Essential Cell Biology

Ch20
Tissue Engineering & Stem Cells

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Questions ?

- How can cell be jointed together robustly?
- Where is builder & architect's plans?
- How different cell types produced in its proper place?

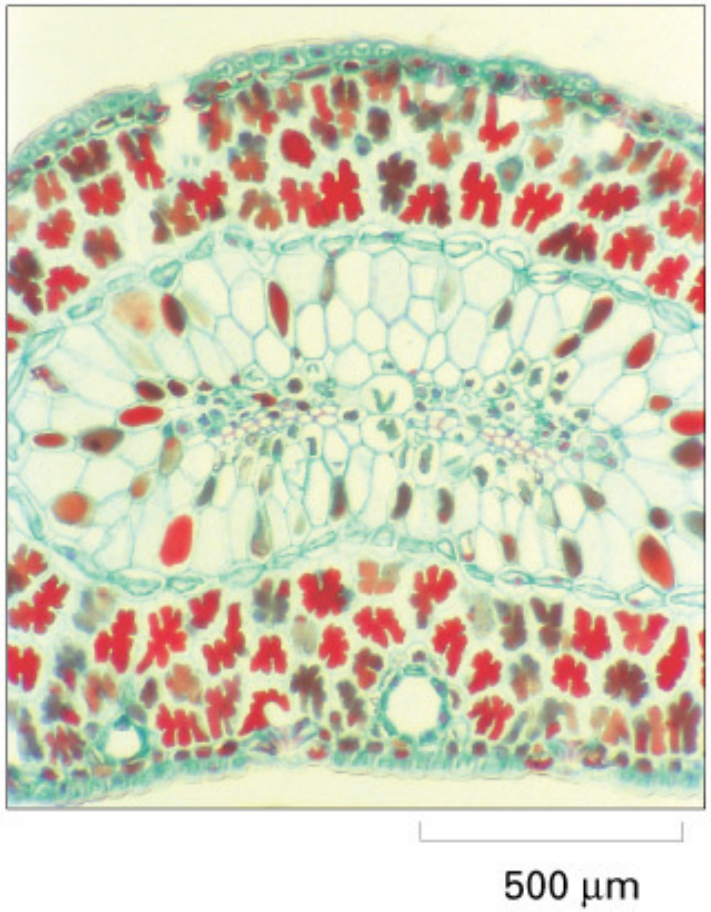
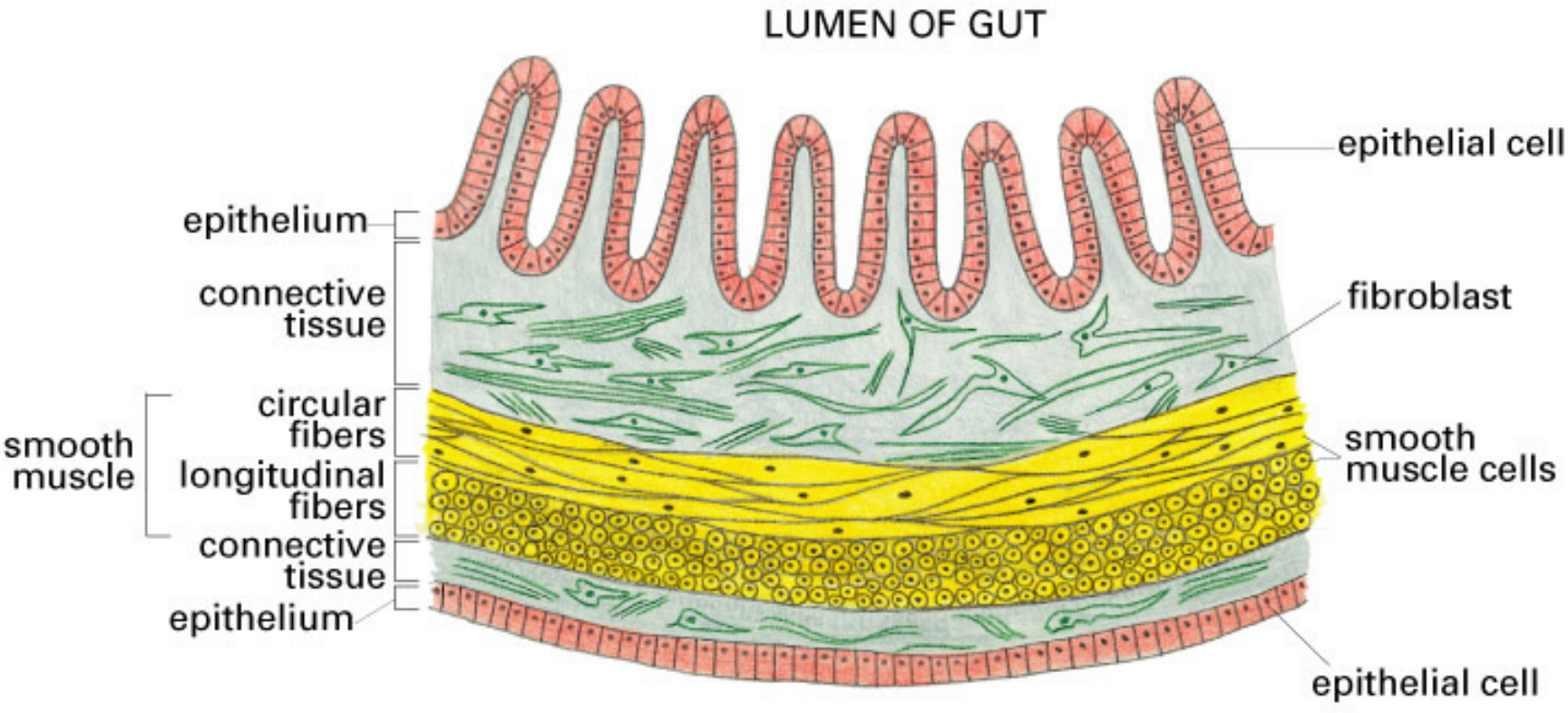


Fig. 20-1

Outline of Ch 20

- Extracellular Matrix (ECM) & Connective Tissue
- Epithelial Sheets & Cell-Cell Junctions
- Tissue Maintenance & Renewal
- Cancer



Tissue: multi-cellular organism

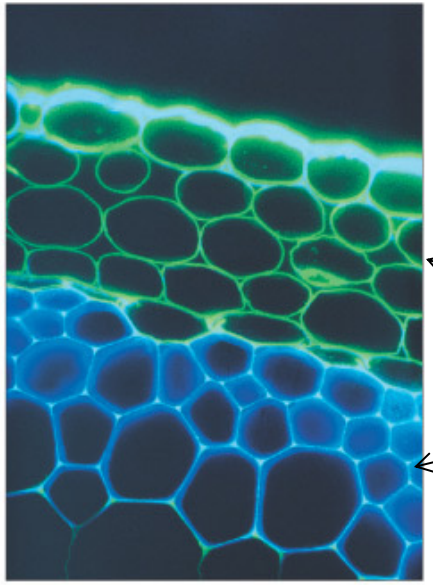
Fig. 20-2

Extracellular Matrix (ECM) & Connective Tissue

- Plant vs. animal cell
- Animal
  1. strong & agile (=swift)
  2. possess rapid movement & change shape quickly
  3. generate & transmit force

- Plant
  1. sedentary
  2. weak cell
  3. strength comes from cell wall
  4. cell wall is a type of ECM that secretes by cell
  5. wood: thick & hard
     leaf: thin & flexible

Arabidopsis



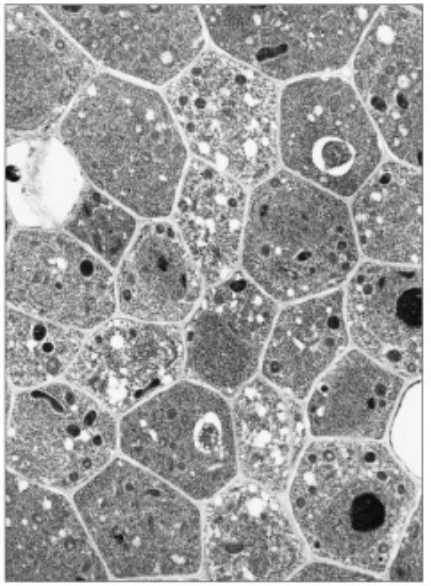


Fig. 20-3 plant cell wall

Extracellular Matrix (ECM) & Connective Tissue

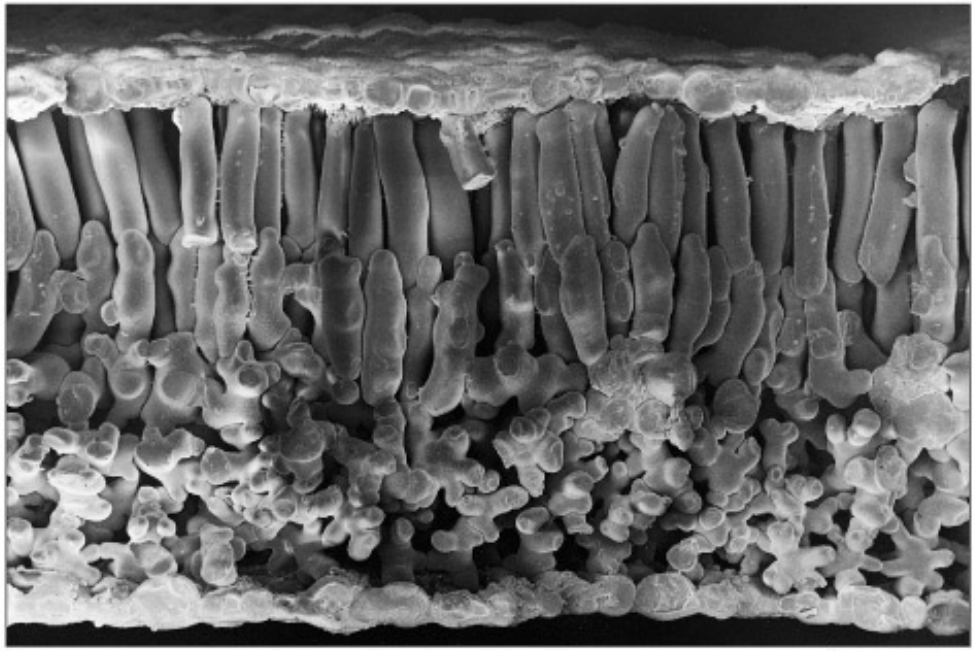
- Plant Cells Have Tough External Walls

Naked plant cell

- delicate & vulnerable
- with care, can be kept in culture
- easily rupture
- small maladjustment of osmotic strength can cause it swell & burst
- cytoskeleton lacks the tension-bearing intermediate filament

Plant cell wall

- Osmotic swelling cell is limited by resistance of cell wall
- Swollen chambers forms semi-rigid tissue



SEM for cells in a crisp lettuce leaf

Fig. 20-4

Extracellular Matrix (ECM) & Connective Tissue

- Cellulose Fibers Give the Plant Cell Wall Its Tensile

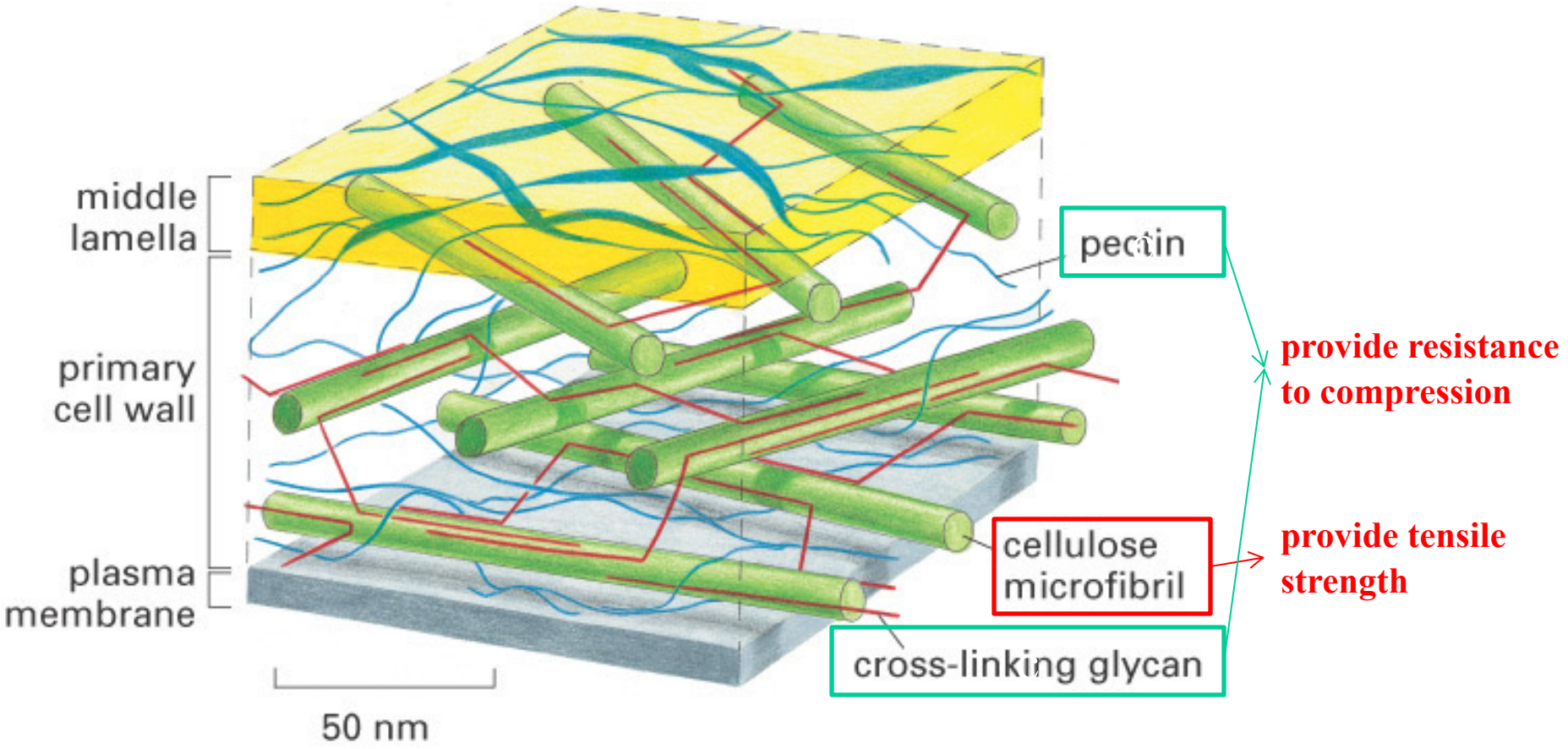


Fig. 20-5

Extracellular Matrix (ECM) & Connective Tissue

- Cellulose Fibers Give the Plant Cell Wall Its Tensile

- Cellulose fiber → resist stretching

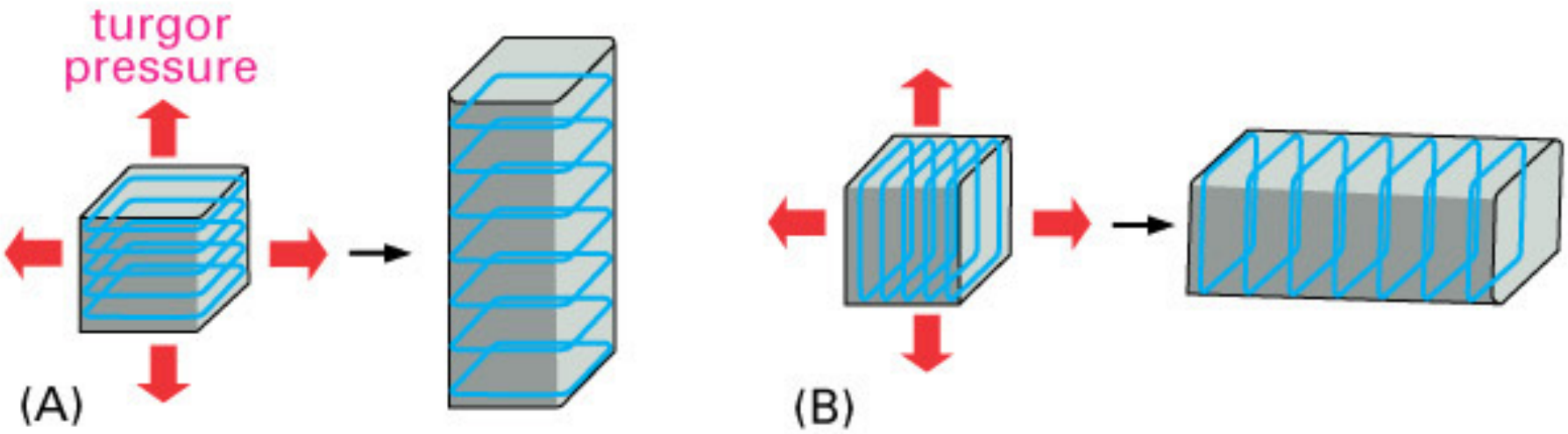


Fig. 20-6

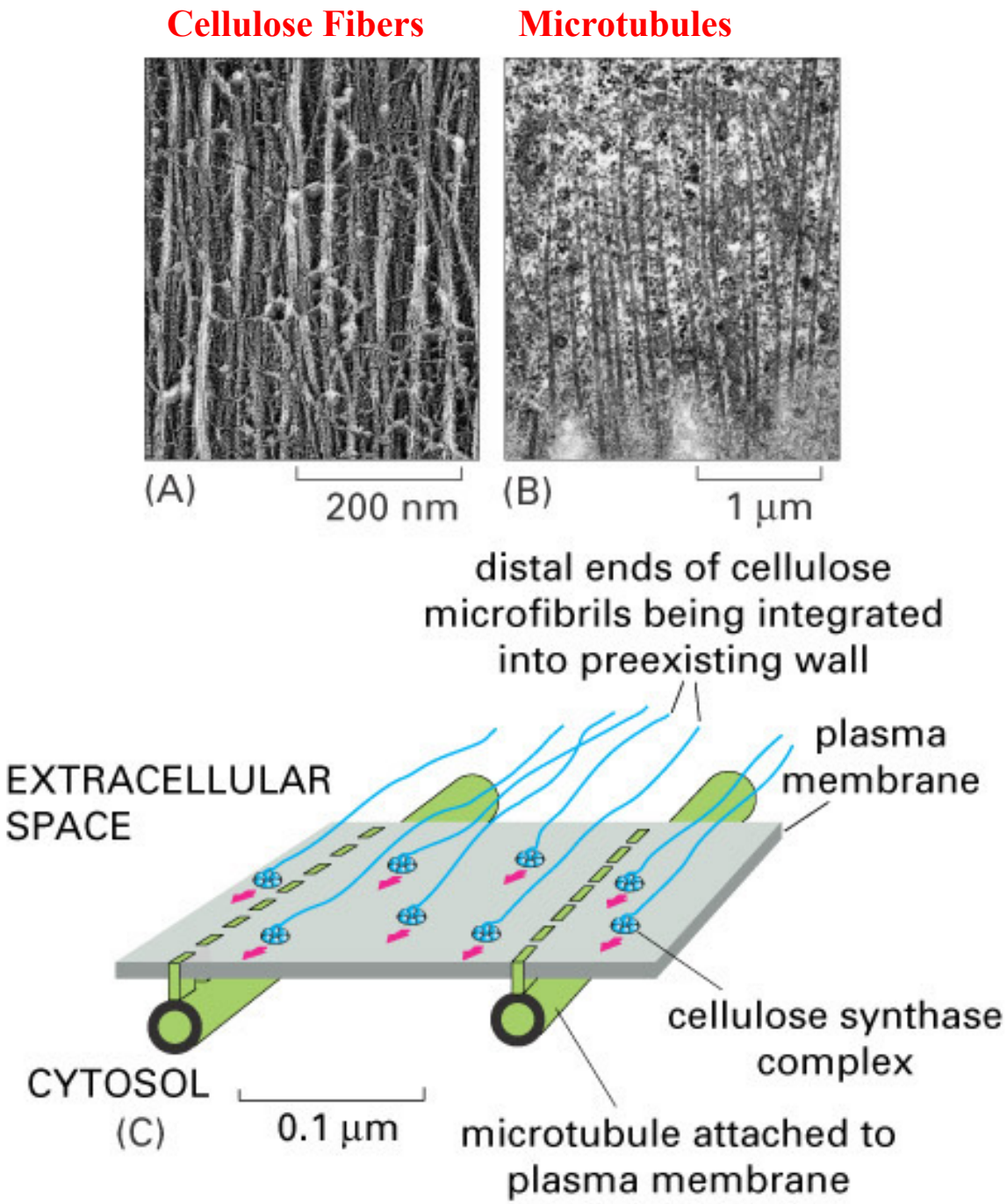

Cellulose Fibers
Microtubules
(A)
200 nm
(B)
1 µm
distal ends of cellulose microfibrils being integrated into preexisting wall
plasma membrane
EXTRACELLULAR SPACE
cellulose synthase complex
CYTOSOL
(C)
0.1 µm
microtubule attached to plasma membrane

