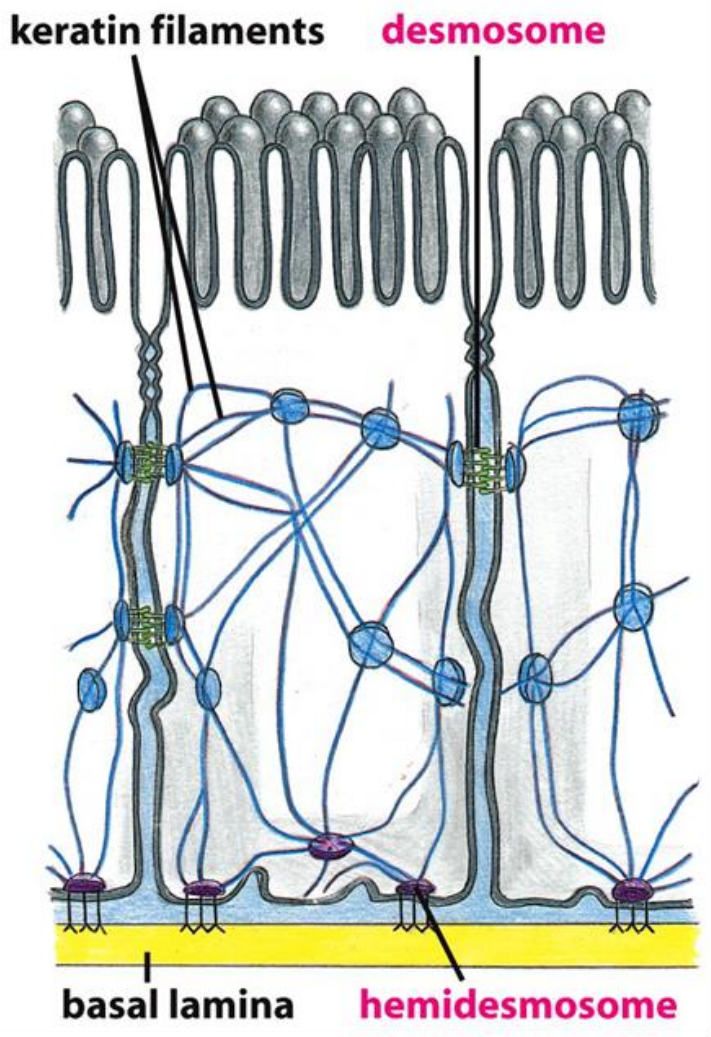
4. Desmosome junctions

- Cadherins links to intermediate filaments
- Give cells mechanical strength
- Plentiful in epithelium, but not found in Drosophila

Structure of desmosome junction



•Desmosome, hemi-desmosome and intermediate filament network



5. Selectins in blood cell adhesion

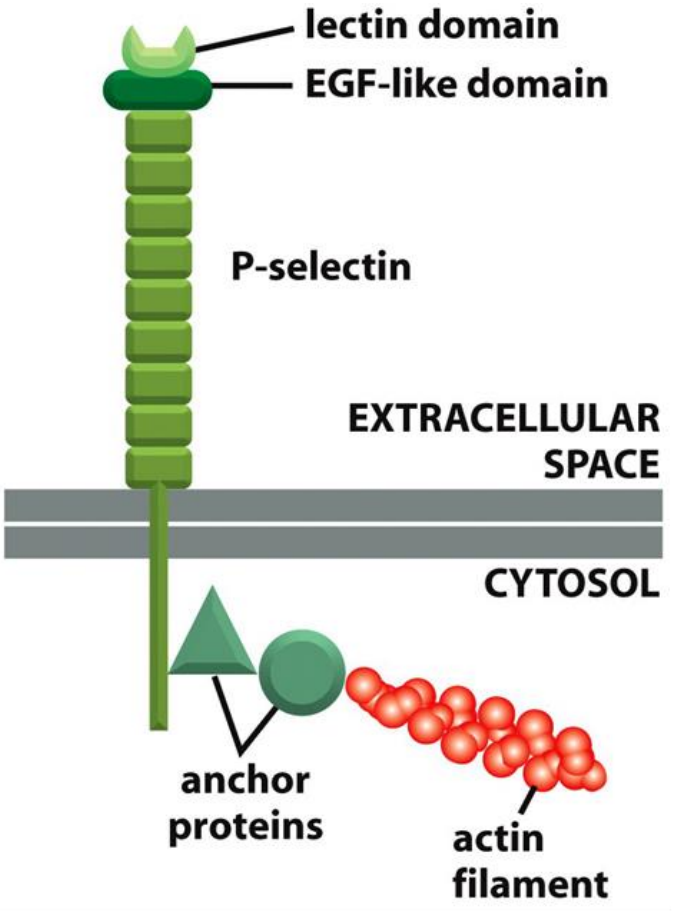
- Ca2+ dependent
- Mediate transient adhesion
- Bind to lectins
- At least 3 types:

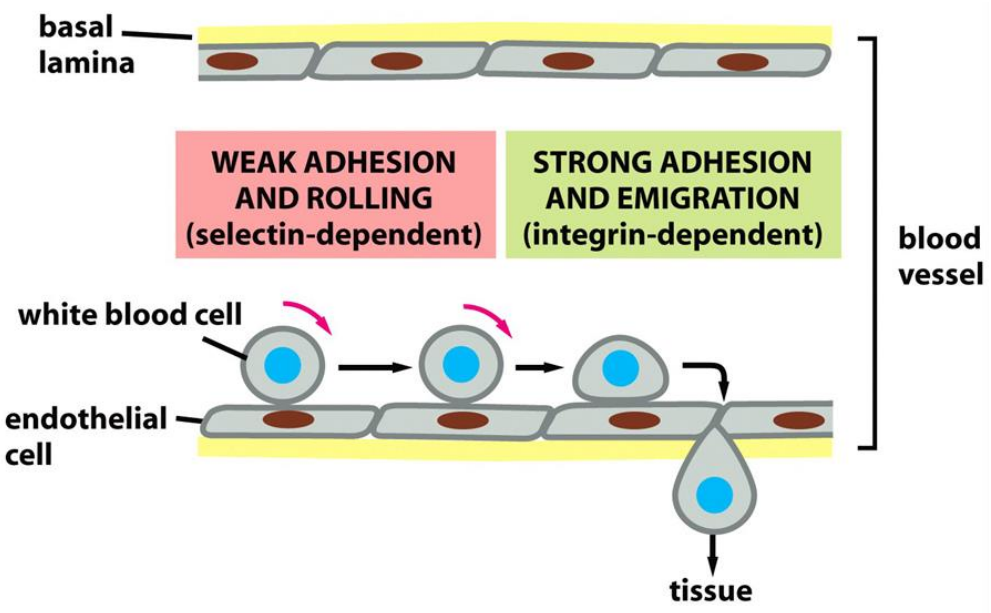
  L-selectin: on white blood cells

  P-selectin: on platelets and endothelial cells

  E-selectin: on activated endothelial cells

The structure and functions for selectins





Selectins binding is weak, they collaborate with Integrin to cause emigration of white blood cells To sites of action.

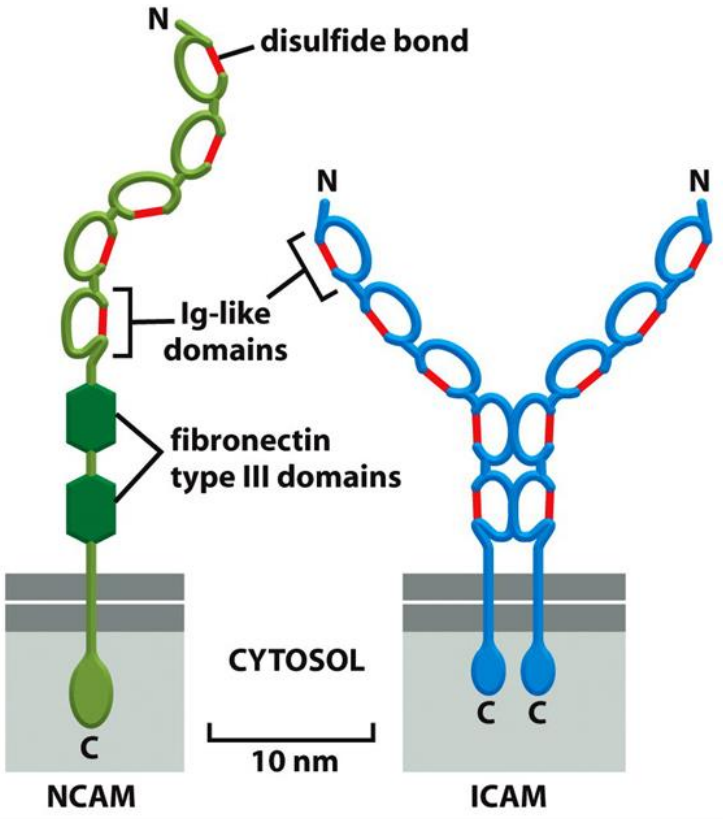
6. Ig superfamily members

- Ca2+ -independent
- Heavy glycosylation, multiple disulfide bonds
- Bind to integrin
- several major proteins:

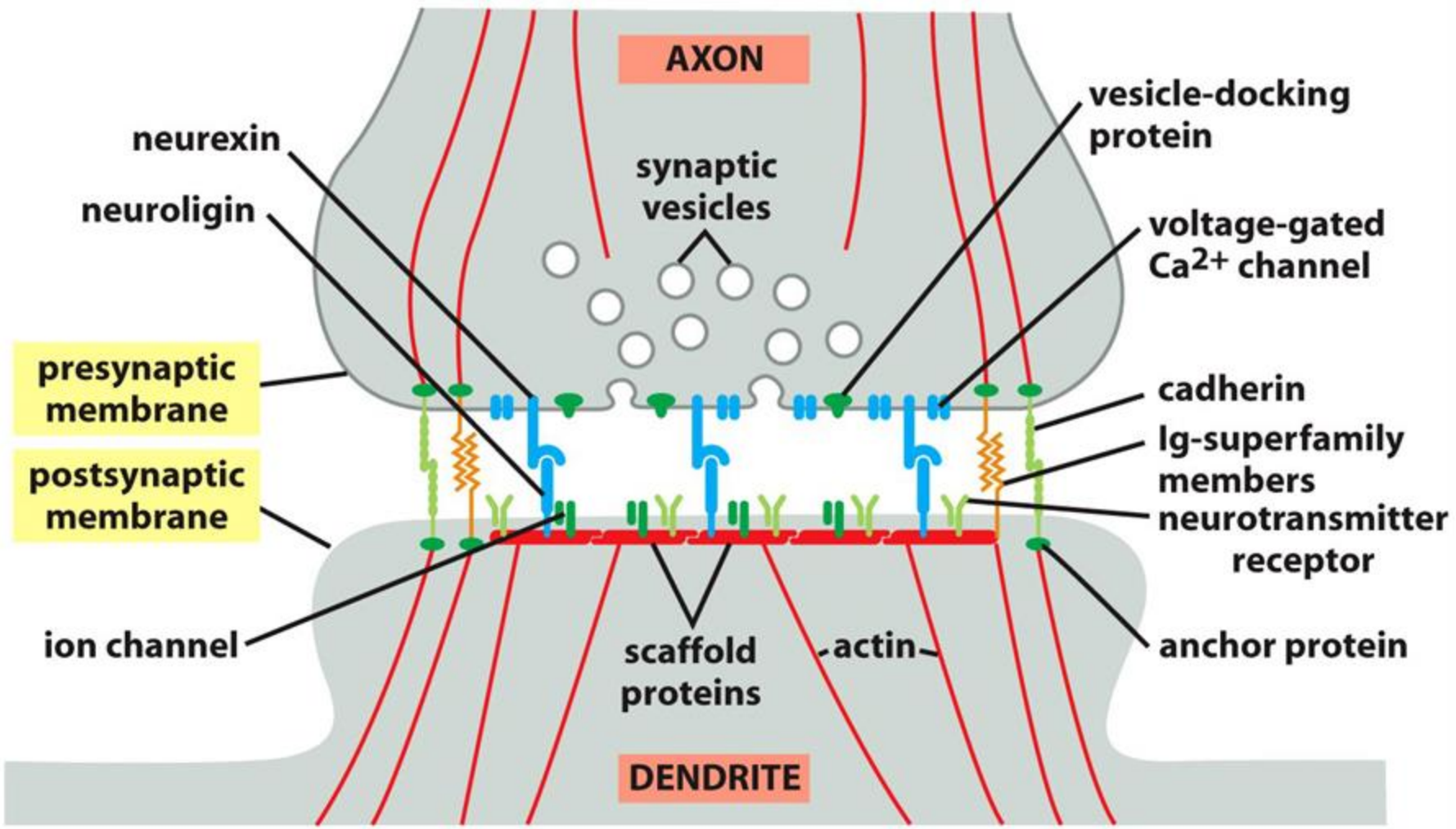
  ICAMs (intercellular cell adhesion molecules)

