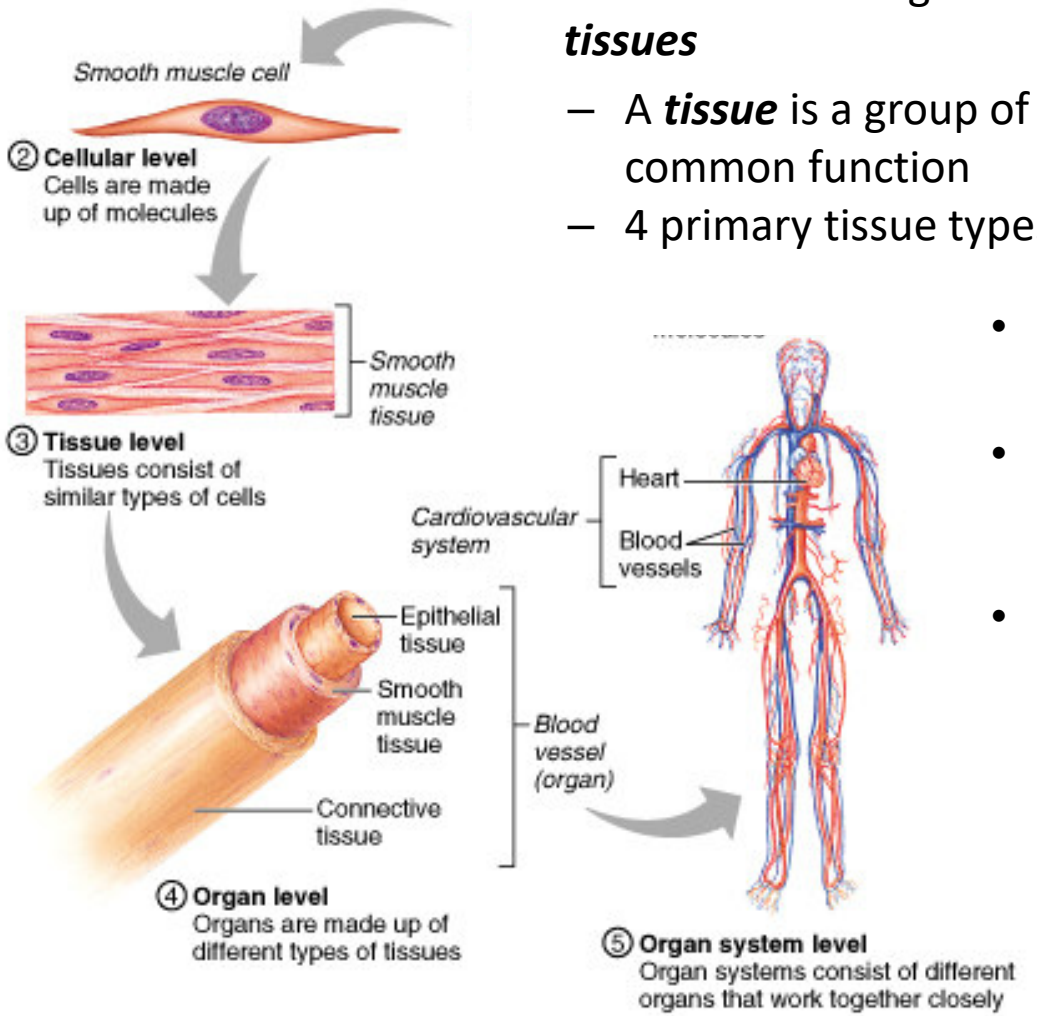
Cells – Tissues - Organs

- The human body contains trillions of cells
  - but only about 200 different cell types
- In multicellular organisms, specialized cells are grouped into ***tissues***
  - A ***tissue*** is a group of cells similar in structure and performing a common function
  - 4 primary tissue types: **Epithelial, Connective, Muscle, Neural**



- **Organs** are comprised of combinations of various tissues
- **Organ systems** include multiple organs working together
- all tissues in the body develop from three *germ layers*
  1. ectoderm - epithelial + neural
  2. mesoderm - connective + muscle + some epithelial
  3. endoderm – epithelial

Form follows function: Types of Epithelia and Epithelial Classification

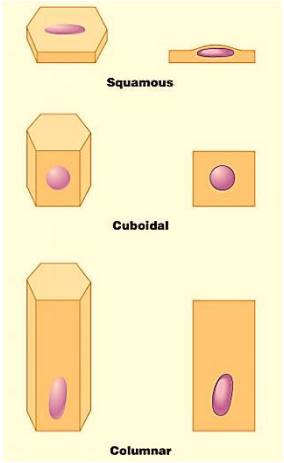
Naming Scheme: first part indicates cell layers, second cell shape

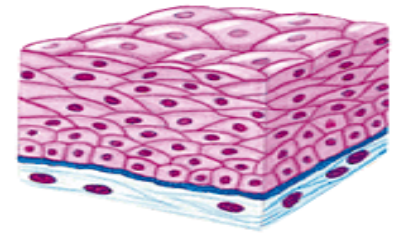
3 types based on layering

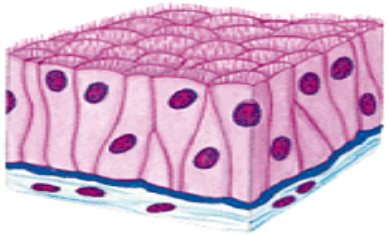
- **Simple** – only 1 layer of cells
- **Stratified** – several layers of cells
- **Pseudostratified** - differently sized cells make it appear multilayered, but all cells contact the basal lamina

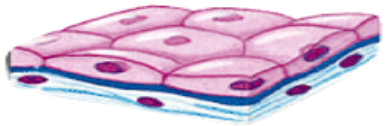
4 types based on cell shapes

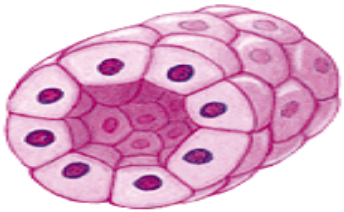
- **Squamous** –thin flat cell
- **Cuboid** –cell height is equal to their width
- **Columnar** – cell height is usually 3-4 times their width
- **Transitional** – cells with varying shapes

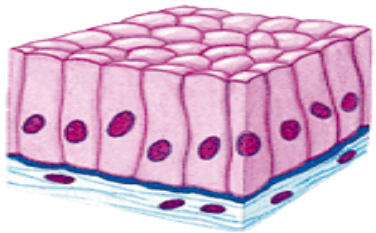


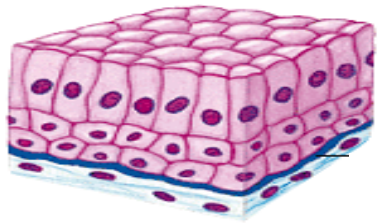

Stratified squamous


Pseudostratified ciliated columnar

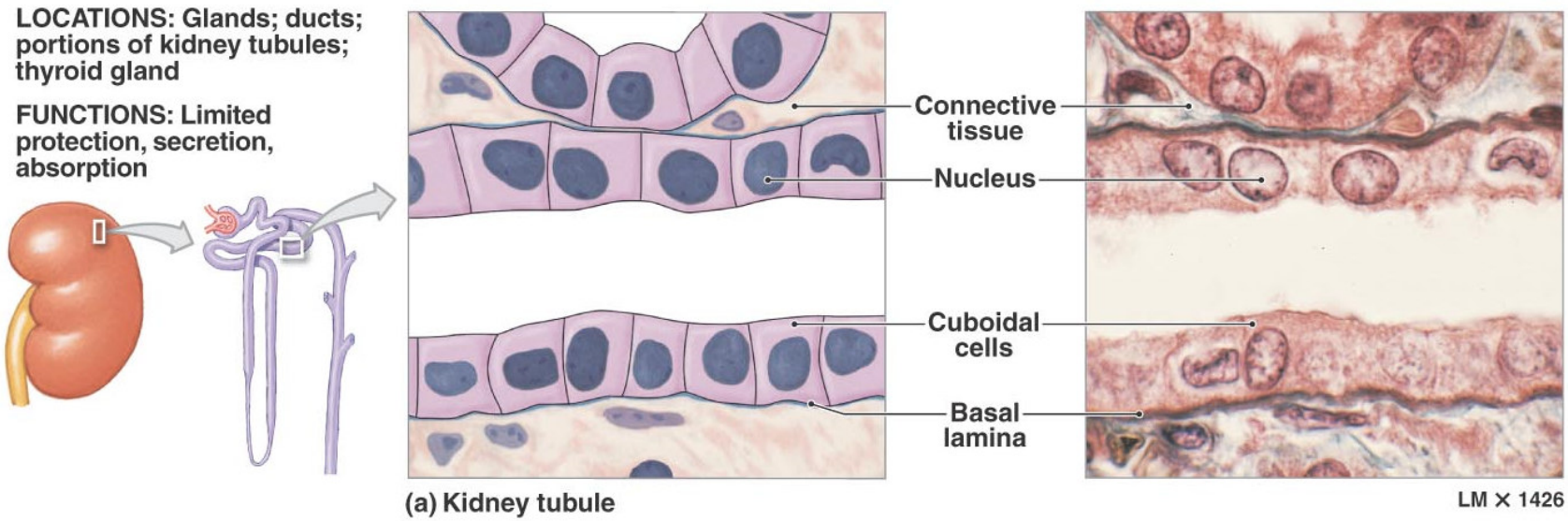

Simple squamous


Simple cuboidal


Simple columnar

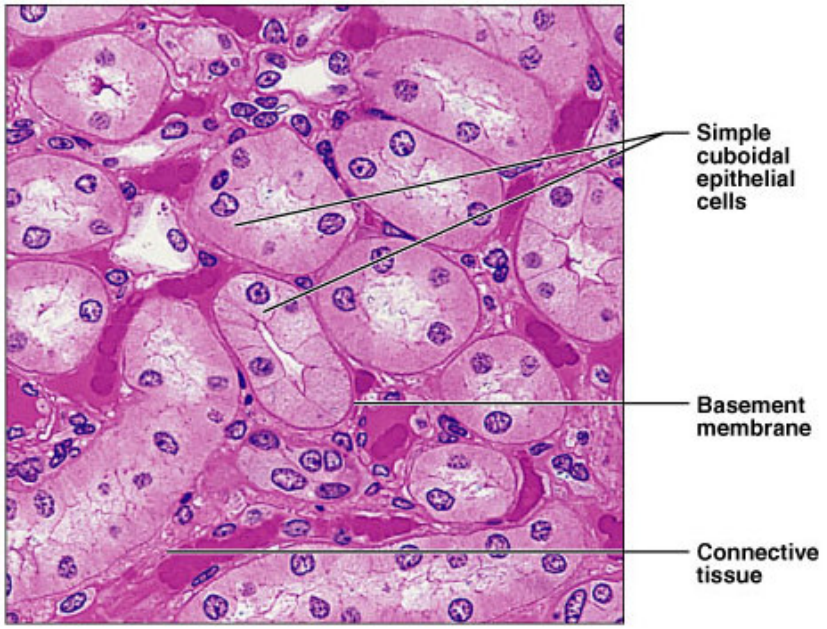

Stratified columnar

SIMPLE CUBOIDAL EPITHELIUM



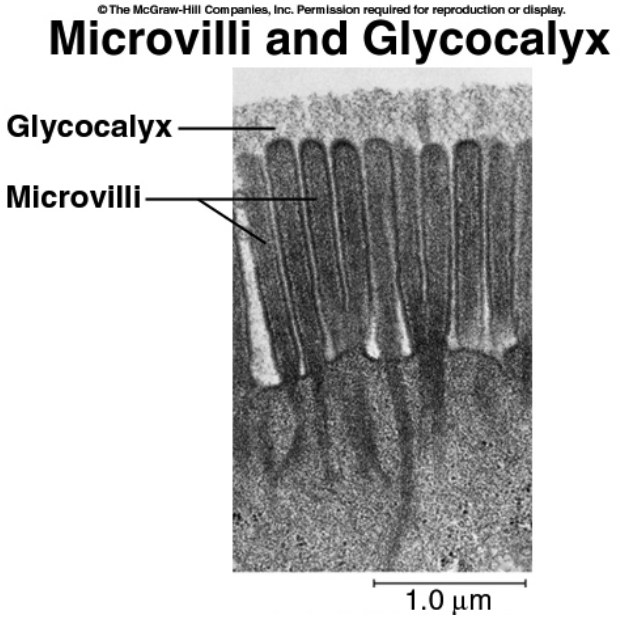
- found in regions where secretion or absorption takes place
- forms the walls of the small ducts of many glands and of kidney tubules

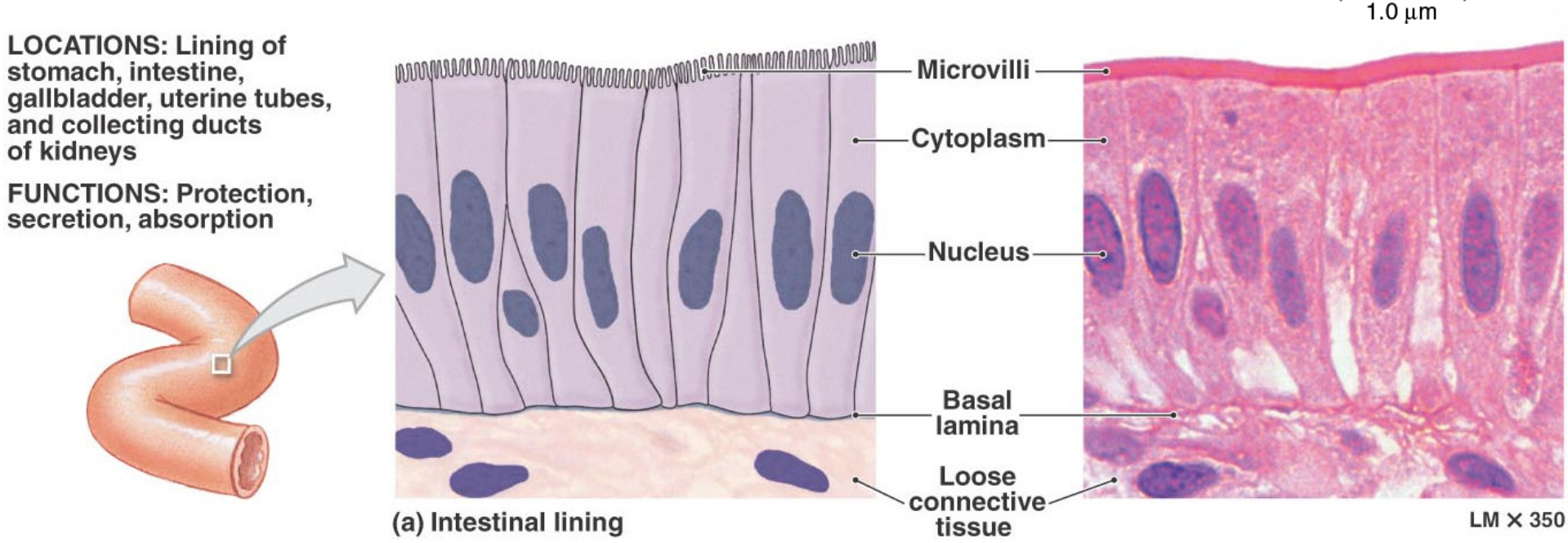
STAINING BASICS H&E:
hematoxylin (blue): stains nuclei
eosin (red): stains proteins; typically cytoplasm faint and extracellular matrix strongly



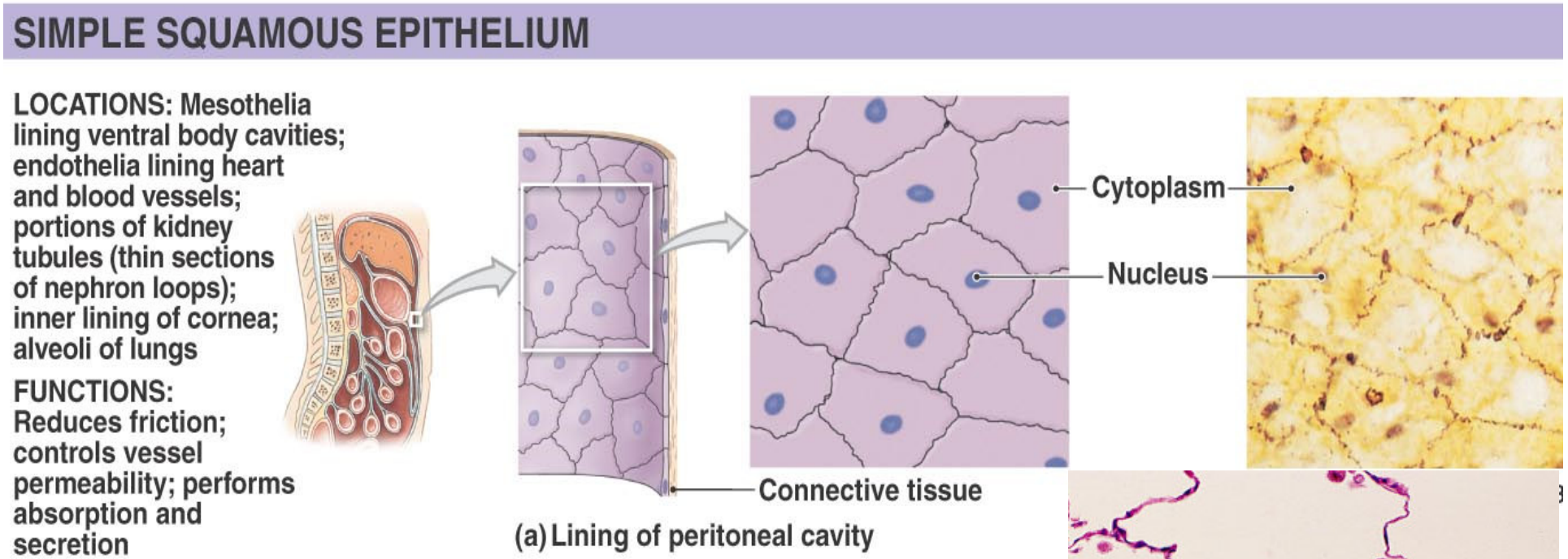
SIMPLE COLUMNAR EPITHELIUM

- Mainly associated with absorption & secretion
- Lines digestive tract (stomach → rectum)
  - Microvilli on apical surface of absorptive cells
  - Mucus-secreting goblet cells
  - May possess cilia

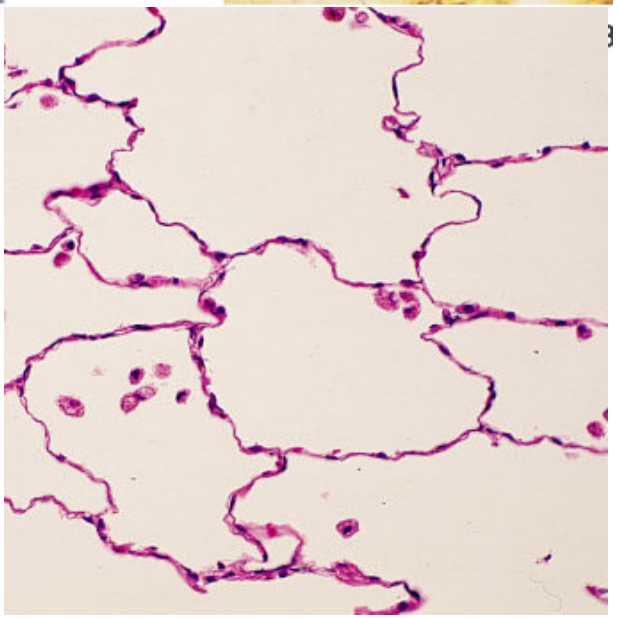




Simple Squamous Epithelium



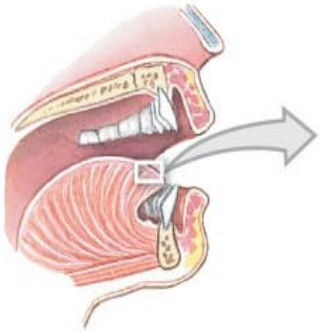
- flat cells with sparse cytoplasm, highly permeable
- found in protected regions where exchange/absorption occurs or a slippery surface reduces friction (i.e. lung aveoli; serous membranes)

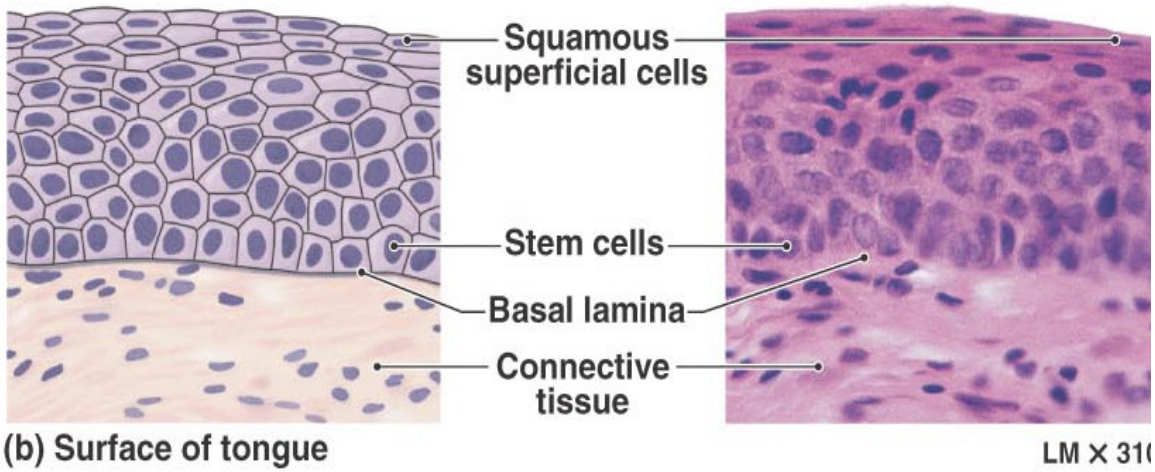


STRATIFIED SQUAMOUS EPITHELIUM

LOCATIONS: Surface of skin; lining of mouth, throat, esophagus, rectum, anus, and vagina

FUNCTIONS: Provides physical protection against abrasion, pathogens, and chemical attack

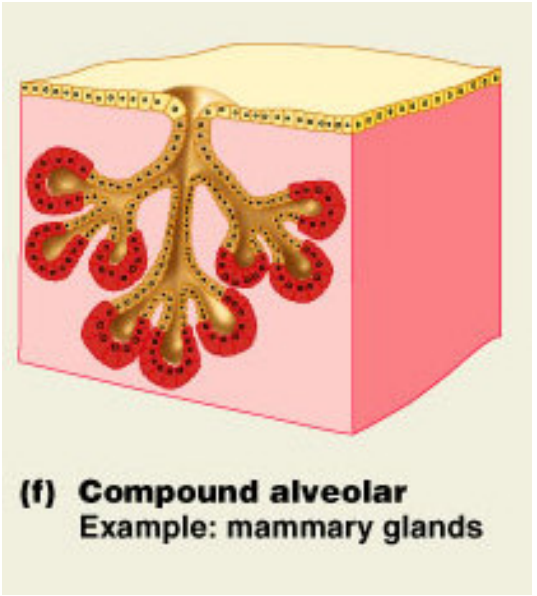




- most widespread type of stratified epithelia, withstands severe mechanical stresses and abrasion
- found in areas subjected to wear and tear: external part of skin, extending into body openings directly continuous with skin (oral cavity, etc.)
- surface cells are squamous (in epidermis even without nucleus) but packed with keratin filaments
- cells in deeper layers are cuboidal or columnar, the most basal layer is usually the only proliferative zone

