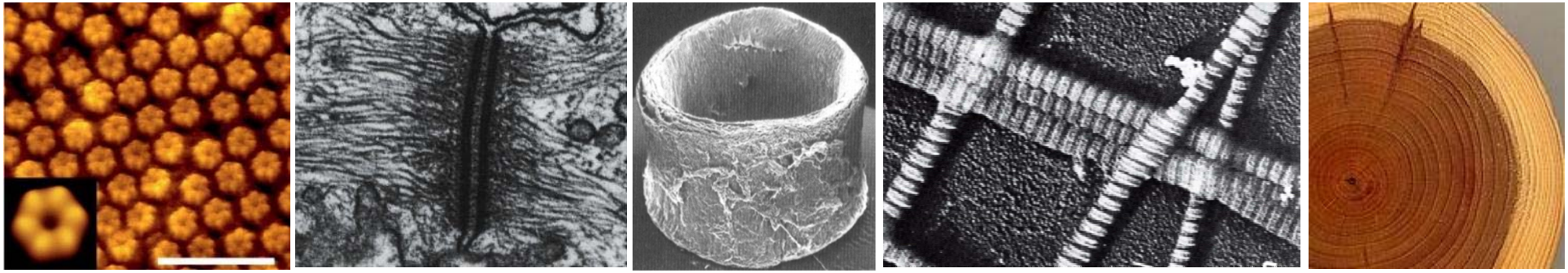
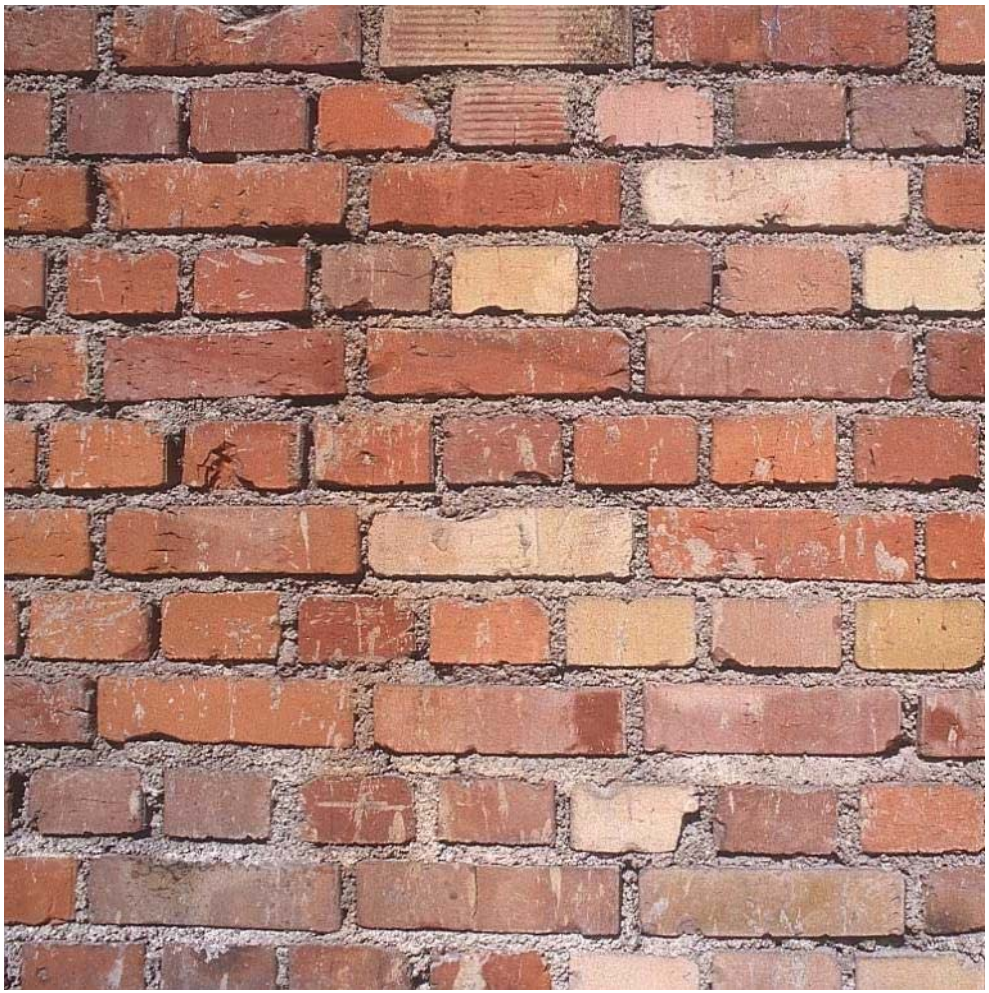


World of the Cell



Chapter 15: Beyond the Cell

王歐力 教授

Oliver I. Wagner, PhD

Professor

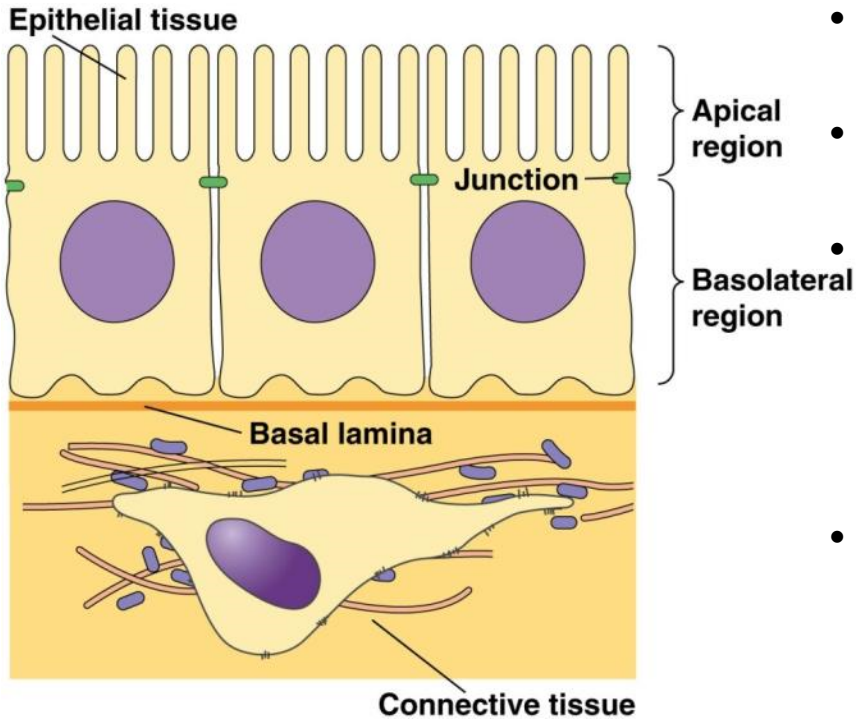
National Tsing Hua University

Institute of Molecular & Cellular Biology

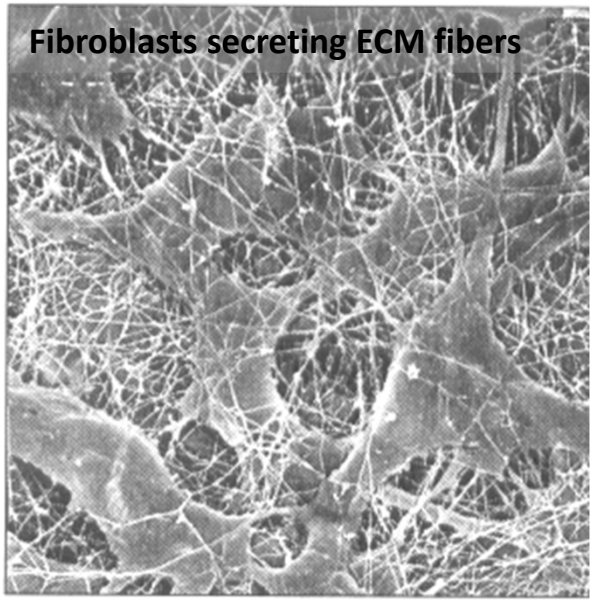
Department of Life Science

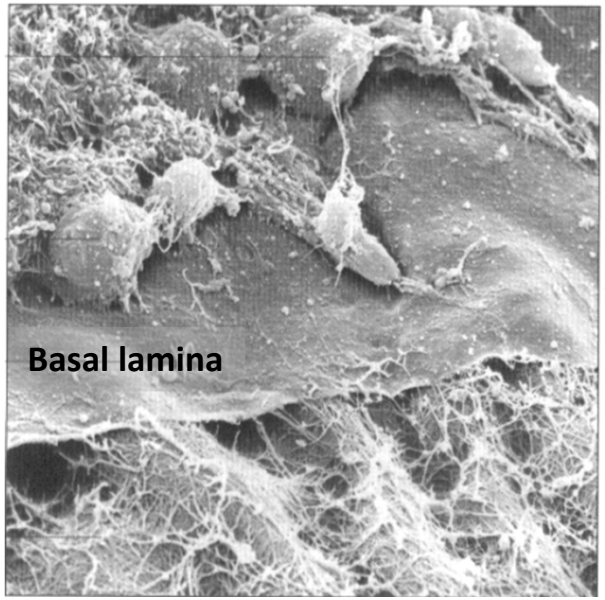
http://life.nthu.edu.tw/~laboiw/

Cell junctions and extracellular matrix (ECM)



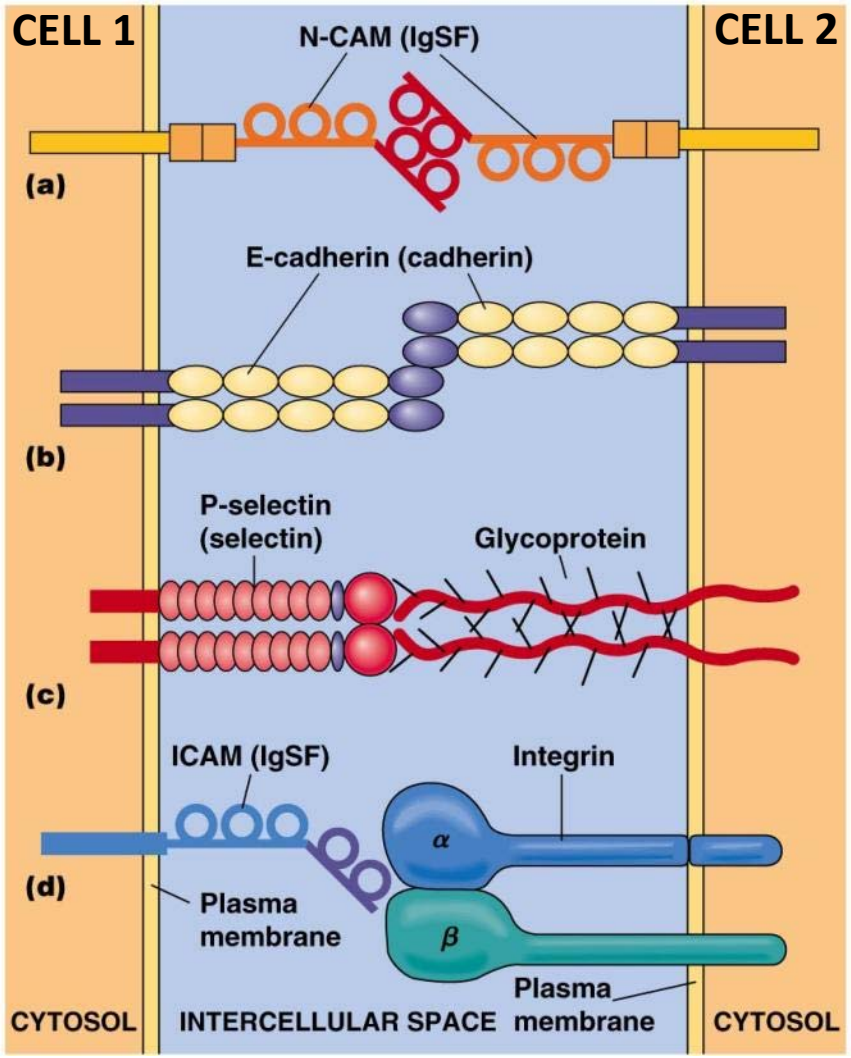
- In animals, cells are usually not alone. They are connected to each other and **form tissues**
- The **extracellular matrix** lies outside of tissues and has basically supportive function
- There are different types of tissues as **epithelial tissues** (ectoderm germ layer: e.g., cells lining the intestine) or **endothelial tissues** (endoderm germ layer: e.g., cells lining blood vessel) or very loosen tissues in the dermis (**connective tissue**)
- Epithelial cells produce a specialized extracellular matrix called the **basal lamina** which acts as a support and tight barrier allowing only water and small molecules to enter





- Cells are connected to each other via specialized **cell junctions** and **adhesion sites**
- Some junctions act as **small channels** for metabolite and electrical current exchange
- Some of the adhesion sites are directly connected to the cytoskeleton **mechanically integrating** neighboring cells

Transmembrane proteins mediate cell-cell adhesion



ECM

Cadherin (green) forms a continuous network that holds the cells together

- Animal cells use specialized adhesions receptors to attach to one another
- Many of the **cell adhesion proteins** are **transmembrane proteins** and the extracellular portions of two matching proteins (from neighboring cells) can interact with each other
- Adhesions are **dynamic structures** and they can quickly assemble and disassemble
- They also act to **assemble cell signaling complexes** and connect to the cytoskeleton
- Thus, cell adhesions act in **cell signaling**, **cell movement**, **cell proliferation** and **cell survival**

Different classes of these proteins exist

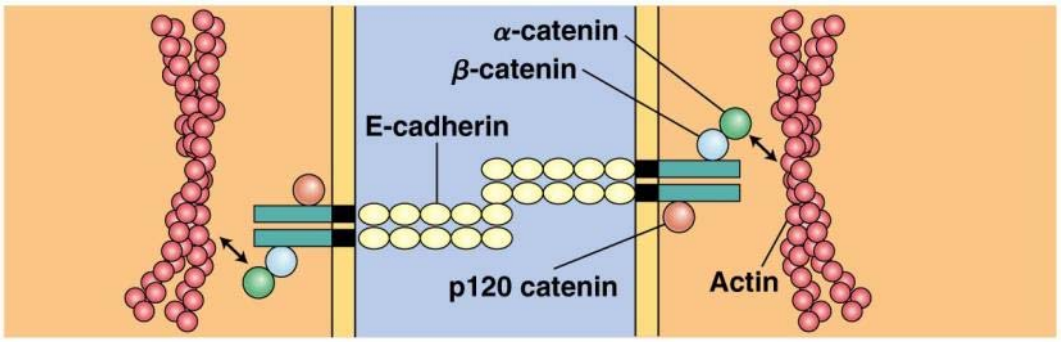
(A) *Homophilic* interactions

- **Immunoglobulin superfamily** (**IgSF**) include **CAM**s (*c*ell *a*dhesion *m*olecules) such as **N-CAM** (*n*eural *c*ell *a*dhesion *m*olecule)
- **Cadherins** as E-cadherin

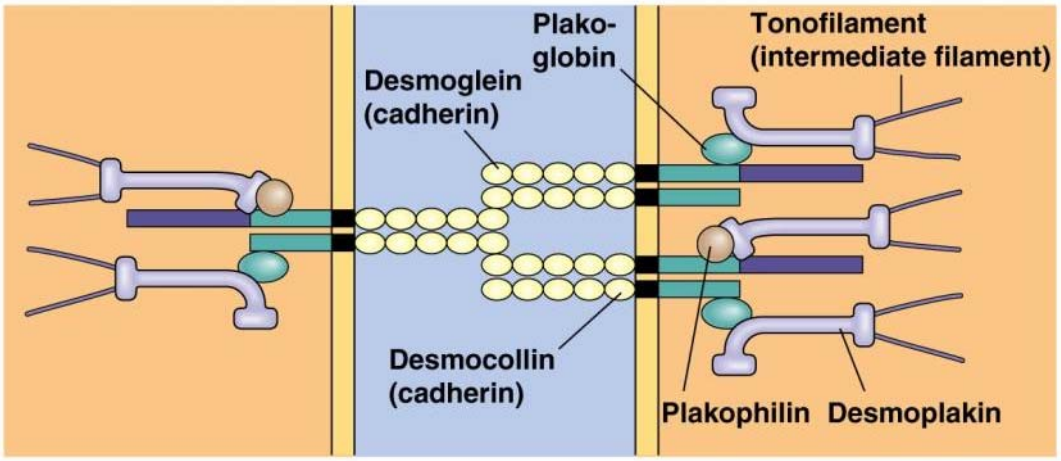
(B) *Heterophilic* interactions

- **Selectins** bind glycoproteins from other cells
- **Integrins** bind to IgSF proteins (e.g., ICAM; *i*ntercellular *a*dhesion *molecule*)

Importance of cadherins

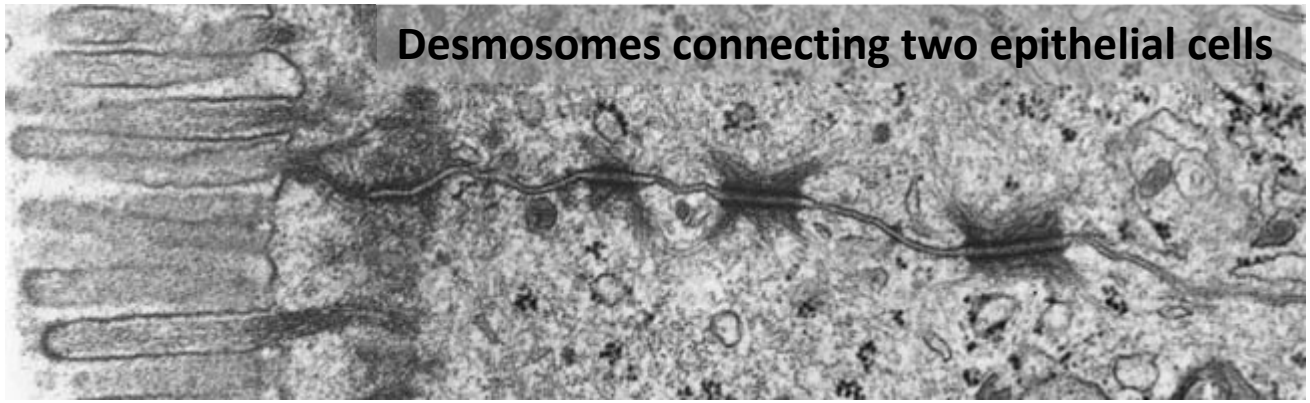


(a) Adherens junction

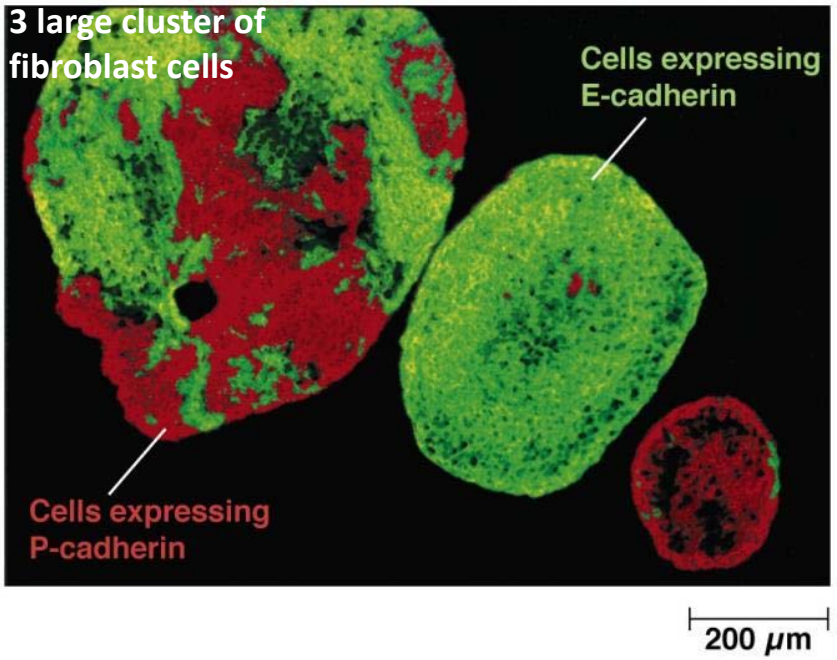


(b) Desmosome

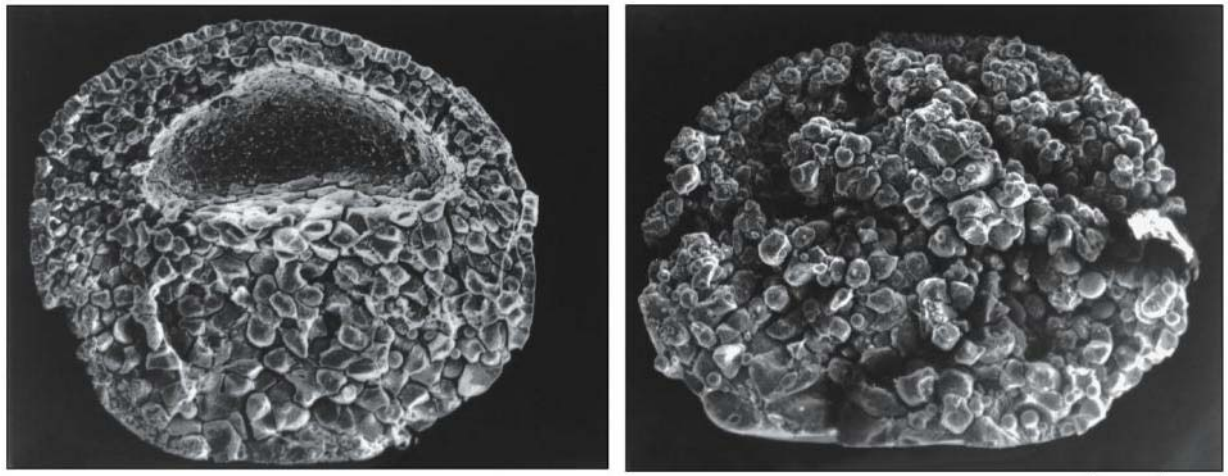
- The <u>difference between cadherins and CAMs</u> is that **cadherins are regulated by Ca^{2+}**
- <u>Cadherins are found in</u> cellular junctions as **adherens junctions** and **desmosomes**
- In <u>adherens junctions</u> **E-cadherin** (*epithelial* cadherin) interacts with **actin** via the proteins **α- and β-catenin**
- In <u>desmosomes</u> the cadherins **desmoglein** and **desmocollin** interact with **intermediate filaments** via **plakoglobin**/**desmoplakin** or via **plakophilin**/**desmoplakin** adaptors



Effect of overexpressing or suppressing cadherins in cells



- **Fibroblasts** are nearly non-adhesive cells and **do not form effective tissues**
- However, if plasmid DNA is introduced (transfection method) that encodes for E- or P-cadherin they form large cell clusters (three cluster shown here)
- Cells expressing **E-cadherin** preferential adhere to other cells expressing **E-cadherin** (and cells expressing **P-cadherin** prefer to interact with cells expressing **P-cadherin**)



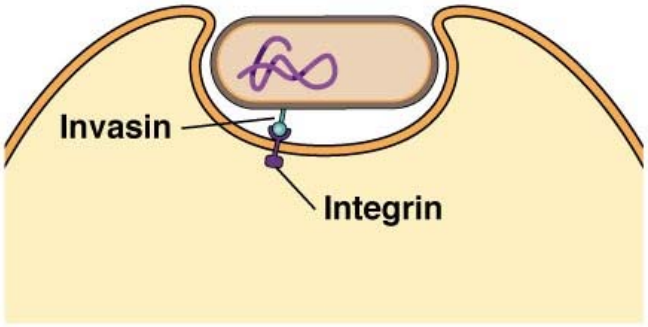
(a) **Wild type (normal gastrulation)**

(b) **Cadherin mutant (RNAi gene knockdown method)**

Cadherins are **important for embryonic development**:
(a): typical frog embryo blastula (cells start to form a hollow sphere)
(b): the production of **E/P-cadherin** is **genetically suppressed** and blastula loses its typical organization

