

# Introduction to tissue biology and epithelial tissues

Prof. Özgür Çınar, M.D.

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“First, I am your professor, not your teacher. There is a difference. Up to now your instruction has been in the hands of teachers, and a teacher’s job is to make sure that you learn... However, things are very different for a university professor. It is no part of my job to make you learn. **At university, learning is your job — and yours alone.** My job is to lead you to the fountain of knowledge. Whether you drink deeply or only gargle is entirely up to you.”

**Keith Parsons, Ph.D.**

Professor of Philosophy,  
College of Human Sciences and Humanities  
University of Houston – Clear Lake

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## What is tissue?

Tissue: *Fr. tissu, woven; L. texo, to weave; Tr. doku*

## Types

- Epithelium (epithelial tissue)
- Connective tissue
- Muscle tissue
- Nerve tissue
- Cartilage
- Bone
- Adipose tissue
- Blood

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## Epithelial Tissue

- is avascular
- covers body surfaces, lines body cavities and tubes
- constitutes glands
- works as receptors for the special senses (smell, taste etc.)

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## What are their functions?

- Protection
- Secretion
- Absorption
- Transportation (on the surface or transepithelial)
- Receptor/Sensory

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## Classification of Epithelial Tissue

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## Fill in the blanks

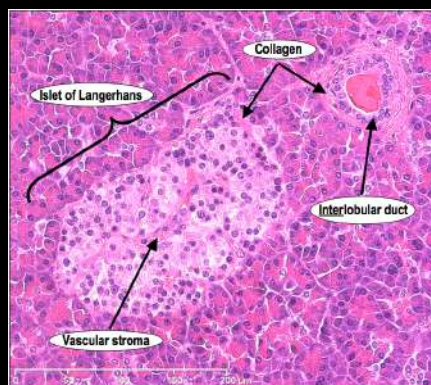
Shapes of the cells	Squamous (Tr. Yassı)	Cuboidal (Tr. Kübik)	Columnar (Tr. Prizmatik, silindirik)	Pseudostratified (Tr. Yalancı çok katlı)	Transitional (Tr. Değişici)
Layer (one or more)					
Simple (Tr. Basit)					
Stratified (Tr. Çok katlı)					

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## Epithelioid Tissue

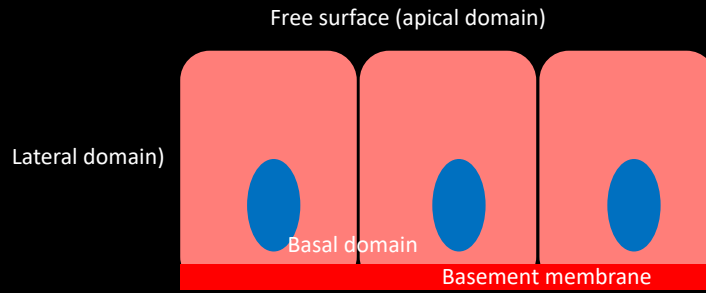
Cells are closely apposed to one another but lack a free surface.

Ex: Leydig cells, islets of Langerhans, anterior lobe of pituitary gland



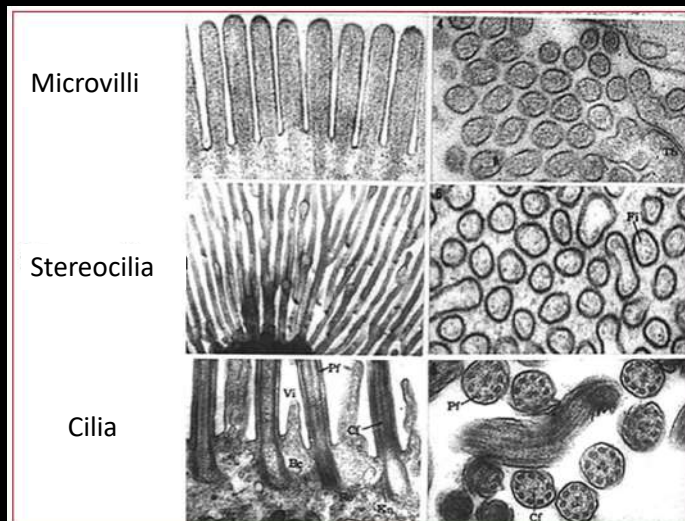
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# Do epithelial cells exhibit polarity?



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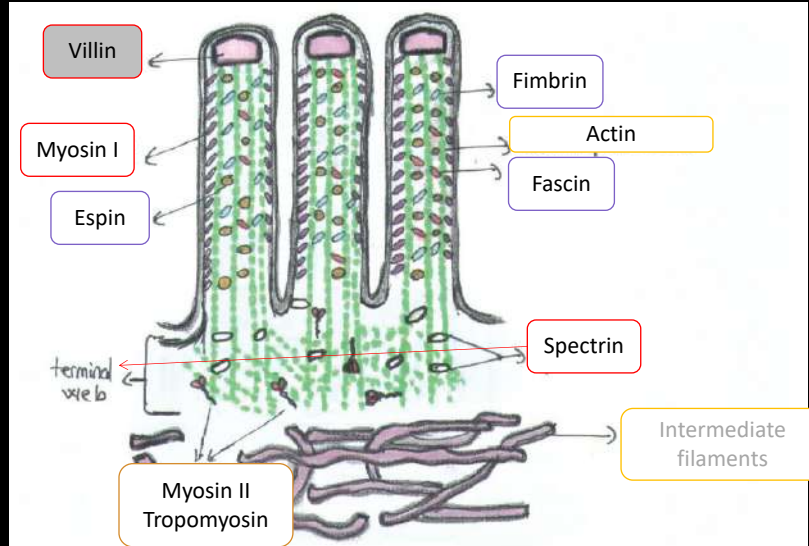
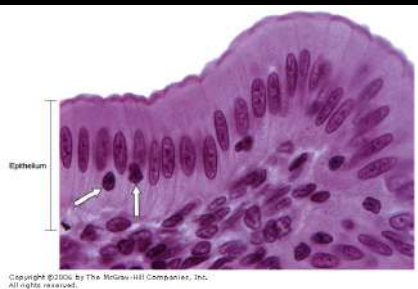
# Surface modifications of apical domain



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# Microvilli (Sing. Microvillus)

Striated border  
Brush border



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https://www.ncbi.nlm.nih.gov/gene/7429

