

Cytology

Definition and basic characteristics of the cell

A cell is the smallest basic structural and functional unit of a living organism.

Most cells are adapted according to structure and function (except undifferentiated cells).

Human cells are 10-30 μm , though some are smaller (erythrocytes: 7.5 μm) or larger (oocytes: 120-150 μm).

The cytoplasmic membrane encloses the cell. It is composed of a phospholipid bilayer with

- embedded proteins
- cholesterol
- oligosaccharides bound to proteins or phospholipids

The basic compartments within the eukaryotic cell are the cytoplasm and the nucleus.

General structure of the cytoplasm

The cytoplasm includes all the material within the cell membrane, but excluding the nucleus. The main components include

- cytosol (gel-like fluid where many cellular processes take place)
- organelles
- inclusions

Cell surfaces and intercellular junctions

Epithelial cells have **apicobasal polarity** - organelles and membrane proteins are unevenly distributed within the cell.

Basal pole

Basement membrane

The **basement membrane** is the means of attachment of the basal poles of epithelial cells with the ECM and surrounding connective tissue. It functions as a selective filter and in communication.

The basement membrane consists of a **basal lamina** (20-100 nm sheet of dense fibrils) and a **reticular lamina** (50-500 nm layer of diffuse fibers).

Layer		Components
Basal lamina	lamina rara externa	laminin, perlecan, fibronectin, syndecans, integrins
	lamina densa	heparansulfate, collagen type IV
	lamina rara interna	hyaluronic acid, thrombospondin, fibronectin, collagen type VII
Reticular lamina		collagen types I, III, VII; fibronectin and versican

Schematic here (https://healthjade.net/wp-content/uploads/2019/11/basement_membrane_structure.jpg).

In some organs, the basal laminae of epithelial layers can fuse. This happens in the Bowman's capsule, cornea, and retina.

Connections

Hemidesmosomes (associated with intermediate filaments) anchor the cytoskeleton of the epithelial cells to the basal lamina via *intermediate filaments*.

Focal adhesions are similar to hemidesmosomes, but are smaller and use *integrins* instead of intermediate filaments.

If the cells detach, programmed cell death - anoikis - happens.

Basal labyrinth

Some epithelia, such as renal proximal and distal tubules, collecting ducts, and striated ducts of salivary glands, also have a **basal labyrinth**. It consists of infoldings of the basal plasma membrane and interdigitations of basal ridges with neighboring cells. This greatly increases surface area, which is necessary for the transcellular transport that these epithelia do. Mitochondria accumulate in this area and align vertically^[1].

Apical pole

The apical pole is opposite to the basal pole and usually has a free surface facing an open space. Specializations include

- **microvilli** (0.1 μm by 1 μm): projections of cytoplasm supported by microfilaments. Increase surface area to facilitate absorption. Organize together into striated border (enterocytes) or brush border (proximal tubule of kidney).
- **stereocilia**: similar to microvilli, but longer (10-50 μm). Function in absorption (ex. epithelia of male reproductive tract) and also in sound detection (cochlea).
- **kinocilia** (0.2 by 5-10 μm): contain axonemal (9 \times 2+2) arrangements of microtubules moved by kinesin and dynein. Found in cuboidal or columnar cells of many epithelia (ex. oviduct); used to move fluid and suspended particles, also function in motion detection in inner ear
- **primary cilium**: non-motile projection for signal transduction ("antenna") found in almost every vertebrate cell

Lateral surfaces

The lateral surfaces touch neighboring cells. There are several types of intercellular adhesions and junctions:

- Tight junctions (aka zonula occludens): tight seal between adjacent cells associated with actin. Most apical.
- Adhesions
 - zonula adherens: points for adjacent cytoskeletons to connect and re-inforce tight junctions
 - macula adherens (aka desmosome) \sim 0.3 μm \times 20-40 nm: associated with intermediate filaments (keratins). Strong intermediate coupling that strengthens tissue.
- Communicating junctions (aka gap junctions or nexons) \sim 0.3 μm diameter, pore diameter is $<$ 1.5nm, intercellular space is between 2-4 nm: made up of connexins; allow transfer of small molecules between cells

Cytoskeleton

Three main kinds of protein polymers make up the cytoskeleton:

- **Microfilaments** (7 nm):
 - G-actin monomers make up F-actin
 - Anchored to cell membrane
 - Fast polymerization/depolymerization
 - Involved in moving the cell, changing its shape, cytokinesis, cytoplasmic transport and streaming.
- **Intermediate filaments** (10 nm):
 - Antiparallel tetramers made of various subunits
 - found throughout cytoplasm and in desmosomes
 - Highly stable structure; disassembly and reassembly not possible
 - Strengthens structure
- **Microtubules** (25 nm):
 - arrangements of 13 heterodimers of α and β tubulin form a hollow tube
 - grow from centrosomes
 - fast polymerization and depolymerization
 - Maintains structure, provides "tracks" for intracellular transport, moves cilia and flagella

Nucleus

The nucleus (5-10 μm) stores the cell's genetic material.

