Epithelial Tissue-1

Hanan Jafar. BDS.MSc.PhD

Introduction

- Epithelial tissues are composed of closely aggregated polyhedral cells adhering strongly to one another and to a thin layer of ECM, forming cellular sheets that **line** the cavities of organs and **cover** the body surface.
- Epithelium lines all external and internal surfaces of the body and all substances that enter or leave an organ must cross this type of tissue.

Functions

- Covering, lining, and protecting surfaces (eg, epidermis)
- Absorption (eg, the intestinal lining)
- Secretion (eg, parenchymal cells of glands)
- Specific cells of certain epithelia may be contractile (myoepithelial cells)
- Some are specialized sensory cells, such as those of taste buds or the olfactory epithelium.

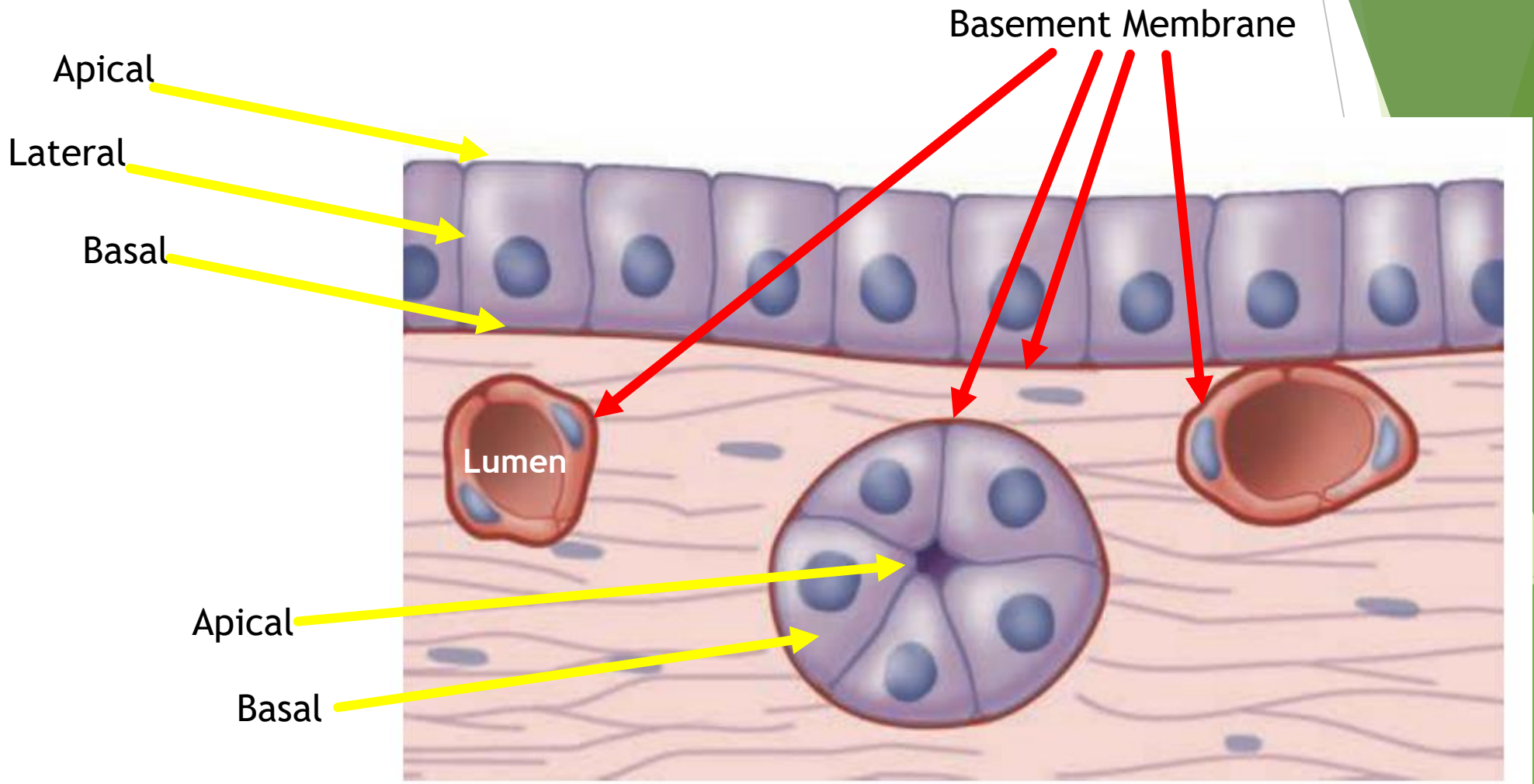
General Characteristics

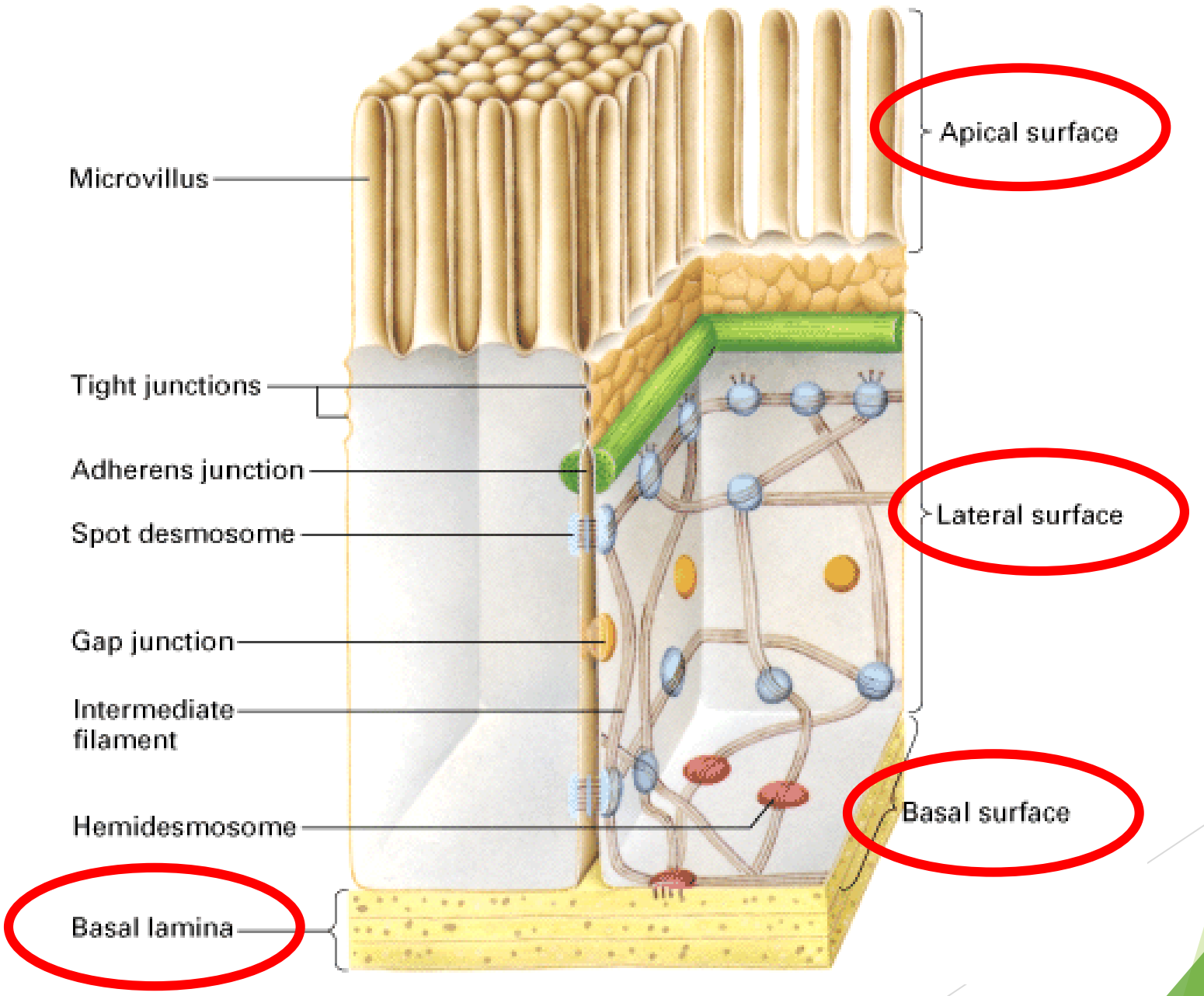
- Epithelium is an **avascular** tissue.
- It forms the **secretory** portion of glands and their **ducts**.
- Specialized epithelial cells function as receptors for the **special senses**.
- Epithelial cells show **polarity** and rest on **basement membrane**.
- Most epithelia are adjacent to connective tissue.
- The connective tissue that underlies the epithelia lining the organs of the digestive, respiratory, and urinary systems is called the **lamina propria**

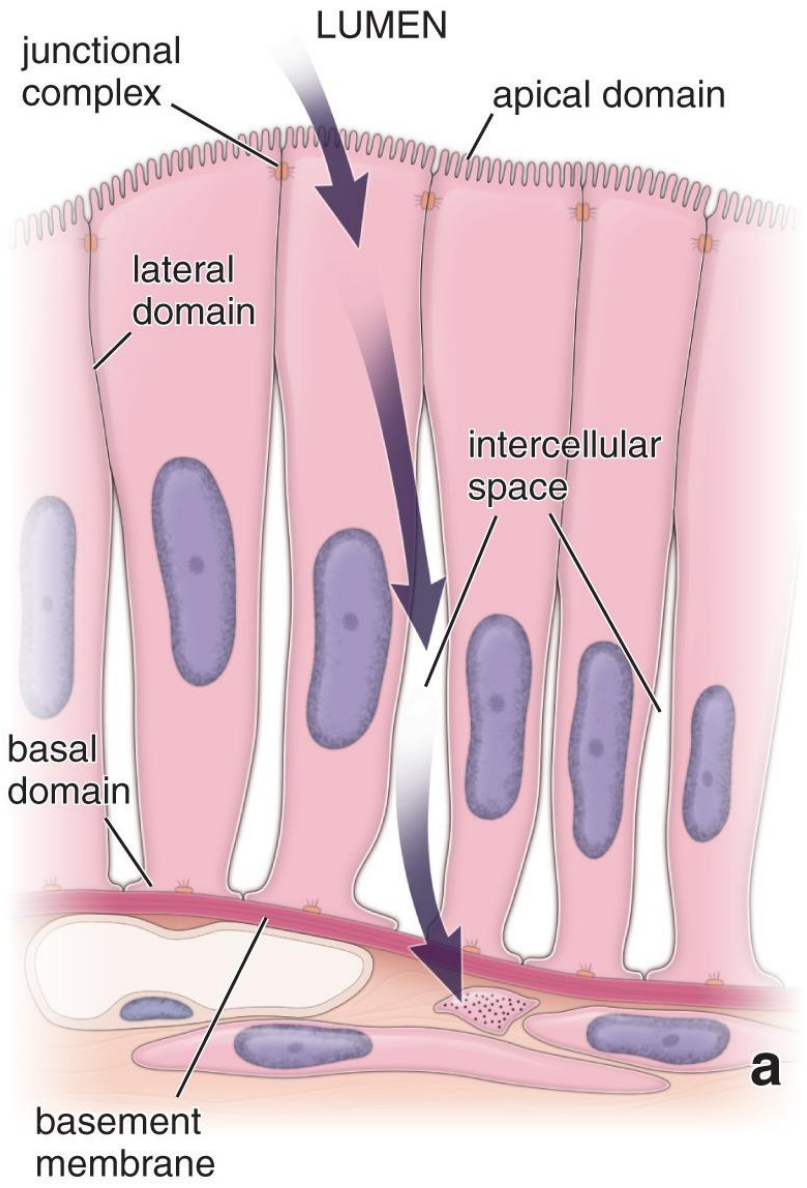
Epithelium creates a selective barrier between the external environment and the underlying connective tissue.

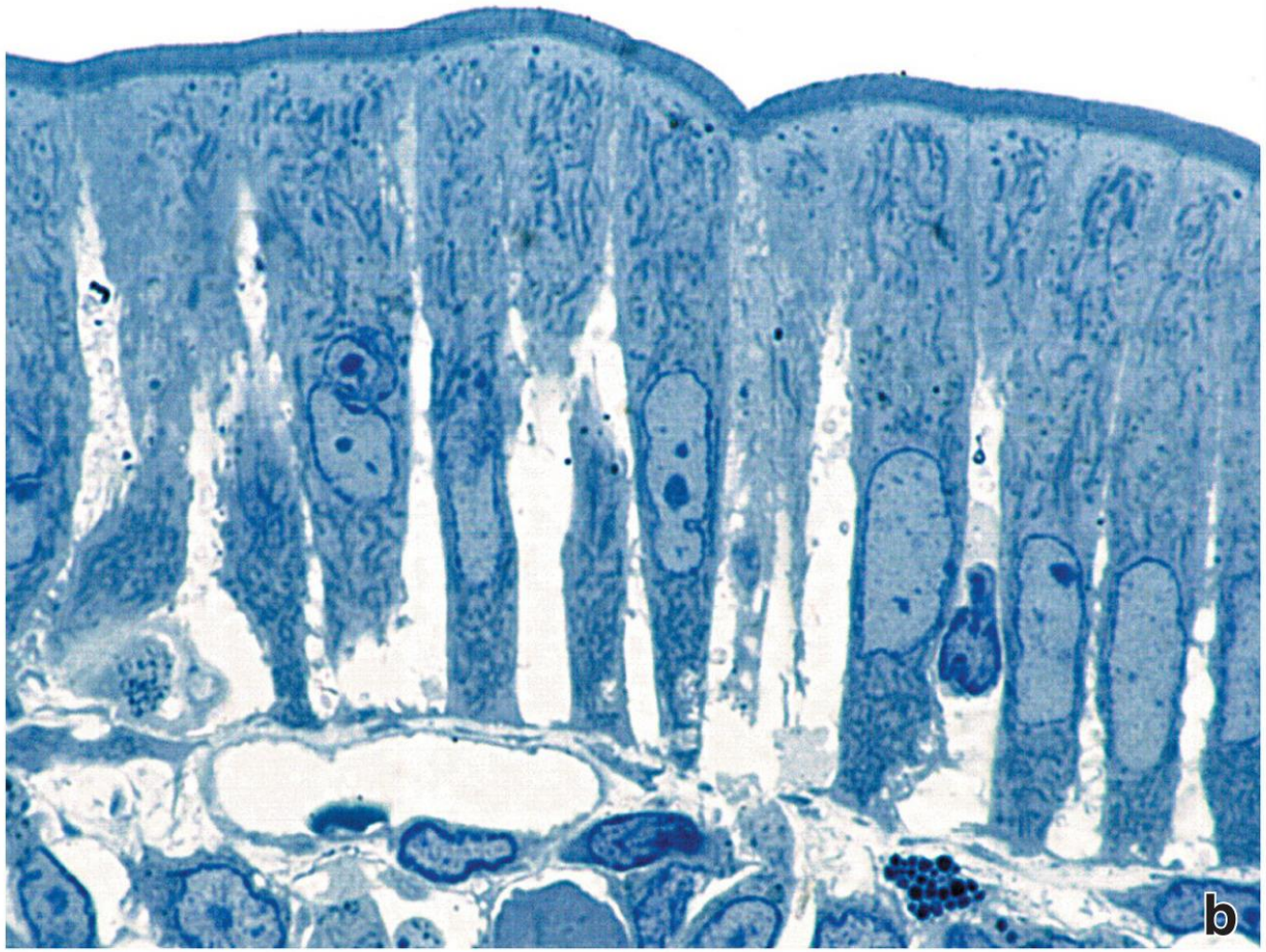
Cell Polarity

- Polarity means that organelles and membrane proteins are distributed unevenly within the cell.
- The region of the cell contacting the ECM and connective tissue is called the **basal pole.**
- The opposite end, usually facing a space, is the **apical pole.**
- Regions of cells that adjoin neighboring cells comprise the cells' **lateral surfaces**.