Glandular Epithelia

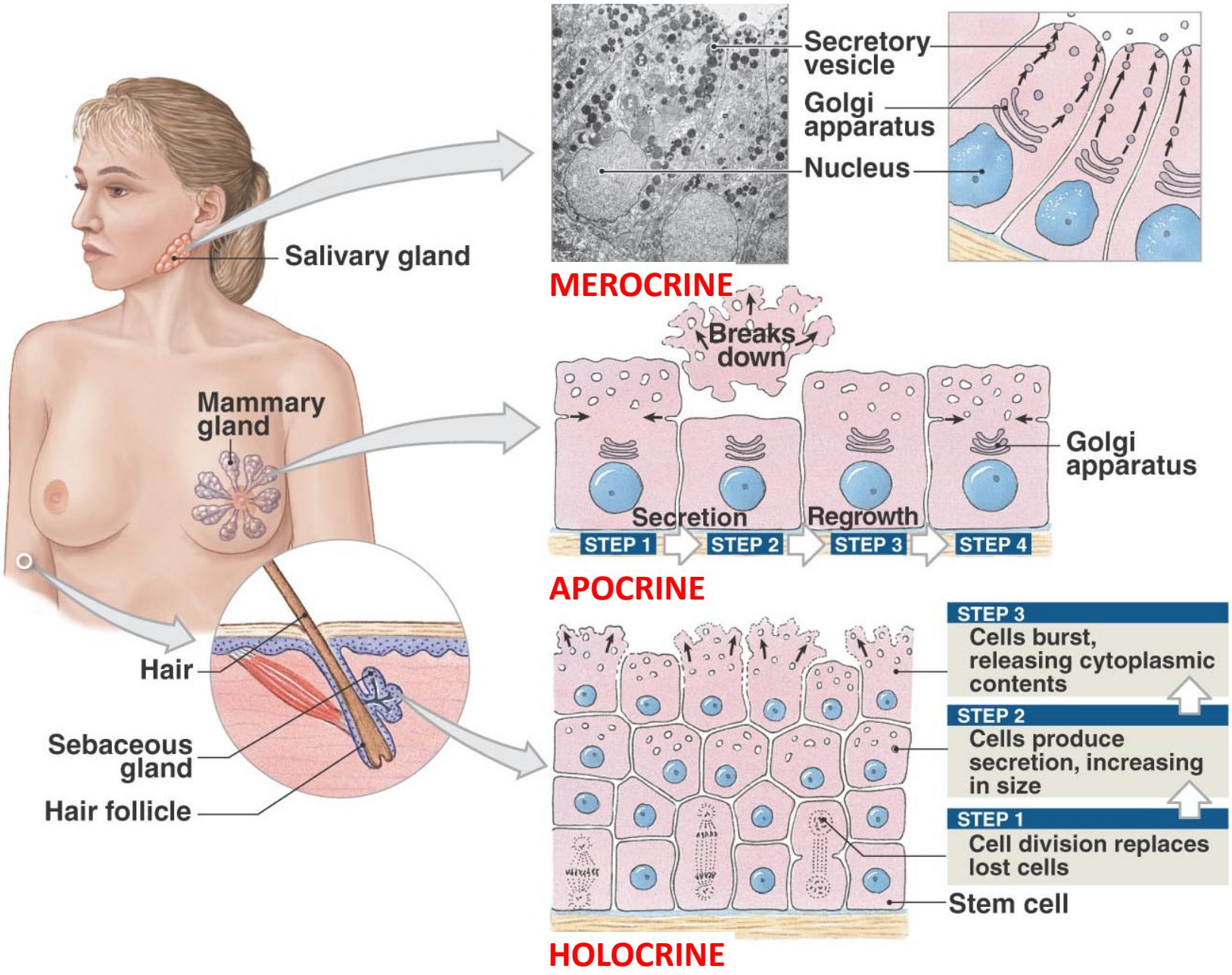
- **Unicellular** – individual secretory cells in epithelia with scattered gland cells: *goblet* and *mucous* cells
- **Multicellular** glands include glandular epithelia and aggregations of gland cells
  - simplest is a secretory sheet that releases secretions into an inner compartment (i.e. protects stomach from acids)
  - most are organized with 2 components, a *secretory portion* (termed ***alveolae*** when forming cyst like structures) and a *duct* to the epithelial surface



(f) Compound alveolar
Example: mammary glands

- Categorized according to their secretion
  - **serous glands** secrete watery fluids rich in enzymes
  - **mucous glands** secrete glycoproteins called mucins that absorb water to form mucus
  - often mixed forms
- **Exocrine glands** discharge secretions onto an epithelial surface (often through an epithelial duct)
- **Endocrine glands** secrete into the fluid surrounding the cell (mostly by exocytosis)

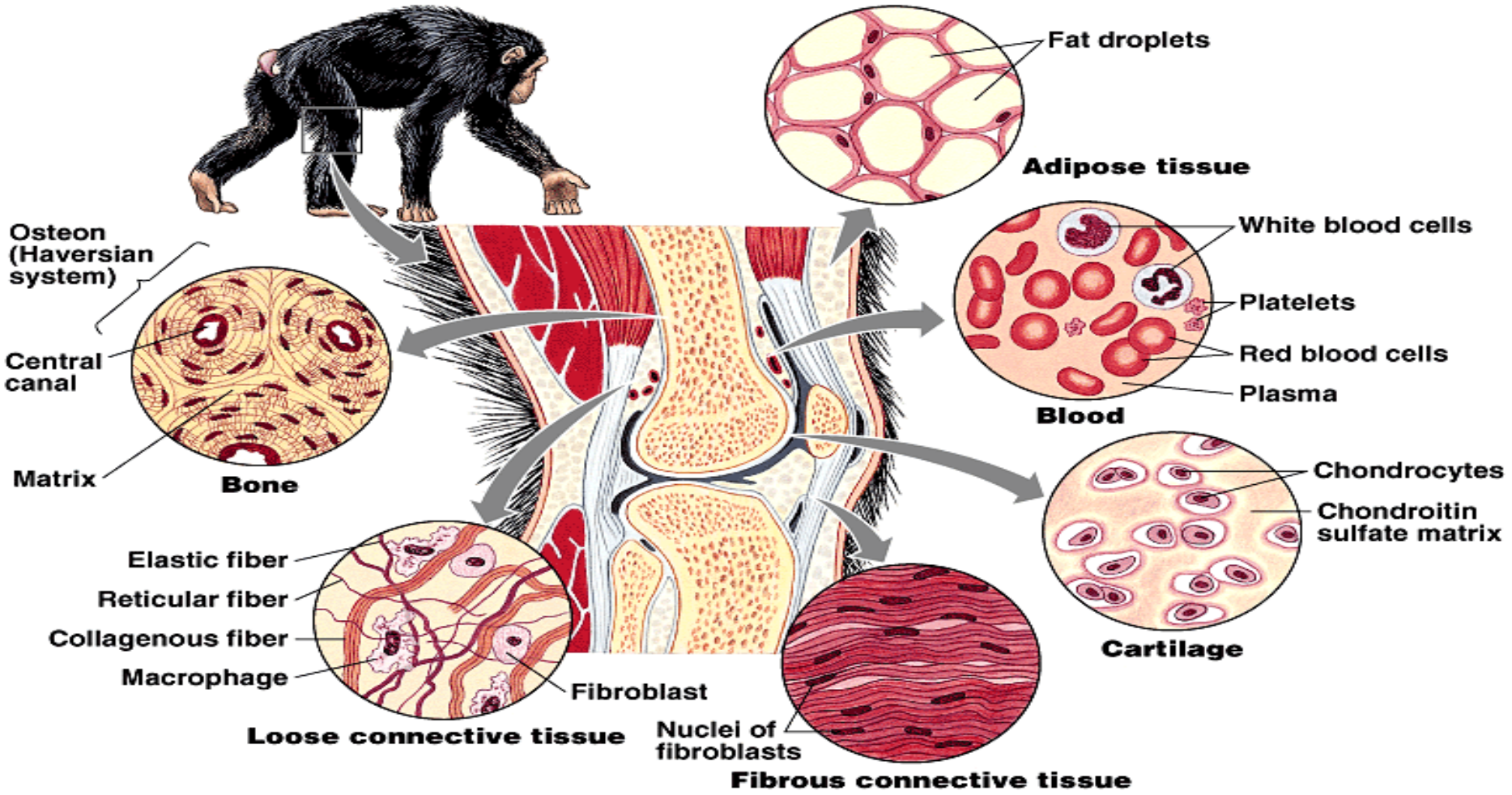
Mechanisms of Glandular Secretion



Modes of Secretion

- **Merocrine** – secretion released through exocytosis
  e.g., Pancreas, sweat & salivary glands
- **Apocrine** – loss of cytoplasm along with secretory product
  - apical portion of the cytoplasm becomes packed with secretory vesicles before it is shed
- **Holocrine** – entire cell becomes packed with secretory products and then bursts apart
  e.g., Sebaceous (oil) glands
  - dying cell replaced by division of remaining cells
  - merocrine and apocrine secretions leave nucleus and Golgi apparatus intact to perform repairs and continue secreting
- Milk production by mammary glands involves both merocrine and apocrine secretions

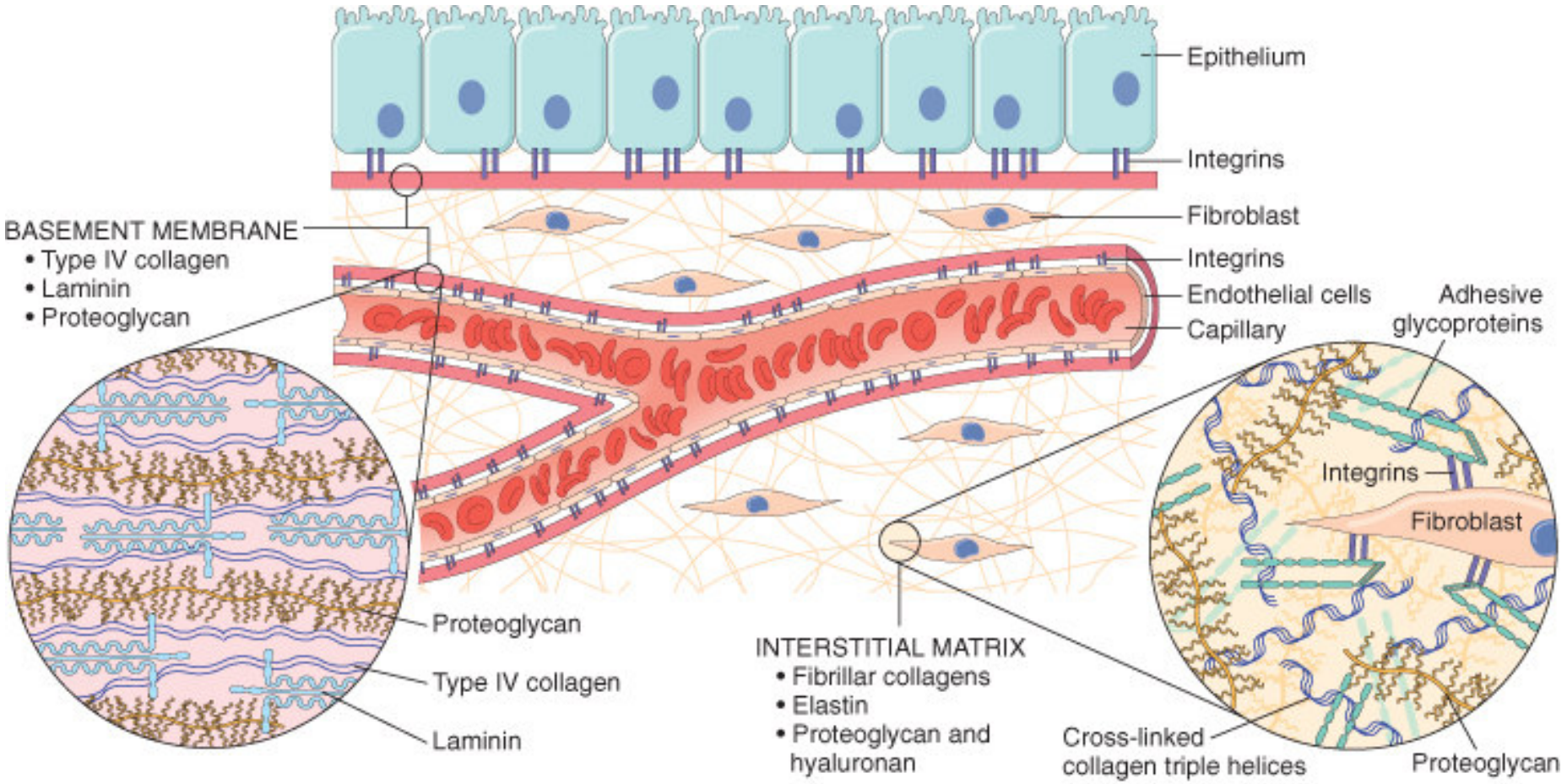
Connective tissue: providing structure and support



Connective Tissues

- Found throughout the body but are never exposed to the outside environment
- Include bone, fat, and blood
- All CT have 3 main components: special **cells**; extracellular (EC) protein **fibers**; **ground substance**
- **matrix** – collective term for the EC component of any CT that is made up of protein **fibers** and the **ground substance** (clear colorless solution of syrup consistency that contains a mixture of glycoproteins and proteoglycans)
- **Loose and Dense CT** depend on proportion of ground substance to cells

The Extracellular Matrix



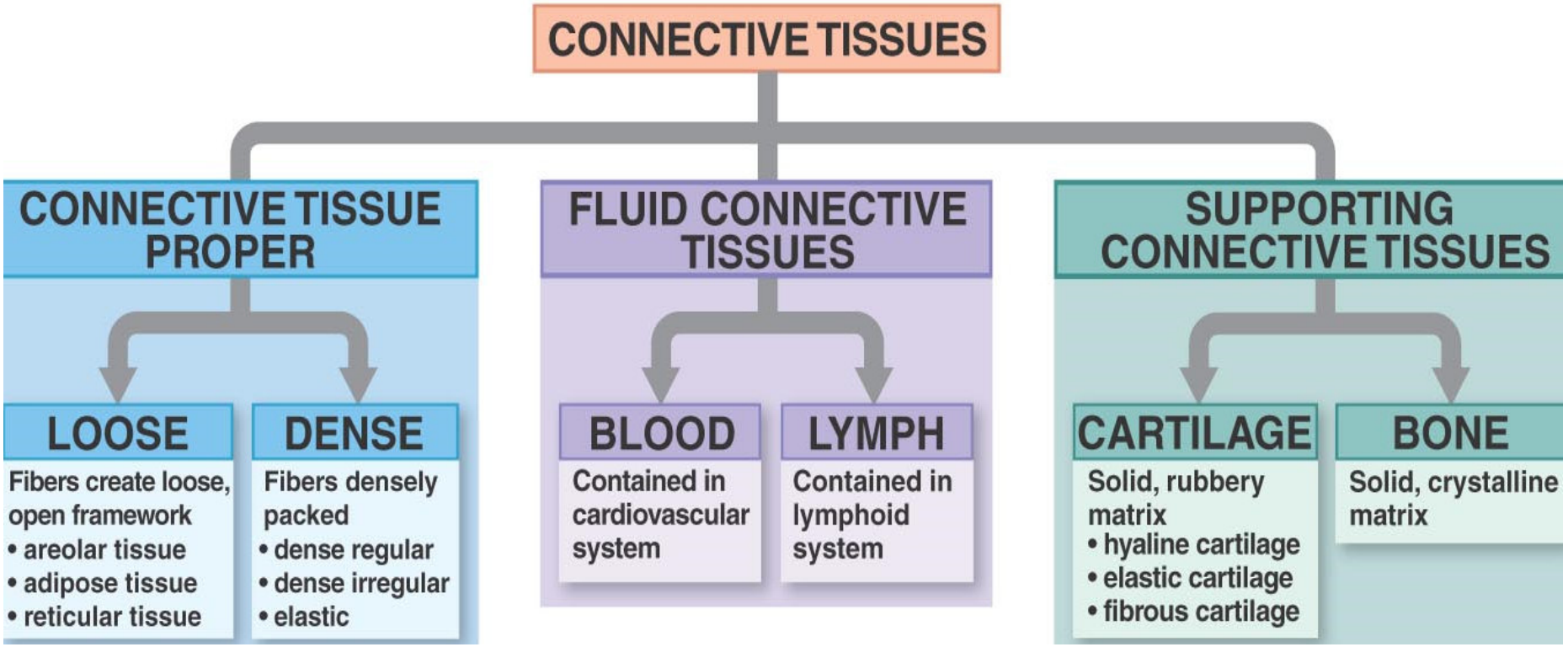
Functions of CTs

- Establishing a structural framework for the body
- Transporting fluid and dissolved materials
- Protecting organs
- Supporting, surrounding, and interconnecting other tissue types
- Storing energy reserves (lipids)
- Defending the body from microorgansims

Note - most CTs have multiple functions, but no single CT performs all of these functions

Classification of CTs

- CT proper – has many cell types and EC fibers in a syrupy ground substance, examples include: adipose (fat) tissue, ligaments, and tendons
- Supporting CT – less diverse cell population than CT proper and a matrix with closely packed fibers: cartilage and bone
- Fluid CT: blood and lymph



CT Proper - Fibers

- **Fibroblasts** (not exclusively) produce all 3 fiber types found in CT
- **Fibrocytes** maintain these CT fibers
- **Collagen** - long, cylindrical fibers made up of 3 subunits coiled around one another (flexible)

  - resists tension and is the most common and strongest fiber
- **Reticular** – thin fibers made up of collagen proteins that form a branching interwoven network

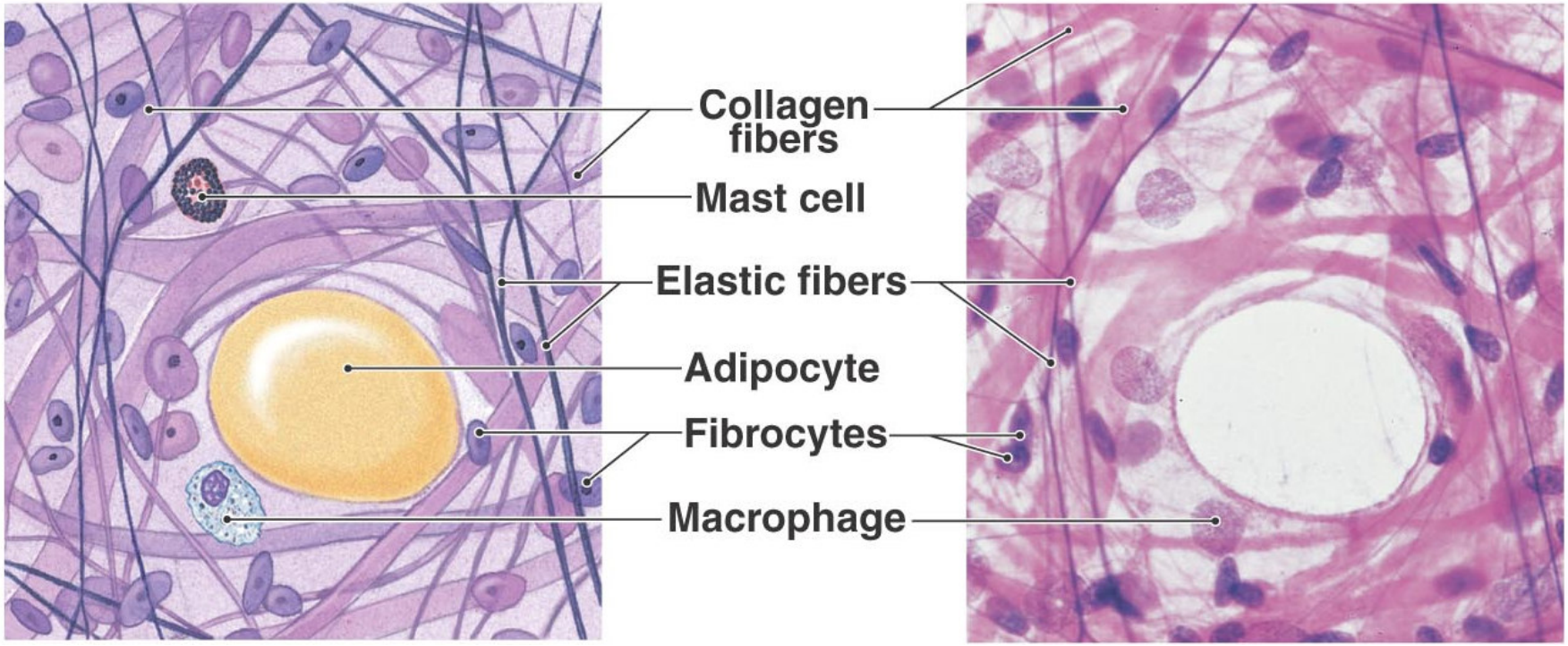
  - abundant in organs such as liver and spleen to create a stroma that resists forces from all directions
- **Elastic** – branching wavy fibers contain the protein elastin

  -stretching up to 150% of their resting length

Areolar – Loose CT

LOCATIONS: Within and deep to the dermis of skin, and covered by the epithelial lining of the digestive, respiratory, and urinary tracts; between muscles; around blood vessels, nerves, and around joints

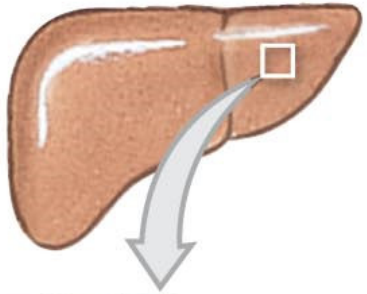
FUNCTIONS: Cushions organs; provides support but permits independent movement; phagocytic cells provide defense against pathogens



