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overview:

- ① 3 characteristics:
- cell junctions
 - polarity (طبقة تكون basement عليها الخلايا تؤمن التصاقها بالنسيج تحتها)
 - Basement membrane

② absence of free surface (epithelioid cells)

في الغدد يوجد free surface حيث أن الخلايا من جهة واحدة
basement membrane ومن جهة الأخرى تطل على تجويف أو سطح خارجي
لنسيج فأحياناً لا يوجد free surface (حتى لو كانت الخلايا من epithelial) وتكون الخلايا عاملة كمسح (زيتي epithelial) تسمىها epithelioid cells

• endocrine glands : e.g

• granuloma

epithelioid macrophages يتشكل مجموعات اسمها macrophages

③ * in terms of layers: - simple - stratified

* in terms of shape of the surface cells:

← شكل الخلية
- squamous مسطحة
- cuboidal
- columnar (pyramidal) مثل مثلثي
قاعدة واسعة مع قمة
زيتي خلايا في stomach تقوم بإفراز HCl متراصة مستطيلة

• بعض الخلايا لو عملت مجموعات ويأخذ epithelial تسمىها
activated macrophage (معبىة) histiocytes
epithelioid زيتي (resembling epithelial cells)

يعني عشت احسن عن ال cells أنهم epithelium لازم:

① cells are closely apposed to one another

② the presence of free surface

③ the presence of basement membrane

close apposition (ملاصقة) ← cells

presence of basement

membrane

cell aggregates تتجمع عنها
epithelioid tissue

Free surface

• epithelioid cells are derived from progenitor mesenchymal cells
(nondifferentiated cells of embryonic origin found in connective tissue)

LECTURE "6"

- epithelioid organization is typical of most endocrine glands; examples of such tissue include the interstitial cells of Leydig in the testis, the lutein cells of the ovary, the islets of Langerhans in the pancreas, the parenchyma of the adrenal gland, and the anterior lobe of the pituitary gland. Epithelioreticular cells of the thymus may be included too.
- Epithelioid patterns are also formed by accumulations of connective tissue macrophages in response to certain types of injury and infections as well as by many tumors derived from epithelium.

3 principal characteristics of the epithelium.

- 1. they're closely apposed and adhere to one another by means of specific cell-to-cell adhesion molecules that form specialized cell junctions.
- 2. they exhibit functional and morphologic polarity. $\Rightarrow$ So that, different functions are associated with three distinct morphologic surface domains: a free surface or apical domain, a lateral domain, and a basal domain. The properties of each domain are determined by specific lipids and integral membrane proteins.
يعني أنه الخلية لها مقدمة وجنب وقاعدة وفراهم
في أن بعض الخلايا تكون خادعة (أرادوا وظيفتها زي intestinal cells تقوم بأشياء من جهة وتفرغ من الجهة الأخرى)
- 3. the basal surface is attached to an underlying basement membrane, a noncellular, protein-polysaccharide-rich layer demonstrable at the light microscopic level by histo-chemical methods.

Histology A Text and Atlas $\leftarrow$ p.123 $\leftarrow$ Fig 5.1
 apical domain/surface : السطح المائل (التيوف أو السطح الخارج)
 lateral domain : الجنب , تكون الخلايا علاقة ببعض
 Basal domain : يكون ملاصق لل basement membrane

* في ال stratified معن الطبقات يكون شكلها مختلف حين أنه الطبقة الأخرى
 لا basement membrane تكون Bordered ولما نتج للأنسجة جهة أخرى ولا maturationaly
 flattened زي في stratified squamous epithelium
 um
 * يسمى ال epithelium وينسب بناءً على شكل آخر طبقة
 squamous عازة
 flat squamous
 (سطح) آخر طبقة مسطحة

→ In a stratified epithelium, the shape and height of the cells usually vary from layer to layer, but only the shape of the cells that form the surface layer is used in classifying the epithelium

يمكن أيضاً تصنيف factor آخر لها تصنيف epithelium (يعني من حيث shape, layer)
 (نوعية layer)

specialization of the apical surface domain

simple columnar ciliated

يعني ممكن نقول

cilia في apical surface domain

أو ممكن تصنيف stratified squamous epithelium

Keratinized and nonkeratinized

لأن للأنسجة التي تتكون من الخلايا
keratin (أنسجة من IF)

يكون في الـ skin, ديس كل keratin

طبقة مهمة للجلد

epidermis e.g

helps prevent dehydration from tissues

- ① + vagina e.g
- ② lining mucosa over the soft palate, cheeks, the floor of the mouth
- ③ the pharynx (or throat)
- ④ the posterior region of the oral cavity leading to the esophagus.
- cervical region around the external os.
- lines moist internal cavities (mouth, esophagus, vaginal)

• The apical ends of many columnar and cuboidal epithelial cells have specialized structures projecting from the cells. These function either to increase the apical surface area for better absorption (microvilli), or to move substance along the epithelial surface (cilia → التنقيص)

special classifications of epithelium.