Basement Membrane
Apical
Lateral
Basal
Lumen
Apical
Basal


Microvillus
Tight junctions
Adherens junction
Spot desmosome
Gap junction
Intermediate filament
Hemidesmosome
Basal lamina
Apical surface
Lateral surface
Basal surface





Apical Domain Modifications/Specializations

- In many epithelial cells, the **apical domain** shows special structural surface modifications to carry out specific functions. They include:

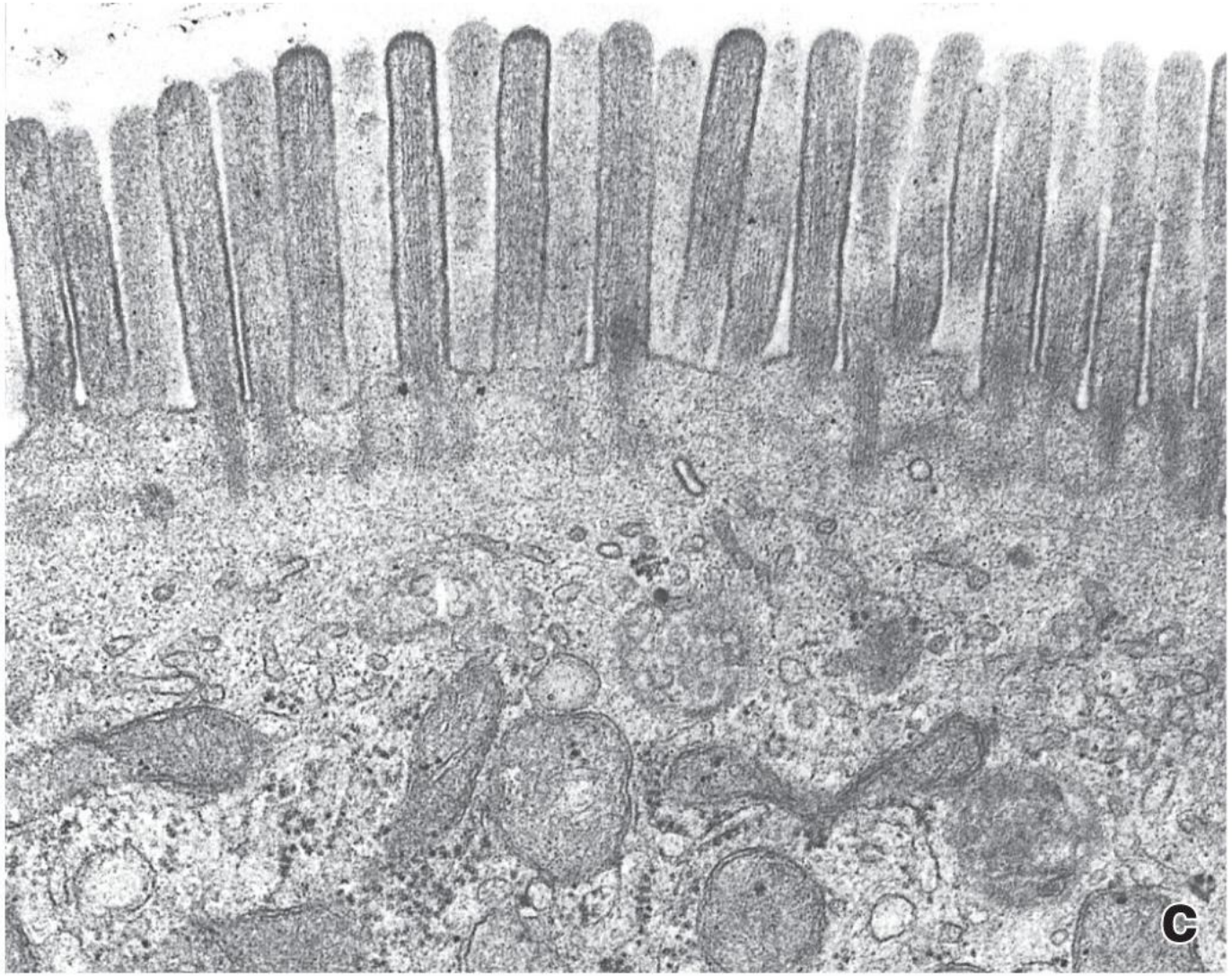
- **Microvilli**, cytoplasmic processes containing a core of actin filaments

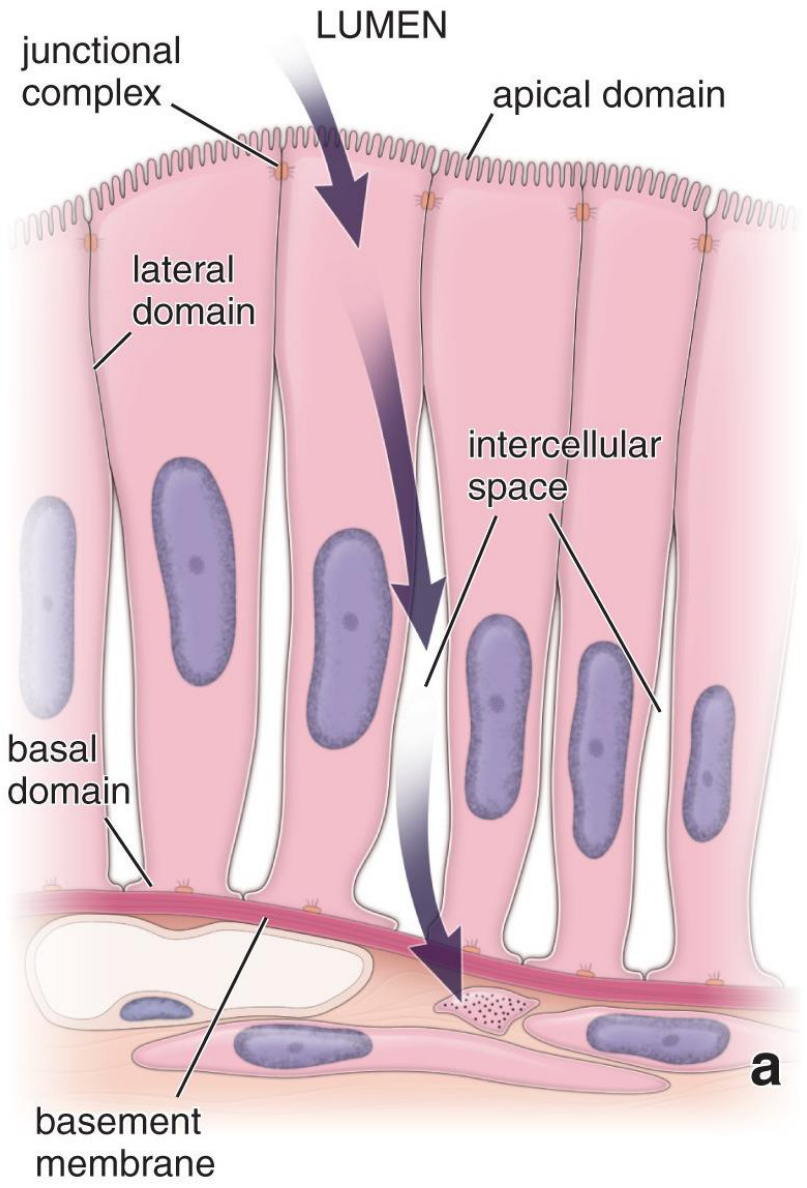
- **Cilia**, cytoplasmic processes containing bundle of microtubules

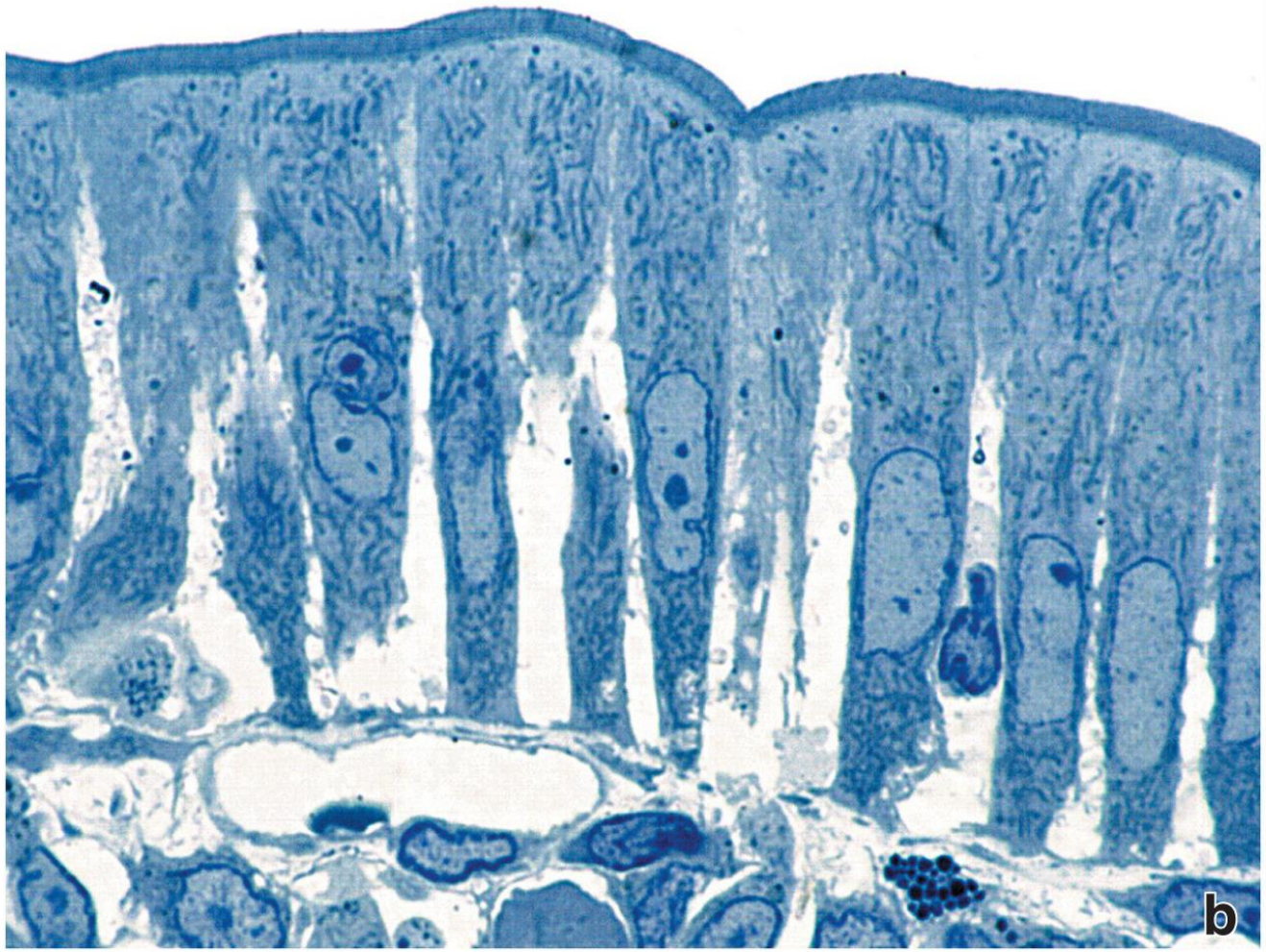
- **Stereocilia**, immobile microvilli of unusual length

Microvilli

- Microvilli are finger-like cytoplasmic projections on the apical surface of most epithelial cells.
- They are tall, closely packed, uniform projections that greatly increase the free cell surface area.
- In general, the number and shape of the microvilli of cell type correlate with the cell's absorptive capacity.
- In intestinal absorptive cells, this surface structure was originally called the **striated border**; in the kidney tubule cells, it is called the **brush border.**
- **They cannot be distinguished individually on LM, but can be seen on EM**



