Histology and Embryology

Lecturers:

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Lecture 1

Introduction

- The object and significance of histology.
- Relevance of histology to other biomedical disciplines.
- History, current state, and future of histology.
- Methodologies to study a structure of cells and tissues.

Cytology

- The cell - definition, characteristics, compartmentalization.
- Cell nucleus - ultrastructure and function, chromosomes, nucleolus.
- Endoplasmic reticulum
- Golgi apparatus
- Centrosome
- Mitochondria
- Lyzosomes + Peroxisomes
- Cytoplasmic inclusions
- Cytoskeleton
- Cell surface specialisations
- Cell cycle, cell division, cell differentiaion

Histology

Microscopic and submicroscopic structure of the body

(cells, extracellular matrix, fluid substances)

Cytology

General aspects of the structures composing the cells and their functioning

General histology

What are the main types of tissues?
What are their functions?
What cell types these tissues are made of?

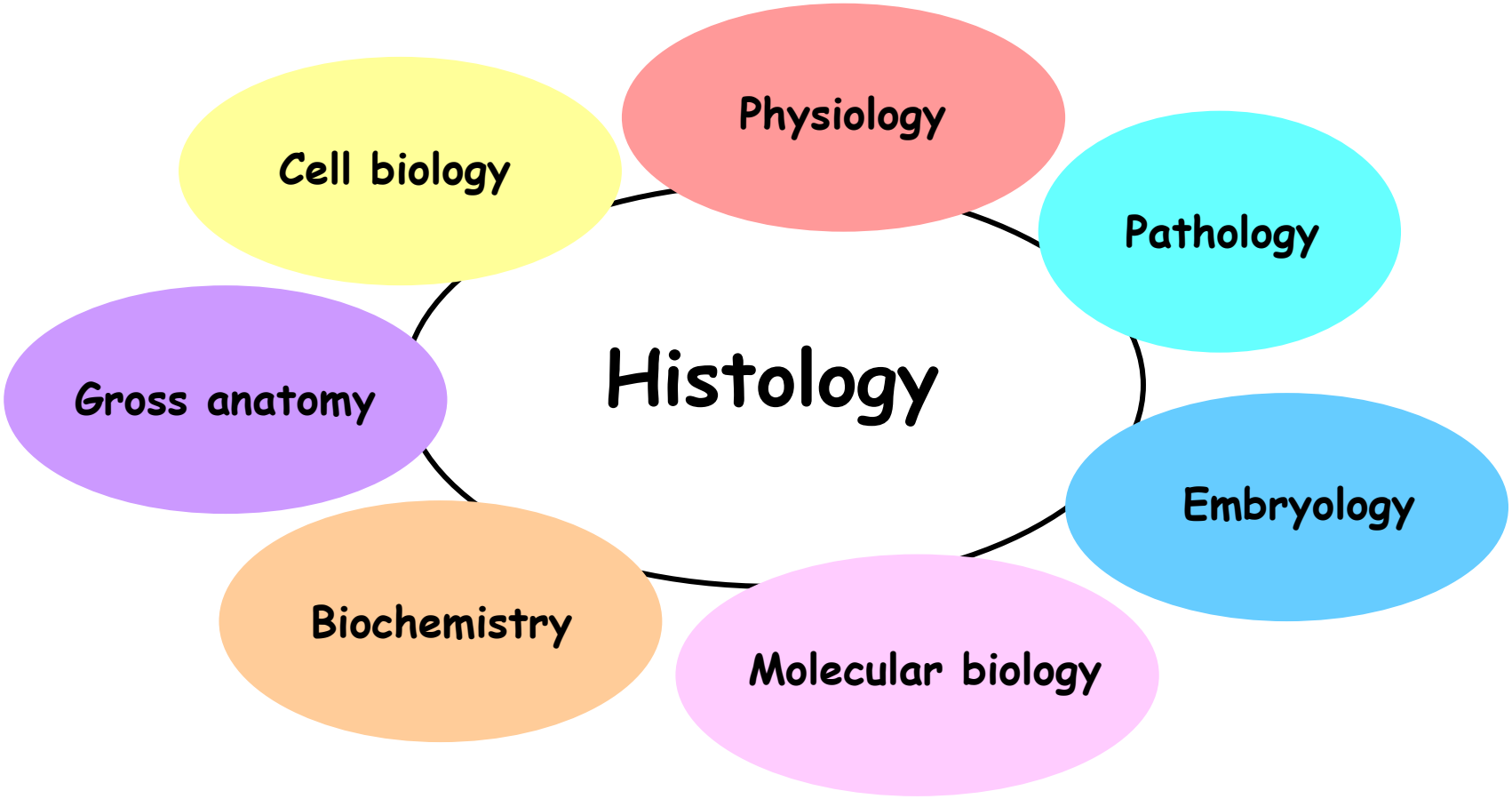
Microscopic anatomy

Composition and structure of organ systems & individual organs

Which tissue types and how organized?
Which special cell types?
Which special structures? (e.g. tubules)
How does it all work?

All this mirrors hierarchical organisation of living organisms

Histology is no longer a static discipline dealing with just the structure !!!



Learn thinking „histologically"

Have the histology in action & in motion

Studying histology was first made mandatory for medical students in 1893 by John's Hopkins Medical School !

Most histologists are Germans primarily because they made great microscopes.

Eponymously theirs…..

Jan Evangelista Purkyně
1787 - 1869

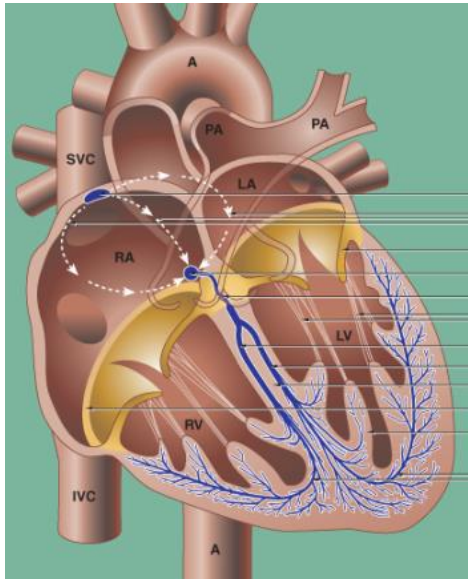
Bohemian physiologist

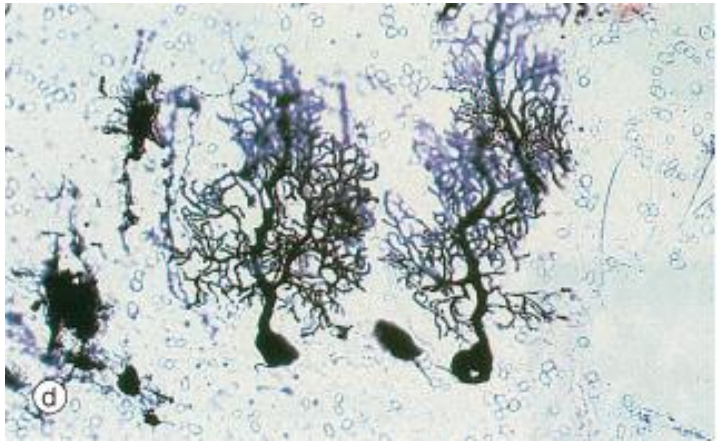
Schwann + Schleiden – 1839 – cell theory