Fig. 20-7

Extracellular Matrix (ECM) & Connective Tissue

- Animal Connective Tissues Consist Largely of ECM

- 4 major types of animal tissue
  connective
  epithelial
  nervous
  muscular

- ECM → bone
- Collagen for tensile strength

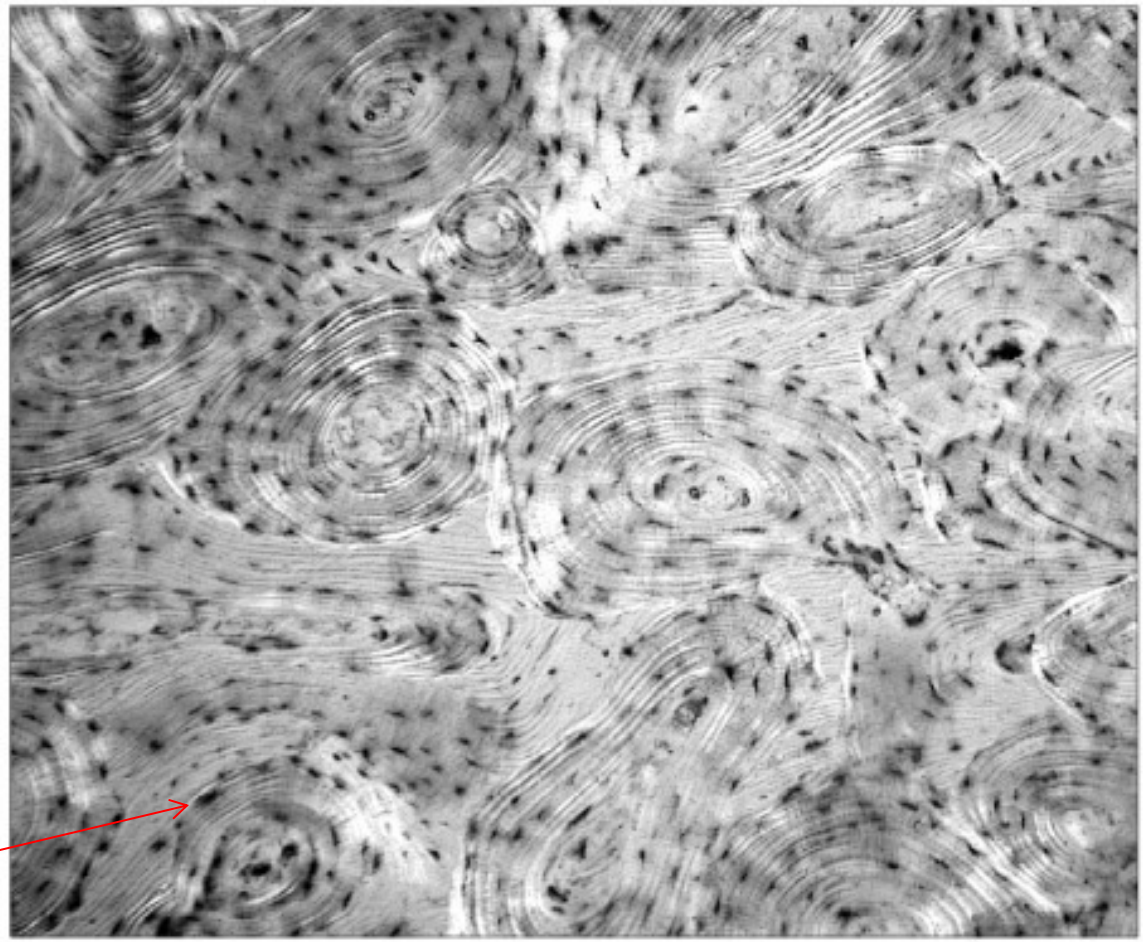


Fig. 20-8

Extracellular Matrix (ECM) & Connective Tissue

- Collagen Provides Tensile Strength in Animal Connective Tissues

- mammals have about 20 different collagen (COL) genes
- consist 25% total protein mass in a mammal
- structure of COL

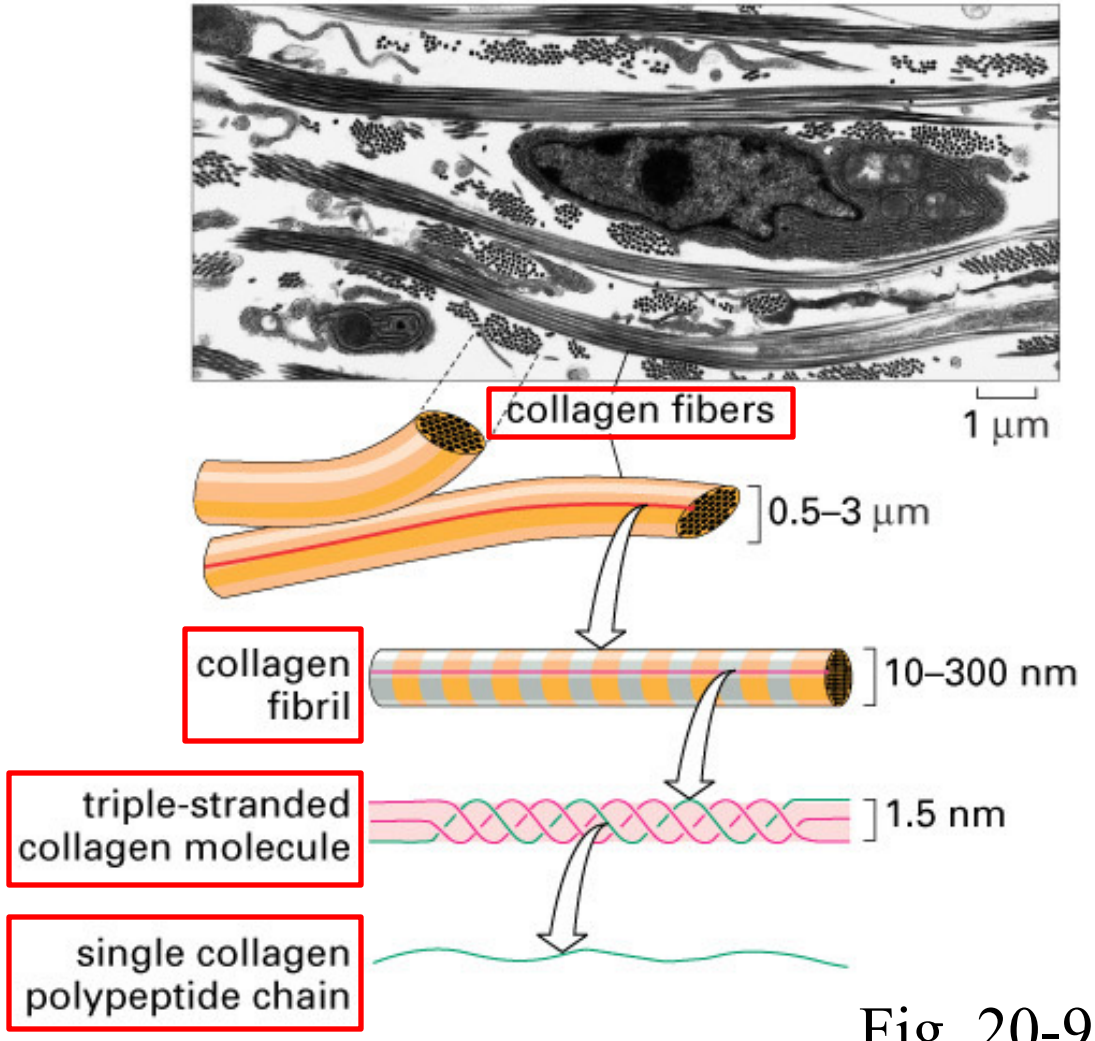
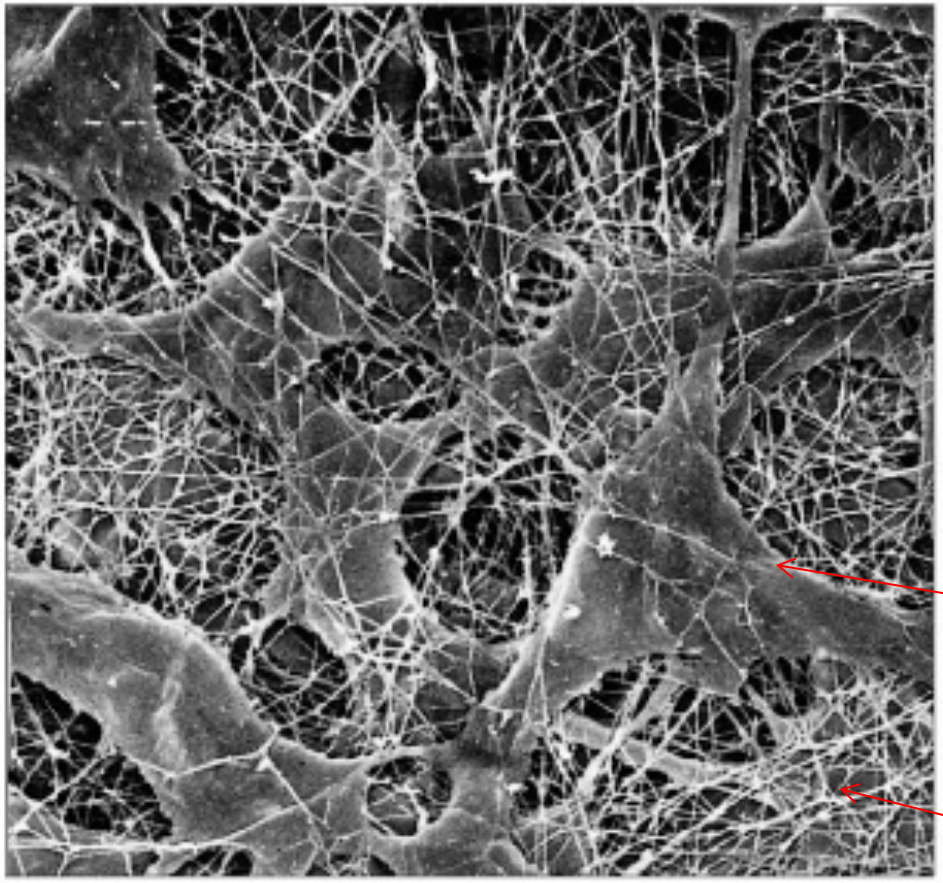


Fig. 20-9

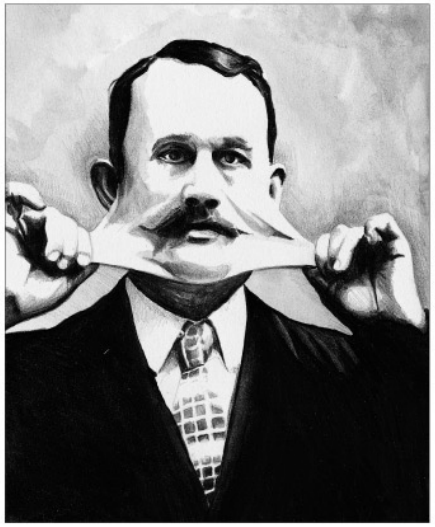
Extracellular Matrix (ECM) & Connective Tissue

- Collagen Provides Tensile Strength in Animal Connective Tissues



rat cornea

Hyperextensible skin
Improper collagen assembly by lack of enzyme to convert procollagen to collagen



Fibroblast

secret ECM (procollagen)

Collagen Fibrils

Fig. 20-10

5 common collagen types:

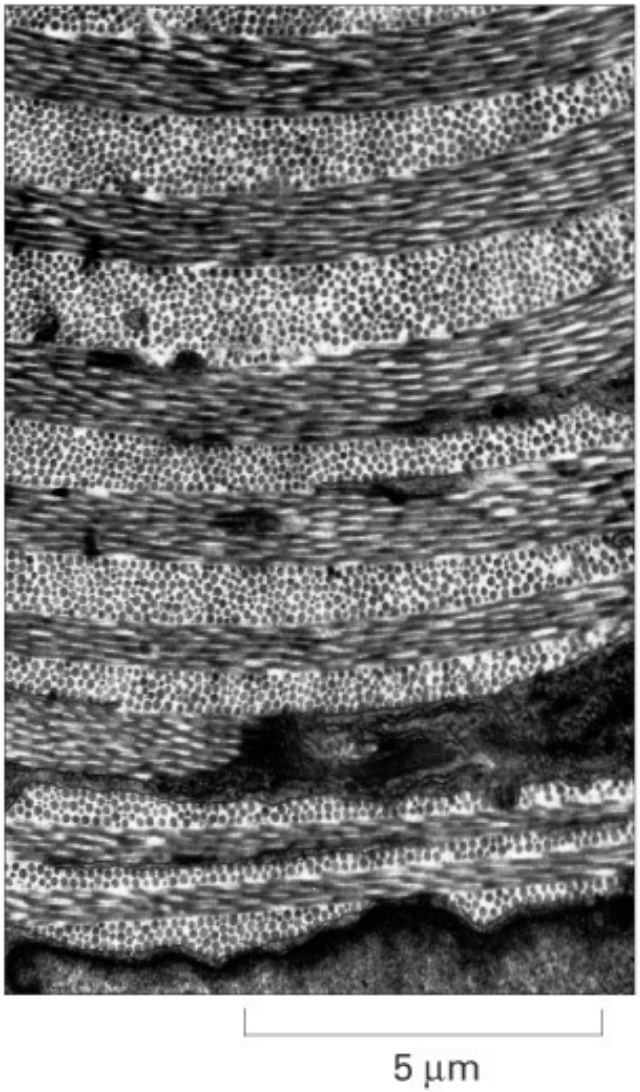
- Collagen I: skin, tendon, vascular ligature, organs, bone (elastic property)
- Collagen II: cartilage
- Collagen III: reticulate (main component of reticular fibers)
- Collagen IV: forms basal lamina, epithelium-secreted layer of basement membrane
- Collagen V: cell surfaces, hair and placenta

Type I collagen products:

Atelocollagen

Extracellular Matrix (ECM) & Connective Tissue

- Cell Organize the Collagen that they Secrete



Collagen fibrils in skin

Fig. 20-12

Alignment

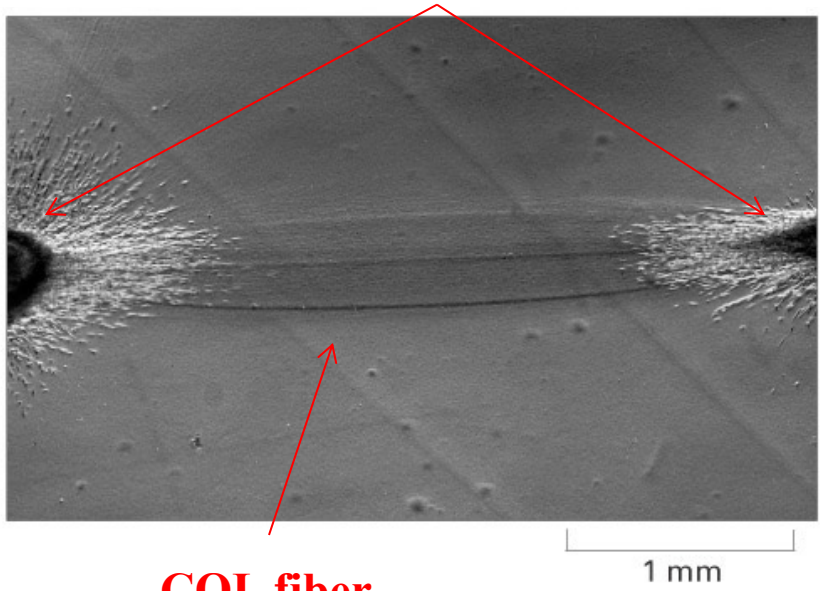
•skin: woven

•tendon: parallel bundles along major axis of tension

Tissue Development

•Fibroblast → secrete COL → crawling & pulling on it → help to compact COL into sheet

Embryonic chick heart (fibroblast & m. cell)

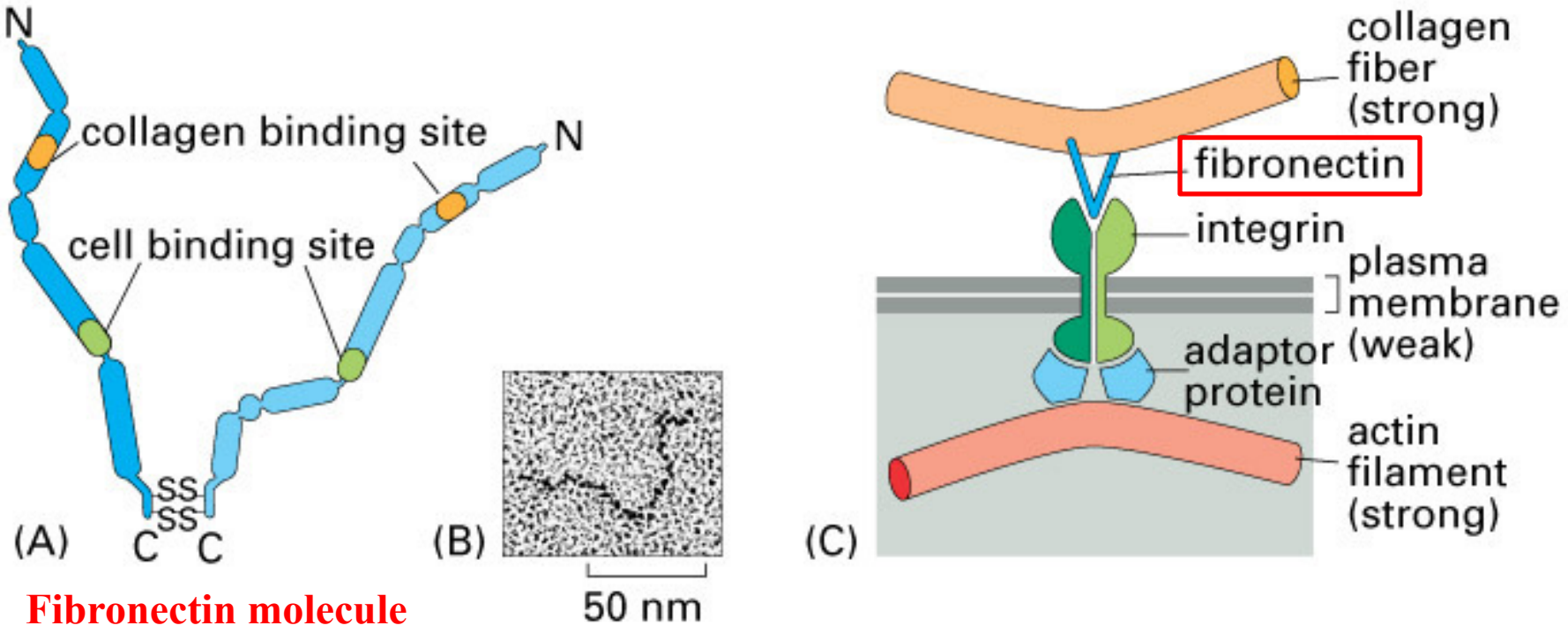


COL fiber

Fig. 20-13

Extracellular Matrix (ECM) & Connective Tissue

- Integrins Couple the Matrix Outside a Cell to the Cytoskeleton Inside It



Fibronectin molecule

- Integrin → transmit stress → cytoskeleton
- Integrin → cell signaling

Fig. 20-14

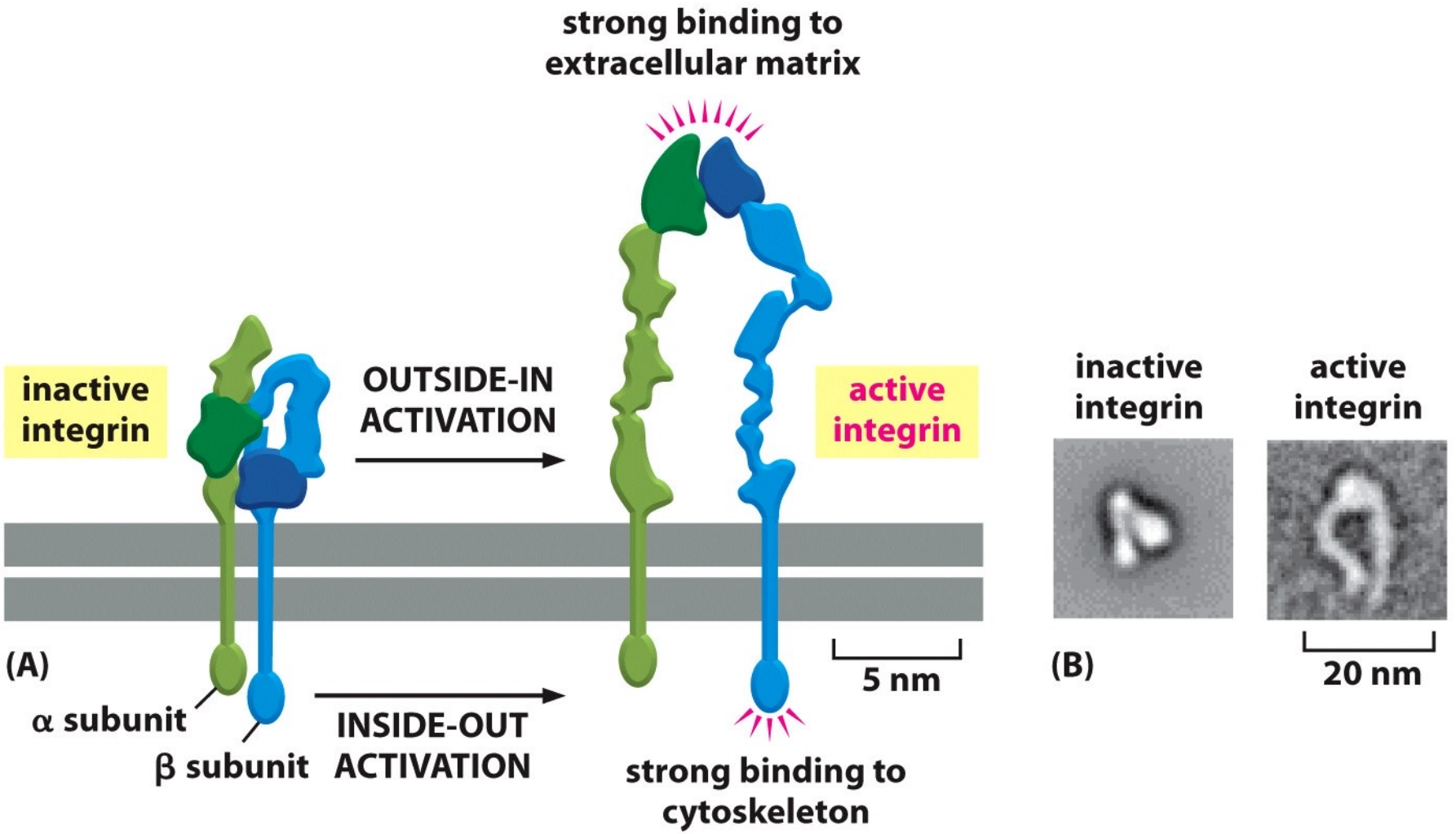


Figure 20-15 *Essential Cell Biology* (© Garland Science 2010)