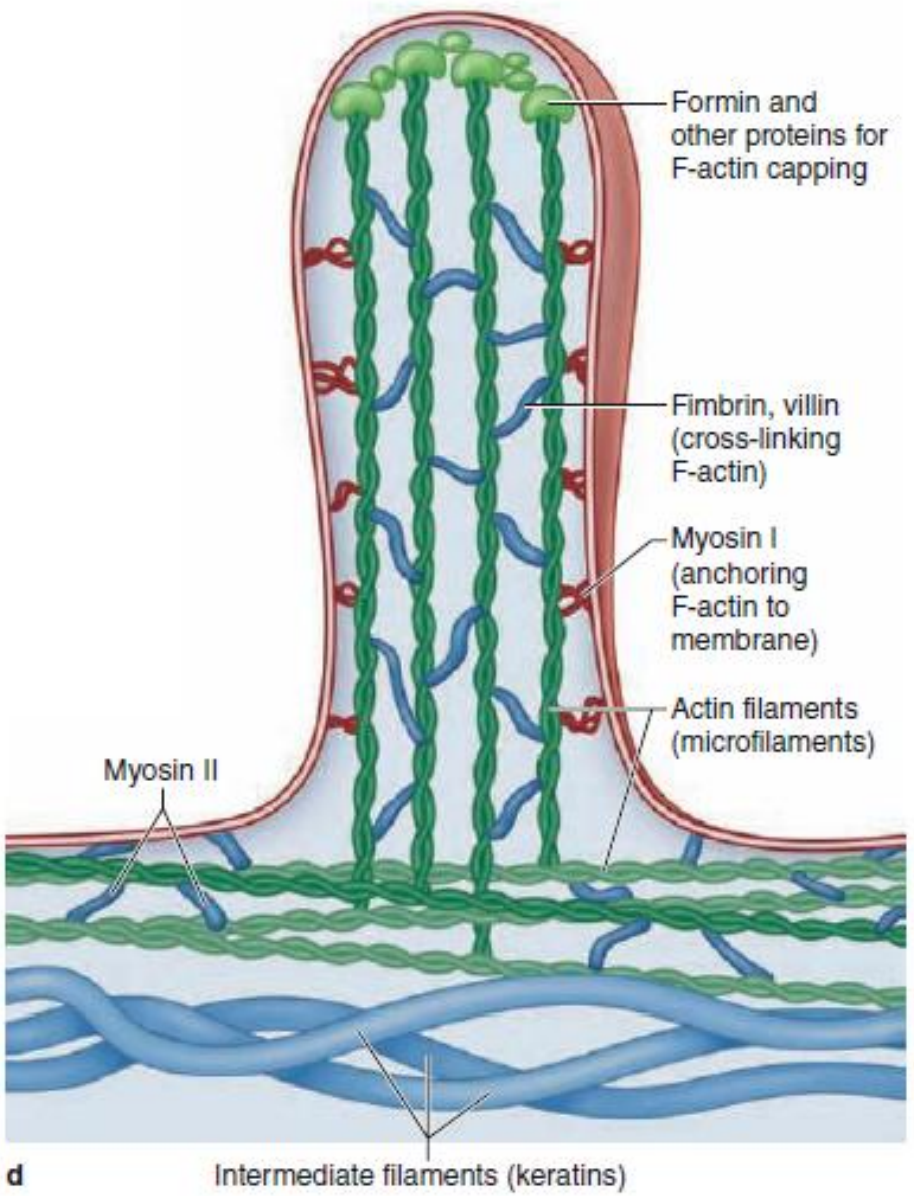


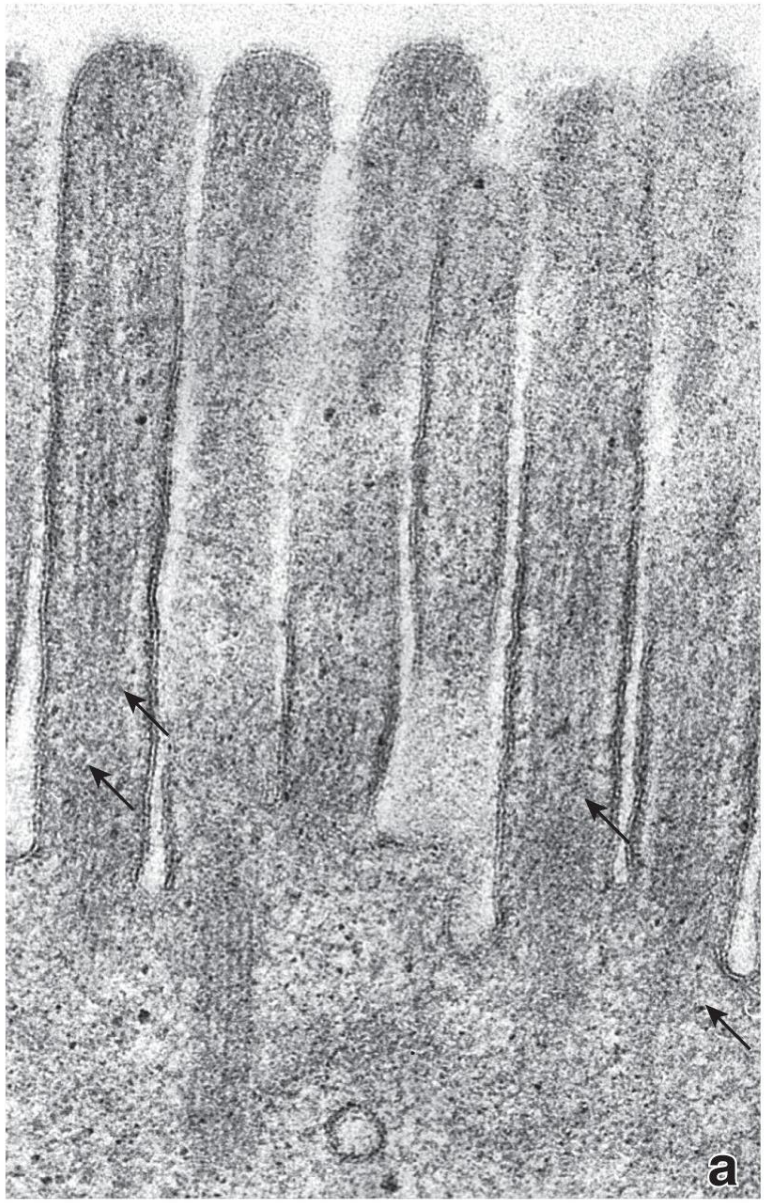


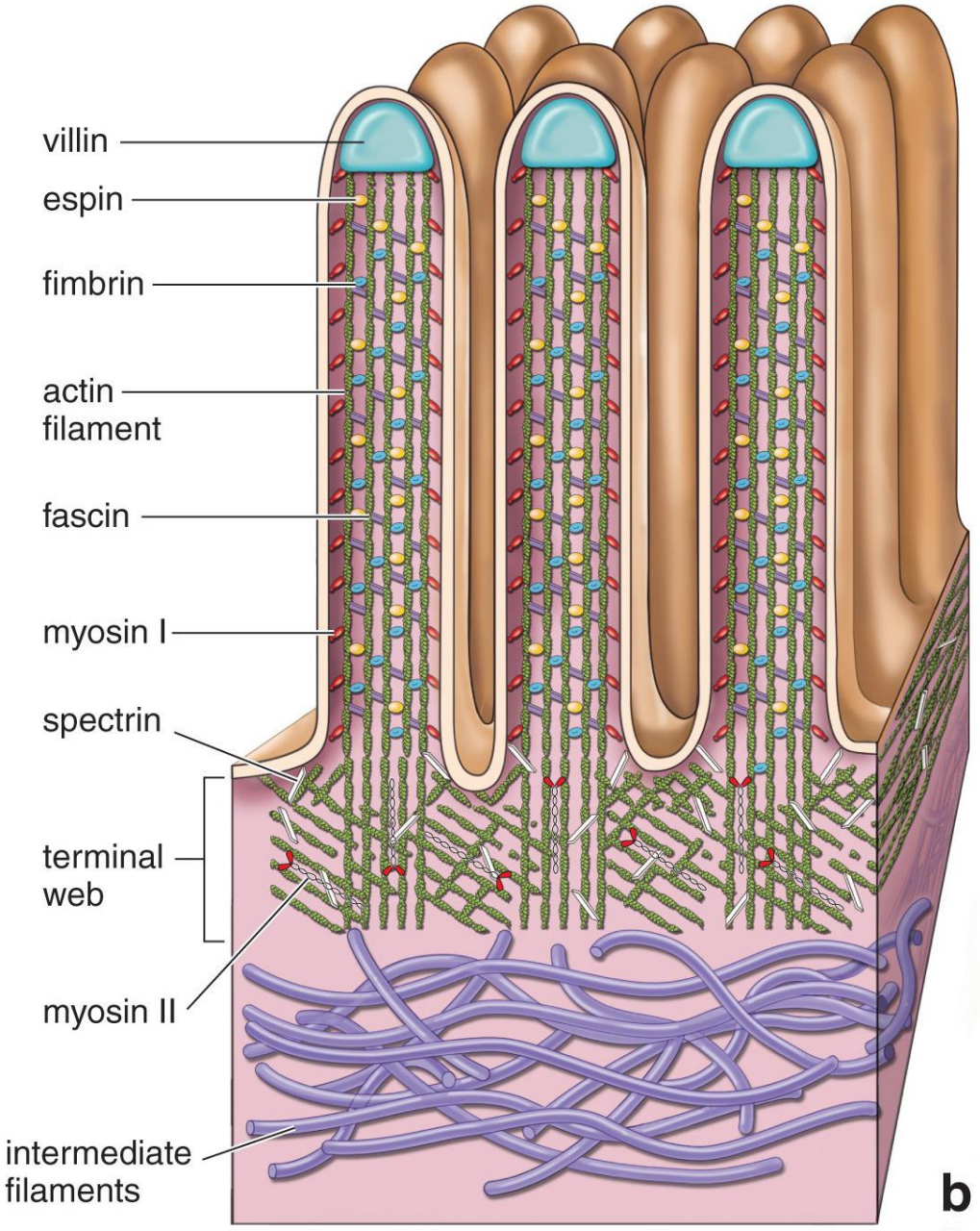
Molecular Structure

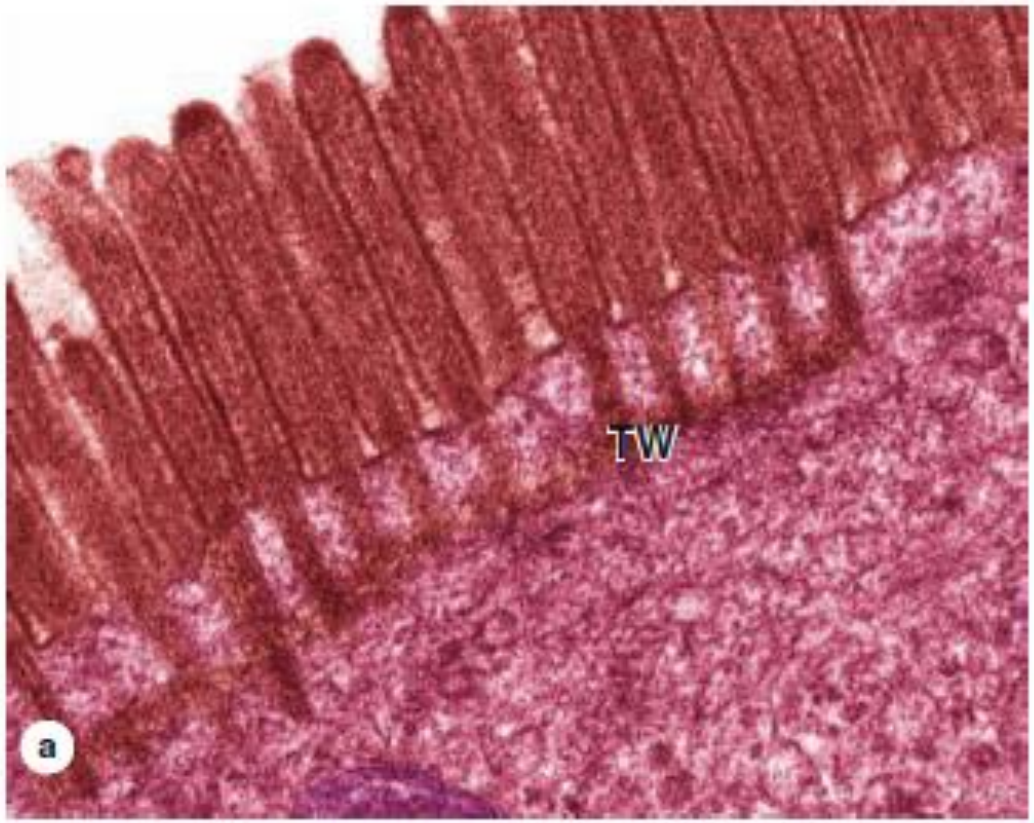
- Each microvillus contains bundled actin filaments **capped** and **bound** to the surrounding plasma membrane by **actin-binding proteins**.

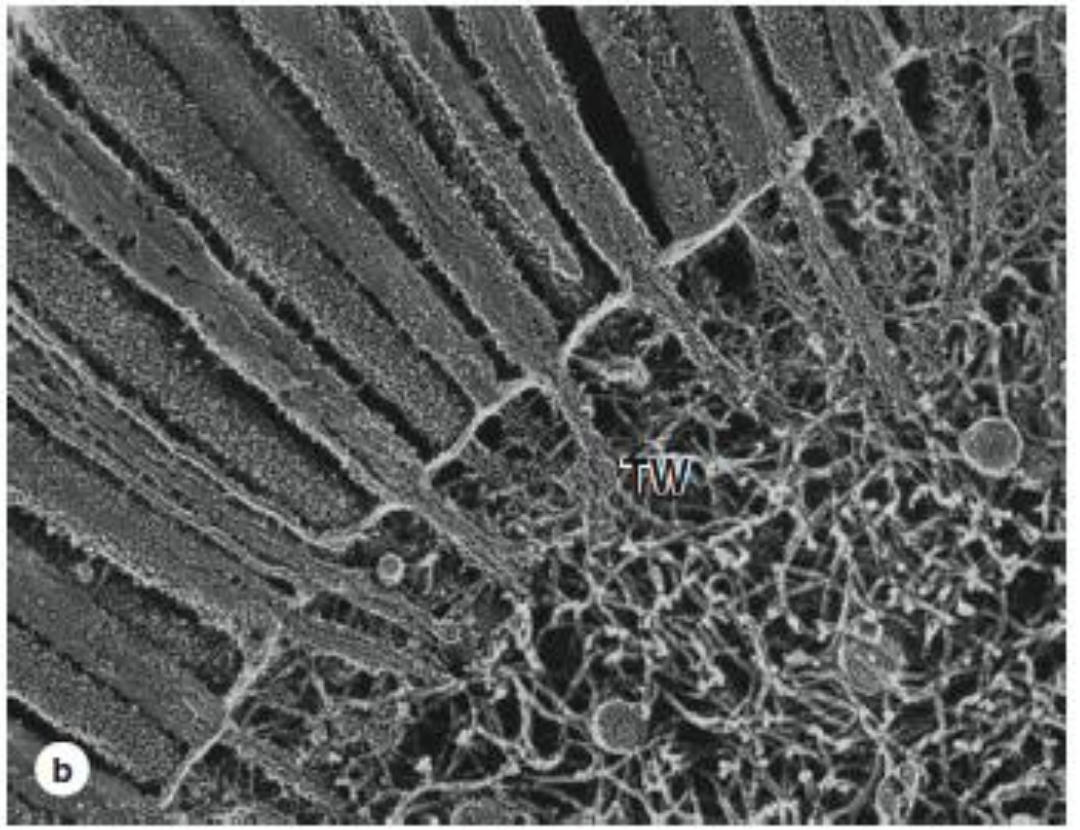
- The actin filaments insert into the **terminal web** of cortical microfilaments at the base of the microvilli.