Gene:  Search

Full Report - Send to:  Hide sidebar >>

**VIL1 villin 1 [Homo sapiens (human)]**  
Gene ID: 7429, updated on 8-Dec-2018

**Summary**

**Official Symbol:** VIL1 provided by HGNC  
**Official Full Name:** villin 1 provided by HGNC  
**Primary source:** HGNC:12652  
**See related:** Ensembl:ENSG00000127831 MIM:193040  
**Gene type:** protein coding  
**RefSeq status:** REVIEWED  
**Organism:** Homo sapiens  
**Lineage:** Eukaryota; Metazoa; Chordata; Craniota; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorhini; Catarrhini; Hominoidea; Homo  
**Also known as:** VIL; D2S1471  
**Summary:** This gene encodes a member of a family of calcium-regulated actin-binding proteins. This protein represents a dominant part of the brush border cytoskeleton which functions in the capping, severing, and bundling of actin filaments. Two mRNAs of 2.7 kb and 3.5 kb have been observed; they result from utilization of alternate poly-adenylation signals present in the terminal exon. [provided by RefSeq, Jul 2008]  
**Expression:** Biased expression in small intestine (RPKM 141.0), duodenum (RPKM 126.6) and 3 other tissues [See more](#)  
**Orthologs:** [mouse](#) [all](#)

**Genomic context**

**Location:** 2q35 See VIL1 in [Genome Data Viewer](#)  
**Exon count:** 20

Annotation release	Status	Assembly	Chr	Location
109	current	GRCh38.p12 (GCF_000001405.38)	2	NC_000002.12 (218419115..218449525)
105	previous assembly	GRCh37.p13 (GCF_000001405.25)	2	NC_000002.11 (219283838..219314248)

Chromosome 2 - NC\_000002.12

Genome Browsers: [Genome Data Viewer](#), [Variation Viewer \(GRCh37.p13\)](#), [Variation Viewer \(GRCh38\)](#), [1000 Genomes Browser \(GRCh37.p13\)](#), [Ensembl](#), [UCSC](#)

Table of contents: [Summary](#), [Genomic context](#), [Genomic regions, transcripts, and products](#), [Expression](#), [Bibliography](#), [Phenotypes](#), [Variation](#), [Pathways from BioSystems](#), [Interactions](#), [General gene information](#), [Markers, Homology, Gene Ontology](#), [General protein information](#), [NCBI Reference Sequences \(RefSeq\)](#), [Related sequences](#), [Additional links](#)

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## Stereocilia

Stereocilia are unusually long, branched microvilli.

They contain ezrin protein to anchor actin filaments to cell membrane.

They do not have villin protein.

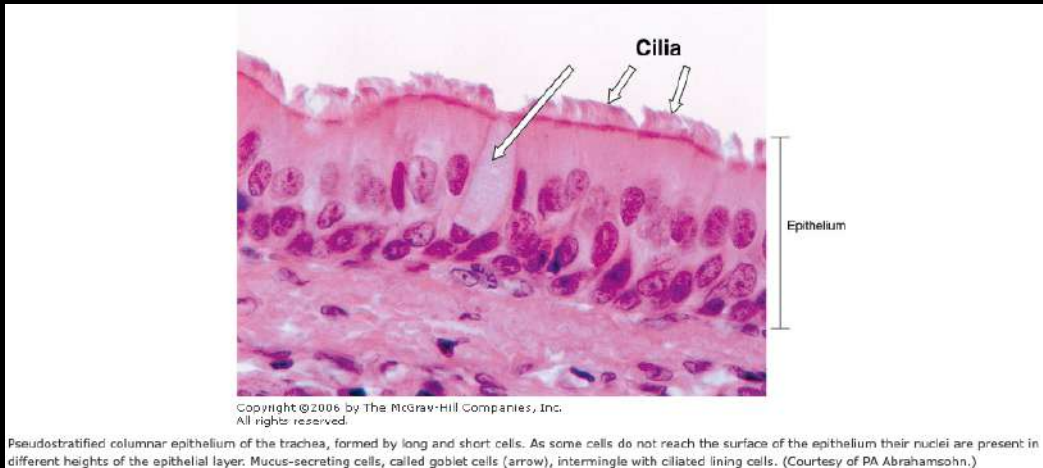
Stereocilia of the sensory epithelium of the ear also derive from microvilli and are sensitive to mechanical vibration.

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The screenshot shows a PubMed search result for the article "Mutations of ESPN cause autosomal recessive deafness and vestibular dysfunction." The article is from J Med Genet, 2004 Aug;41(8):591-5. The authors listed are Naz S<sup>1</sup>, Griffith AJ, Riazuddin S, Hampton LL, Battey JF Jr, Khan SN, Riazuddin S, Wilcox ER, and Friedman TB. The abstract states: "We mapped a human deafness locus DFNB36 to chromosome 1p36.3 in two consanguineous families segregating recessively inherited deafness and vestibular areflexia. This phenotype co-segregates with either of two frameshift mutations, 1988delAGAG and 2469delCTCA, in ESPN, which encodes a calcium-insensitive actin-bundling protein called espin. A recessive mutation of ESPN is known to cause hearing loss and vestibular dysfunction in the jerker mouse. Our results establish espin as an essential protein for hearing and vestibular function in humans. The abnormal vestibular phenotype associated with ESPN mutations will be a useful clinical marker for refining the differential diagnosis of non-syndromic deafness." The PMID is 15286153, PMCID is PMC1735855, and DOI is 10.1136/jmg.2004.018523. There are links for "Free PMC Article" and "Add to Favorites".

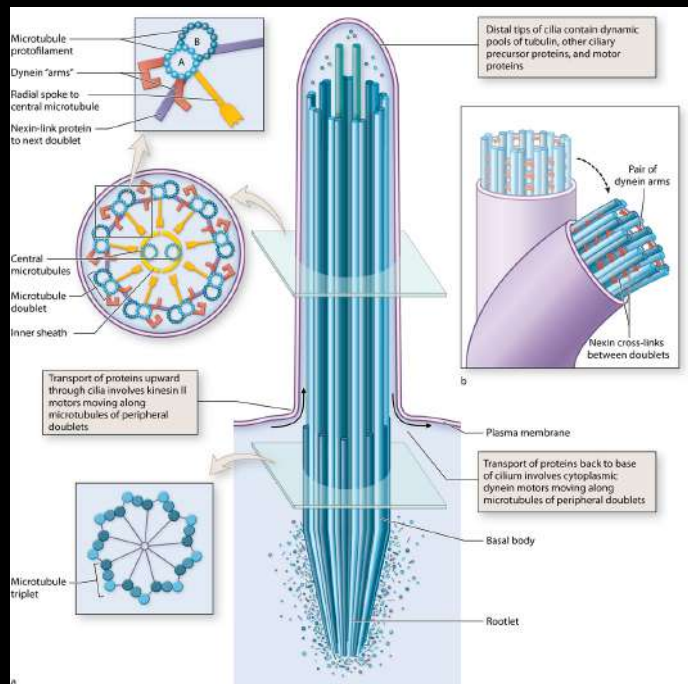
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# Cilia (sing. Cilium)