① Pseudostratified epithelium كاذب

→ كل الخلايا تكون في basement membrane لكن في جزء منها يصل

لا lumen, آخره فميت كل nucleus متكون في level مختلفة

فالتالي في light microscope فينك أنها عبة طبقات مو أنها طبقة

it's actually simple epithelium - don't reach the free surface and rest on basement membrane

- distribution in the body is limited + difficult to know whether all

identification of these cells depends on knowing where it's normally found ← cells contact basement membrane or not

منها صغيرة
سبب الوضعية

② **Transitional epithelium (urothelium)** (a term applied to the epithelium lining the lower urinary tract, extending from minor calyces of the kidney down to the proximal part of the urethra)

- has specific morphologic characteristics that allow it to distend urinary bladder
بيني urinary bladder ويتغير ويتمدد (وهذا يكون فقط في cells كيس) فآخر طبقة لها تكون فارغة يكون كروية تقريباً لكن لها تمانيد (ال bladder) يتمدد الخلايا وتبسط flat تقريباً.

Specific names: يمكن ترجعوا 125 م. لكن تشووا صورة نواح epithelium

① **Endothelium** → simple squamous → vascular system

- تبطن ال blood vessels لكن من دائماً ال endothelium يكون squamous
يمكن يكون cuboidal زي lymph node

- the epithelial lining of the blood and lymphatic vessels
- exceptions → simple squamous ما يكون endothelium
① in postcapillary venules of certain lymphatic tissues, these venules are called **high endothelial venules (HEV)** → cuboidal
② in the spleen in which endothelial cells of the venous sinuses are red-shaped and arranged like the staves of a barrel.

② **Endocardium**: the epithelial lining of ventricles and atria of the heart
تبطن تجاويف القلب

③ **Mesothelium** is the epithelium lining the walls and covers the contents of the closed cavities of the body (abdominal "peritoneal", pericardial and pleural cavities)

- endothelium, endocardium and mesothelium are almost always simple squamous epithelia.

Diverse epithelial functions:

عشر epithelium موجود تقريباً في

① **secretion (glands)** → e.g.: columnar epithelium of the stomach and the gastric glands

كل أجزاء الجسم نباتاني في تنوع حشري الوظائف

② **absorption** → e.g.: the columnar epithelium of the intestines and proximal convoluted tubules in the kidney.

③ **Transportation** → e.g.: transport of materials or cells along the surface of an epithelium propelled by motile cilia (transport of dust particles in the bronchial tree)

The transport of materials across an epithelium (pino- or endocytosis) to and from connective tissues.

- ④ **mechanical protection** → e.g.: the stratified squamous epithelium of the skin (epidermis) and the transitional epithelium of the urinary bladder.
 القدم تكون عدة طبقات من الكيراتين
 Keratin
- ⑤ **receptor function**: to receive and transduce external stimuli → e.g.: the taste buds of the tongue, olfactory epithelium of the nasal mucosa, and the retina of the eye.

ملاحظات:

- ① Epithelia involved in secretion or absorption are typically simple → pseudostratified
 نحن أحياناً نكوننا
- ② The height of cells often reflects the levels of secretory or absorptive activity
- ③ simple squamous epithelia are compatible with high rate of transepithelial transport.
- ④ Stratification of the epithelium usually correlates with transepithelial impermeability
- ⑤ in some pseudostratified epithelia, basal cells are the stem cells that give rise to the mature functional cells of the epithelium, thus balancing cell turnover.

The apical domain and its modifications:

- In many epithelial cells, the apical domain exhibits special structural surface modifications to carry out specific functions.
- apical domain may contain specific enzymes (hydrolases), ion channels and carrier proteins (glucose transporters)

cytoplasmic

3 structures / modifications في هنا

processes with a core of actin filaments

① microvilli

② stereocilia

③ cilia

of microtubule

cytoplasmic processes containing bundle

- finger-like cytoplasmic projections on the apical surface of most epithelial cells → جدران ذات فعالية أداء الوظيفية وخاصة امتصاص

- with the electron microscope (EM), microvilli vary widely in appearance. In some cell types, microvilli are short, irregular, bleb-like projections. In other cell types, they are tall, closely packed, uniform projections that greatly increase the free cell surface area. => لش بنزید مساحة السطح، عشن هیک هیكون عنا عدد بروتینات ومستقبلات = أكثر فبالتالی عنا مساحة أكبر لاداء وظائف أكثر زی فی القنوات والمضخات صح انه المساحة محدودة لكن لها القدرة على اداء كم كبير من الوظائف
- the number and shape of the microvilli of a cell correlate with the cell's absorptive capacity. Thus, cells that transport fluid and absorb metabolites have many closely packed, tall microvilli. Cells in which transepithelial transport is less active have smaller, more irregularly shaped microvilli.
یعنی انه شکل ال microvilli هیتغیر حسب وظيفتها یعنی ممکن یكون عنا شی بسیط کمن وحدة وممكن یكون عنا عدد كبير ومنظم ومتطور منهم وی فی ال epithelium of the small intestine لانه هناك هتكون وظيفتها الامتصاص من السائل اللى فیهِ المواد الغذائية ولازم تتم العملية بكفاءة
- Cytoplasmic extension like a tube fragile structure وبالتالی بده دعم عشن هیک
The internal structure of microvilli contains a core of 20 -30 actin filaments that are cross-linked by several actin-bundling proteins.
- Their **barbed (plus)** ends are anchored to **villin** (bundling protein located at the tip of the microvilli). **The other end interacts with the terminal web** (a horizontal network of actin filaments, which lies just below the base of the microvilli = close to the apical surface of the cell).
- The actin filaments inside the microvillus are cross-linked at 10-nm intervals by other actin-bundling proteins such as fascin, espin, and fimbrin. This cross-linkage provides support and gives rigidity to the microvilli.
- Among the fluid transporting epithelia (epithelium of the intestine and kidney tubules), a distinctive border of **vertical striations at the apical surface** of the cell, representing an astonishing number of 15,000 close-packed microvilli, is easily seen in the light microscope. In intestinal absorptive cells, this surface structure was originally called **the striated border**; in the kidney tubule cells, it is called **the brush border**.
- microvilli are usually short and not numerous, which explains why they may escape detection in the light microscope.
- The microvilli of the intestinal epithelium (striated border) are the most highly ordered and are even more uniform in appearance than those that constitute the brush border of kidney cells.