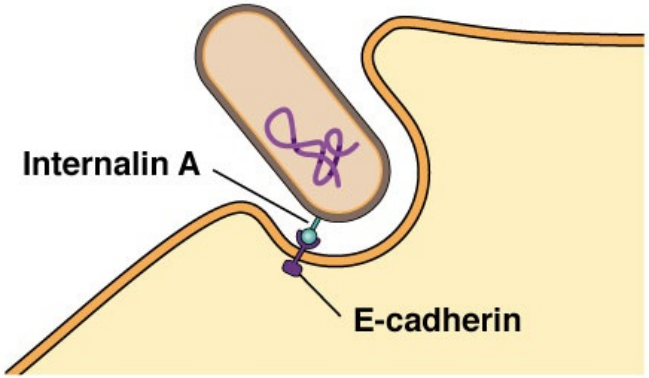
(*narrated*)

Cell adhesions and diseases



(a) ***Yersinia***

- Some **bacteria** express molecules on their surfaces that perfectly bind to cell adhesion molecules on **host cells**
- For example ***Yersinia pseudotuberculosis*** expresses a protein **invasin** that recognizes and binds to **integrins**
- *Yersinia* is an enteropathogenic bacteria and infects intestinal cells resulting in gastroenteritis with diarrhea and vomiting
- Infection of *Yersinia* occurs via contaminated water and food
- Similar mechanism is used by the enteropathogenic bacteria ***Shigella flexernii***

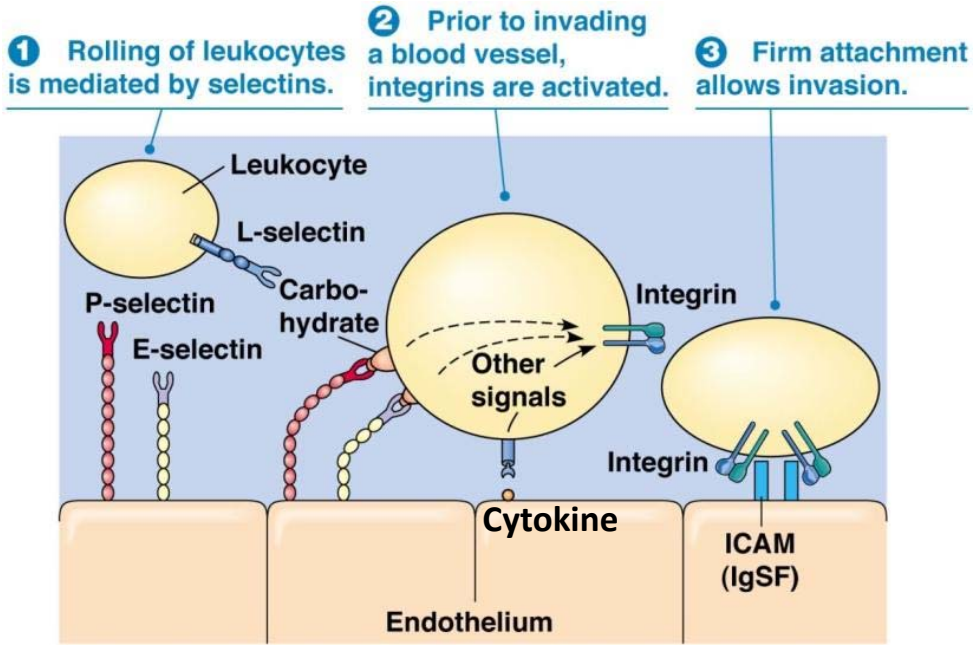


(b) ***Listeria monocytogenes***

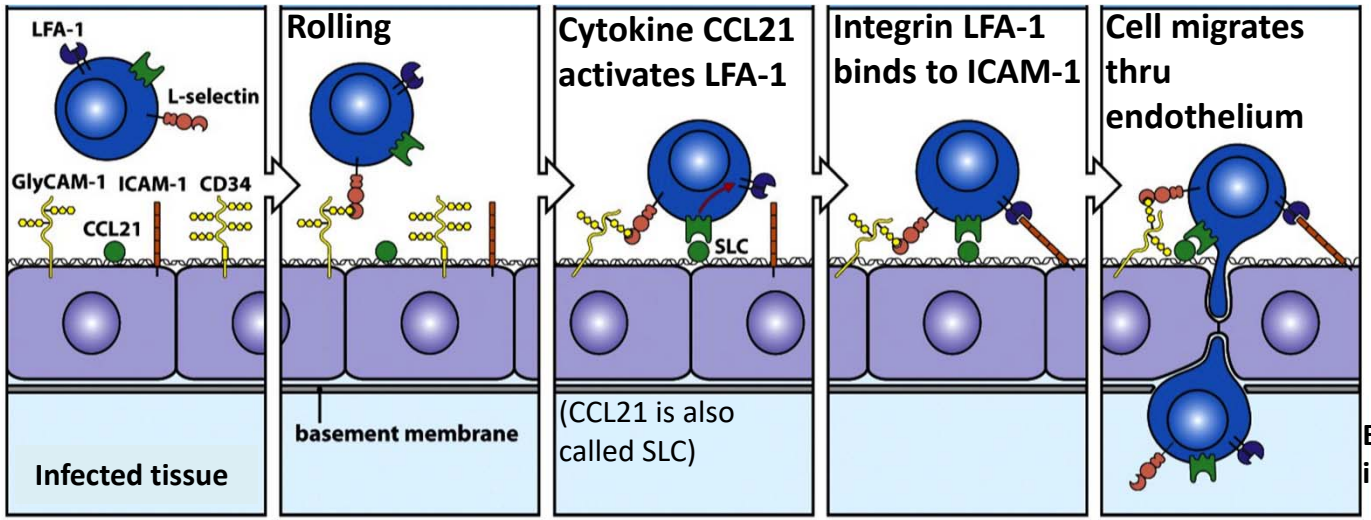
- ***Listeria monocytogenes*** expresses **internalin A** which is able to recognize and tightly bind to **E-cadherin**
- *Listeria* not only "hijacks" the cell adhesion system but also "hijacks" the cytoskeleton system to boost its motility in the host (as shown earlier)

Y. pestis (that caused the plague) has been evolved from Y. pseudotuberculosis

Leukocyte rolling



- **Leukocytes** continuously **roll along the walls of blood vessels** to seek for sites of inflammation
- This process is mediated by selectins that are able to bind to carbohydrates (glycoproteins) on cell surfaces
- **P-selectin** and **E-selectin** on the endothelium recognizes sugars-chains on the leukocyte, and **L-selectin** recognizes sugar-chains on the endothelium
- When an inflammation site is detected (cytokine signals) leukocytes **stop rolling** and make tight attachments via **integrins** (leukocyte) and **ICAMs** (endothelium)
- Leukocytes then **migrate** ("diapedesis") **thru the endothelium** to the site of inflammation



Leukocyte rolling

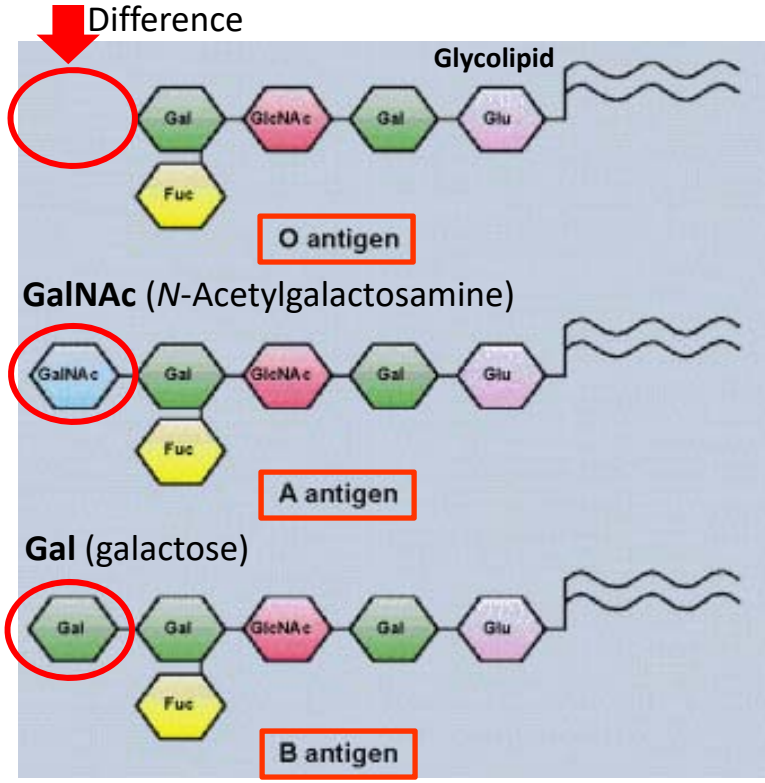
Importance of cell surface carbohydrates in blood types

Blood Type	Antigen (RBC membrane)	Antibody (plasma)	Can receive blood from	Can donate blood to
A (40%)	A antigen	Anti-B antibodies	A, O	A, AB
B (10%)	B antigen	Anti-A antibodies	B, O	B, AB
AB (4%)	A antigen, B antigen	No antibodies	A, B, AB, O	AB
O (46%)	No antigen	Both Anti-A and Anti-B antibodies	O	O, A, B, AB

Cannot receive from "B" because "B" has Anti-A antibodies

Cannot donate to "O" because "O" has Anti-B antibodies

Specific **carbohydrate side chains** present on a glycolipid on the erythrocyte surface **determines the blood** type of a person



- **A Type**: **antibodies against Gal** in their blood. **B Type**: has **antibodies against GalNAc**.
- **O Type**: **both antibodies**. **AB Type**: **no antibodies**.
- Detection of these antibodies in the blood of a person identifies the blood group
- If an **A Type** would be transfused with blood from a **B Type**, the **anti-A** antibodies in the B-blood would lead to blood clumping and possibly death of the A-person

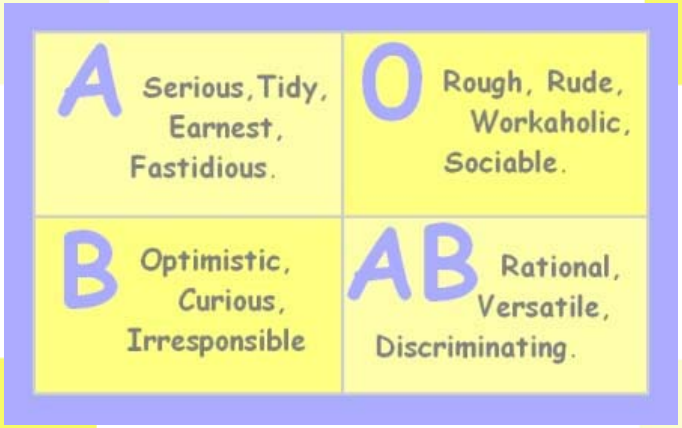
Blood type occurrences in Taiwan and blood type personalities in Japanese culture

	O+	A+	B+	AB+	O−	A−	B−	AB−
World	36.44%	28.27%	20.59%	5.06%	4.33%	3.52%	1.39%	0.45%
Taiwan	43.90%	25.90%	23.90%	6.00%	0.10%	0.10%	0.01%	0.02%

Additional blood system: Rh- or Rh+ = Rhesus factor or D-antigen (either you have it or not)

- Considerate about everything
- Prefer peaceful human relations
- Slow to trust people
- Observe social rules and customs
- Regard social order as important
- Restrain action and expression

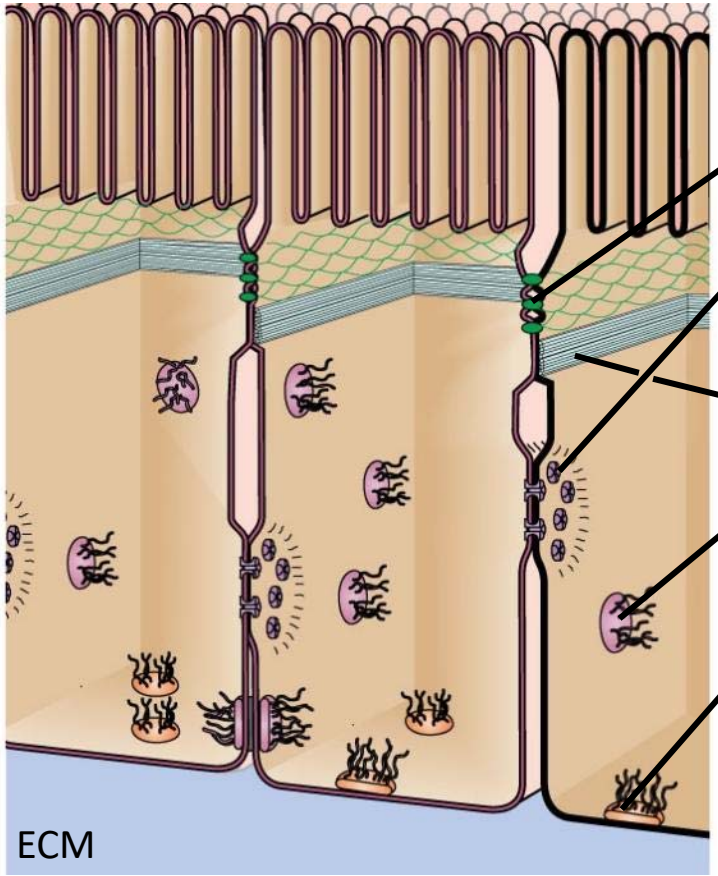
Blood Type and Personality in Japanese Culture



- Strongly purpose-oriented
- Straight desire
- Conscious of power relationship
- Know how to take chances
- Dislike to be subordinate
- Expressive

- Dislike restrictions and one's own way
- Non-stereotyped action
- Non-stereotyped thinking
- Self-conscious and not warped expressions
- Makes less distinction of things
- Not conscious of circumstances
- Don't care social rules and customs

- Rational thinking
- Good critic and analyst
- To participate and contribute to the society
- Good at adjusting human relations
- Hope to be in harmony with the society
- Feels distant from the society



Types of cell junctions

Tight junction: impermeable seal

Gap junction: ion exchange and electrical connection

Adherens junction: a belt (ring) of actin filaments

Desmosome: button-type of connections (bind to intermediate filaments)

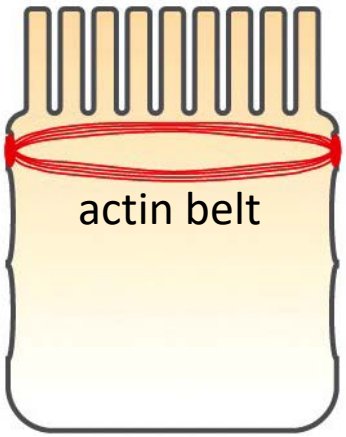
Hemidesmosome: connect cell to basal lamina (bind to intermediate filaments)

Focal adhesion: connect cell to ECM (bind to actin) (not shown)

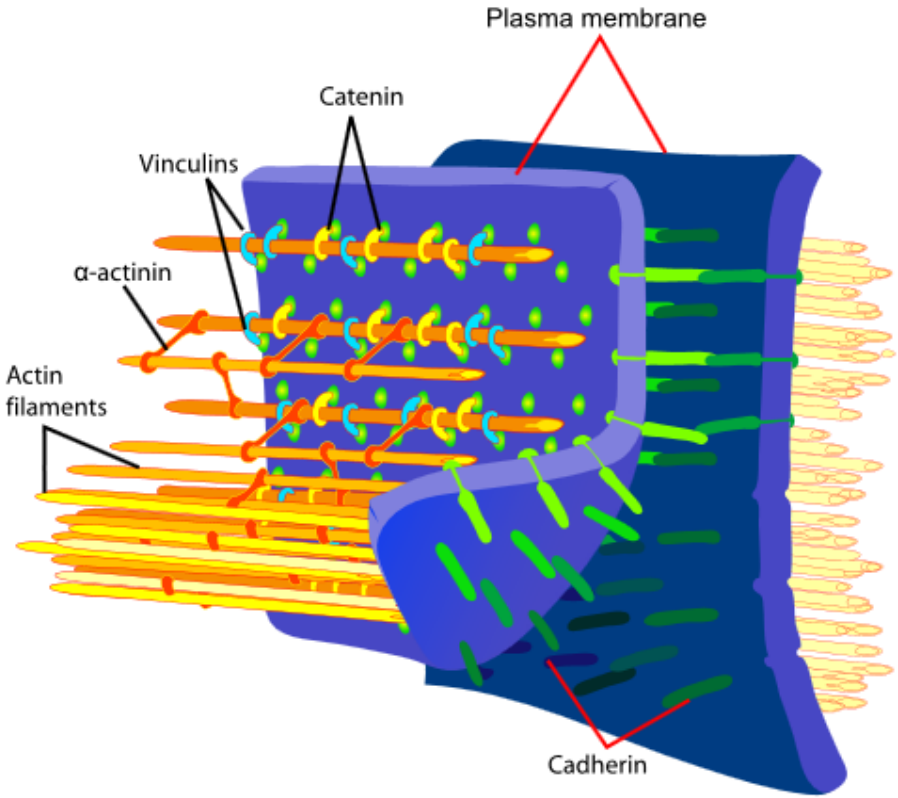
Adhesive junctions

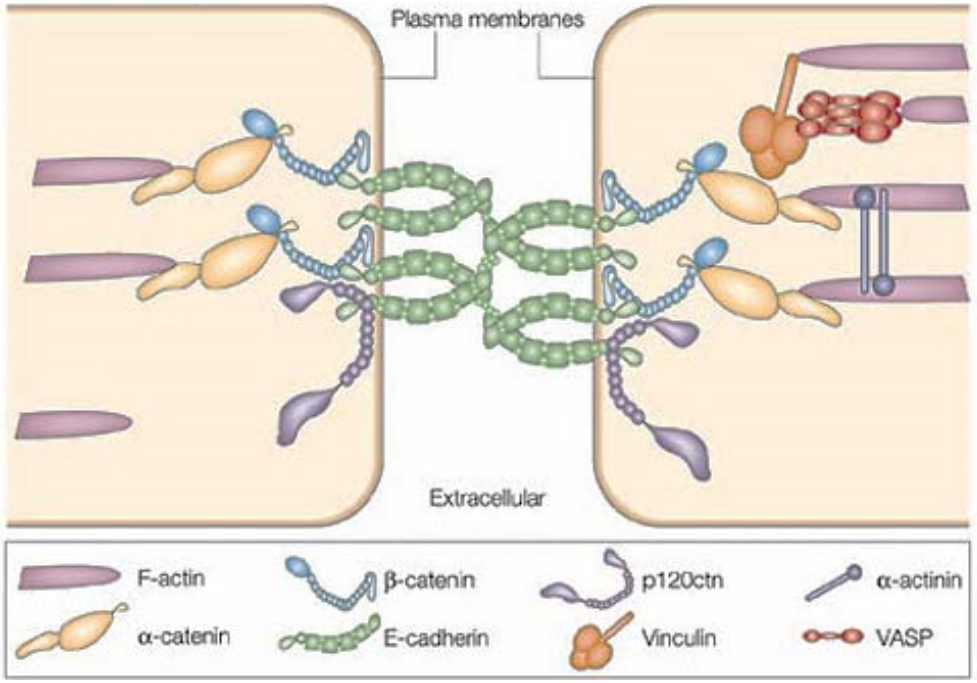
Type of Junction	Main Function	Intermembrane Features	Space	Associated Structures
Adhesive junctions				
Focal adhesion	Cell-ECM adhesion	Localized points of attachment	20–25 nm	Actin microfilaments
Hemidesmosome	Cell–basal lamina adhesion	Localized points of attachment	25–35 nm	Intermediate filaments (tonofilaments)
Adherens junction	Cell-cell adhesion	Continuous zones of attachment	20–25 nm	Actin microfilaments
Desmosome	Cell-cell adhesion	Localized points of attachment	25–35 nm	Intermediate filaments (tonofilaments)
Tight junction	Sealing spaces between cells	Membranes joined along ridges	None	Transmembrane junctional
Gap junction	Exchange of ions and molecules between cells	Connexons (transmembrane protein complexes with 3-nm pores)	2–3 nm	Connexins in one membrane align with those in another to form channels between cells

Structure and function of adherens junctions



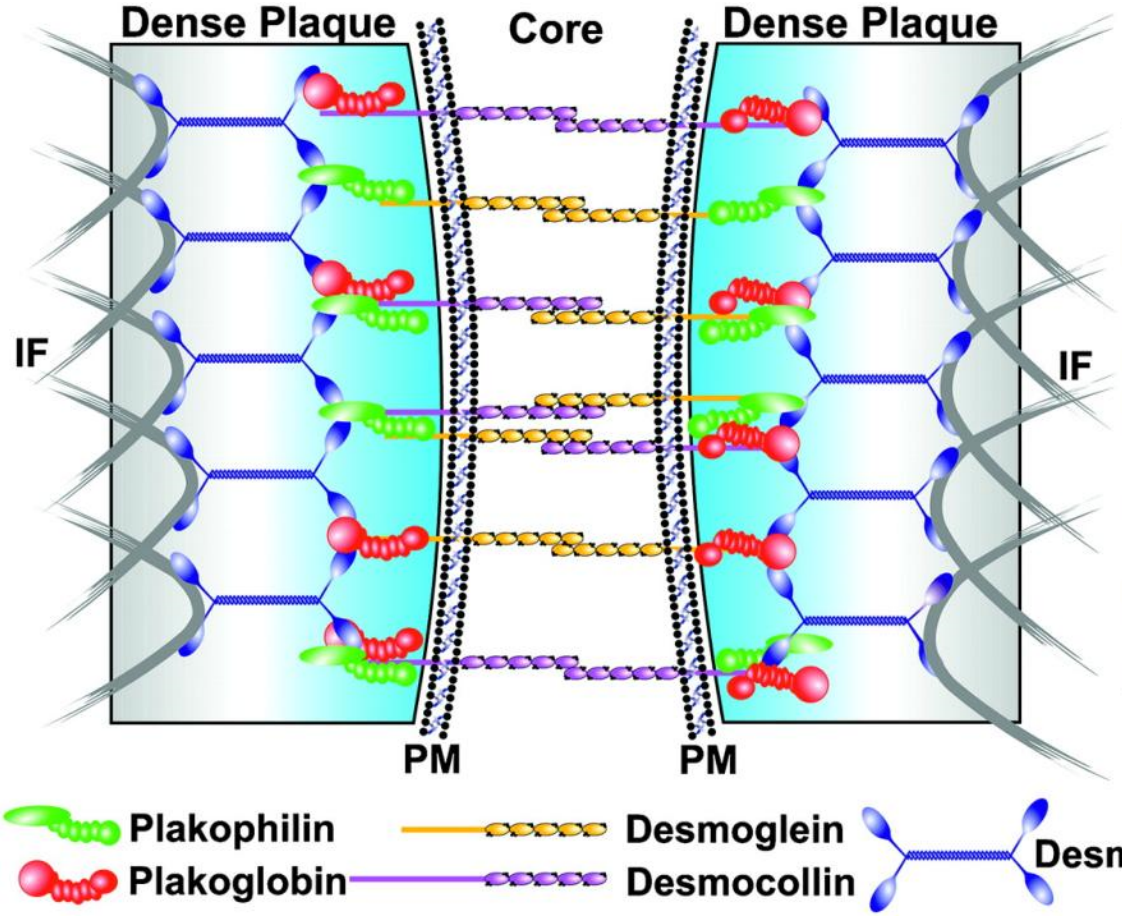
- Adherens junctions are mostly found in epithelial cells
- They form close connections points via **cadherins** and **catenins** and connect to a supportive **actin belt**
- The actin belt provides tissue integrity and mechanical resistance
- At the connection site **E-cadherins** bind to **β-catenin** that connects to the actin-binding protein **α-catenin**
- **α-actinin** is important for actin bundling and **p120 catenin** stabilizes cadherins near the plasma membrane