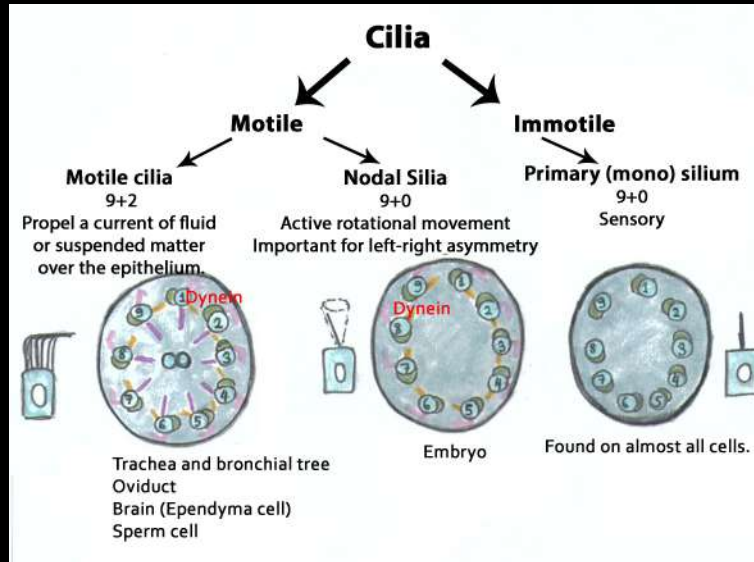
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# Cilia



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- Kartagener's syndrome

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Related disease - Polycystic Kidney Disease

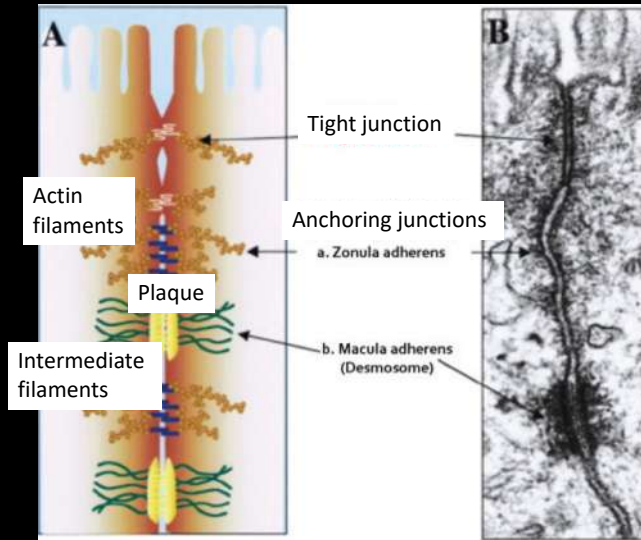
In humans, mutations in two genes, ADPKD1 and ADPKD2, appear to affect development of these **primary cilia**, leading to polycystic kidney disease (PKD).

The proteins encoded by these genes, polycystin-1 and polycystin-2, respectively, are **essential in the formation of the calcium channels associated with primary cilia**.

This autosomal recessive disorder is characterized by **multiple expanding cysts in both kidneys**, which ultimately **destroy the renal cortex and lead to renal failure**.

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## The Lateral Domain and Intercellular Junctions



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## Tight (Occluding) Junction

**Tight junctions** are circumferential belts at the apical domain of epithelial cells and linking adjacent endothelial cells. Tight junctions seal the space between epithelial cells and regulate the passage of water and flux of ions between adjacent epithelial cells (**paracellular pathway**). Molecules across the cell follow a **transcellular pathway**.

Afadin-nectin complex is anchored to ZO-1. Nectins form **cis-homodimers**, which interact with each other (**trans-homo interaction**) through the extracellular region.

Junctional adhesion molecules (JAMs) are associated to afadin and ZO-1. JAMs **cis-homodimers** interact with each other (**trans-homo interaction**) and determine the formation of cell polarity.

Occludin and claudins are the molecular basis for the formation of tight junction strands seen in freeze-fracture preparations.

Zonula occludens proteins (ZO-1, ZO-2, and ZO-3) facilitate the reciprocal interaction of occludin, claudins, and JAMs with F-actin.

Occludin and claudins are members of the **tetraspanin** family of proteins, containing four transmembrane domains, two loops, and two cytoplasmic tails.

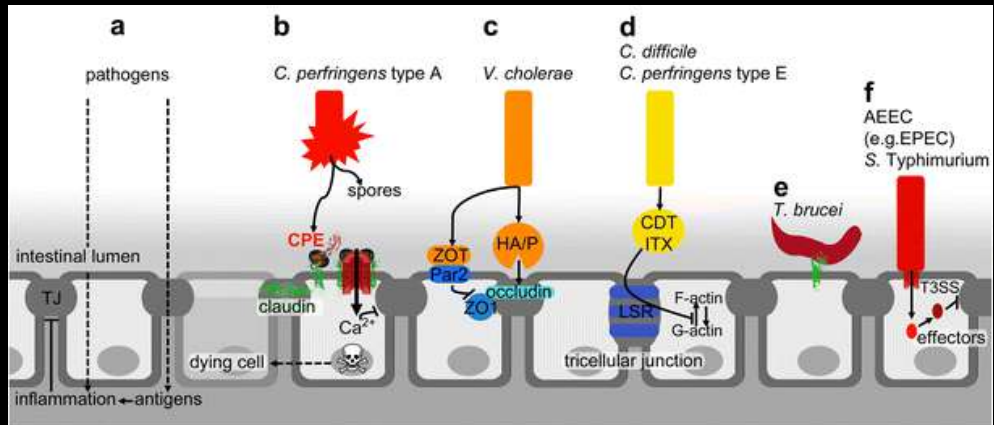
Nectins and JAMs are members of the **immunoglobulin** subfamily. Their structure is characterized by immunoglobulin loops, each stabilized by disulfide bonds. Nectins and JAMs **cis-homodimers** mediate **trans-homo cell-cell adhesion**.

Paracellular pathway

Transcellular pathway

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## Tight (Occluding) Junction



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## Adherens (Anchoring) Junction

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**Epidermal layers:** Stratum corneum, Stratum granulosum, Stratum spinosum, Stratum basale.