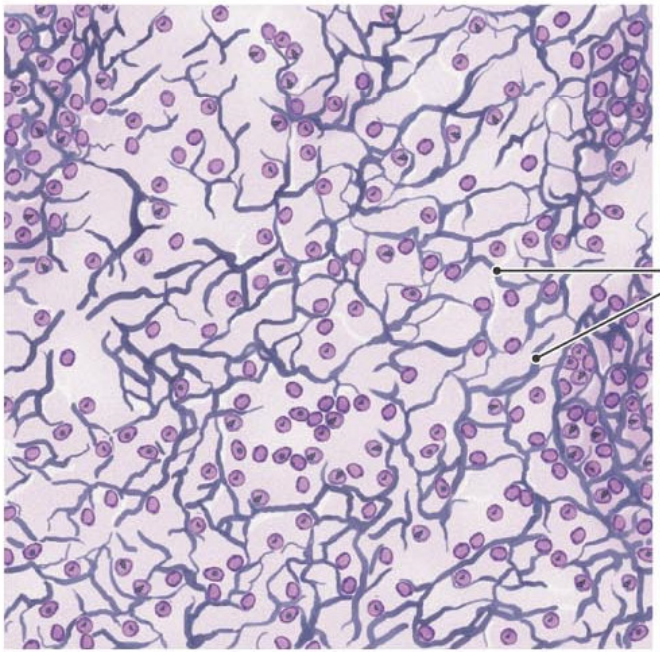
Reticular – Loose CT

LOCATIONS: Liver, kidney, spleen, lymph nodes, and bone marrow

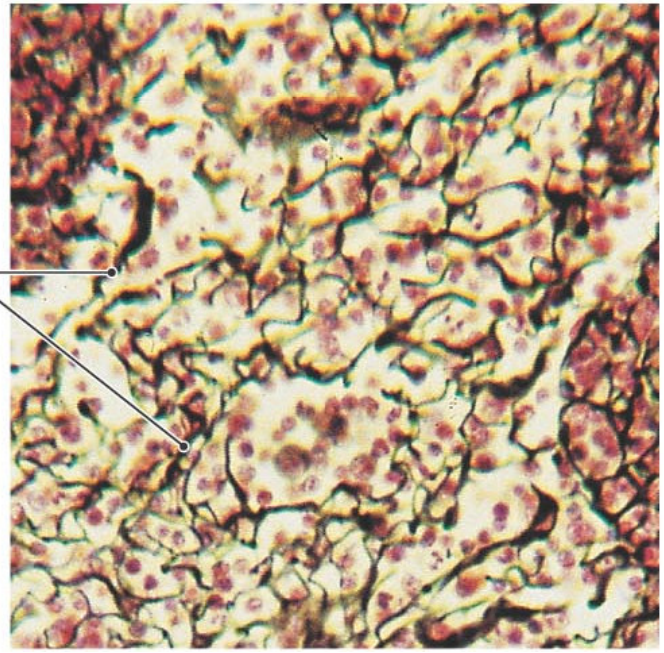
FUNCTIONS: Provides supporting framework



Reticular tissue from liver



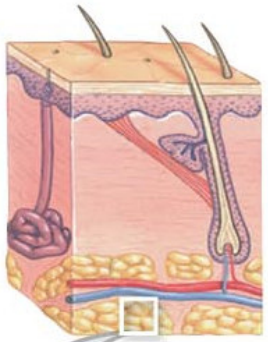
Reticular fibers

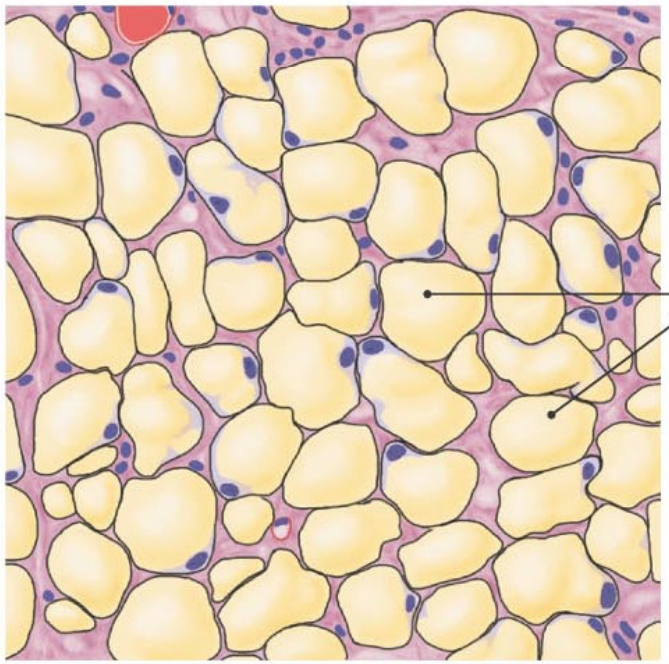


Adipose – Loose CT

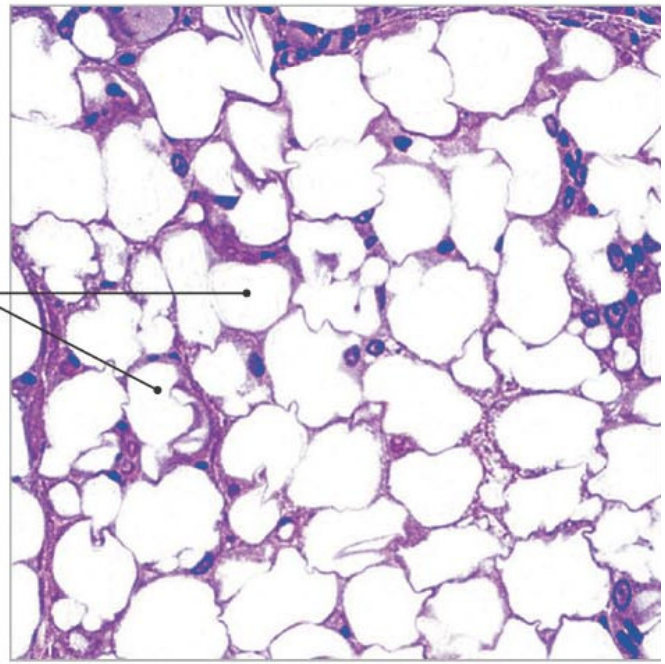
LOCATIONS: Deep to the skin, especially at sides, buttocks, breasts; padding around eyes and kidneys

FUNCTIONS: Provides padding and cushions shocks; insulates (reduces heat loss); stores energy





Adipocytes (white adipose cells)

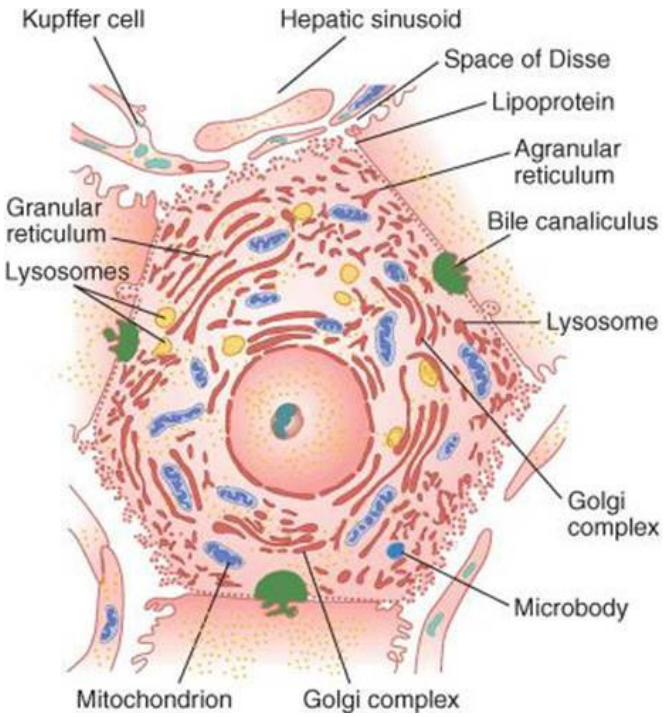


The liver

The liver is one of the largest and most important organs functioning as **exocrine gland** (bile production), **endocrine gland** (metabolic activity) and **blood filter**. The liver is critical for maintaining physiological homeostasis by controlling the metabolite content of the blood, storing nutrients absorbed after a meal and releasing them in a regulated manner between meals.

The liver has a diversity of functions:

- formation and secretion of bile into the intestine (for digestion and absorption of fats and for excretion of lipid-soluble waste products).
- storage of glycogen, buffer for blood glucose.
- synthesis of urea.
- metabolism of cholesterol and fat.
- processing of several steroid hormones and vitamin D.
- detoxification of many drugs and other poisons.
- volume reservoir for blood.
- synthesis and endocrine secretion of many plasma proteins, including albumin, complement proteins and clotting factors.
- catabolism of hemoglobin from worn-out red blood cells.
- cleansing of bacteria from blood.



The hepatocyte, a metabolic power house

The liver lobules

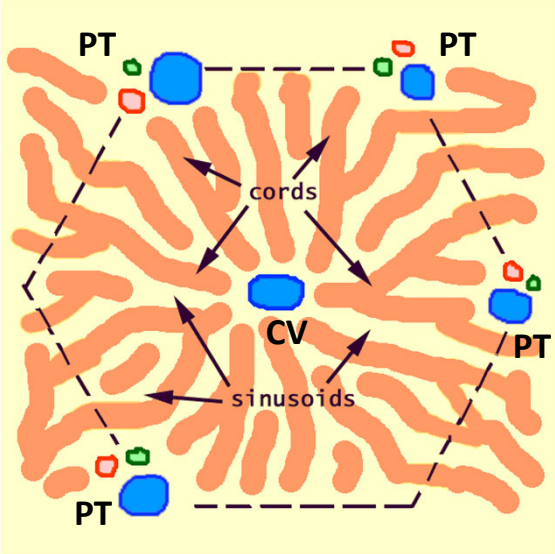
The liver is organized into **lobules** which take the shape of polygonal prisms. Each lobule is typically hexagonal in cross section and contains a **central vein (CV)** which is a branch of the hepatic vein.

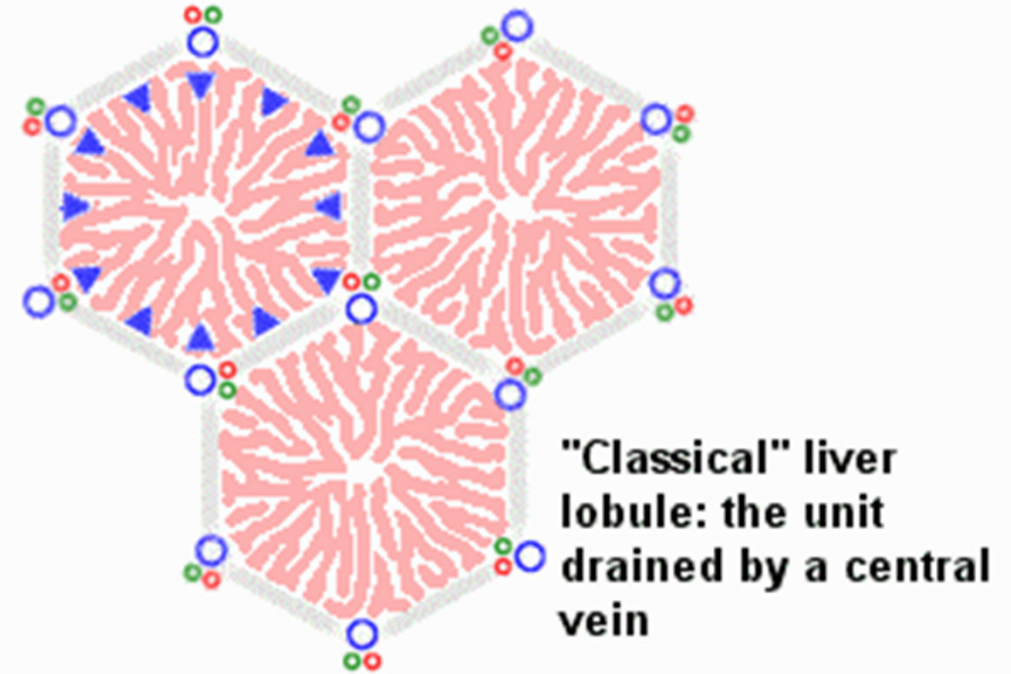
Within lobules, hepatocytes are arranged into 1-cell-thick **hepatic cords** separated by adjacent **sinusoids**.

A fenestrated endothelium lines the sinusoids, with no basement membrane and practically no intervening connective tissue, so that each hepatocyte is exposed on two faces to blood plasma.

At the corners between adjacent lobules are **portal triads (PT)** which include branches of the **bile duct**, the **portal vein**, and the **hepatic artery**.

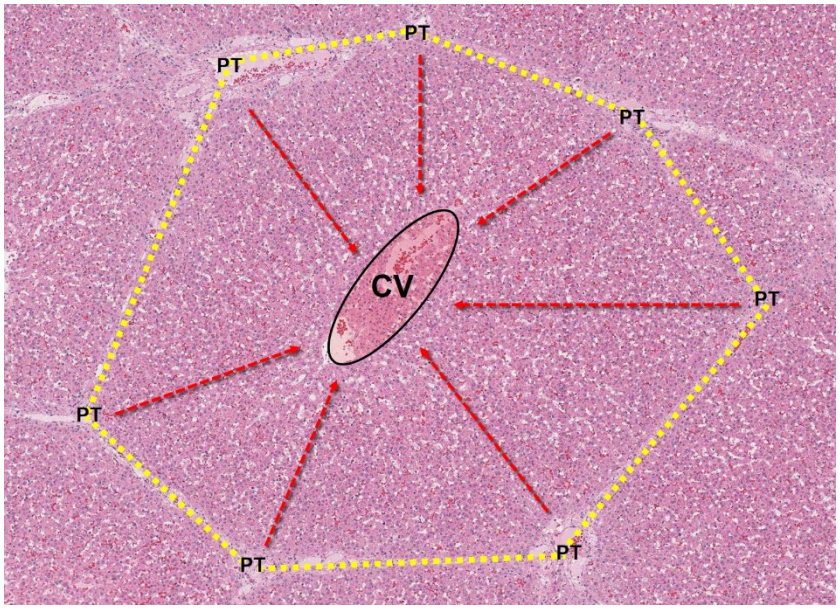
Associated with the sinusoids are stellate **Kupffer cells** -- liver macrophages which extend protrusions into the lumen of the sinusoids where they effectively catch and destroy bacteria which entered the blood in the intestine or aged blood cells.



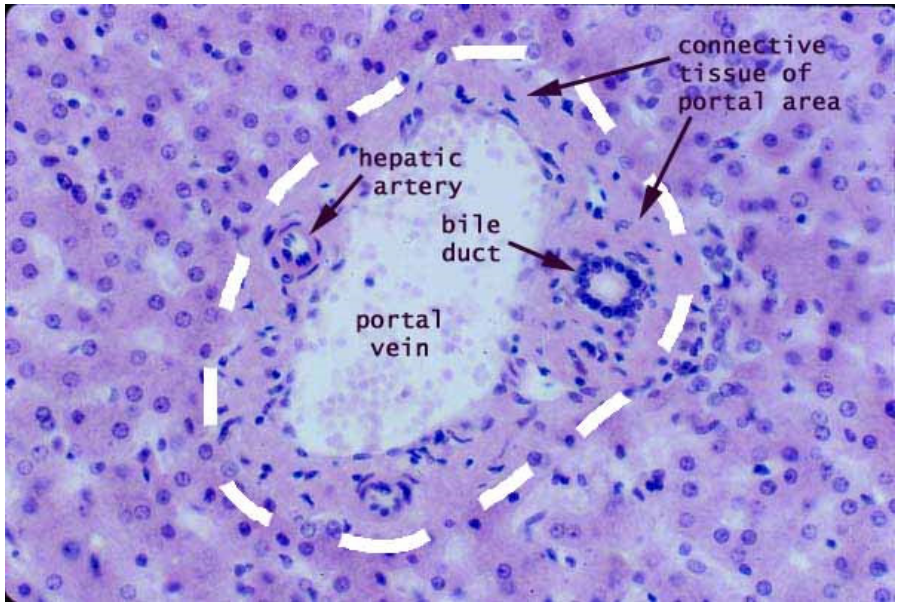


The liver lobule - histology

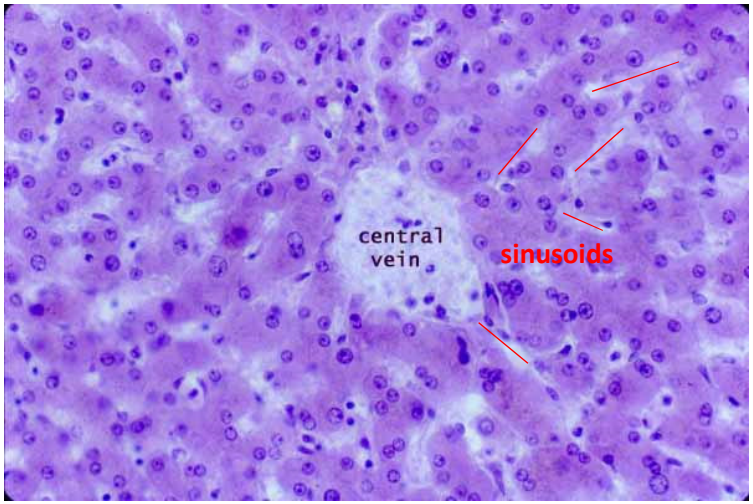
Hexagonal liver **lobule** with **central vein (CV)** and **portal triads (PT)**



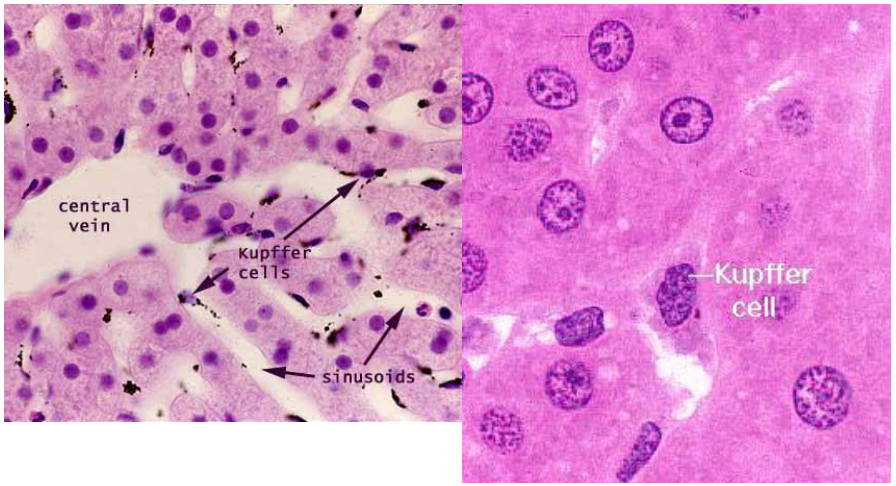
Portal triad with **bile duct**, **portal vein**, and **hepatic artery**



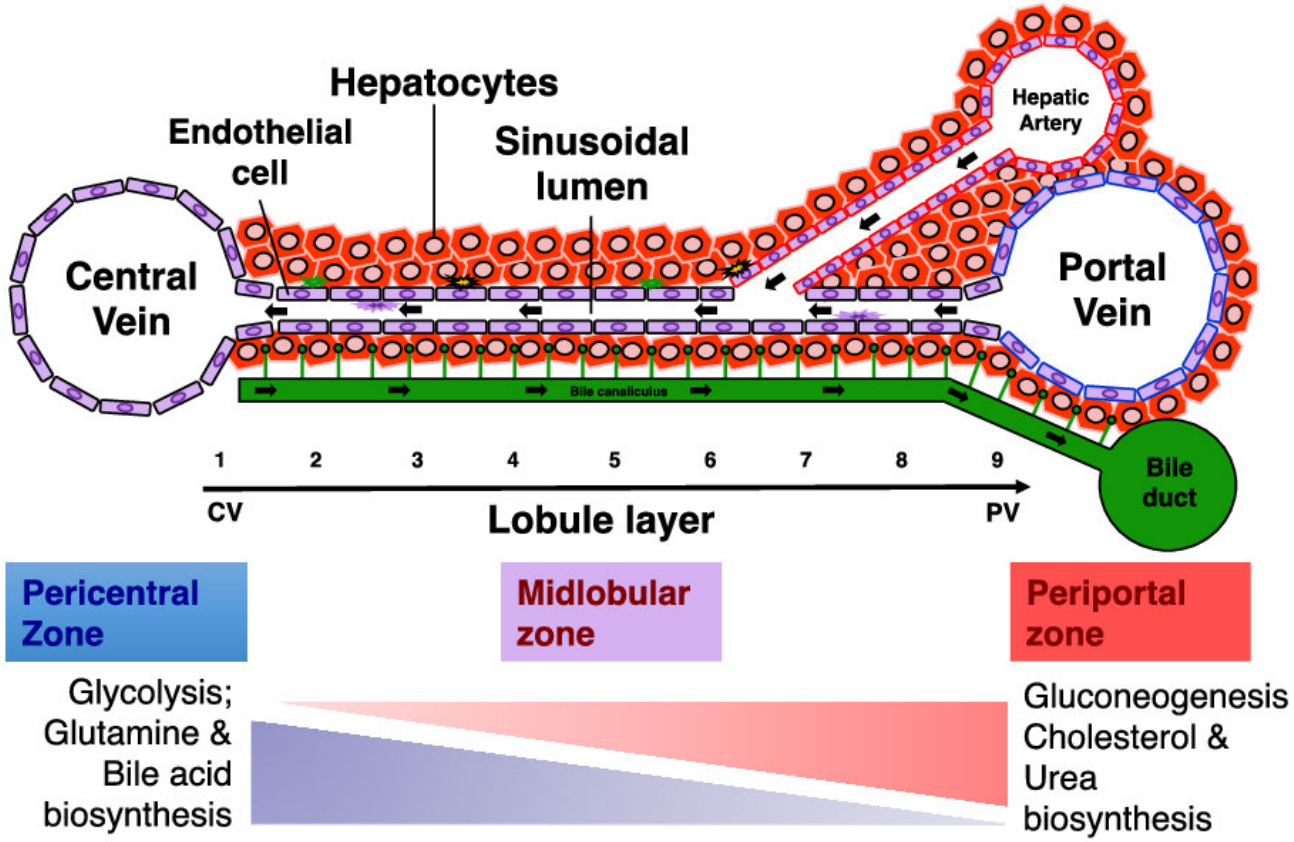
Central vein



Kupffer cells (on the left with phagocytosed carbon particles)



General structure of the liver and liver zonation



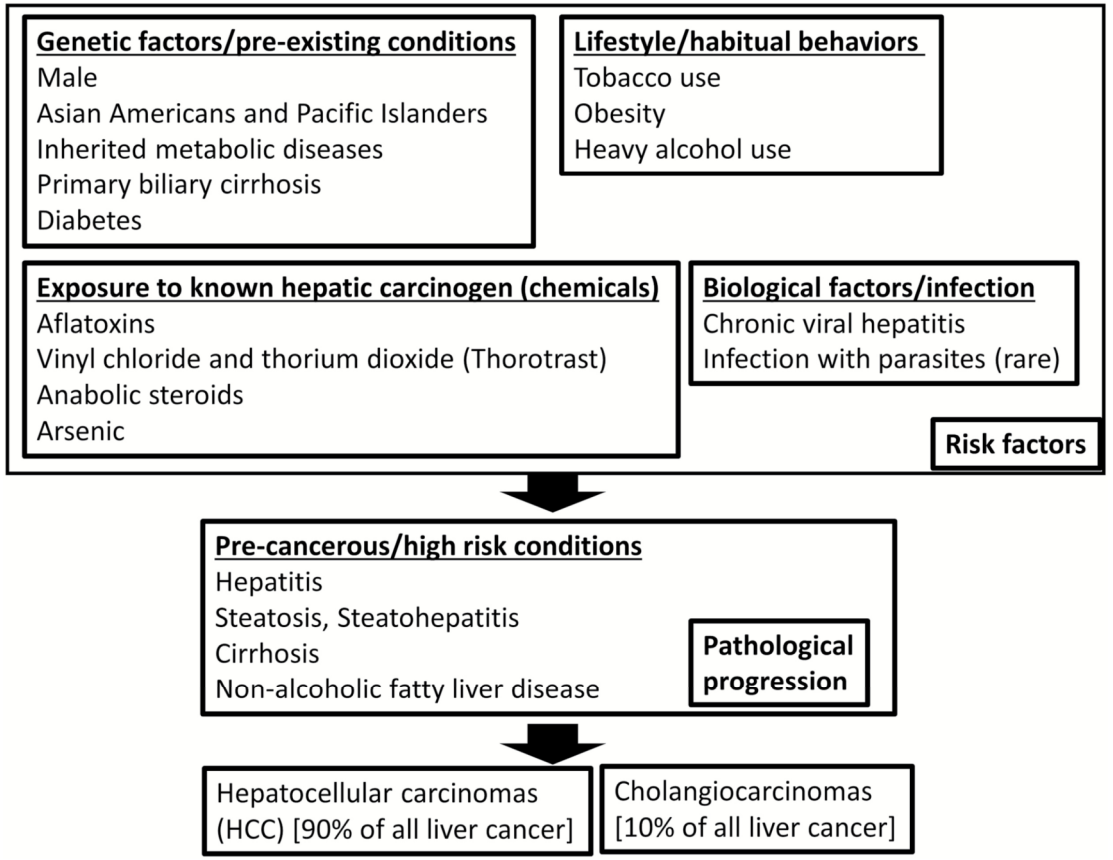
The liver serves as a **filter** for blood coming from the gastrointestinal tract (via the portal vein) and which is (potentially) contaminated by microbiota and toxic molecules and before this blood can reach the rest of the body. This blood is mixed (3:1) with arterial blood and passes through sinusoids between plates of hepatic cells and eventually drains into the hepatic vein. During its passage, the blood is extensively modified chemically and bile is formed on the other side at each plate which will be released into the intestine via the hepatic duct. The liver consumes over 20% of the body's resting oxygen consumption. Hepatocytes residing along the portal-central axis are exposed to different microenvironments (oxygen concentrations), resulting in spatial **zonation** of liver metabolic tasks. About 50% of hepatocyte genes are expressed in a zonated manner creating specialized, functional sub-units.