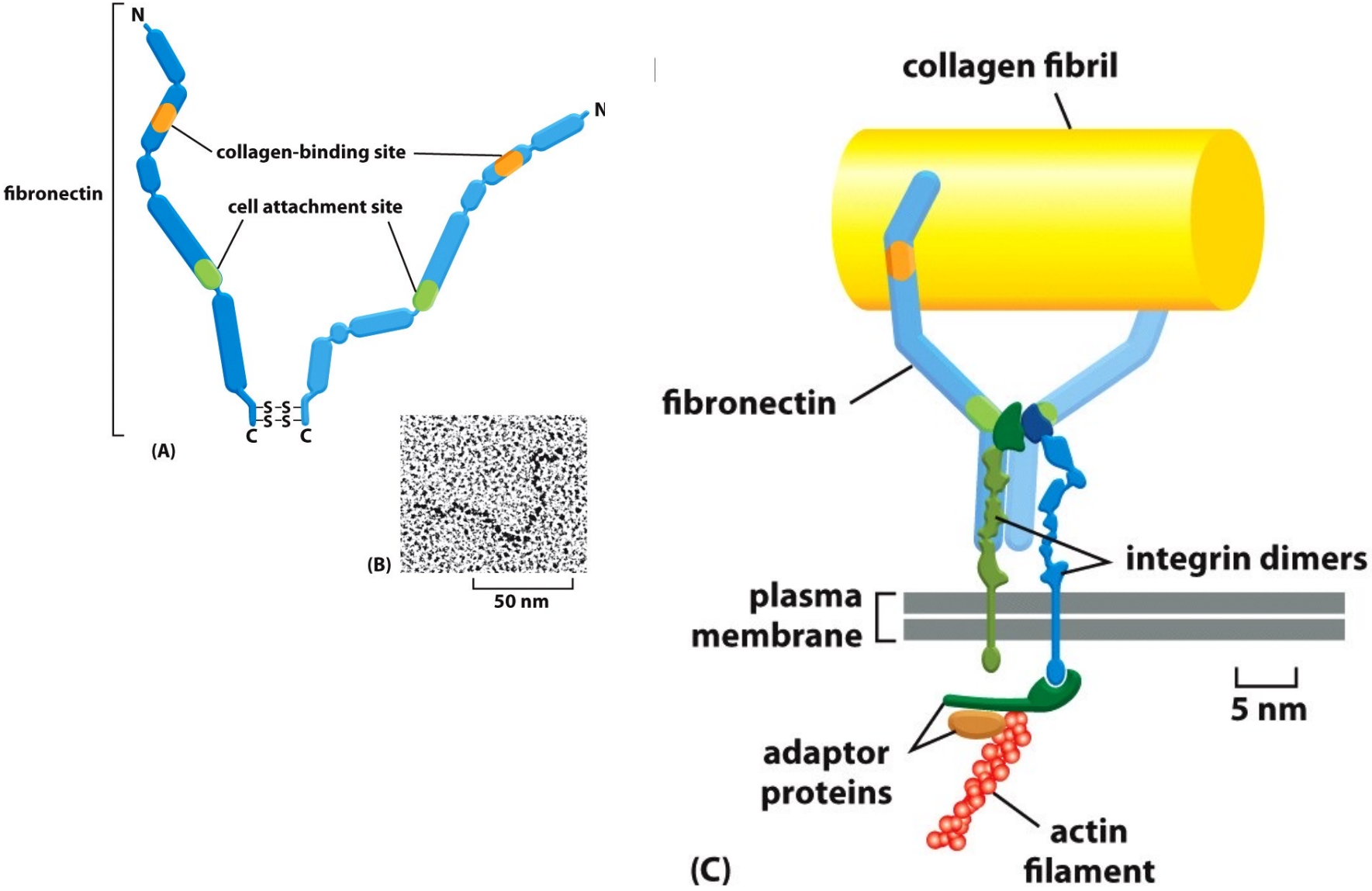
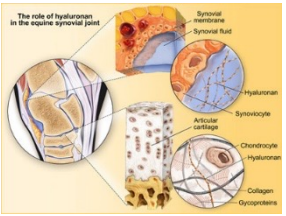


Figure 20-14 *Essential Cell Biology* (© Garland Science 2010)

Extracellular Matrix (ECM) & Connective Tissue

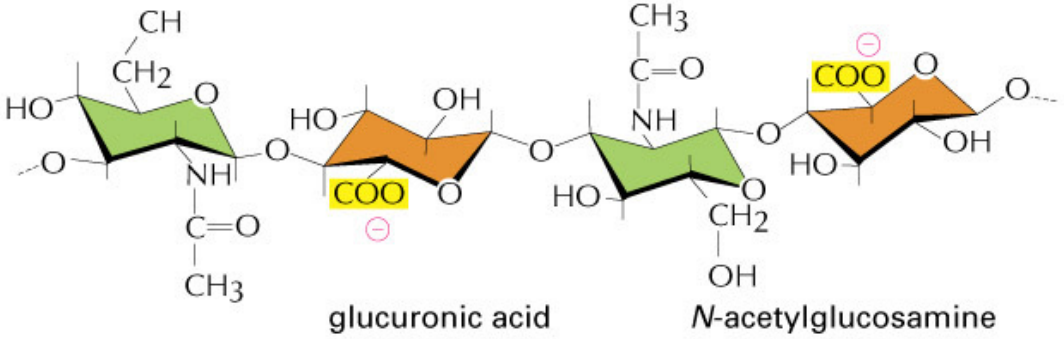
- Gels of Polysaccharide and Protein Fill Spaces and Resist Compression

- Proteoglycans: extracellular proteins link to a special class of complex negatively charged polysaccharides → glycosaminoglycans (GAGs)



repeating disaccharide

Hyaluronan (HA)



Negative Charge

↓

Hydrophilic

↓

Osmotically active

↓

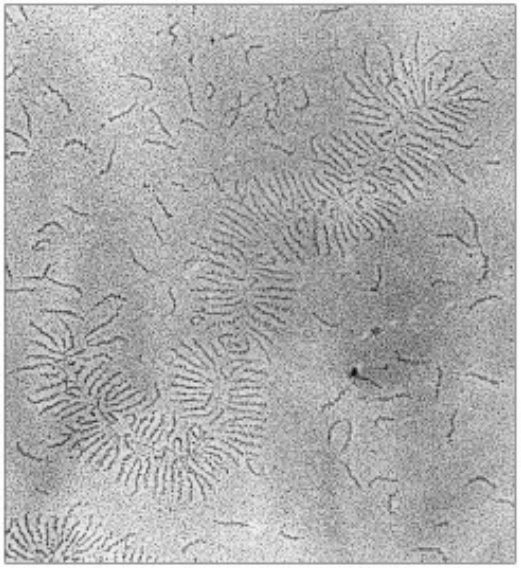
Suck water

↓

↑ volume

↓

Bear compression



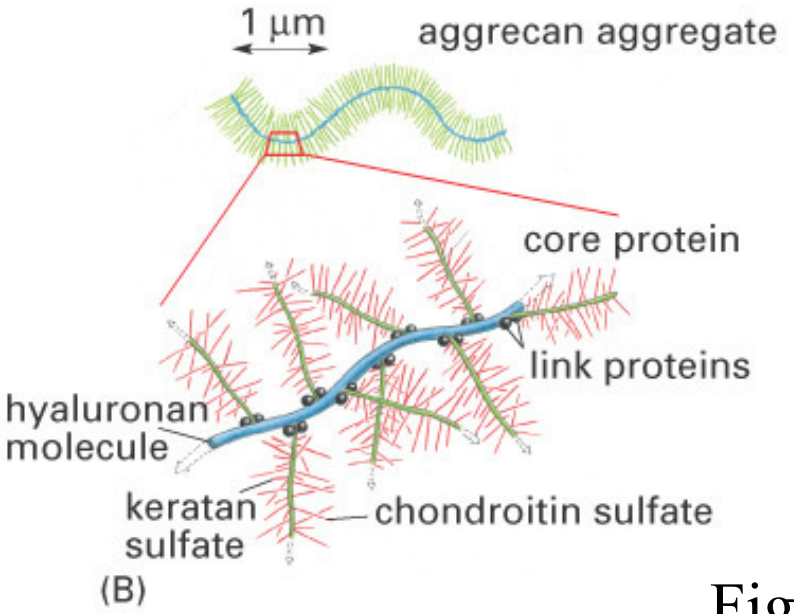
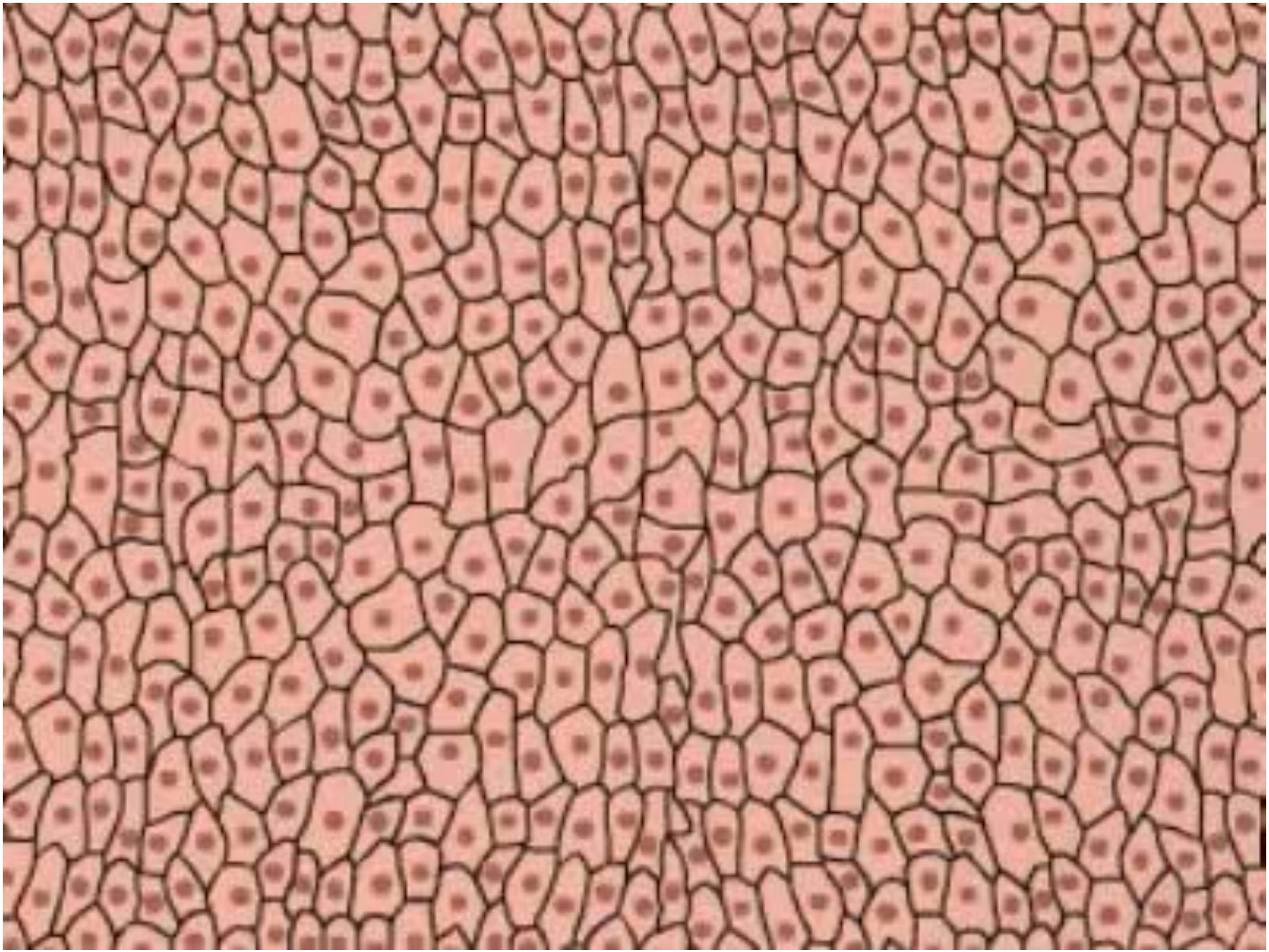


Fig. 20-17



Epithelial Sheets & Cell-Cell Junctions

- Cover the external surface of the body
- Line internal cavity
- Sheet → create a barrier

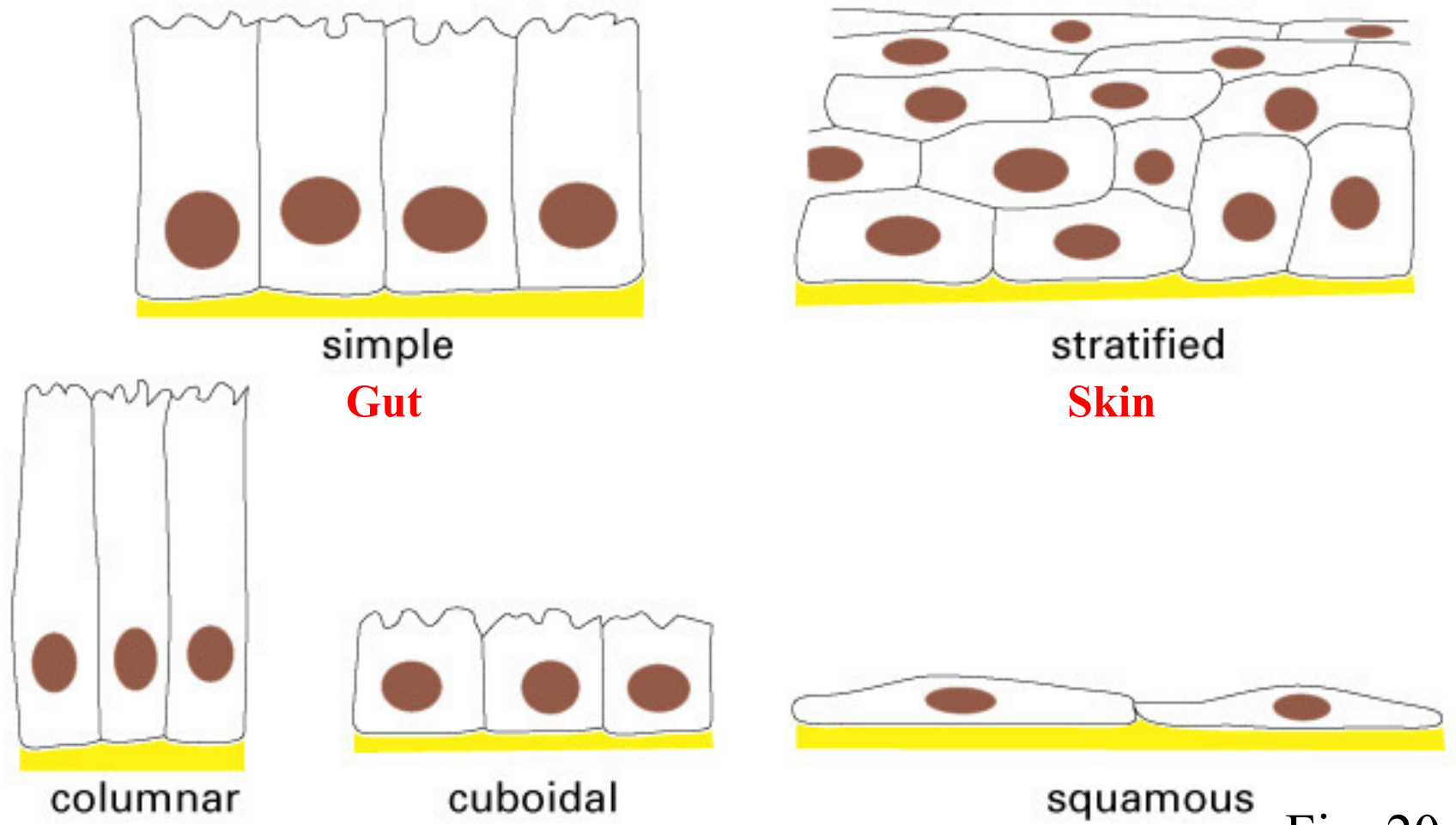


Fig. 20-18

Epithelial Sheets & Cell-Cell Junctions

- Epithelial Sheets are Polarized and Rest on a Basal Lamina

- Epithelial sheet
  apical surface: free & exposed to air or watery fluid
  basal surface: rest/attach on other tissue (connective tissue)
- Basal Lamina (COL IV + Laminin)