**Associated conditions:**

- Epidermolytic plantar/epidermal keratoderma (EPPK):** Keratin 9 (plantar/epidermal epidermis)
- Epidermolytic hyperkeratosis (EH):** Keratins 1 and 10
- Epidermolysis bullosa simplex (EBS):** Keratins 5 and 14

**Clinical Photos:**

- Epidermolysis bullosa simplex (EBS):** Mutation of keratins 5 and 14. Blisters develop soon after birth at sites subject to pressure or rubbing. Blisters can be seen on the fingers of an infant.
- Epidermolytic hyperkeratosis (EH):** Mutation of keratins 1 and 10. Excessive keratinization causes a breakdown of the epidermis.
- Epidermolytic plantar/epidermal keratoderma (EPPK):** Mutation of keratin 9. This disorder is restricted to the epidermis of the palms and soles.

**Histology of Pemphigus foliaceus:** An autoantibody-mediated blistering disease in which antibodies against desmoglein 1 cause a loss of adhesion of keratinocytes in the superficial layers of the epidermis. Desmoglein 1 predominates above the stratum spinosum. Desmoglein 3 predominates in the strata basale and spinosum.

**Layers of the epidermis:** Stratum corneum, Stratum granulosum, Stratum spinosum, Stratum basale.

**Other labels:** Dermis, Basal lamina, Epidermis, Blister.

Kierszenbaum & Tres: Histology and Cell Biology: An Introduction, 2002

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## Cell adhesion molecules

Calcium

Dependent

Independent

Cadherin

Selectin

Integrin

Immunoglobulin superfamily

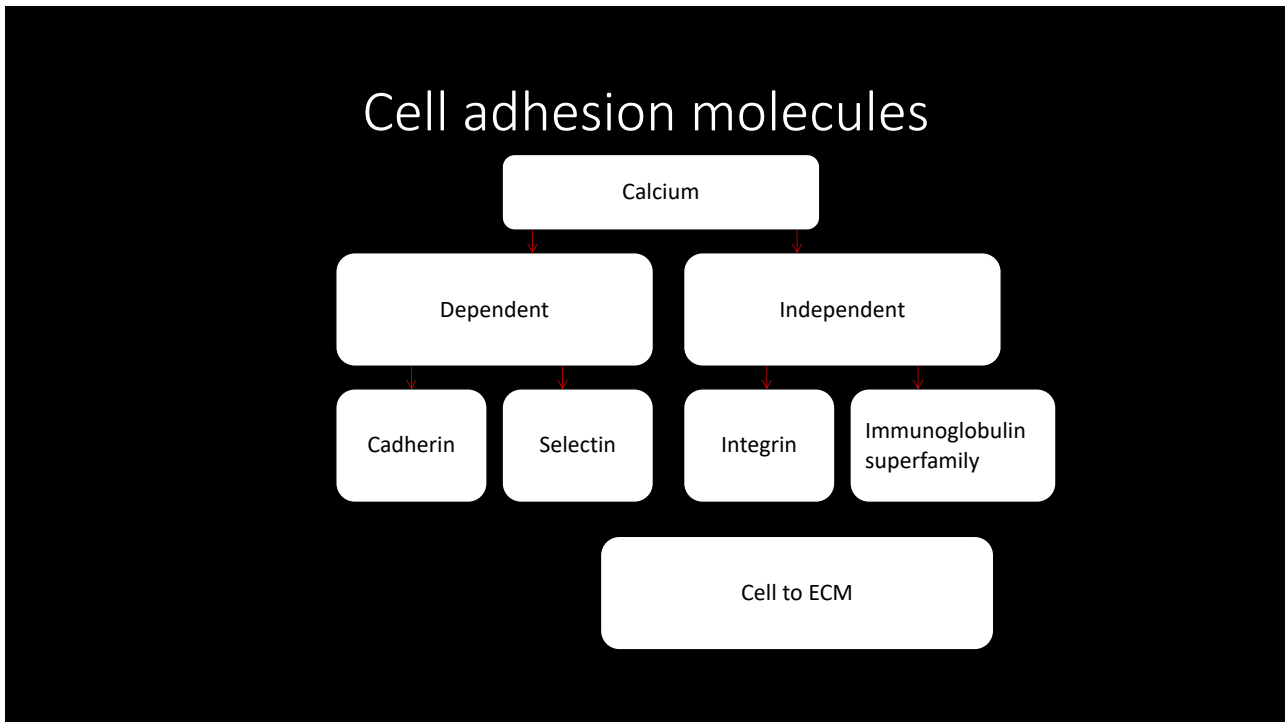
Homophilic interactions

Heterophilic interactions  
Leukocytes, endothelial cells

**A** Homotypic (Homophilic) / Heterotypic (Heterophilic)

**B** Homophilic / Heterophilic

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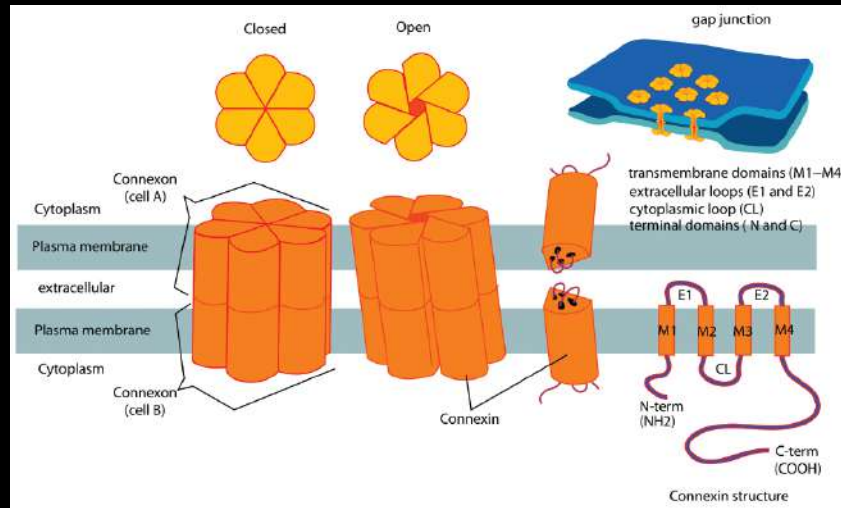
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### Immunoglobulin superfamily (Cellular Adhesion Molecules)

- Vascular,
- Inter-cellular,
- Neural,
- Cellular (C-CAM),
- Down Syndrome (DS-CAM),
- Platelet Endothelial (PE-CAM)
- Junctional Adhesions Molecules (JAM)