The nuclear **envelope** forms a boundary continuous with the endoplasmic reticulum. It is made up of two lipid membranes separated by a perinuclear space (30-50 nm) and perforated by nuclear pore complexes (100-125 nm). The **lamina** (80-100 nm) is a meshwork of proteins (ex. lamins) that strengthens the envelope and serves as anchorage for chromatin. Cryofracture is particularly useful in visualizing the lipid membrane and associated structures.

Chromatin includes the DNA and associated proteins. **Euchromatin** is transcriptionally active - the chromosomes are uncoiled, and therefore it is invisible with light microscopy. **Heterochromatin** is transcriptionally inactive, the DNA is coiled around histones and visible as dark dense granules.

The **nucleolus** is a non-membrane-bound structure, where rRNA is synthesized (pars fibrosa) and ribosomes are assembled (pars granulosa). It disappears during prophase, since the DNA needs to condense into chromosomes.

Organelles

Organelles are metabolically active structures within the cytoplasm.

Endoplasmic reticulum

- Membranous network of tubuli and vesicles that empty into cisterns
- Continuous with nuclear envelope
- Site of protein synthesis and modification via ribosomes (Rough ER)
- Site of lipid metabolism, glycogen breakdown, drug detoxification (Smooth ER)

Golgi apparatus

- Consists of stacks of disk-shaped membranous cisternae
- receives incoming vesicles from the RER at the cis face
- modifies and packages the proteins
- sends proteins in vesicles to their destination from the trans face

Mitochondria

- 0.5-1 μm diameter, up to 10 μm long
- Outer membrane encloses intermembrane space
- Inner membrane lies beneath, many folds (cristae) increase surface area and project inward
- Contains own circular mtDNA in matrix
- Functions in the Krebs cycle, oxidative respiration, and apoptotic pathway

Lysosomes

- 0.05-0.5 μm
- Membrane-limited vesicles with over 50 types of acidic (pH 5) hydrolases
- Abundant in phagocytic cells
- Degrades excess or nonfunctional components of cytoplasm via autophagy: a lipid bilayer forms around the component and then fuses with a lysosome to form an autophagosome (aka secondary lysosome)
- Contents are recycled in the cytoplasm; the "trash" remains in the residual body as lipofuscin

Peroxisome

- Single-membrane vesicle
- contains oxidases that form H_2O_2 while oxidizing substrates
- catalases break down peroxide
- functions in detoxification and beta-oxidation of fatty acids

Cell inclusions

Cytoplasmic inclusions contain substances but are not metabolically active. Most are not enclosed by a membrane. There are several different types:

- Secretory granules: contain compounds destined for secretion out of cell
- Storage compounds
 - Glycogen
 - glucose polymer linked by $\alpha(1\rightarrow4)$ glycosidic bonds
 - alpha-glycogen granules (up to 200 nm): rosette-like aggregations in hepatocytes
 - beta-glycogen granules (15-20 nm): spherical aggregations in skeletal and cardiac muscle^[2]
 - Lipids
 - one large droplet in white adipocytes
 - multiple smaller droplets in brown adipocytes
 - also present in cells of adrenal cortex and liver
 - Protein crystals
- Pigments
 - Endogenous
 - autogenous (ex: melanin)
 - hematogenous (ex: hemoglobin decomposition)
 - Exogenous (from environment; ex: carotenes, inhaled particles)
- Exocytic vesicles: contain substances targeted for exocytosis; vesicle fuses with membrane and buds off of cell
- Endocytic vesicles: incoming substances get engulfed by membrane that fuse with the membrane; the formed vesicle buds off

Vital manifestation of the cell

- Movement (of the cell itself, of substances outside and inside it)
- Metabolism
- Response to stimuli
- Growth
- Differentiation
- Division

References

Mescher, A. and Junqueira, L., 2018. *Junqueira's basic histology*. New York: McGraw-Hill, pp. 17-68

1. https://link.springer.com/chapter/10.1007/978-3-211-99390-3_93#:~:text=The%20basal%20labyrinth%20is%20a,surfaces%20of%20the%20epithelial%20cells.
2. <http://www.drjastrow.de/WAI/EM/EMGlykogenE.html>