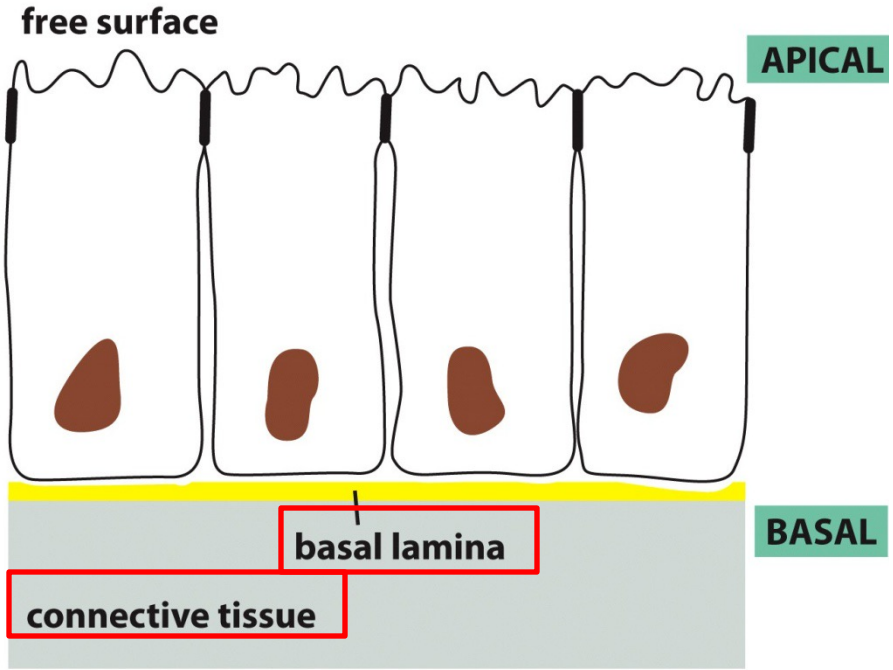


Fig. 20-19

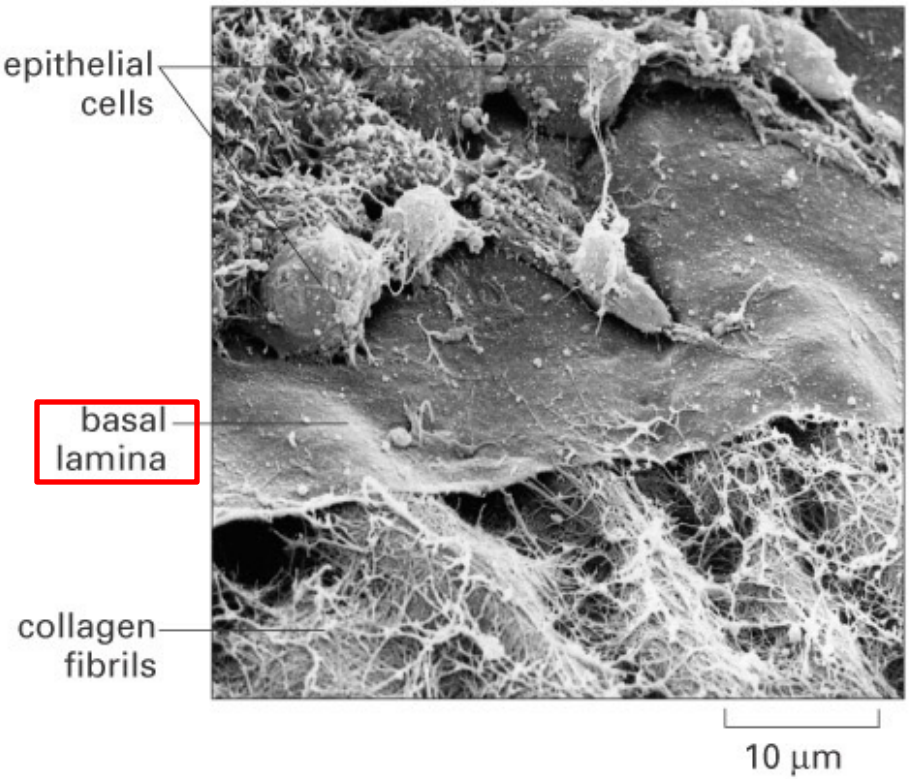


Fig. 20-20

Epithelial Sheets & Cell-Cell Junctions

- Epithelial Sheets are Polarized and Rest on a Basal Lamina

- 2 intermingles cell types

  absorptive cell: uptake nutrients

  goblet cell: secrete mucus to protect & lubricate gut

  asymmetrical organize of Golgi apparatus & cytoskeleton

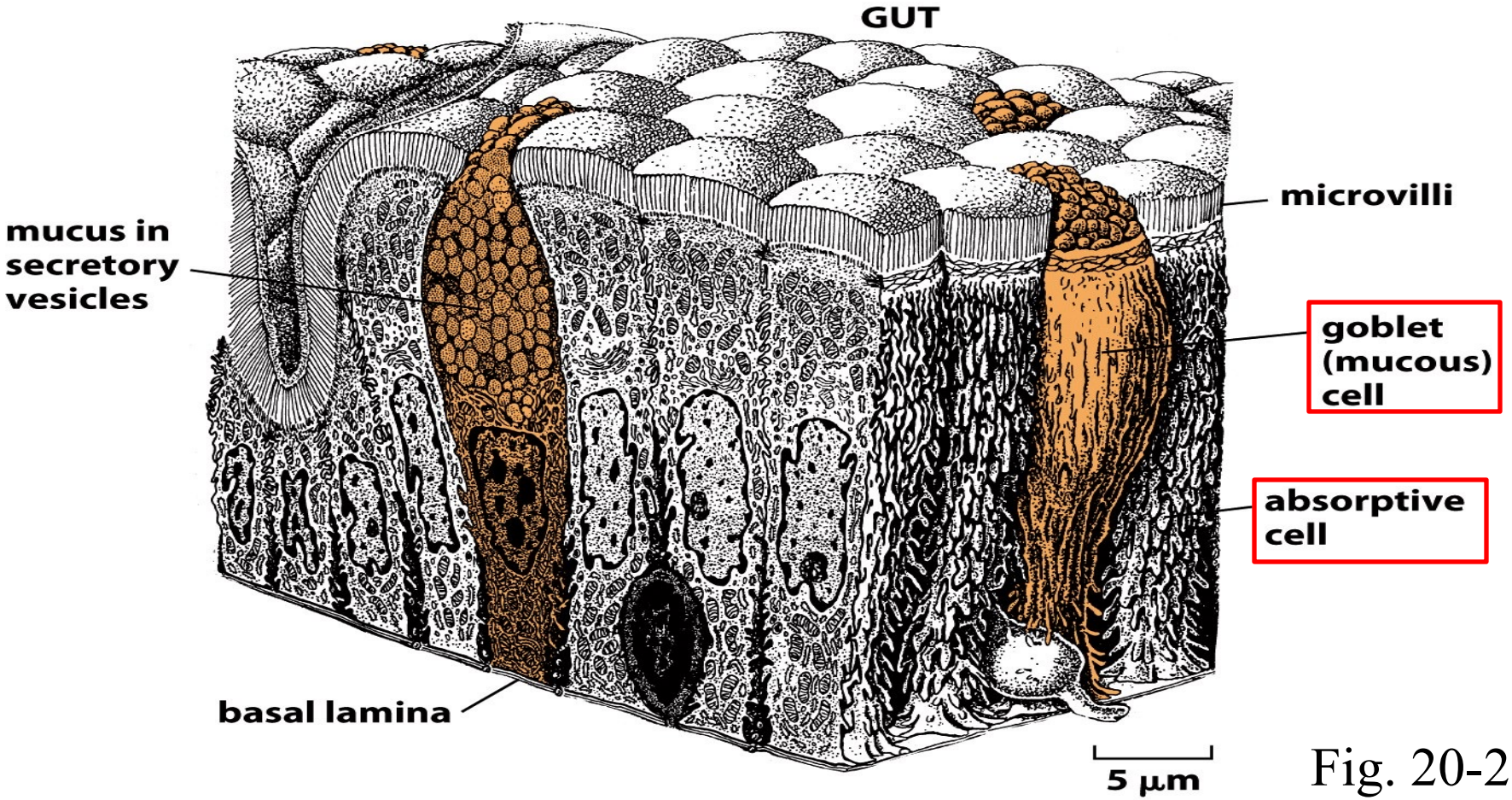


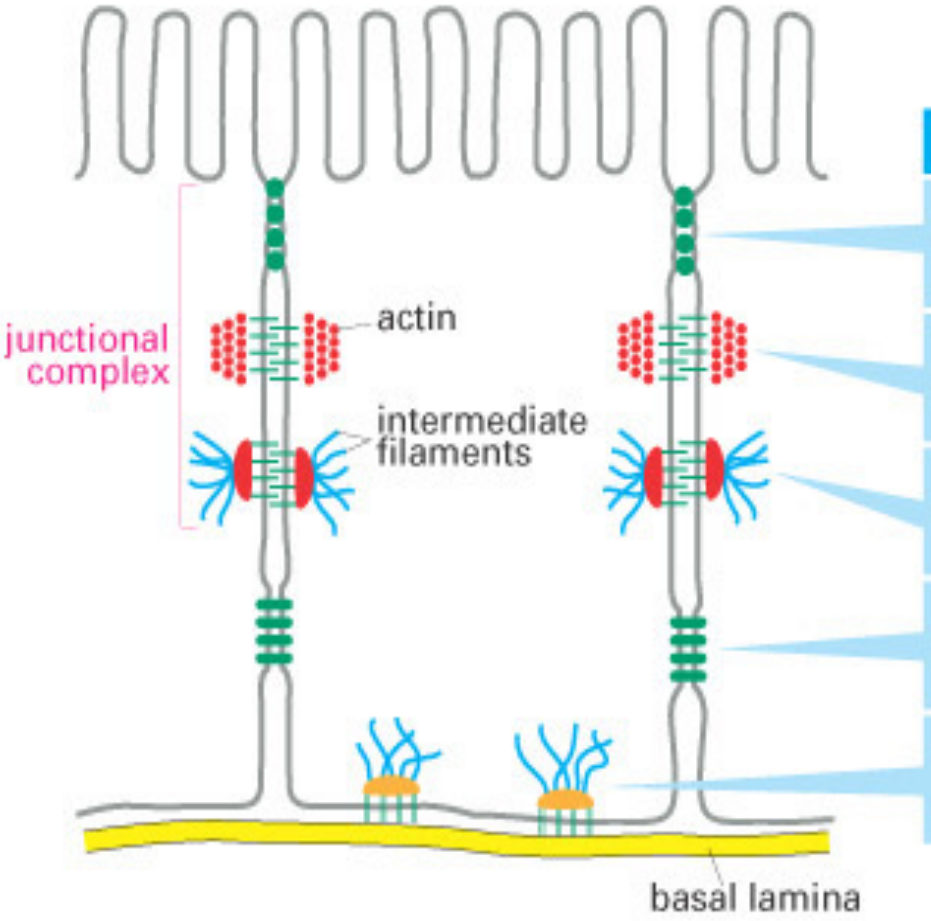
Fig. 20-21

Epithelial Sheets & Cell-Cell Junctions

- Tight Junction Make an Epithelium Leak-proof and Separate its Apical & Basal Surfaces

Epithelial cell junction

- Seal: tight junction
- Mechanical attachment
- Intimate chemical communication



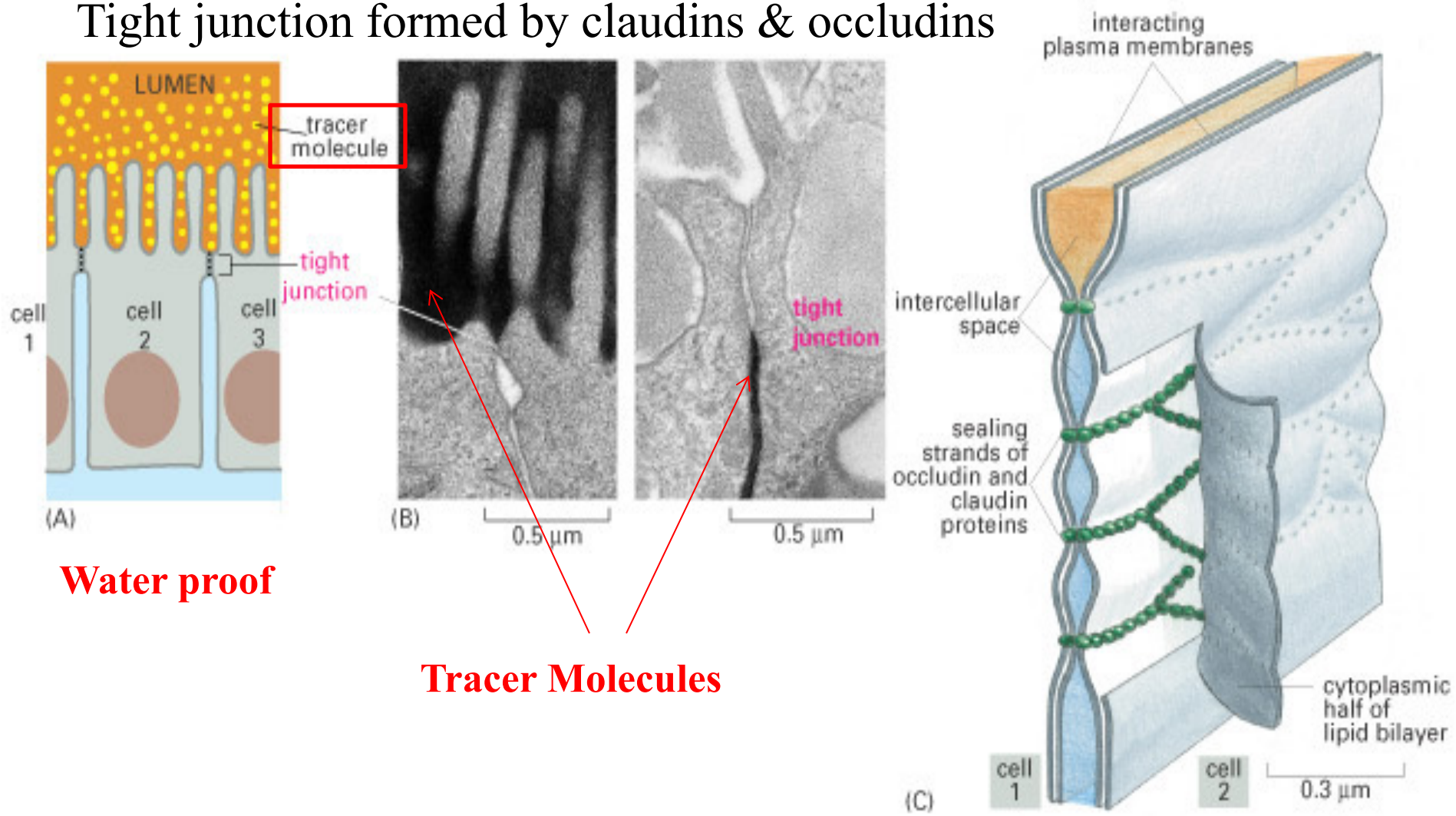
name	function
tight junction	seals neighboring cells together in an epithelial sheet to prevent leakage of molecules between them
adherens junction	joins an actin bundle in one cell to a similar bundle in a neighboring cell
desmosome	joins the intermediate filaments in one cell to those in a neighbor
gap junction	allows the passage of small water-soluble ions and molecules in the cytosol
hemidesmosome	anchors intermediate filaments in a cell to the basal lamina

Fig. 20-22

Epithelial Sheets & Cell-Cell Junctions

- Tight Junction Make an Epithelium Leak-proof and Separate its Apical & Basal Surfaces

Tight junction formed by claudins & occludins



Water proof

Tracer Molecules

Fig. 20-23

Epithelial Sheets & Cell-Cell Junctions

- Cytoskeleton-linked Junctions bind Epithelial Cells Robustly to one another and to the Basal Lamina

3 main types of mechanical attachments:

1. adherens junctions
2. desmosome junction

] bind one epithelial cell to another

3. hemidesmosomes → bind to basal lamina

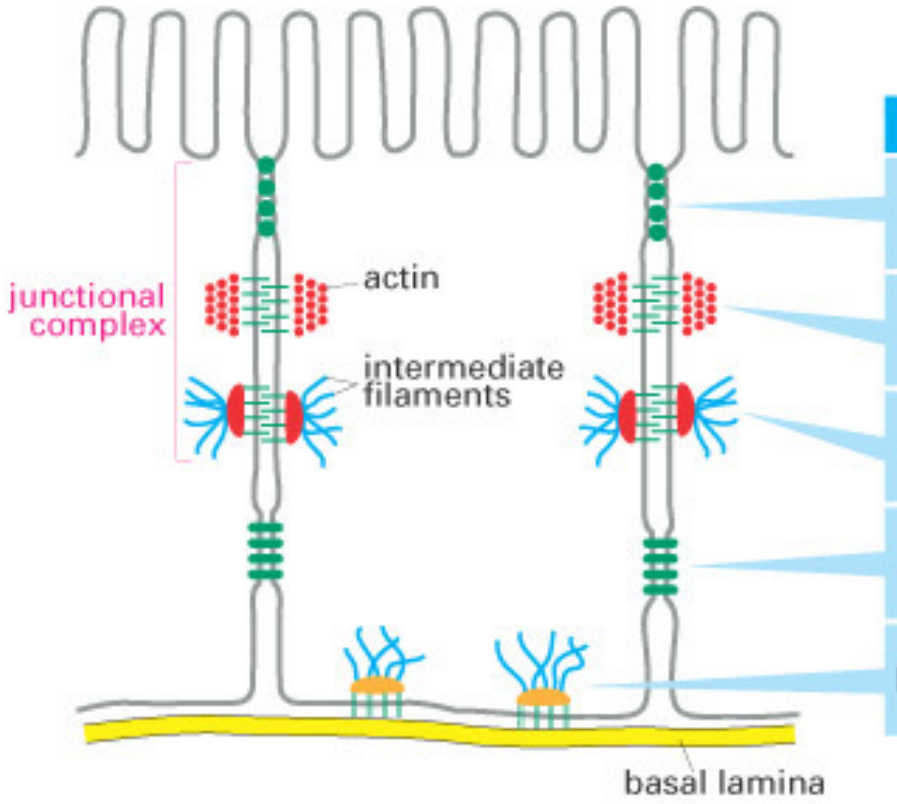


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Fig. 20-22

Epithelial Sheets & Cell-Cell Junctions

- Cytoskeleton-linked Junctions bind Epithelial Cells Robustly to one another and to the Basal Lamina

adherens junctions

- provide mechanical strength
- linked to cytoskeletal filaments
- insert on plasma membrane
- built by cadherin → binding → homophilic
- binding require Ca2+

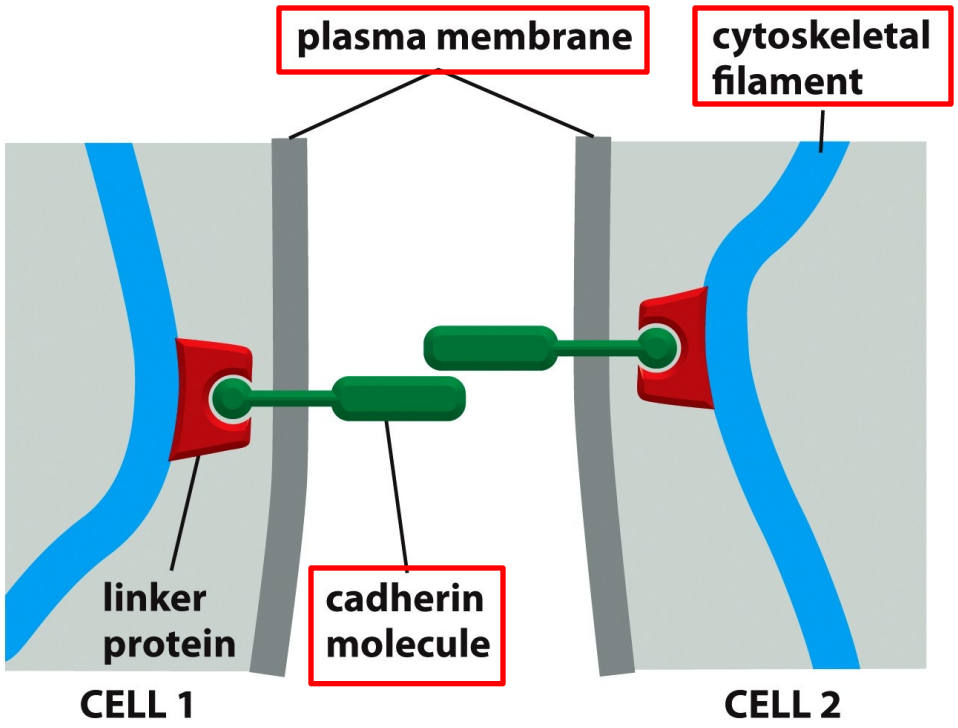
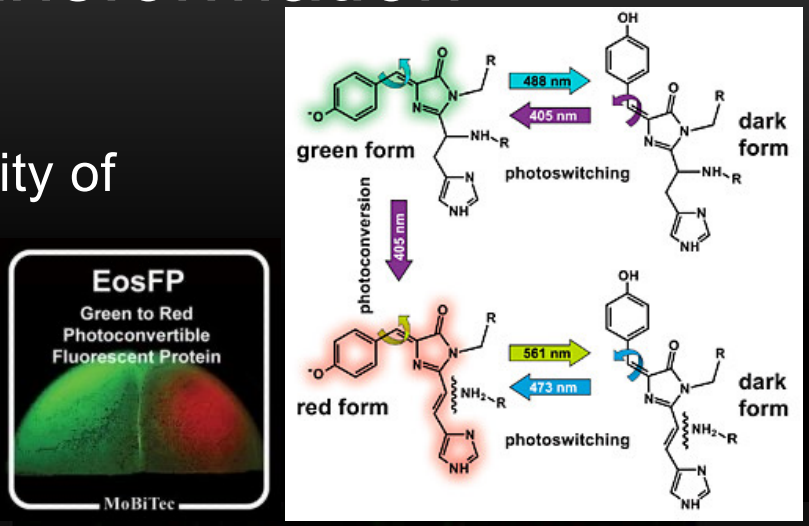
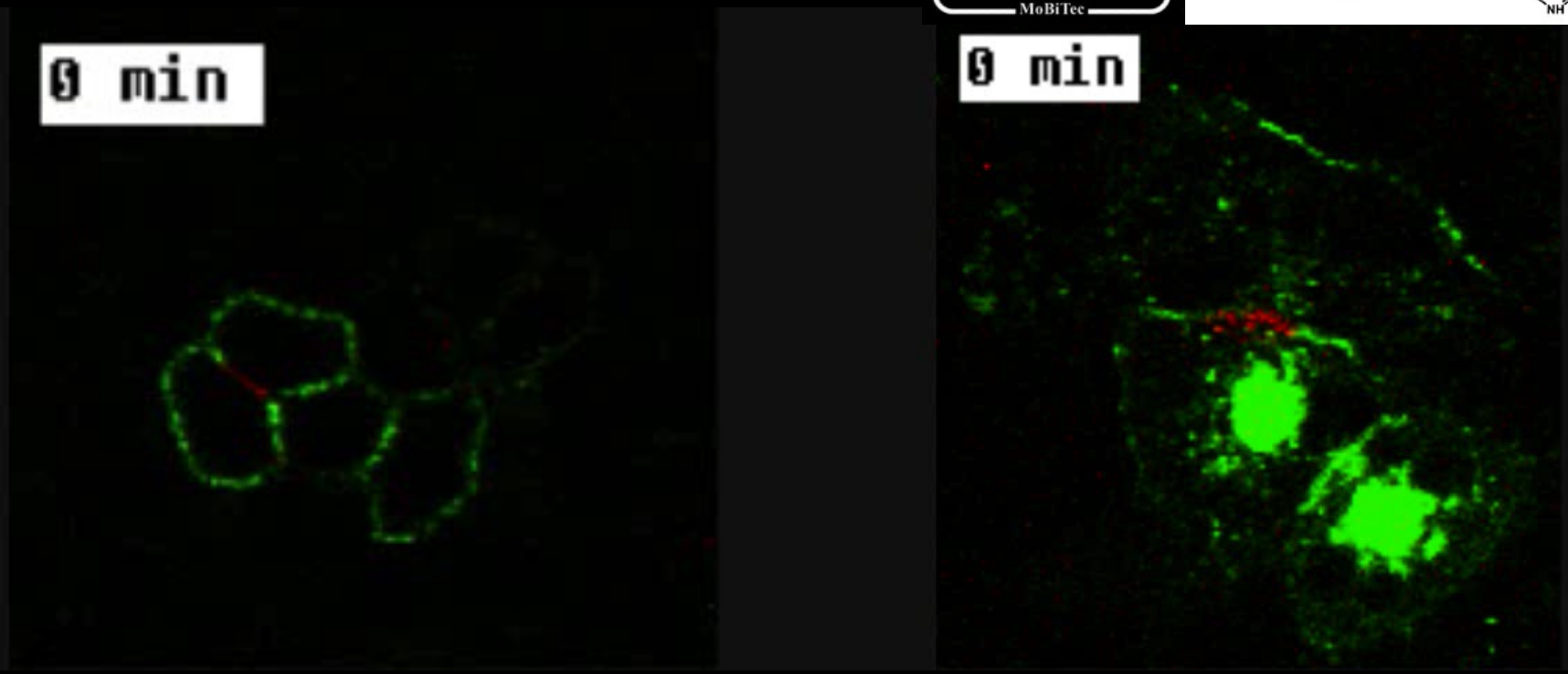


Fig. 20-24

mEosFP for Green/Red transformation

- Photocovertion fluorescent probe
- Ecadh-mEosFP → DDR1 reduces mobility of membrane bound E-cad





Yeh YC et al. (2011) Mol Biol Cell

Epithelial Sheets & Cell-Cell Junctions

- Cytoskeleton-linked Junctions bind Epithelial Cells Robustly to one another and to the Basal Lamina

Adhesion belt

- actin filament
- near apical end
- below tight junction
- potentially contractile
  - → tension
  - → shrinking apical surface (one axis)
  - → rolling into tube