Liver cancer

Liver cancer has the second-highest worldwide cancer mortality. In contrast to an overall decreasing trend in cancer deaths, the incidence of and deaths by liver cancer have increased in recent years.

Liver cancer is highly resistant to conventional chemotherapy and radiotherapy. For all stages combined, the 5-year survival rate is only 15–17%. Heterogeneity, which can originate from genomic instability, is one reason for this poor outcome.

About 80–90% of liver cancers are hepatocellular carcinoma (HCC), but liver cancer is highly heterogeneous in terms of morphology, genome composition and mutated genes and typically is characterized by intra-patient heterogeneity and clonal evolution.

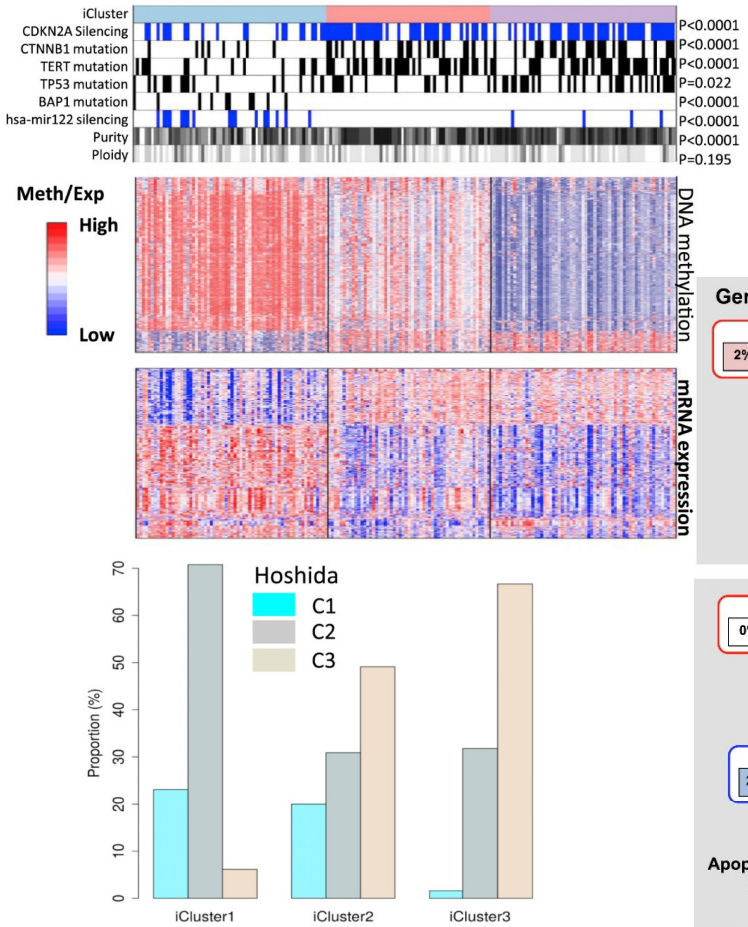


Rao et al., Carcinogenesis 2017

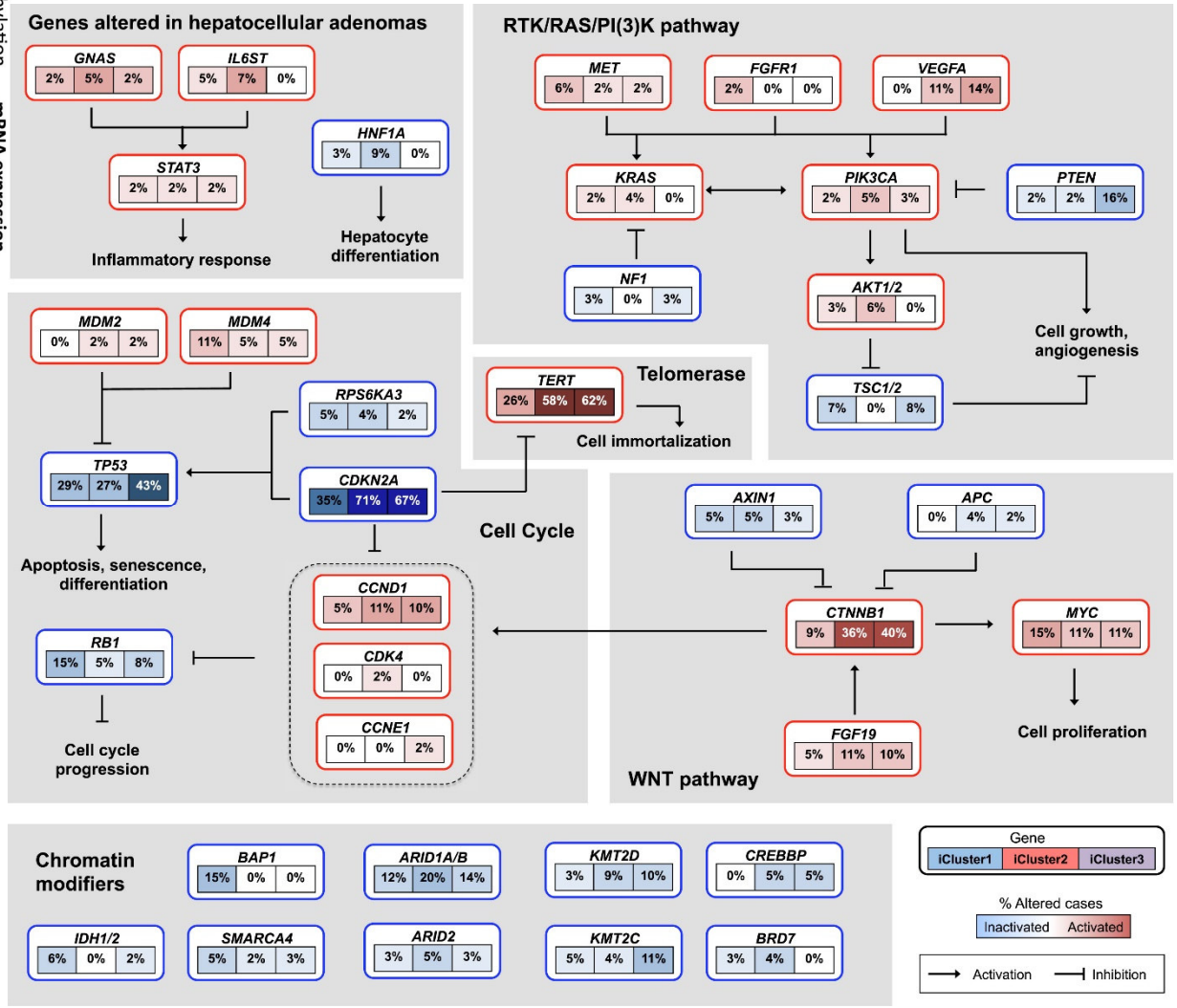
Risk factors and known causes for HCC include genetic factors (e.g. male gender, metabolic syndrome and diabetes), carcinogens (e.g. aflatoxin), lifestyle/habitual behaviors (e.g. tobacco smoking, alcohol abuse and obesity) and biological factors/infection (e.g. hepatitis virus HBV or HCV). These lead to pathological conditions (hepatitis, cirrhosis, steatosis, non-alcoholic fatty liver disease) which typically precede formation of liver cancer.

Liver cancer genetics

WNT pathway members were frequently (44%) mutated or subject to copy number alterations. Other key pathways included cell cycle regulators, RTK kinase signaling and chromatin modifiers. Promoter mutation of TERT is a frequent event.



Three subtypes/clusters of hepatocellular carcinoma were identified based on DNA methylation, mRNA expression, copy number alterations and gene mutations. Cluster1 had significantly worse prognosis and exhibited features such as higher tumor grade and invasion and had the lowest fraction of differentiated cells by Hoshida classification.

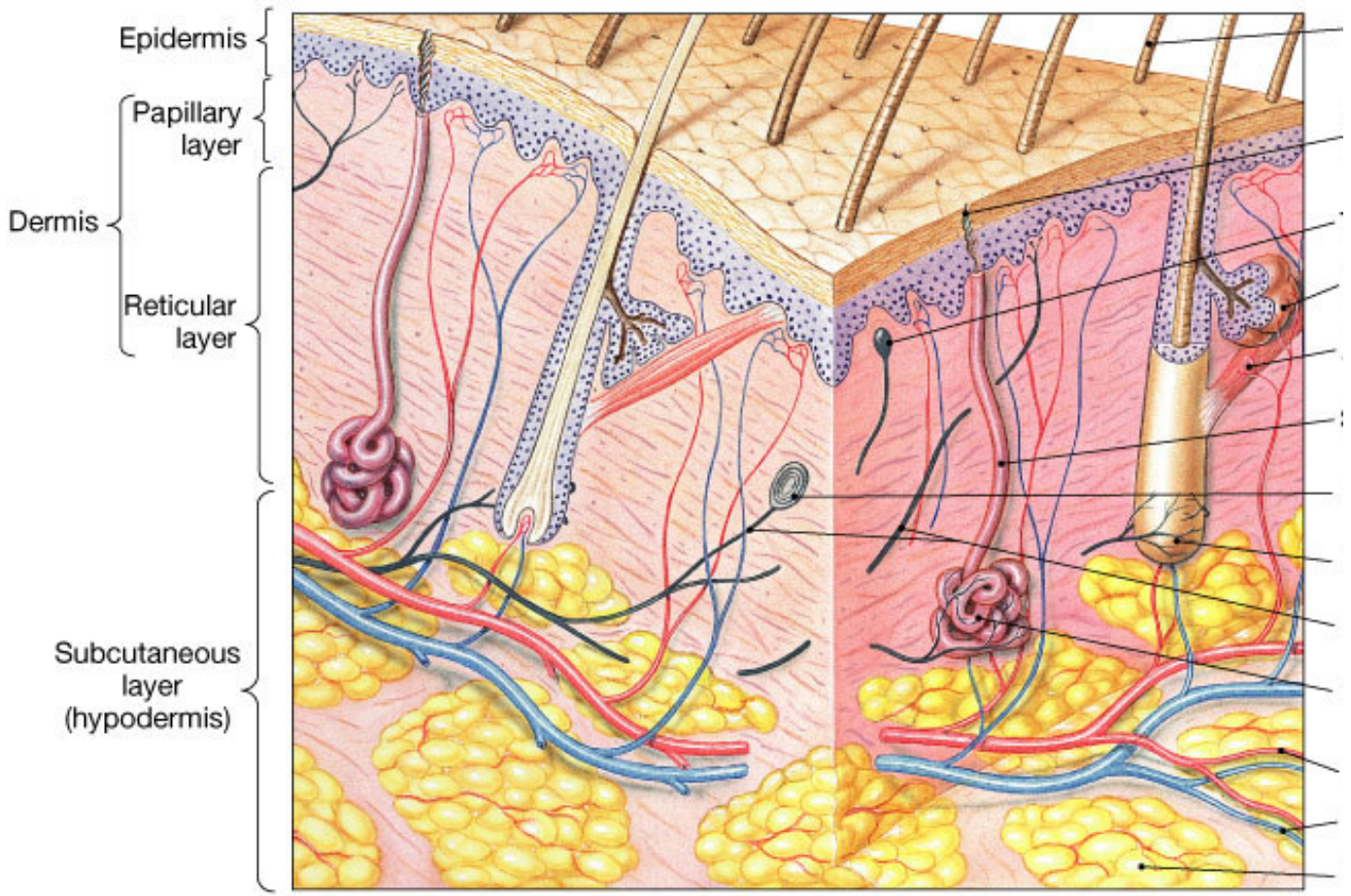


Ally et al., Cell 2017

SKIN

- ~16 % of total body weight ; 1.2- 2.3 m^2 in adults
- Physical protection:
  - Barrier against bacteria, UV, chemicals, friction
- Hydroregulation:
  - Prevents water loss (due to keratin and sebum); but also takes part in gas exchange
- Thermoregulation:
  - Helps regulate body temperature through radiation, evaporation, skin capillaries dilation/constriction
- Cutaneous absorption:
  - Only lipid based chemicals penetrate (significantly) the skin
- Synthesis:
  - Skin synthesizes melanin (color) and Vitamin D (Calcium metabolism)
- Sensory reception:
  - Senses touch, pressure, heat, cold and tissue damage (pain)
- Communication:
  - Reflects emotions through facial expressions, gland secretions (pheromones)

General structure



the skin consists of

- **epidermis**: an epithelial layer of ectodermic origin
- **dermis**: a layer of connective tissue of mesenchymal origin
- **hypodermis** or subcutaneous tissue: a layer of loose connective tissue that may contain pads of adipose cells, the **panniculus adiposus**

- **skin appendages -** either **keratinised** (hair and nails) or **glandular** (sebaceous and sudoriferous glands)

Epidermis

stratified squamous epithelium

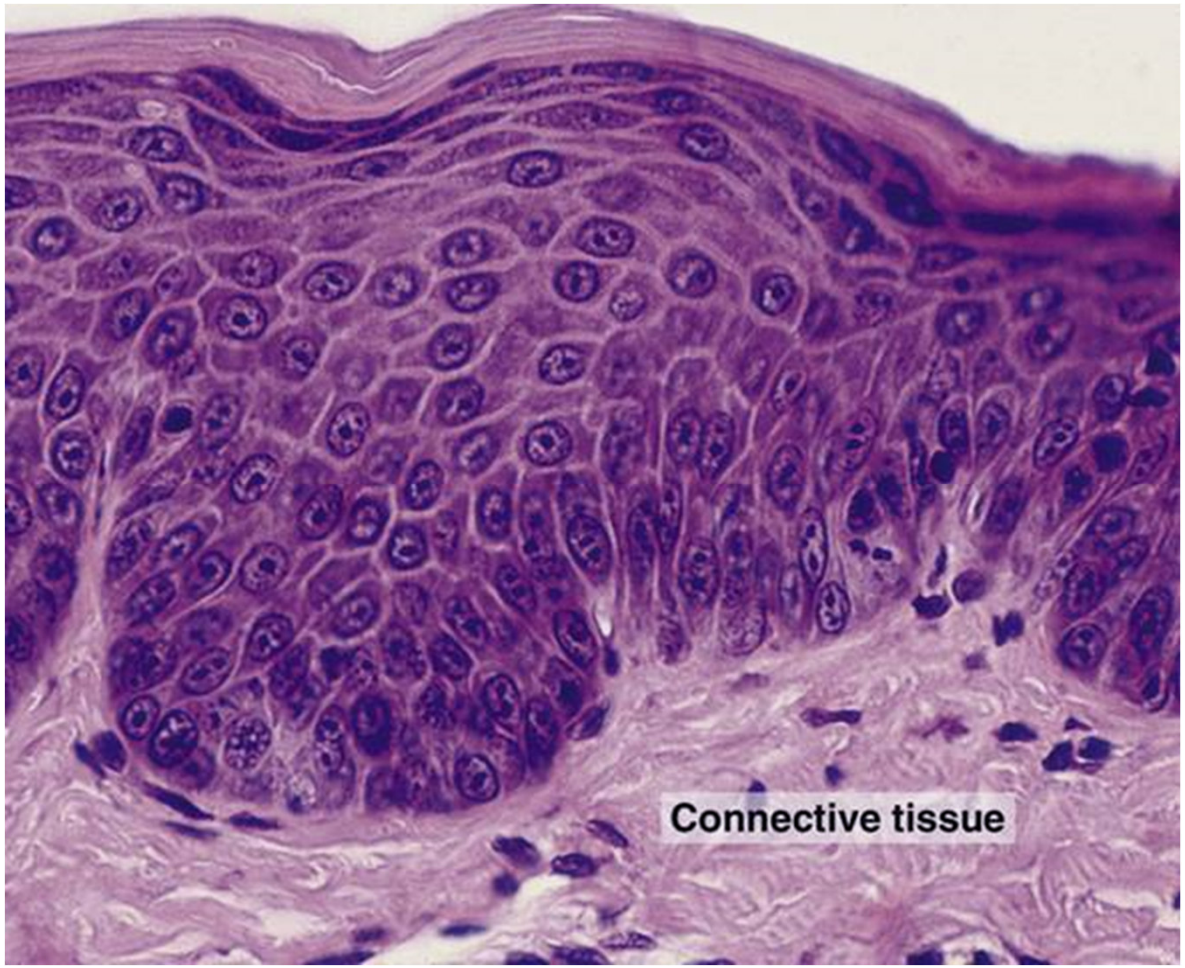
cells are called **keratinocytes**

contains 3 less abundant cell types:
melanocytes, **Langerhans cells**, and **Merkel´s cells**

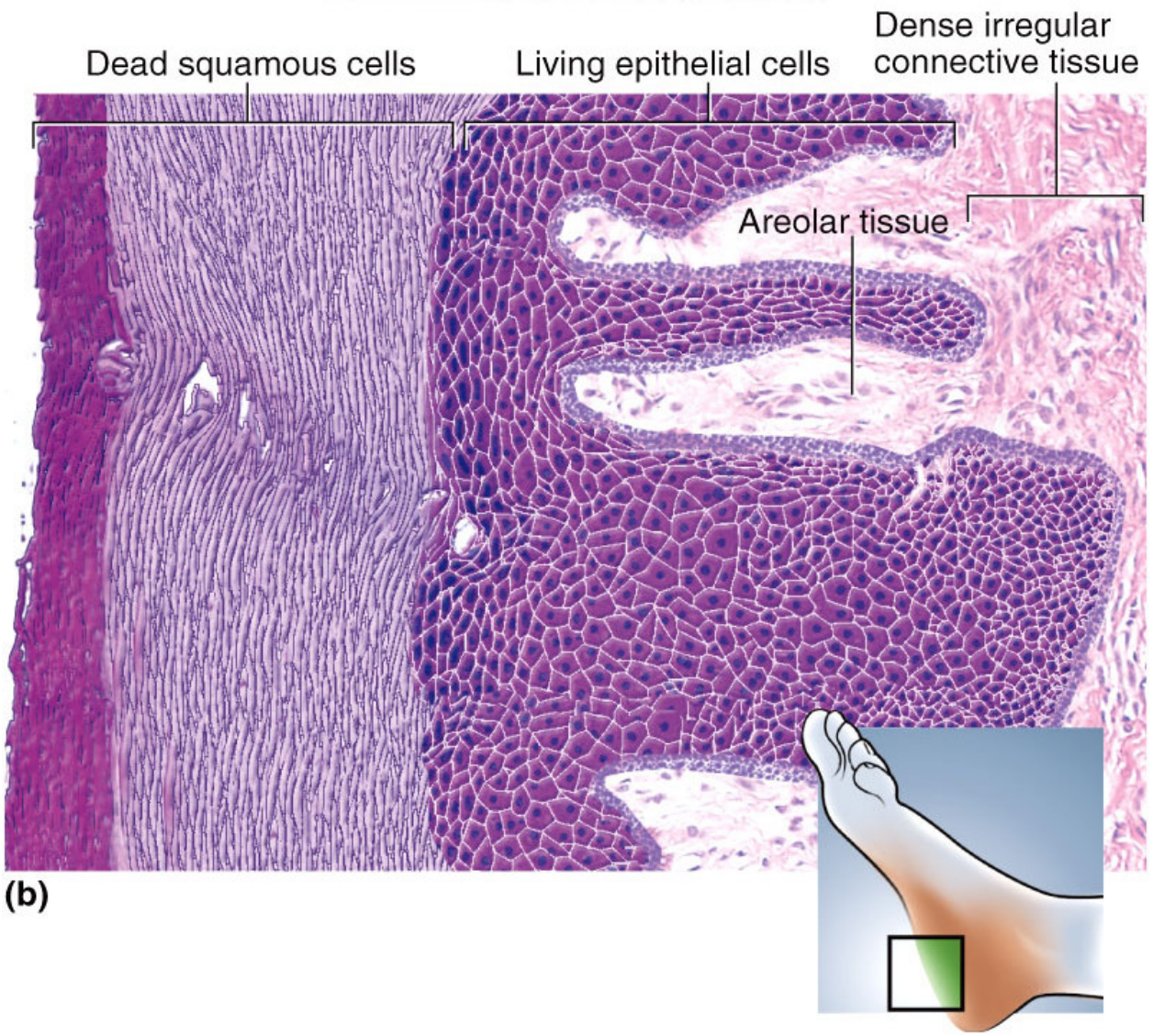
2 types of the skin are distinguished:

the **thick (glabrous) skin** (*600-800 µm)*
- found on palms and soles

the **thin (hairy) skin (***75-150 µm)*
- found elsewhere on the body surface



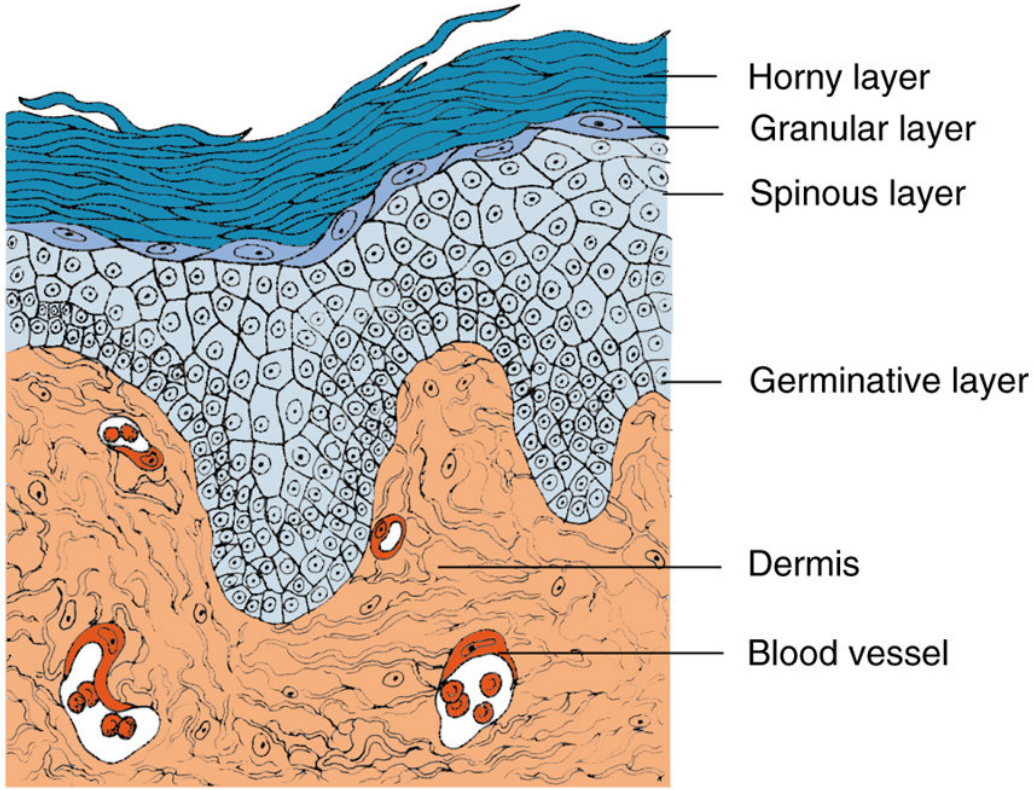
Glabrous skin



How does skin develop and differentiate?