- Pioneer in histological techniques
  First to use something like a **microtome**

- Introduced the term **plasma**

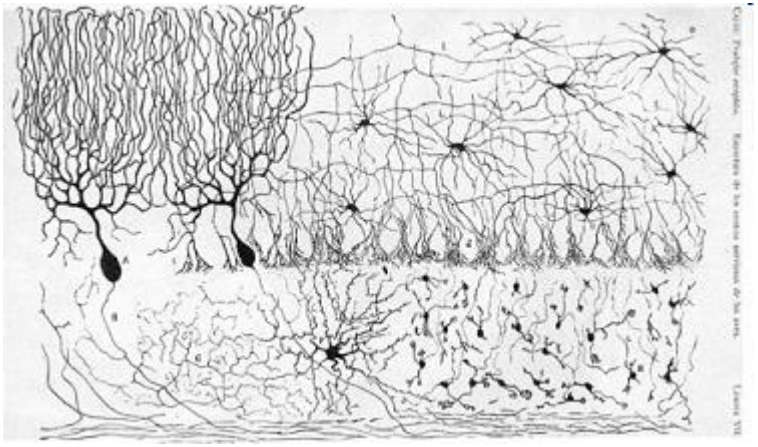
- Found **Purkinje fibers** of the heart →
- Found **Purkinje cells** of the cerebellar cortex

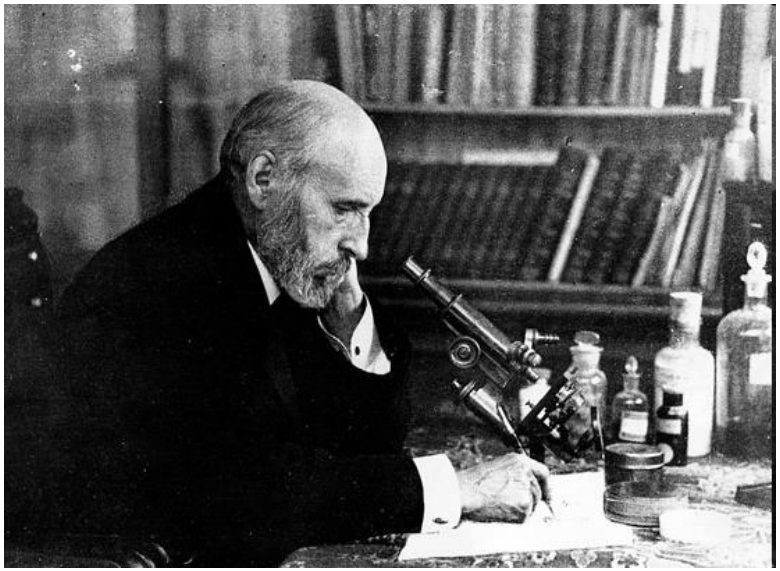




Santiago Ramón Y Cajal
1852 - 1934

Spanish physician and anatomist





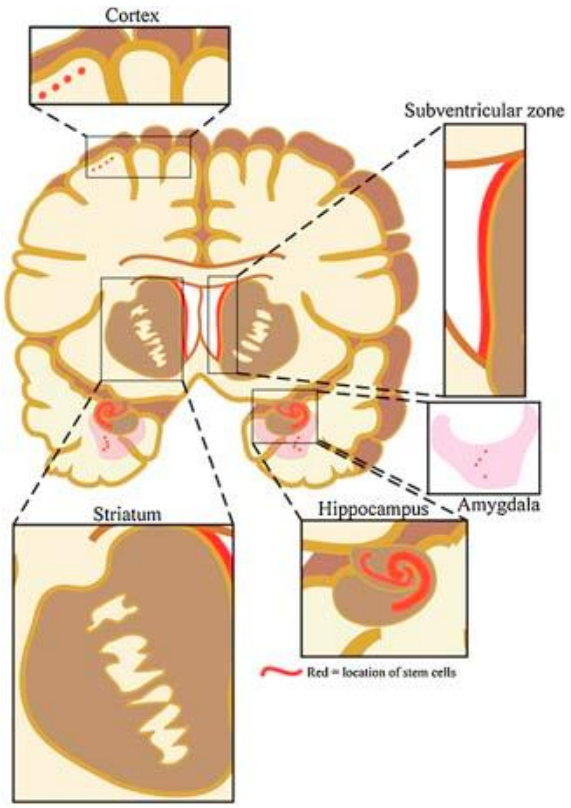
He established the neuron as the primary structural and functional unit of the nervous system.
Nobel Prize in 1906

"Once the development was ended, the founts of growth and regeneration of the axons and dendrites dried up irrevocably. In the adult centers, the nerve paths are something fixed, ended, and immutable. Everything may die, nothing may be regenerated. It is for the science of the future to change, if possible, this harsh decree."

Making unexpected discoveries

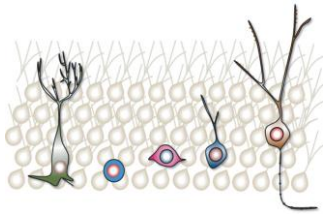
(since early 1990s)

The existence of multipotent self-renewing progenitors residing in the postantal and adult nervous system



DEFINITELY IN:

- Subventricular zone of the lateral ventricle
- Subgranular zone of the dentate gyrus of the hippocampus



POSSIBLY IN:

- Cortex ?
- Amygdala ?

Our view on the organization of the central nervous system has been dramatically changed !!!

Methodologies to study cells and tissues 1

Making it observable

Stabilization of the structure

Fixation

Making the objects smaller – transmissible for the light

Embedding + Sectioning

Making the structures well visible

„Staining"

Enlargement

Utility of Microscopes

Light (optical) microscopes

(interaction of photons with a matter)

Resolution 0.1 μm

- Equipped for visible light only
- Equipped for fluorescence
- Confocal laser scanning

Electron microscopes

(interaction of electrons with a matter)

Resolution 0.1 nm (in practice 1 nm)

- Transmission
- Scanning

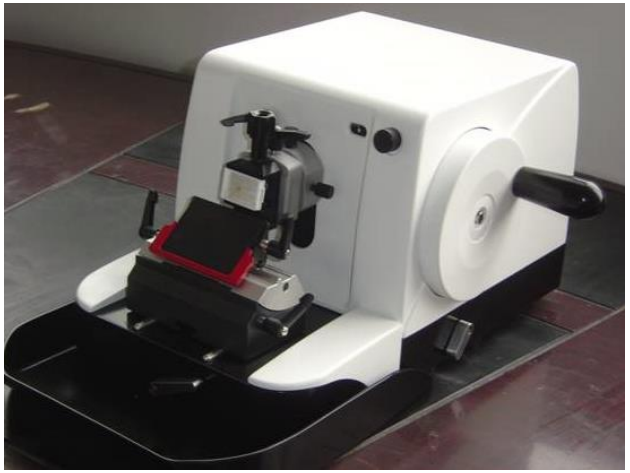
Methodologies to study cells and tissues 2