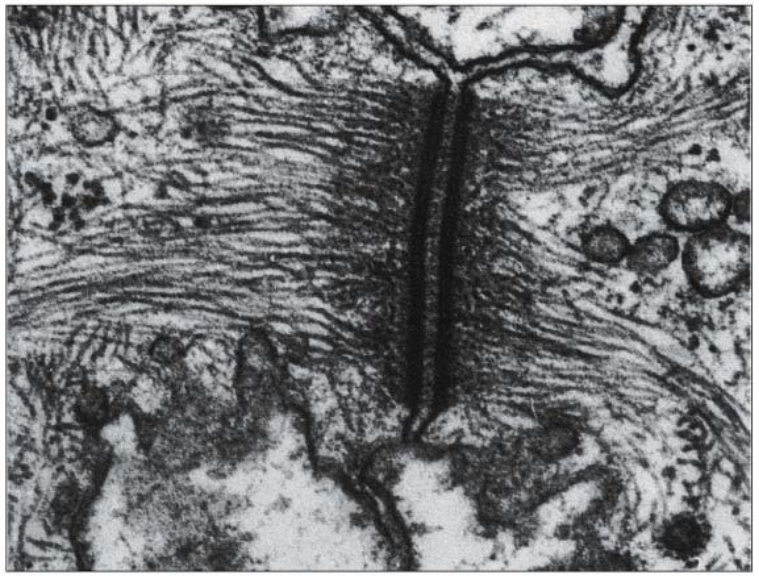




Structure and function of desmosomes

- **Desmosomes** are knob-like attachment points of cells connecting to IFs (keratin e.g.)
- The result is **tissue integrity** and **resistance to mechanical stress**
- Two cadherins **desmoglein** and **desmocollin** form heterophilic interactions in the extracellular space ("desmosome core")
- Attached to these cadherins are **plakophilin** and **plakoglobin** (β-catenin family) that bind to **desmoplakin** (visible in electron dense *desmosome plaques* in TEM images)

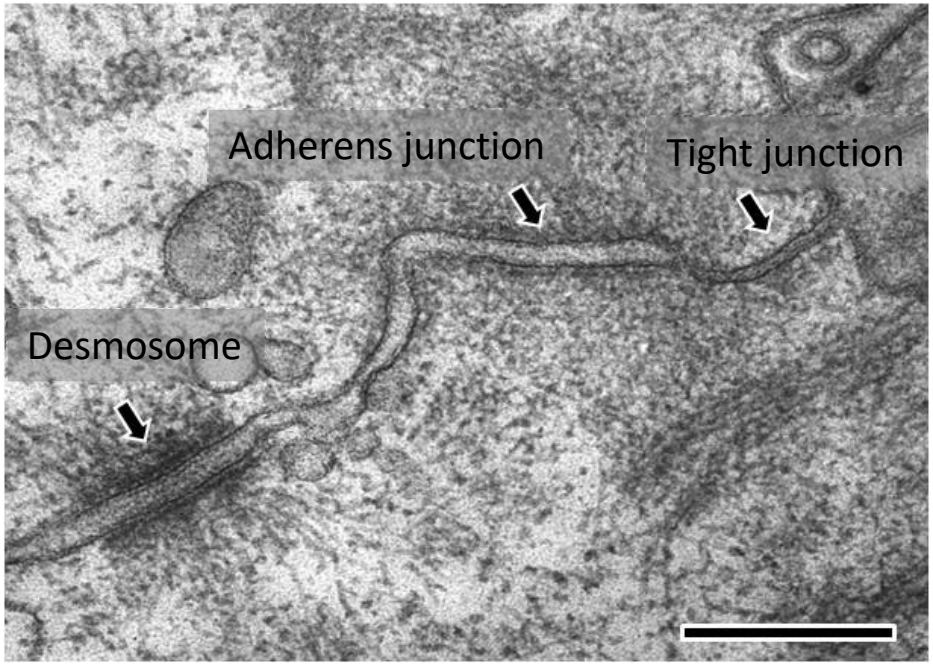


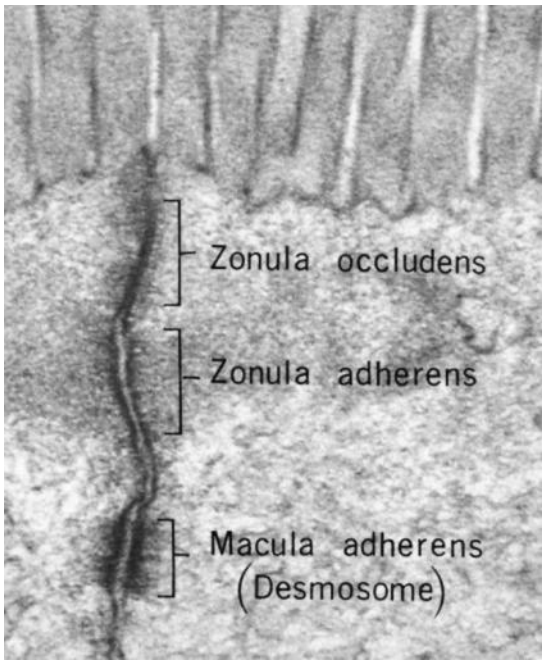


Especially in skin, heart muscle and uterus

Structure and function of desmosomes

- Desmosomes form the largest extracellular space with 25-35 nm followed by adherens junctions with 20-25 nm and the gap junctions with only 2-3 nm (tight junction = no space)
- Depending on the cell type **tonofilaments** (IFs) can be keratin, vimentin or desmin

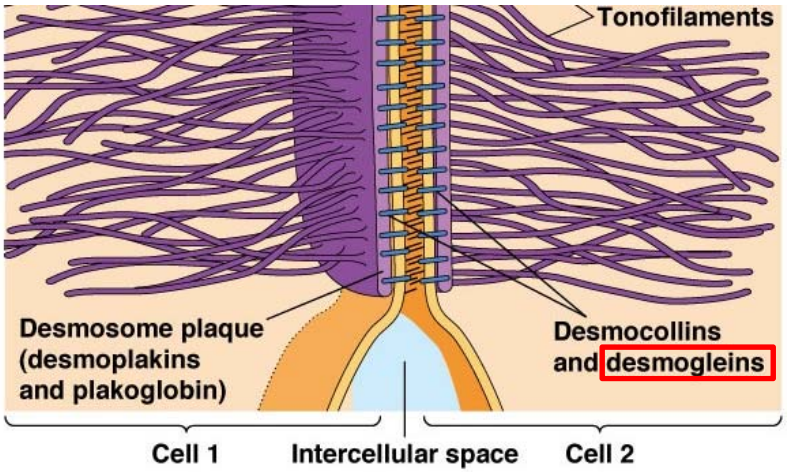


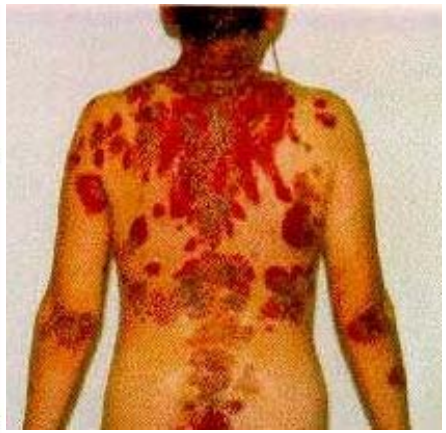


Older names:
tight junction = *zonula occludens*

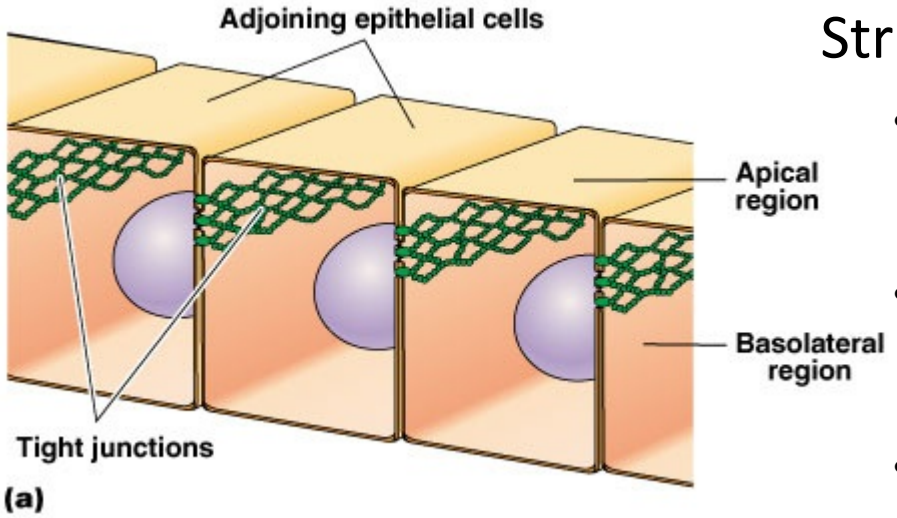
adherens junction = *zonula adherens*

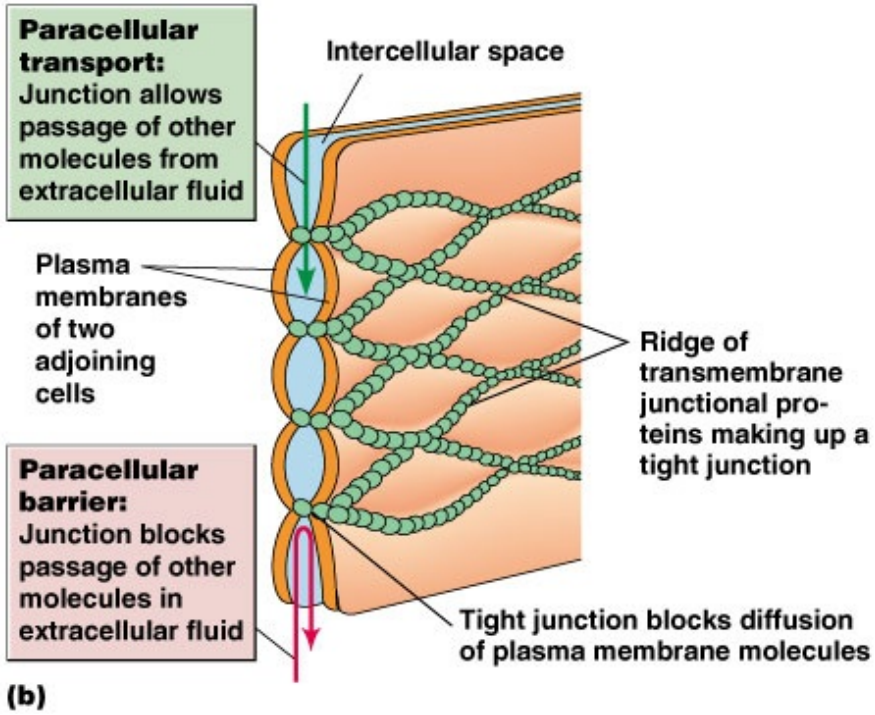
desmosomes = *macula adherens*





- *Pemphigus vulgaris* is an autoimmune disease.
- Antibodies directed against **desmoglein** result in the detachment of keratinocytes from the epidermis.
- **Severe skin blistering** is the result.

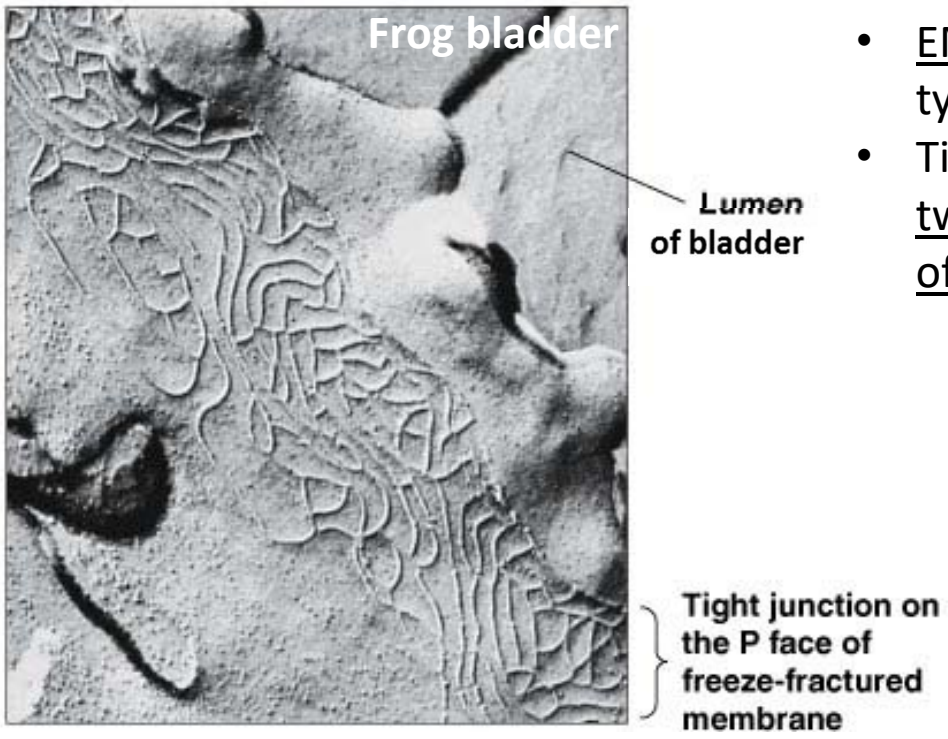




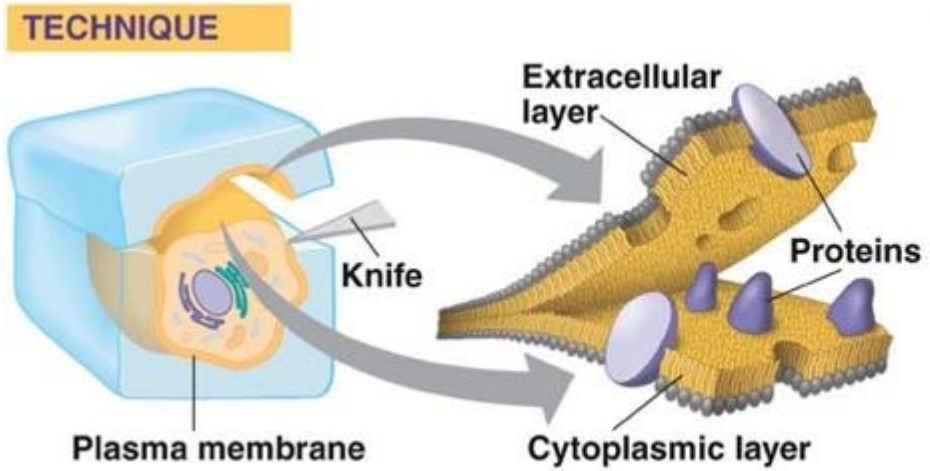
Structure and function of tight junctions

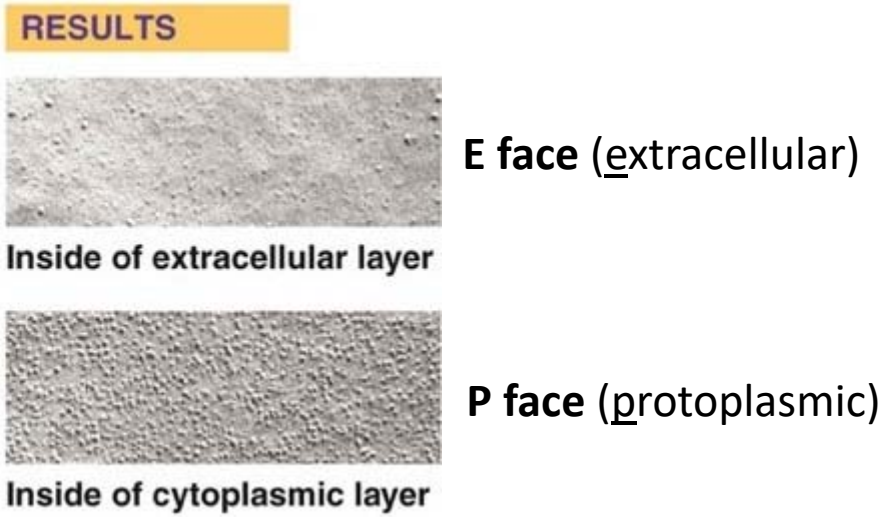
- Tight junctions act as **very efficient barriers** to prevent unwanted molecules passing thru the intercellular space of two adjacent cells
- This is especially important in tissues of the intestinal tract, liver, pancreas or urinary bladder
- Transmembrane proteins of 3-4 nm form a **network of ridges** (脊狀) sealing the membranes at defined areas
- This tight belt forces molecules to pass thru the apical cell membrane and not thru the space between two cells = **paracellular barrier**
- Specific ions, however, are allowed to pass via **paracellular transport** (mediated by specialized tight junction proteins)
- Also lateral movement of lipids or membrane proteins is blocked (“*small mesh-sized fence blocks passage of a soccer ball*”)

Making tight junctions visible in the EM



- EM freeze fracture method reveals the ridge-type structure of tight junctions
- Tight junctions can be imagined as if placing two corrugated (波狀的) metal plates on top of each other

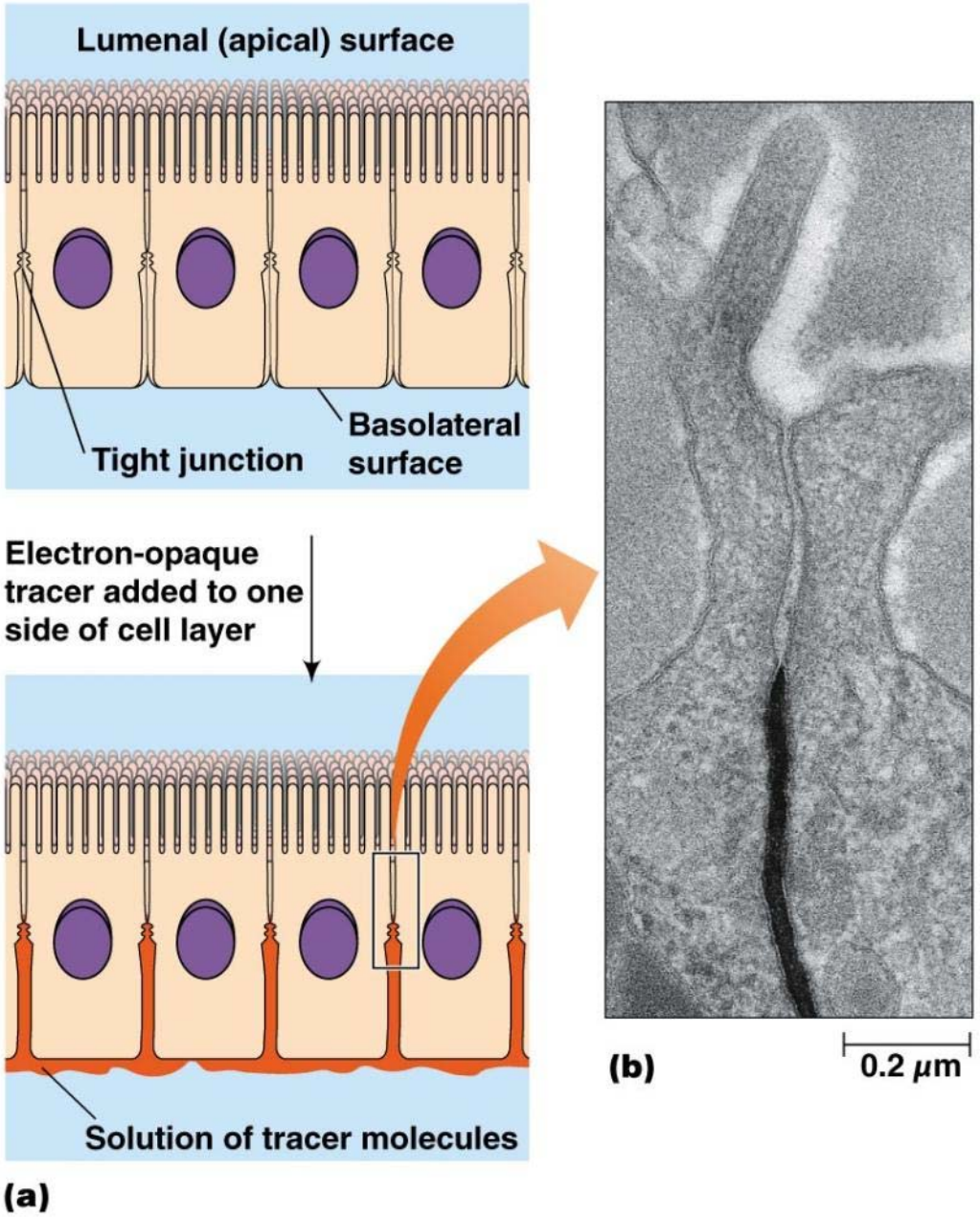




E face (extracellular)

P face (protoplasmic)

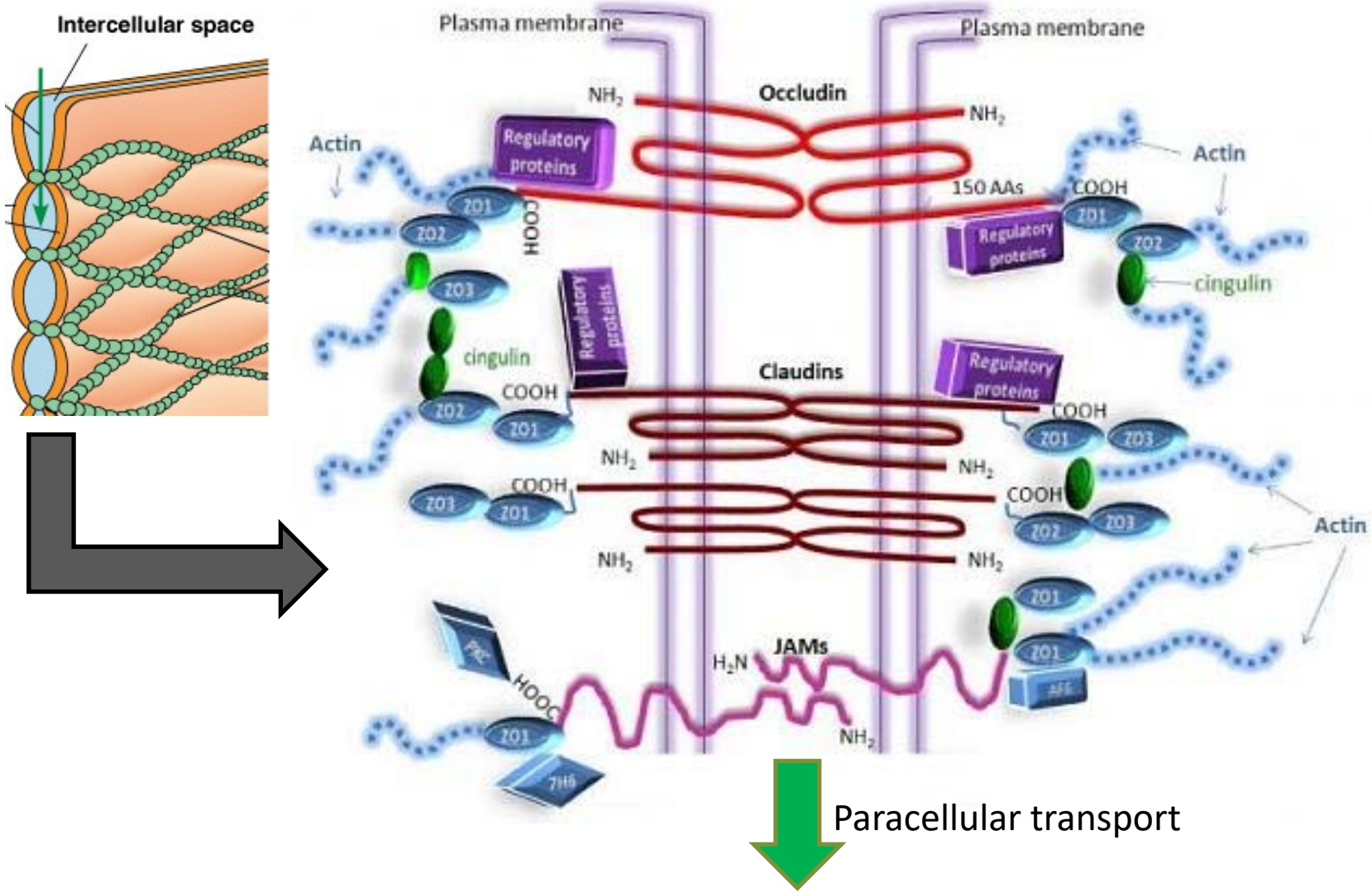
How tight are tight junctions?