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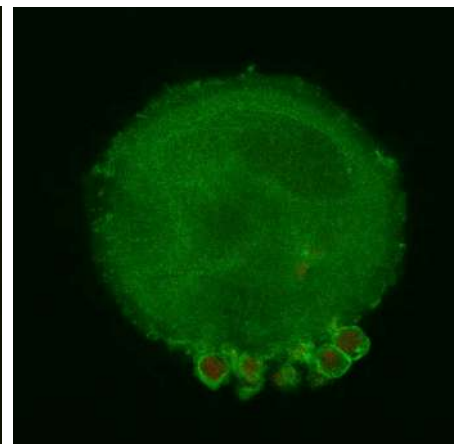
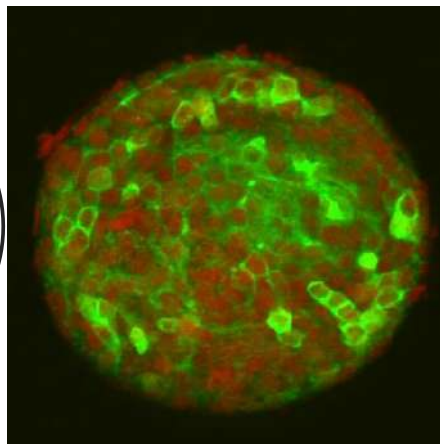
# Communicating (Gap) Junction (Nexus)



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What is known?

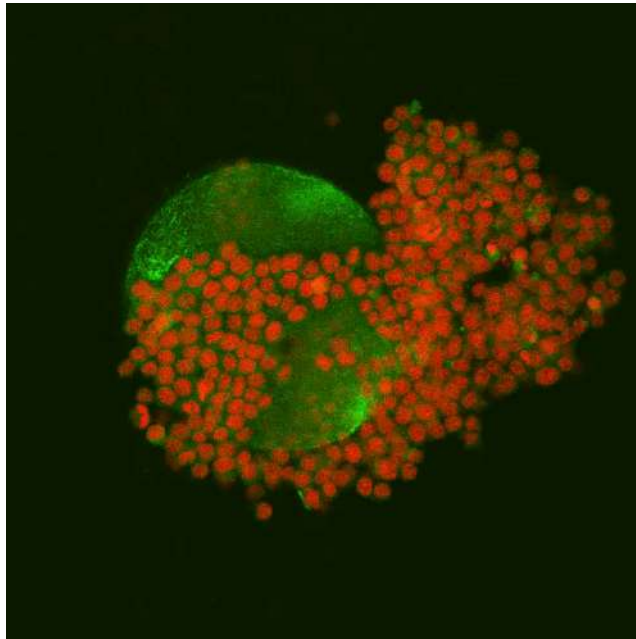
GJs



Connexin 43

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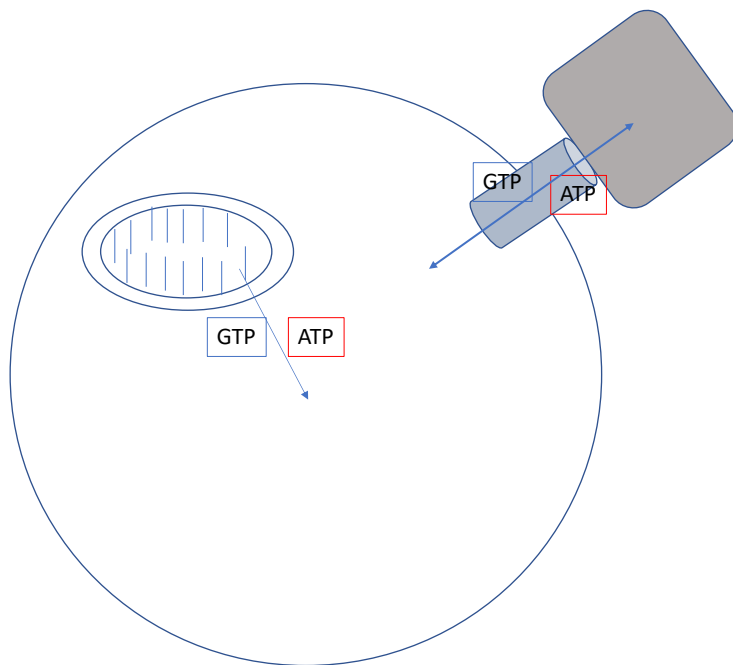
What is known?  
GJs



Connexin 32

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What is known?



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**Table 1**  
Genetic disorders caused by human connexin mutations.

Gene	Chromosome	Protein	Disorder(s)	OMIM
GJA1	6q22.31	Cx43	Craniometaphyseal dysplasia, autosomal recessive	218400
			Erythrokeratoderma variabilis et progressiva	133200
			Oculodentodigital dysplasia	164200
			Oculodentodigital dysplasia, autosomal recessive	257850
			Palmarplantar keratoderma with congenital alopecia	104100
GJA3	13q12.11	Cx46	Cataract	186100
GJA4	1p34.3	Cx37	Cataract	601885
GJA5	1q21.2	Cx40	Atrial fibrillation, familial, 11	614949
			Atrial standstill, digenic (GJA5;SCN5A)	108770
GJA8	1q21.2	Cx50	Cataract	116200
GJA9	1p34.3	Cx59	Cataract	602540
GJA10	6q15	Cx62	Cataract	148210
GJB1	Xq13.1	Cx32	Charcot-Marie-Tooth neuropathy, X-linked 1	302800
			Bart-Pumphrey syndrome	149200
GJB2	13q12.11	Cx26	Deafness, autosomal dominant 3A	601544
			Deafness, autosomal recessive 1A	220290
			Hypsic-like ichthyosis with deafness	602540
			Keratitis-ichthyosis-deafness syndrome	148210
			Keratoderma, palmarplantar, with deafness	148350
			Vohwinkel syndrome	124500
GJB3	1p34.3	Cx31	Perikeratotic eccrine ostial and dermal duct nevus	612644
			Deafness, autosomal dominant 2B	220290
GJB4	1p34.3	Cx30.3	Deafness, digenic (GJB2;GJB4)	133200
			Erythrokeratoderma variabilis et progressiva	133200
GJB5	1p34.3	Cx31.1	Deafness, autosomal dominant 3B	612643
GJB6	13q12.11	Cx30	Deafness, autosomal recessive 1B	612645
			Deafness, digenic (GJB2;GJB6)	220290
GJB7	6q14.3-q15	Cx25	Ectodermal dysplasia 2, Clouston type	129500
GCF1	17q21.31	Cx45	Leukodystrophy, hypomyelinating, 2	608804
GCT2	1q42.13	Cx47	Spastic paraplegia 44, autosomal recessive	613206
			Lymphedema, hereditary, KC	613480
GCC3	7q22.1	Cx30.2		
GDD2	15q14	Cx35		
GDD3	17q21.2	Cx31.9		
GDD4	10p11.21	Cx40.1		
GDF1	6q24.1	Cx23		