Formin and other proteins for F-actin capping
Fimbrin, villin (cross-linking F-actin)
Myosin I (anchoring F-actin to membrane)
Actin filaments (microfilaments)
Myosin II
Intermediate filaments (keratins)
d





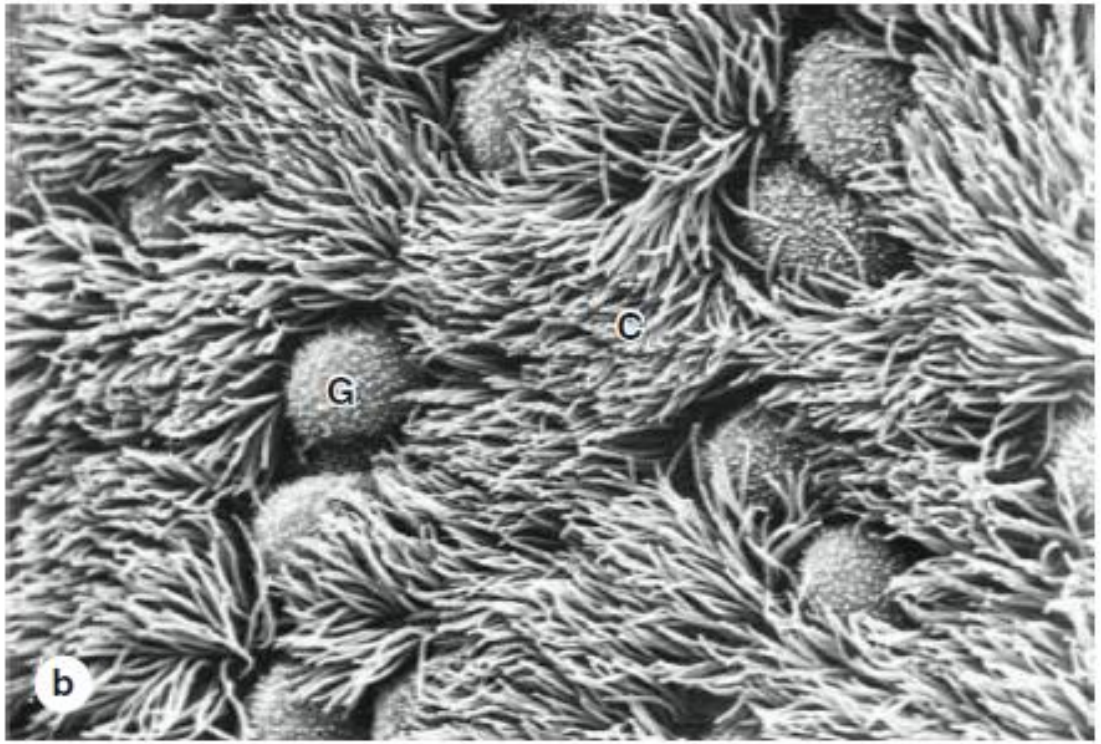

TW
a

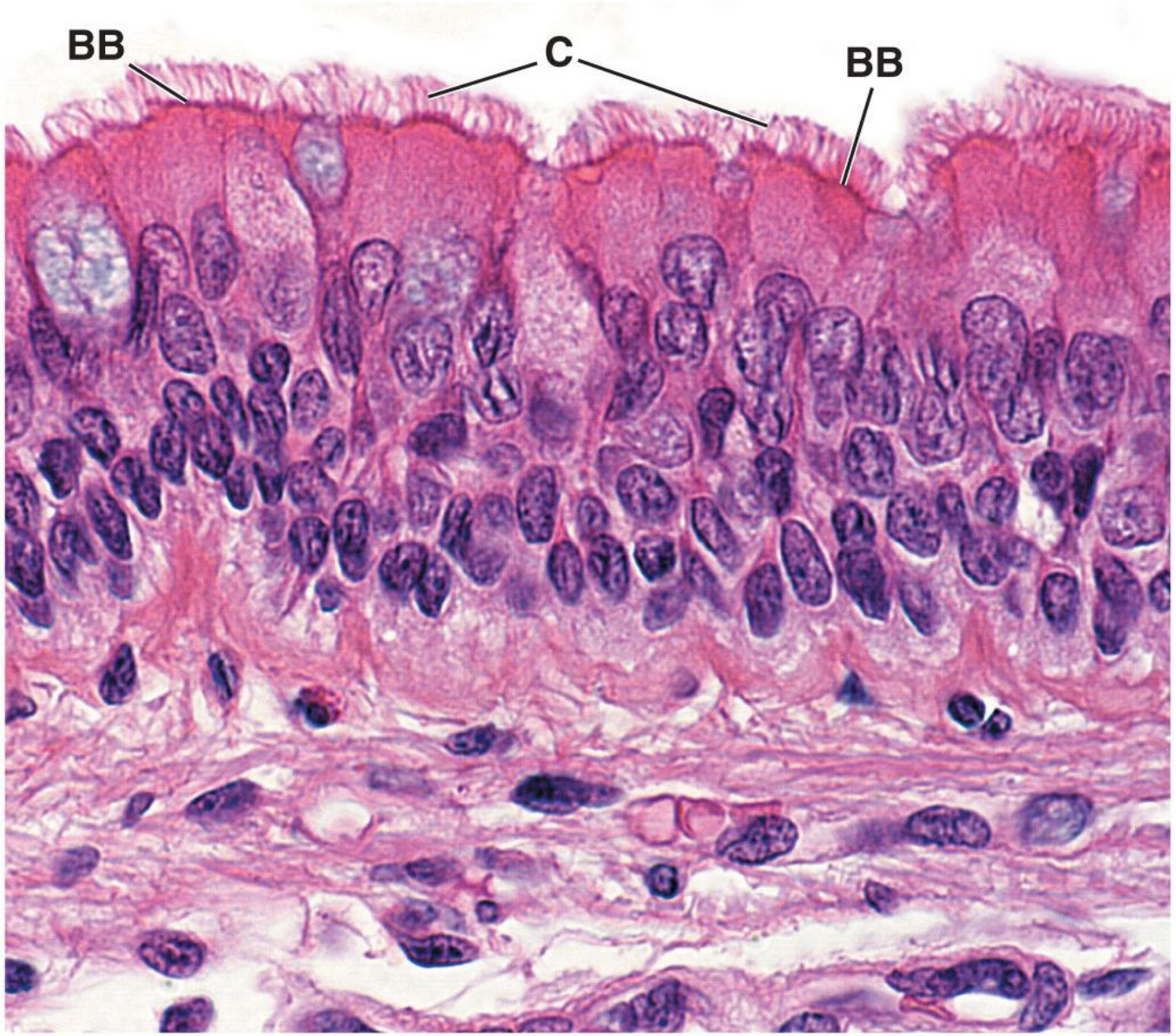

TW
b

Cilia

- **Cilia** are long, highly motile apical structures, larger than microvilli, containing internal arrays of microtubules not microfilaments.
- Motile cilia are abundant on cuboidal or columnar cells of many epithelia.


C
G
a


C
G
b



Molecular Structure

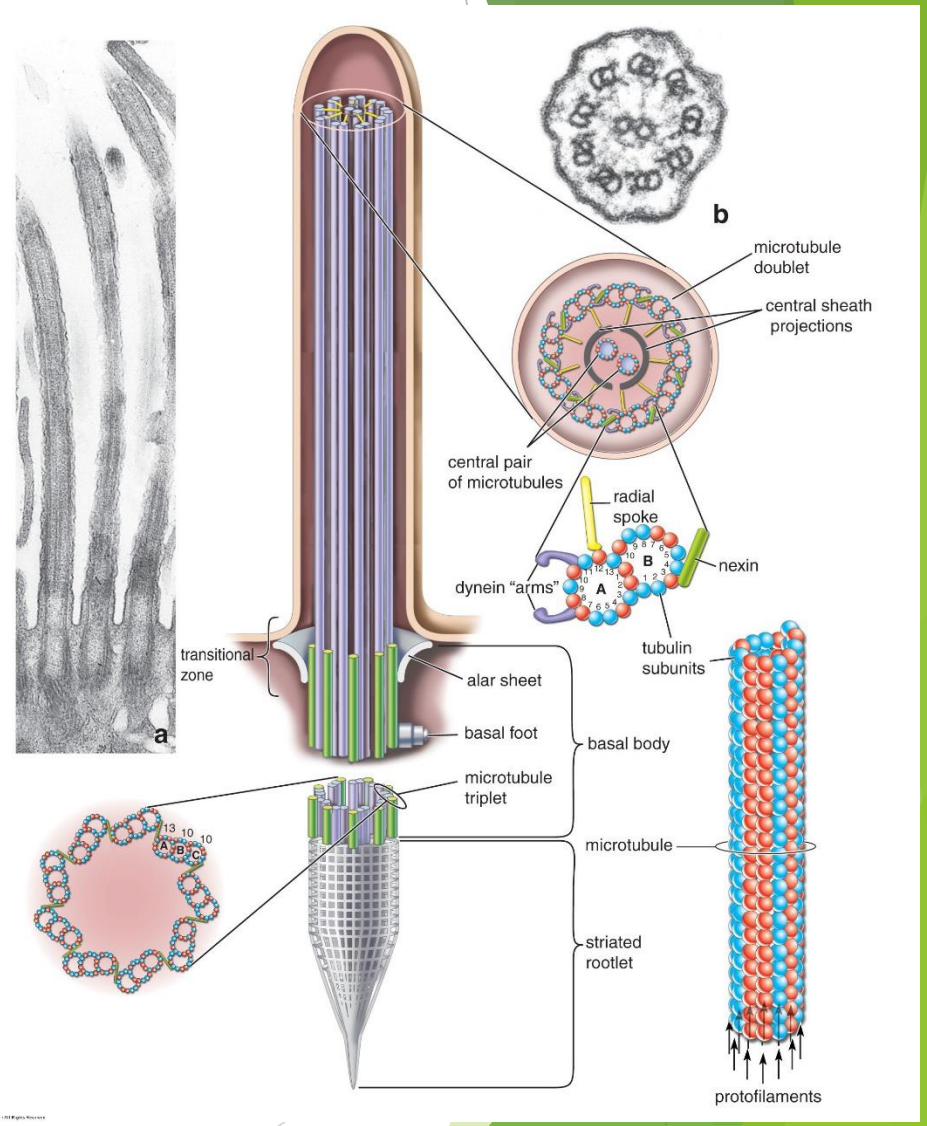
- Each cilium has a core structure consisting of nine peripheral microtubule doublets arrayed around two central microtubules.
- This **9 + 2 assembly** of microtubules is called an **axoneme.**
- Microtubules of axonemes are continuous with those in **basal bodies**, which are apical cytoplasmic structures just below the cell membrane.
- Basal bodies have a structure similar to that of centrioles, with triplets of microtubules forming rootlets anchoring the entire structure to the cytoskeleton.

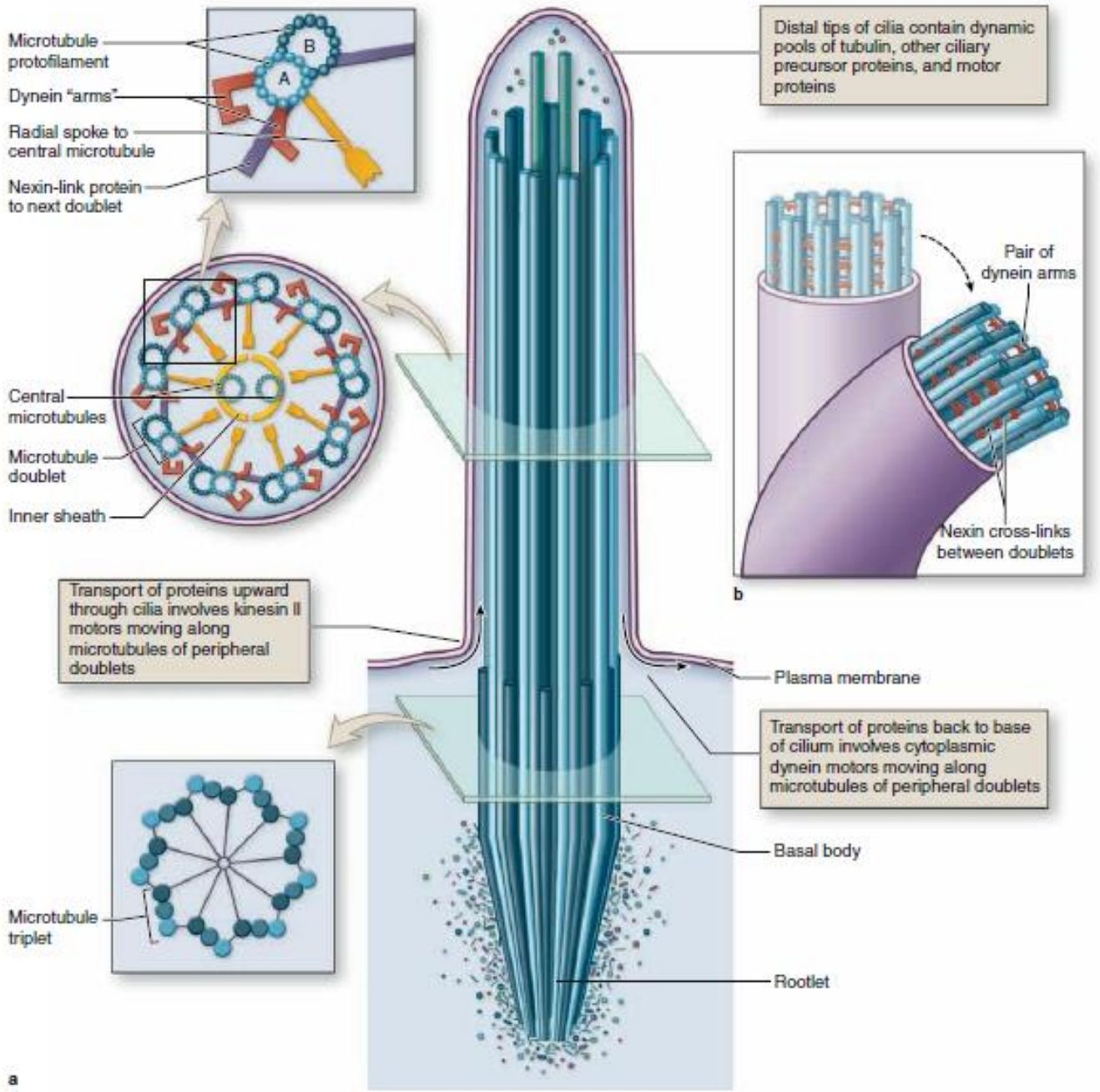
Note that the **A microtubule** of the doublet is composed of **13** tubulin dimers arranged in a side-by-side configuration (*lower right*), whereas the **B microtubule** is composed of **10** tubulin dimers and shares the remaining dimers with those of the A microtubule.

The **dynein arms** extend from the A microtubule and make temporary cross-bridges with the B microtubule of the adjacent doublet.

The basal body is anchored by the striated rootlet within the cell cytoplasm.

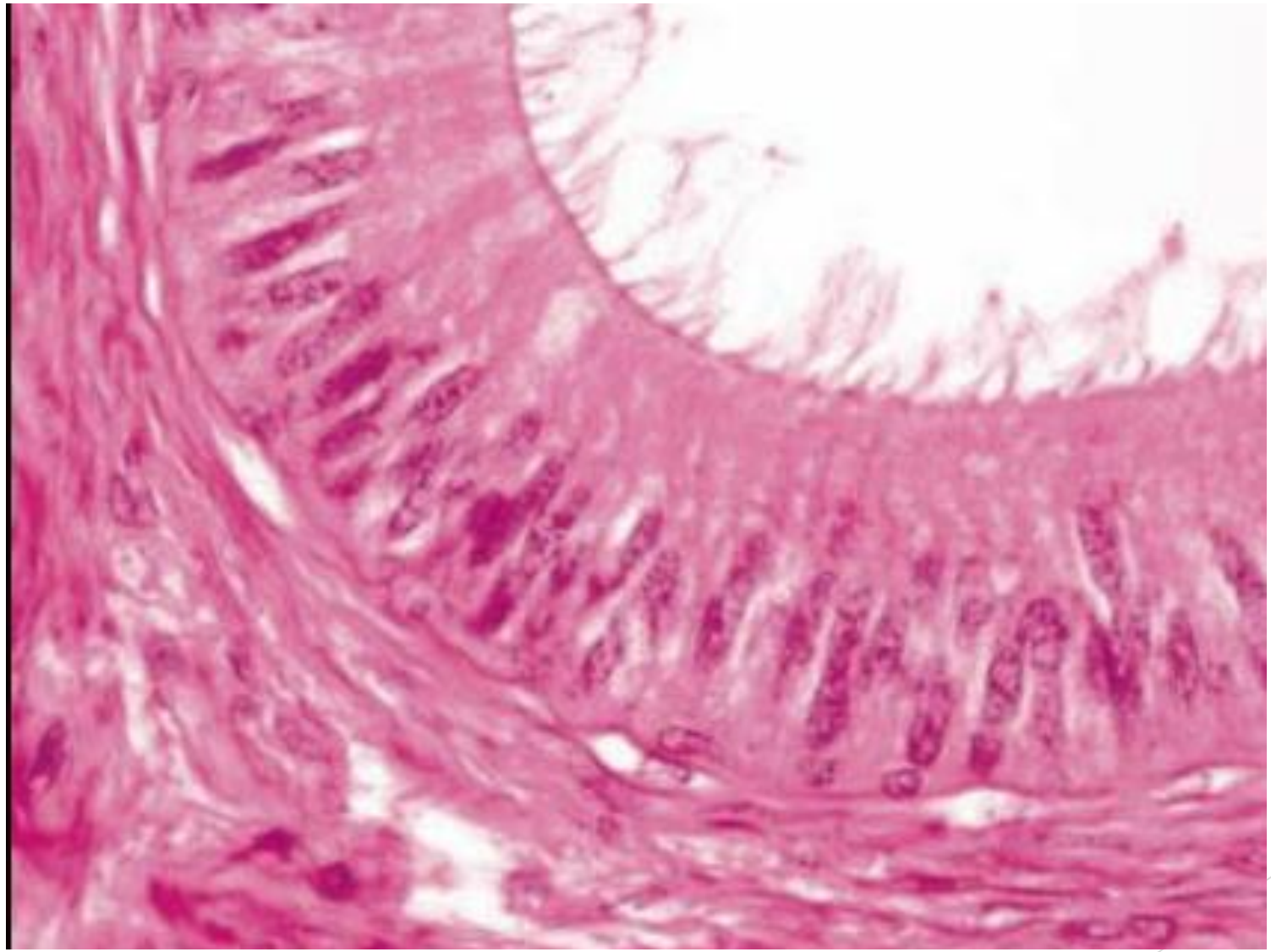
A cross section of the basal body (*lower left*) shows the arrangement of nine microtubule triplets. These structures form a ring connected by **nexin** molecules.