  VCAMs(vascular cell adhesion molecules)

  NCAM (neural cell adhesion molecule)



- Many types of adhesion molecules act together to create a synapse



III. Integrins in cell–matrix adhesion

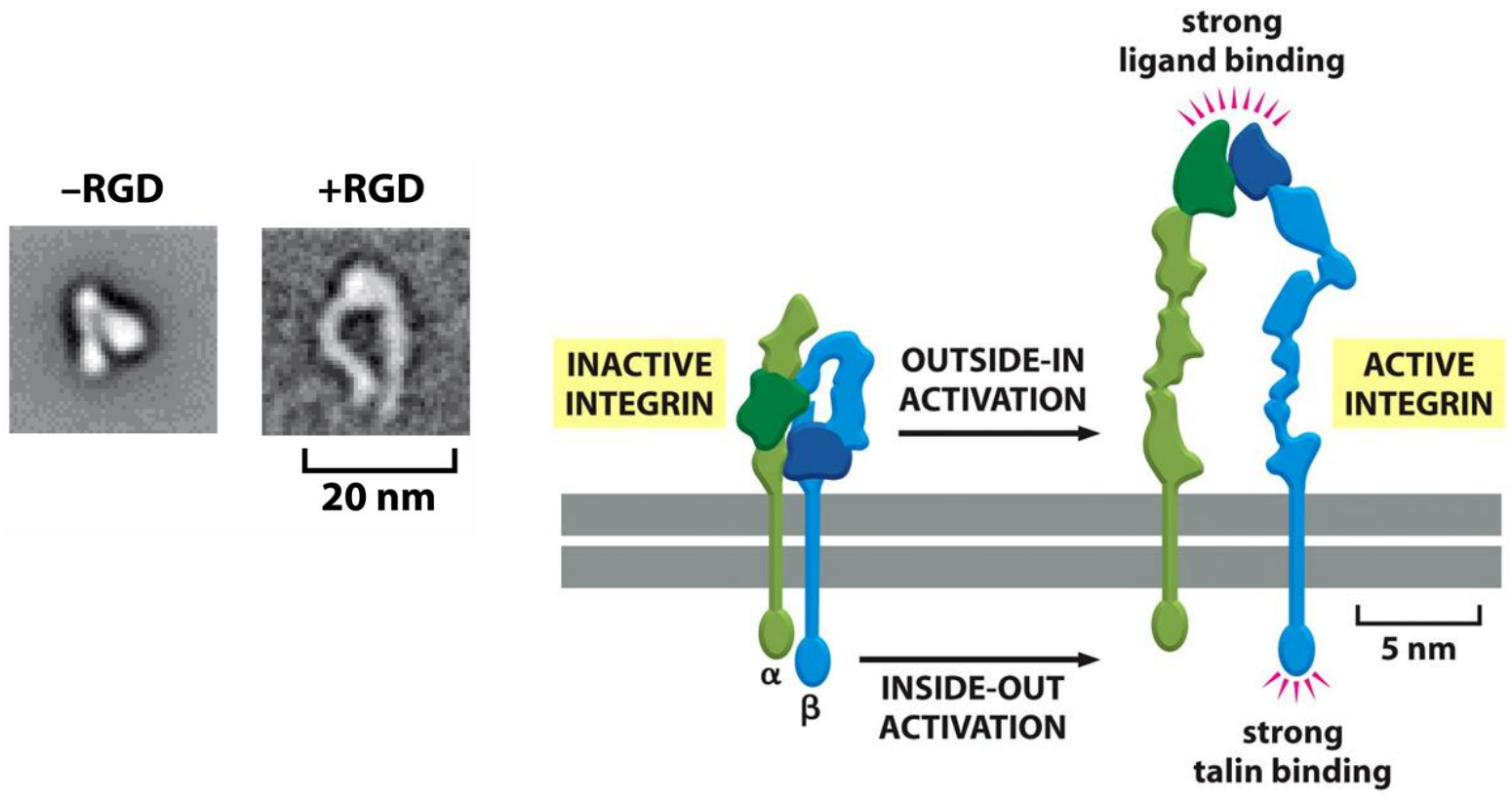
- Integrins are transmembrane proteins composed of α- and β- subunits
- Bind to extracellular matrix proteins.
- Play important role in regulating cellular function
- Defects in integrins signaling cause many genetic diseases