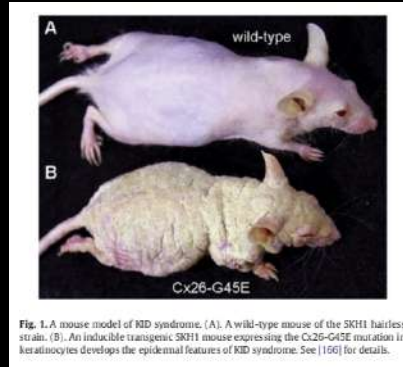


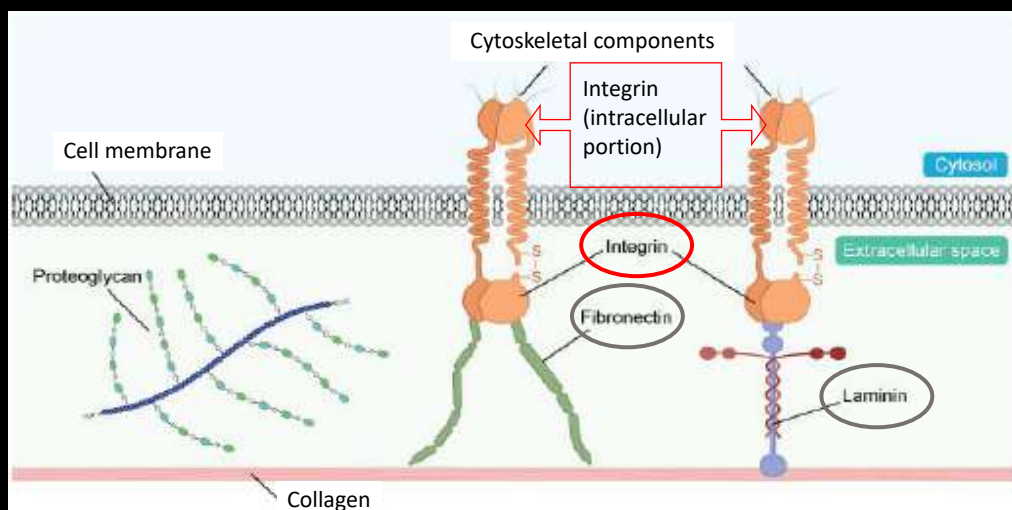
Fig. 1. A mouse model of KID syndrome. (A). A wild-type mouse of the SKH1 hairless strain. (B). An inducible transgenic SKH1 mouse expressing the Cx26-G45E mutation in keratinocytes develops the epidermal features of KID syndrome. See [106] for details.

KID: Keratitis-ichthyosis-deafness syndrome

M. Srinivas et al. / Biochimica et Biophysica Acta 1860 (2018) 192–201

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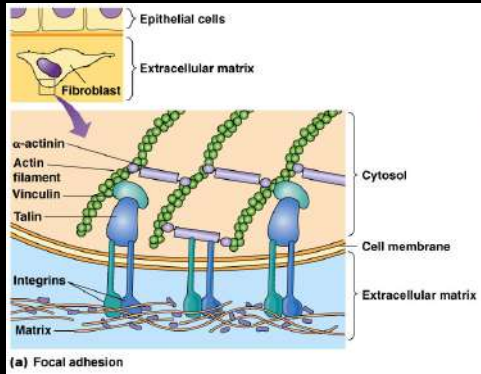
## Basal domain and cell to ECM adhesions



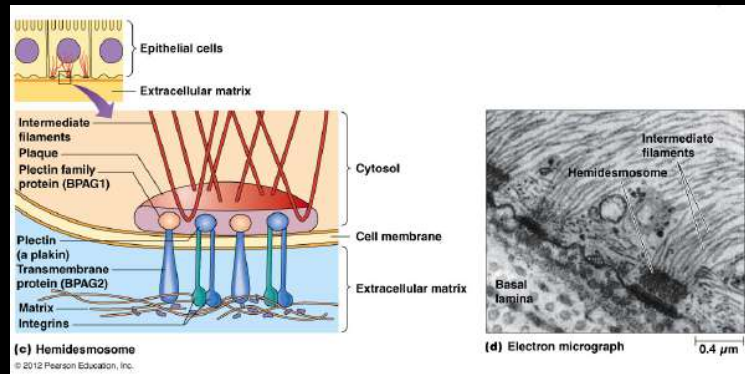
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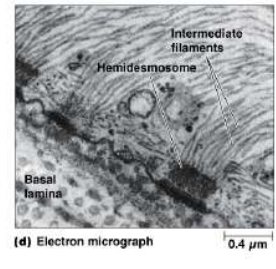
## Cell to ECM adhesions: focal adhesion and hemidesmosome



**focal adhesions**, which anchor actin filaments of the cytoskeleton into the basement membrane; and

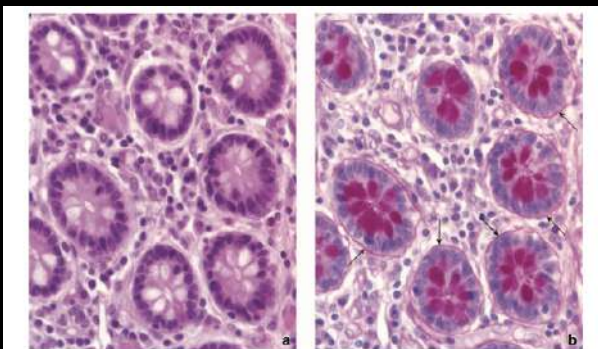


**hemidesmosomes**, which anchor the intermediate filaments of the cytoskeleton into the basement membrane.



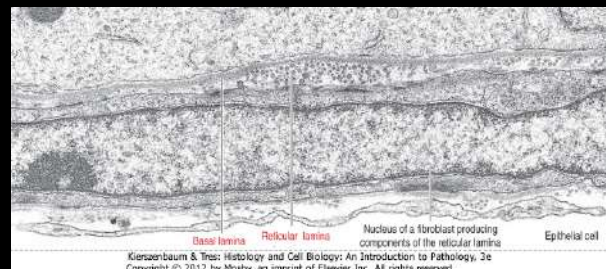
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## Basement membrane (basal lamina)



**FIGURE 5.26** Photomicrographs showing serial sections of intestinal glands of the colon. The glands in this specimen have been cross-sectioned and appear as round profiles. **a**, This specimen was stained with H&E. Note that neither the basement membrane nor the mucin that is located within the goblet cells is stained.  $\times 550$ . **b**, This section was stained by the PAS method. It reveals the basement membrane as a thin, magenta layer (arrows) between the base of the epithelial cells of the glands and the adjacent connective tissue. The mucin within the goblet cells is also PAS positive.  $\times 550$ .