Fixation (denaturation)

- **Organic solvents** (EtOH, MetOH, Aceton,…)
- **Aldehydes** (form-, paraform-, glutar-aldehyde, …)
- **Organic acids** (acetic, picric, …)
- **Heavy metals** (salts of mercury, chrome, osmium, …)

Embedding + Sectioning

- **Paraffine wax**
- **Celloidine** (=cellulose nitrate)
- **Durcupan** (synthetic polymer)
- **LR White** (synthetic polymer)
- **others**



„Staining"

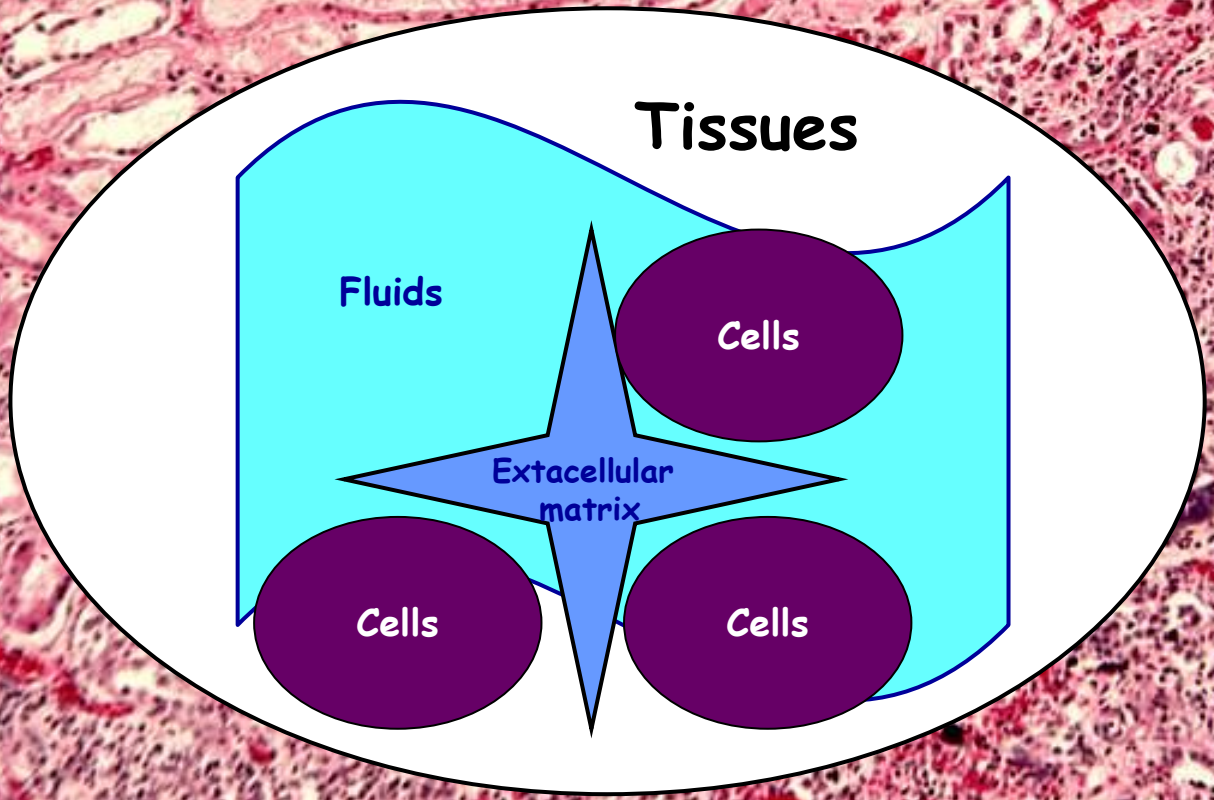
Chemical stains (H+E, Azan, van Gieson, …)

Histochemical stains (for proteins/enzymes, sugars, lipids, …)

Immunochemical visualization (labeled antibodies)

Heavy metals (for TEM – salts of uranium, lead, wolfram, …)

Understanding the complex systems can only be built on understanding its components



Fluids
- Interstitial fluid
- Plasma (in blood)
- Lymph (in lymph vessels)
- Cerebrospinal fluid
- Intracellular fluid (cytosol)

The cells make it all !

Living organisms are composed of cells

Long way to this discovery:

Robert Hooke
1665

He for the first time observed
the structure of cork - cell

Antonie van Leeuwenhoek
1678

He for the first time observed
microscopical organisms
(bacteria, protozoa)

1839

Matthias Schleiden

Theodor Schwann

All organisms are composed
of one or more cells

Rudolph Virchow
1855

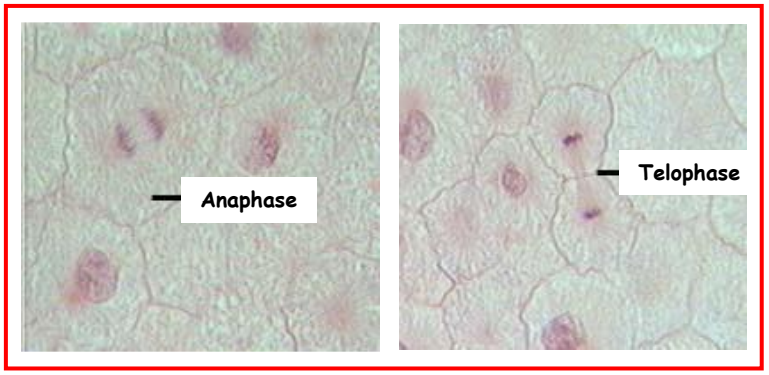
Cell can develop only from preexisting cells
„Omnis cellula e cellula"

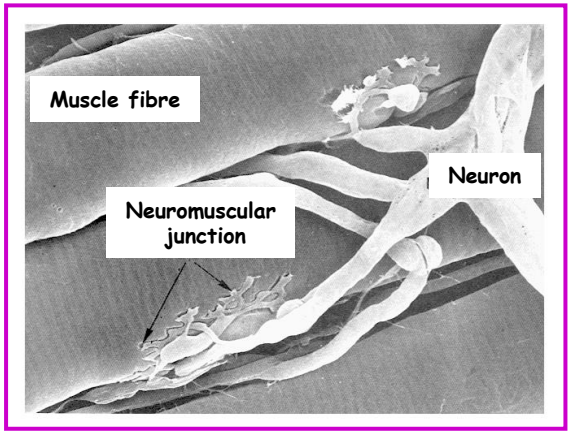
Cell is unifying theme/element of life

(cells are very similar among each other: small + specialized functions)

Current cell theory – 6 principles on which it is built

- Cell is the smallest structural and functional unit capable of life functions
- Function of each cell is given by its specific structure
- Cells are bulding units of all multicellular organisms – cells are responsible for all processes taking place in the organisms
- Structure and function of all organisms is based on structural and functional properties of cells from which they are composed
- All new cells originate from preexisting cells
- Thanks to the continuity of life on the Earth, all cells are in principle the same (universal genetic code and its expression)