microvilli تبس intestine ال **Fig 5.2** ← **p.127** ← // **انتلا حظ انه ال** numerous, uniform, and regularly arranged **منظمة ومتقاربة (ح) خلاف البانی**

② **Stereocilia**
(misnomer) **اسمها مضلل فهي** **cilias** فيوحى أنها متحركة **immitile microvilli** **لكنها في الحقيقة**

- long, immotile microvilli
- It was given the name cilia عشن اول حد شاقها كانت بتتحرك لكن فيما بعد تبين أنها مش متحركة
- are not widely distributed among epithelia and limited to the epididymis (convoluted channel), the proximal part of the ductus deferens of the male reproductive system, and the sensory (hair) cells of the inner ear.
- Because electron microscopy reveals their internal structure to be that of unusually long microvilli, some histologists now use the term **stereovilli**. Seen in the light microscope, these processes frequently resemble the hairs of a **paintbrush** because of the way they aggregate into pointed bundles.
- are supported by internal bundles of actin filaments that are cross-linked by fimbrin. The actin filaments' barbed (plus) ends are oriented toward the tips of the stereocilia and the pointed (minus) ends at the base.
- Stereocilia of the sensory epithelium of the ear are sensitive to mechanical vibration and serve as **sensory mechanoreceptors** rather than absorptive structures. They are uniform in diameter and organized into ridged bundles of increasing heights, forming characteristic staircase patterns.
- actin-binding protein, ezrin, closely associated with the plasma membrane of stereocilia, anchors the actin filaments to the plasma membrane.
- The difference between microvilli and stereocilia, other than size and the presence of ezrin, is the absence of villin from the tip of the stereocilium.

3 cilia

Cilia:

- are common surface modifications present on nearly every cell in the body.
- are hair-like extensions of the apical plasma membrane containing an **axoneme** (microtubule-based internal structure). The axoneme extends from the **basal body** (a centriole-derived, microtubule-organizing center (MTOC) located in the apical region of a ciliated cell)
- Cilia + basal bodies + basal body-associated structures = ciliary apparatus
- cilia are classified as **motile**, **primary**, or **nodal**

1 Motile cilia

2 primary cilia

3 Nodal cilia

لها 3 أنواع:

→ (مطلوب تعريف سغلاية
لبطة عنها)

• Nodal cilia:

- are found in the embryo on the bilaminar embryonic disc

لها علاقة بتطور ال embryo

• Motile cilia:

- short, fine, hair-like structures $0.25 \mu\text{m}$ in diameter and 5 to $10 \mu\text{m}$ in length
- Motile cilia and flagella possess a typical 9+2 axonemal organization (A => 13 protofilament, B => 10 protofilament) with microtubule-associated motor proteins that are necessary for motility
- Basal bodies and basal body-associated structures firmly anchor cilia in the apical cell cytoplasm
- The basal body, a modified centriole, functions as an MTOC consisting of nine short microtubule triplets arranged in a ring
- A and B microtubules are continuous with two of the triplet microtubules of the basal body. The third incomplete C microtubule in the triplet extends from the bottom to the transitional zone at the top of the basal body near the transition between the basal body and the axoneme
- responsible for moving mucus over epithelial surfaces or facilitating the flow of fluid and other substances through tubular organs and ducts
- give a "crew-cut" appearance to the epithelial surface

Fig 5.6 ← p. 131

صورة مبيّنة لـ pseudostratified respiratory epithelium (منظر cut surface) بلفقر نتونه

tissue
connective

بتلاحظ أنه انخرأ كلها (الانفصال basement membrane التي تفرز) وجزء منها يعمل للأخرى (الغذاء) ومستويات مختلفة

• Primary cilia (monocilia):

- are solitary projections found on almost all eukaryotic cells
- a single cilium per cell on the apical part
- contain a 9+0 pattern of microtubules
- are immotile because of different arrangements of microtubules in the axoneme and lack of microtubule-associated motor proteins.
- function as **chemosensors**, **osmosensors**, and **mechanosensors**, and they mediate light sensation, odorant, and sound perception in multiple organs in the body.