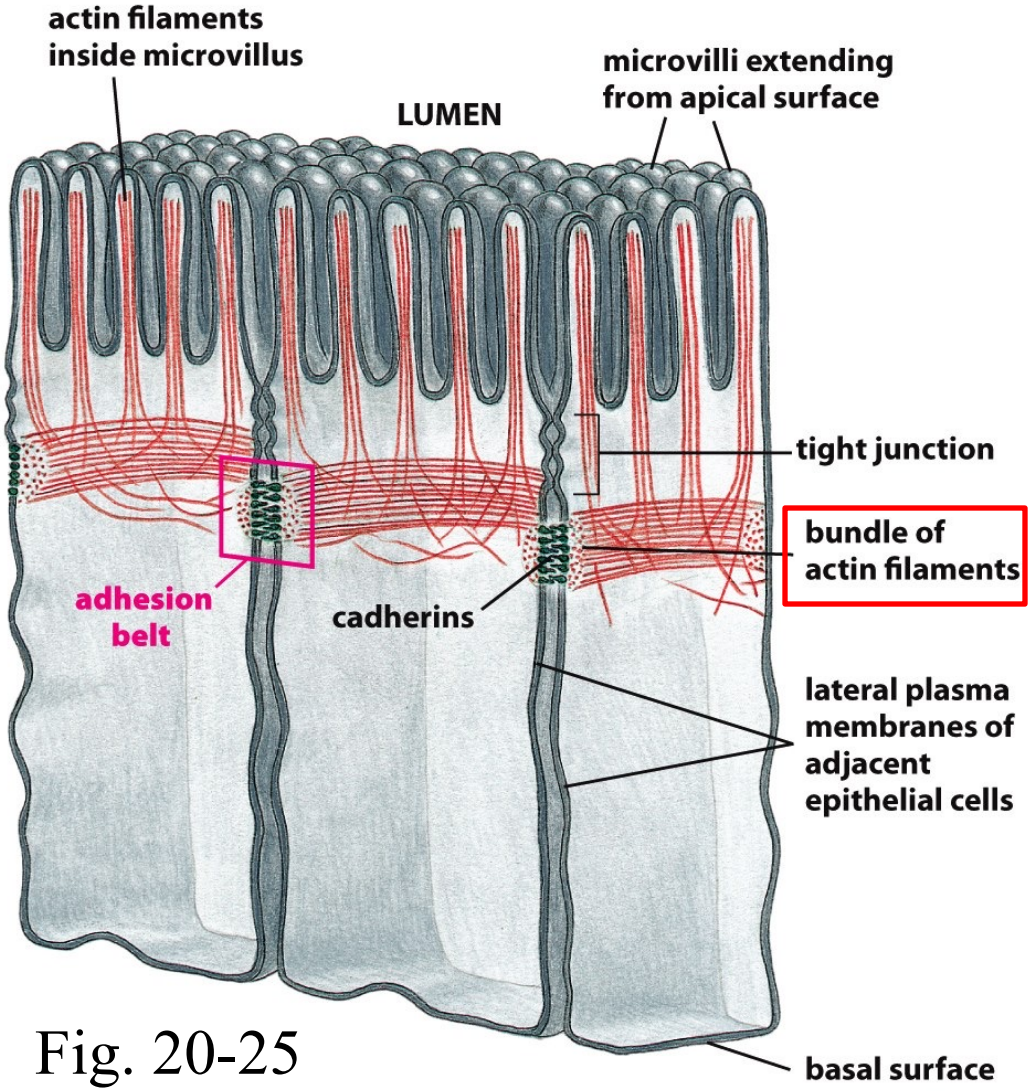
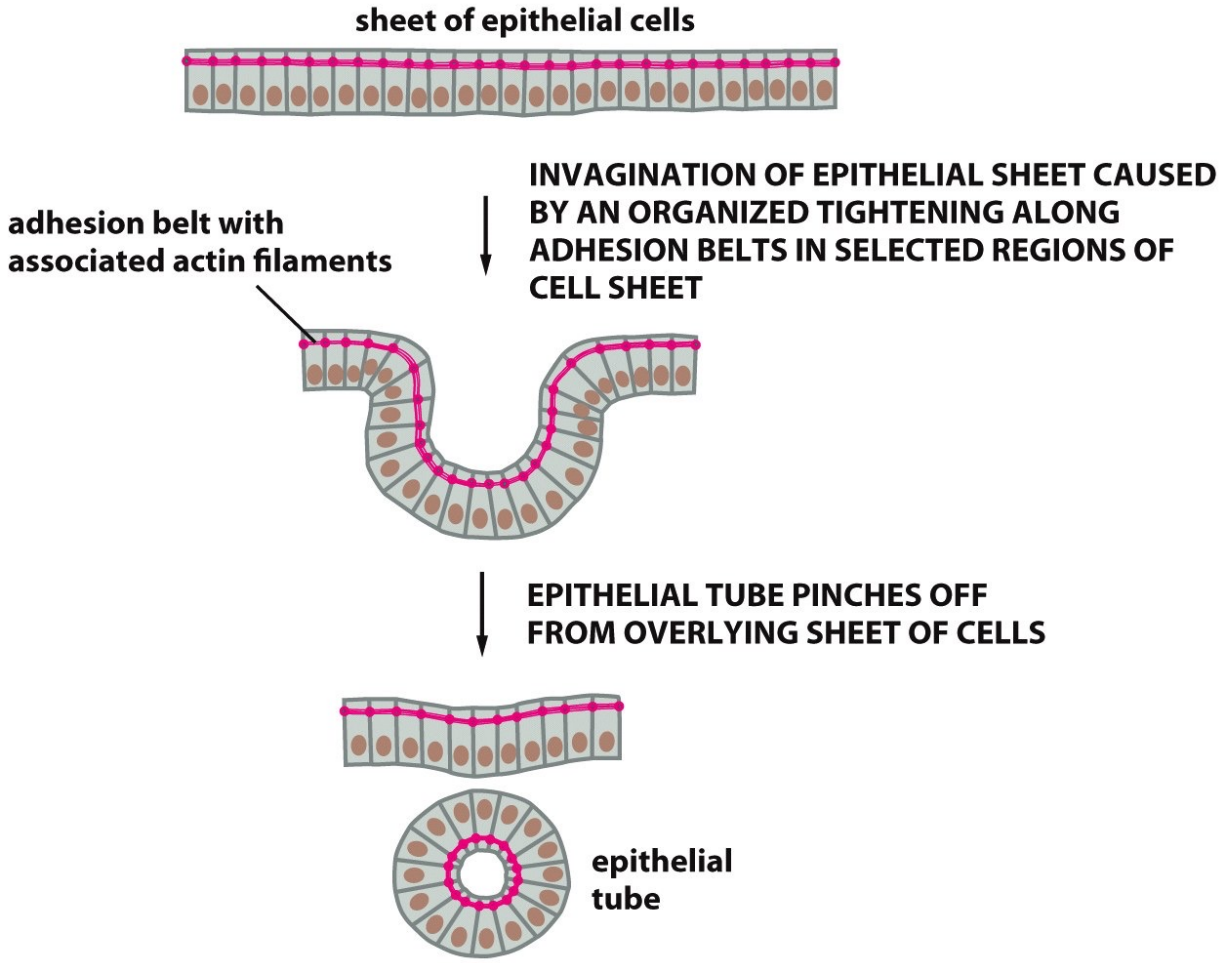


Fig. 20-25

Epithelial Sheets & Cell-Cell Junctions

- Cytoskeleton-linked Junctions bind Epithelial Cells Robustly to one another & to Basal Lamina



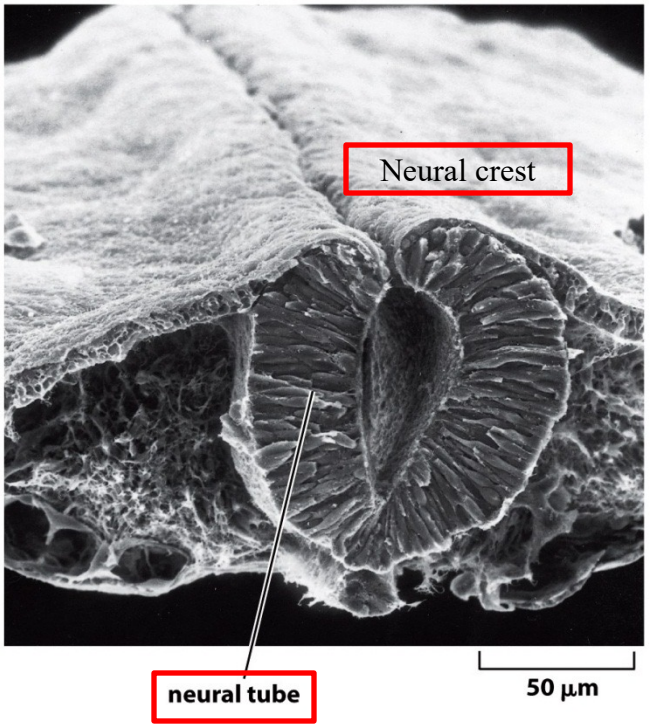


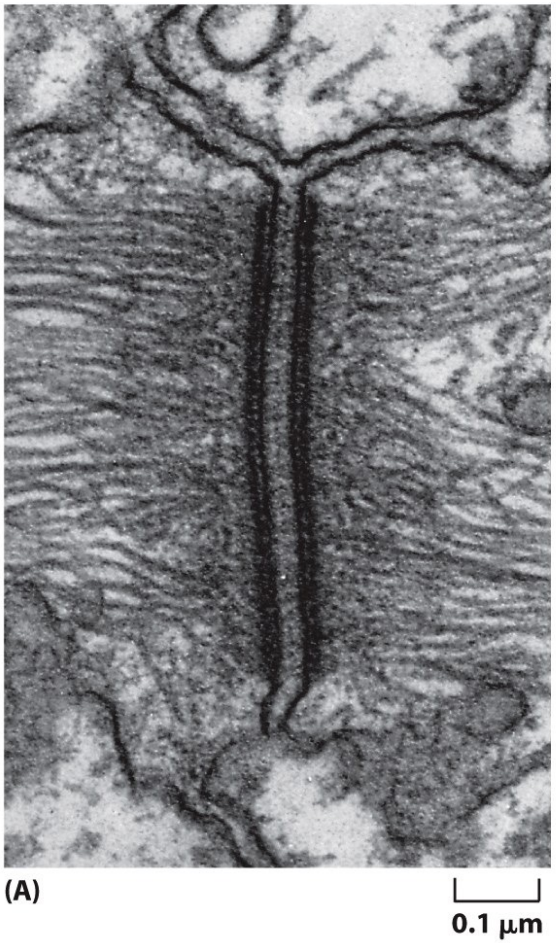
Fig. 20-26

Epithelial Sheets & Cell-Cell Junctions

- Cytoskeleton-linked Junctions bind Epithelial Cells Robustly to one another and to the Basal Lamina

desmosome junction

- Cadherins are anchored to intermediate filament (Keratins)
- Epidermis of skin



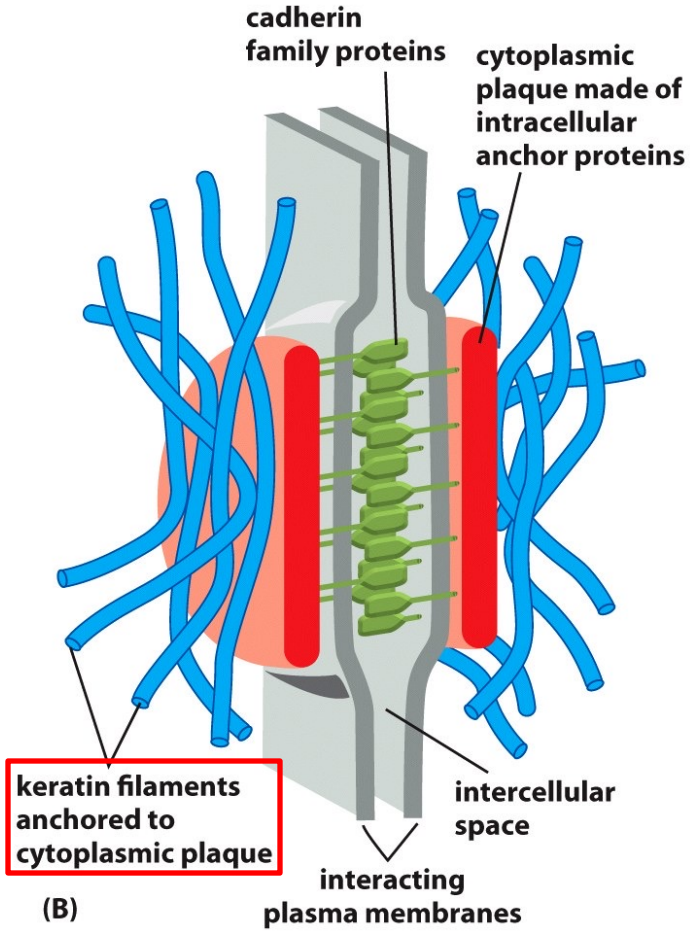


Fig. 20-27

Epithelial Sheets & Cell-Cell Junctions

- Cytoskeleton-linked Junctions bind Epithelial Cells Robustly to one another and to the Basal Lamina

Hemidesmosomes

- anchored to the basal membrane by integrin
- intermediate filament (Keratins)
- Blister (水泡)→ not enough epithelial cell for cell-cell junction & attachment to basal membrane

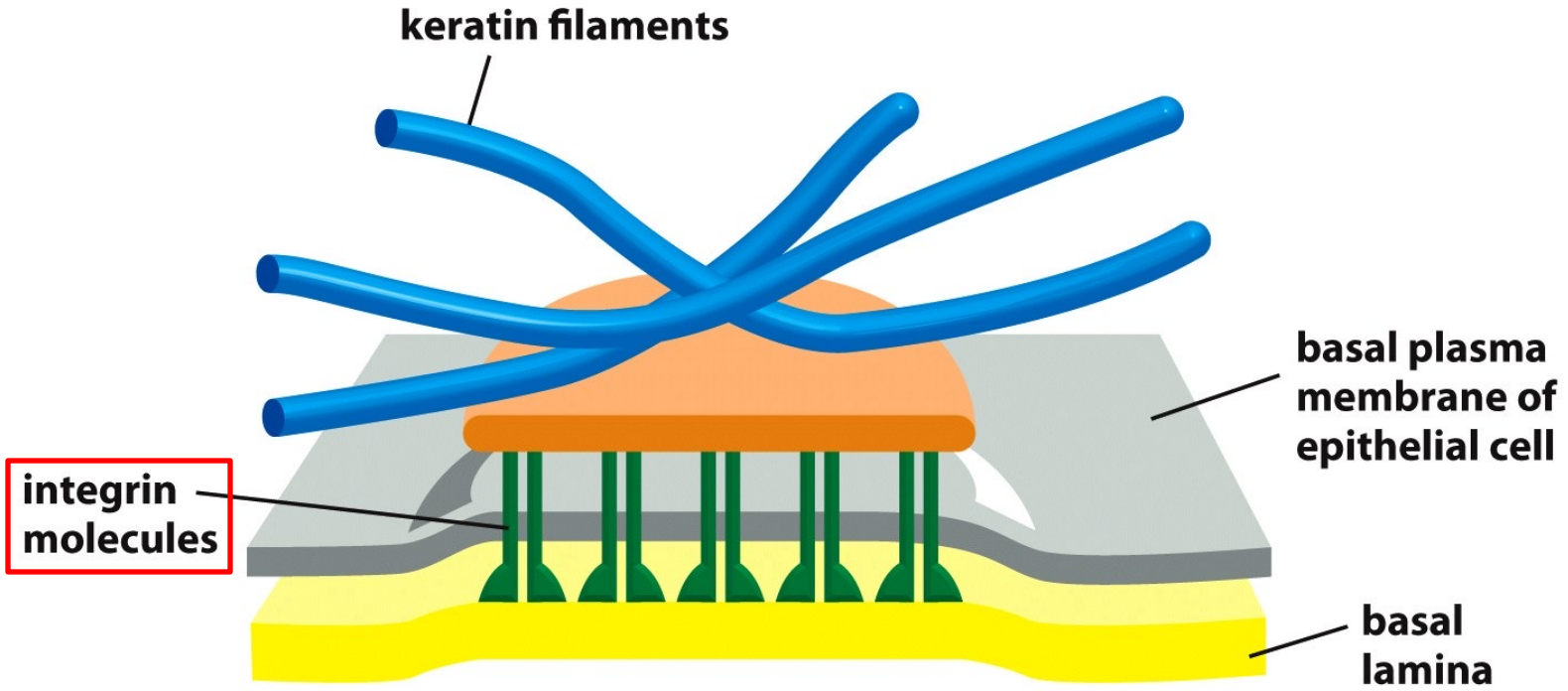
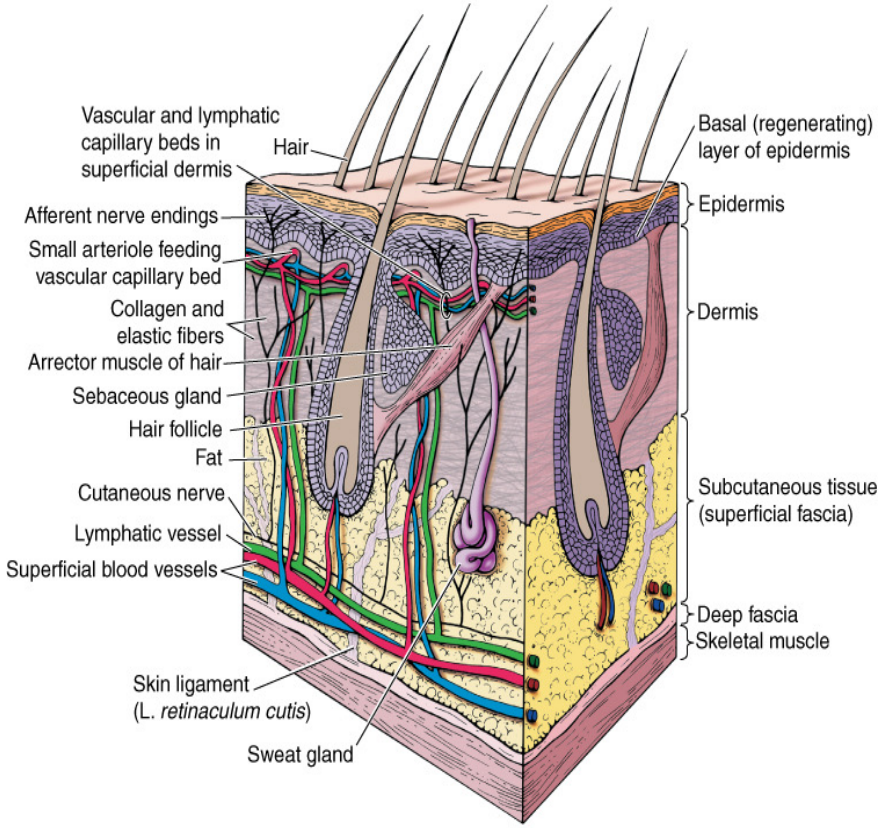


Fig. 20-28

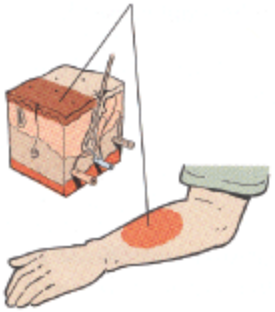


Recognizing burns

Use the size and symptoms of the burn to determine its degree. The cause of the burn will give clues as to severity and whether the injury is critical.

First-degree burn

Only the top layer of the skin is damaged.

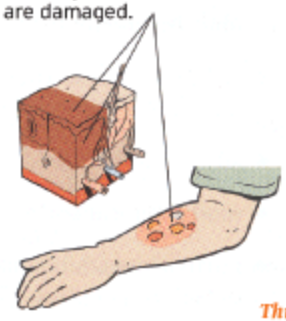


First-degree symptoms

- skin color is pink to red
- slight swelling
- skin is dry
- burn can be anywhere from tender to severely painful

Second-degree burn

Both layers of the skin are damaged.

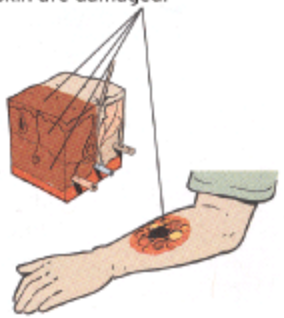


Second-degree symptoms

- skin looks raw and is mottled red in color
- skin is moist
- blisters contain clear fluid
- severe to extreme pain

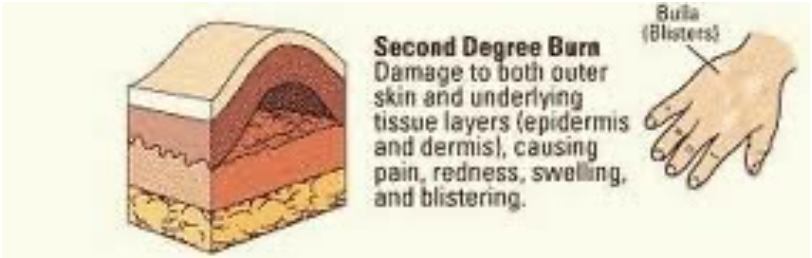
Third-degree burn

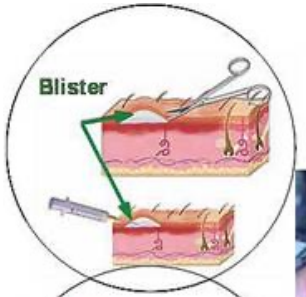
The full thickness of the skin, including tissues under the skin are damaged.