Epidermis: the largest derivative of ectoderm forms the outer layer of the skin.
It is an epithelium and cells are connected by desmosomes and tight junctions.

The epidermis consists initially of two layers: periderm (a temporary outer layer) and the germinative layer below. The germinative layer contains stem cells that divide actively to produce differentiated progeny. The basal layer develops from the germinative layer (it contains stem cells in the adult).



Spinous layer forms as cells are squeezed out of the basal layer. They become large and differentiate.

Granular layer starts making keratin granules

Cornified or horny layer is composed of dead cells that are filled with keratin

It takes cells about 7 days to journey through the skin

Epidermal layers

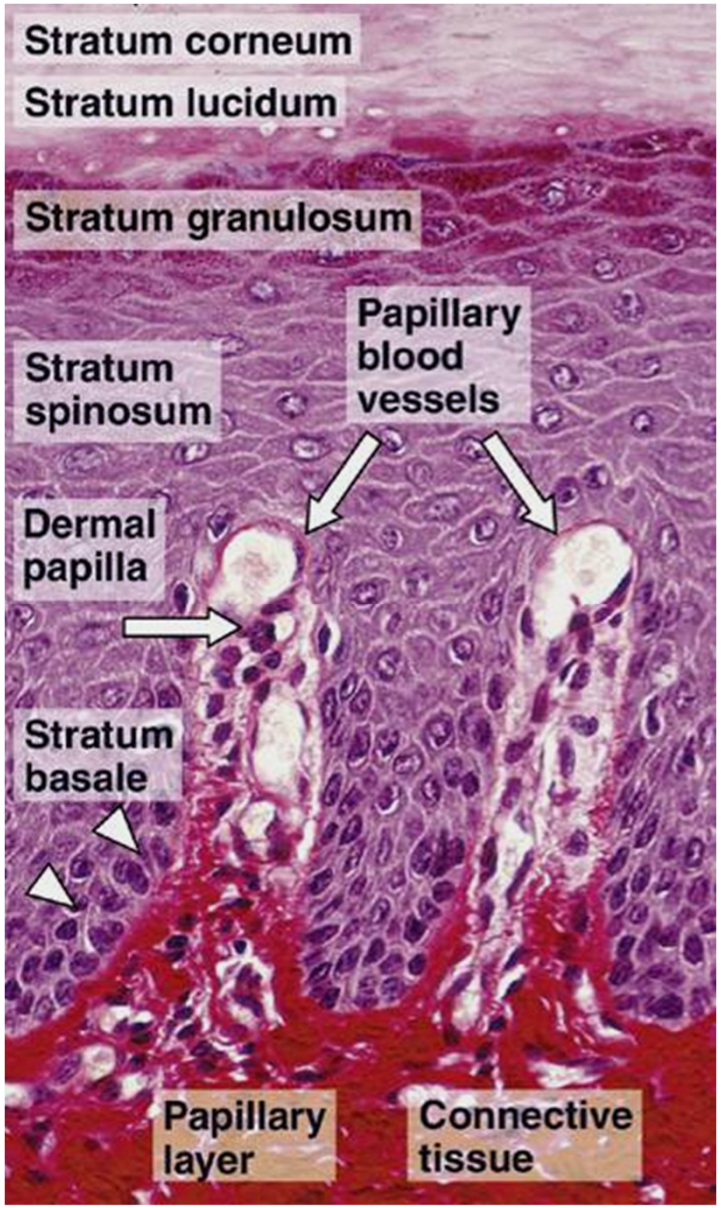
5. Stratum corneum: lies at the surface, consists of 15-20 layers of flattened , non-nucleated keratinised cells whose cytoplasm is filled with a birefringent filamentous scleroprotein **– keratin**

4. Stratum lucidum : translucent and thin, it lacks regularly in the thin skin; the layer contains dead, anucleated and eosinophilic cells, desmosomes are still evident

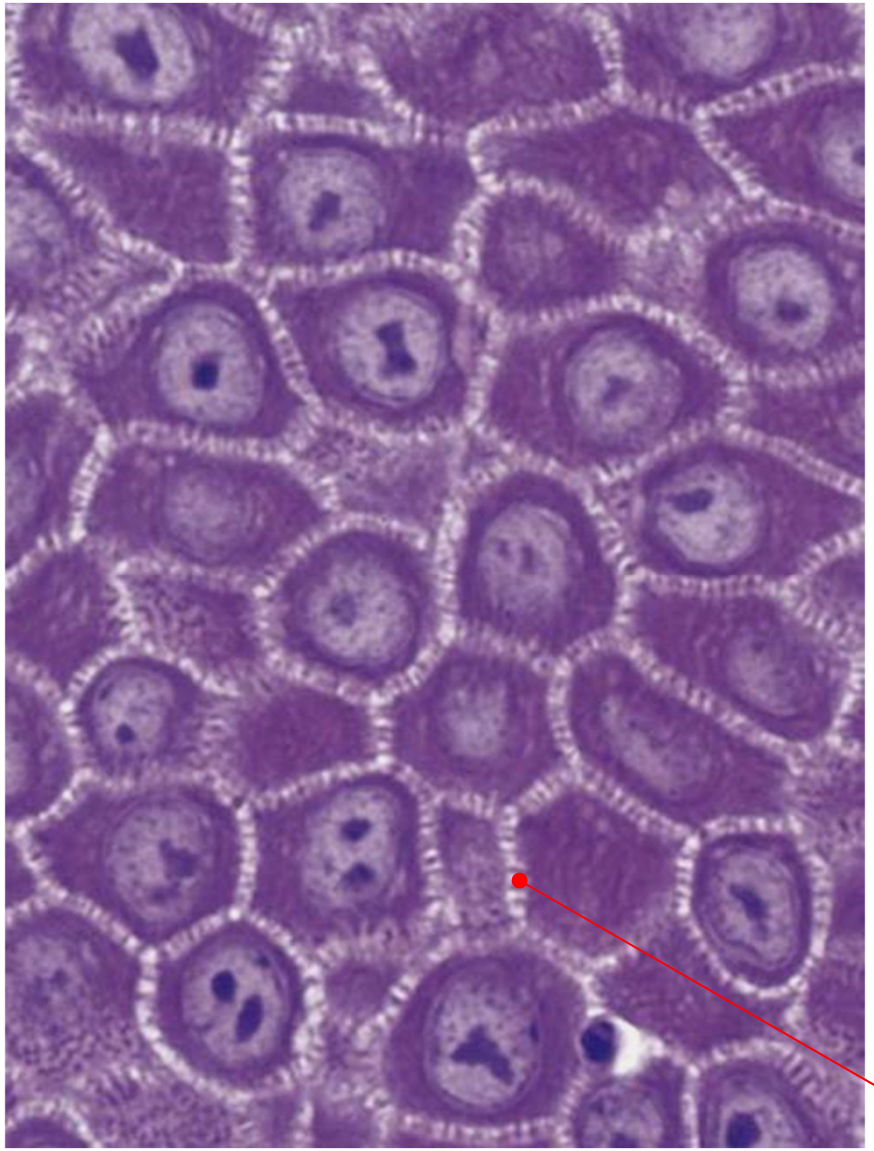
3. Stratum granulosum: 3 - 5 layers of flattened polygonal cells with **keratohyalin granules** and **membrane-coated lamellar granules** (composed of lamellar discs formed by lipid bilayers)

2. Stratum spinosum: consists of cuboidal, polyhedral, or slightly flattened cells, the cytoplasm projects into processes that are filled with bundles of tonofilaments (under light microscope as tonofibrils), contains cytokeratin filaments and numeruous desmosomes

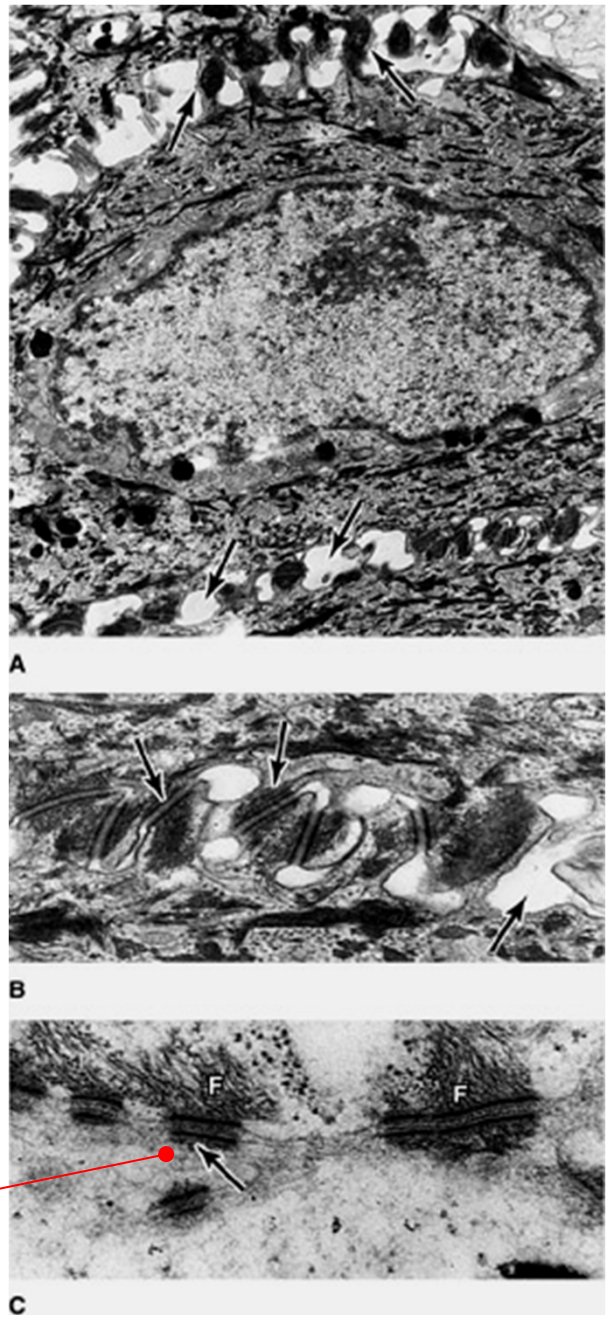
1. Stratum basale (stratum cylindricum): a single layer of basophilic columnar or cuboidal cells, intense mitotic activity



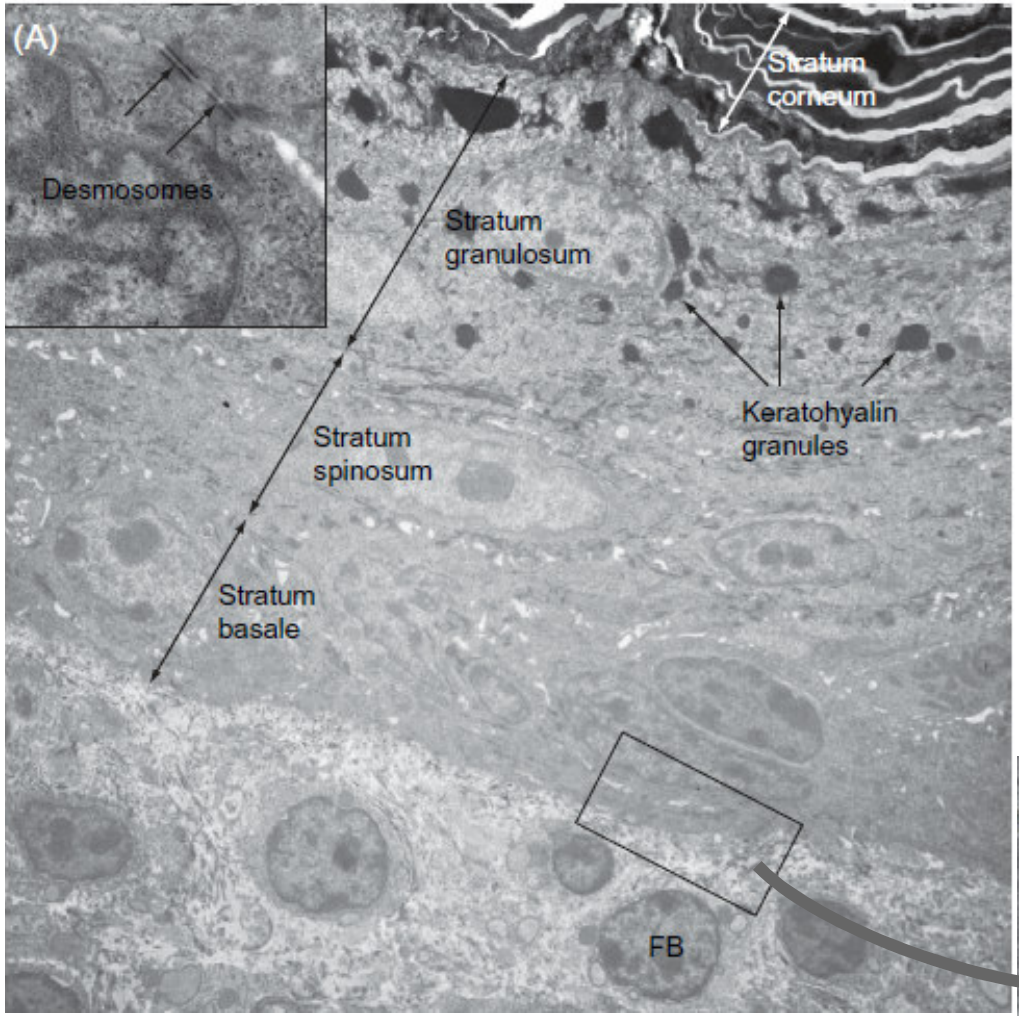
Stratum spinosum



desmosomes

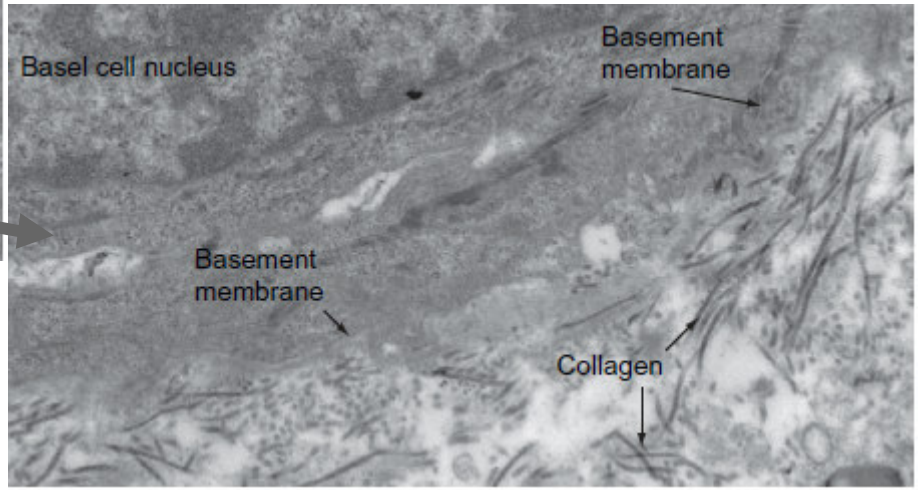


Basic ultrastructure of the skin



transmission electron micrograph of the epidermis with basement membrane, stratum basale, stratum spinosum (cells held together by desmosomes; insert), stratum granulosum, and stratum corneum

below the basement membrane are a mixture of fibroblasts (FB) and collagen bundles

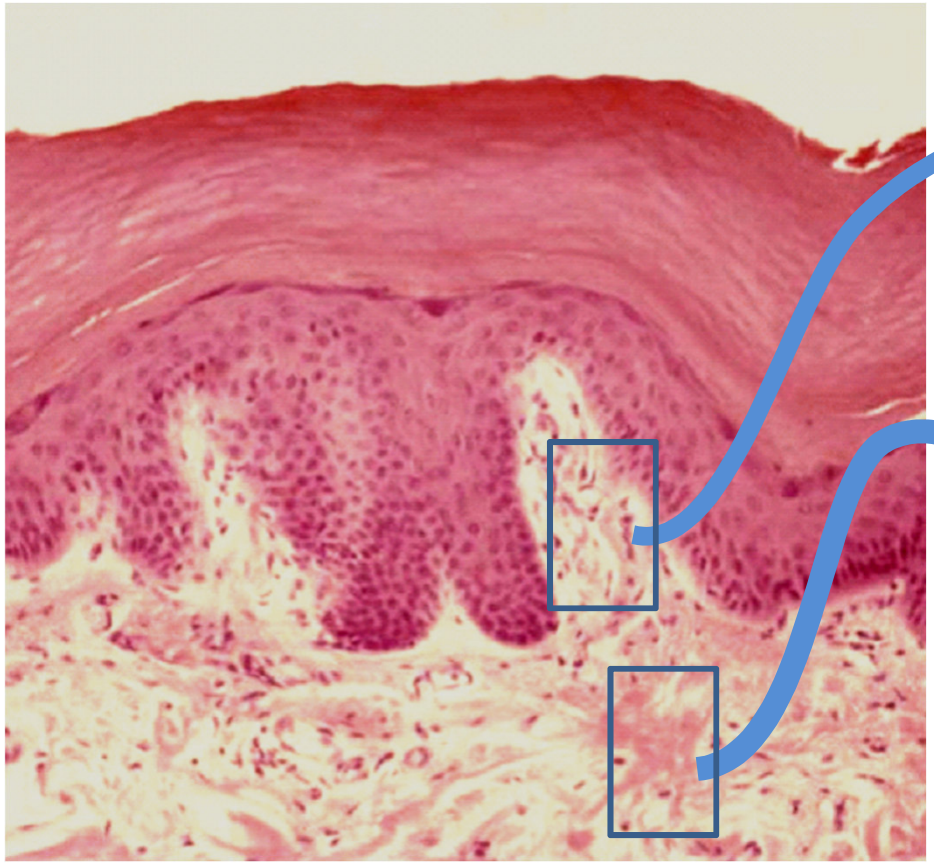


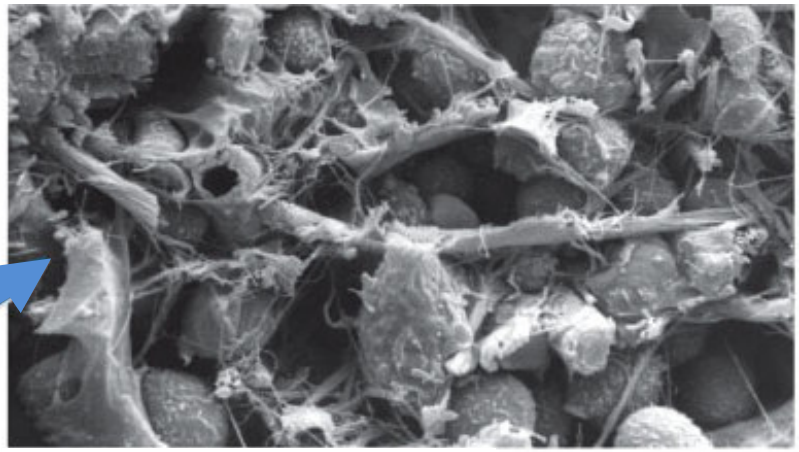
Dermis

it supports the epidermis and reaches a thickness of about 2-4 mm

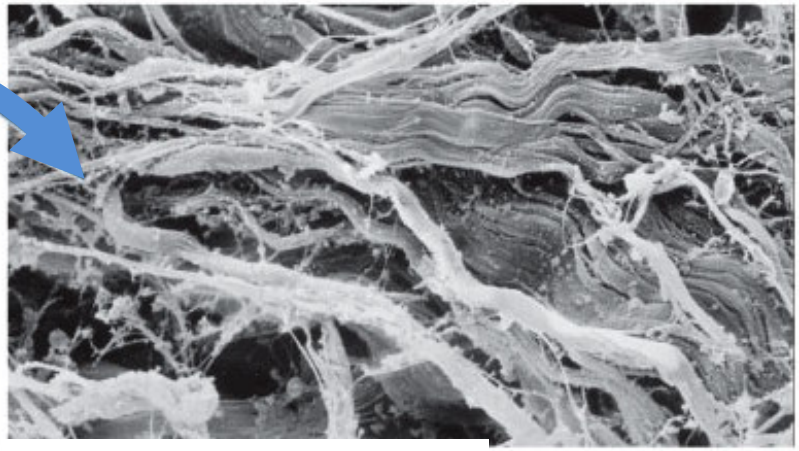
2 layers with rather indistinct boundaries:

- the outermost **papillary layer** (stratum papillare corii) - of loose connective tissue with networks of elastic and reticular fibers
- the deeper **reticular layer** (stratum reticulare corii) - of irregular dense connective tissue (collagen I)
- the principal glycosaminoglycan of the dermis is dermatan sulfate