التي يكتسب الخلايا صفة الحياة انها بتكون قادرة على ضبط وسطها الداخلي بمعزل عن الوسط الخارجي وهاد بيتهم من خلال sensors من خلال ال primary cilia حيث انها تكتشف وسط الخلية من ناحية ال chemicals, osmotic pressure and mechanical forces عشن تضبط وضعها

Fig 5.9 ← p. 133

صورة بـ EM لا primary cilia وموجود أيضاً basal bodies بتونها

The lateral domain and its specialization in cell-to-cell Adhesion:

- The lateral domain is characterized by the presence of unique proteins => cell adhesion molecules (CAMs) that are part of junctional specializations.
الخلايا لو لم قدرت تتجمع وتلتصق مش هتقدر تعمل وظائفها
- The molecular composition of the lipids and proteins that form the lateral cell membrane differ significantly from the composition of those that form the apical cell membrane. هيكون مختلف لانه كل وحدة لها وظيفتها الخاصة فيها
- The lateral cell surface membrane in some epithelia may form folds and processes, invaginations, and evaginations that create **interdigitating** and **interleaving** tongue-and-groove margins between neighboring cells.
سطح plasma membrane يكون متعرج ومتاخرل معه بشكل متطابق سطح الخلية المجاورة وهاد بيعمل على زيادة مساحة ال interaction بين الخلايا وبيعطي mechanical support لانه هيك بكون في مساحة احسن لل junctions تتكون
- Junctional complexes are responsible for joining individual cells together. There are three types of junctional complexes: Occluding junctions, Anchoring junctions and Communicating junctions.

① occluding junctions

• Occluding junctions:

- impermeable and allow epithelial cells to function as a barrier
- called tight junctions and form the primary **intercellular diffusion barrier** between adjacent cells.

they maintain physico-chemical separation of tissue compartments
Because they are located at the most apical point between adjoining epithelial cells, occluding junctions prevent the migration of lipids and specialized membrane proteins between the apical and lateral surfaces, thus maintaining the integrity of these two domains

apical part ال apical part يكون بمعزل تام عن ال lateral part
recruit various signaling molecules to the cell surface and link them to the actin filaments of the cell cytoskeleton

E.g. **zonula occludens** (pl., zonulae occludentes) represents the most

apical component in the junctional complex between epithelial cells
At high resolution, the zonula occludens appears not as a continuous seal but as a series of **focal fusions** created by transmembrane proteins of adjoining cells that join in the intercellular space.

- The arrangement of these proteins in forming the seal is best visualized by **the freeze fracture technique**.
- When the plasma membrane is fractured at the site of the zonula occludens, the junctional proteins observed on the P-face appear as ridge-like structures. The opposing E-face surface of the fractured reveals complementary grooves resulting from detachment of the protein particles from the opposing surface.

منه بيرصدر
جزء للواد لكن
يتحكم
material

transcellular
من داخل
الخلية
وفارص

intestine
حيث انه
عملية مرور
اغوار تكون
منظمة
وبالتفلا

طاقة

لكن
الزيت
phospholipid
موجود
في
الخلية
بالكامل

وظائفه
مختلفة

sealing of intercellular space

* بروتينات zonula occludens لها دور في توصيل ^{cells} signal حيث تقع receptors في منطقة معينة

* تقنية freeze fracture تفضل سطوح وفتحات و ^{خنادق} grooves و ^{جوان بارزة} ridges و ^{خاو} الخاو والمسطح المقابل للخلية يوجد ما يسمى

interactions between transmembrane proteins claudin and occludin سببها tight junctions
 " ← p. 140 ← Fig 5.15 (c)
 عبارة عن تقنية freeze fracture

② anchoring junctions → basal domain (موجودة في)
 ال PM يعتبر fragile فتحة فيكون anchoring junctions
 e.g. Zonula adherens → mechanical support لتعطى

وتصل الخلايا ببعضها في جوانبها
 تكون متصلة بالخلية المقابلة ومن الداخل مع cytoskeleton يعطى unity
 للخلية حتى تعمل معاً وتكون مترابطة كيميائياً وميكانيكياً
 ولها دور في signal transduction

- provide lateral adhesions between epithelial cells that link into the cytoskeleton of adjacent cells → provides mechanical stability
- 2 types: ① Zonula adherens (pl, zonulae adherents) (interacts with the network of actin filaments) ② macula adherens (pl, maculae adherents) or desmosomes (interacts with intermediate filaments)
- important in creating and maintaining the structural unity of the epithelium
- can be found on the lateral cell surface but also on the basal domain
- Through their signal transduction capability, anchoring junctions play important roles in cell-to-cell recognition, morphogenesis, and differentiation.

" " ← p. 145 ← Fig 5.19
 مقطع EM الجزء من PM التي فيه é dense filaments and granules

تبين نقاط اتصال ما بين cytoskeleton junctions

③ communicating junctions

cardiac muscle مثلاً يكون فيها اتصالات وأنسجة لنقل العنصر في إشارات كهربية تصل من أول خلية إلى آخر خلية (يفترض بدافعة طويلة) لكن هنا روابط أو فتحات بين cells فتتصل ال signal بسرعة ← من غير أن أجساد تتفتق من الفتحة وأخرى تتنبسط (يعني من خلاصوا) ← فهي توصل توصل سريع وانتقال المواد وال signals بسرعة.

- allow direct communication between adjacent cells by diffusion of small molecules (e.g. ions, amino acids, sugars, nucleotides, second messengers, metabolites)
- This type of intercellular communication permits the coordinated cellular activity that's important for maintaining organ homeostasis.

Zonula occludens: (ZO) → mechanical support

- joining of transmembrane proteins in the intercellular space
- occludin → claudin → junctional adhesion molecule (JAM)
- ZO1 and ZO3 (occludin and claudin interact with actin through them)

- The extracellular portions of these transmembrane proteins function as a zipper and seal the intercellular space between 2 adjacent cells.