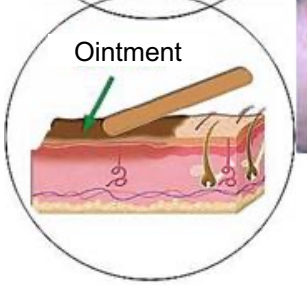


Third-degree symptoms

- skin is pearly-white, tan-coloured or charred
- skin is dry and leathery
- blood vessels and bones may be visible under the skin
- little or no pain, as nerve endings are destroyed







Epithelial Sheets & Cell-Cell Junctions

- Gap Junctions Allow Ions & Small Molecules to Pass from Cell to Cell

Gap Junctions

- 2-4 nm gap
- connexon: channel across 2 plasma membrane
- heart m. cell → electrical coupling

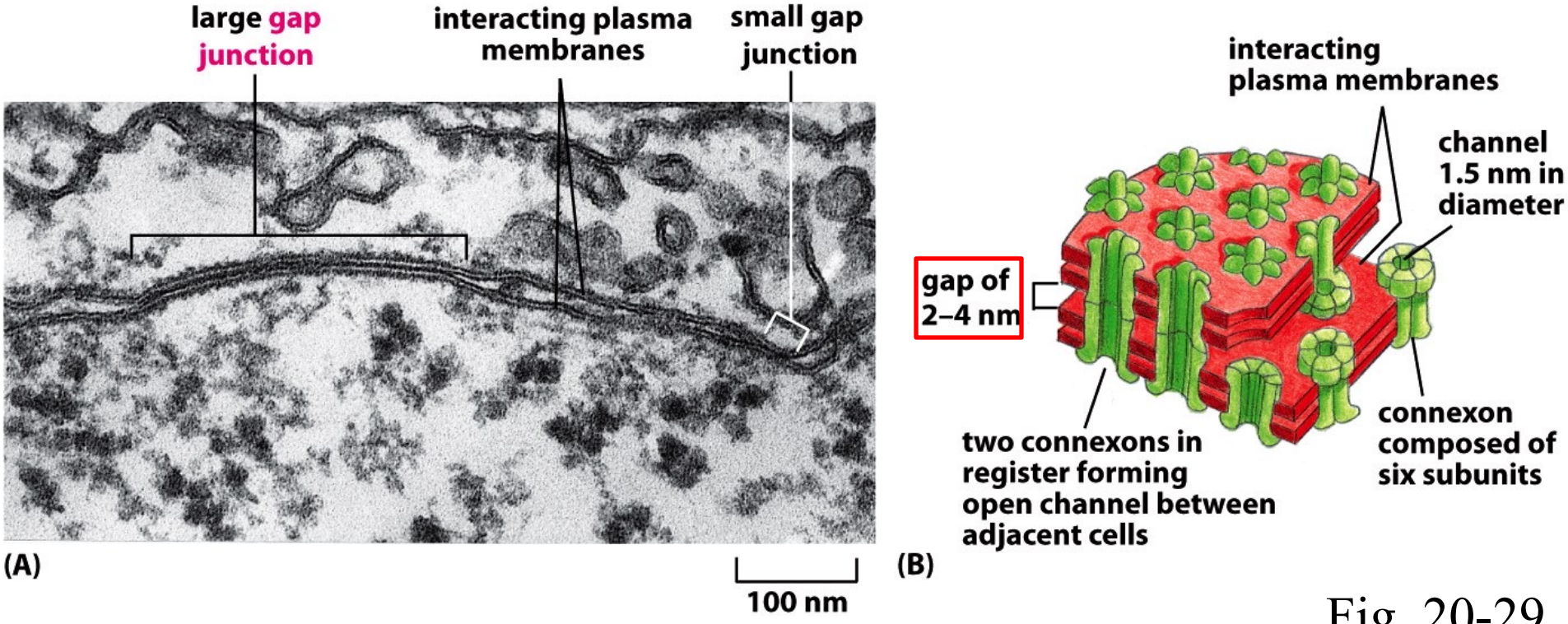
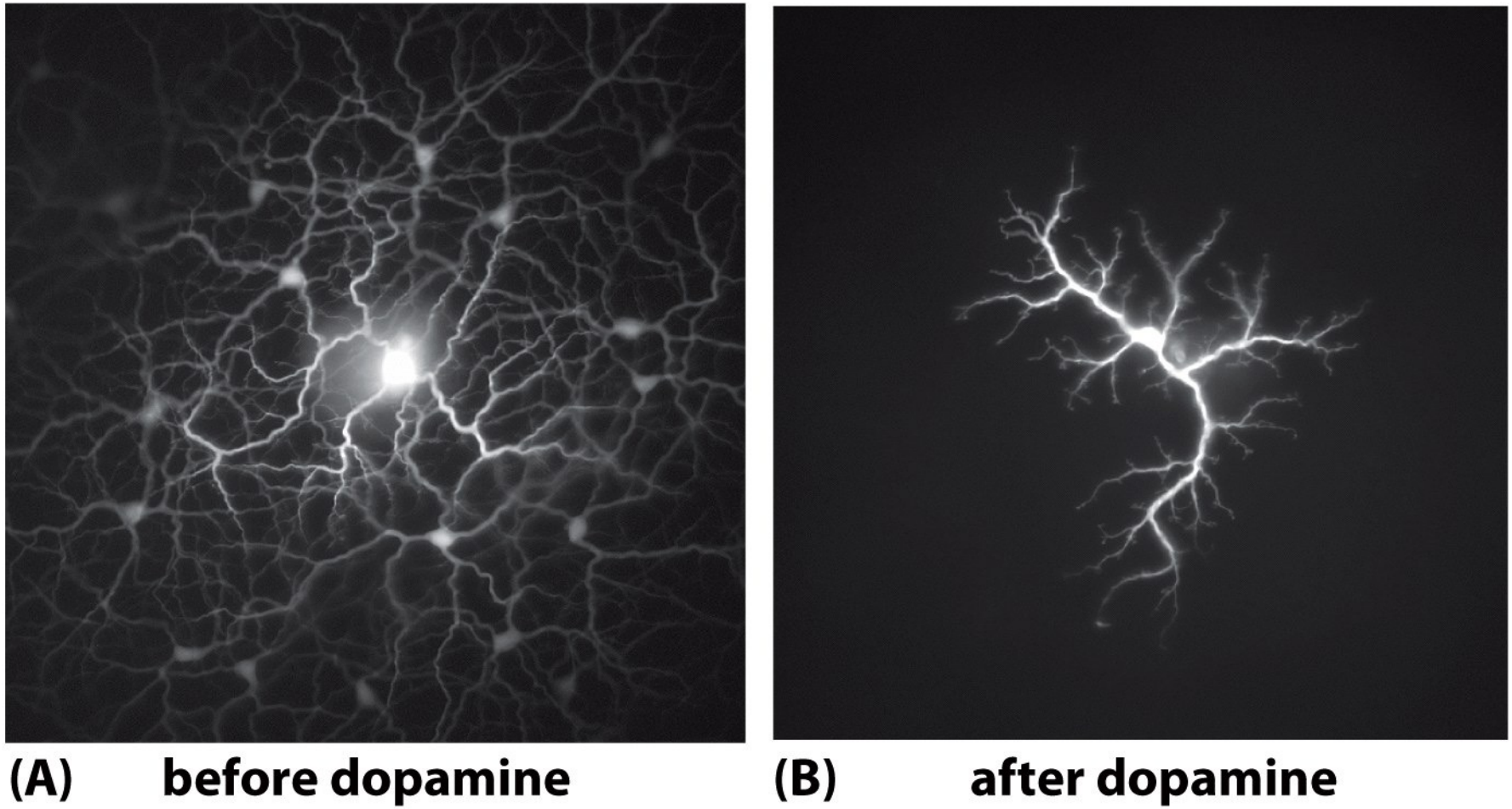


Fig. 20-29

Epithelial Sheets & Cell-Cell Junctions

- Gap Junctions Allow Ions & Small Molecules to Pass from Cell to Cell

Dopamine → ↓ gap-junction communication



(A) before dopamine (B) after dopamine

Rat retina, inject Lucifer yellow into neuron

Fig. 20-30

Epithelial Sheets & Cell-Cell Junctions

- Gap Junctions Allow Ions & Small Molecules to Pass from Cell to Cell

Plant cell

- *plasmodesmata*
- pass ions & small molecules

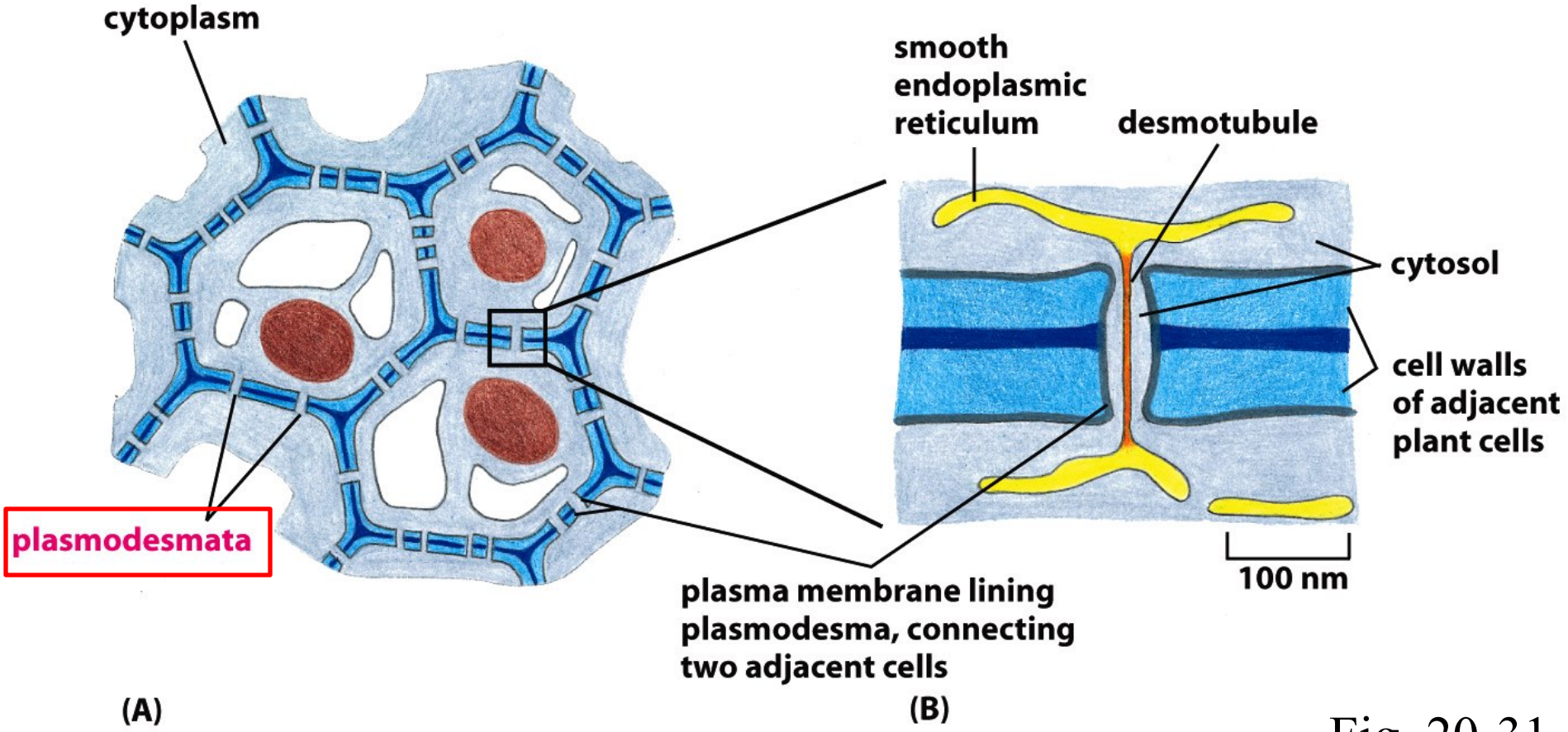
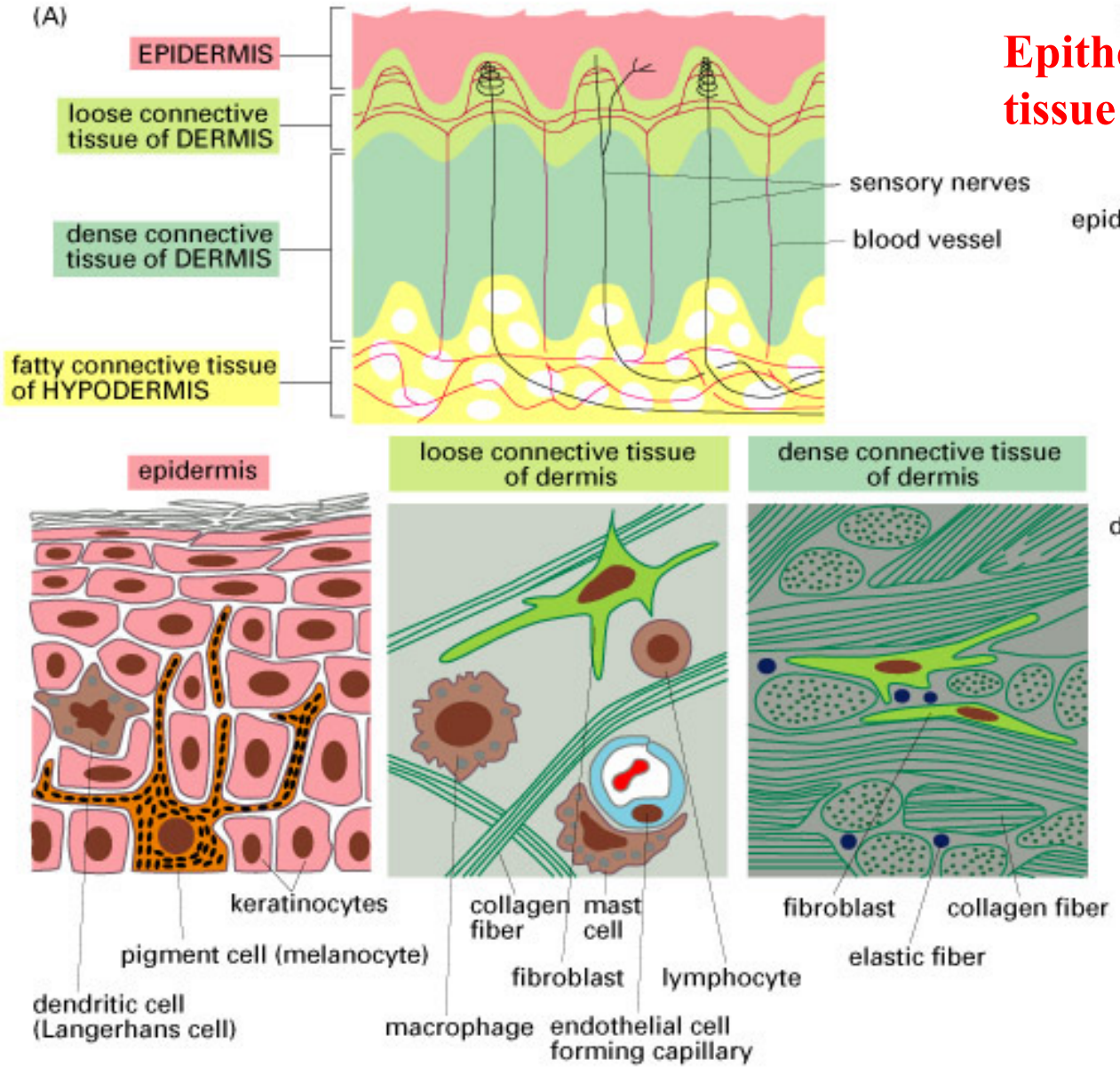
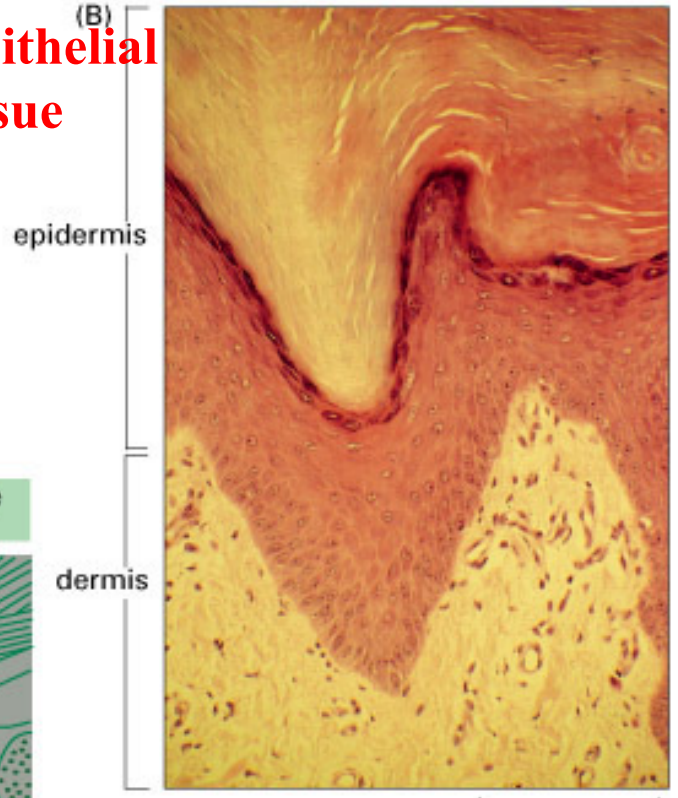


Fig. 20-31

Tissue Maintenance & Renewal

- Tissue are Organized Mixtures of Many Cell Types





Epithelial tissue

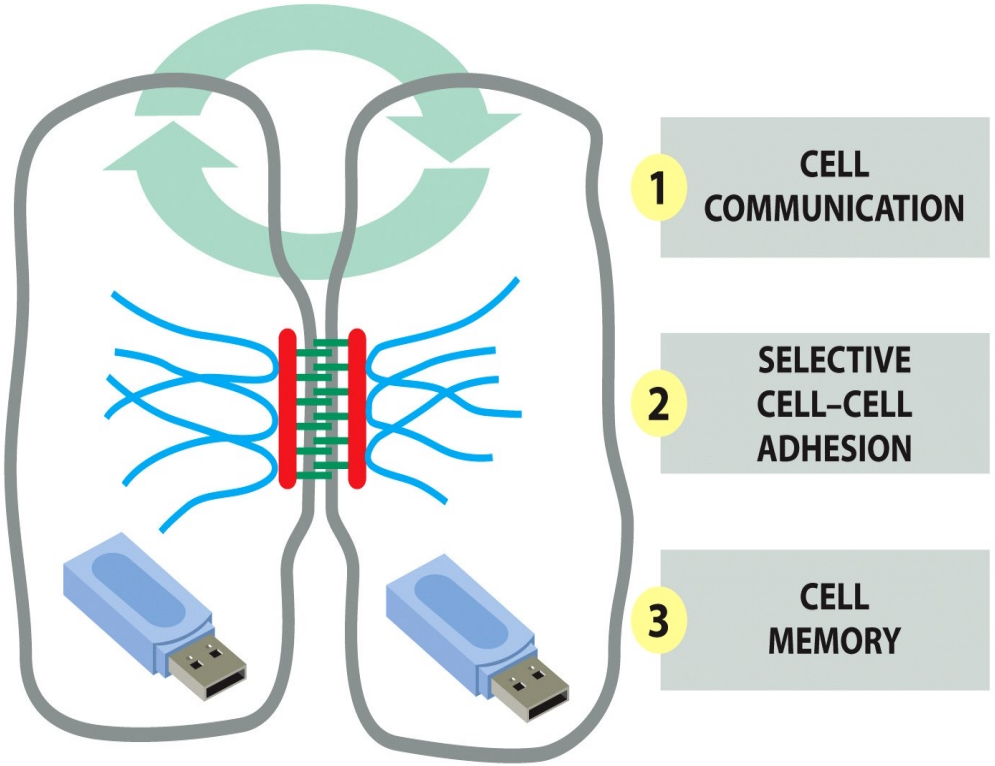
Connective Tissue

Mammalian Skin

Fig. 20-33

Tissue Maintenance & Renewal

- Tissue are Organized Mixtures of Many Cell Types



3 major factors for organization of structure stability

1.Cell communication
environmental signal → produce & survive new cell

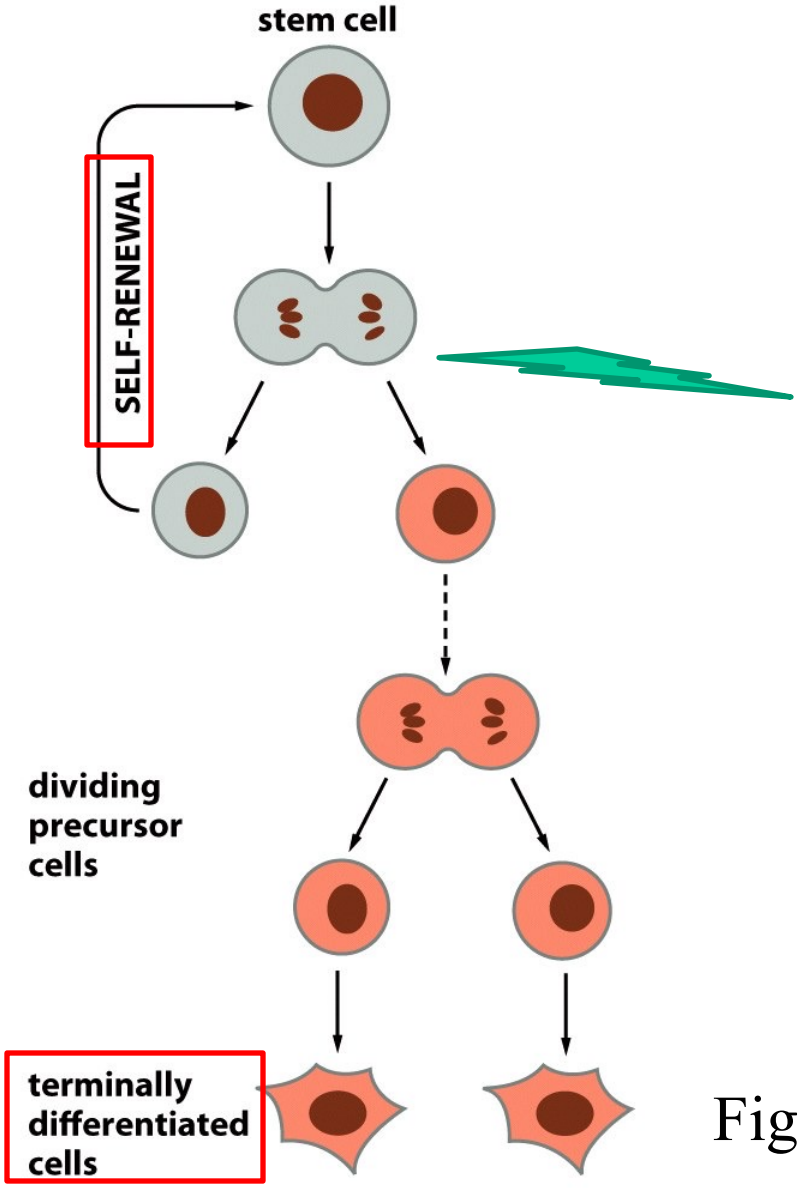
2.Selective cell-cell adhesion
cadherin

3.Cell memory
autonomously preserve distinctive character & pass it on

Fig. 20-34

Tissue Maintenance & Renewal

- **Different Tissue are Renewed at Different Rates**
- **Stem Cells Generate a Continuous Supply of Terminally Differentiated Cells**



What signal for decision making ?