The basal lamina in nonepithelial cells is referred to as the **external lamina**.



### Basal lamina (lamina densa):

- 3- to 4-nm filaments
- composed of
- laminin, fibronectin, laminin receptors etc.
- type IV collagen, and other collagens
- various associated proteoglycans
- glycoproteins (entactin/nidogen)

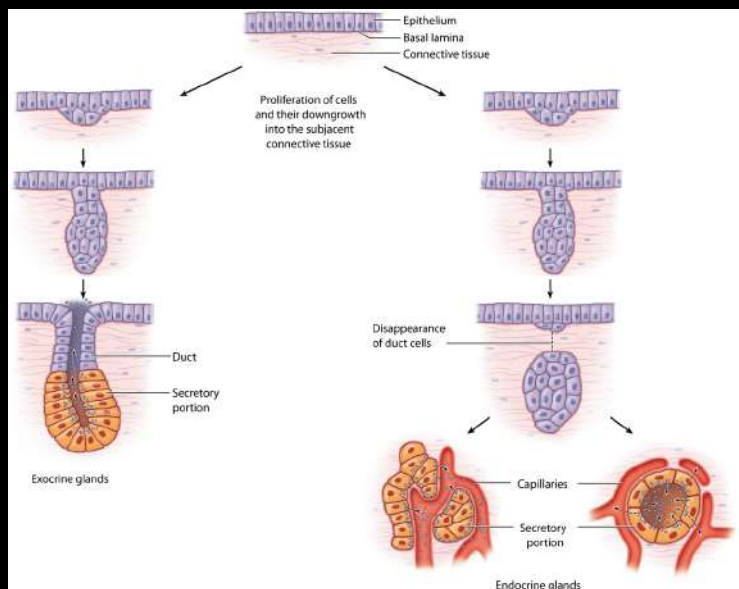
**Reticular lamina:** type III collagen (reticular fibers)

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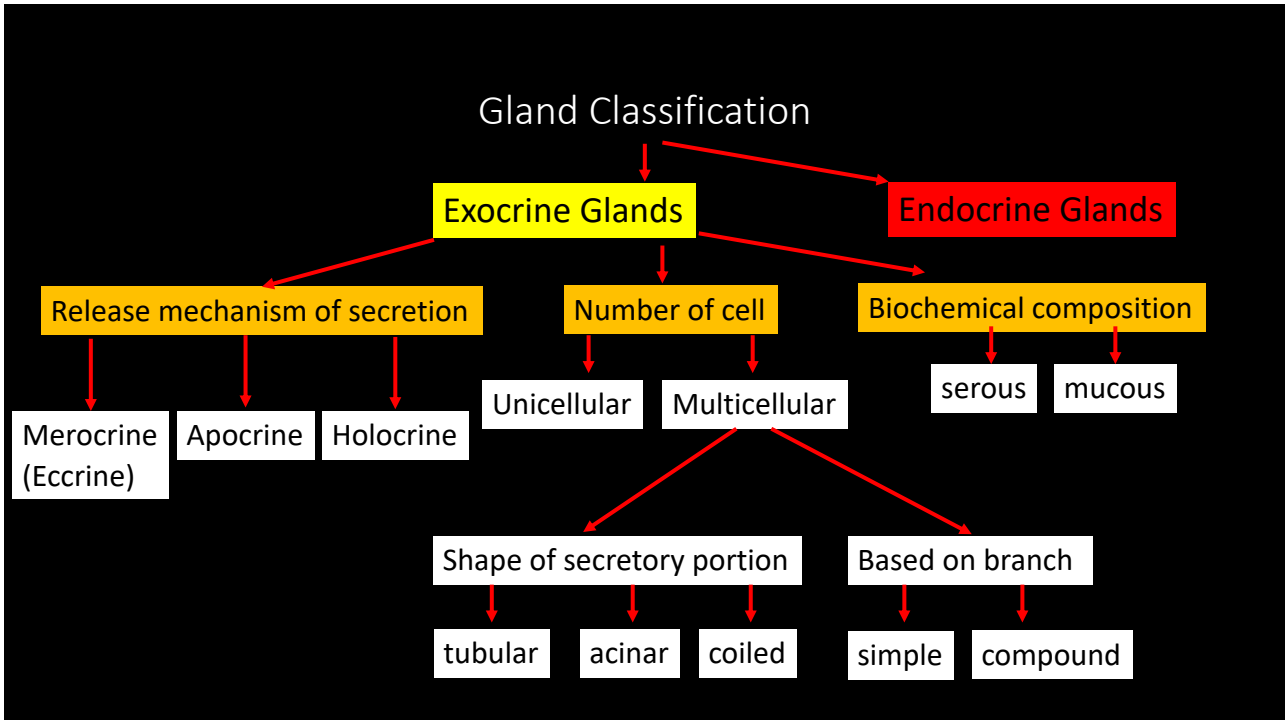
The screenshot shows a PubMed search result for the article "Anti-Glomerular Basement Membrane Disease" by McAdoo SP and Pusey CD. The article is from the *Clin J Am Soc Nephrol*, published in 2017. The abstract describes anti-GBM disease as a rare small vessel vasculitis affecting the capillary beds of the kidneys and lungs, caused by pathogenic autoantibodies. It notes that environmental factors like infection may trigger the disease in susceptible individuals. Treatment involves plasma exchange, steroids, and cytotoxic therapy. The article also mentions that relapse and recurrent disease after kidney transplantation are uncommon, and that ANCA-associated vasculitis and membranous nephropathy can co-present with anti-GBM disease.