Table 19–4 Some Types of Integrins

INTEGRIN	LIGAND*	DISTRIBUTION	PHENOTYPE WHEN α SUBINUT IS MUTATED	PHENOTYPE WHEN β SUBUNIT IS MUTATED
α5β1	fibronectin	ubiquitous	death of embryo; defects in blood vessels, somites, neural crest	early death of embryo (at implantation)
α6β1	laminin	ubiquitous	severe skin blistering; defects in other epithelia also	early death of embryo (at implantation)
α7β1	laminin	muscle	muscular dystrophy; defective myotendinous junctions	early death of embryo (at implantation)
αLβ2 (LFA1)	Ig superfamily counterreceptors (ICAM)	white blood cells	impaired recruitment of leucocytes	leucocyte adhesion deficiency (LAD) impaired inflammatory responses; recurrent life-threatening infections
αIIbβ3	fibrinogen	platelets	bleeding; no platelet aggregation (Glanzmann's disease)	bleeding; no platelet aggregation (Glanzmann's disease); mild osteopetrosis
α6β4	laminin	hemidesmosomes in epithelia	severe skin blistering; defects in other epithelia also	severe skin blistering; defects in other epithelia also

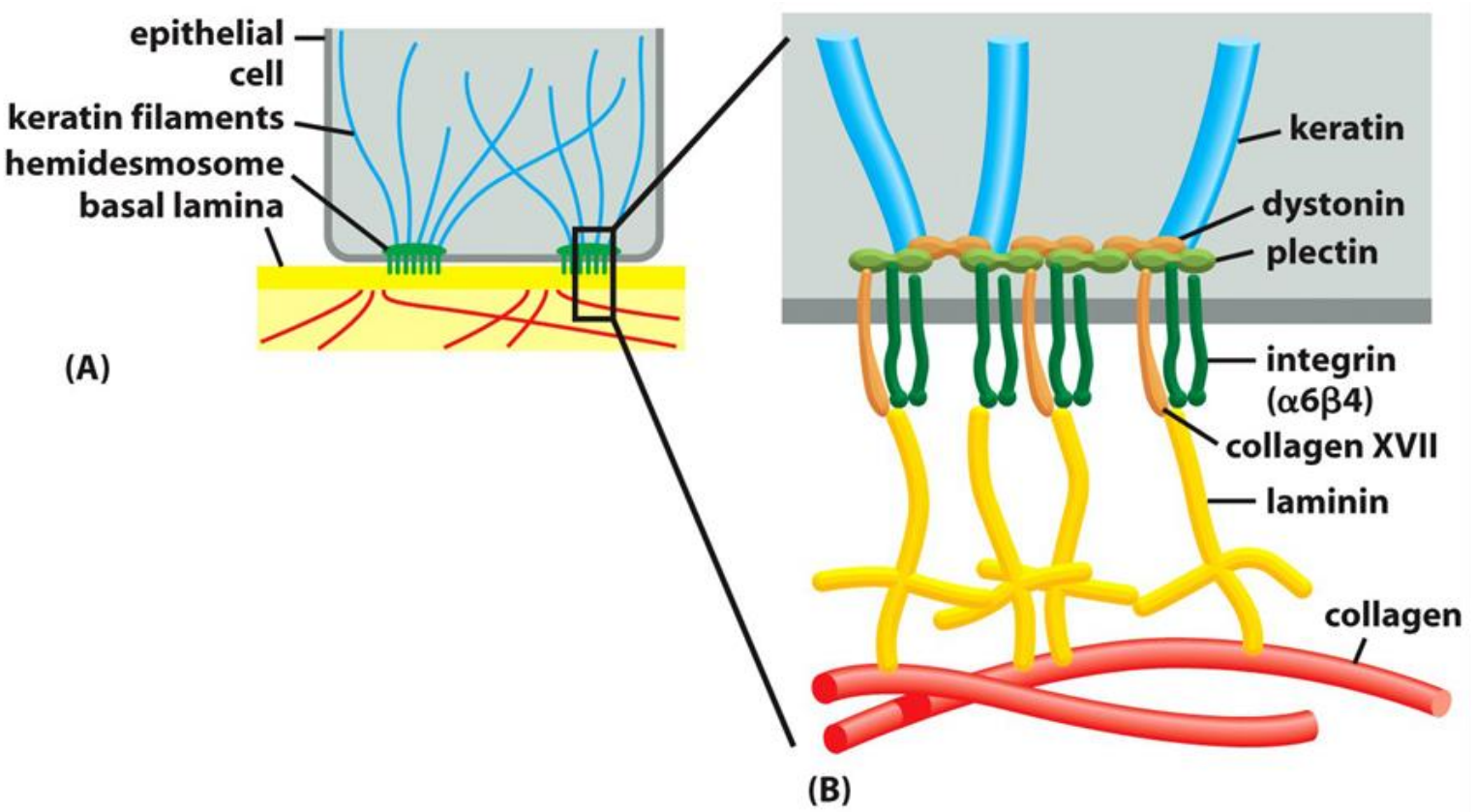
*Not all ligands are listed.