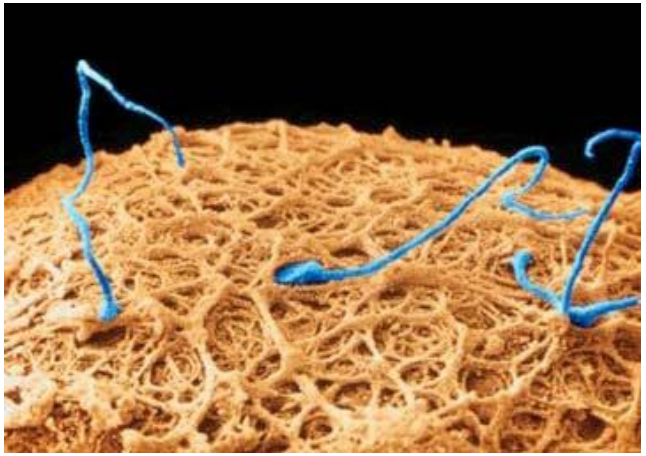


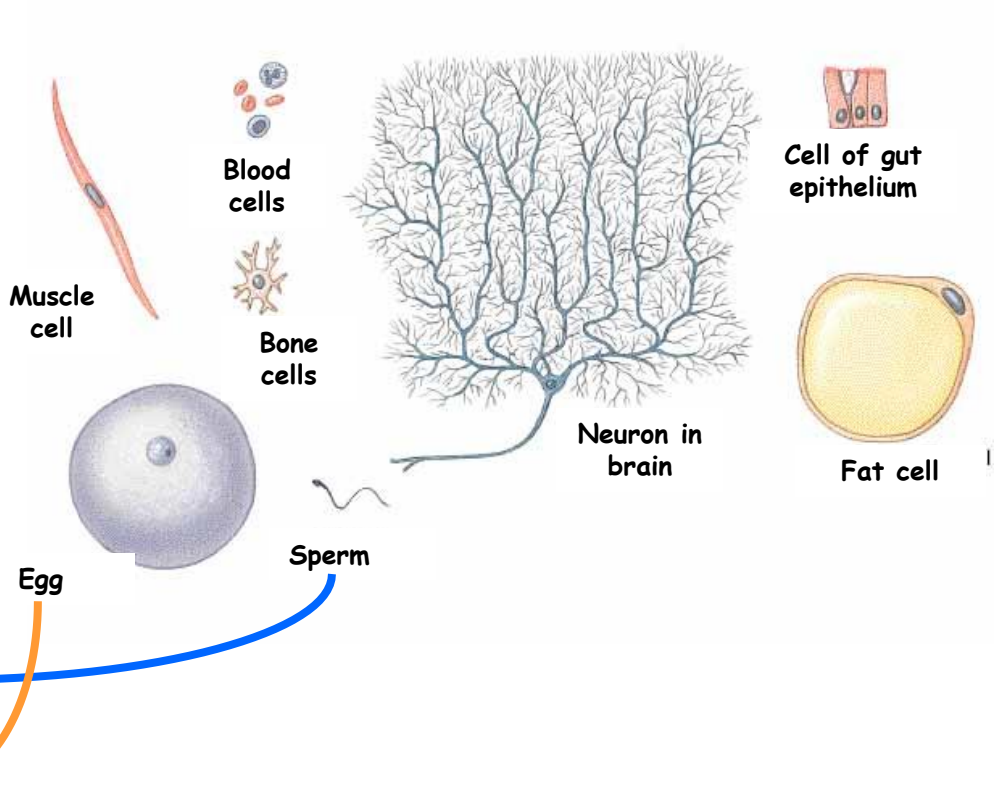


Despite of their common scheme, structural and functional diversity is a typical feature of all eukaryotic cell types

The cells of human tissues and organs are also structurally and functionally very diverse

Such diversity is critical for an ability of cells to serve various functions in human body



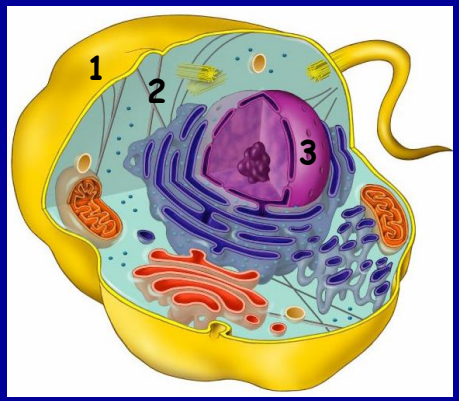


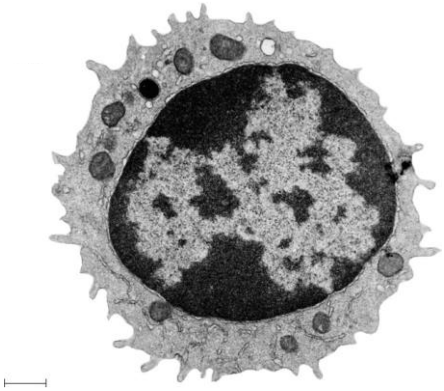
No cell is exactly like all others, but cells do have many common structural and functional features.

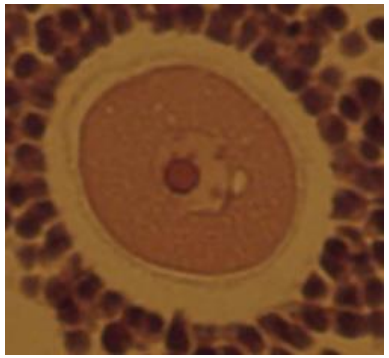
Keep in mind that not all cells contain all the structures we will discuss !

All cells have 3 major parts:

1. PLASMA MEMBRANE
2. CYTOPLASM
3. NUCLEUS (eukaryotic)







Cellular organization is based on COMPARTMENTALIZATION

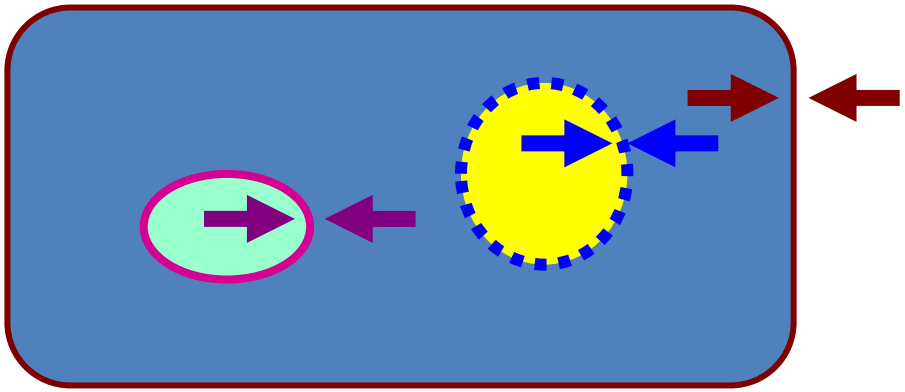
Specialized functions can be carried out in different locations

Membranes make up boundaries between the compartments

Unique protein and lipid components and unique function

Unique control of the movement of molecules

Unique composition of the surrounded interior



Compartments & Membranes

Many small compartments are better

More membrane surface per volume surrounded

More space for:

- **regulation**
- **nutrients exchange**
- **waste removal**

Surface area is proportional to the ***square*** (r^2) of its diameter.
Volume is proportional to the ***cube*** (r^3) of its diameter.