- In an experiment <u>electron-dense</u> **tracer molecules** are applied to one side of a tissue (basolateral surface) know to contain tight junctions
- EM imaging reveals that the <u>tracer travels thru the paracellular space until it encounters a tight junction</u>
- Thus, in the intestine tight junctions **force the absorption of digested food from the apical surface** (and not from the intercellular space)
- Similar, in <u>bladder cells</u> the barrier provided by tight junctions would <u>prevent leaking of urine</u>

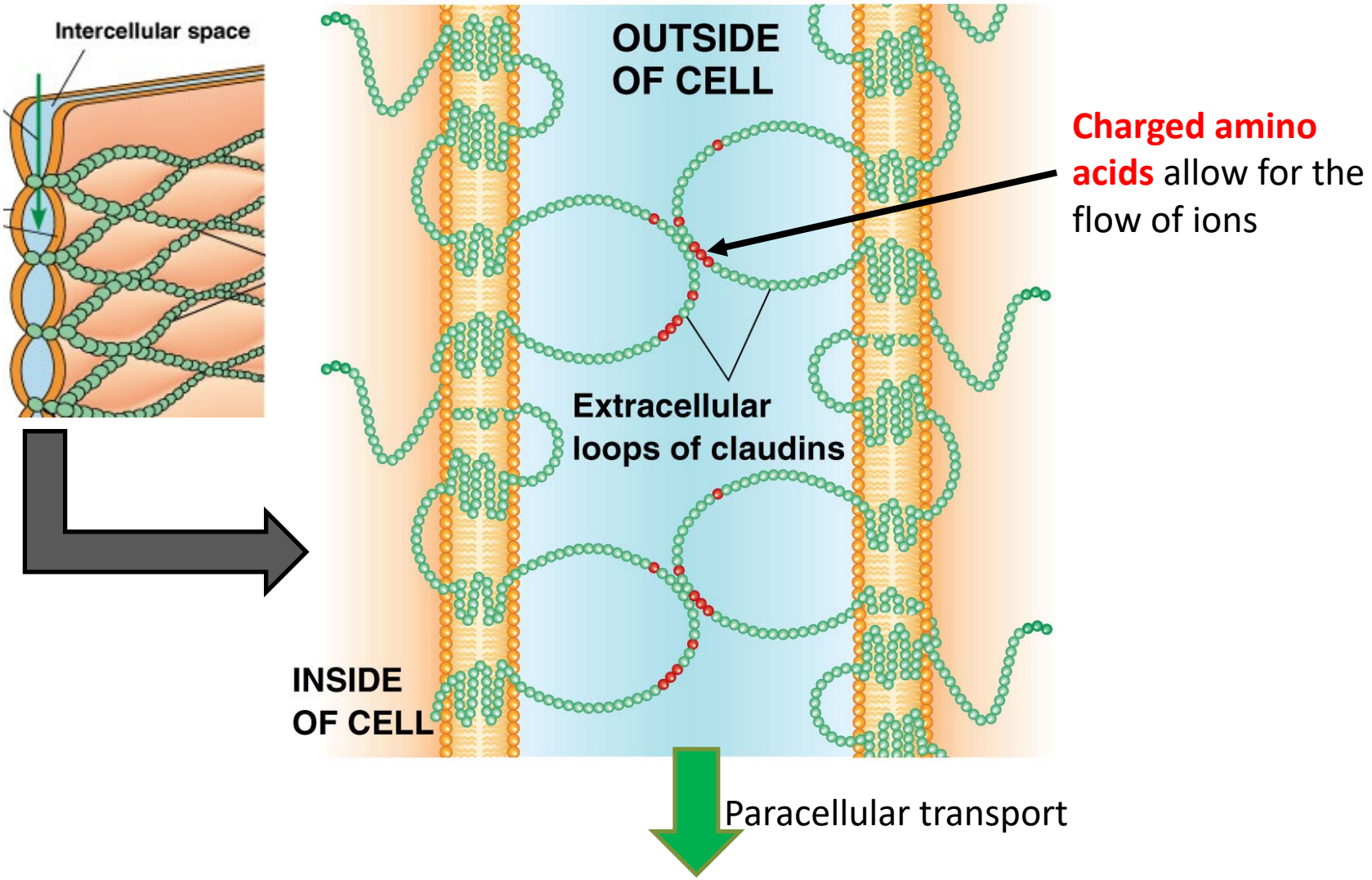
Paracellular transport through tight junctions

- Three types of transmembrane proteins can be found in tight junctions: **occludin**, **claudin** and **JAMs** (junctional adhesion molecules)
- The cytosolic portion of claudins can also bind to actin filaments

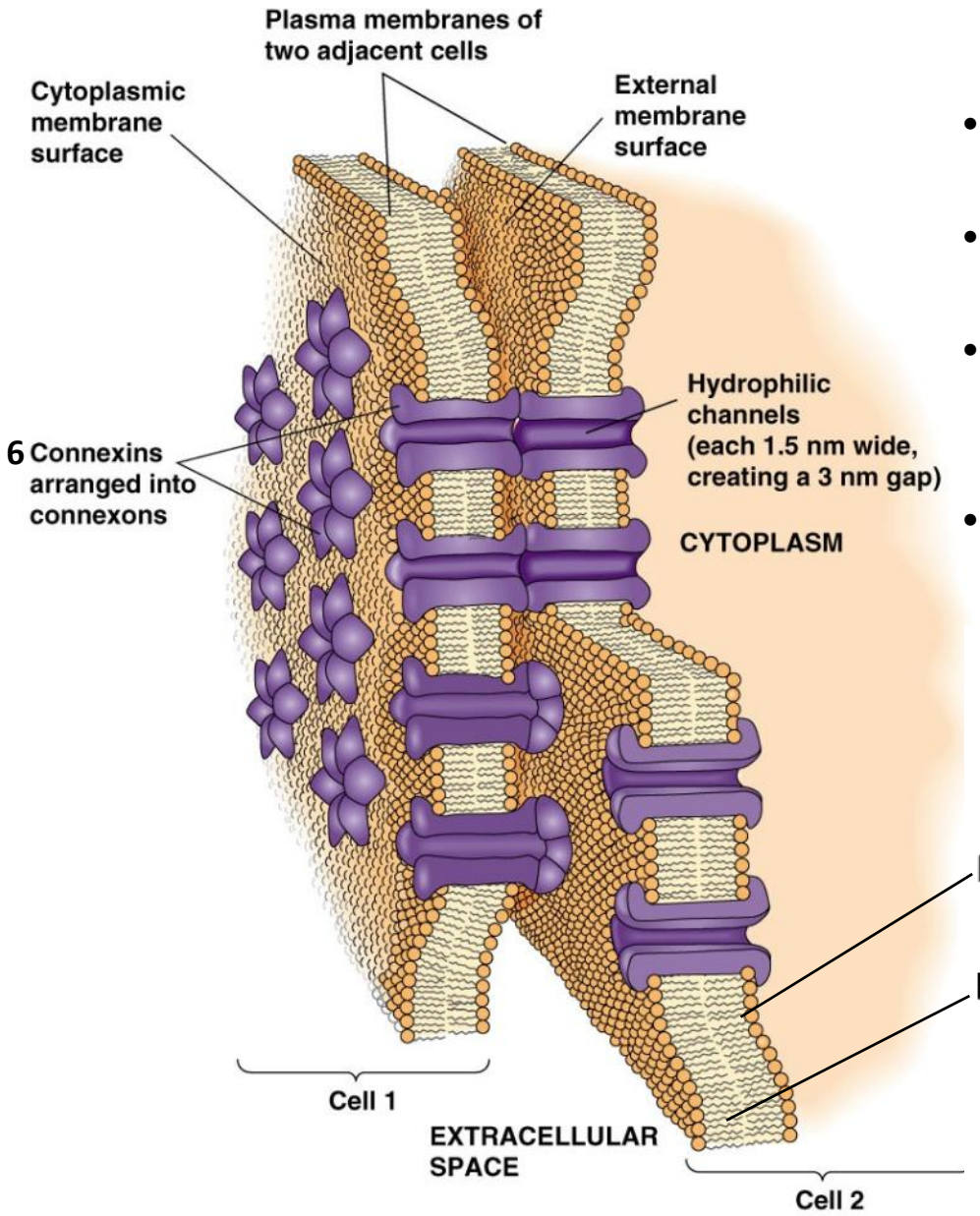


Paracellular transport through tight junctions

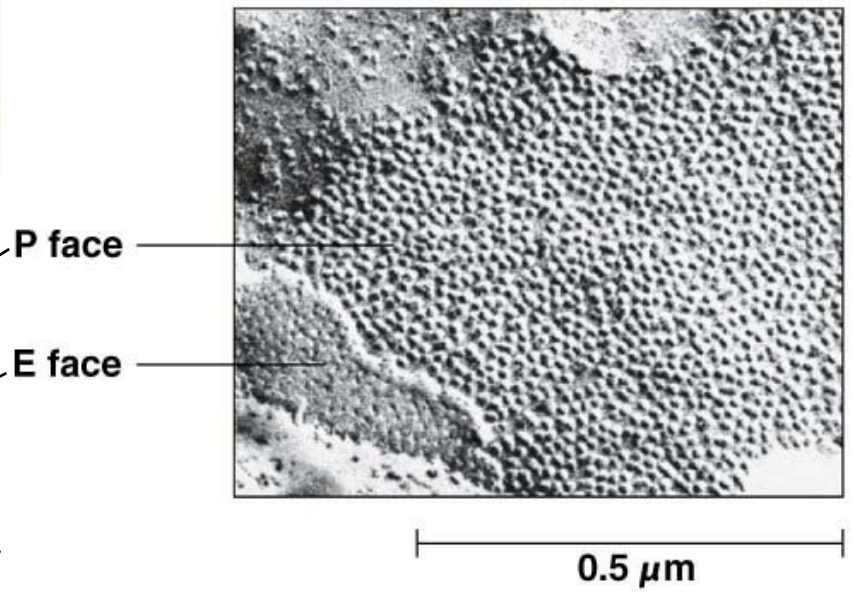
- Claudin has four transmembrane-spanning domains and a large and **charged extracellular loop** that facilitates passing of ions thru the intercellular space (**paracellular transport**)
- Mutations in claudin result in a **disease** (**FHHNC**) with severe Mg^{2+} and Ca^{2+} imbalance



Structure and function of gap junctions



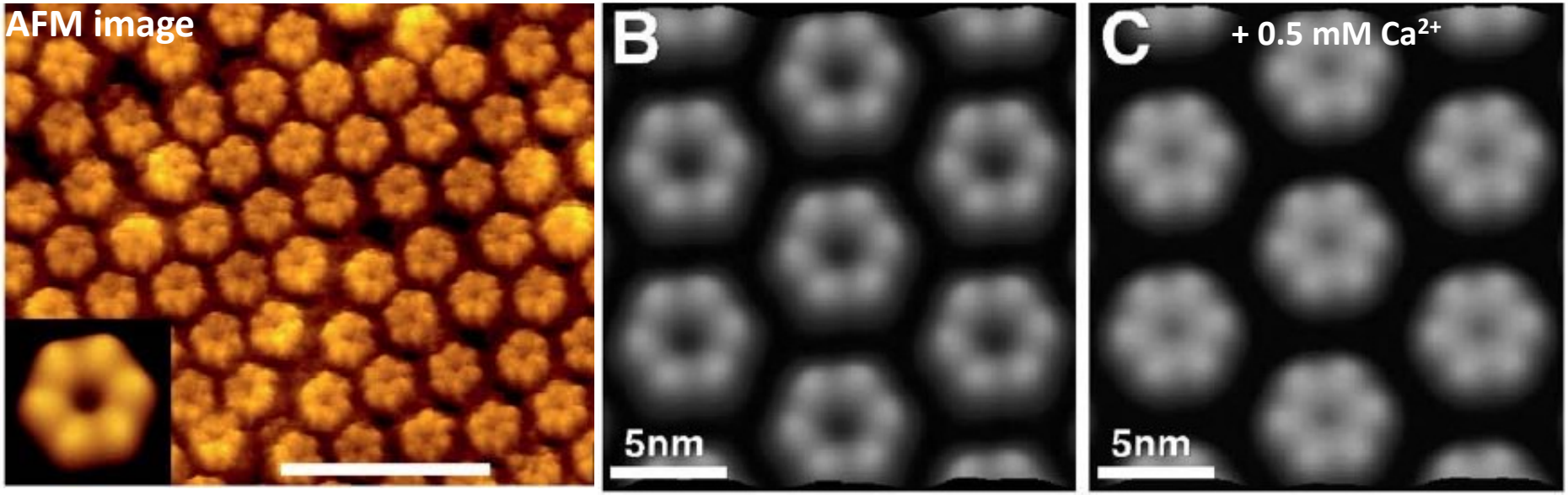
- Gap junctions are cell-cell junctions with the smallest known intercellular space (gap): 2-3 nm
- Gap junctions are composed of small channels made of (hexagonal) **connexons**
- Each connexon is made of six **connexin** subunits
- These channels let ions and small molecules pass (including **single sugars**, **amino acids** and **nucleotides**)
- They serve as **chemical and electrical connections** between two cells



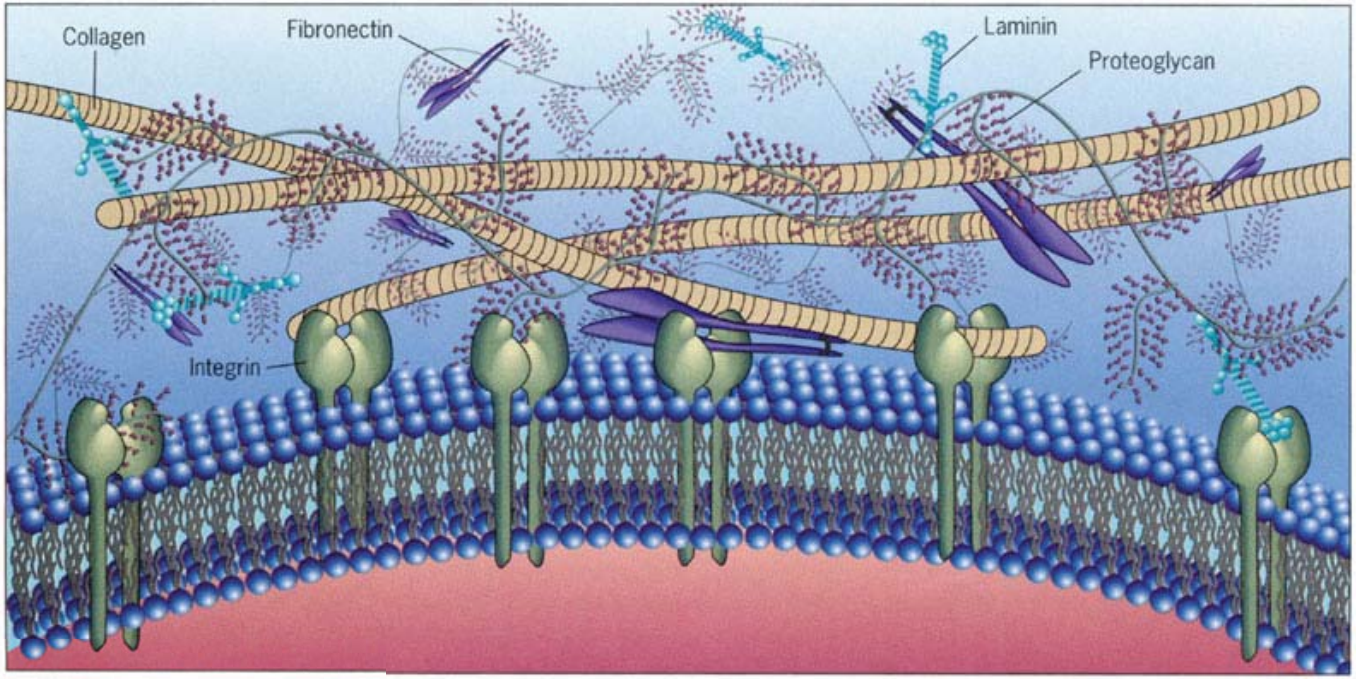
Structure and function of gap junctions

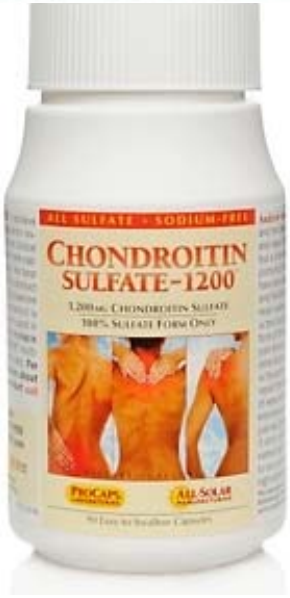
- Especially important are gap junctions in **heart muscle** and **nerve tissues** where fast communication is necessary ("electrical synapse")
- Several **human diseases** are associated with gap junctions involving the demyelinating of neurons, skin diseases, cataracts (clouding of the eye lens) and deafness
- Gap junction channels **are able to open and close** (controlled by calcium, second messengers and the electrical potential)

Atomic force microscopy allows for high resolution imaging of connexons closing and opening



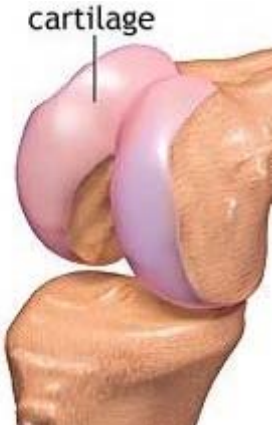
The extracellular matrix

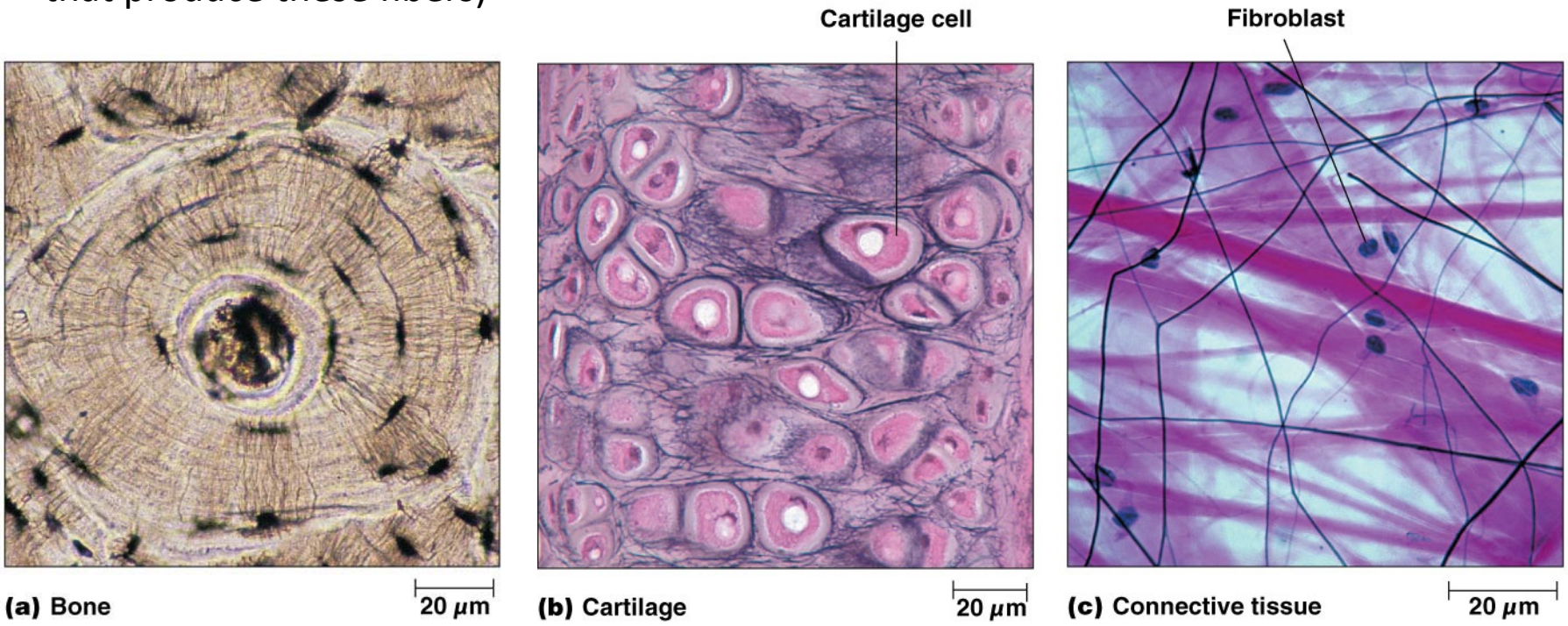




Introduction to the extracellular matrix (ECM)

- Tissues are not only composed of tightly interacting cells
- All tissues are embedded and interact with the **extracellular matrix** (**ECM**)
- The **calcified bone tissue** is one of the hardest tissues and is mainly composed of ECM (with only few cells - osteoblasts - spread in)
- Also the **cartilage** (more softer and flexible than bone tissue) is almost entirely composed of ECM (lots of **proteoglycan**)
- The **connective tissue** surrounding glands and blood vessels has a gelatinous character and mainly contains the ECM protein **collagen** and **fibroblasts** (cells that produce these fibers)