- Integrin activation can result from both inside-out and outside-in mechanisms

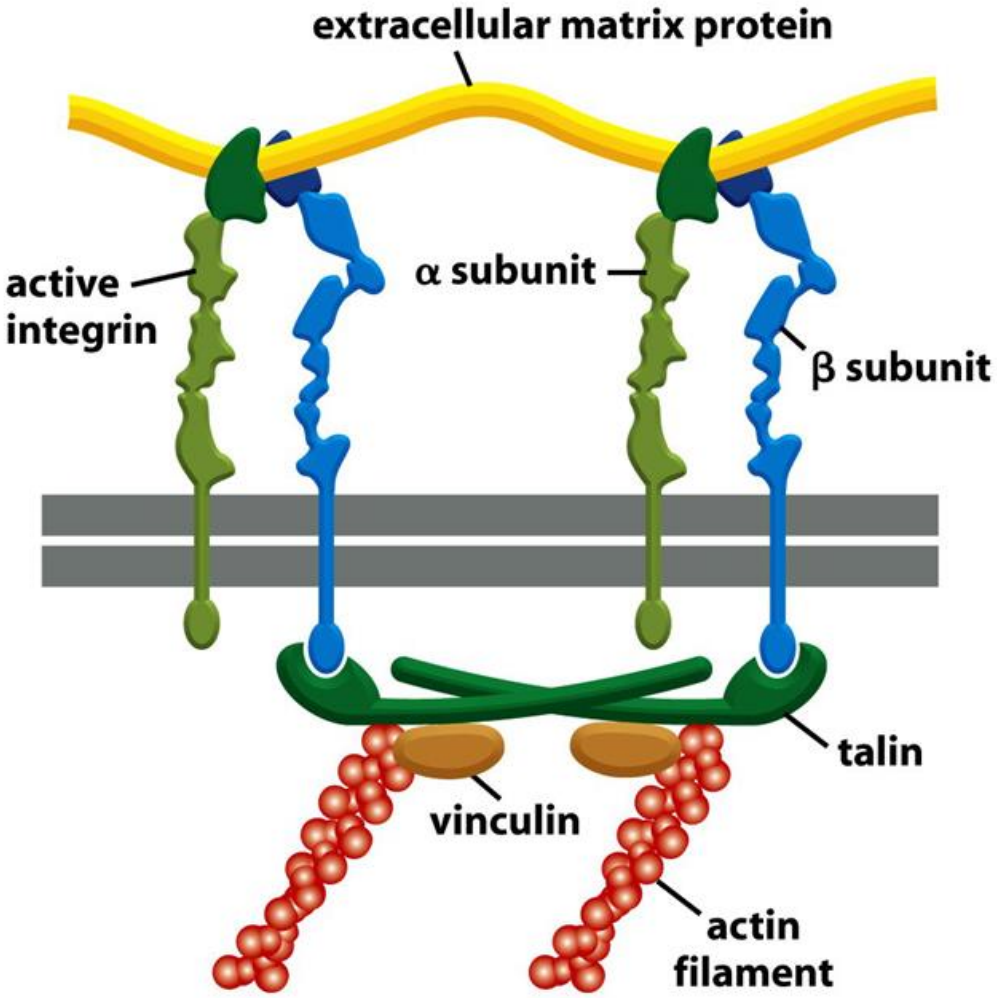


1. Outside-in activation: extracellular ligand binding
2. Inside-out: strong talin binding in response to intracellular signaling molecules such as PIP2, etc.