Zonula adherens: interacts with actin (cytoskeleton)

macula adherens: (desmosomes) → ترتبطها ونظامها
وظيفتها متشابهة للzonula adherens لكنها تكون على شكل بقعة spot على PM وليس زوناً حلقية حيث أنه الخلية المجاورة يردا يكون عليها بقعة متشابهة ويرتبطوا سوا

focal adhesions hemidesmosomes

anchoring junctions

" " ← p.147 ← Fig 5.21

thick/dense layer صورة للmacula adherens يكون على PM ومقابلها نفس الشيء ويكون بينهم ارتباط من خلال adhesion molecules ومن الداخل تكون على cytoskeleton

CAMs: cell adhesion molecules

- Transmembrane proteins (about 50 CAMs have been defined)
- binding between different types of CAMs → heterotypic binding
- binding between CAMs of the same type → homotypic binding
- e.g. cadherins, Integrins, selectins, Ig superfamily

حسب المكان التي ترتبط فيها أول مرقم لتسميتها لتذكر CAM

ca $\rightarrow$ calcium

دور Ca^{2+} مع لقم الوظيفية

cadherins:

- are represented by transmembrane Ca^{2+} -dependent CAMs localized mainly within the zonula adherens.
- maintain homotypic interactions with similar proteins from the neighboring cell
- are associated with a group of intracellular proteins (catenins) that link cadherin molecules to actin filaments of the cell cytoskeleton
- convey signals that regulate mechanisms of growth and cell differentiation

Integrins:

- are represented by 2 transmembrane glycoprotein subunits consisting of α and β chains.
- This composition allows for the formation of different combinations of integrin molecules that are able to interact with various proteins (heterotypic)
- interact with ECM molecules (collagens, laminin, and fibronectin) and with actin and IF.
- regulate cell adhesion, control cell movement and shape, and participate in cell growth and differentiation.

Selectins:

- are expressed on WBC (leukocytes) and endothelial cells and mediate neutrophil - endothelial cell recognition. This heterotypic binding initiates neutrophil migration through the endothelium of blood vessels into the ECM.
microorganism/ inflammation $\rightarrow$ neutrophils تحتاج أحياناً لتغادر blood vessels لتدخل في
vascular structures endothelium) و leukocytes فخرجها يتطلب interaction بين
selectins وما بين دور
• involved in directing lymphocytes into accumulations of lymphatic tissues (homing procedure) $\rightarrow$ تواصل lymphocytes مع lymph node

Immunoglobulin superfamily (IgSF)

- one of the largest gene families in the human genome.
- eg: ICAM $\rightarrow$ intercellular CAM, E-CAM $\rightarrow$ cell CAM, VCAM $\rightarrow$ vascular CAM, DSCAM $\rightarrow$ Down syndrome CAM, PECAM $\rightarrow$ platelet endothelial CAM, JAM $\rightarrow$ junctional CAM

Macula adherens (desmosomes)

- anchoring sites for IFs
- These junctions are localized on the lateral domain of the cell, much like a series of spot welds, and membrane of each of the adjoining cells is a disc-shaped structure consisting of very dense material called the desmosomal attachment plaque. → anchor IFs
- The filaments appear to loop through the attachment plaques and extend back out into the cytoplasm.

يعتقد أن لهم دور في

dissipating physical forces throughout the cell from the attachment site

- each attachment plaque is composed of several constitutive proteins, mainly desmoplakins and plakoglobins, which are capable of anchoring IFs.
- The intercellular space of the macula adherens is wider than that of the zonula adherens and is occupied by a dense medial band, the intermediate line. This line represents extracellular portions of transmembrane glycoproteins, the desmogleins and desmocollins, which are members of the cadherin family of Ca^{2+} dependent CAM.

communicating junctions:

- Where high coordination is required
تؤمن التوافق بين خلايا -
Heart muscle زب السلام زب لتؤدي وظيفتها بشكل السليم زب
- accumulation of transmembrane channels
القنوات بين الخلايا تؤمن نقل المواد بسرعة عالية

- passage of signaling molecules

- low resistance to electricity
زب من القلب اذ مساره عبارة عن تيار كهربائي لما يلائم المسافات ذات resistance سوا يبين فيها فصل بينه اثنان نوع بكفاءة أكبر

- 12 subunits of connexin protein family
المادة الواحدة تتكون من نصف قناة كل نصف قناة فيها 6 connexin
2 connexons = قناة

- tightly packed channels

→ 6 symmetrical subunits of integral membrane protein.

morphologic specializations of the lateral cell surface

Fig 5.24 ← p. 150

- lateral surface lateral surface فيا تخرجان فالخلايا داخلية ببعض له دور مهم في رفع كفاءة العمل
- ① has a boundary as a result of infoldings or plicae along the border of each cell with its neighbor
 - ② these infoldings increase in the lateral surface area of the cell and are particularly prominent in epithelia that are engaged in fluid and electrolyte transport, such as the intestinal and gall bladder epithelium

the basal domain:

- ① basement membrane يوجد basement membrane برا الخلية
 - ② junctions: focal adhesions + hemidesmosomes
- بعمية فلاك عمتن desmosomes تكون بين dense plaque في خلية مع plaque في الخلية الأخرى لكن الثاني basal domain في خلية مقابلها connective tissue وكانا نص يعني hemi
- ← BM أحيانا يكون prominent وينشوفة في Light ميكروسكوب دون تقينا خاصة حين أنه ثنائي صورة (pseudostriated) كان لونه pink و هو بكل عام في respiratory epithelium يكون واضح لكن غالباً عت تنشفه كذا نأخذ صبغات خاصة زي PAS فيصبح الكربوهيدرات و التي صرودة بنسبة sufficient في BM و تنشفه أرممكن silver salt فيترسب على BM و يبرزه عن الميكروسكوب
- ← كما شغل أن BM ممكن تلاحظه في connective tissue (لكن طبيعتها مختلفة عن epithelia فممكن تكون خلايا منتشرة أو جملعات صغيرة) المهم ممكن نأخذ وحة من الصبغين PAS أو silver salt و نأكد أنه BM مثلاً: خلايا supporting حول nerve cells لها BM و adipocytes لها BM و صيغارة عن نسيج دهني و muscle cells لها طبقة متجهة لل BM