Fig. 20-35

Stem Cell

Requirement

1. **"multipotency": able to differentiate into multiple mature cell types**
2. **"stemness": self-renewal**

- ***Embryonic Stem Cell (ESC)***

  pluripotency: able to differentiate three germ layers of cells

  Ectoderm – brain, eyes

  Mesoderm – bone, muscle, heart, kidney

  Endoderm – liver, pancreas, lung, GI tract

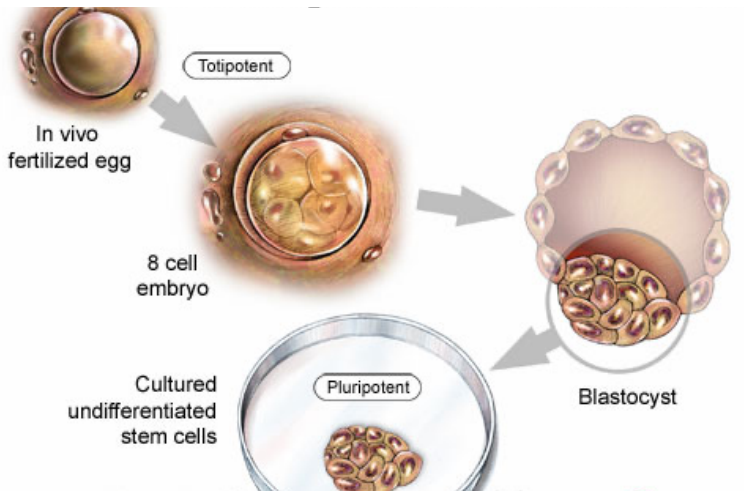
embryonic
stem cell

Tissue Maintenance & Renewal

- Stem Cells can be Used to Repair Damaged Tissues

Embryonic stem cell (ES cell)

- can differentiation into all cell types, including germ cell
- skeletal m. fiber → muscular dystrophy
- nerve cell → Parkinson's disease
- insulin-secreting cell → type I diabetics
- cardiac m. cell →
  heart attack



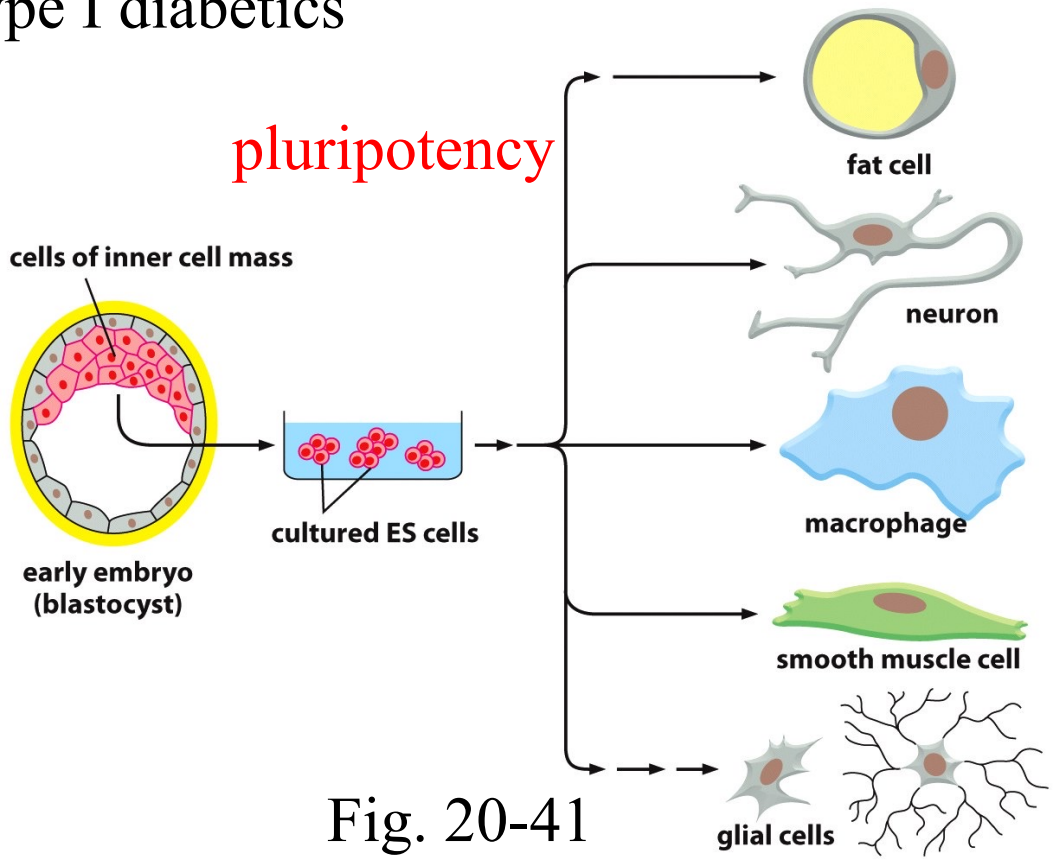
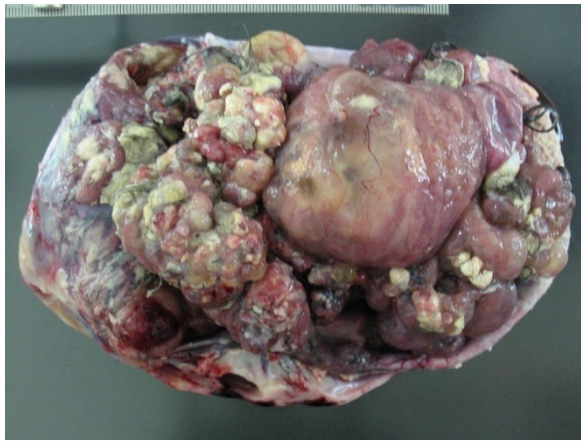
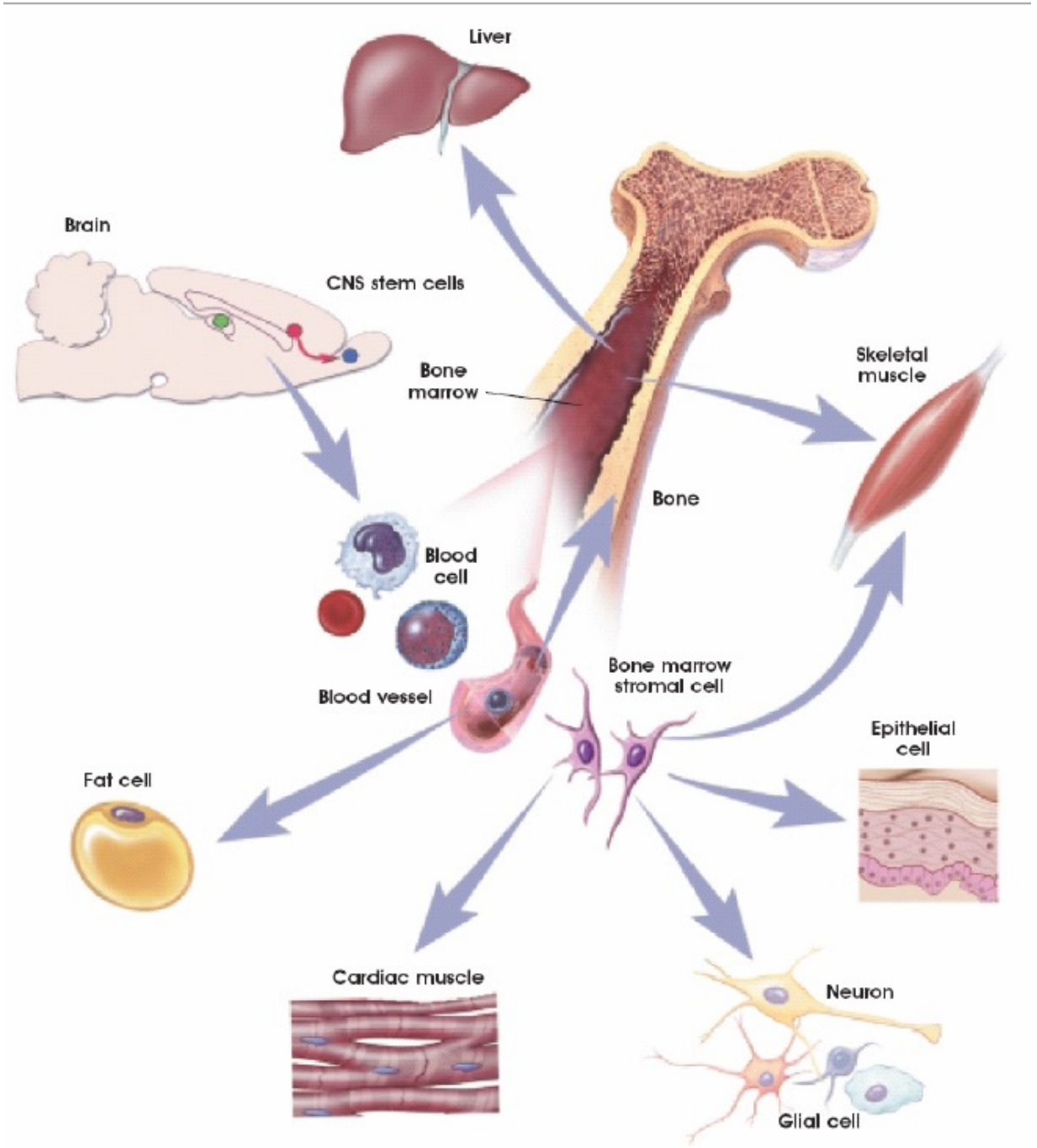


Fig. 20-41

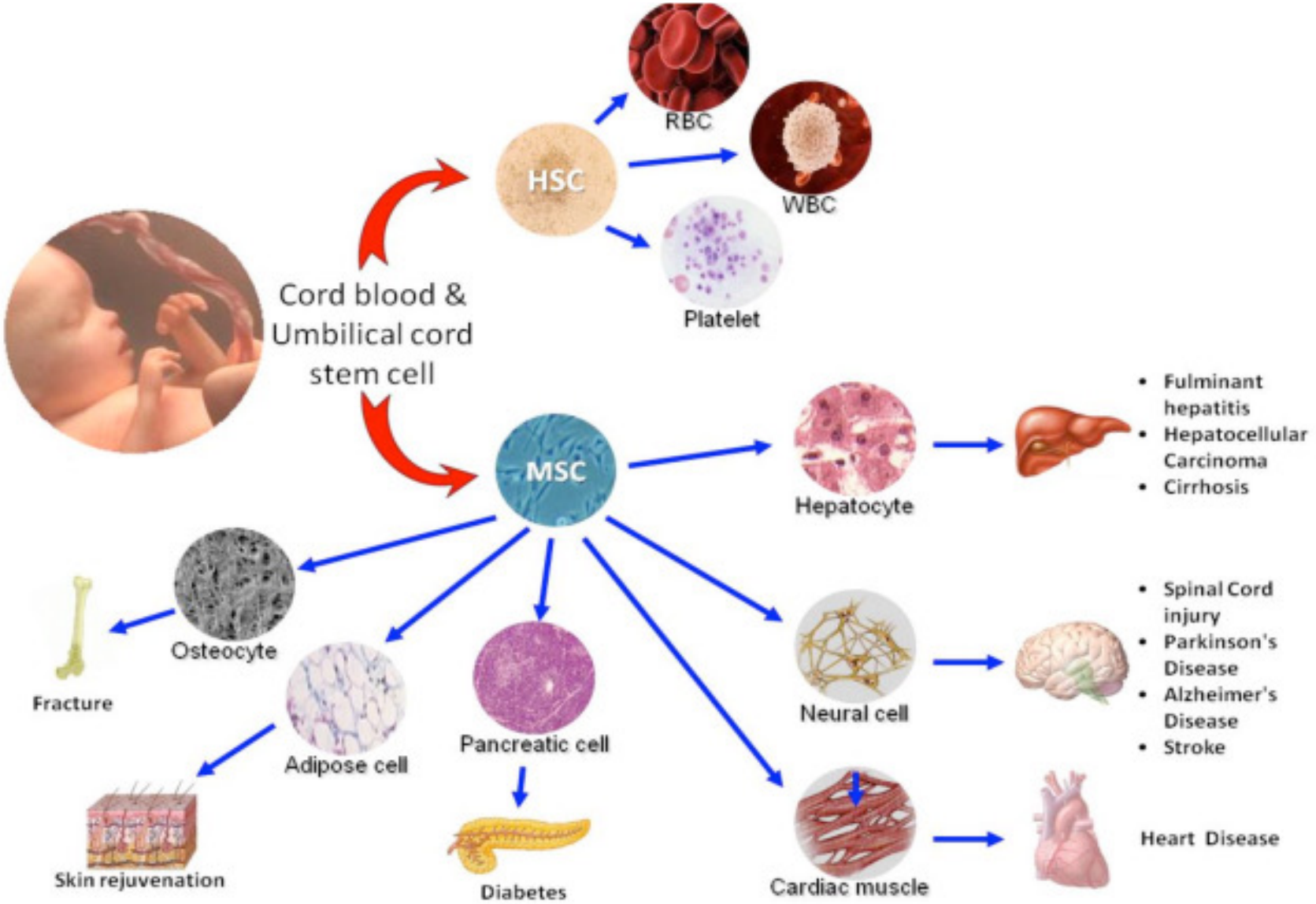


Zygote
Blastocyst
Gastrula
Ectoderm (external layer)
Mesoderm (middle layer)
Endoderm (internal layer)
Germ cells
Skin cells of epidermis
Neuron of brain
Pigment cell
Cardiac muscle
Skeletal muscle cells
Tubule cell of the kidney
Red blood cells
Smooth muscle (in gut)
Pancreatic cell
Thyroid cell
Lung cell (alveolar cell)
Sperm
Egg

Adult Stem Cell



Other Adult Stem Cell: Cord blood



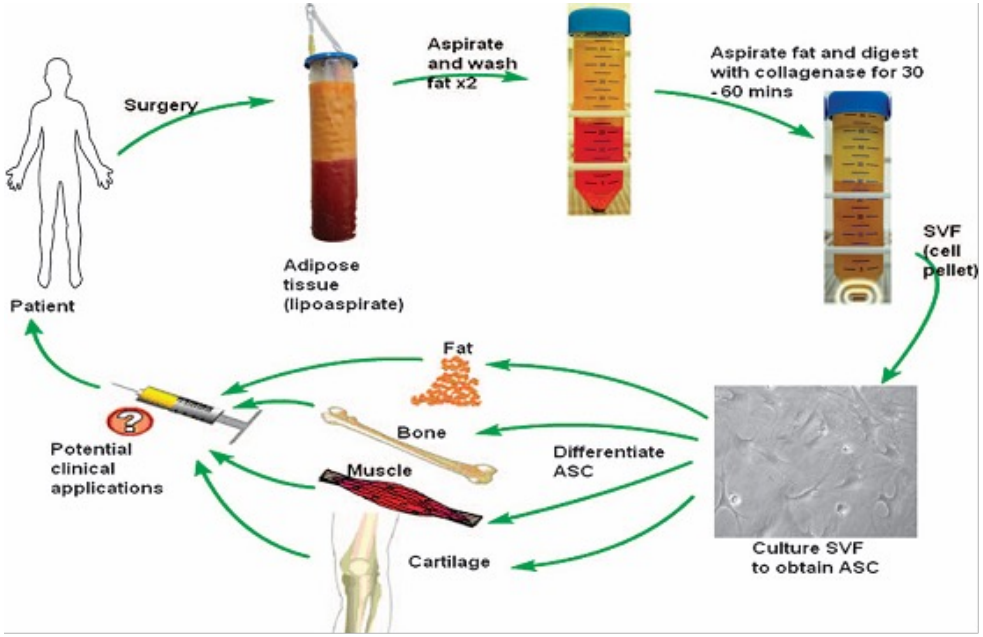
Other Adult Stem Cell

PDMC (placenta-derived multipotent cells)

紫河車

本草綱目》解釋，「天地之先，陰陽之祖，乾坤之始，胚胎將兆，九九數足，胎兒則乘而載之」，其遨遊於西天佛國，南海仙山，飄蕩於蓬萊仙境，萬里天河，故稱之為河車。母體娩出時為紅色，稍放置即轉紫色，因此，入藥時稱為「**紫河車**」。

ASC (adipose-derived stem cells)



Tissue Maintenance & Renewal

- **Nuclear Transplantation Provides a Way to Generate Personalized ES cell: the Strategy of Therapeutic Cloning**

Cloning?

Biology term: a set of individuals that are genetically identical by virtue of their descent from a single ancestor

Cloning entire multicellular animal → reproductive cloning

Nuclear Transplantation

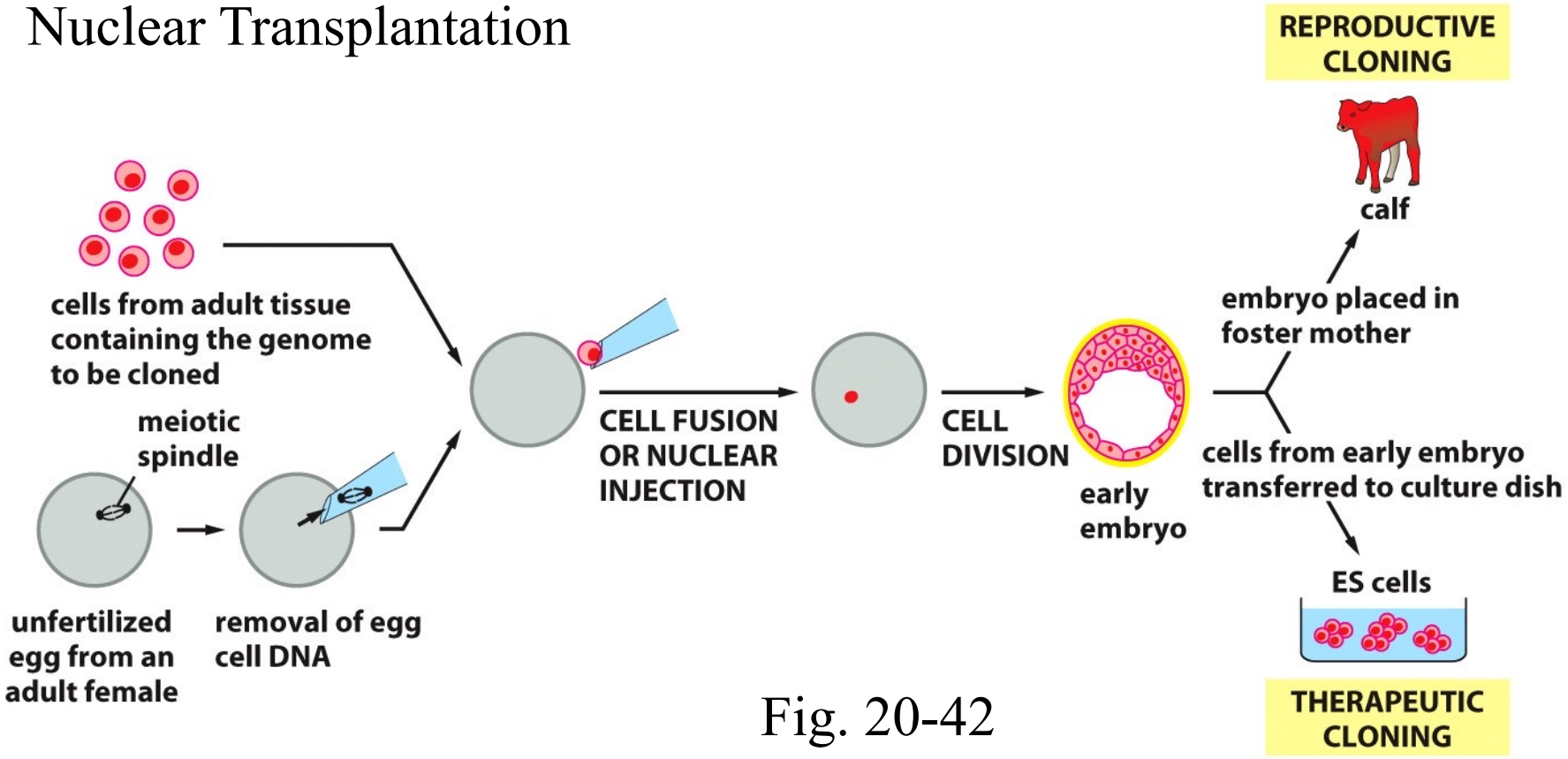
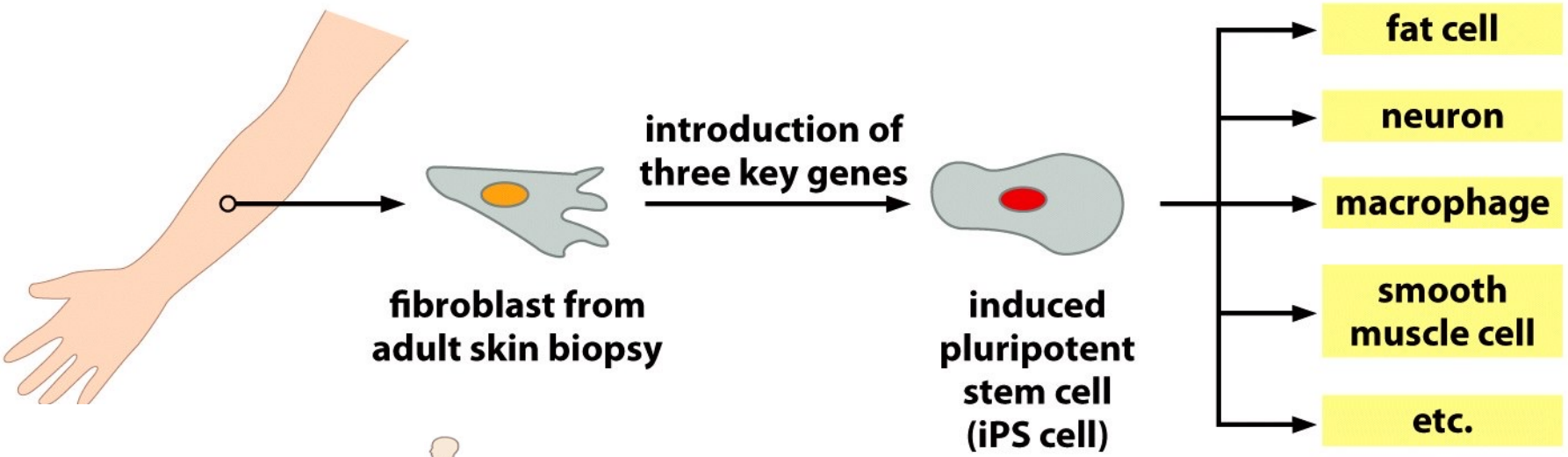