Microtubule protofilament
Dynein "arms"
Radial spoke to central microtubule
Nexin-link protein to next doublet
B
A
Central microtubules
Microtubule doublet
Inner sheath
Microtubule triplet
a
Distal tips of cilia contain dynamic pools of tubulin, other ciliary precursor proteins, and motor proteins
Pair of dynein arms
Nexin cross-links between doublets
b
Transport of proteins upward through cilia involves kinesin II motors moving along microtubules of peripheral doublets
Plasma membrane
Transport of proteins back to base of cilium involves cytoplasmic dynein motors moving along microtubules of peripheral doublets
Basal body
Rootlet

Stereocilia

- Stereocilia resemble microvilli in containing microfilaments and actin-binding proteins, with similar diameters, and with similar connections to the cell's terminal web.
- Like microvilli, stereocilia increase the cells' surface area, facilitating absorption.
- However, stereocilia are typically much longer and less motile than microvilli, and may show branching distally.
- They are best seen on the absorptive epithelial cells lining the male reproductive system




Stereocilia (microvilli)
Principal cells
Smooth muscle cells
Basal cells

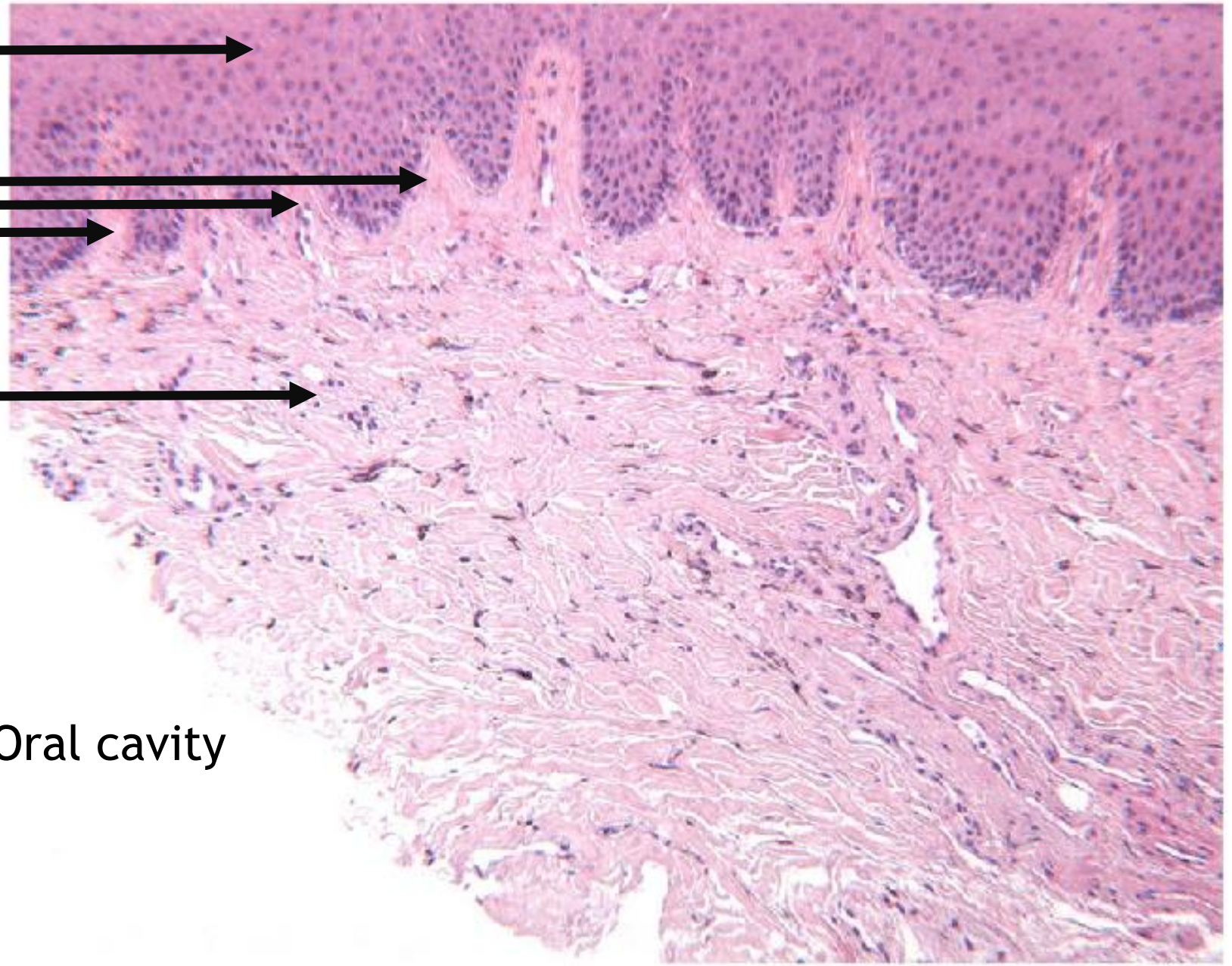
Lamina propria

- The connective tissue that underlies the epithelia lining the organs of the digestive, respiratory, and urinary systems is called the **lamina propria**
- The area of contact between the two tissues may be increased by small evaginations called **papillae** projecting from the connective tissue into the epithelium
- Papillae occur most frequently in epithelial tissues subject to friction, such as the covering of the skin or tongue.

Epithelium (stratified squamous non-keratinized)