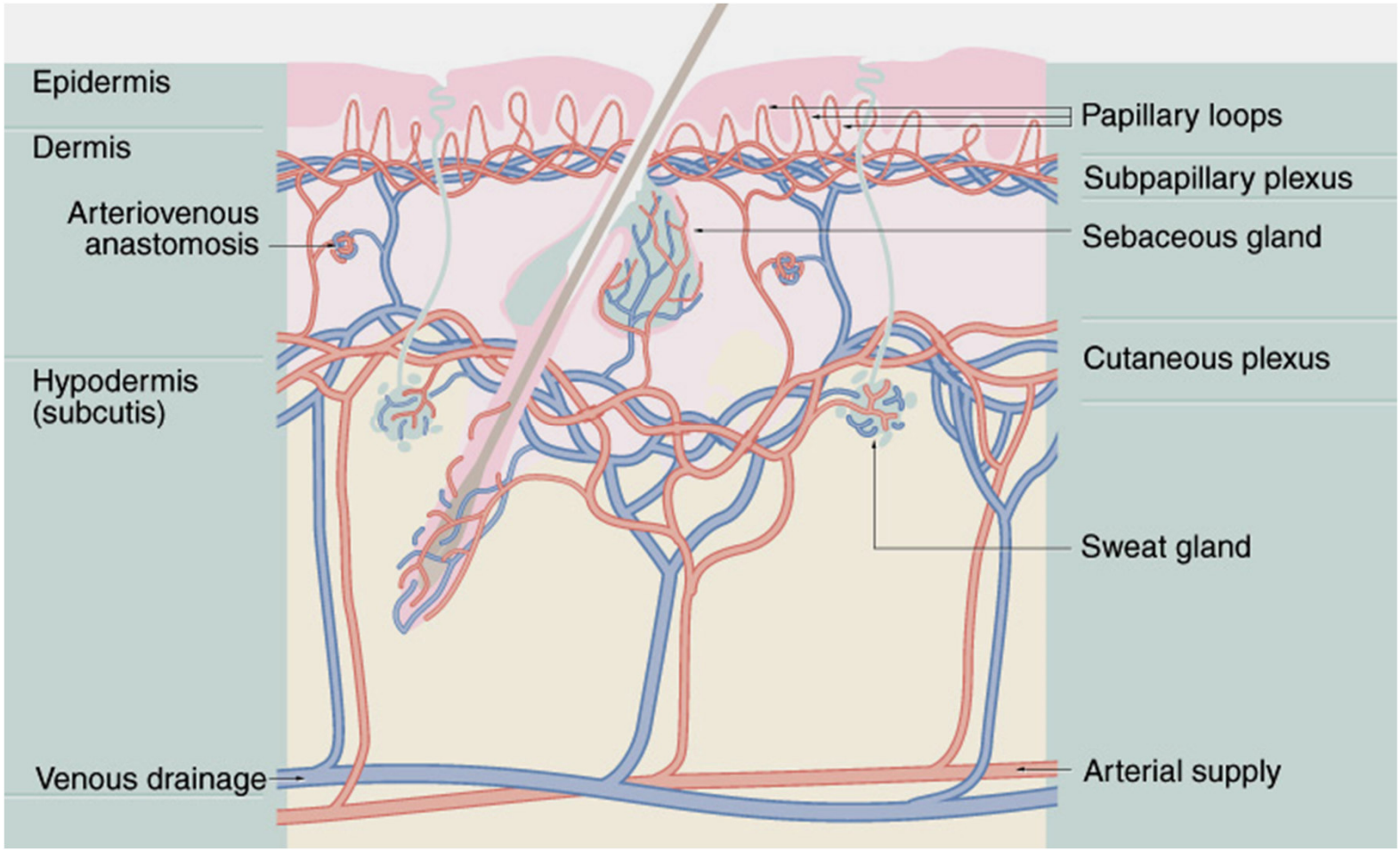
papillary layer of dermis



reticular layer of dermis

Blood supply

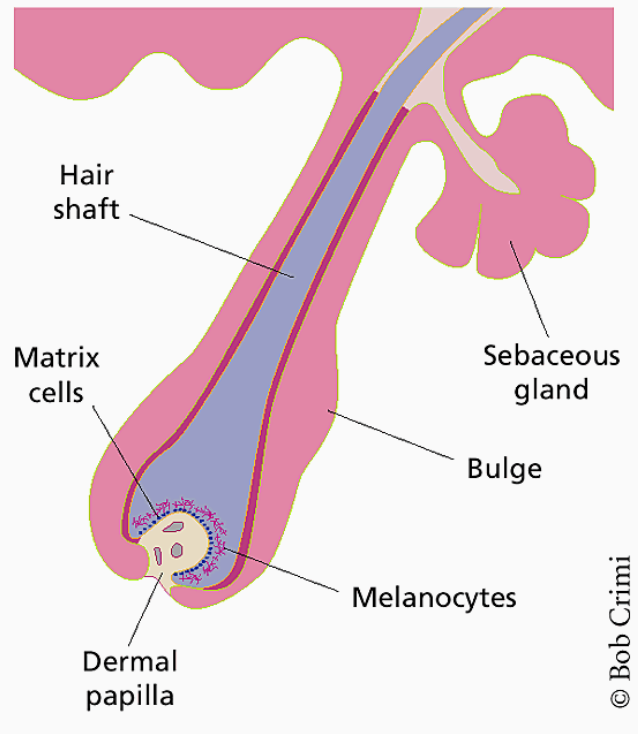
- the epidermis is free of vasculature
- the dermis has a rich network of blood and lymph vessels
- blood may pass through capillaries or directly from arteries to veins via arteriovenous anastomoses or shunts
- these play a very important role in temperature and blood pressure regulation

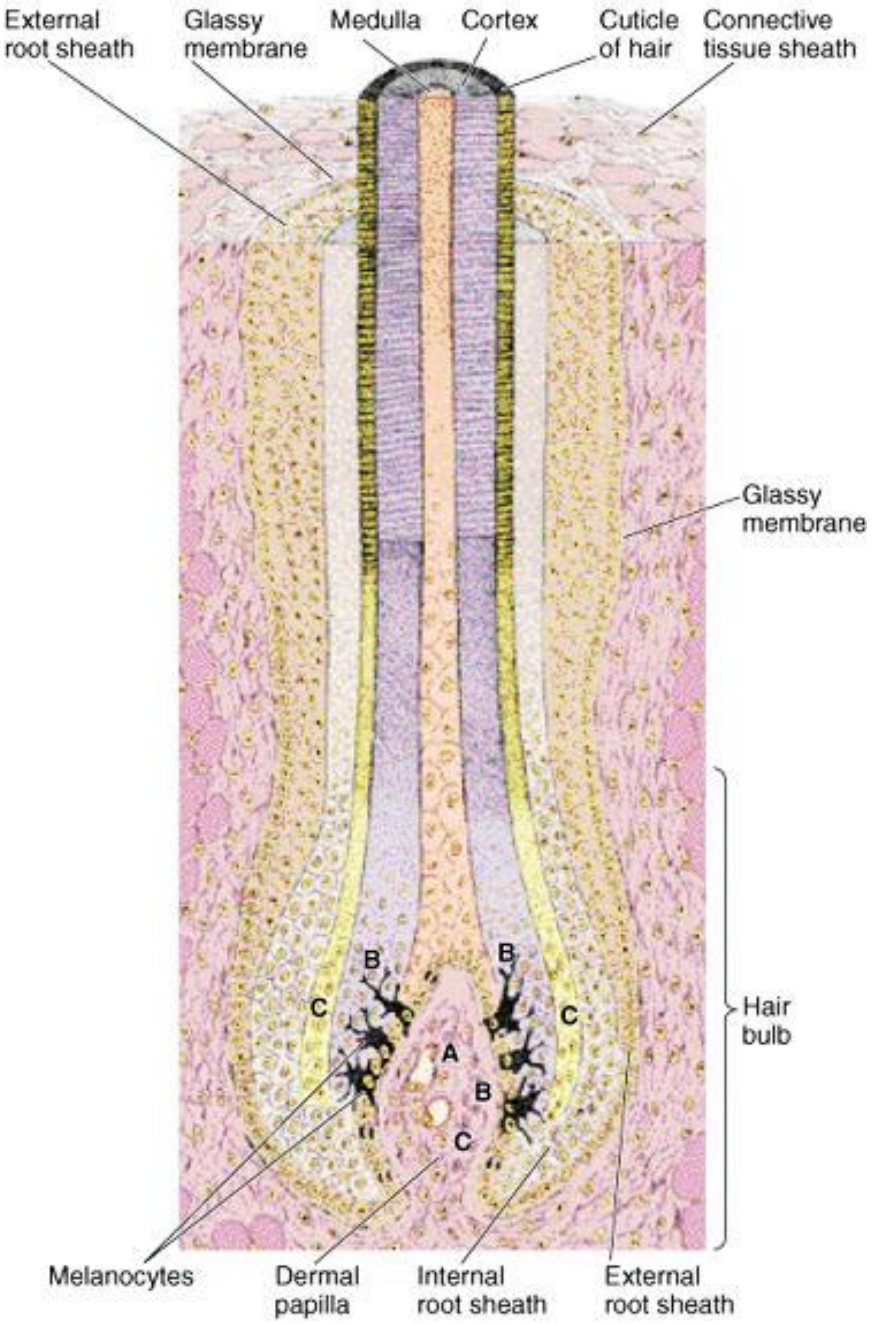


How Hair is Formed

a hair is formed by division of the well-nourished stratum basale epithelial cells in the growth zone, or **hair bulb matrix**, at the inferior end of the follicle.

- as the daughter cells are pushed farther away from the growing region, they become keratinized and die.
- thus, the bulk of the hair shaft is dead material and almost entirely protein





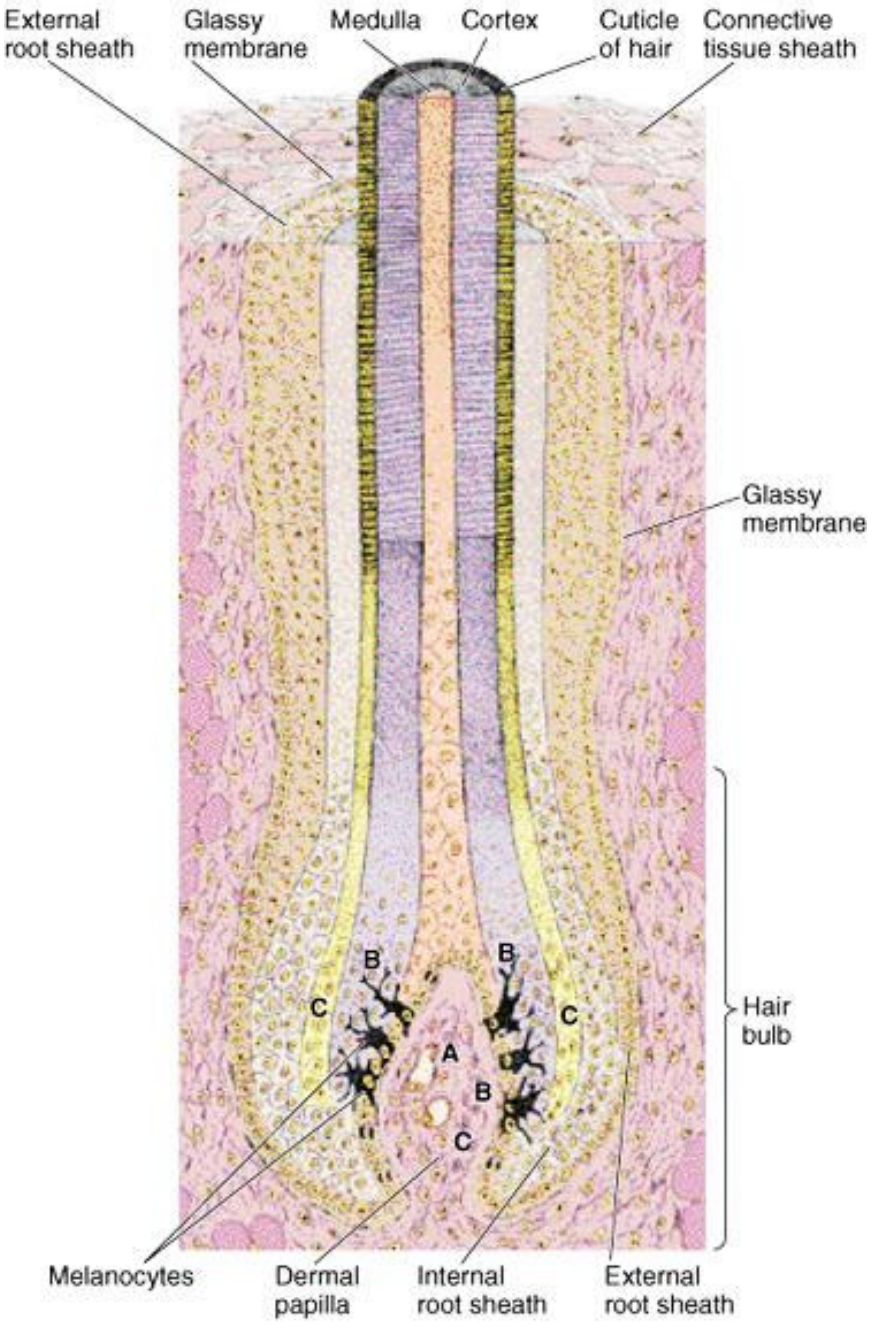
Hair follicle structure

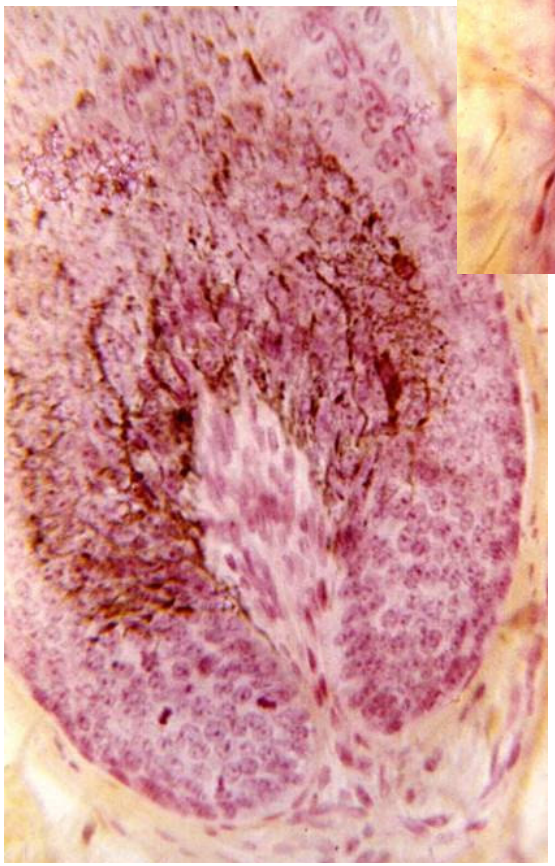
the **hair follicle** envelopes the hair root

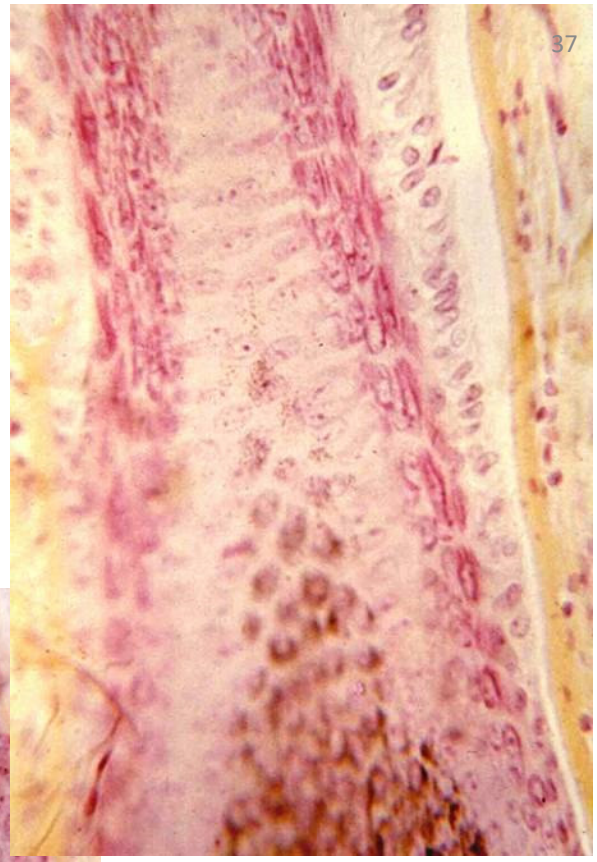
the **internal root sheath** lies close to the hair and comprises three layers: **Henle's** and **Huxley's layers**, which contain eosinophilic trichohyaline granules, and the **cuticle** of keratinised cells; the internal root sheath grows from the hair bulb and its cells gradually keratinise towards the neck of the hair follicle (the neck = region of the opening of sebaceous gland)

the **external root sheath** is continuous with the germinal epidermal layer and thins towards the hair bulb; it consists of lightly stained cells and the basement membrane

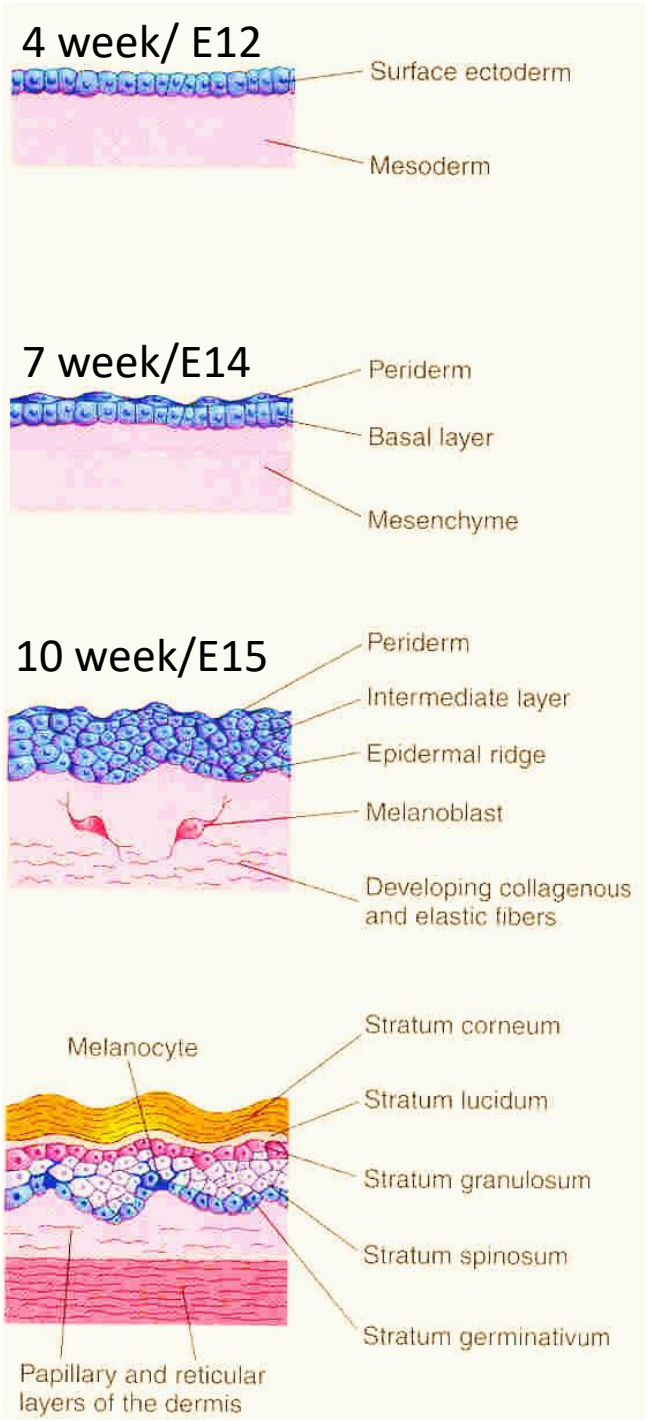
the **connective tissue sheath** is a thin leaf of dense collagen tissue that links the hair to its surrounding tissue


External root sheath
Glassy membrane
Medulla
Cortex
Cuticle of hair
Connective tissue sheath
Glassy membrane
Hair bulb
A
B
C
Melanocytes
Dermal papilla
Internal root sheath
External root sheath

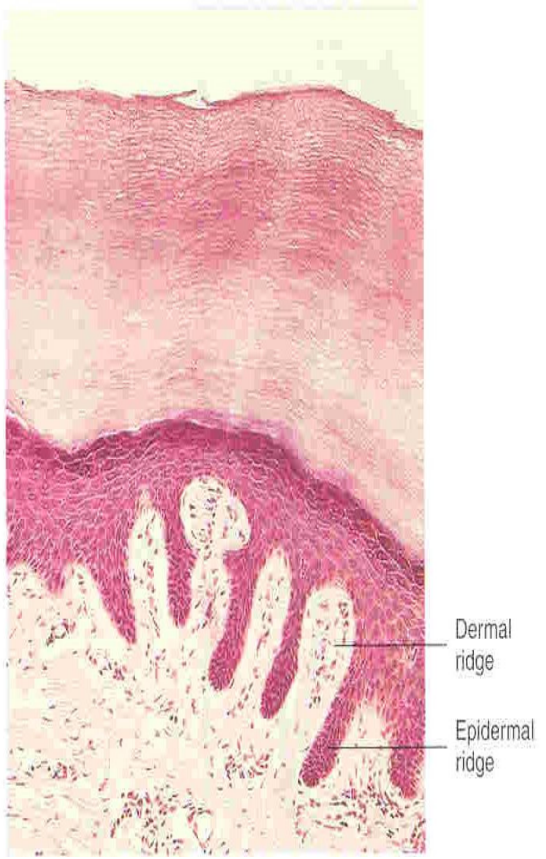




Skin development



- the epidermis derives from the surface ectoderm
- the dermis is derived from mesoderm
- the embryonic skin initially consists of a single layer of surface ectoderm overlying the mesenchyme
- these ectodermal cells proliferate and form a layer of squamous epithelium (periderm) and a basal layer (germinative)
- the cells of the periderm undergo keratinization and desquamation and are replaced by cells arising from the basal layer
- proliferation of stratum germinativum cells form epidermal ridges (in humans) which extend into the developing dermis and are macroscopically visible as fingerprints

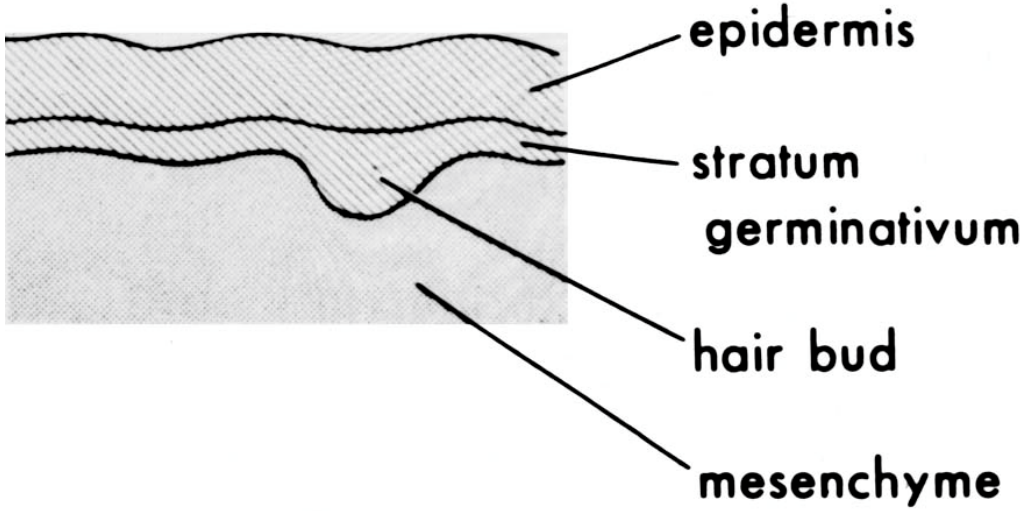


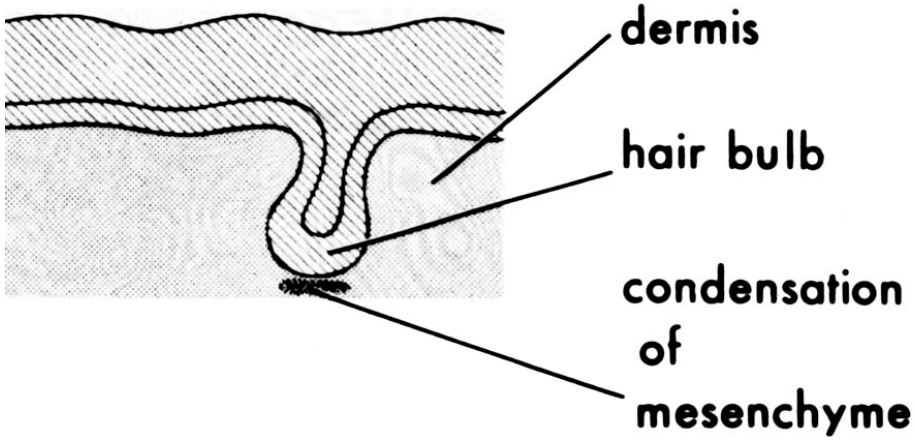
Hair development

The dermis induces a variety of epidermal structures depending on the species (feathers, hair, scales).

a hair follicle begins to develop as a solid downgrowth of the stratum germinativun of the epidermis called the **hair bud**,

it extends into the underlying dermis.