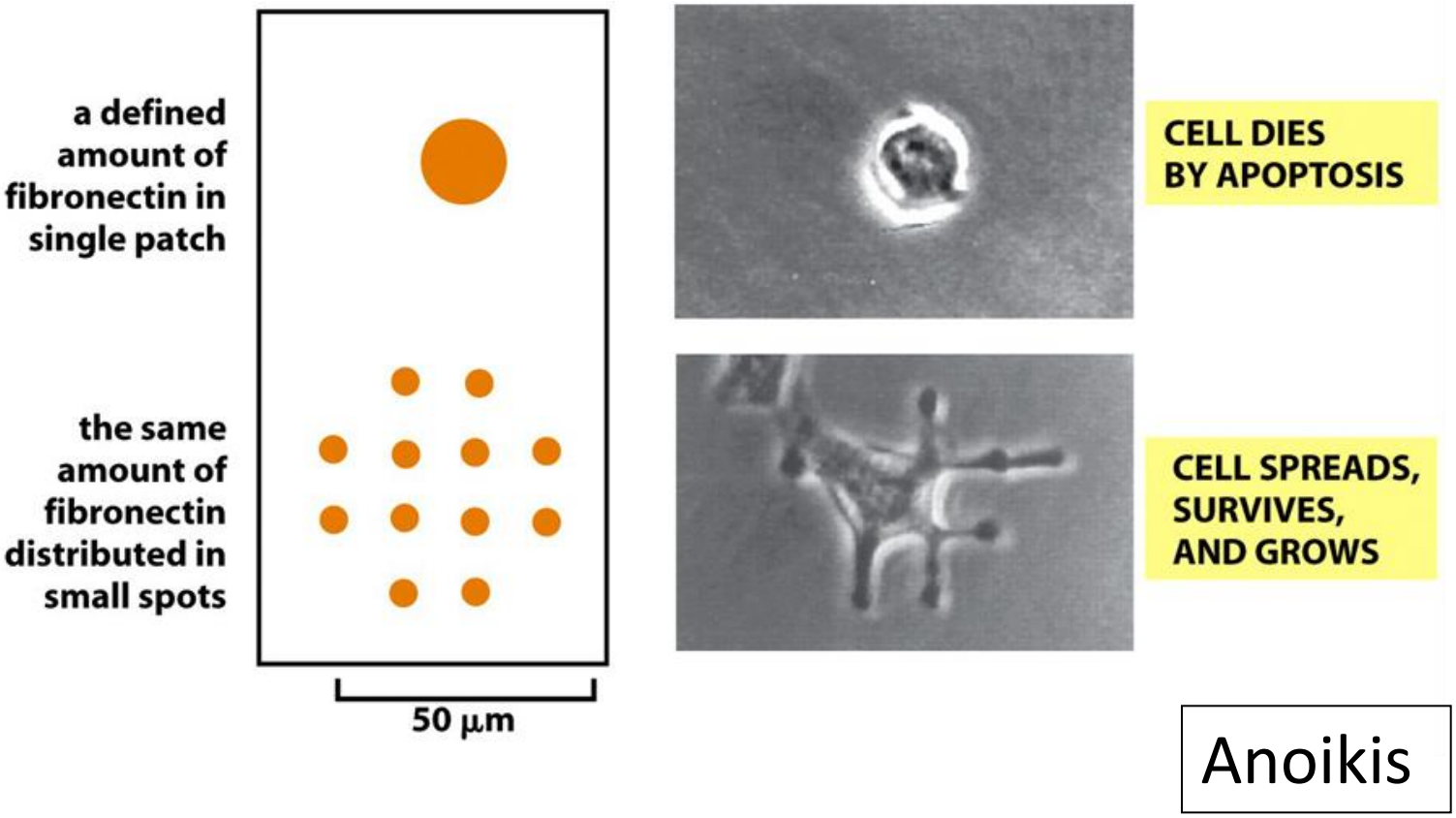
Integrins in hemidesmosomes



•Integrins links extracellular matrix to intracellular actin cytoskeleton



Integrin signaling controls cell proliferation an survival



Anoikis

Cells without attachment will die by apoptosis

Cells with attachment and activated integrin signaling survive and proliferate.