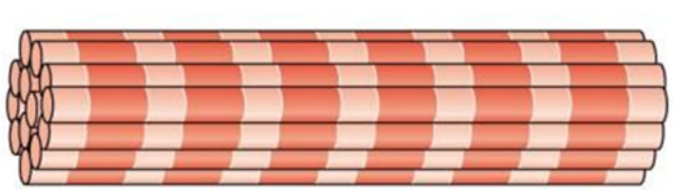


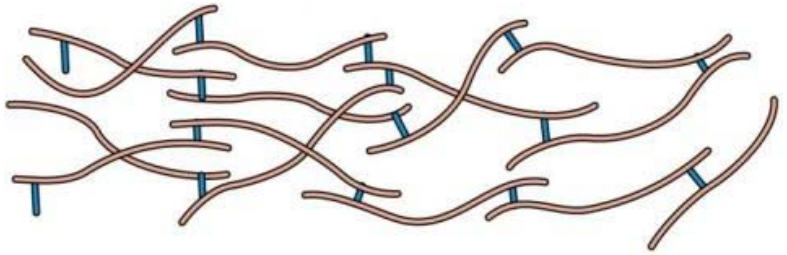


The basic proteins forming the extracellular matrix (ECM)

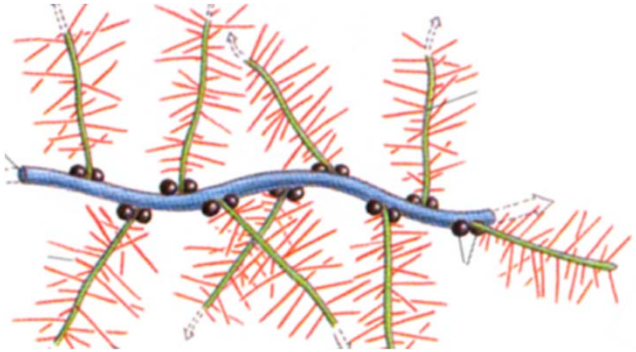
The ECM can be subdivided into three major classes of molecules

(1) Structural proteins: **collagens** and **elastins** for strength and flexibility of the ECM

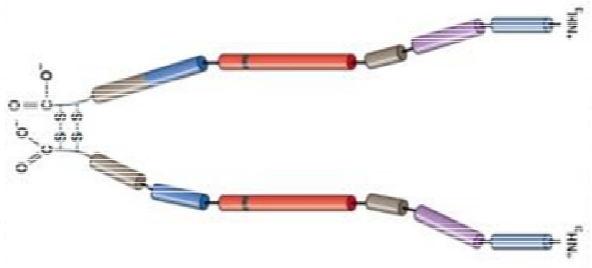


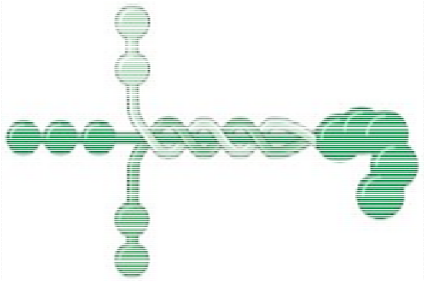


(2) Protein-polysaccharides (**proteoglycans**) create the matrix for structural proteins

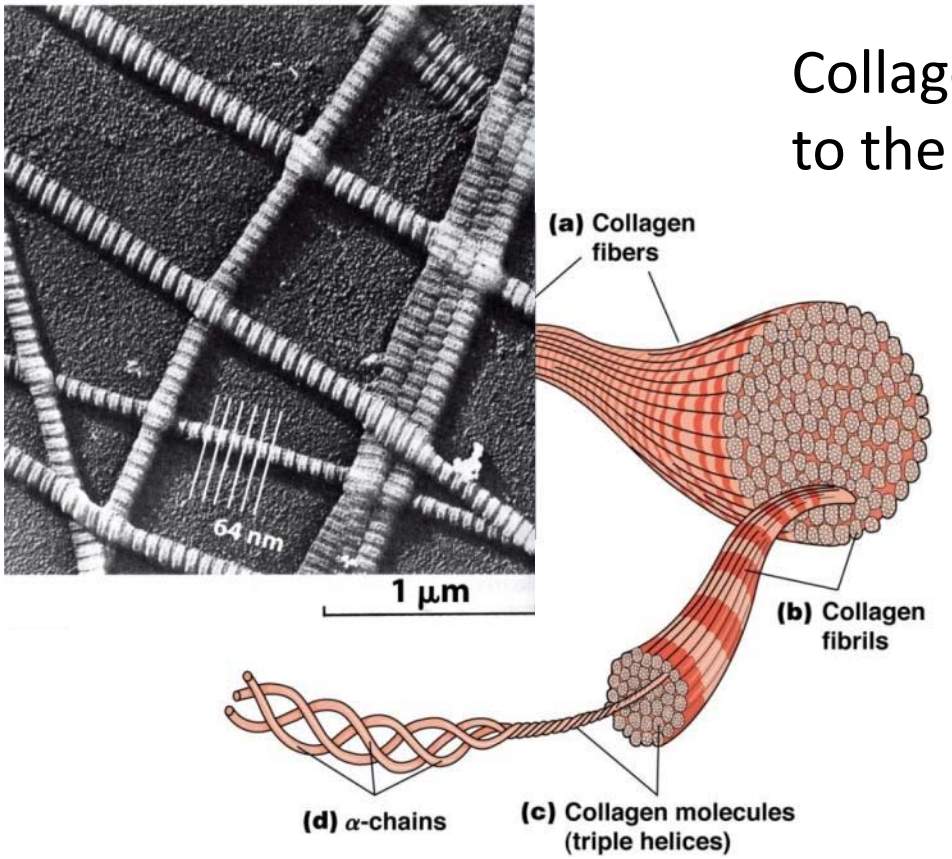


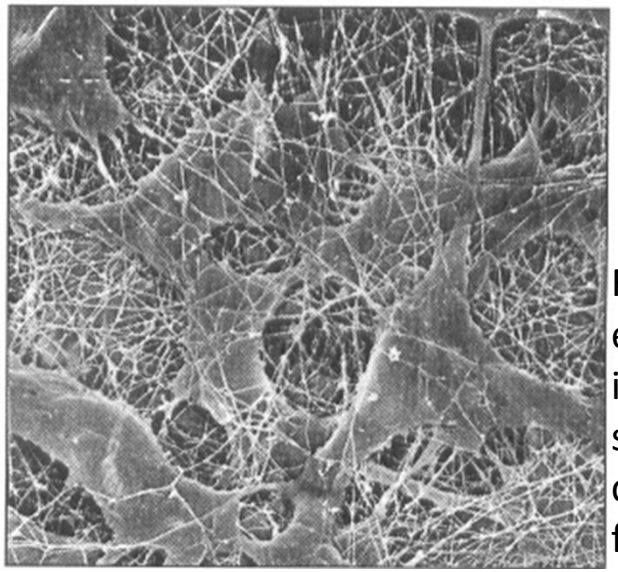
(3) Adhesive glycoproteins: **fibronectin** and **laminins** that attach cells to the matrix





Collagens provide strength and flexibility to the ECM



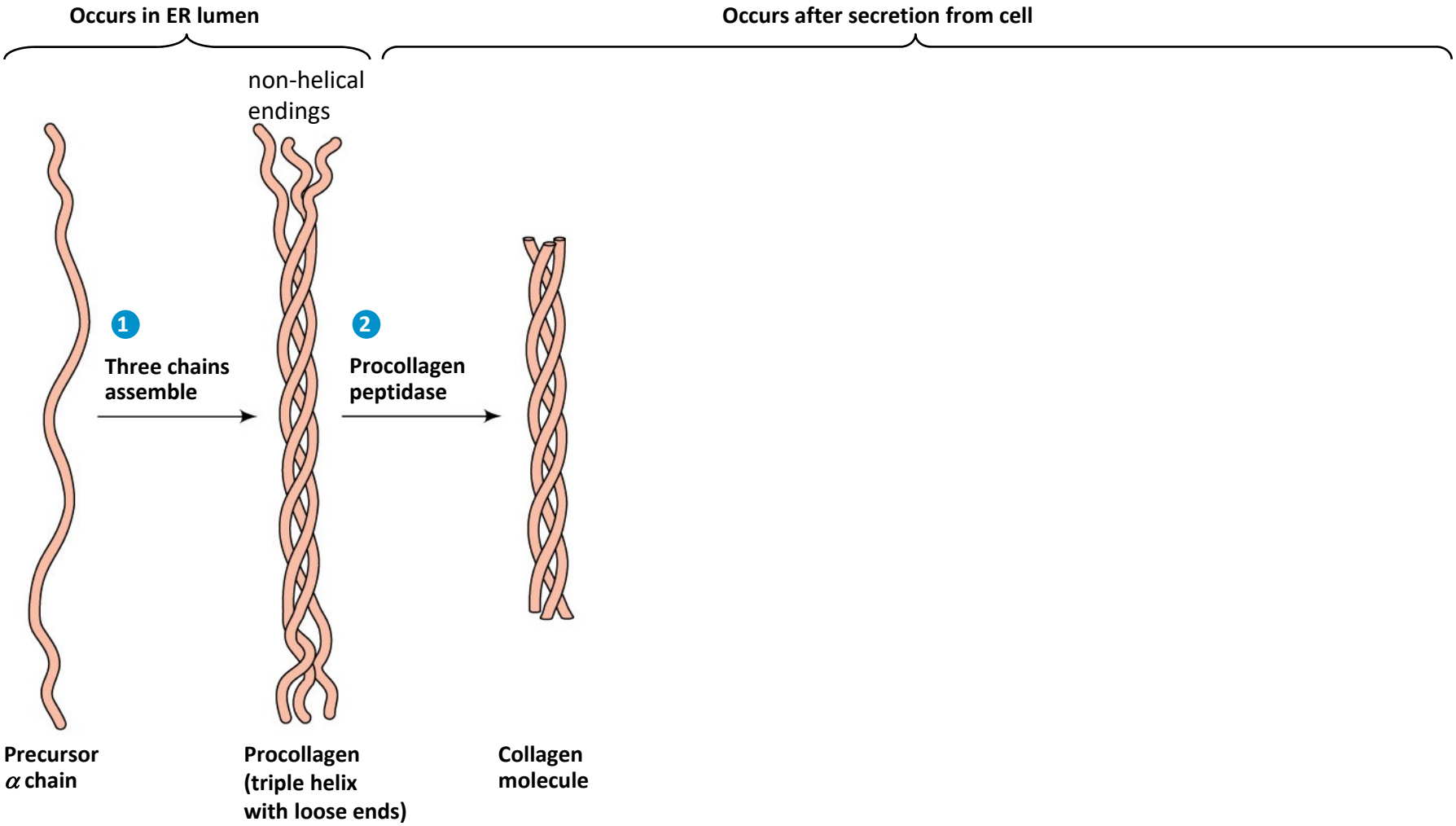


Fibroblasts embedded in their own secreted collagen fibers

- Collagens are very abundant in the ECM (in fact most abundant protein in our body covering 20-25% of total protein)
- These fibers have **high tension strength**: a fiber of 1 mm in length can easily resist a pulling force of 9 kg
- Collagens are **secreted by fibroblasts** which are embedded in the ECM
- **3 α-chains** are intertwined to form the characteristic **triple helix** of collagen
- Many collagens form the collagen **fib*ril***
- These fibrils assembly into the final collagen **fib*er***
- In EM images, collagen fibers exhibit a characteristic **striation** (based on the assembly pattern of the triple helices)
- **Vitamin C** is an essential cofactor for collagen synthesis and lack of vitamin C results in the "*sailor and pirate disease*" **scurvy** (impairment of wound healing)

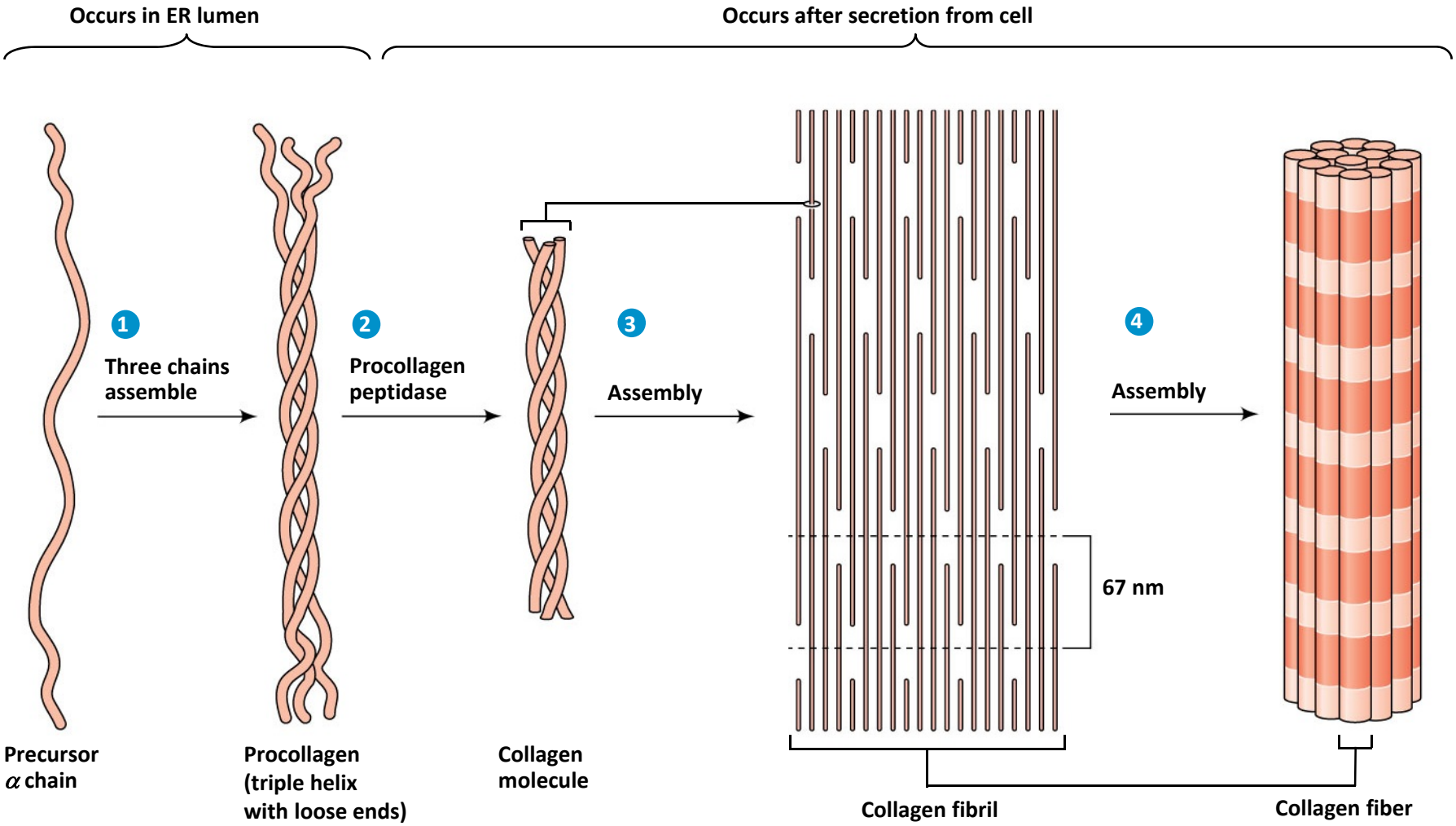
Collagen assembly

- Collagen assembly takes part **inside** as well as **outside** of the cell
- **ER lumen**: **precursor α-chains** are assembled to **procollagen** (**triple helix**)
- After secretion from the cell, procollagen is **converted to collagen** by a peptide cleavage process (**peptidase**) (non-helical endings prevent spontaneous assembly into collagen)



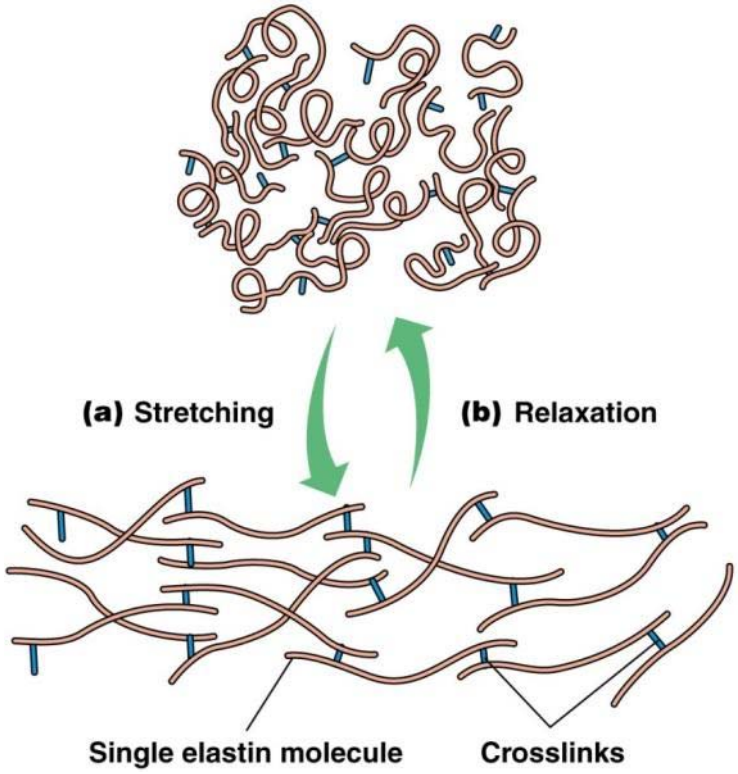
Collagen assembly

- In the intercellular space, collagen molecules (also called tropocollagen) spontaneous self-assemble into **collagen fibrils**
- The collagen fibrils then assemble laterally into the **final collagen fiber** (diameter varies between 30-300 nm)

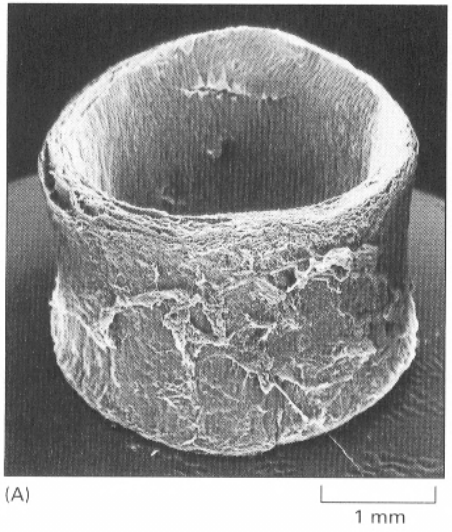


Elastin is the most s t r e t c h a b l e molecule in the ECM

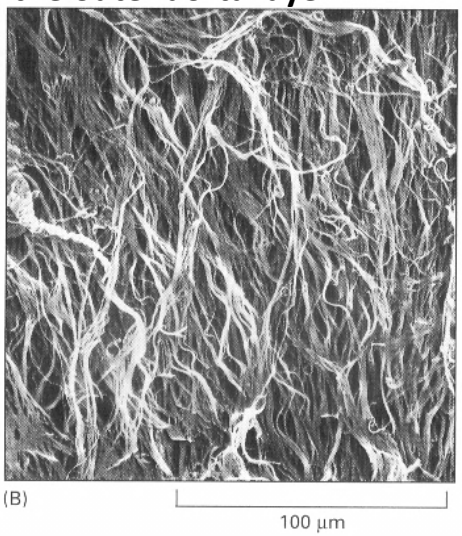
- In organs as lungs, arteries, skin and intestine tissue **elasticity** and **flexibility** is important
- **Elastins** are very stretchable fibers and are able to provide elastic features for tissues
- For example the **aorta** must somehow manage strong and alternating **blood pressure**
- **Elastin** molecules are long and floppy chains cross-linked to one another by covalent bonds
- Tension on this network will **stretch** it, and when the tension is released the network will **relax back** to its initial state
- **Over age**, elastins are lost from tissues (e.g., the skin) and at the same time collagen becomes more crosslinked and inflexible => **skin becomes wrinkled**



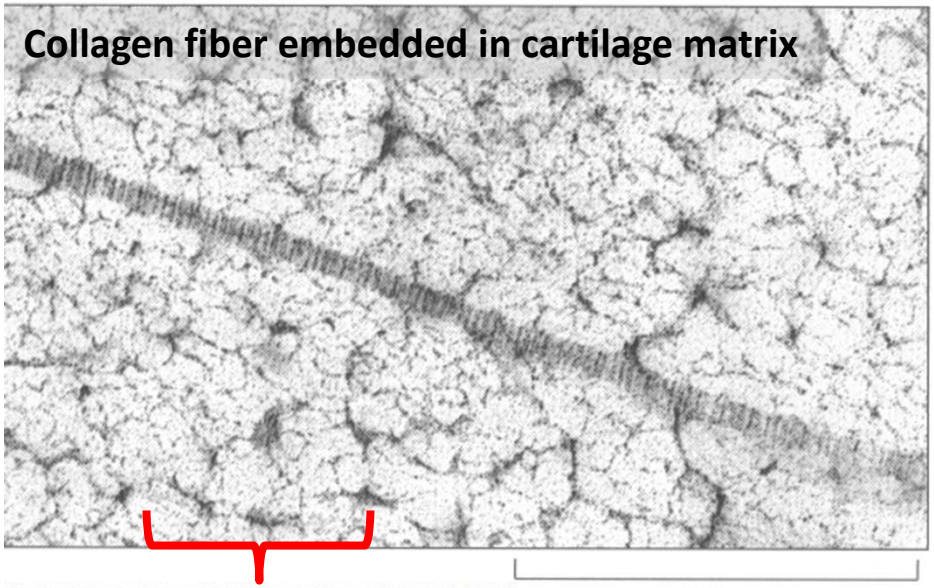
Elastic aorta to handle alternating blood pressure

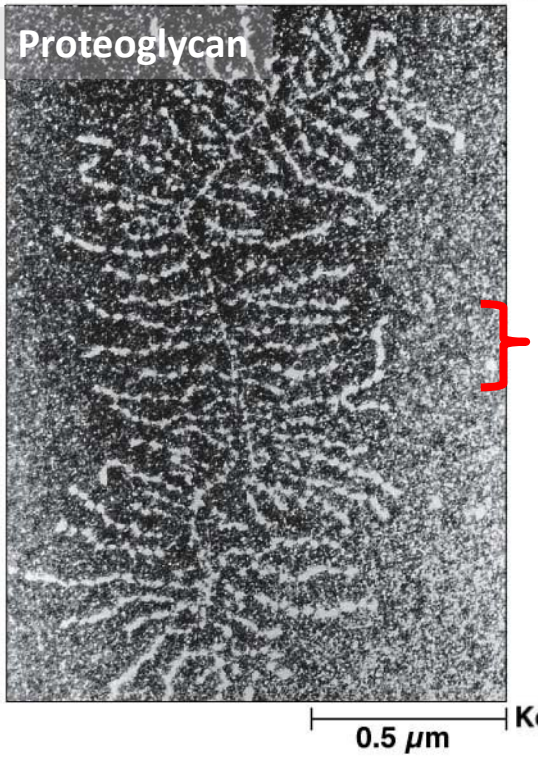


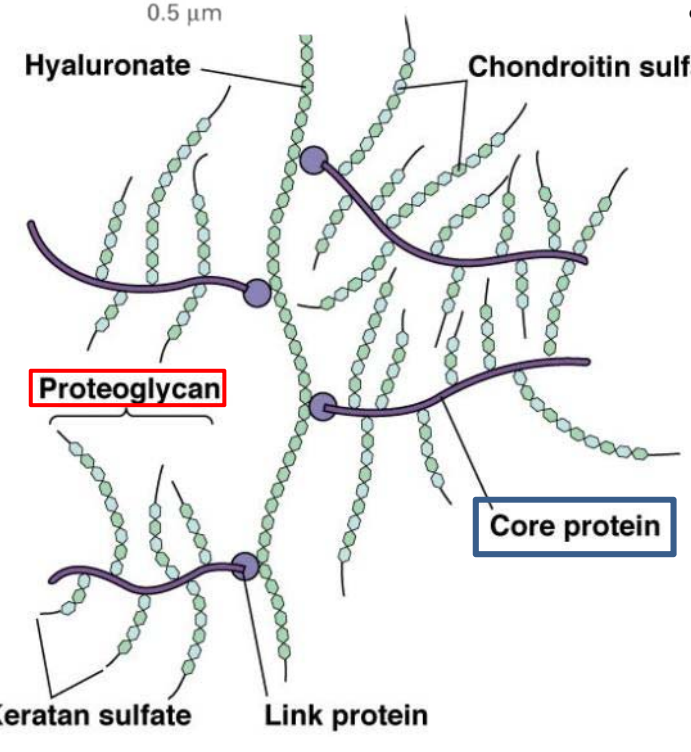
Elastic fibers (elastin) in the outer aorta layer