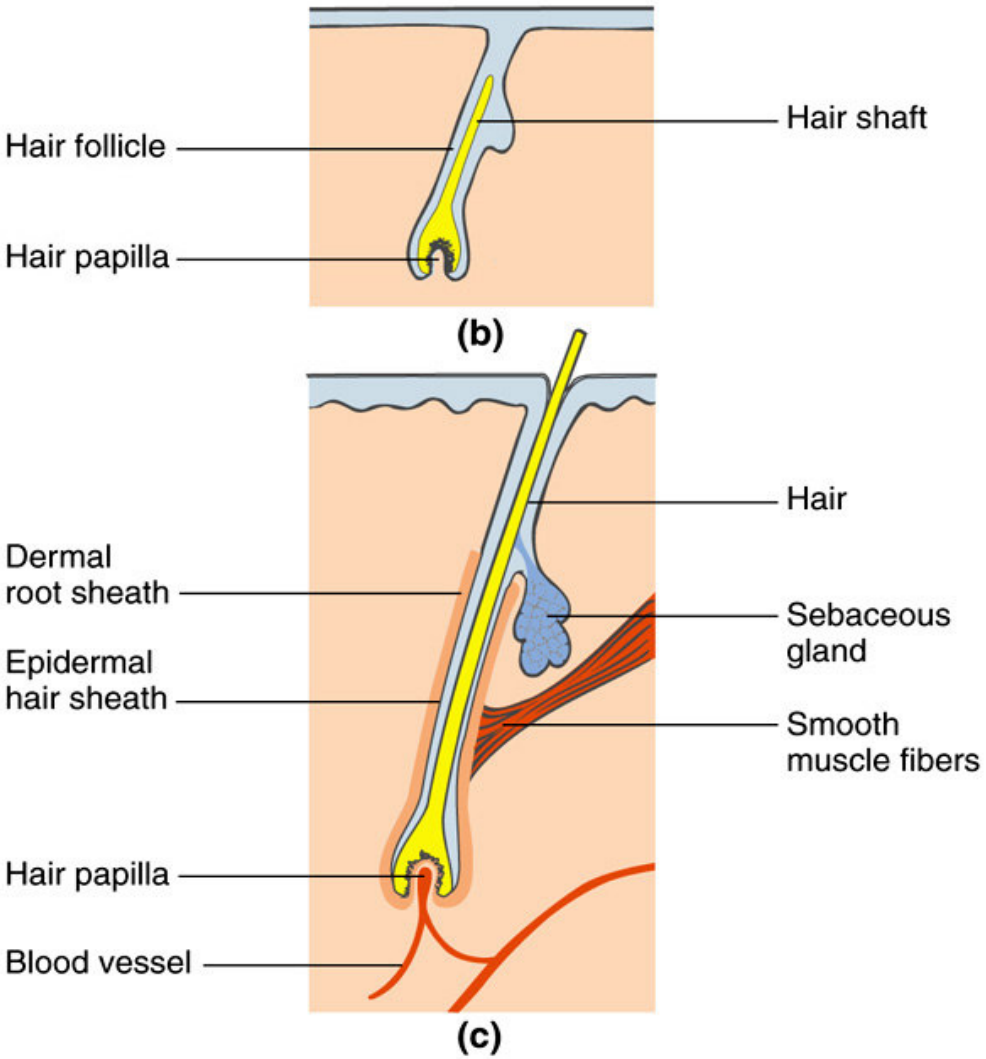


the deepest part of the **hair bud** soon becomes club-shaped, forming a **hair bulb**

the epithelial cells of the centre of the hair bulb constitute the germinal matrix - it gives rise to proper **hair**

the hair bulb that penetrates the dermis then envelopes these cells to form a **hair papilla**

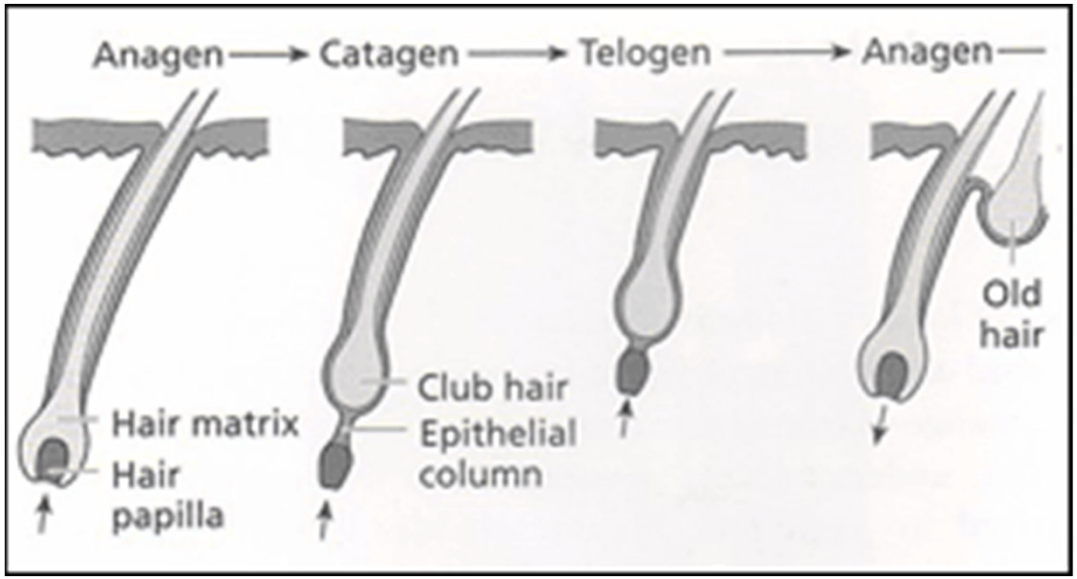
Hair development



The hair follicle is formed when the inner cells overlying the papilla start to differentiate and produce keratin in the form of hair. The continued production of keratin by the cells at the base of the shaft causes the hair to grow longer.

the peripheral cells of the developing hair bud (follicle) form the epithelial root sheath
the surrounding mesenchymal cells differentiate into the dermal (connective tissue) root sheath apocrine sweat glands (axilla, pubic region, anal region, areolae) develop from the hair follicle as well as sebaceous glands

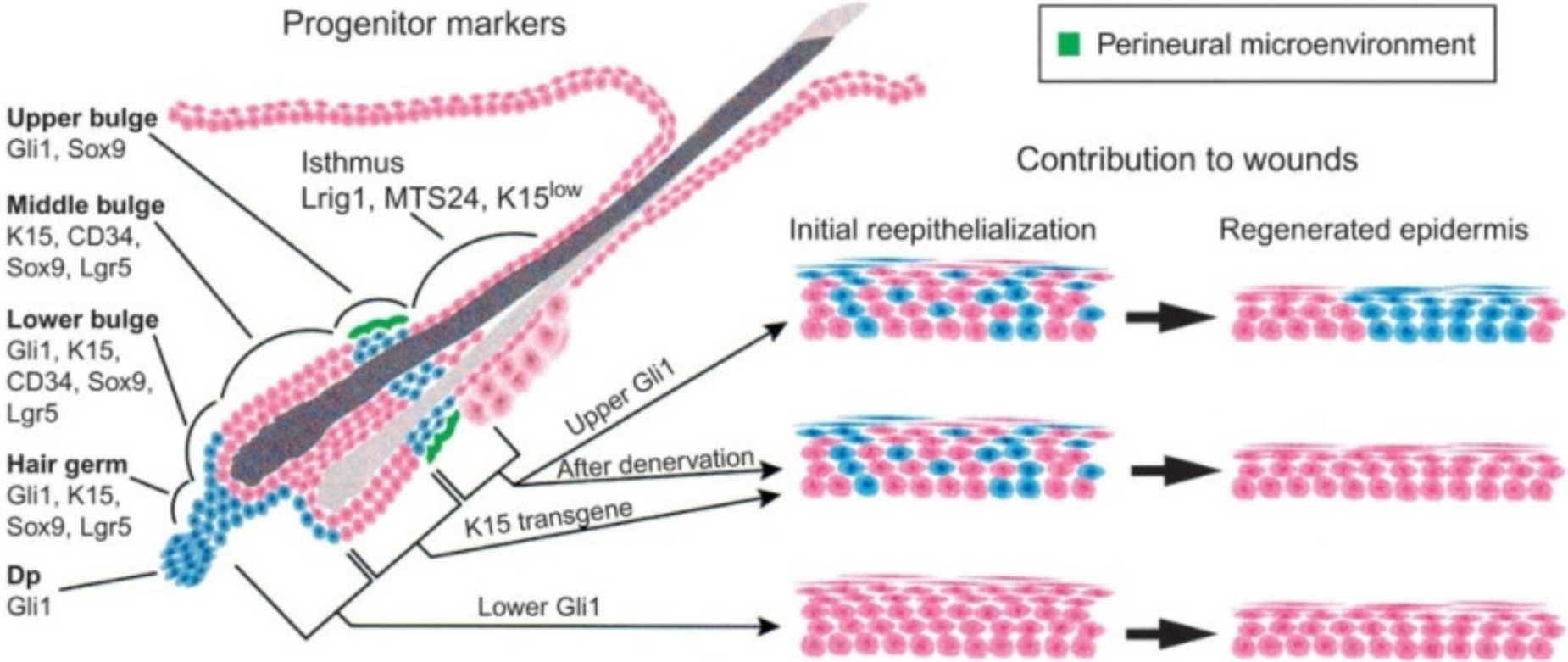
Hair follicle growth cycle



- 100 to 150,000 follicles on the scalp
- ~95% of them are in an active growth phase called Anagen and which lasts 2-3 years
- ~5% completed their growth phase
- during Catagen most follicle cells are lost by apoptosis and the follicle shortens, leaving the dermal papilla behind

- Telogen hair typically remains in the skin for about three months before it is shed
- each hair is replaced by a new hair that pushes the old hair shaft out from the follicle, the total number of hair is slowly decreasing with age
- shampooing, combing or brushing typically releases hair at a rate of about 50 to 80 per day.

Numerous stem cell populations in the hair follicle



- different stem cell domains (markers shown) contribute to varying degree to regeneration of the follicle and of the interfollicular epidermis
- in particular after wounding, the contribution to epidermal repair varies between no, transient or stable contribution
- the cells of the upper Gli 1 domain are the only bulge cells capable of contributing to regenerated epidermis after injury; these cells are unique in being signaled by SHH from sensory neurons in that domain

Skin derivatives of glandular type

glands of the skin are of 2 types:

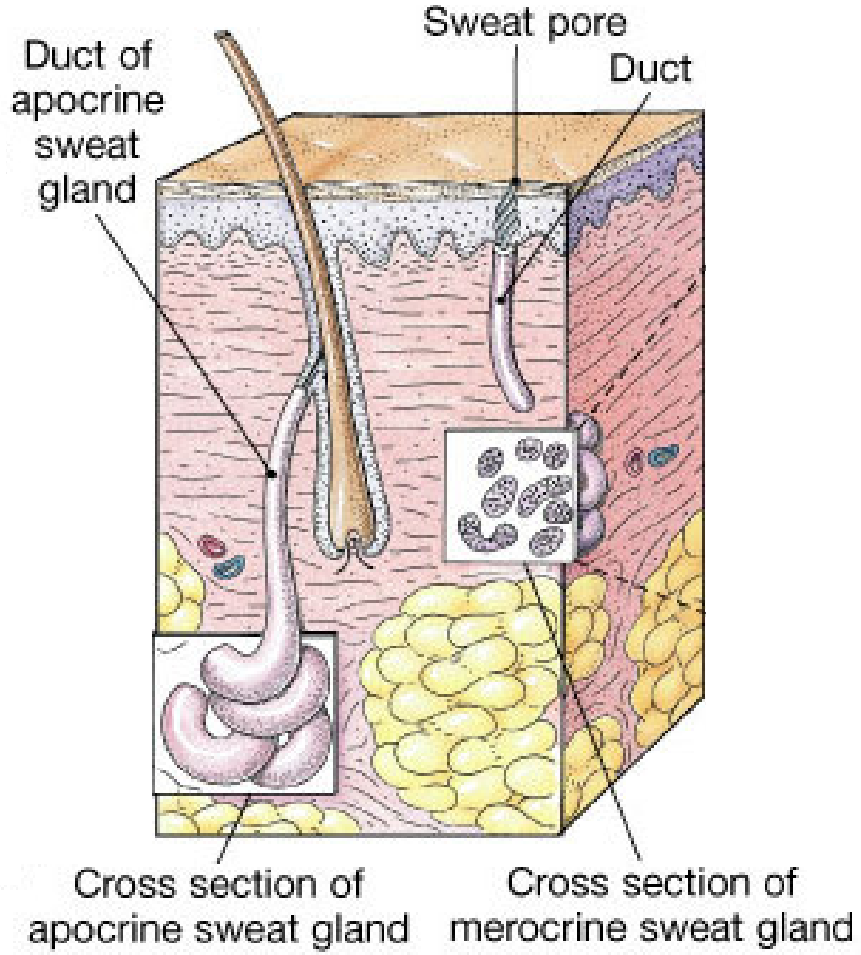
- **sweat glands**
- **sebaceous glands**

sweat glands - widely distributed throughout the body, specialized for production of sweat that cools the body by evaporation, and other complex secretions

eccrine/merocrine sweat glands duct directly to the surface

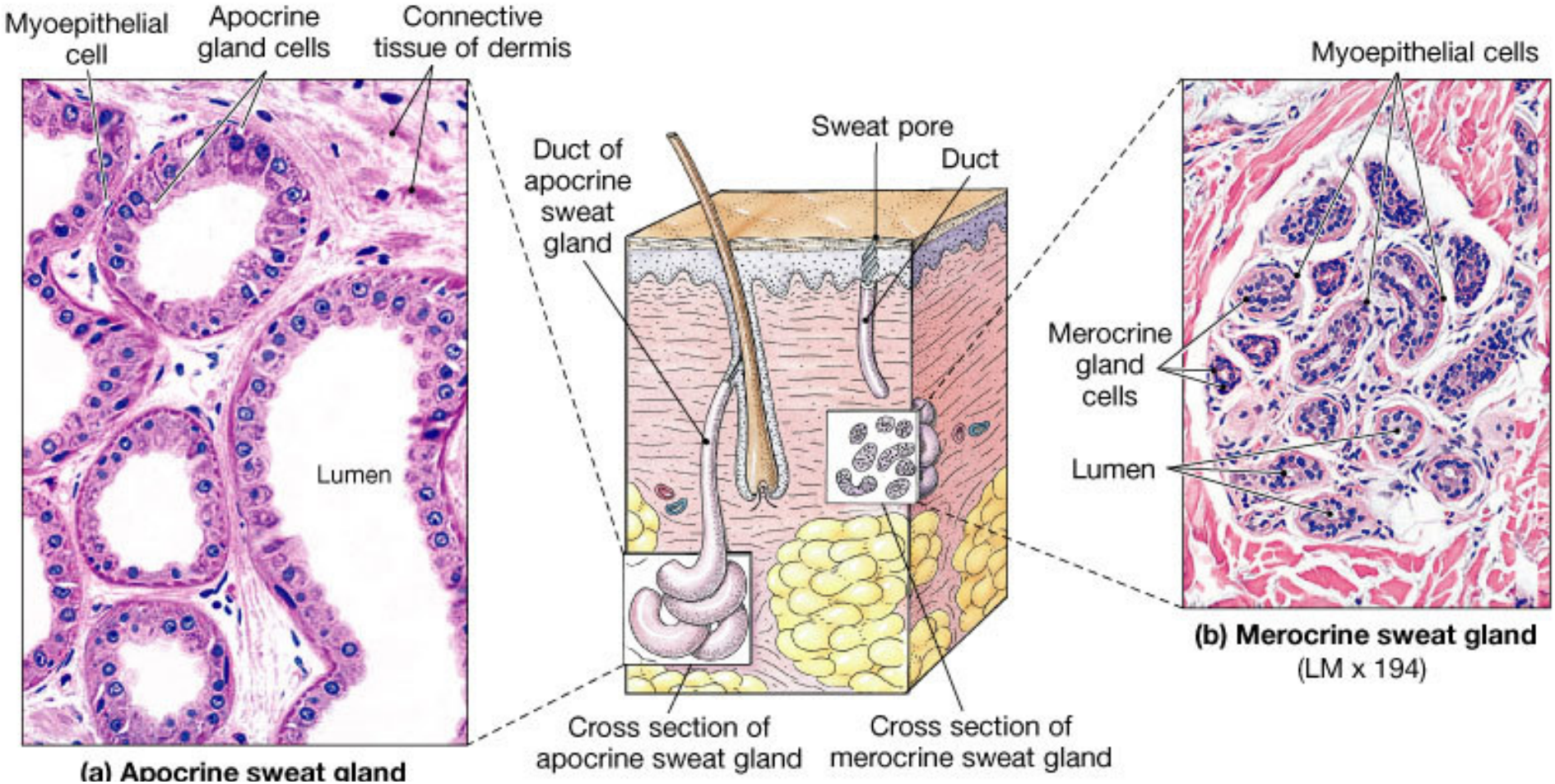
sebaceous glands produce oil that lubricates and waterproofs the hair

sebaceous glands and apocrine sweat glands open towards the hair follicle



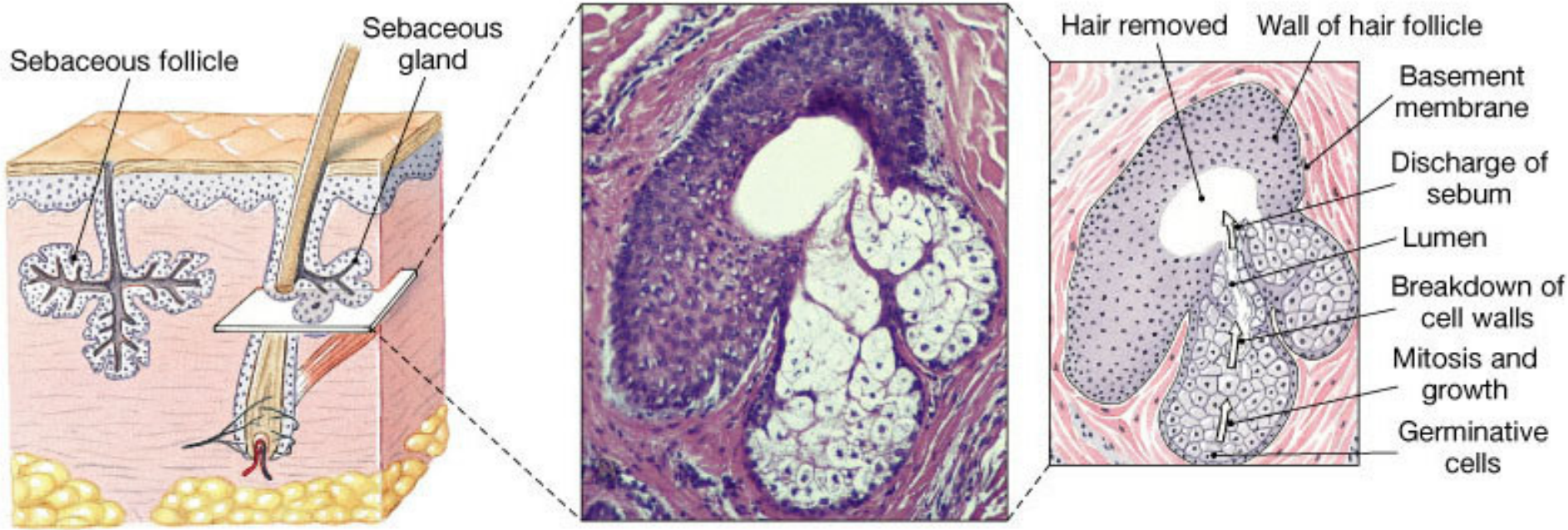
Sweat glands

- Eccrine/merocrine sudoriferous gland
  - Distributed all over the body (sweaty palms, back, cc.)
  - Non-smelly, not viscous, little protein (H_2O, NaCl, urea, ammonia, and uric acid)
- Apocrine sudoriferous gland
  - Armpits (axillary) and pubic regions – open into a hair shaft
  - Smelly sweat