Lamia propria papillae

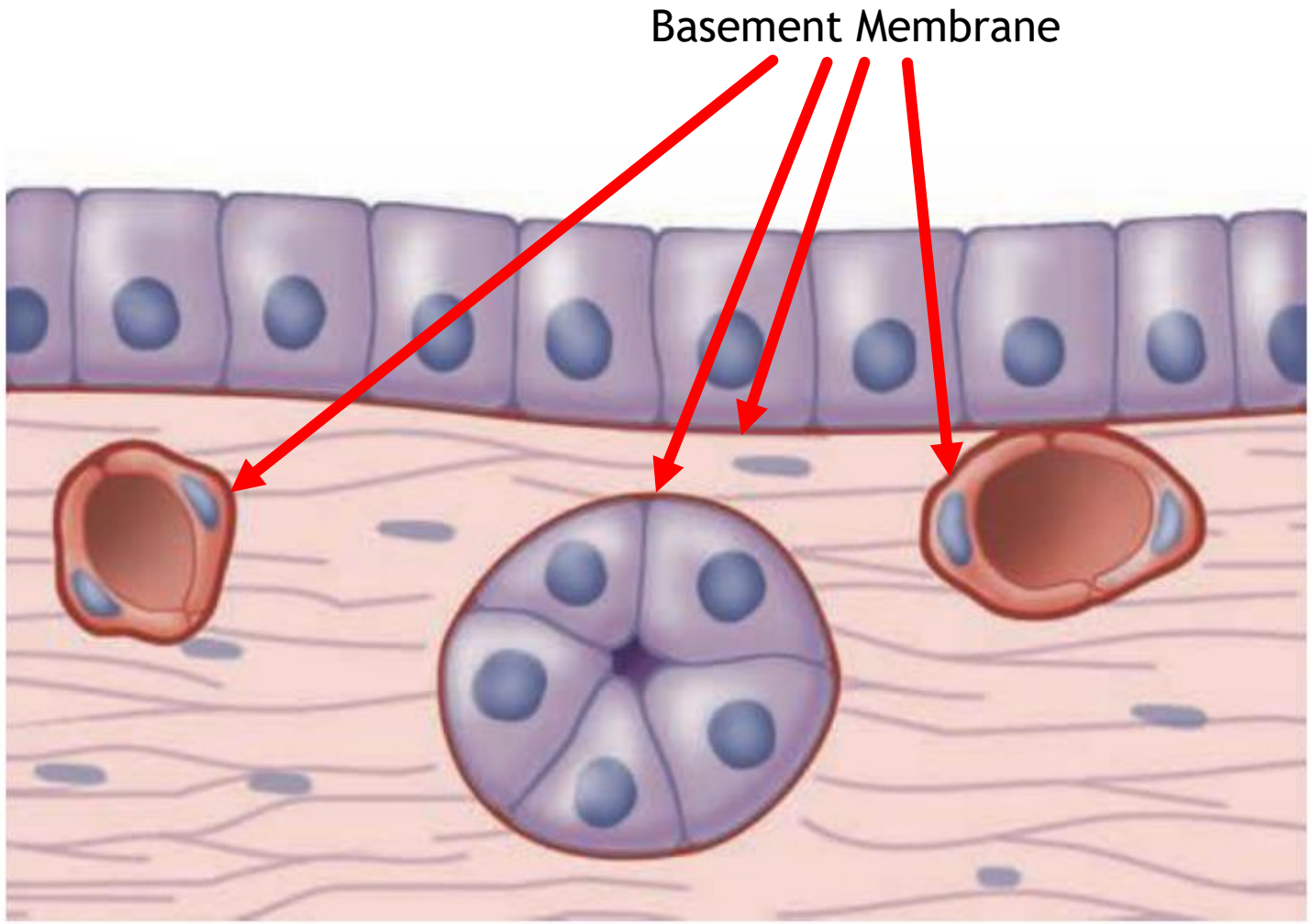
Connective tissue

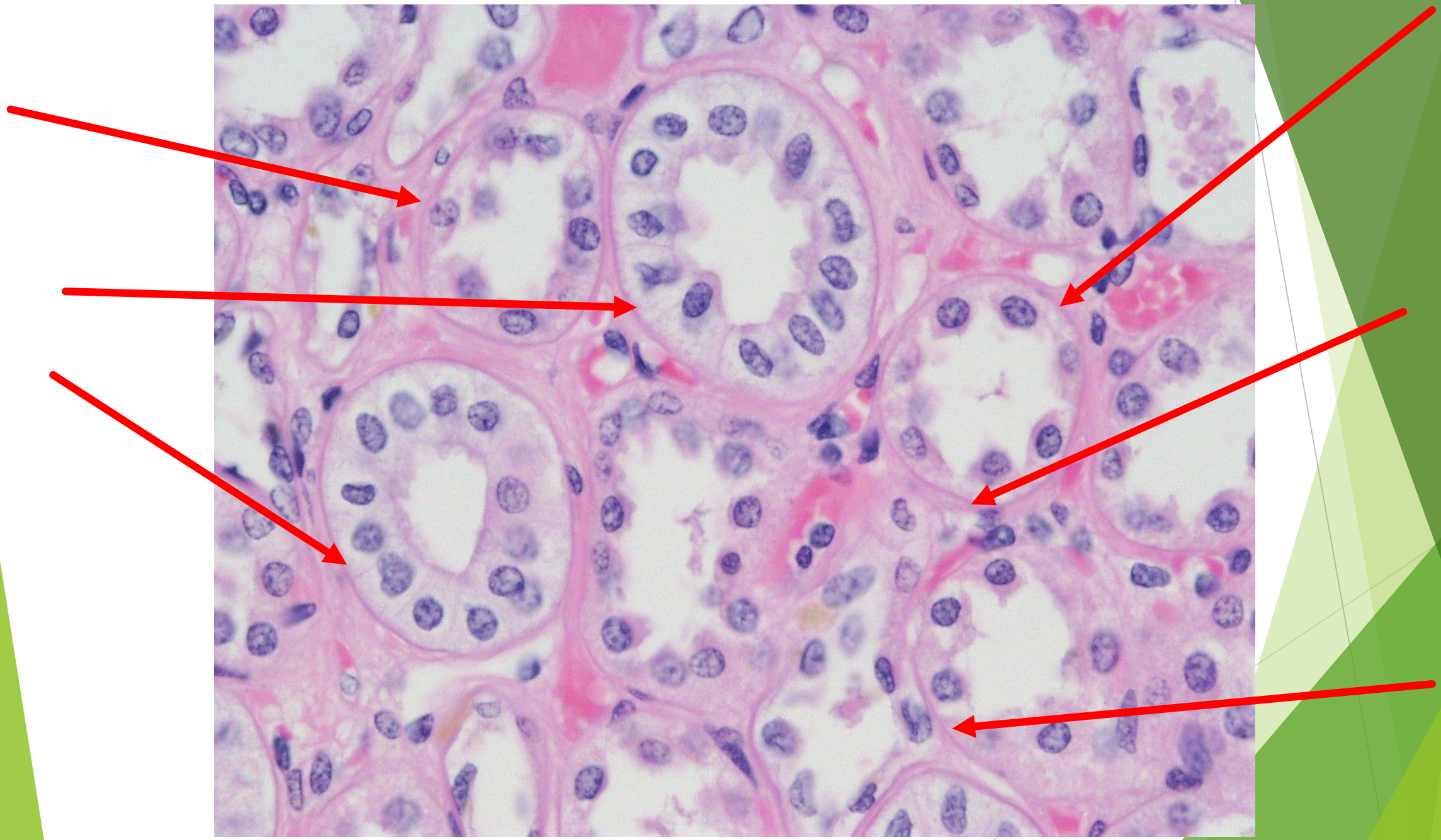


Oral cavity

Basement membrane

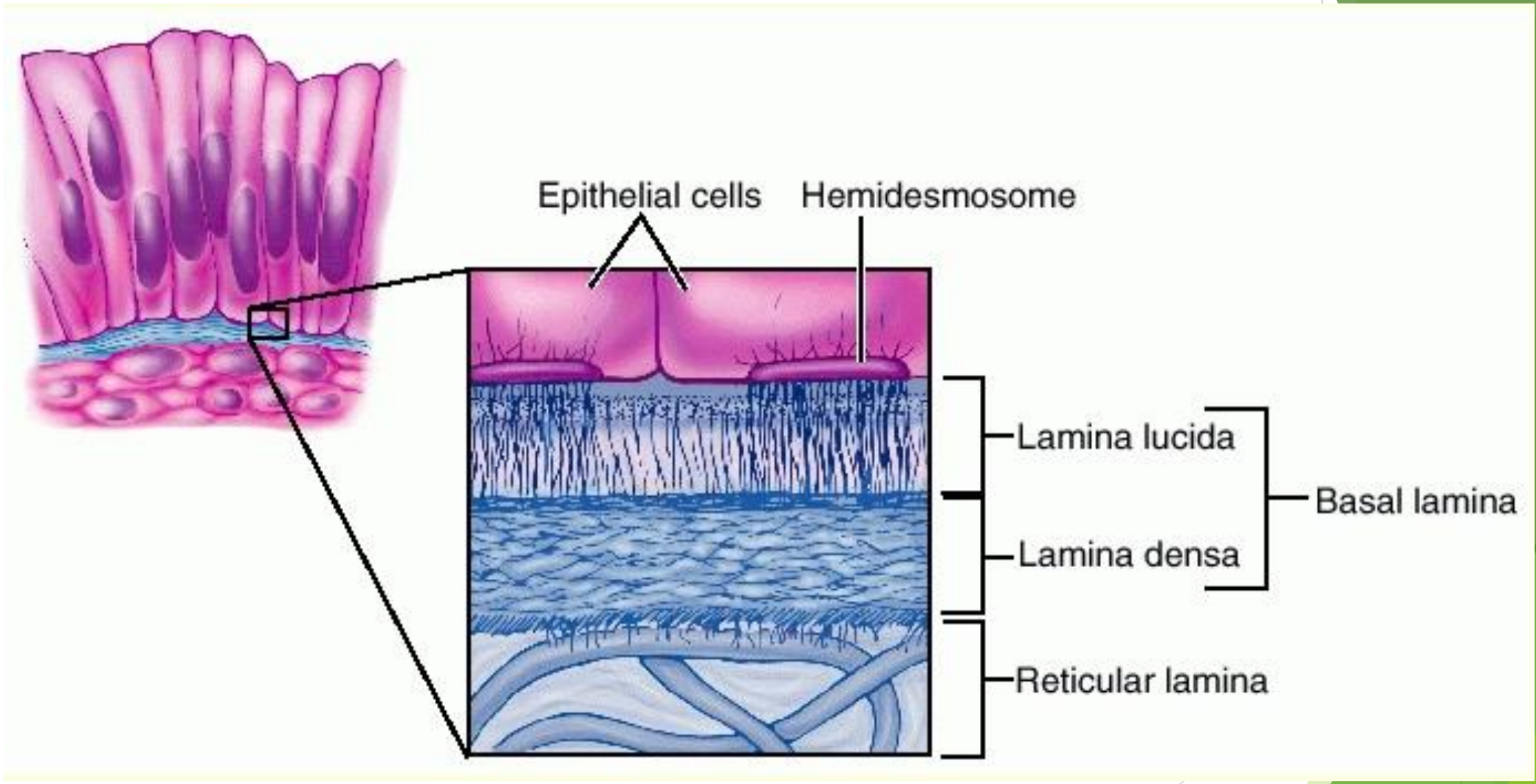
- The basal surface of all epithelia rests on a thin extracellular sheet of macromolecules referred to as the **basement membrane**
- The **basement membrane** a semipermeable filter for substances reaching epithelial cells from below.
- Glycoproteins and other components in this structure can often be stained and visualized with the light microscope using special stain for carbohydrate such as PAS, so we call it PAS positive


Basement Membrane



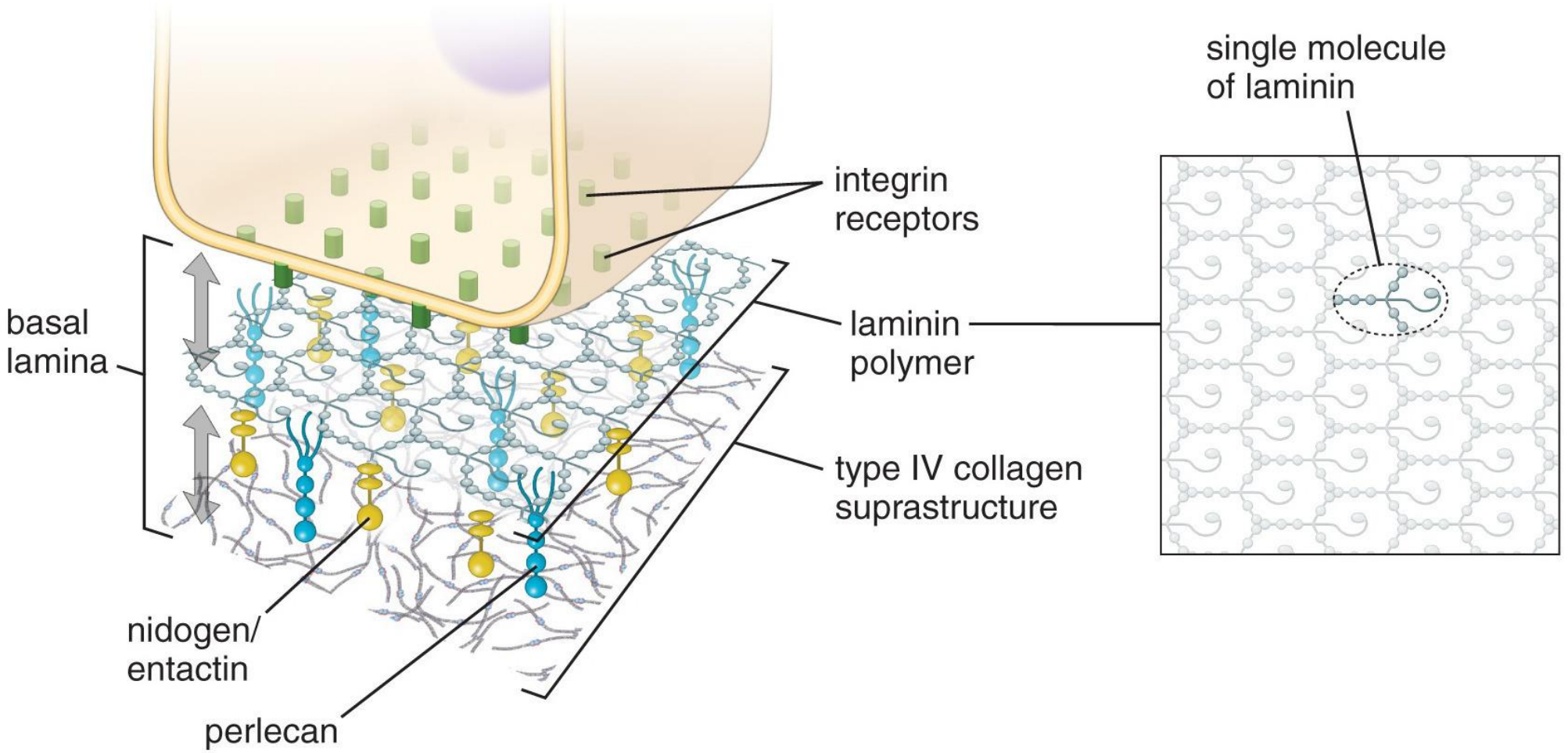
Basal lamina

- With the transmission electron microscope (TEM) two parts of the basement membrane may be resolved.
- Nearest the epithelial cells is an electron-dense layer, consisting of a network of fine fibrils that comprise the **basal lamina**
- Beneath this layer is a more diffuse and fibrous **reticular lamina**
- The macromolecules of the basal lamina are secreted from the basal sides of the epithelial cells


Epithelial cells
Hemidesmosome
Lamina lucida
Lamina densa
Basal lamina
Reticular lamina

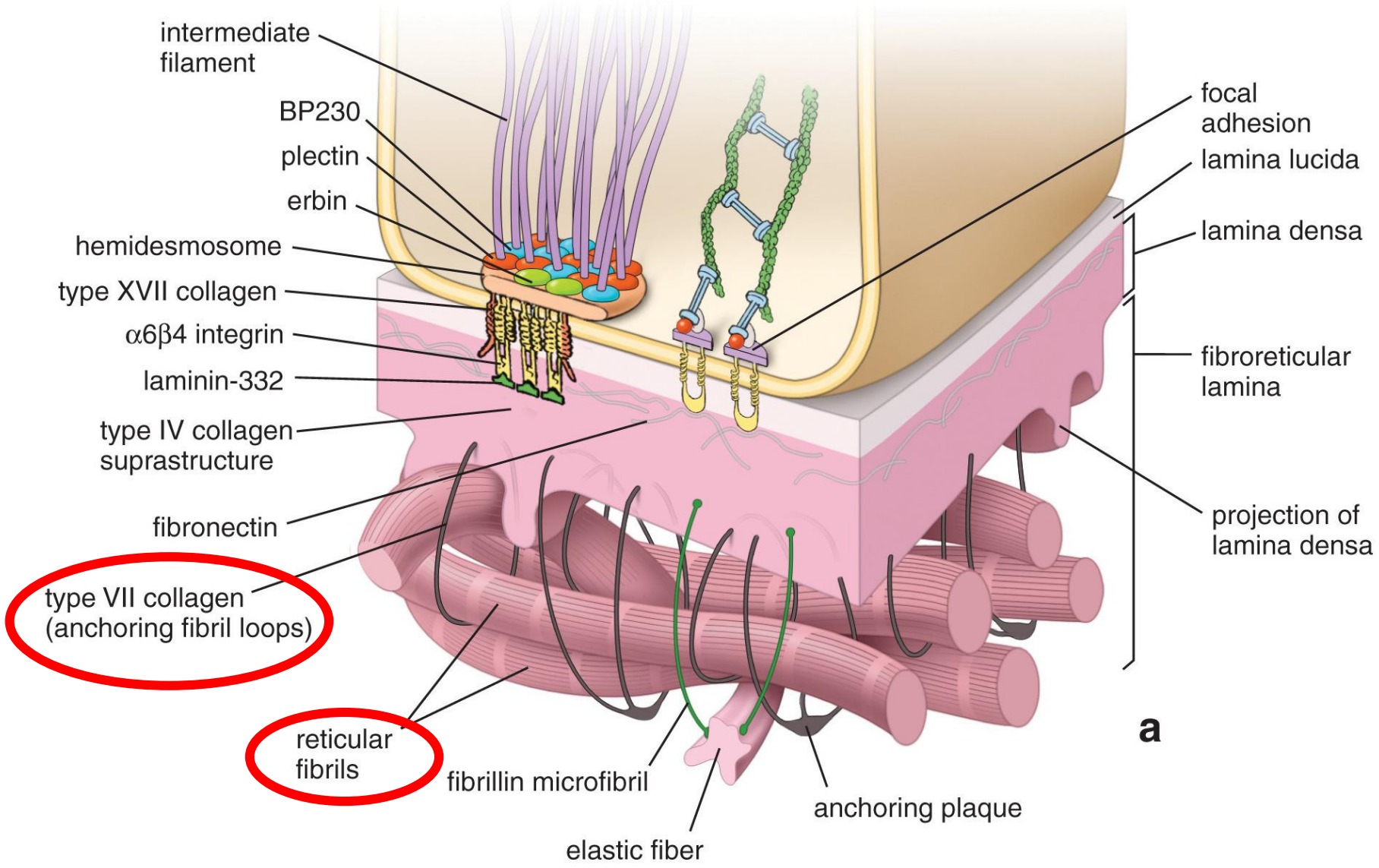
Basal lamina components

- **Type IV collagen:** Monomers of type IV collagen self-assemble into a two-dimensional network of evenly spaced subunits.
- **Laminin:** These are large glycoproteins that attach to transmembrane proteins called **integrins** at the cells' basal surface and project through the network of type IV collagen.
- **Nidogen (entactin)** and **perlecan:** Respectively a short, rod-like protein and a proteoglycan, both of these cross-link laminin to the collagen network and help determine the porosity of the basal lamina and the size of molecules able to filter through it.



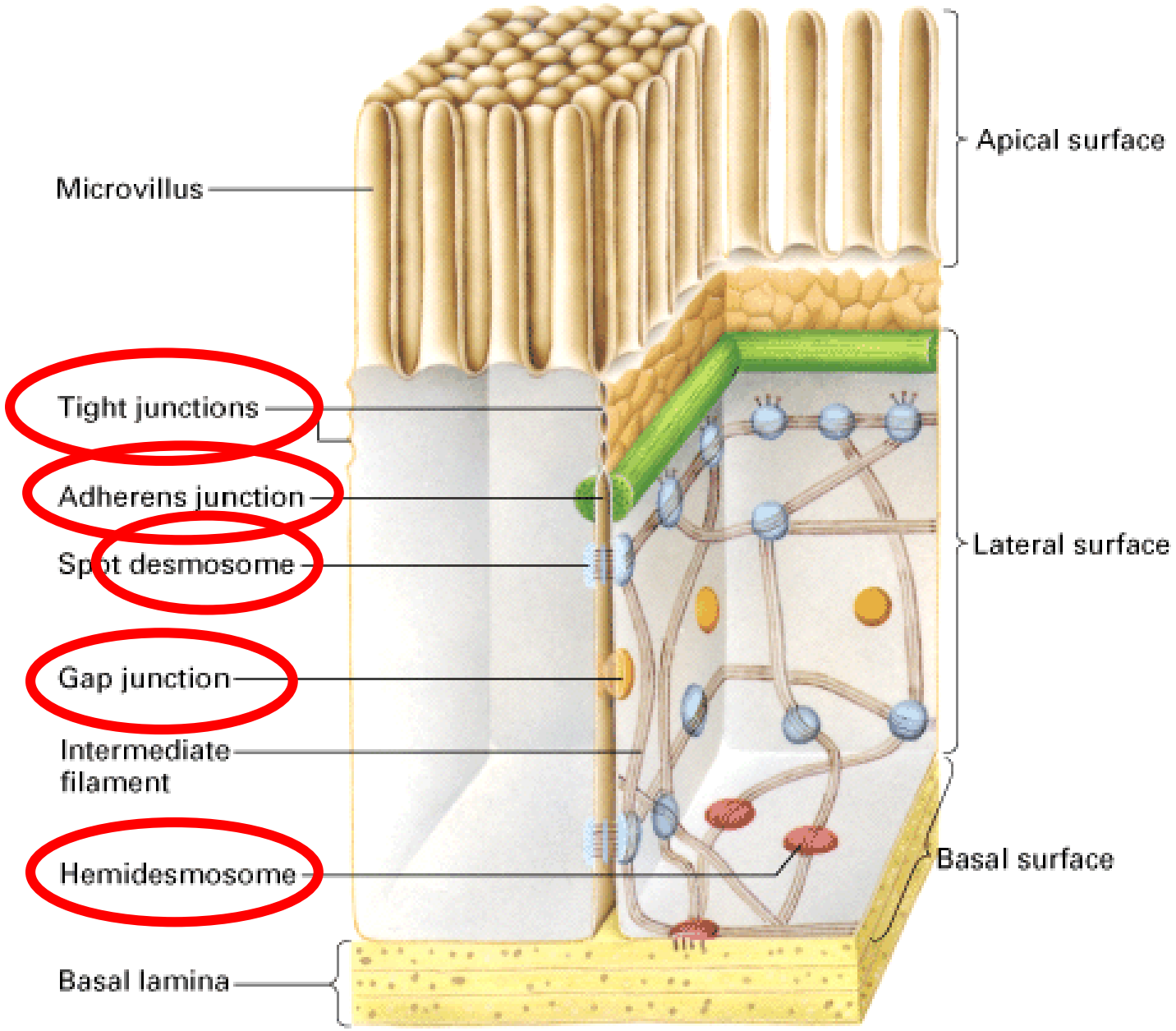
Reticular lamina

- Has reticular fibers (collagen III)
- Anchoring fibrils of type VII collagen link the basal lamina with the reticular fibers of the reticular lamina
- Both reticular fibers and anchoring fibrils are produced by cells of the connective tissue


intermediate filament
BP230
plectin
erbin
hemidesmosome
type XVII collagen
α6β4 integrin
laminin-332
type IV collagen suprastructure
fibronectin
type VII collagen (anchoring fibril loops)
reticular fibrils
fibrillin microfibril
elastic fiber
anchoring plaque
focal adhesion
lamina lucida
lamina densa
fibroreticular lamina
projection of lamina densa
a