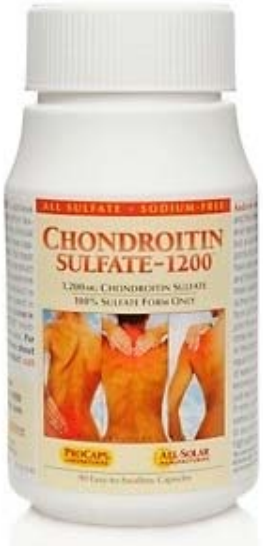
Collagen and elastin are often embedded in a matrix of proteoglycans





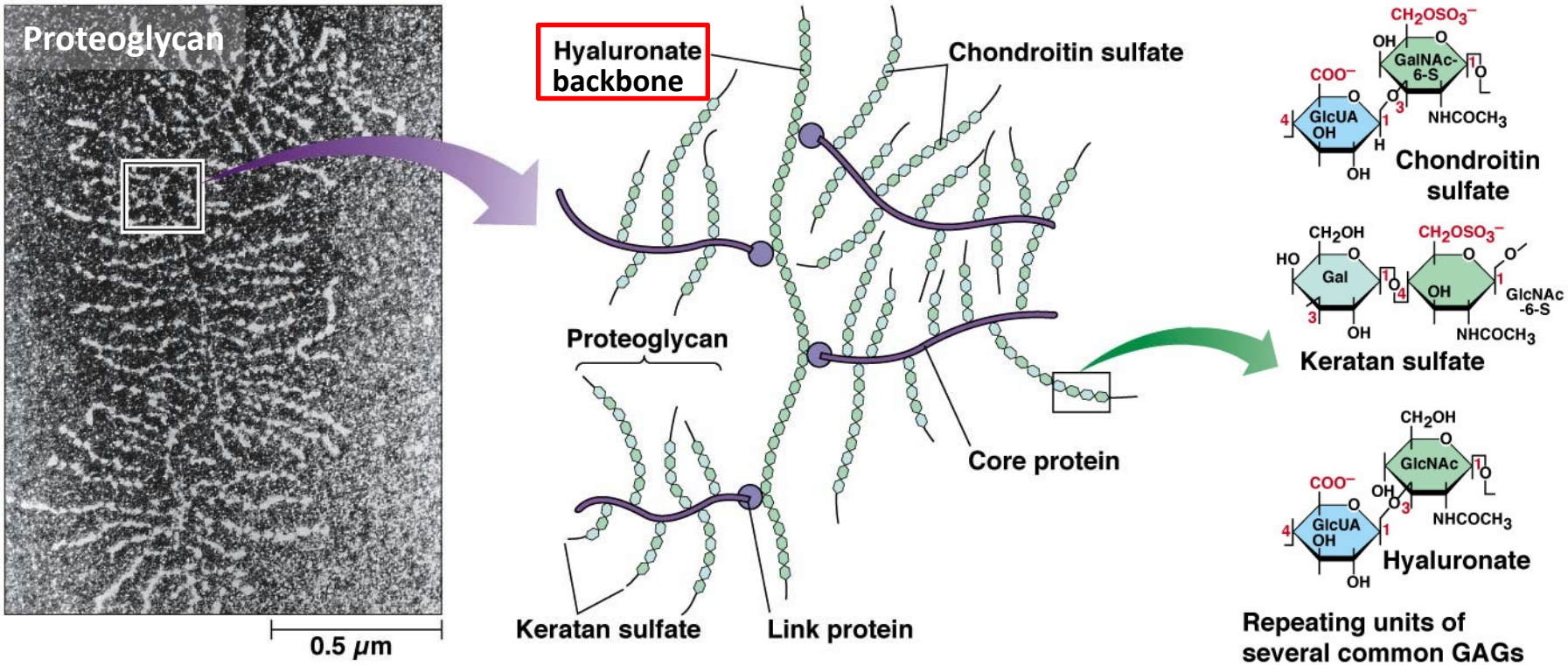


- Collagen and elastin fibers are found in **hydrated**, **gel-like matrices**, e.g., cartilage
- These gel-like matrices are basically composed of **proteoglycan proteins**
- Proteoglycans have a core protein to which long chains of **GAGs** (**glycosaminoglycans**) associate
- Example of GAGs are **hyaluronate**, **chondroitin sulfate** and **keratan sulfate** (which differ in lengths)



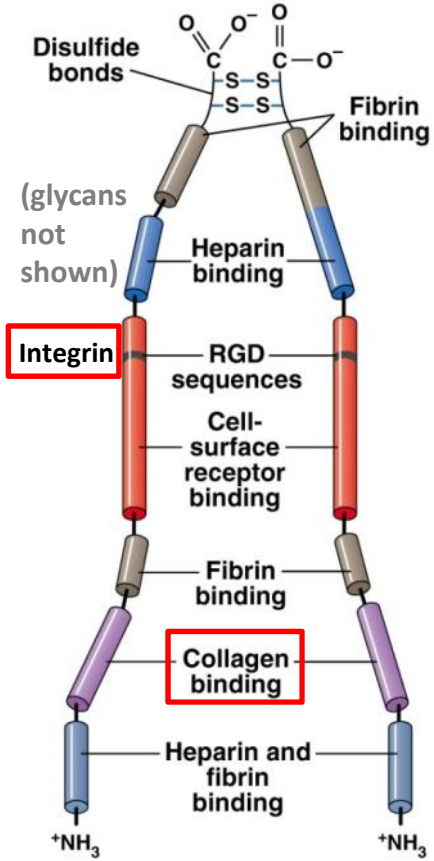
Many proteoglycans are linked to a long hyaluronate backbone

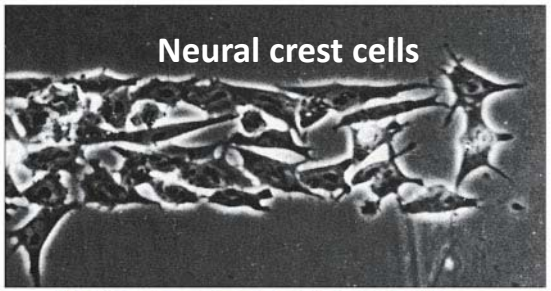
- Several proteoglycans are connected to a **hyaluronate backbone** via **link proteins**
- This makes the cartilage proteoglycans huge molecules with the **size of a bacterium**!
- GAGs are long **carbohydrates** characterized by **repeating disaccharide units**
- The disaccharide always contains **one amino sugar**, either ***N*-Acetylgalactosamine** (***GalNAc***) or ***N*-Acetylglucosamine** (***GlcNAc***). The **other sugar** is usually a sugar acid (**glucuronate**, **GlcUA**) or a monosaccharide (**galactose**, **Gal**).
- Because GAGs are **hydrophilic** with many negatively charged groups, they **attract** both **water and cations** contributing to the **gelatinous** and **hydrated matrix**

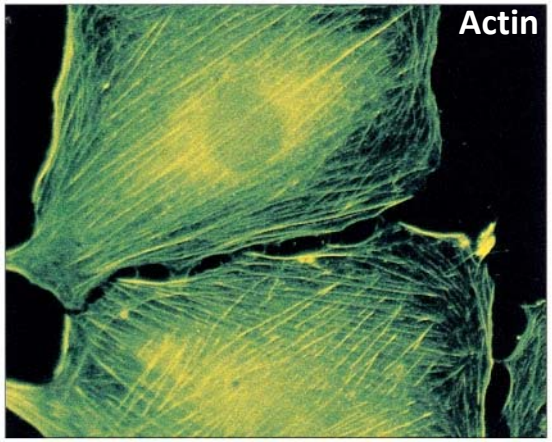


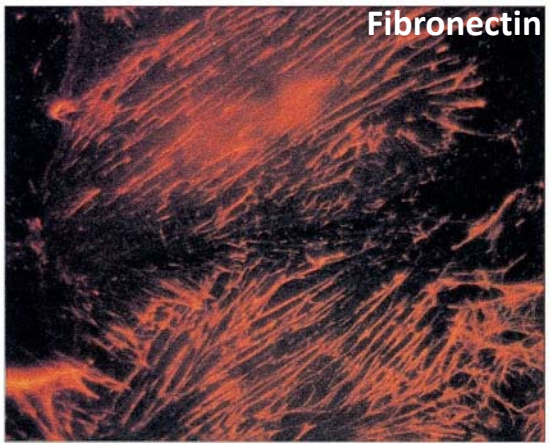
Fibronectin connects cells to the ECM and guides cell migration

- Fibronectin is a an **adhesive glycoprotein** found in ECM substrates
- 2 large polypeptides (each 2500 aa) linked by **disulfide bonds** at the C-terminal end
- Several domains bind to different **ECM** molecules such as **collagen**, **heparin** (anticoagulant) and **fibrin** (blood clotting)
- **RGD** (arginine-glycine-aspartate) **sequences** bind to **integrins** on cell surfaces
- Based on these binding properties **fibronectin** can be considered as a bridging molecule that **connects cells to the ECM**







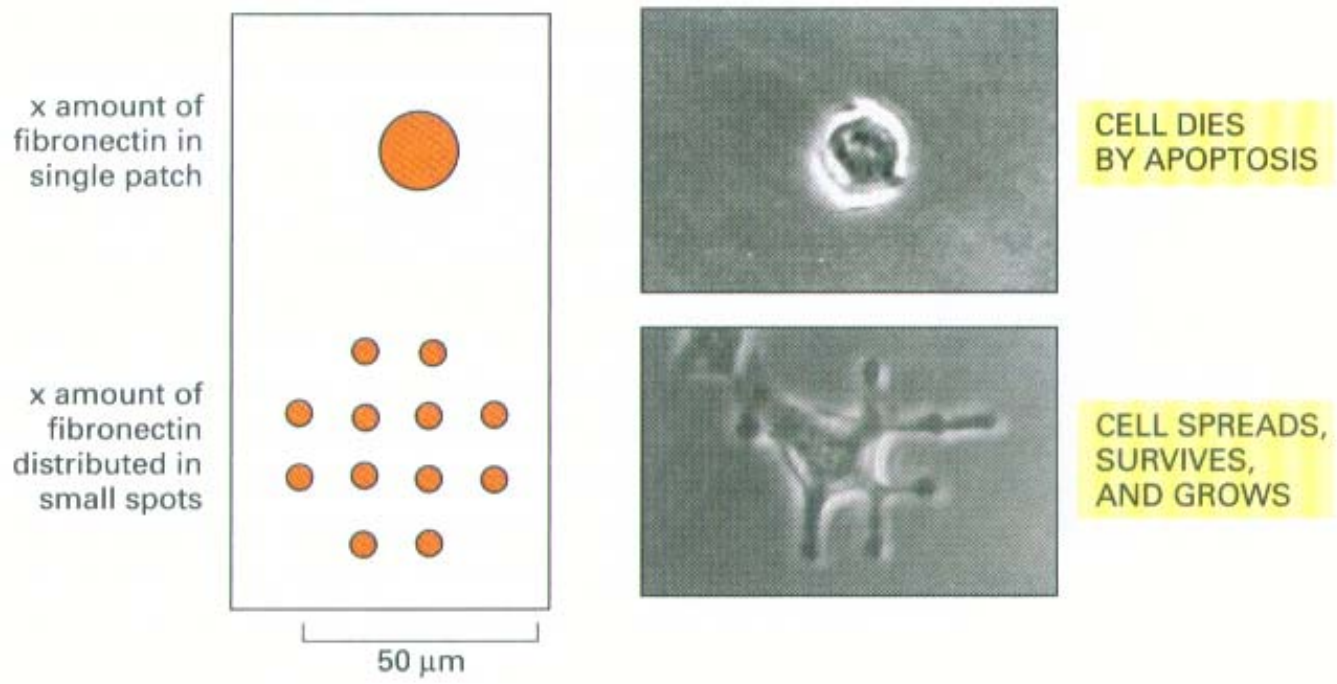


- Fibronectin has the ability to **guide migrating cells** (e.g., neural crest cells)
- Cells preferably attach to surfaces coated with fibronectin and tend to **align their actin fibers** along the **fibronectin network**

Fibronectin make a flexible and stretchable fibrous network

Fibronectin facilitates cell spreading important for cell viablity

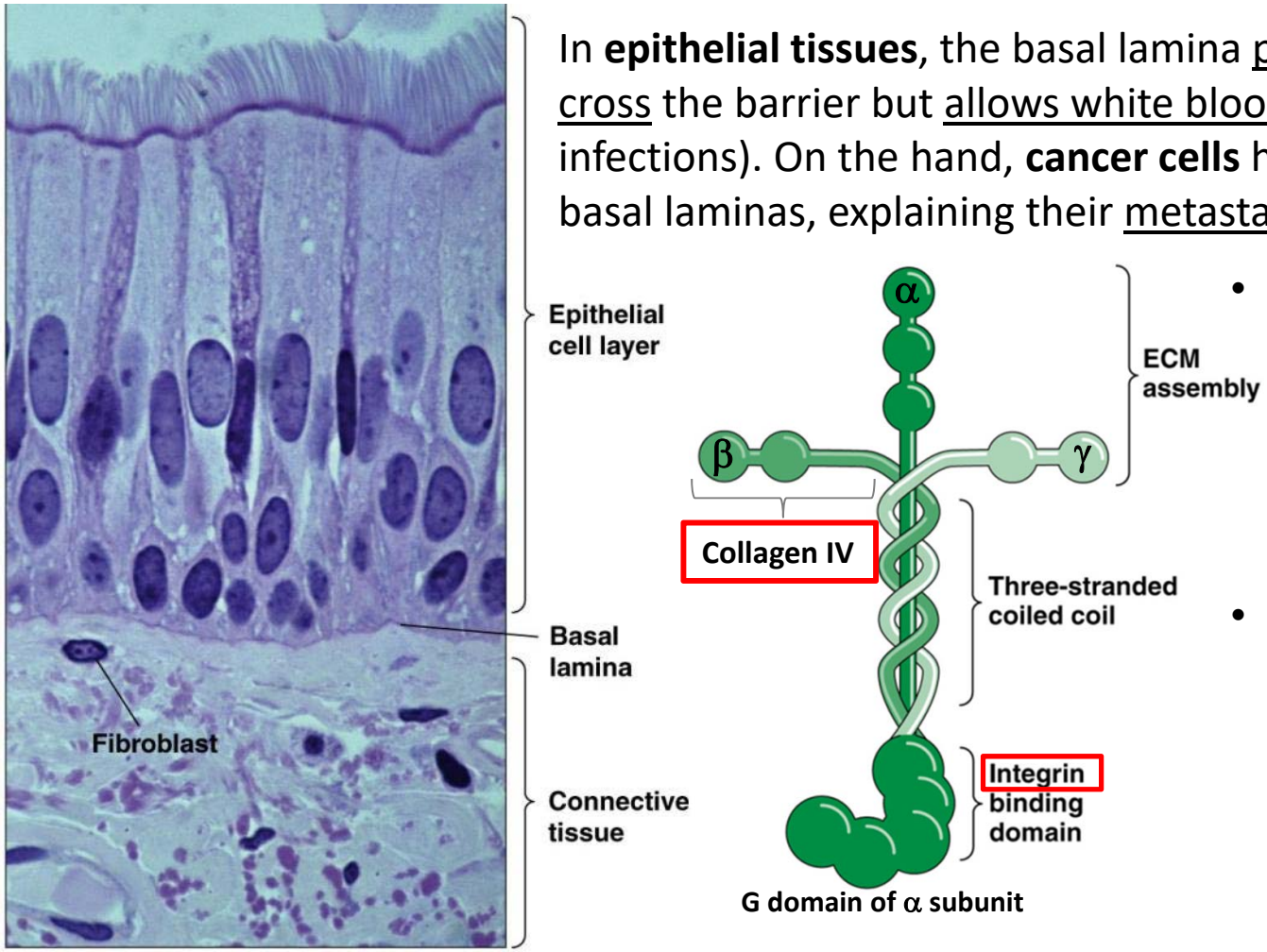
- The interaction of cells with fibronectin in the ECM seems to be important for **cell survival**
- If a cell in a culture dish cannot spread out it will **die by apoptosis** (programmed cell death)
- On the other hand if a cell is able to spread (even with a small amounts of fibronectin) it will **survive** and **proliferate** (cell growth)
- Some cancer cells lack the ability to produce fibronectin and easily detach from ECM surfaces that may contribute to their uncontrolled migration behavior



To survive and proliferate cells need to spread out. Even small amounts of fibronectin (that can be "searched and captured") are sufficient for the cell to create new anchor points.

Laminins are bridging proteins that link cells to basal laminas

- Similar to fibronectin, **laminins** have two binding sites that allows for connecting cells to the ECM. However, laminins are specialized for only one type of ECM: the **basal lamina**
- Basal laminas act as a **permeability barrier** between two tissues of different functionalities
- For example, in the **kidney** basal laminas prevent blood from entering into the urine (but allow for the bidirectional flow of small molecules)

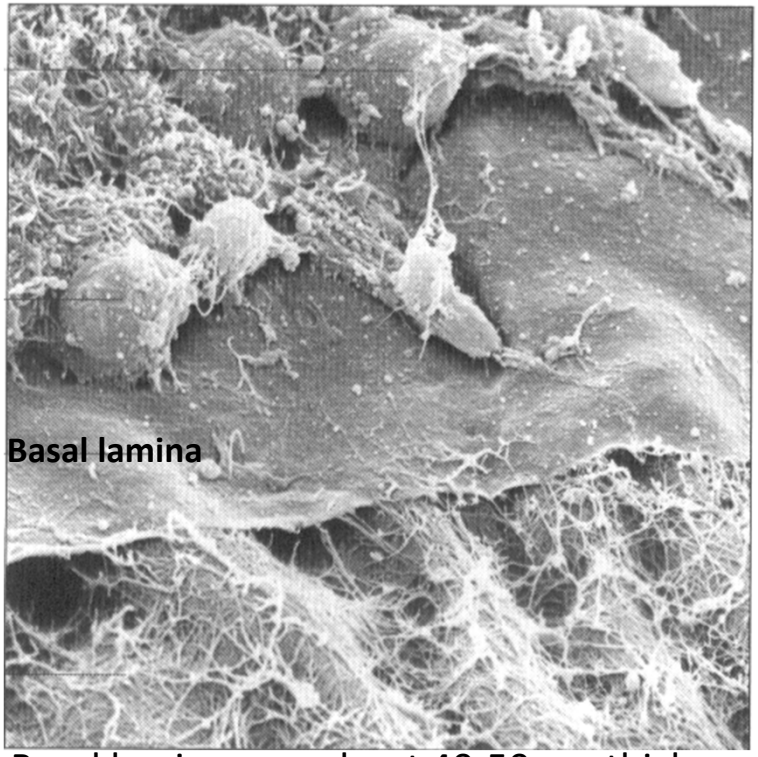


In **epithelial tissues**, the basal lamina prevents fibroblasts to cross the barrier but allows white blood cells to enter (to fight infections). On the hand, **cancer cells** have a strong affinity to basal laminas, explaining their metastatic potential.

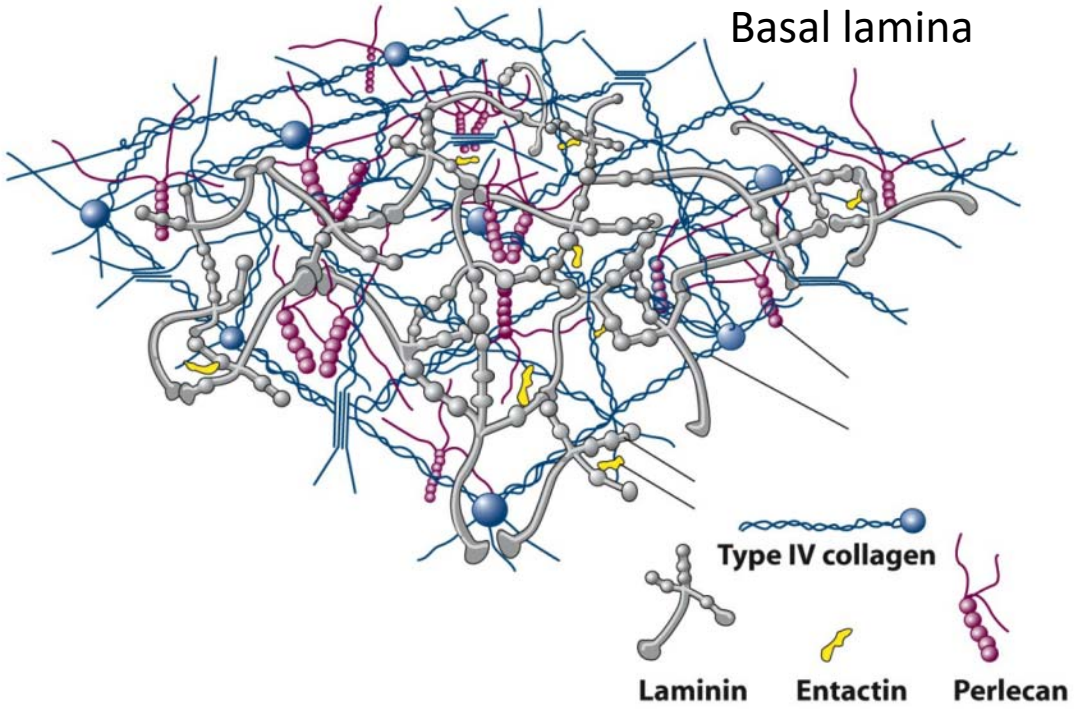
- Laminins are large molecules (850 kD) composed of **three intertwined polypeptide chains** (α, β and γ) that **form a cross**
- Laminins have binding sites for **integrins**, **type IV collagen** (arms of β and γ), **heparin**, **haparan sulfate** and **entactin**