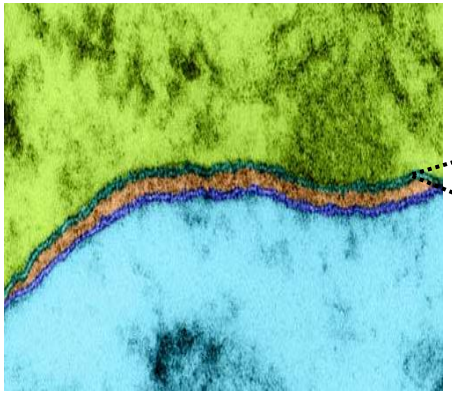
Amplification X Reduction of selected compartments

Specialization of cells for different functions

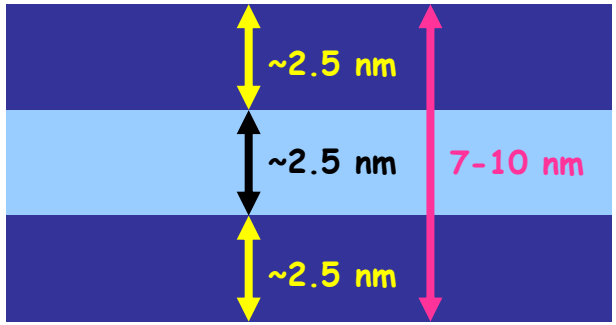
Cell differentiation

Rough ER in secretory cells
Mitochondria in cardiac musle cells

Biological membrane structure 1



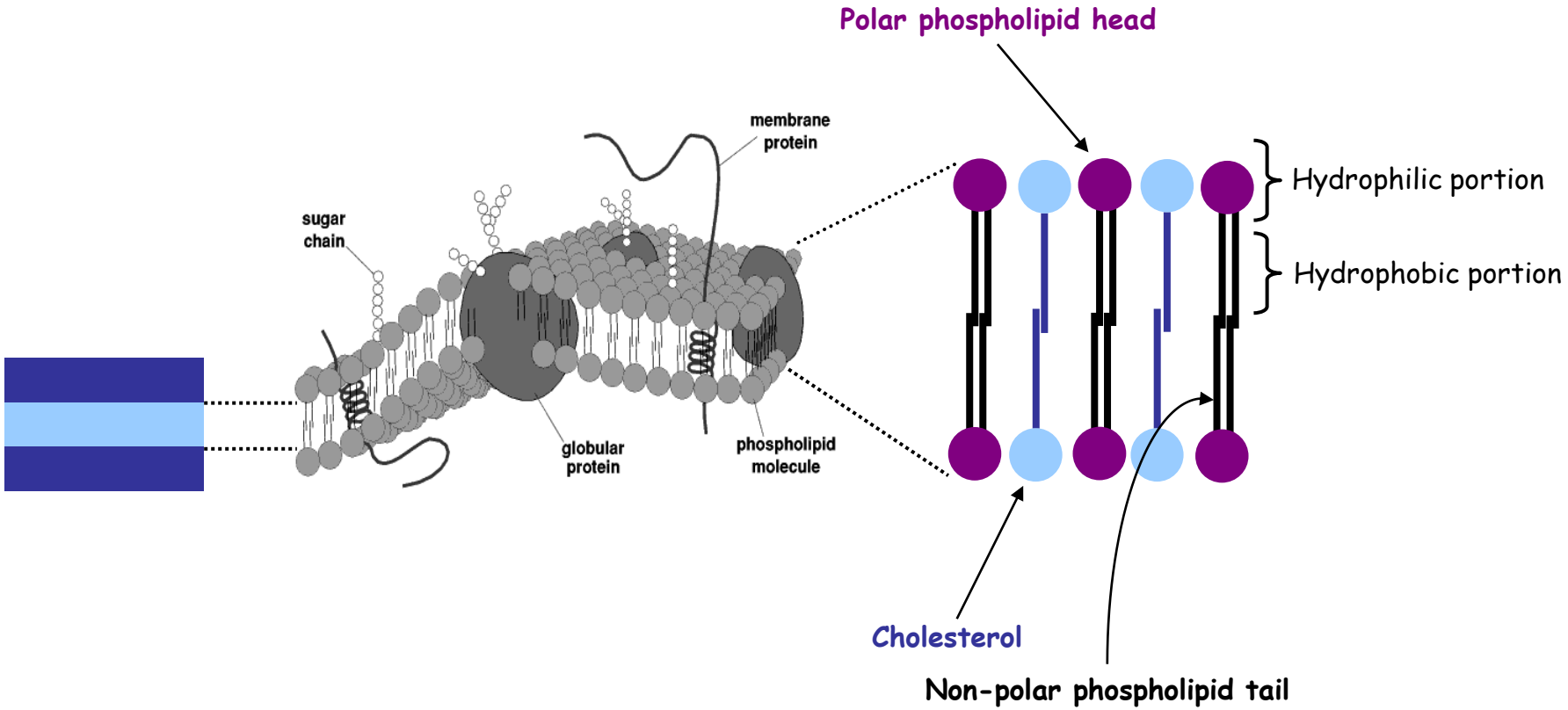
Cell membranes seen
in electron microscope
(pseudocolored)



Unit membrane
common to all membranes

Biological membrane structure 2

Fluid mosaic - A bilayer of lipids with mobile globular proteins



Membrane structure 3

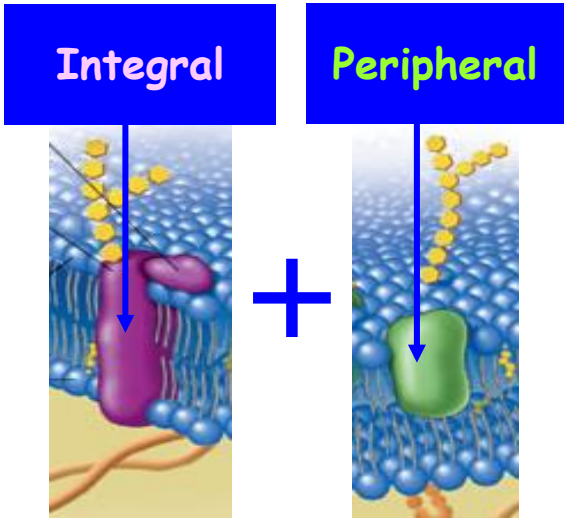
Membrane lipids

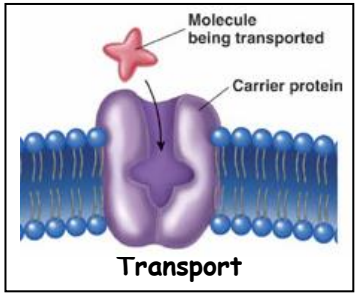
Make up 90-99% of molecules in membrane (in numbers).