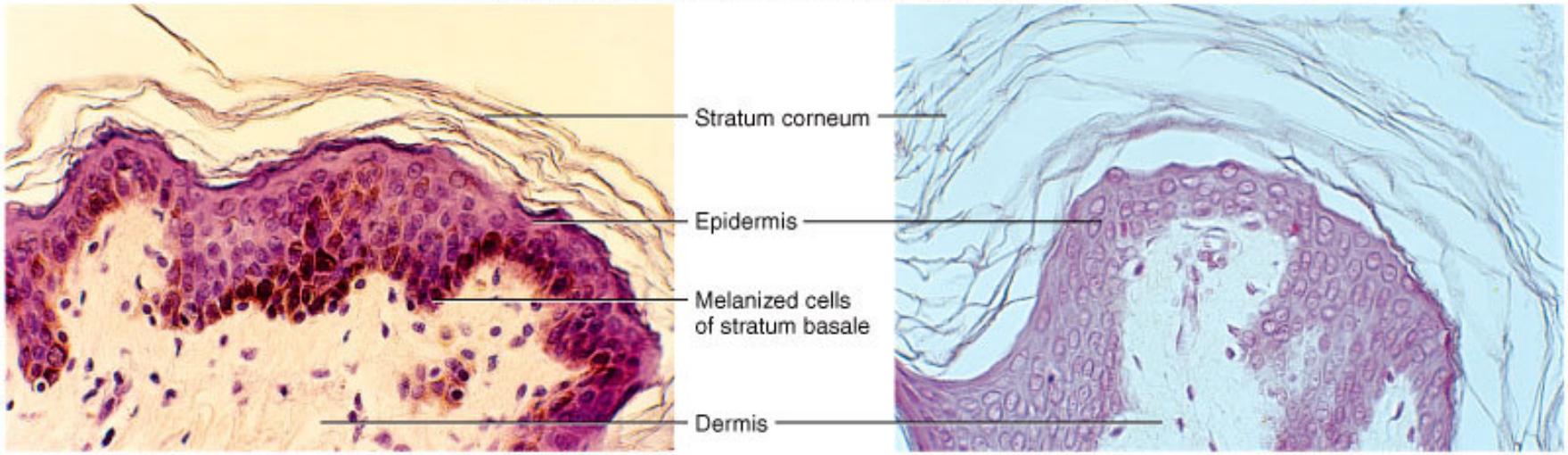
Sebaceous glands

- oil glands of the **holocrine type** secrete “sebum” (lipid-rich secretion that lubricates & waterproofs the hair shaft)
- occur practically on all body surfaces except the palms of the hands and soles of the feet
- consist of several **alveolae (acini)** and a **short duct** that opens in the **upper portion of the hair follicle** and is lined by a stratified squamous epithelium
- acini are composed of two types of cells: outer stem cells (basal cells) and central cells that accumulate lipid and disintegrate to produce sebum (holocrine secretion)
- sebaceous glands begin to function at puberty causing acne in teenagers



Sebaceous gland (LM × 150)

Skin pigmentation



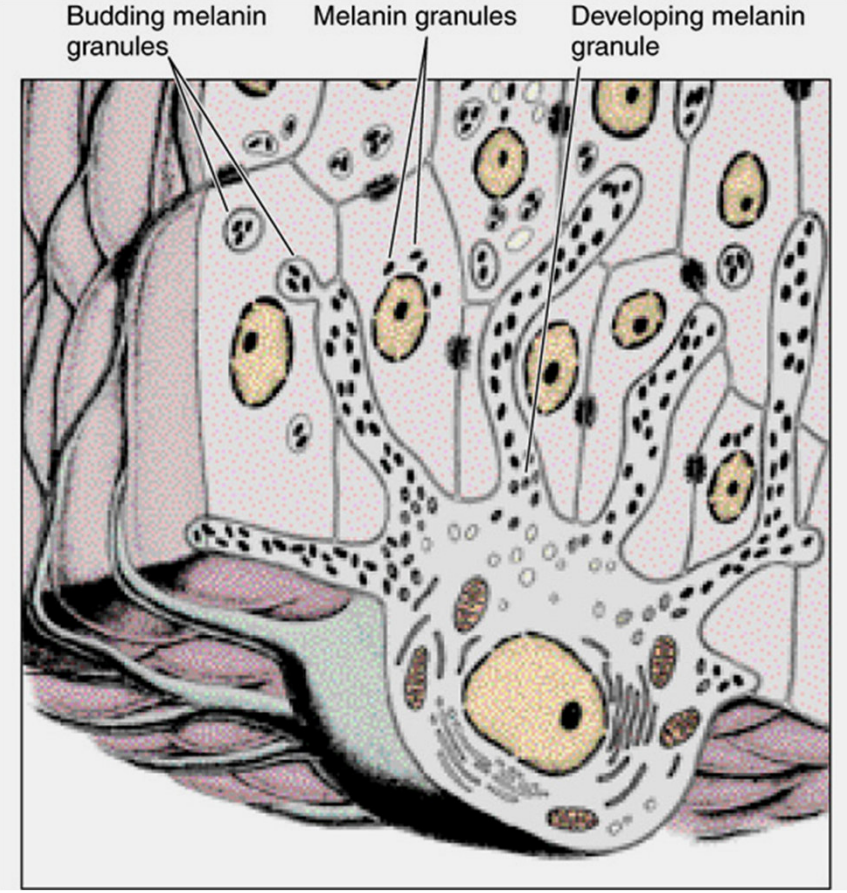
Note the difference between the melanized cells of the stratum basale between the two skin tones. Also recall that the stratum corneum is transparent.

Melanin production

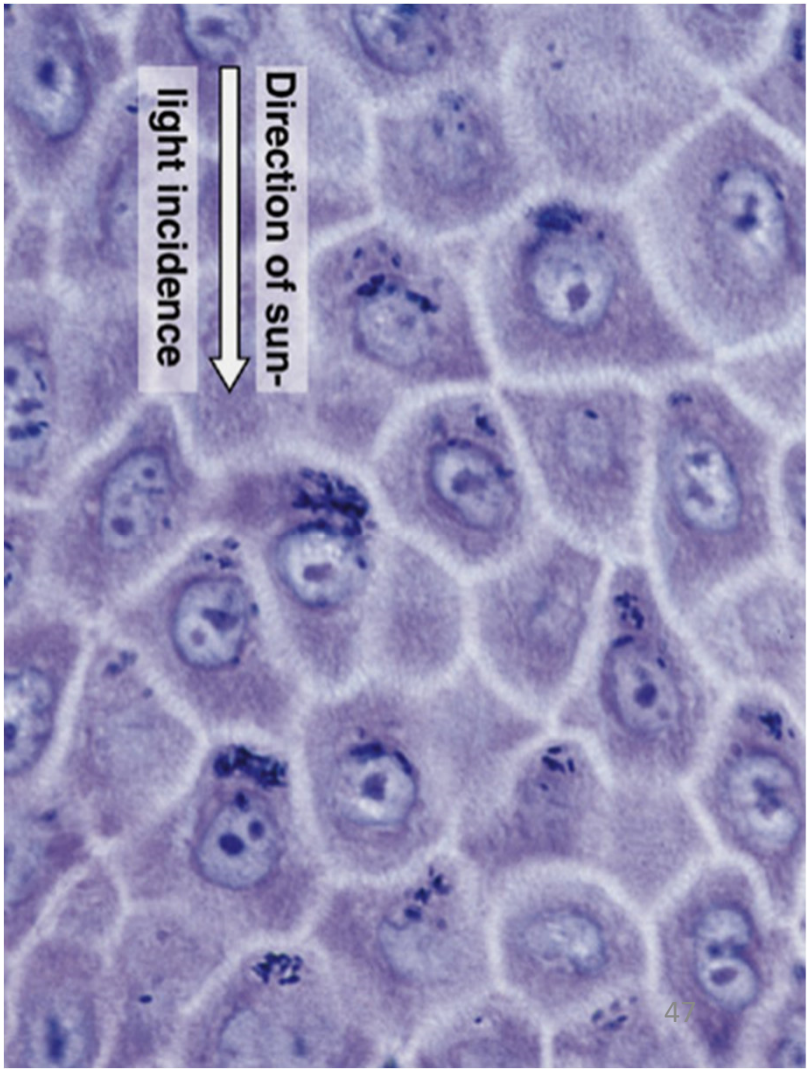
Melanocytes are located beneath or between cells of the stratum basale and in hair follicles

synthesize and produce eumelanin

melanin granules are then injected in the cytoplasm of keratinocytes



supra-nuclear location of granules



Skin tumors (benign and not)

- **Warts**: due to papilloma virus, treated by cryosurgery

- **Skin cancers**
  - Basal cell carcinoma: most common, due to UV exposure, arises from basal cell, easily treated
  - Squamous cell carcinoma: from cells above basal cells, more invasive but cervical SCC (HPV) are often more aggressive
  - Malignant melanoma:
    derived from melanocytes (changing moles)
    often very invasive

Bowen's disease

- Bowen's disease is intraepidermal squamous cell carcinoma (carcinoma-in situ)
- may progress into squamous cell carcinoma (approximately 5%)
- presents as a pink or red ,irregular scaly patch in sun-exposed area
- most common (benign) skin cancer

Basal cell carcinoma

- Affects fair skinned adults who have had a lot of sun exposure or repeated episodes of sunburn
- **Gorlin's syndrome**-inherited tendency to multiple BCCs by **mutations in the Hh pathway**
- BCCs grow slowly over months or years; bleed or ulcerate easily

- Metastasis exceedingly rare but BCCs can cause destructive changes in surrounding tissues

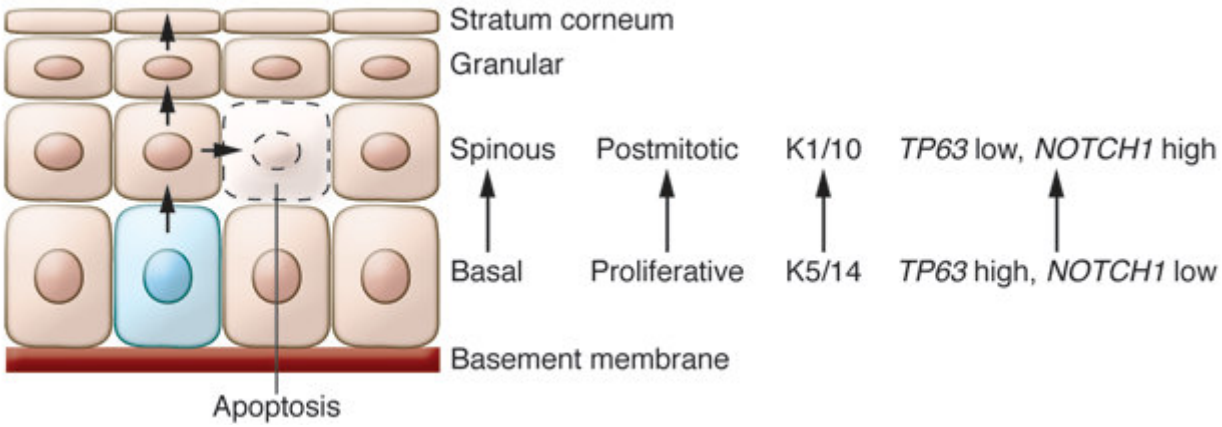
Squamous cell carcinoma (SCC)

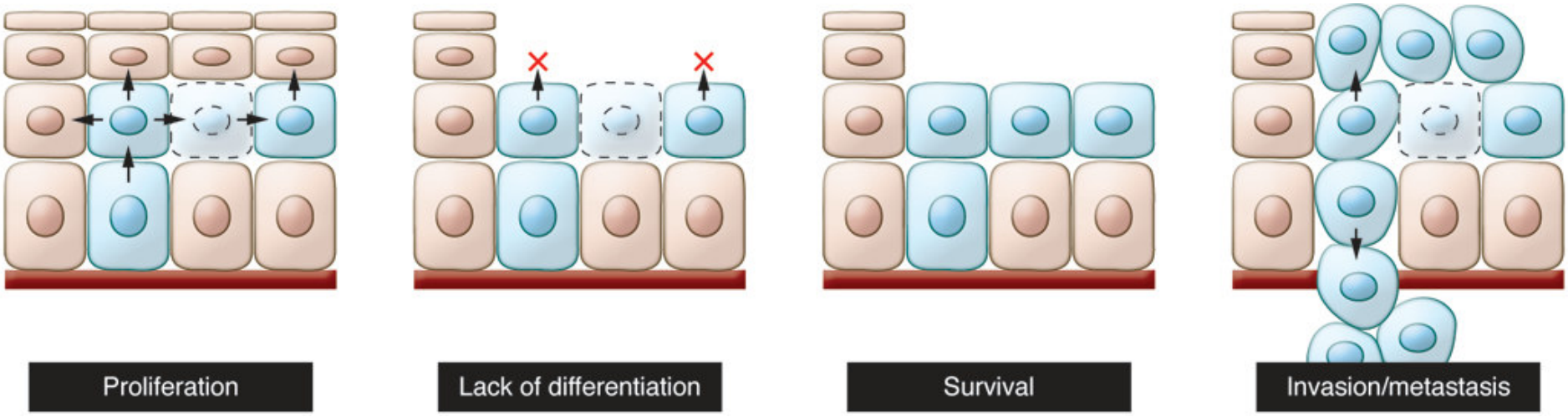
- SCC is a common type of skin cancer; develops in the epidermis from squamous cells which produce keratin
- Usual presentation is a slowly–growing scaly or crusted lump
- Can present as a non-healing sore or ulcer “punched out” in appearance
- Sometimes growth is rapid over a matter of weeks
- 5% SCCs metastazise, more frequent for oral SCC
- SCC may develop in an actinic keratosis or patch of Bowen’s disease

Risk factors:

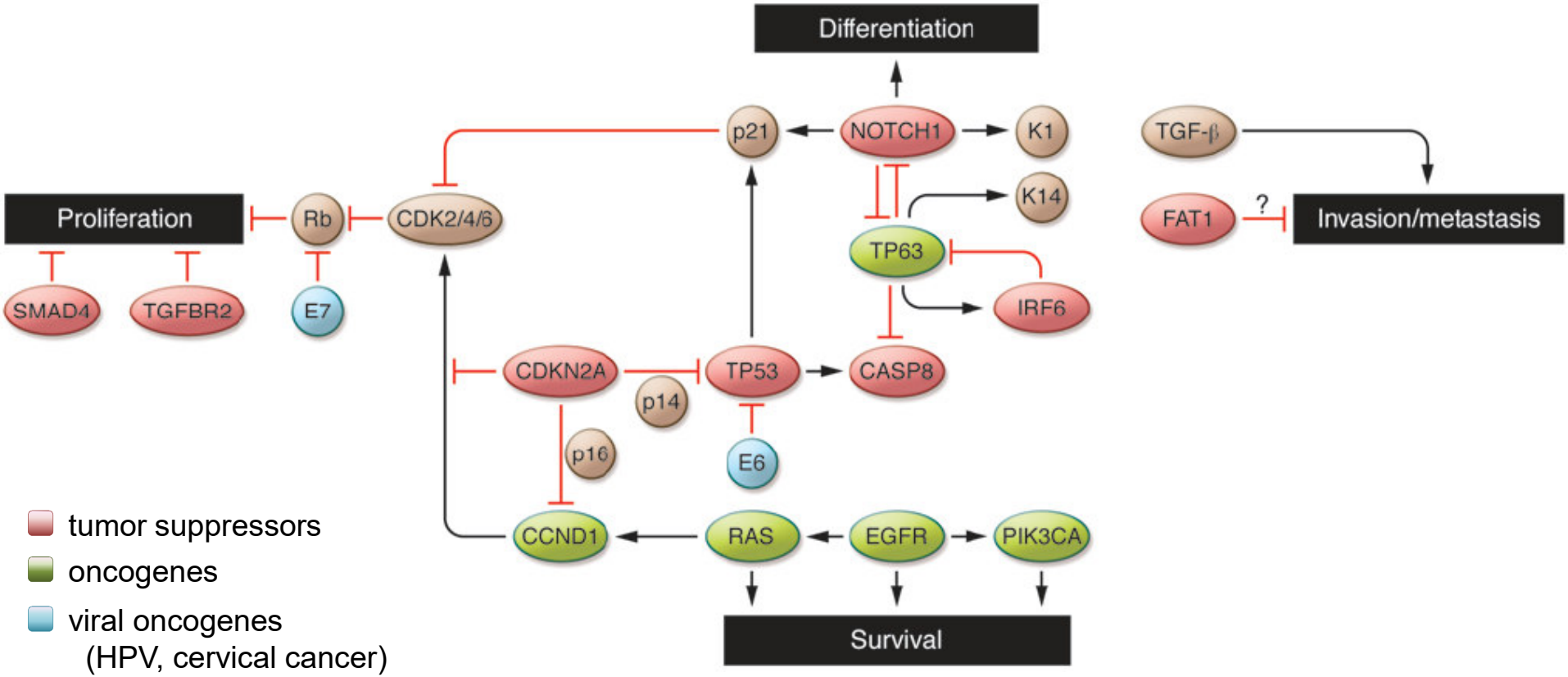
- Genetic predisposition to develop SCCs
- UV radiation damages DNA in skin
- Smoking-especially SCC lip
- Thermal burns
- Chronic leg ulcers
- Immunosuppression-Azathioprine/Ciclosporin.
  Organ transplantation patients highly susceptible
- HPV infection implicated in genital SCCs
- Pre-existing skin conditions eg lichen sclerosus and lichen planus can predispose to development of genital and oral SCCs

Stratified organization coupled to growth vs. differentiation

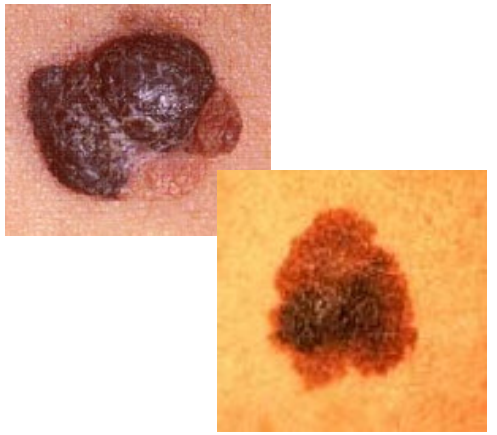




Major players in squamous cell cancers



Malignant melanoma



- Non-cancerous growth of melanocytes results in moles or freckles
- Cancerous growth of melanocytes results in malignant melanoma

Risk factors

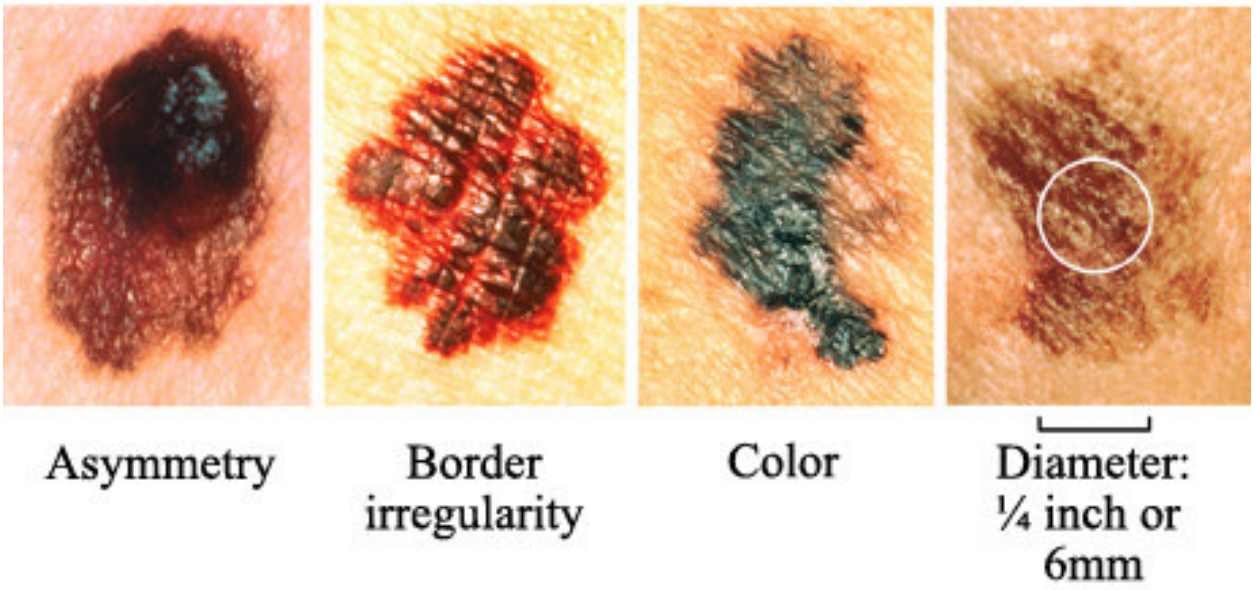
- Sun exposure, blistering sunburn, especially when young
- previous non-melanoma skin cancer
- large numbers of moles/ dysplastic moles

Treatment

- surgical excision with 2-3 mm margin; wider excision if histology confirms melanoma
- thicker melanomas >1mm: wider excision + sentinel node biopsy

Diagnosis: The ABCDE of melanoma

- A Asymmetry
- B Border irregularity
- C Colour variation
- D Diameter over 6mm
- E Evolving (enlarging or changing)

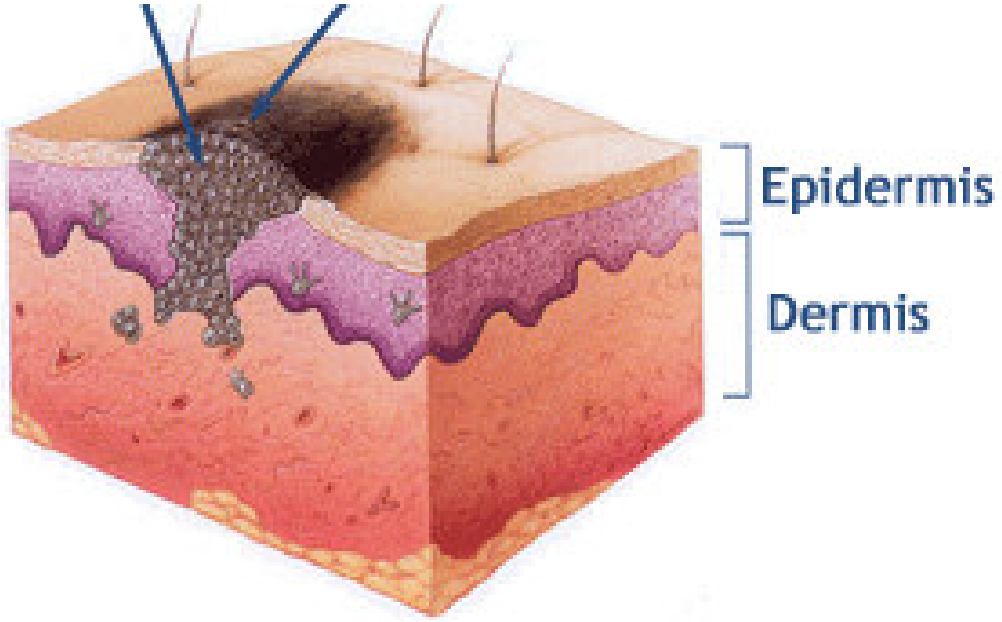


Melanoma: histological classification

Breslow thickness: thickness of the melanoma in mm

Clark's level:

- This describes which layer of skin has been breached
- Clark's level 1 - epidermis (melanoma in situ)
- Clark's level 2 - dermal invasion
- Clark's level 5 - invasion of subcutaneous fat



Horizontal growth within epidermis=melanoma in situ

Vertical growth through basement membrane into dermis = invasive melanoma

Once melanoma penetrates dermis, it spreads via lymphatic and blood stream = metastatic melanoma

Prognosis:

- Breslow thickness **< 1mm** (level 1), almost 100% 5 year survival
- Breslow thickness **> 4mm** (level 2), only 50% 5 year survival

Melanoma genetics