Fig 5.25 ← p. 150 " " thick band of eosinophilic/pink material

- ← العرف تنوف BM في light ميكروسكوب (دون بائيل صلبة لكن أحيانا بيفترسب) أه نأخذ صبغة خاصة فتي صورة Fig 5.26 ← عن glands لا color موجودة في gastrointestinal system إذا + نأخذنا PAS تظن انطحولين الخلايا أنها كلها موجودة في BM

- focal adhesions: anchor actin filaments of the cytoskeleton into the BM
- hemidesmosomes: anchor intermediate filament of the cytoskeleton into the BM.

THE BASAL DOMAIN AND ITS SPECIALIZATIONS IN CELL-TO-EXTRACELLULAR MATRIX ADHESION

The basal domain of epithelial cells is characterized by several features:

- The **basement membrane** is a specialized structure located next to the basal domain of epithelial cells and the underlying connective tissue stroma.
- **Cell-to-extracellular matrix junctions** anchor the cell to the extracellular matrix; they are represented by focal adhesions and hemidesmosomes.
- **Basal cell membrane infoldings** increase the cell surface area and facilitate morphologic interactions between adjacent cells and extracellular matrix proteins.

Basement Membrane Structure and Function

- The term basement membrane was originally given to an amorphous, dense layer of variable thickness at the basal surfaces of epithelia.
- Although a prominent structure referred to as basement membrane is observed with hematoxylin and eosin (H&E) stain in a few locations such as the trachea (respiratory epithelia) and, occasionally, the urinary bladder and ureters, basement membrane requires special staining to be seen in the light microscope.
- This requirement is caused, in part, by its thinness and by the effect of the eosin stain, which makes it indistinguishable from the immediately adjacent connective tissue.
- In contrast to H&E, the **periodic acid-Schiff (PAS)** staining technique results in a positive reaction at the site of the basement membrane. It appears as a thin, well-defined magenta layer between the epithelium and the connective tissue. The stain reacts with the sugar moieties of proteoglycans, accumulating in sufficient amounts and density to make the basement membrane visible in the light microscope.
- Techniques involving the reduction of **silver salts** by the sugars blacken the basement membrane and are also used to demonstrate this structure. Although the basement membrane is classically described as exclusively associated with epithelia, similar PAS-positive and silver-reactive sites can be demonstrated surrounding peripheral nerve supporting cells, adipocytes, and muscle cells; this helps to delineate them from the surrounding connective tissue in histologic sections.

The examination of the site of epithelial basement membranes with the EM reveals:

- a discrete layer of electron-dense matrix material 40- to 60-nm thick between the epithelium and the adjacent connective tissue called the basal lamina or, sometimes, lamina densa.
- When observed at high resolution, this layer exhibits a network of fine, 3- to 4-nm filaments composed of laminins, a type IV collagen molecule, and various associated proteoglycans and glycoproteins.
- Between the basal lamina and the cell is a relatively clear or electron-lucent area, the lamina lucida (also about 40 nm wide). The area outlined by the lamina lucida contains extracellular portions of CAMs, mainly fibronectin and laminin receptors. These receptors are members of the integrin family of transmembrane proteins.
- With the development of new EM preparation techniques, the lamina lucida appears to be an artifact of fixation; in the living state, the basal lamina is composed of a single layer of the lamina densa.

endothelium

p. 155 ← Fig 5.32

Blood vessel → capillary → filtration
endothelial cells → مع
basal lamina → دمج لا
epithelium → (يتم فيه ترشيح الدم ليتركز البول)
glomerules
special BM → نسيج النقا
2 epithelium → عشرين ميلان
2 lamina → رeticular lamina من متراكبين من وجود

epithelial cell processes فيه cell processes اسمها
(foot processes) podocyte
the basal lamina is interposed between the capillary endothelial cell (En) and the cytoplasmic processes (podocytes) of epithelial cells.
endothelium فيزي فضاء من خلافا غير الدم يتم ترشيحه

Basement membrane: basal lamina

multi-adhesive glyco-
proteins + fibronectin

- consists of approximately 50 different proteins: collagens, laminins, glycoproteins, and proteoglycans (أعلى كبريتات وحمضية بروتين)
- consists of molecules that come together to form sheet-like structure
بروتين متصل بسلاسل طويلة من
polysaccharides

reticular lamina: قد تكون artifact

Cell to ECM junctions: anchoring junctions:

- ① hemidesmosomes → desmosomes من بنية structure
- IF to the BM → IF → looping → desmo → lamina
- on the basal cell surface → provide increased adhesion to the basal
- exhibits an intracellular attachment plaque on the cytoplasmic side of the basal PM
- the protein structure composition of the plaque is similar to the desmosomal plaque as it contains a desmoplakin-like family of proteins capable of anchoring IF.
- 3 major proteins have been identified in the plaque: plectin, BP 230, perlecan
- transmembrane proteins - desmosomes → cadherin family of Ca²⁺-dependent molecules
- Hemidesmosomes → majority belong to the integrin class of cell matrix receptors