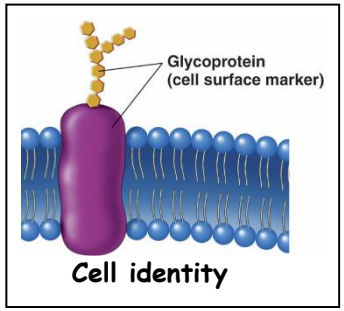
- **Phospholipids** - 75% of lipids
- **Cholesterol** - 20%
- **Glycolipids** - 5% - only on cytoplasmic membrane - GLYCOCALYX

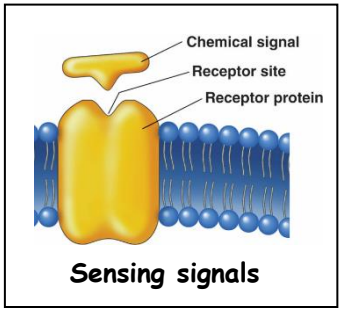
Membrane proteins

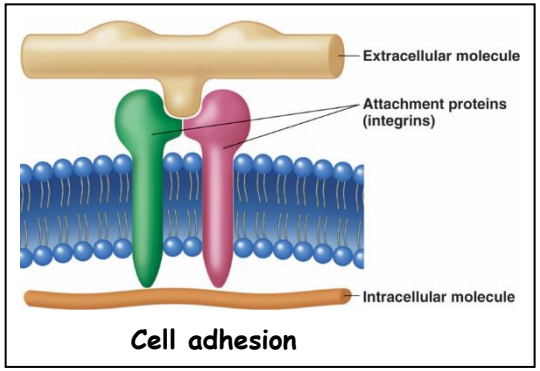
Constitute 1-10% of total molecules but 50% of the weight because of their larger size.

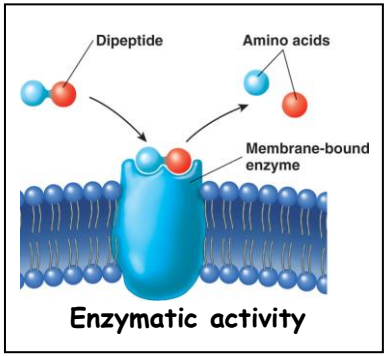












Organelles

Specialized internal structures with specialized functions

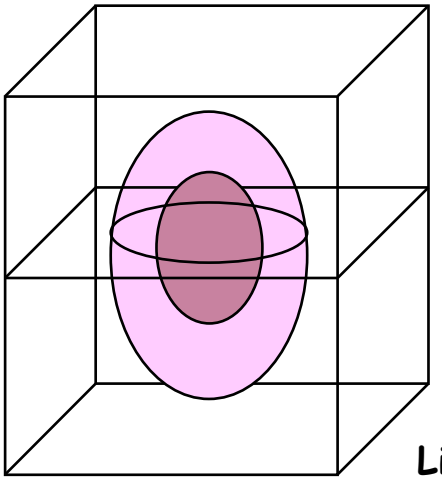
Membranous

- Endoplasmic reticulum
- Golgi apparatus
- Lysosomes
- Endosomes
- Peroxisomes
- Mitochondria

Non-membranous

- Ribosomes
- Centrosomes
- Centrioles
- Basal bodies

Related to specific structure and function of the cell
e.g., much energy needed → many mitochondria

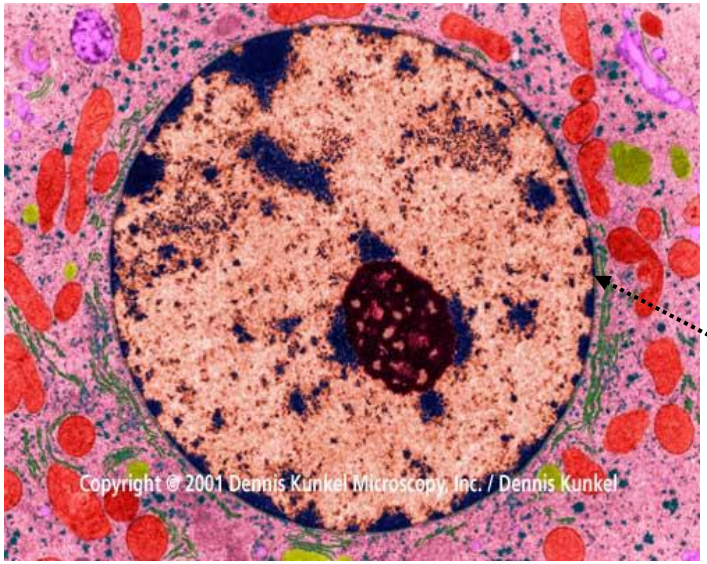


Nucleus 1
Envelop-bounded structure

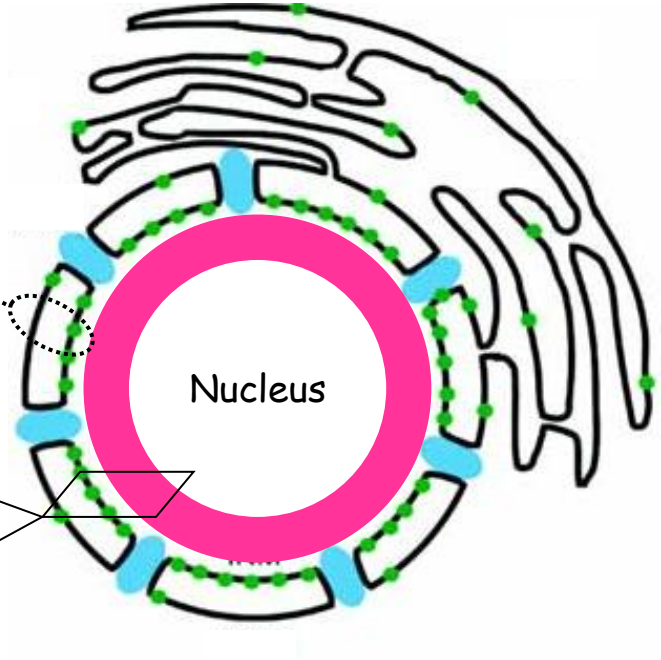
Mostly:

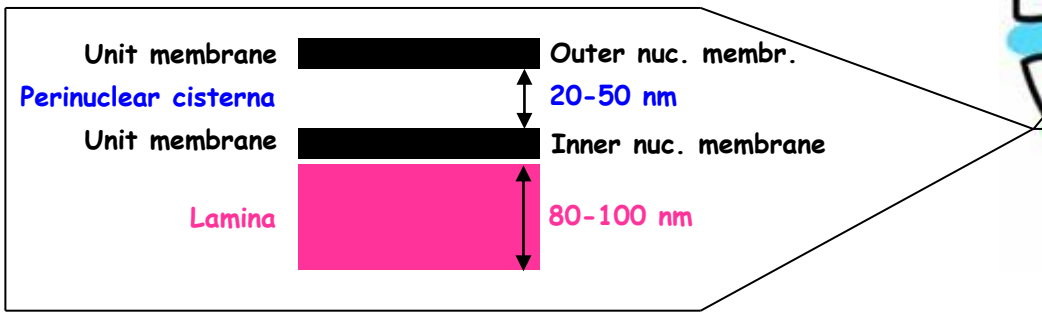
- Spheherical (5-10 μm) (lobular, twisted, disk-shaped,...)
- Located centrally
- One per cell (osteoclast more, erythrocyte none)

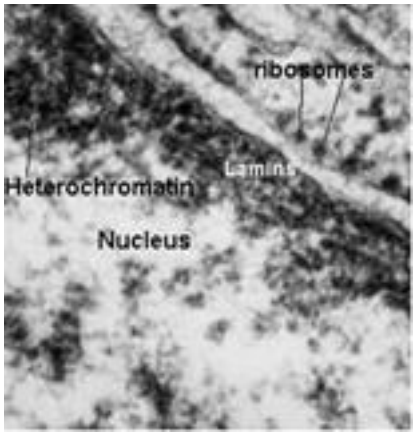
Liver cell nucleus



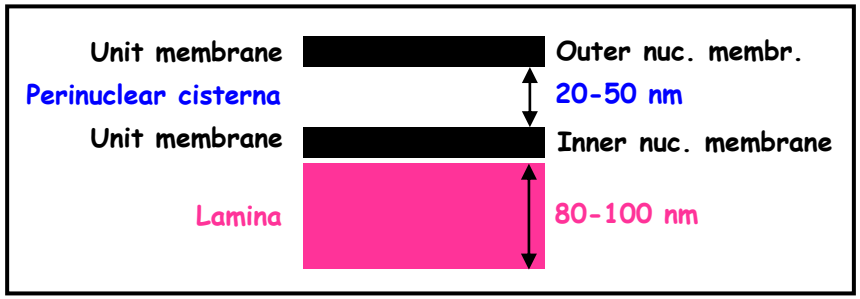
Nuclear envelope

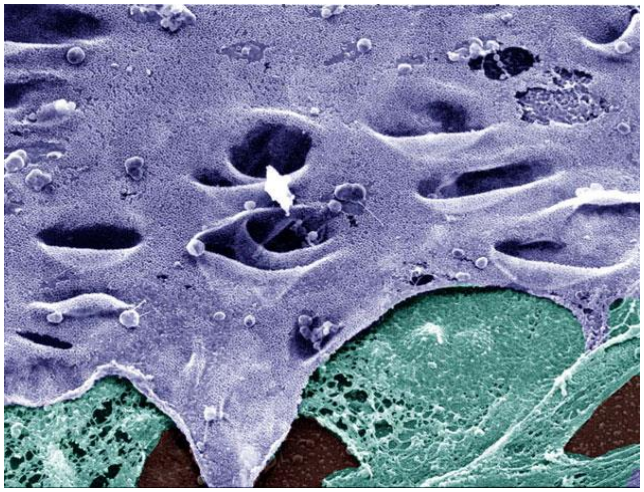




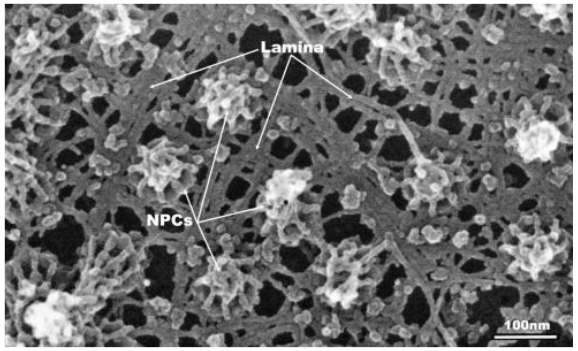


Nucleus 2
Continuation on nuclear envelop

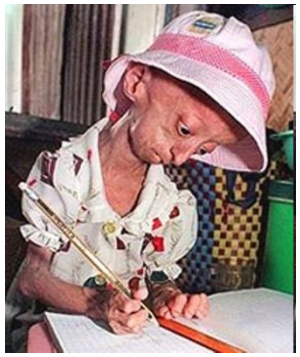




Lamins:
- Intermadiate filament proteins (A, B, C)
- Form meshwork inside of INM, some extend into nucleoplasm
- Nuclear strength and architecture
- Anchorage sites for chromatin
- DNA replication and mRNA transcription
- Involved in apoptosis



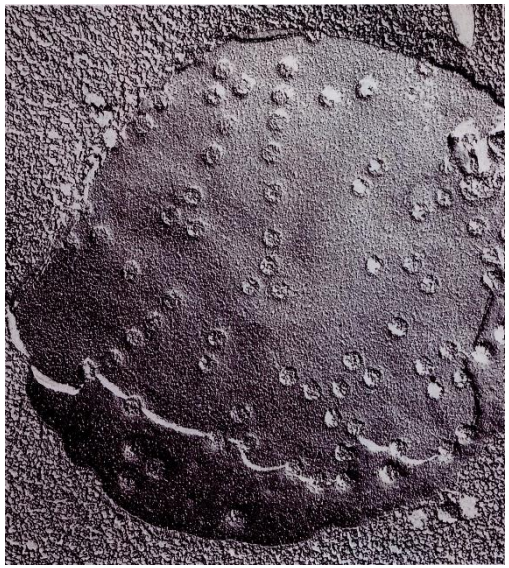
Laminopathies
- Human diseases (at least 13 known)
- Mutations in lamin genes (almost 200 mutations known)
- Deregulated gene expression
- Premature aging