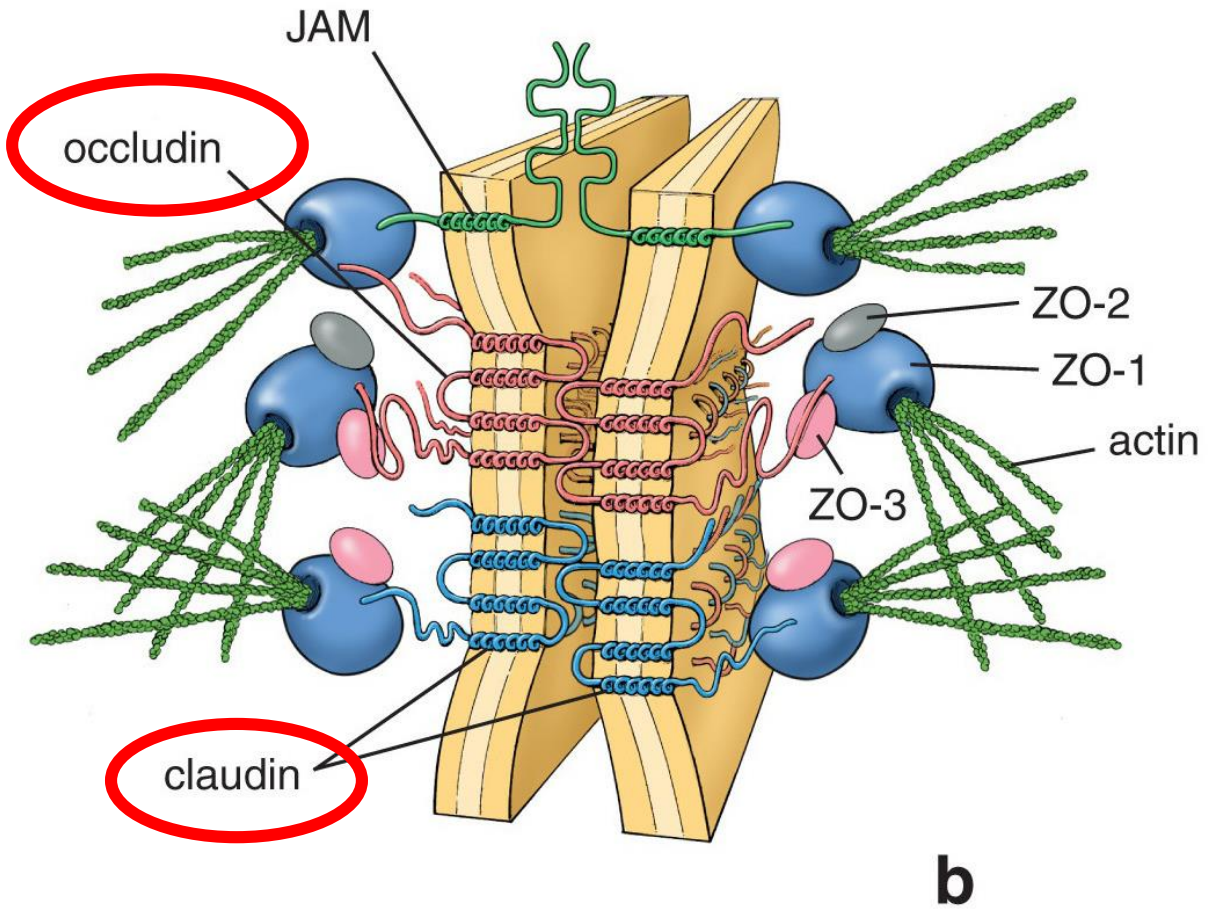
Junctional complexes

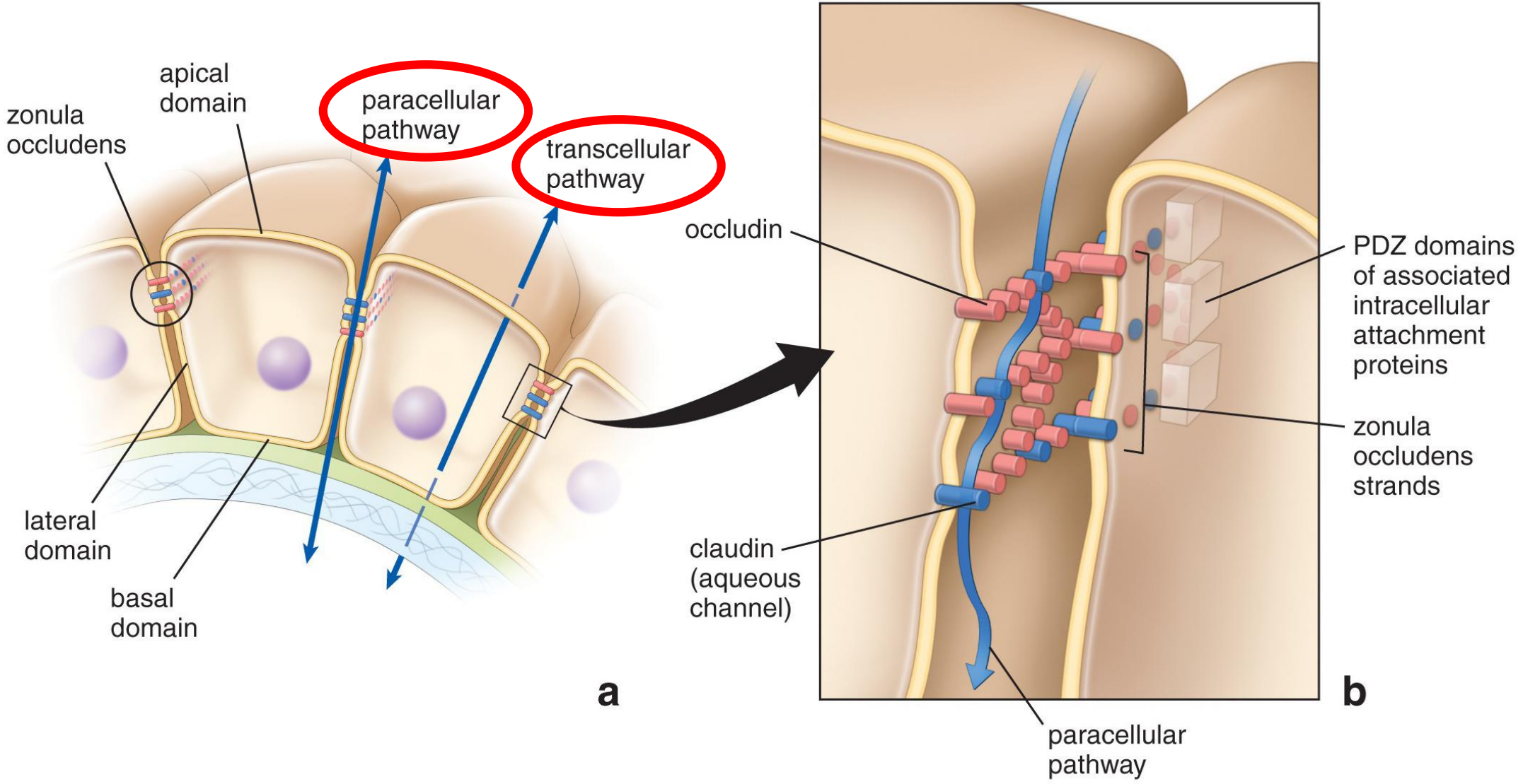
- Several membrane-associated structures provide adhesion and communication between cells.
- Epithelial cells adhere strongly to neighboring cells and basal laminae, particularly in epithelia subject to friction or other mechanical forces
- These junctions include:
  - Tight junctions (Zonula occludens)
  - Adherent junctions (Zonula adherens)
  - Desmosomes (Macula adherens)
  - Gap junctions (Nexus)
  - Hemidesmosomes


Microvillus
Apical surface
Tight junctions
Adherens junction
Spot desmosome
Lateral surface
Gap junction
Intermediate filament
Hemidesmosome
Basal surface
Basal lamina

Tight junctions (Zonula occludens)

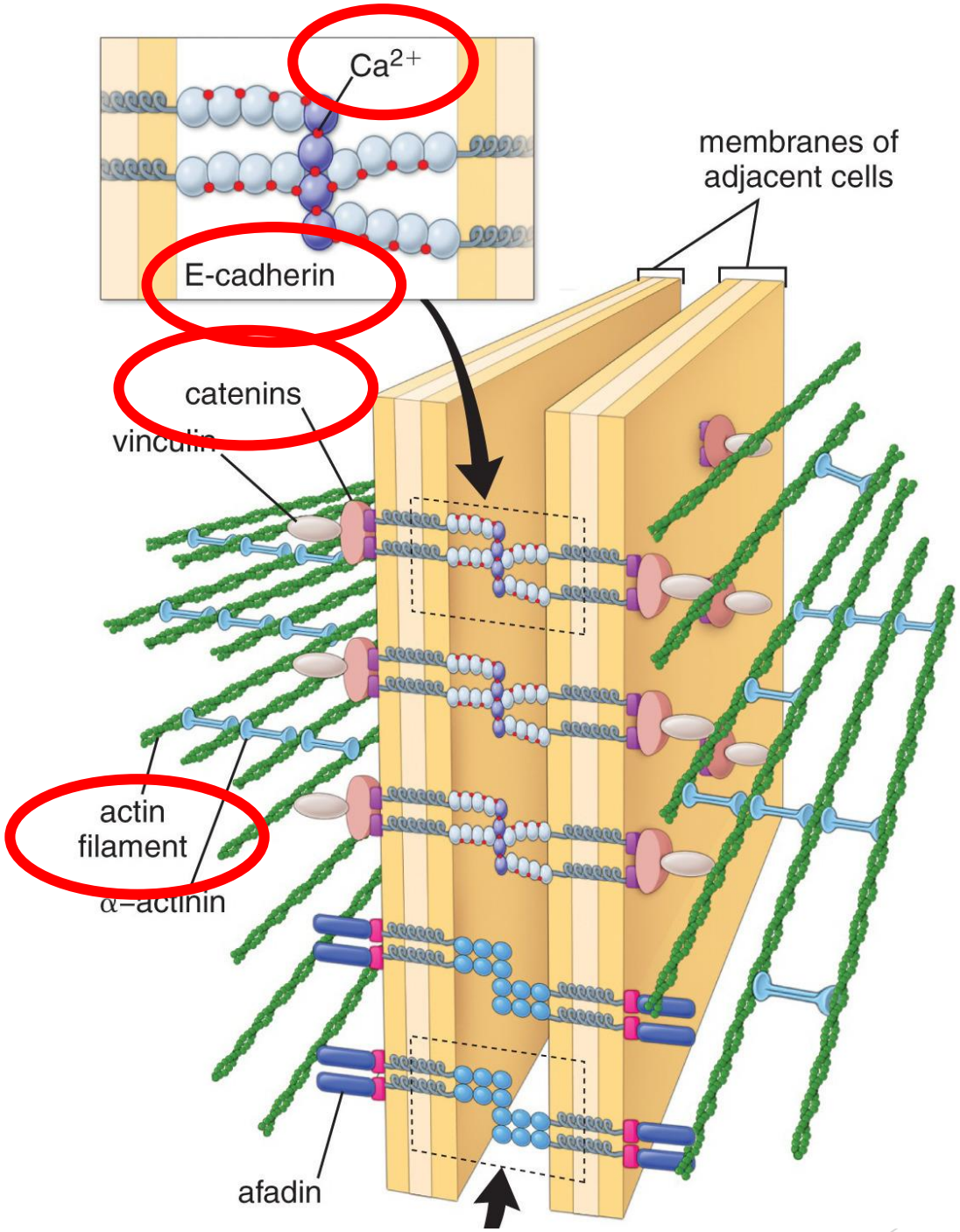
- **Tight** or **occluding junctions** form a seal between adjacent cells.
- **They** are the most apical of the junctions.
- The term “zonula” indicates that the junction forms a band completely encircling each cell
- In TEM the adjacent membranes at these junctions appear fused
- The seal between the two cell membranes is due to tight interactions between the transmembrane proteins **claudin** and **occludin**
- The intercellular seal of tight junctions ensures that molecules crossing an epithelium in either direction do so by going *through* the cells (a transcellular path) rather than *between* them (the paracellular pathway).