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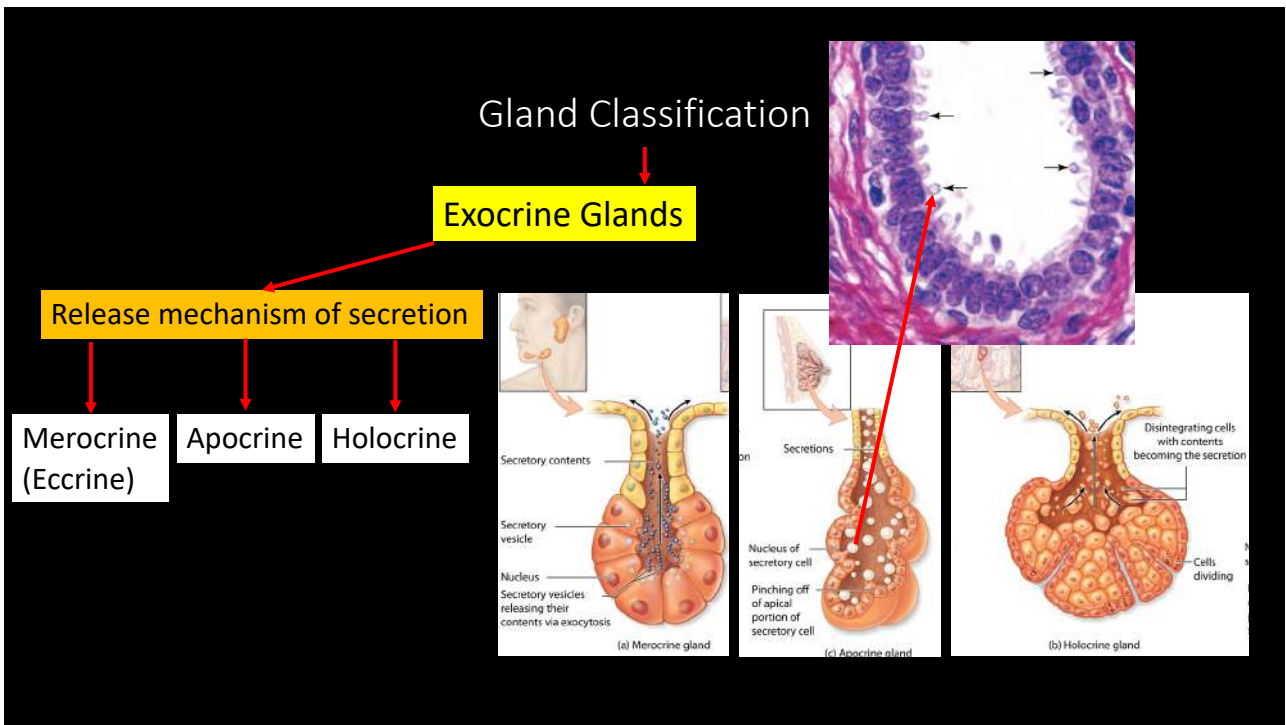
# GLANDS (Tr. Bezler)



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**Mucous secretory portion (sublingual gland):** The sublingual gland contains mucous secretory portions that possess a **basophilic** appearance. The **apical portion** of the mucous-containing secretory vesicles. The **basophilic appearance** is due to the presence of the **basophilic** secretory cells. The secretory content can be demonstrated by the PAS reaction, which stains glycoproteins. Myoepithelial cells are also present around the mucous secretory portions.

**Mucous acinar cell:** Mucus product, Irregularly shaped and basally located nucleus.

**Serous secretory portion (parotid gland):** The parotid gland contains serous secretory portions. The serous-secreting cells have a **large spherical nucleus**, a basal region in which the rough endoplasmic reticulum predominates, and an apical region with well-developed **zymogen granules**. Zymogen granules represent secretory vesicles containing enzyme precursors.

**Serous acinar cell:** Golgi apparatus, Secretory granules, Rough endoplasmic reticulum.

**Mixed secretory portion (submandibular or sublingual gland):** The submandibular gland contains both serous and mucous secretory portions and they produce a seromucous secretion delivered into the same lumen. Mixed secretory units are made up of mucous coils and a small cap of serous cells on one side. The cap is called a **serous demilune** because of its crescent moon shape. Surrounding each secretory unit and the initial portion of the excretory duct are the **myoepithelial cells**. Myoepithelial cells are placed between the secretory cells and the basal lamina and their long and branched cytoplasmic processes form a loose basket. Their function is to contract and squeeze the secretion out of the secretory portion and along the duct system.

**Biochemical composition:** serous, mucous

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### Gland Classification

**Exocrine Glands**

**Number of cell**

- Unicellular
- Multicellular
  - Goblet cell**
  - Shape of secretory portion
    - tubular
    - acinar
    - coiled
  - Based on branch
    - simple
    - compound

**Histological Labels:** Mucus, Cilia, Terminal bars, Epithelial cell, Goblet cells, Basal cell, Basement membrane, Lamina propria.

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## Gland Classification

### Exocrine Glands

#### Number of cell

#### Multicellular

#### Shape of secretory portion

#### Based on branch

tubular

acinar

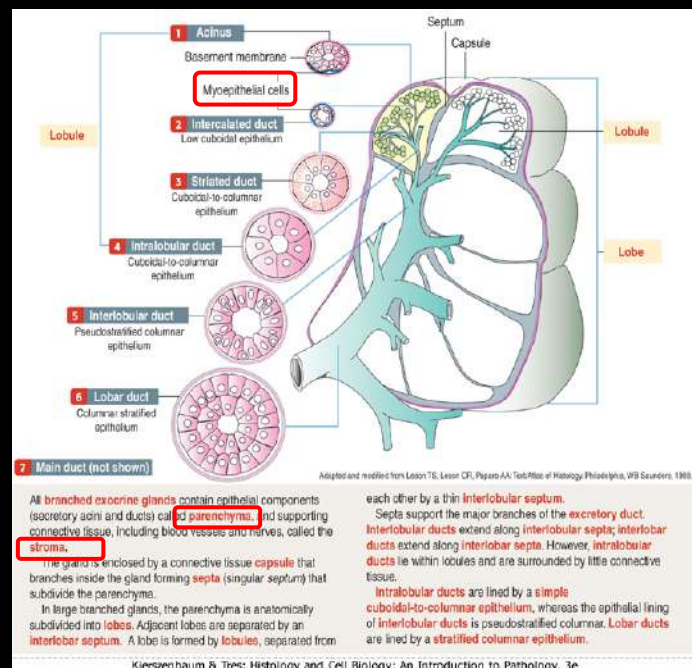
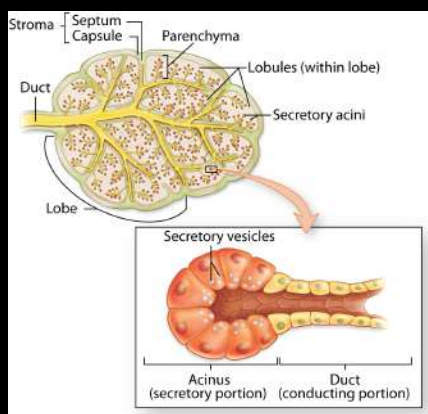
coiled

simple

compound

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## Structure of an exocrine gland



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