→ protein complex

② focal adhesion

- Actin into the BM (ارتبط مع ECM من خلال integrins)
- The main family of transmembrane proteins is integrins, which are concentrated in clusters within areas where the junction can be detected.

modifications of basal cell surface:

• في lateral side يوجد interdigitations مهمة لزيادة مساحة surface ويمكن support (لما يكون متداخلة مع الخلية المتاخمة)
وفي ال basal في الخلية التي يكون فيها transport of fluid في proximal tubules of الكلى filtration حيث يتم ترشيح ephrine kidney

النموذجي ~~التي~~ بالتكامل عدد الخلية والارتباطات التي حجمها كبير
فالسائل الذي ينتج ultrafiltrate يشار امتصاص الموارد المقيمة
منه عسكن يقطع في نقل الموارد التي بدو يبرلها elimination وتقطع
لبر الجسم وعن هذه tubules يتم فيها عملية الامتصاص كثير فيكون
فيها modification ← يكون في foldings في basal side تزود كفاءة
عملية النقل

Fig 5.37 ← p.160 ← "

المسافات بين interdigitations و PM يوجد mitochondria موجود بشكل
مكثف حتى تزود عملية النقل بالطاقة لثم (ازودنا مساحة الطح عسكن عسكن
نقل أكثر)

Many cells that transport fluid have **infoldings** at the basal cell surface. They significantly increase the surface area of the basal cell domain, allowing for more transport proteins and channels to be present. These basal surface modifications are prominent in cells that participate in active transport of molecules (e.g., in proximal and distal tubules of the kidney and in certain ducts of the salivary glands). mitochondria are typically concentrated at this basal site to provide the energy requirements for active transport. The mitochondria are usually oriented vertically within the folds. The orientation of the mitochondria, combined with the basal membrane infoldings, results in a **striated appearance** along the basal aspect of the cell when observed in the light microscope. Because of this phenomenon, the salivary gland ducts that possess these cells are referred to as striated ducts.

Glands: ^{غدد خلية الظهارة} epithelial

① **exocrine:** تطلق المحتويات من الخلية للجسم أو لتتوحد
واله عدة أشكال:

- **merocrine:** vesicles تتكون في cytoplasm وتقترب من PM تلتصق به وتفرغ
محتوياتها بال exocytosis وفاد mechanism منتشرة في الجسم وبنادقها
في salivary glands و pancreatic glands

- **apocrine:** products accumulate at the cells' apical ends, portions of which
are then extruded to release the product together with small amount
of cytoplasm and cell membrane. يعني إما أن apical part تلتصق بال PM تلتصق
بفتحة lumen أو كجزء من apical part مع PM تنفصل
وفاد mechanism مثل صجودة بكل مكان بالجسم ومثال عليها: breast
وفي genital area ← axillary apocrine glands

- **holocrine:** الخلية يتم فيها secretion كدماء فتلتصق بكل كامل وبلاخر
ببركها apoptosis الخلية نقطة lumen المطلوب
eg. skin hair follicle → sebaceous glands → sebum
يتم إنتاج sebum بهذه mechanism

② **endocrine:** blood vessels
محتوى خلايا يتم إنزاله في

③ **paracrine:** nearby خلايا product يتوجه خلايا

④ **autocrine:** منتج يؤثر على الخلية نفسها حيث أنه يكون لها receptors
على سطحها ويتفرز المادة وتأثر فيها وبيرتوي من feedback حتى
يتم ضبط كمية secretions.

توزيع الأنواع المختلفة p. 161 ← Fig 5.38

junqueira's Basic histology ← p. 102 (pdf) ← Fig 4-21

90 د

توزيع 3 mechanisms exocrine secretion

junqueira's ← p. 103 ← Fig 4-23 + Fig 4-22

بلا حظ أنه ال mammary gland فيه فتود تنفصل ويخرج داخل
lumen

GLANDS:

1. **Exocrine glands** secrete their products onto a surface directly or through epithelial ducts or tubes that are connected to a surface
 - **Merocrine secretion:** This secretory product is delivered in membrane-bounded vesicles to the apical surface of the cell. Here vesicles fuse with the plasma membrane and extrude their contents by exocytosis. This is the most common mechanism of secretion and is found, for example, in pancreatic acinar cells.
 - **Apocrine secretion:** The secretory product is released in the apical portion of the cell, surrounded by a thin layer of cytoplasm within an envelope of plasma membrane. This mechanism of secretion is found in the lactating mammary gland, where it is responsible for releasing large lipid droplets into the milk.
 - **Holocrine secretion:** The secretory product accumulates within the maturing cell, which simultaneously undergoes destruction orchestrated by programmed cell death pathways (apoptosis). Both secretory products and cell debris are discharged into the lumen of the gland. This mechanism is found in sebaceous glands of skin and the tarsal (Meibomian) glands of the eyelid.
2. **Endocrine glands** lack a duct system. They secrete their products into the connective tissue, from which they enter the bloodstream to reach their target cells. The products of endocrine glands are called hormones.
3. **Paracrine signaling:** In some epithelia, individual cells secrete substances that do not reach the bloodstream but rather affect other nearby cells. The paracrine secretion has very limited signaling range; it reaches the target cells by diffusion.
4. **autocrine signaling:** many cells secrete molecules that bind to receptors on the same cell that release them. In many instances, signaling molecules (autocrines) initiate negative feedback pathways to modulate their own secretion. This signaling mechanism is frequently used by cells of the immune system and involves the family of interleukin signaling molecules.