Laminin and type IV collagen form the complicated basal lamina

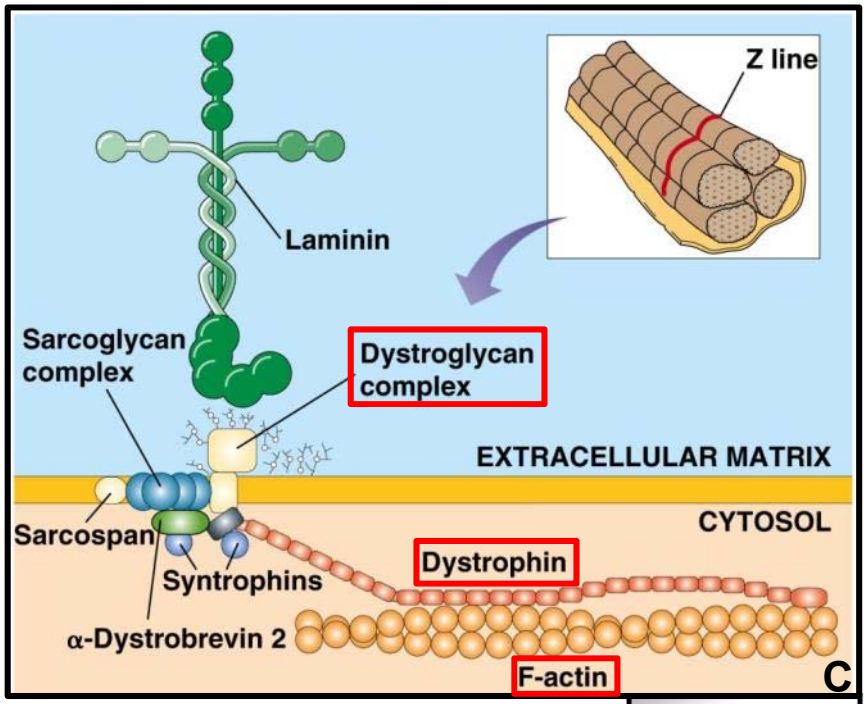
- **Type IV collagen** plays an important role in the formation of a tight network
- **Entactin** and **perlecan** bind to both **type IV collagen** and **laminin** which reinforces the network
- **Secreting enzymes** can alter the properties of basal laminas
- One example is the **matrix metalloproteinase** (**MMP**). This enzyme (requires metal ions as cofactors) can degrade the basal lamina locally to **let cells pass thru** (important for leucocytes to invade insured tissues)
- Highly metastatic **melanoma cells** have high MMP activity



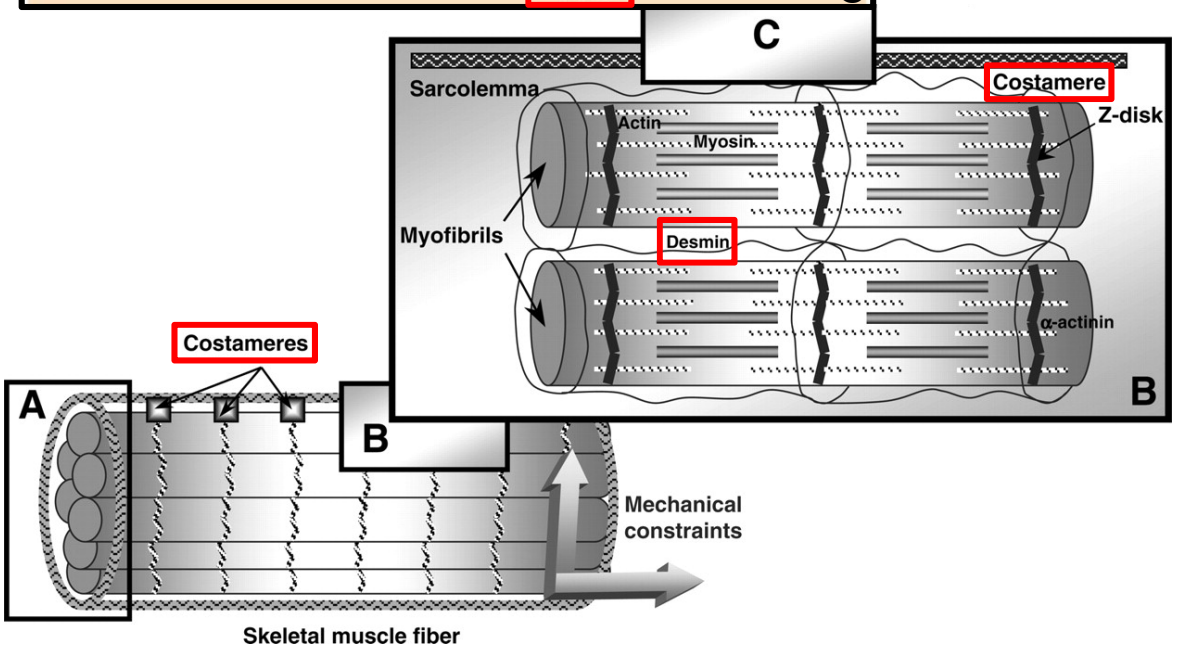
Basal laminas are about 40-50 nm thick



Laminins also connect muscle fibers to the ECM



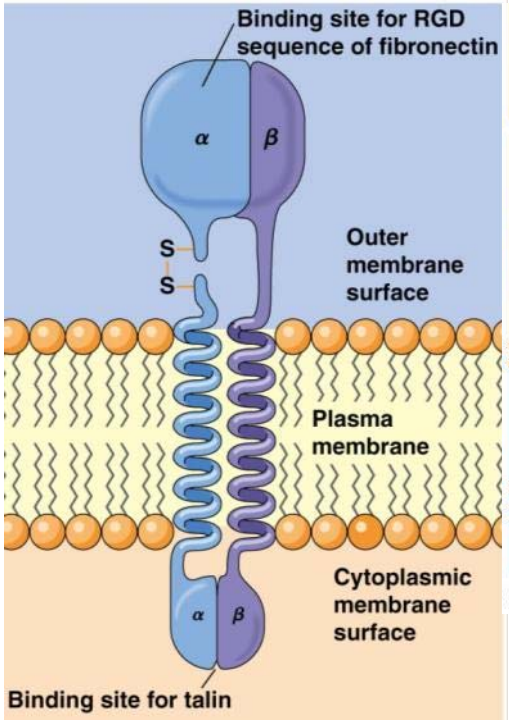
- **[A]** Near the sarcolemma, **costamers** appear that are in close proximity to Z-discs
- **[B]** Myofibrils are bundled via the intermediate filament protein **desmin**
- **[C]** Besides proteins that are found in focal adhesions, costamers also contain **dystrophin**
- Dystrophin binds to **actin** and to the **dystroglycan complex** (that **binds laminin**) via a series of other proteins

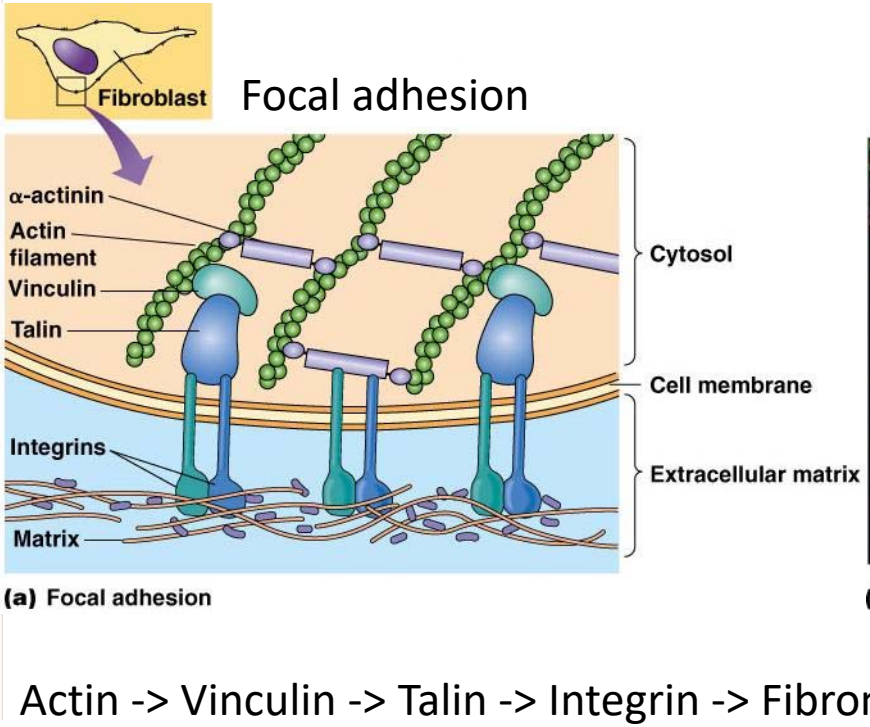


- Mutations in dystrophin causes a major type of **muscular dystrophy** (DMD, *Duchenne muscular dystrophy*)
- DMD patients undergo progressive muscle degeneration often leading to loss of the ability to walk and even death (e.g., unable to swallow)

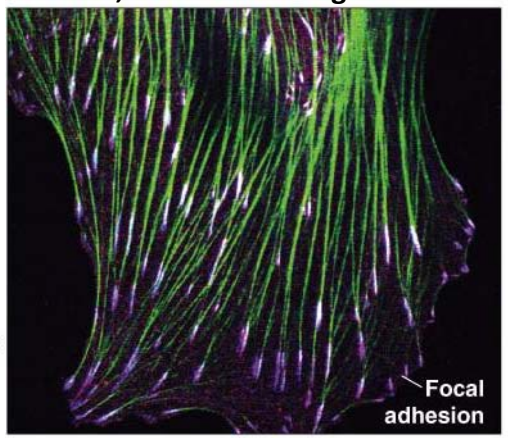
Structure and function of integrins

- How do cells recognize and bind to collagen, fibronectin and laminins in the ECM?
- Cells use receptor molecules (called **integrins**) on their cell surface to bind to the ECM
- Besides the function of integrins as cell adhesion molecules (rolling of leucocytes) they also act as **integrators** to connect cells to the ECM
- Integrins are composed of **two large polypeptides** spanning across a membrane
- The **α subunit** is most critical for binding to ECM molecules (e.g., **RGD of fibronectin**)
- The cytosolic portion binds to **cytoskeletal adaptor proteins** so the cytoskeleton (e.g., F-actin) is mechanically linked (thru the plasma membrane) to the ECM
- In many migrating cells several adaptors as **talin**, **vinculin** and **α-actinin** are necessary to form tight attachment points with ECM surfaces called **focal adhesions**





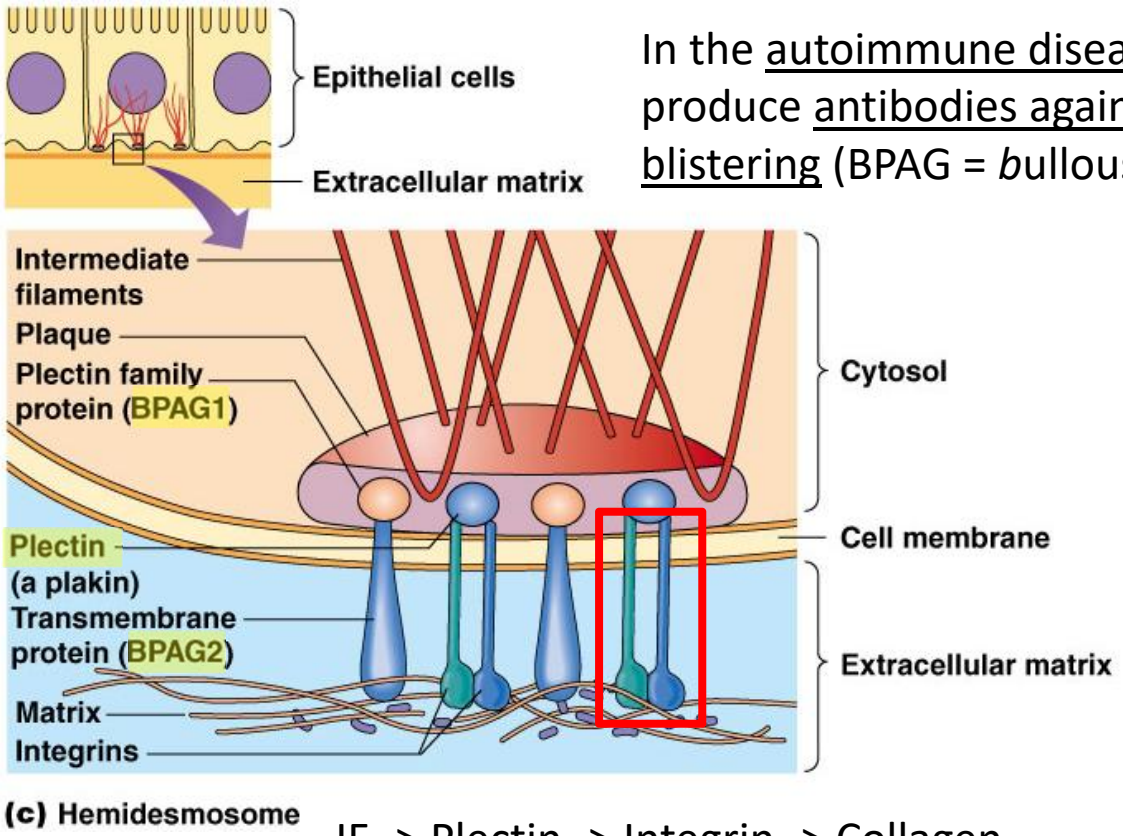
Green = actin, blue = integrin, red = vinculin, white = all merged



Actin -> Vinculin -> Talin -> Integrin -> Fibronectin -> Collagen

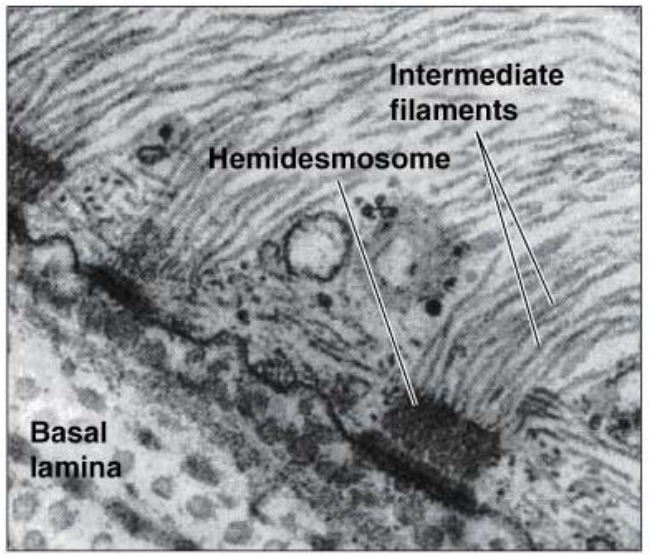
Integrins can be also found in hemidesmosomes

- Besides focal adhesions, integrins are also a major component of **hemidesmosomes** that **link epithelial cells to the ECM** (specifically to laminin in the basal lamina)
- Hemidesmosomes contain electron dense plaques (similar to desmosomes) that bind to **intermediate filaments** (IF). However, hemidesmosomes do not contain cadherins but **plectins** (IF binding protein and plakin family member) that bind to **integrins**
- In addition to integrins, hemidesmosomes also contain **BPAG2** that directly binds to the ECM and is anchored to the plaque via **BPAG1** (plectin family member)



(c) Hemidesmosome

In the autoimmune disease ***bullous pemphigoid*** patients produce antibodies against BPAG proteins resulting in skin blistering (BPAG = *b*ullous *p*emphigoid *a*ntig*e*n)



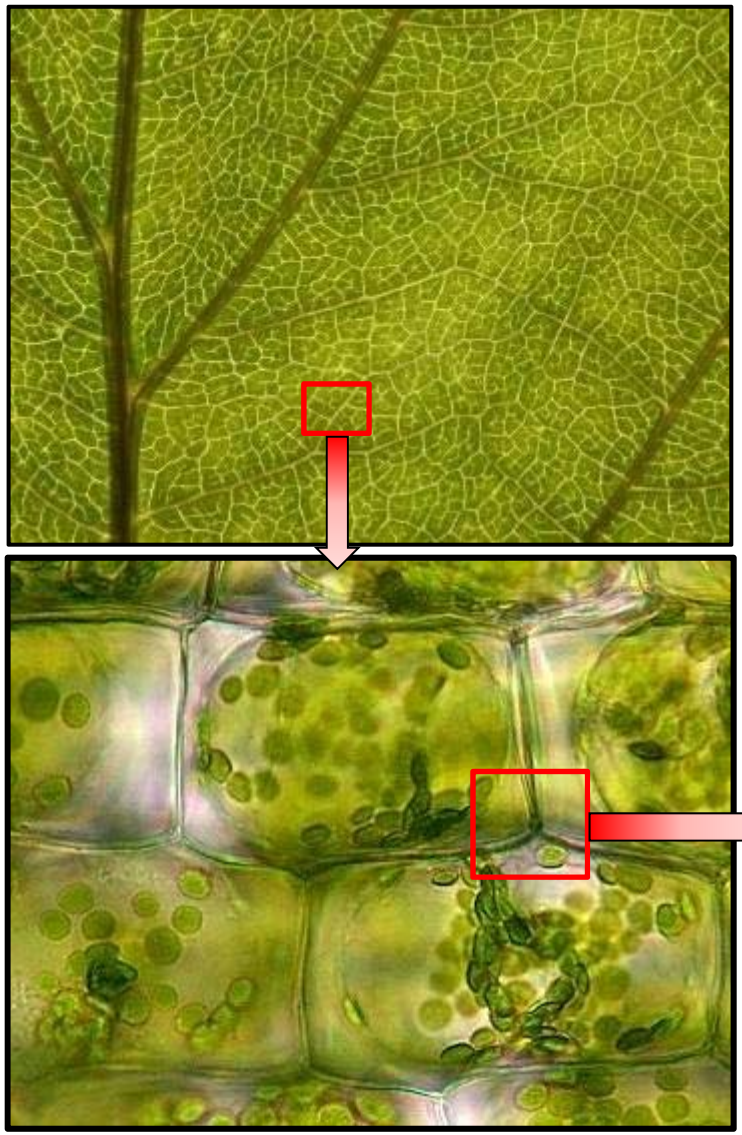
(d) Electron micrograph

IF -> Plectin -> Integrin -> Collagen

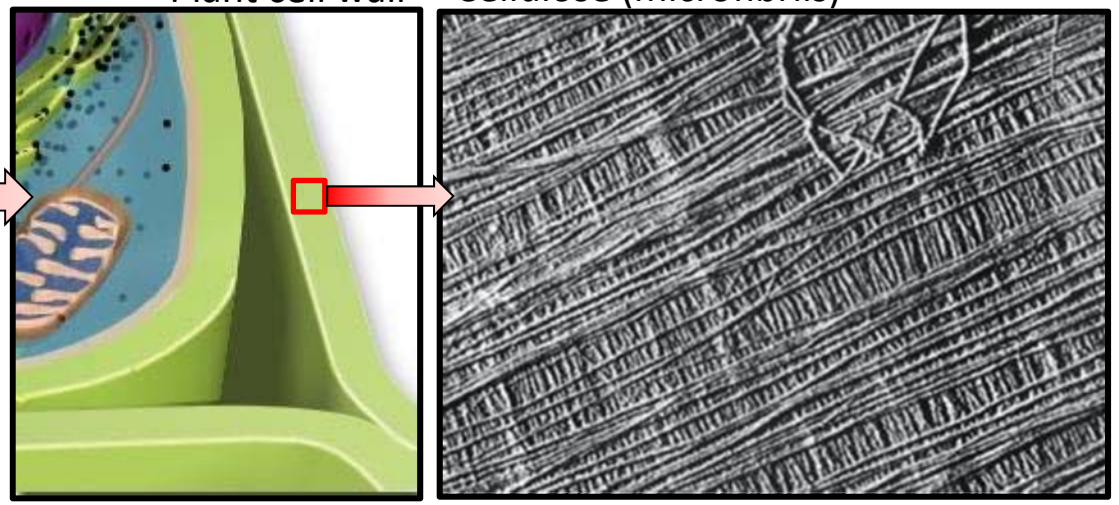

A journey into the cell
8 min full version:
https://www.youtube.com/watch?v=B_zD3NxSsD8

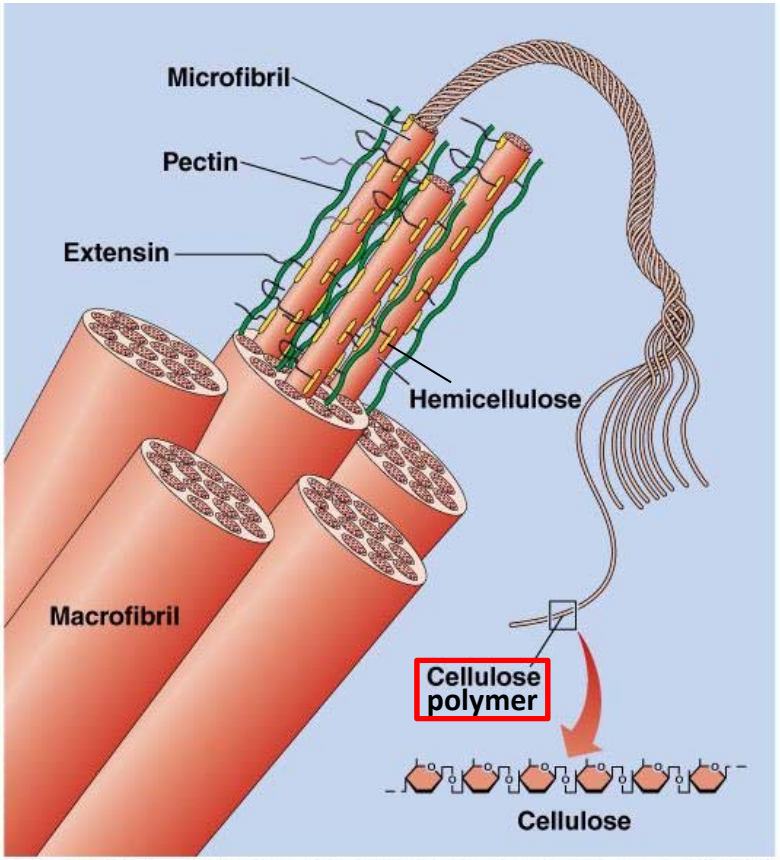
The plant cell surface: organization of the plant cell wall

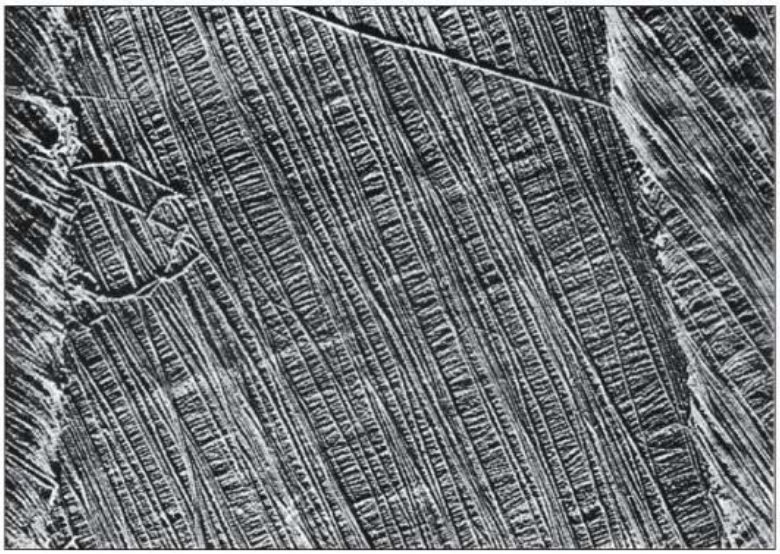
Unlike animals, plants have no bones or other skeletal structures. The **rigidity** in plants is **provided by** the strong **cell walls**, however, making them unable to move.