JAM
occludin
ZO-2
ZO-1
actin
ZO-3
claudin
b



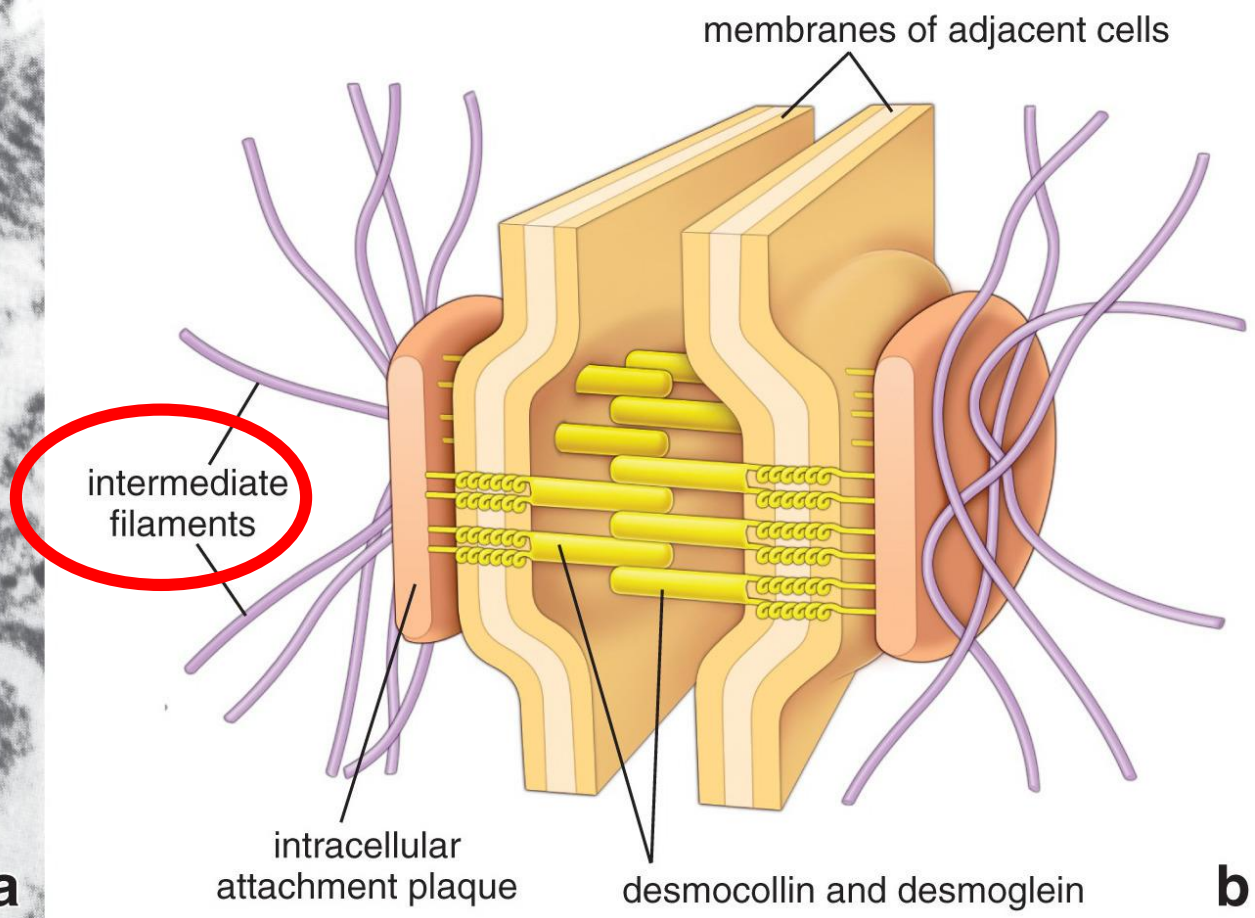
Adherent junctions (Zonula adherens)

- Adherent junctions also encircle the epithelial cell, usually immediately below the tight junction.
- They firmly anchor a cell to its neighbors.
- Cell adhesion is mediated by **cadherins (E-cadherin)**, transmembrane glycoproteins of each cell that bind each other in the presence of Ca2+.
- At their cytoplasmic ends, cadherins bind **catenins** that link to actin filaments with actin-binding proteins.
- The actin filaments linked to the adherens junctions form part of the “terminal web,” a cytoskeletal feature at the apical pole in many epithelial cells.


Ca^{2+}
E-cadherin
membranes of
adjacent cells
catenins
vinculin
actin
filament
α–actinin
afadin

Desmosomes (Macula adherens)

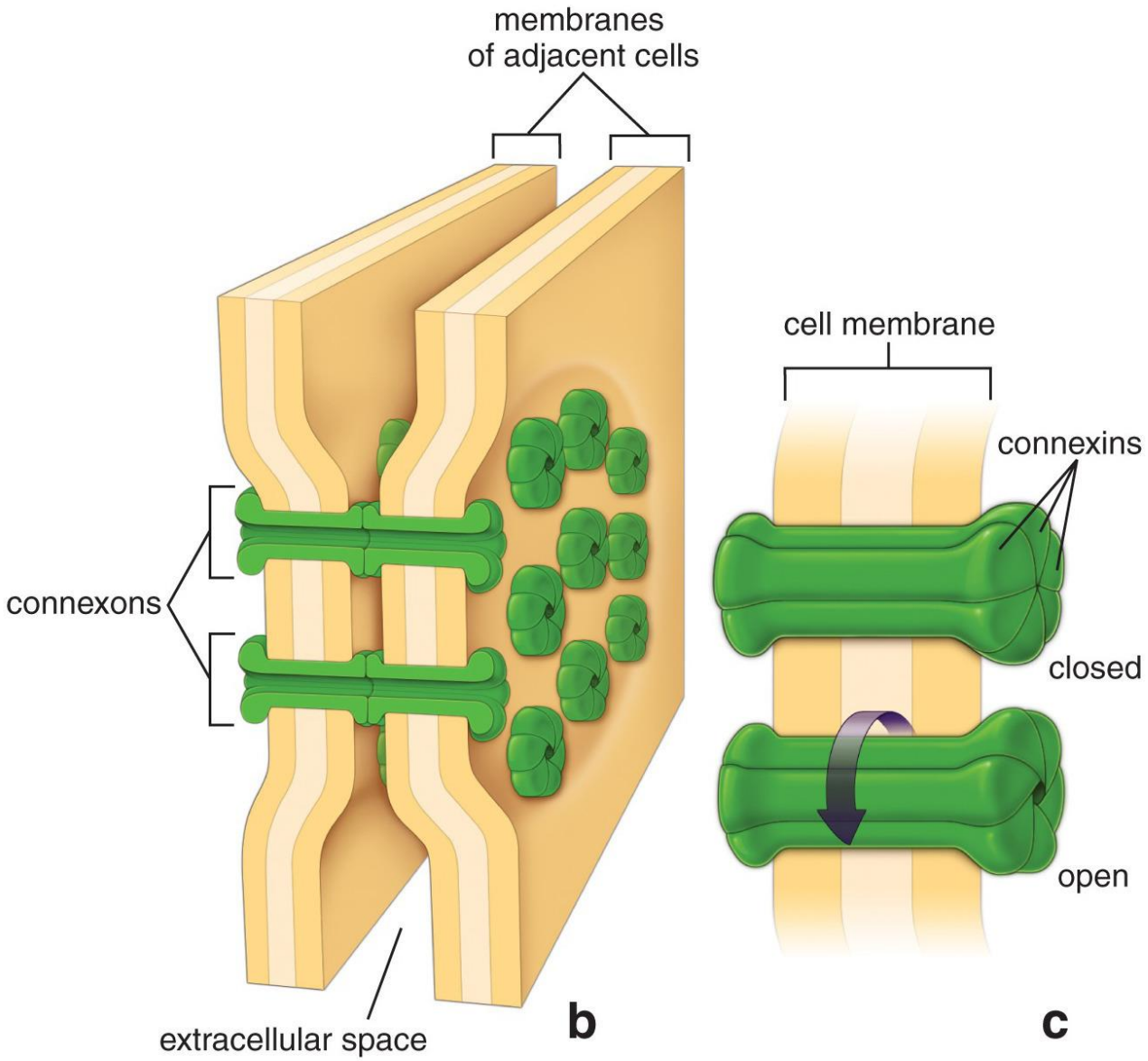
- This junction resembles a single “spot-weld” and does **not** form a belt around the cell.
- Desmosomes are disc-shaped structures at the surface of one cell that are matched with identical structures at an adjacent cell surface
- Desmosomes contain larger members of the cadherin family called desmogleins and desmocollins.
- The cytoplasmic ends of these transmembrane proteins bind a catenin-like protein which bind intermediate filament proteins rather than actins.




MV
TJ
AJ
IF
D

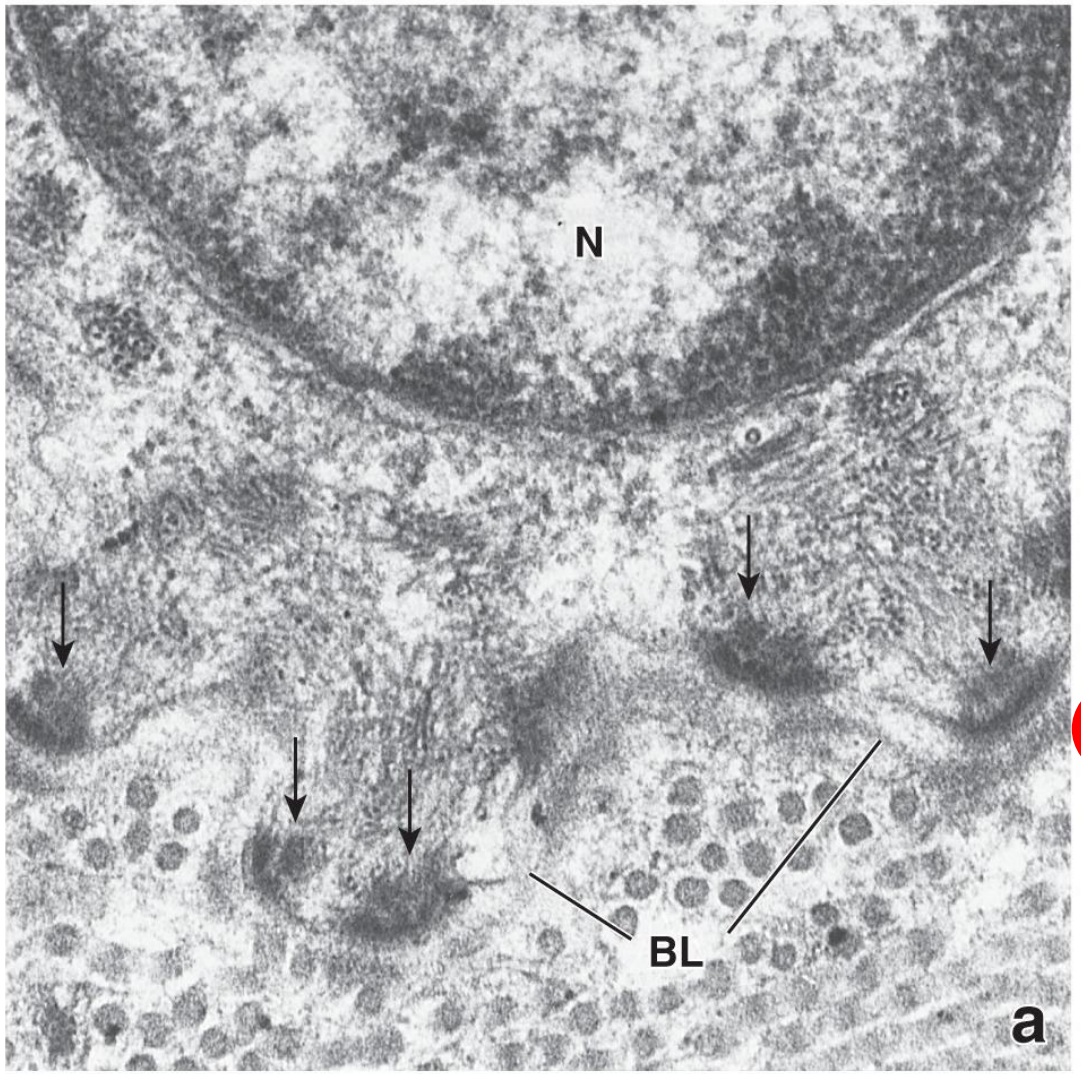
Gap junctions (Nexus)

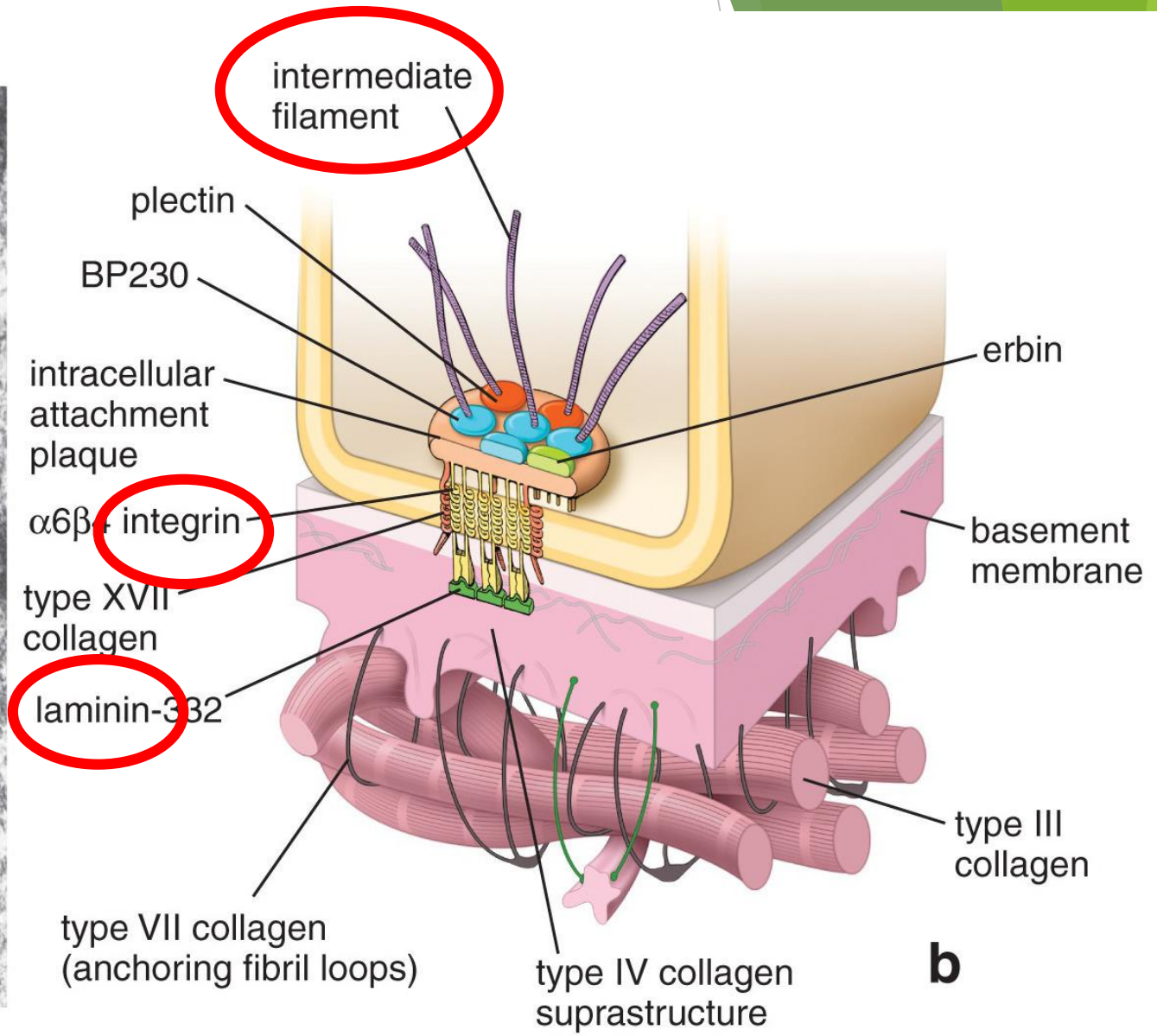
- **Gap junctions** mediate intercellular communication rather than adhesion or occlusion between cells.
- Gap junctions are functionally important in nearly all tissues.
- The transmembrane gap junction proteins, **connexins**, form hexameric complexes called **connexons**, each of which has a central hydrophilic pore about 1.5 nm in diameter.
- Gap junctions permit intercellular exchange of molecules with small (< 1.5 nm) diameters.


membranes
of adjacent cells
connexons
extracellular space
b
cell membrane
connexins
closed
open
c

Hemidesmosomes

- On the basal epithelial surface, cells attach to the basal lamina by anchoring junctions called **hemidesmosomes**
- These adhesive structures resemble a half-desmosome ultrastructurally, but unlike desmosomes the clustered transmembrane proteins that indirectly link to cytokeratin intermediate filaments are **integrins** rather than cadherins.
- The integrins of hemidesmosomes bind primarily to laminin molecules in the basal lamina





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