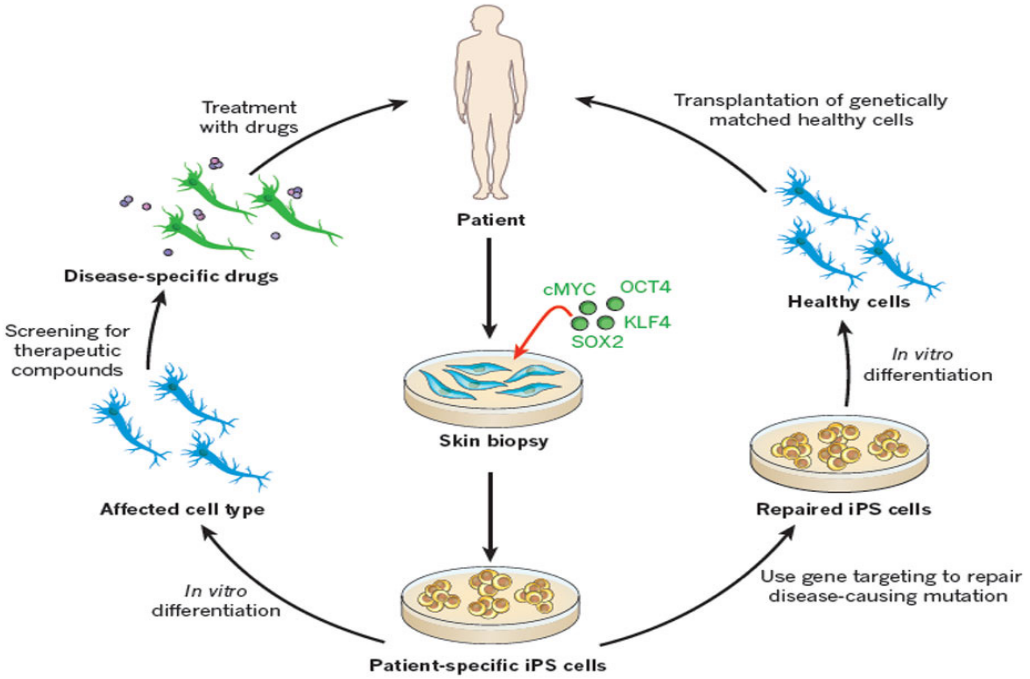
Fig. 20-42

Tissue Maintenance & Renewal

- iPS: induced pluripotent stem cell

Fig. 20-43



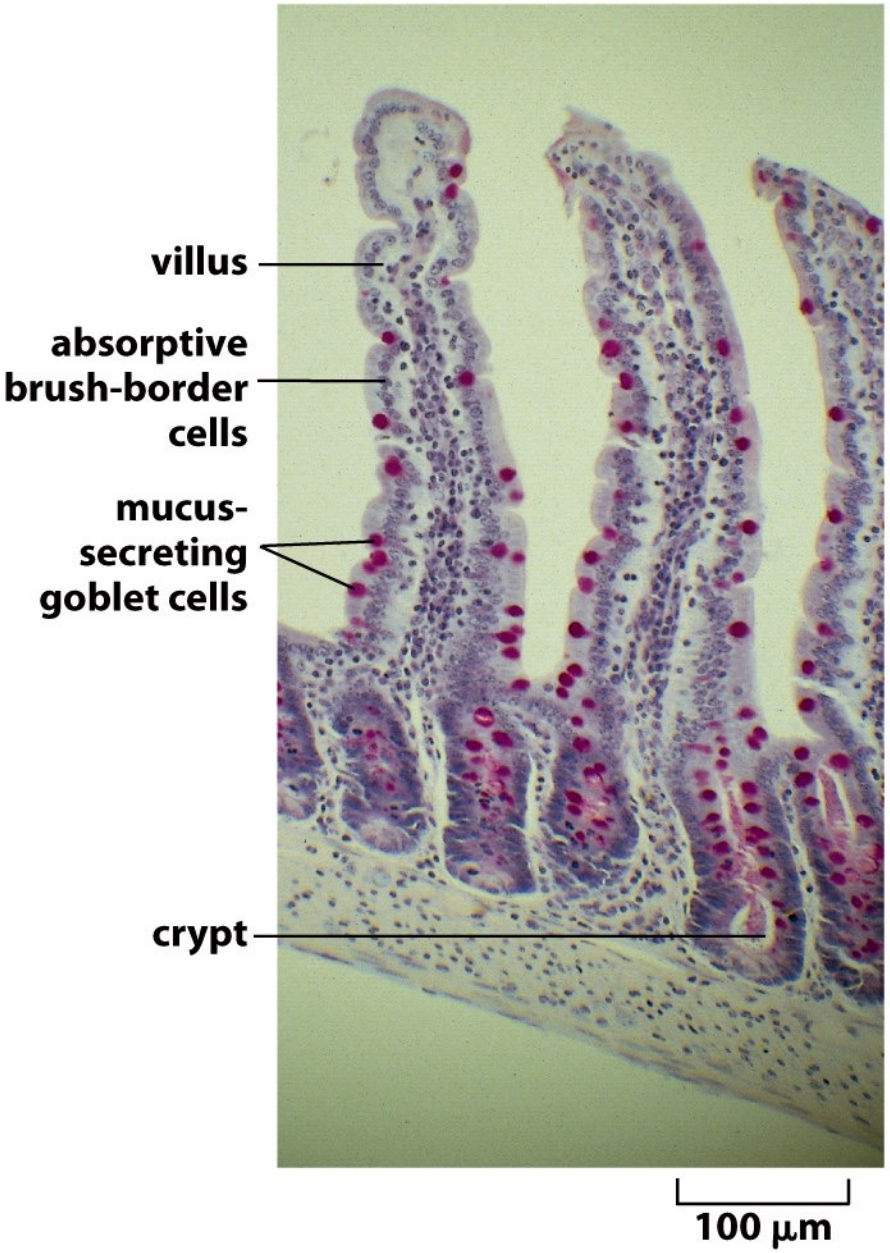


Center for iPS Cell Research and Application
CiRA Kyoto University

Shinya Yamanaka

Tissue Maintenance & Renewal

- Stem Cells Generate a Continuous Supply of Terminally Differentiated Cells



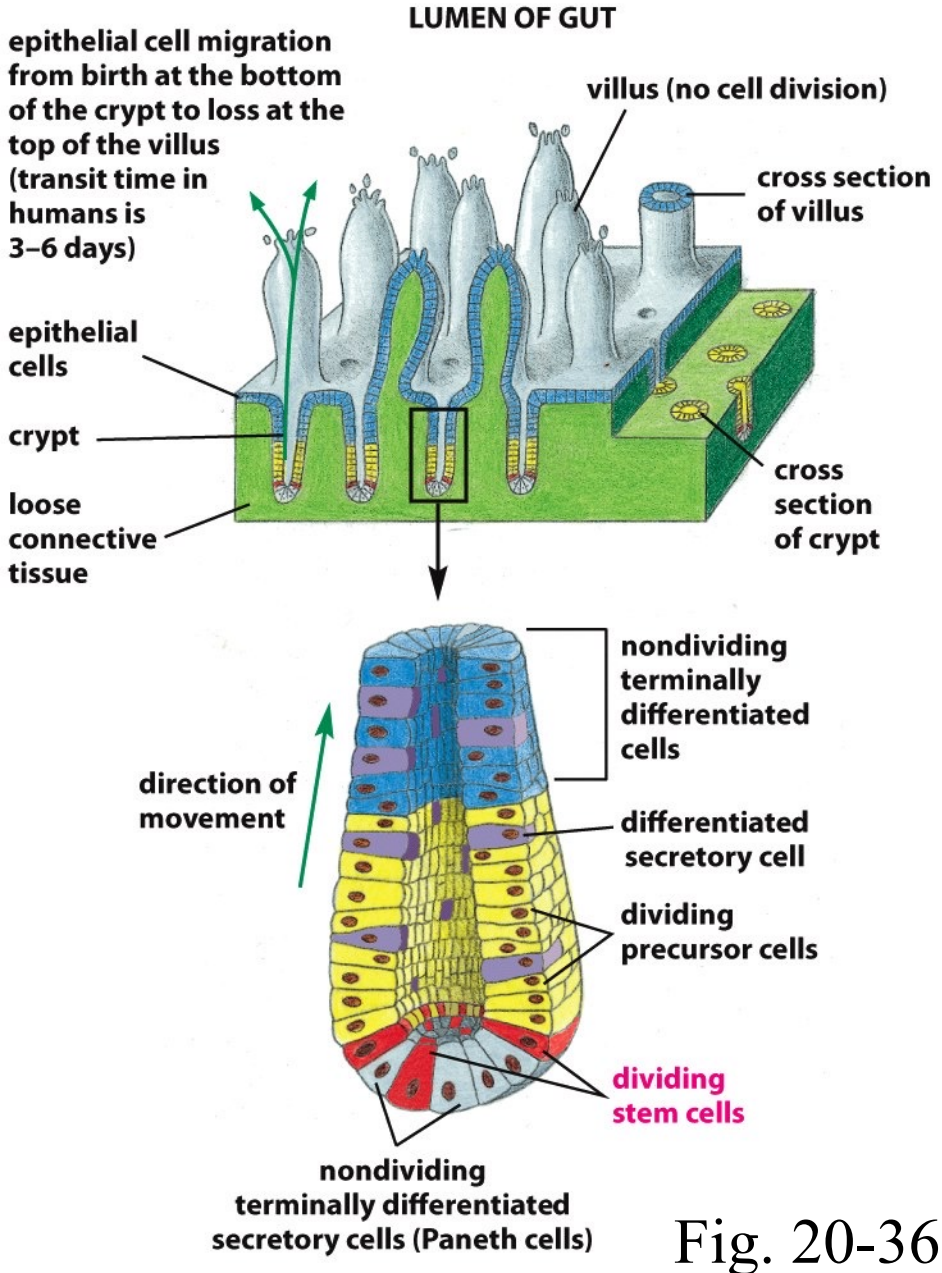


Fig. 20-36

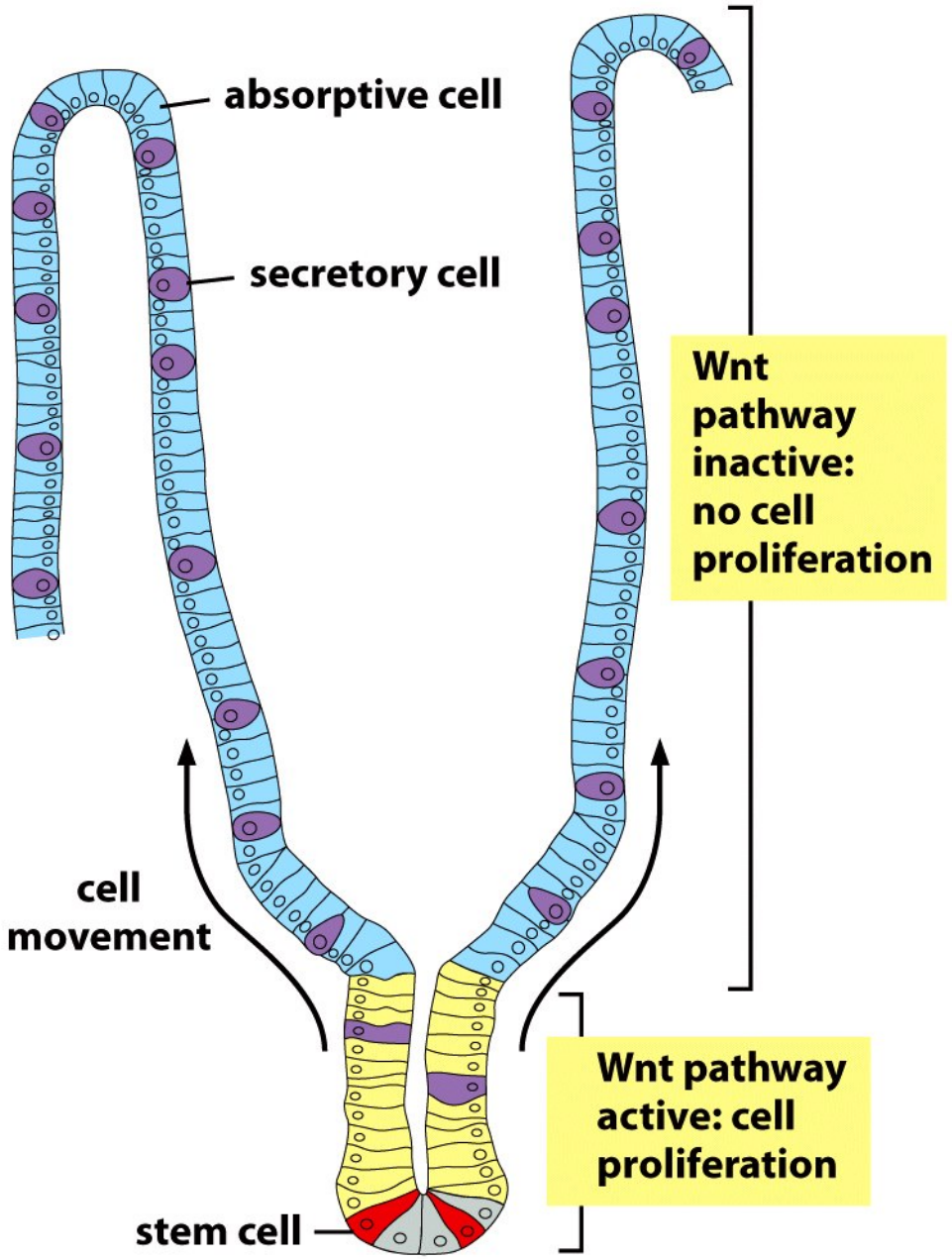


Figure 20-40 *Essential Cell Biology* (© Garland Science 2010)

Tissue Maintenance & Renewal

- Stem Cells Generate a Continuous Supply of Terminally Differentiated Cells

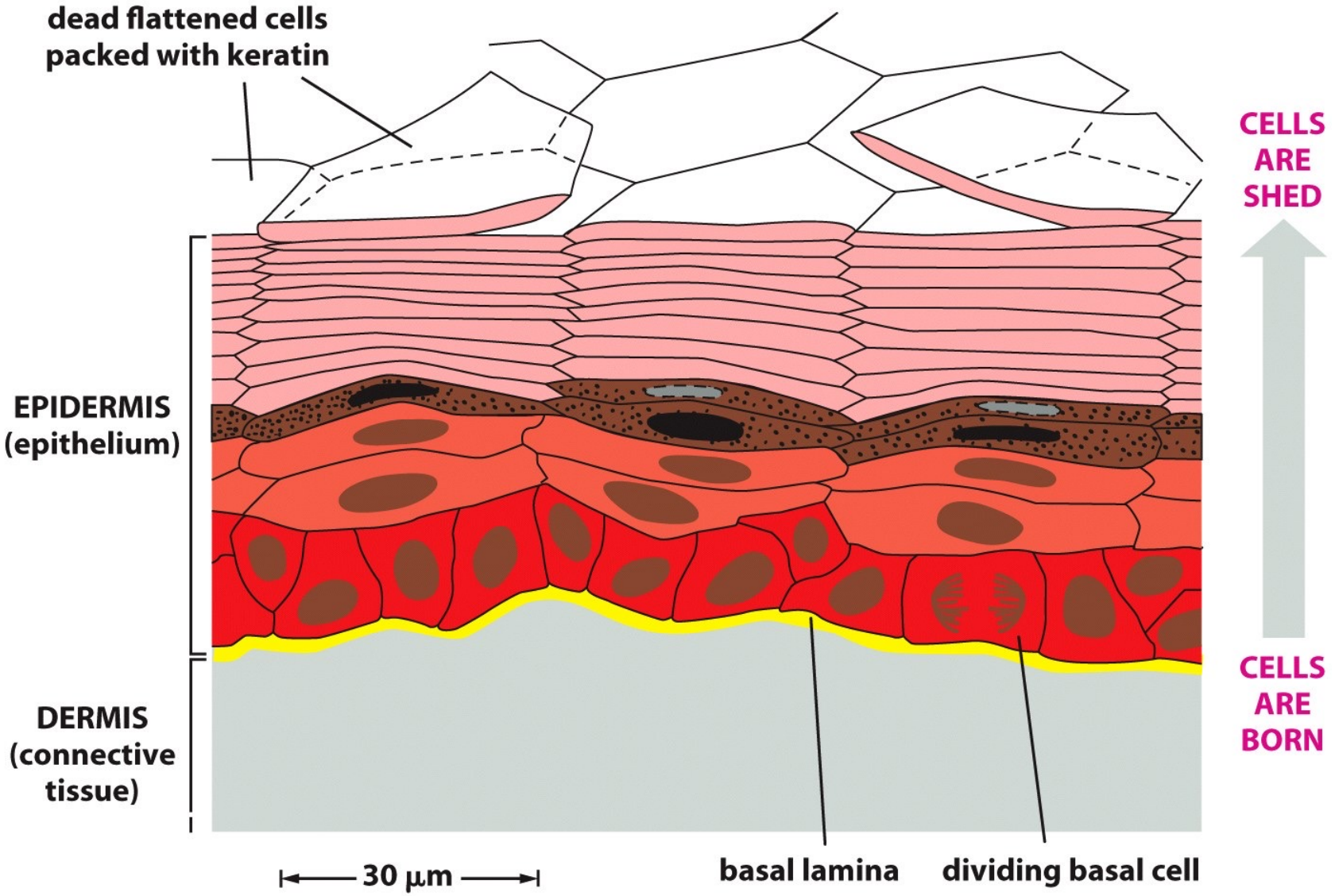
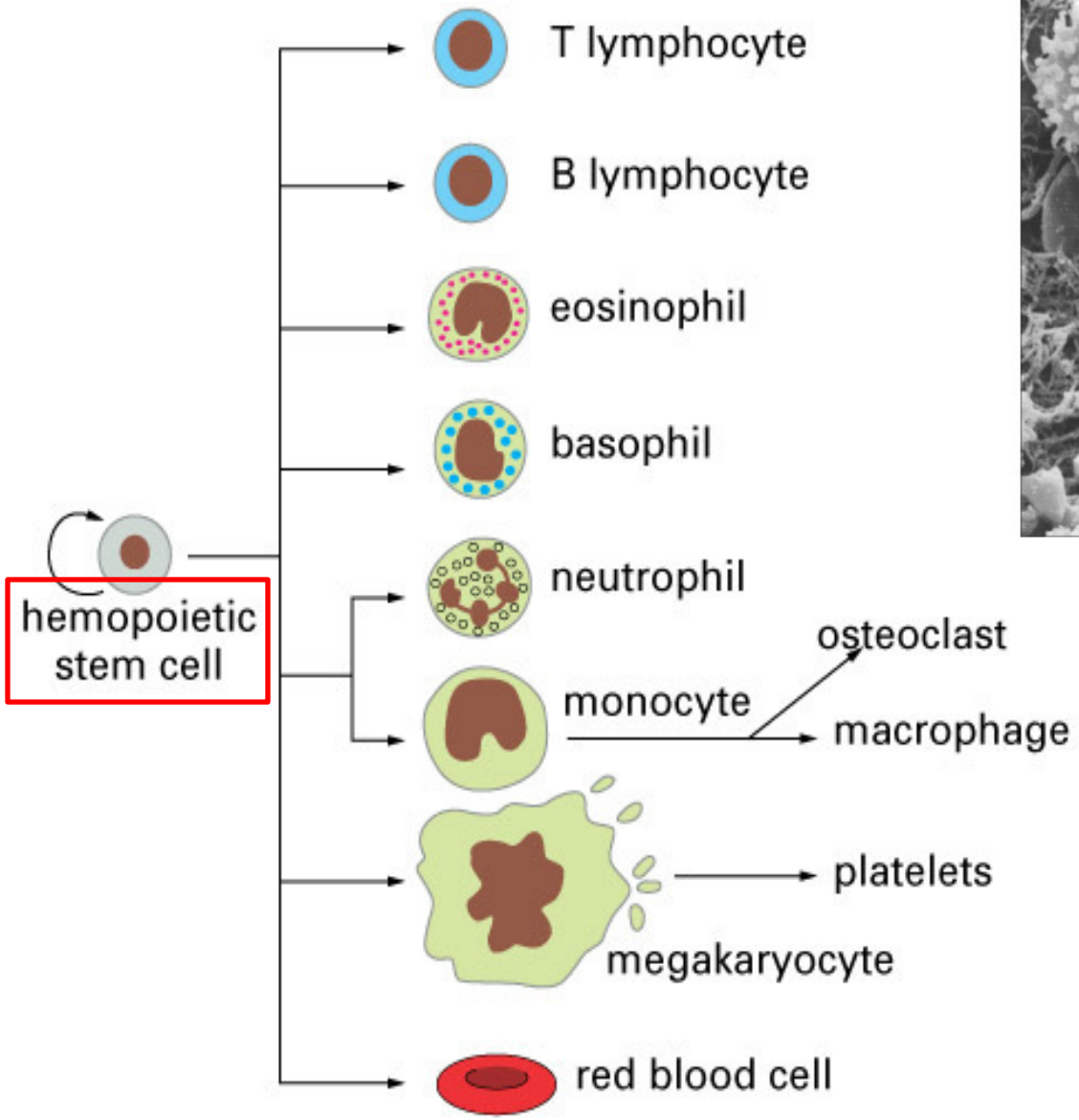
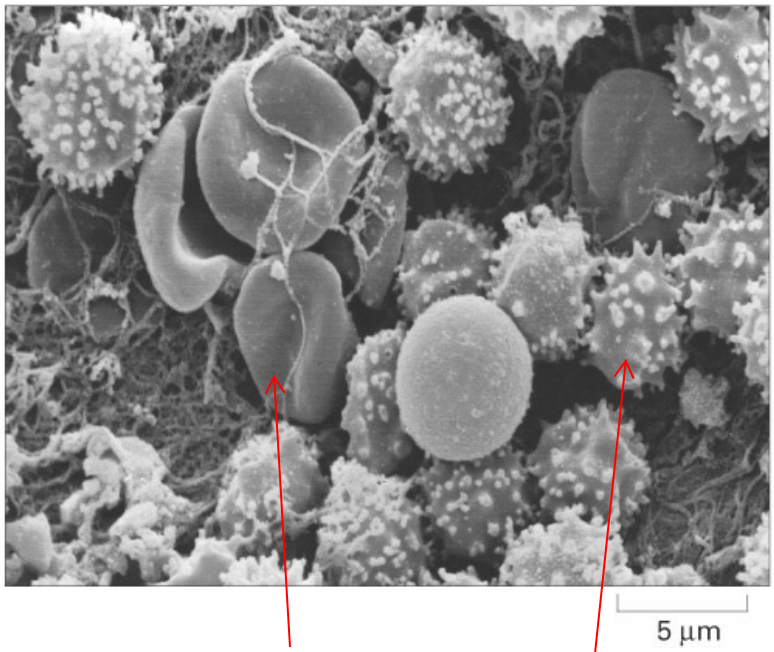


Fig. 20-37

Tissue Maintenance & Renewal

- Stem Cells Generate a Continuous Supply of Terminally Differentiated Cells





Transfusing HSC into irradiated mouse to rescue blood stem cell

Fig. 20-38