- The sturdy cell walls are also important to withstand the high inner pressure of plant cells (**turgor pressure**) which comes from the water uptake
- Turgor pressure is important for cell expansion
- Cell wall acts also as a **permeability barrier**; still it is well permeable for water, small molecules, amino acids and sugars
- **Similar to the ECM of animal cells** the plant cell wall is composed of fibers (**cellulose**) that are embedded in a matrix (**hemicellulose** and **extensins**)



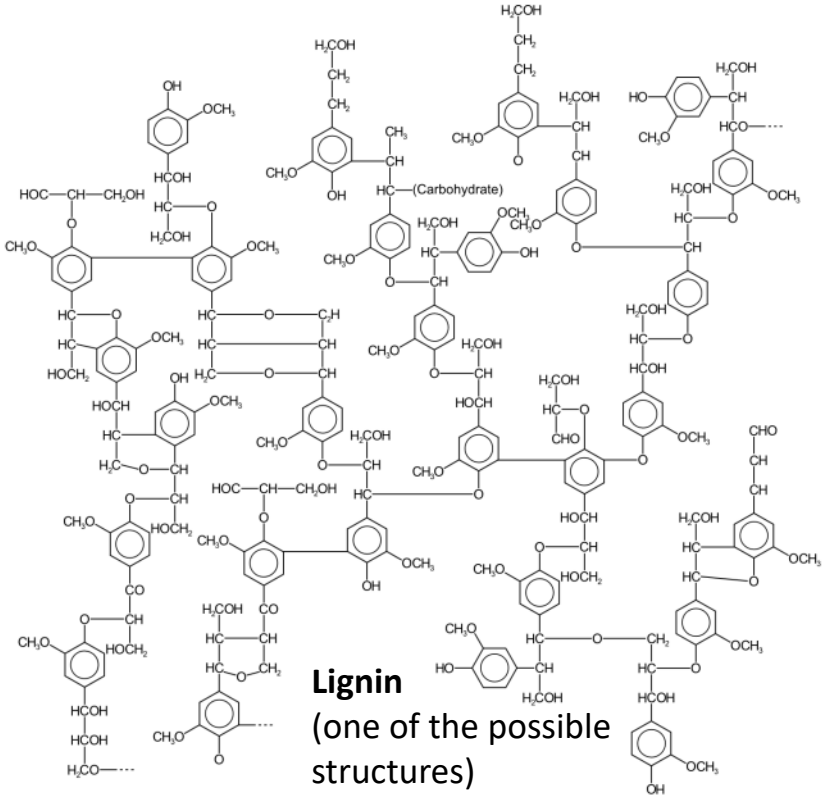




Structure of cellulose and its matrix

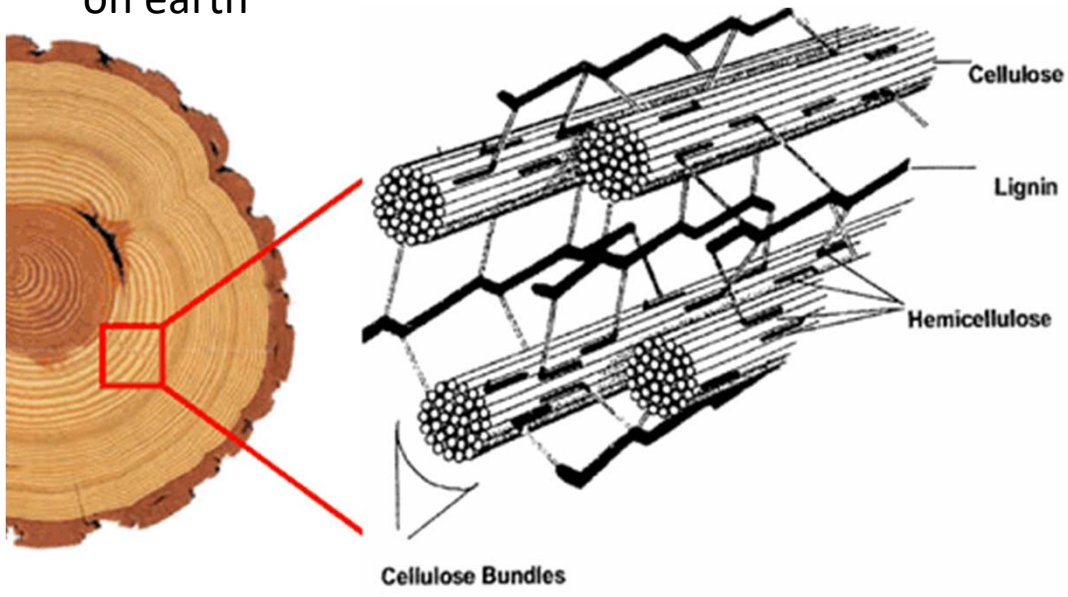
- Cellulose is the definite most abundant organic molecule on earth
- Cellulose is an unbranched polymer consisting of thousands **β-D-glucose units** linked together by β(1->4) bonds
- 50-60 of **cellulose polymers** form **cellulose microfibrils** which (often) form **macrofibrils** with an enormous strength (comparable to steel)
- The microfibrils are embedded in a matrix of polysaccharides (**hemicellulose** and **pectin**) and glycoproteins (**extensins**)
- **Pectins** are branched polysaccharides composed of *rhamnogalacturonans* (**galacturonic acid** and **rhamnose**)
- **Hemicellulose** are branched polysaccharides which basically contain **glucose** but also **xylose**
- **Pectins** are highly negatively charged and **trap and bind water** molecules providing a **sticky, gel-type matrix** for cellulose microfibrils (pectin is used in making jams and jellies)

Lignin makes up the matrix for cellulose in wood



Lignin
(one of the possible structures)

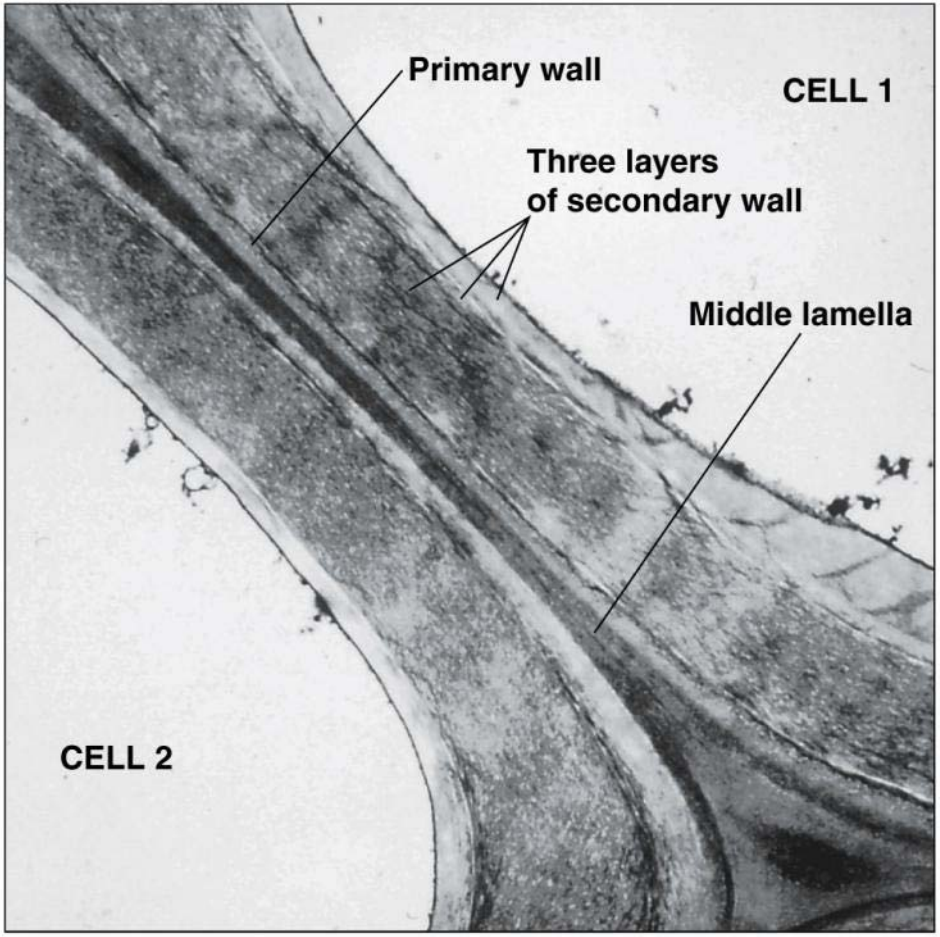
- **Lignins** are also found in cell walls, however, mostly in <u>woody tissues</u>
- Lignins are **polymers of aromatic alcohols** and are the <u>second most abundant organic molecule</u> on earth

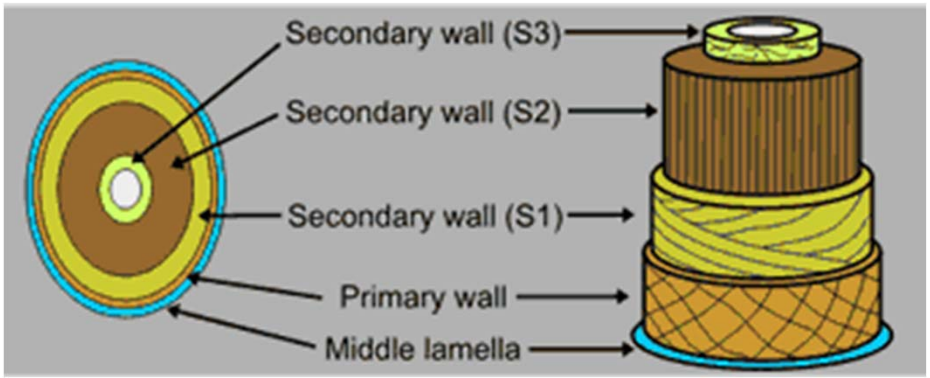


ECM animal cells compared to ECM plant cells

Kind of Organism	Extracellular Structure	Structural Fiber	Components of Hydrated Matrix	Adhesive Molecules
Animals	Extracellular matrix (ECM)	Collagens and elastins	Proteoglycans	Fibronectins and laminins
Plants	Cell wall	Cellulose	Hemicelluloses and extensins	Pectins

Organization and synthesis of the cell wall

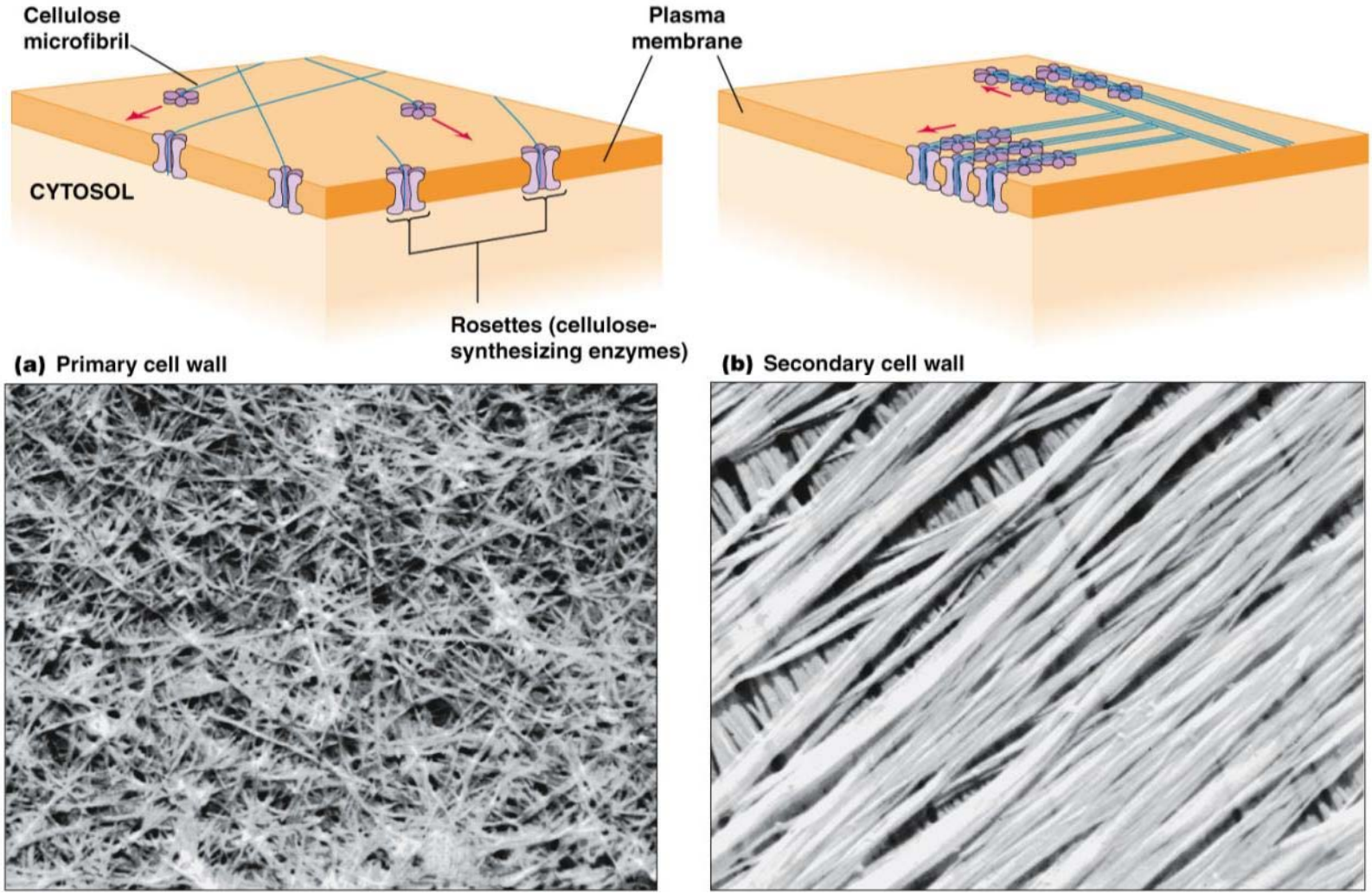




- Cell wall synthesis starts with the **middle lamella** which is shared by neighboring cells
- The **middle lamella** consists mainly of **sticky pectins** which binds the two neighboring cells tightly together
- The **primary wall** forms next which is composed of loosen networks of **cellulose**
- Cellulose is synthesized by **enzyme complexes** called **rosettes** (arrays of **cellulose synthase** enzymes) located in the plasma membrane
- When the cell has stopped growing, a thicker layer of **secondary cell wall** is produced
- **Lignins** are responsible to make the secondary cell wall hard and rigid in woody plants

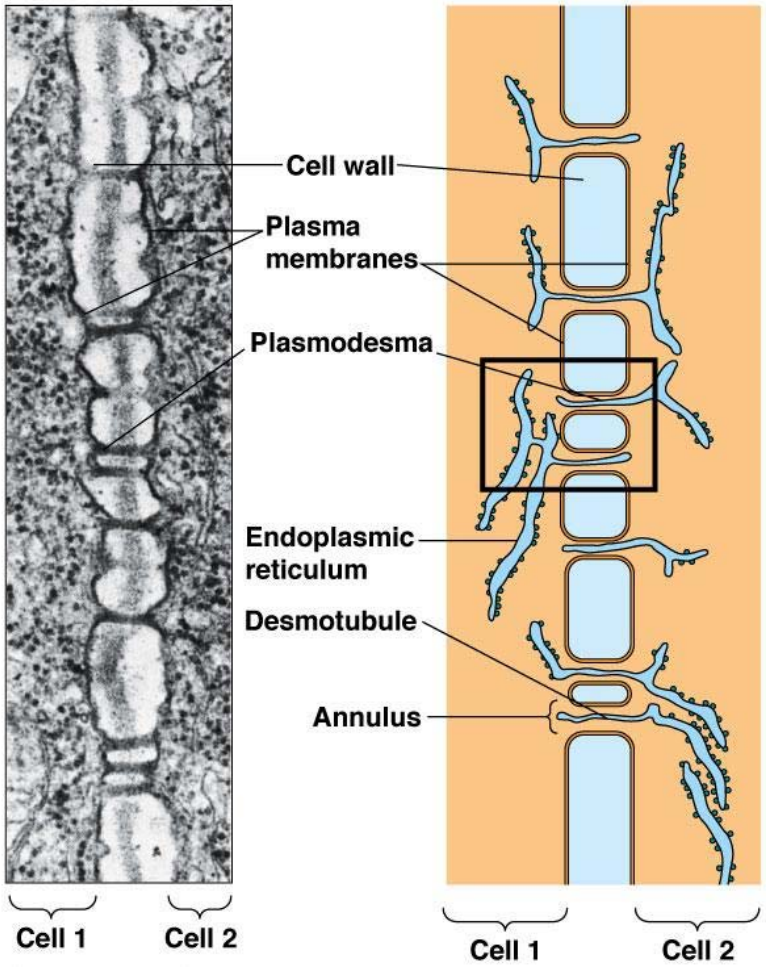
Organization and synthesis of the cell wall

- During the synthesis of **cellulose microfibrils**, rosettes are moving in the plasma membrane as the cellulose microfibrils are extending (similar to “spinning of a spider web”)
- For synthesis of larger cellulose **microfibrils bundles** (**macrofibrils**) in secondary cell walls, rosettes form aggregates and movements is guided by underlying **microtubules**

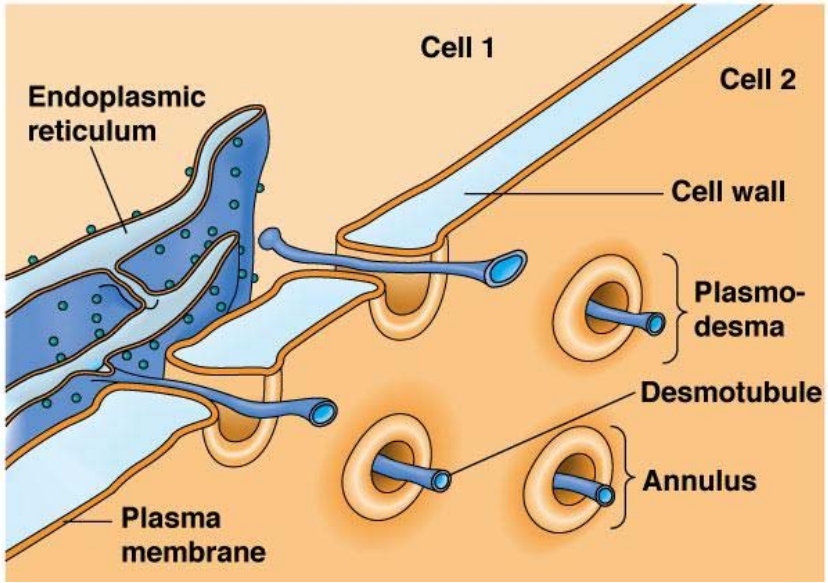


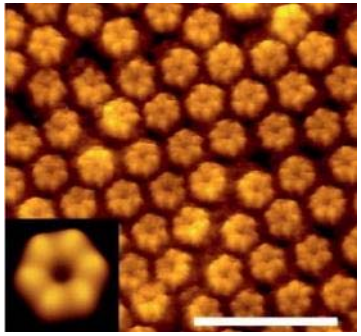
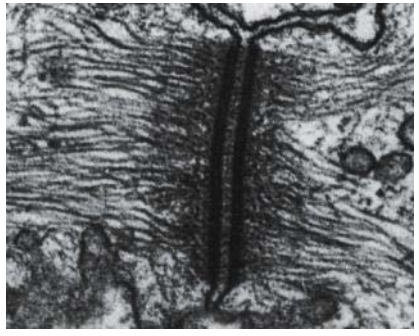
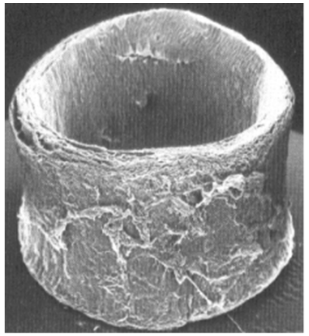
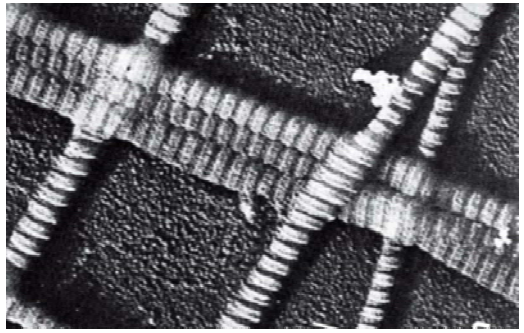
Plasmodesmata provide the basis for intercellular communication

Analog to gap junctions in animal cells, **plasmodesmata** allow for intercellular communication

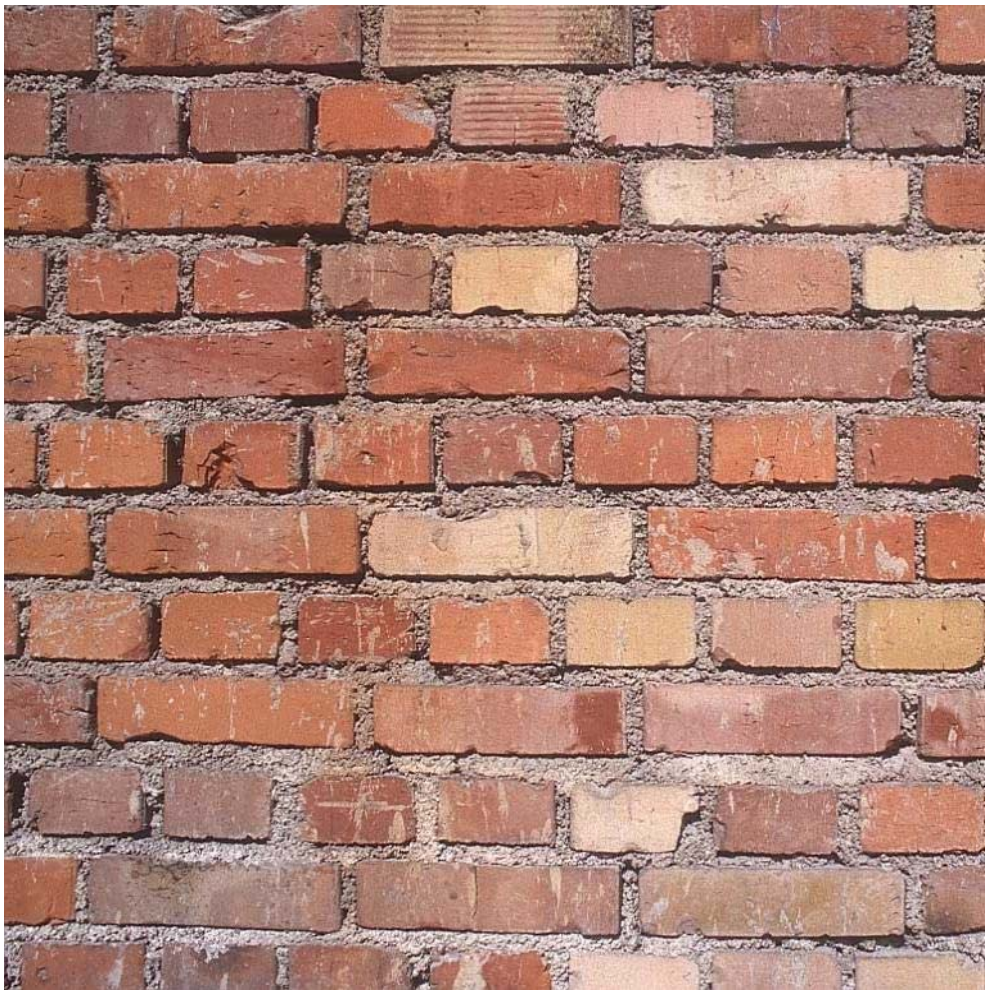


- The pore of a plasmodesma is relatively large compared to gap junctions (20-200 nm)
- In the central channel of the plasmodesma a tubular structure lies, called **desmotubule**
- Near the desmotubule often ER can be found
- Similar to gap junctions, plasmodesmata are important for the **electrical connectivity** of cells (though plant cells do not have a nervous system)
- Besides the flow of **small ions**, also large molecules as **signaling molecules**, **RNA**, **transcription factors** and even **viruses** can pass these channels




World of the Cell



The end of chapter 15

Thank you!