Exocrine:

- ① unicellular → goblet cells → internal surface || internal organs
- ② multicellular
 - simplest arrangement → sheet (e.g. gastric surface and pits)
 - tubular (simple → 1 tubule, compound → more than 1 tubule and share a common duct or excretory system)
 - acinar, acinar → flask/grape
 - tubuloacinar → mix of all in combination

EXOCRINE:

- Exocrine glands are classified as either unicellular or multicellular.
- Unicellular glands** are the simplest in structure. In unicellular exocrine glands, the secretory component consists of single cells distributed among other nonsecretory cells. A typical example is the goblet cell, a mucus-secreting cell positioned among other columnar cells. Goblet cells are located in the surface lining and glands of the intestines and in certain passages of the respiratory tract.
- Multicellular glands** are composed of more than one cell. They exhibit varying degrees of complexity. The simplest arrangement of a multicellular gland is a cellular sheet in which each surface cell is a secretory cell. For example, the lining of the stomach and its gastric pits is a sheet of mucus-secreting cells. Other multicellular glands typically form tubular invaginations from the surface. The end pieces of the gland contain the secretory cells; the portion of the gland connecting the secretory cells to the surface serves as a duct. If the duct is unbranched, the gland is called simple; if the duct is branched, it is called compound. If the secretory portion is shaped like a tube, the gland is **tubular**; if it is shaped like a flask or grape, the gland is **alveolar or acinar**; if the tube ends in a sac-like dilation, the gland is **tubuloalveolar**. Tubular secretory portions may be straight, branched, or coiled; alveolar portions may be single or branched. Various combinations of duct and secretory portion shapes are found in the body.

Fig 5.39 p. 161

microvilli ← columnar cells ← small intestine ← سطح داخل small intestine
brush border

↓
dispersed among them goblet cells

من قوت والسعة من قوت بتضيق وتكون معجزة
secretion → compress nucleus against basal part (الجزء القاعية)

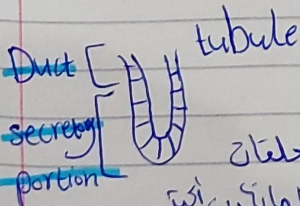
Fig 4-17 p. 97

crew-cut → cilia / أنوية مستوية مختلفة
pseudostratified

Fig 4-18(b) p. 98

dispersed goblet cells → filled by mucus secretion

cilia تتحرك من الداخل للخارج وعليها mucus التي فيه حافة particles
يتم دفعها للخارج لتخلط منها



coiled tubule → e.g. sweat glands (exocrine)

لما تأخذ مقطع تكون شكل حبات ← Exocrine glands

كلمة compound تستخدمها أيضاً (Table 5.5) لما تكون أكثر

منهجة تكرر وتتركب من نقطة تفرع واحدة

branched ← sebaceous gland

Good luck ت

وبس ...

table 55 ← p. 162 ← " (يوجد الاستكشاف لوانواع)
table 4-4 ← p. 101 ← ج. (يوجد انواع بكلام غيبا بالجدول)

mucus ← المادة الغضائية التي يفرها secretion
mucous acinus → round cluster of cells

Fig 4-25 ← p. 105 ← ج.
acini Lie ← النواة، bluish background
pushed against basal part ← بيب secretions

Mucous and serous glands are so named because of the type of secretion produced. The secretory cells of exocrine glands associated with the various body tubes are often described as being mucous, serous, or both.

- **Mucous secretions** are viscous and slimy, whereas serous secretions are watery. Goblet cells, secretory cells of the sublingual salivary glands, and surface cells of the stomach are examples of mucus-secreting cells.
- The mucous nature of the secretion results from extensive glycosylation of the constituent proteins with anionic (negative charge) oligosaccharides.
- The mucinogen granules, the secretory product within the cell, are therefore PAS positive.
- they are water soluble and lost during routine tissue preparation. For this reason, the cytoplasm of mucous cells appears to be empty in H&E-stained paraffin sections.
- Another characteristic feature of a mucous cell is that its nucleus is usually flattened against the base of the cell by accumulated secretory product.
- **serous cells** produce poorly glycosylated or nonglycosylated protein secretions. The nucleus is typically round or oval.
- The apical cytoplasm is often intensely stained with eosin if its secretory granules are well preserved. The perinuclear cytoplasm often appears basophilic because of an extensive rough endoplasmic reticulum, a characteristic of protein-synthesizing cells.
- Serous cell-containing acini (sing., acinus) are found in the parotid gland and pancreas.
- Acini of some glands, such as the submandibular gland, contain both mucous and serous cells (serous cells predominate).
- The sublingual gland is mixed serous and mucous tubuloacinar gland in which mucous cells predominate.
- In routine tissue preparation, the serous cells are more removed from the lumen of the acinus and are shaped as crescents or demilunes (half-moons) at the periphery of the mucous acinus. => artcraft تكون في submandibular gland
الخلايا تكون على نفس ال BM مختلفين ال mucous and serous لكن أثناء ال processing
ال serous ينفصلوا ويحيطوا في ال acinus زي هلال