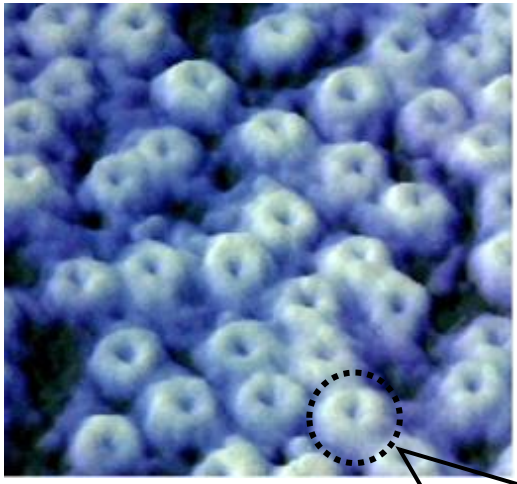


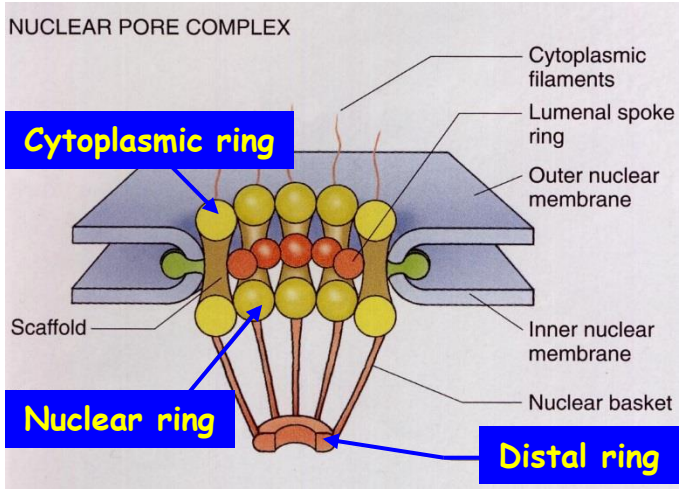
Hutchinson-Gilford progeria

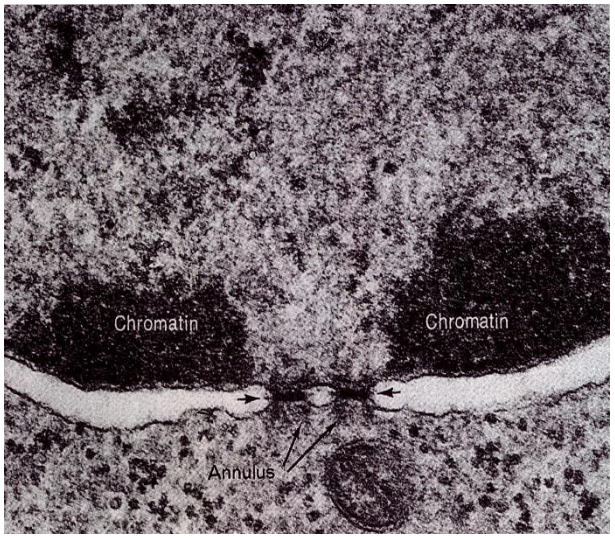
Rare - 1-4 per 8 milion of newborns
Missense mutation in A-type lamin

Nucleus 3
Nuclear pore complex









Diameter ~ 100 – 125 nm

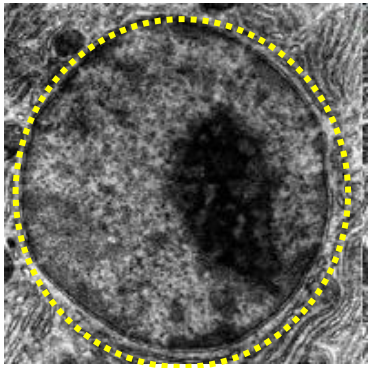
Three rings (8 subunits each)

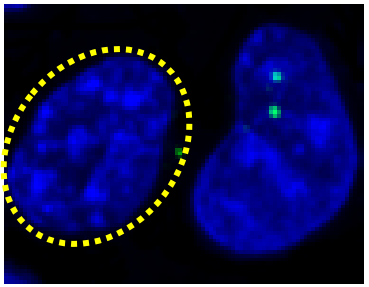
Inner filamentous basket

Transport via nuclear pores
(Nucleocytoplasmic shuttling)

- Proteins, RNAs, ribosome subunits
- Bidirectional
- Needs nuclear localization/export signals
- Helped by importins/exportins
- Regulated by Ran GTPases

Nucleus 4
Chromatin





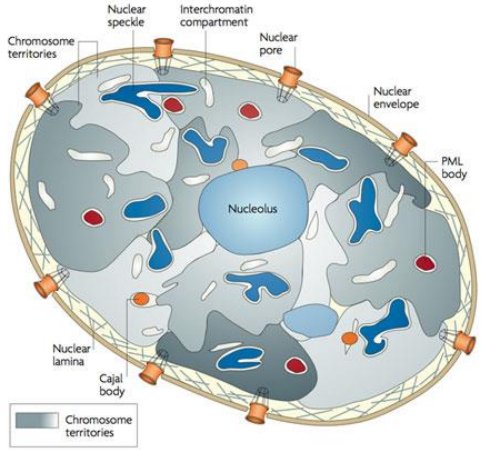
Interphase nucleus

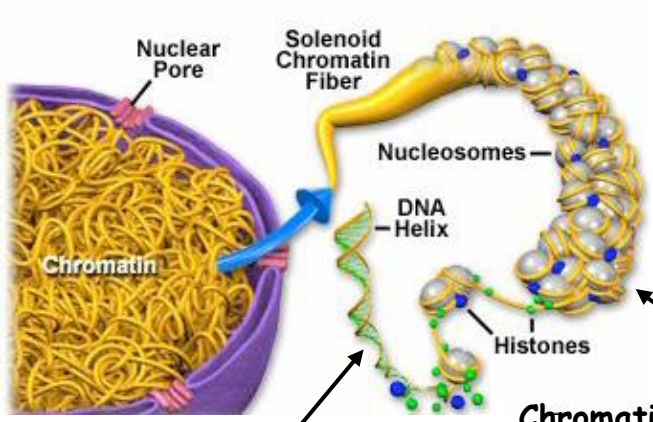
Heterochromatin

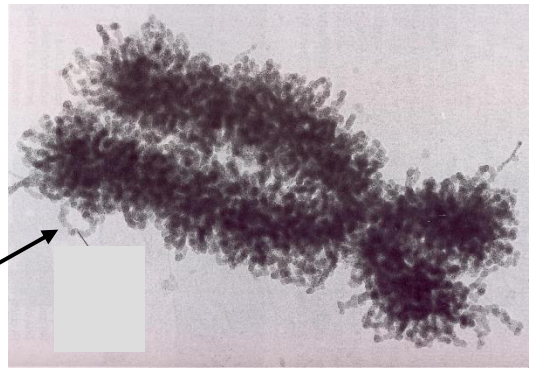
Feulgen positive – dark in light microscope
Dark/dense granular in TEM
Transcriptionally inactive

Euchromatin

Invisible in light microscope
Relaxed uncoiled chromosomes
Transcriptionally active

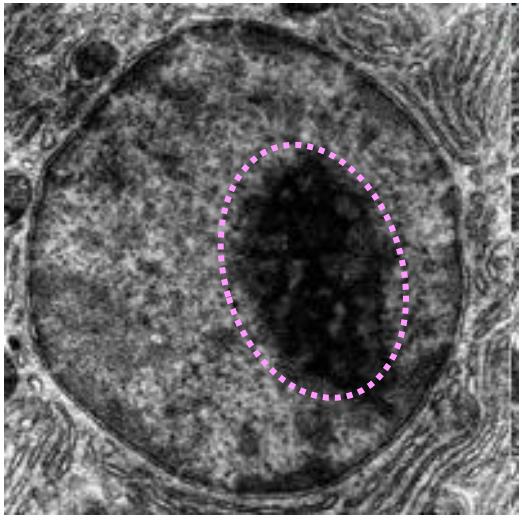






2 nm
DNA double helix

30 nm
Chromatin fiber of packed nucleosomes

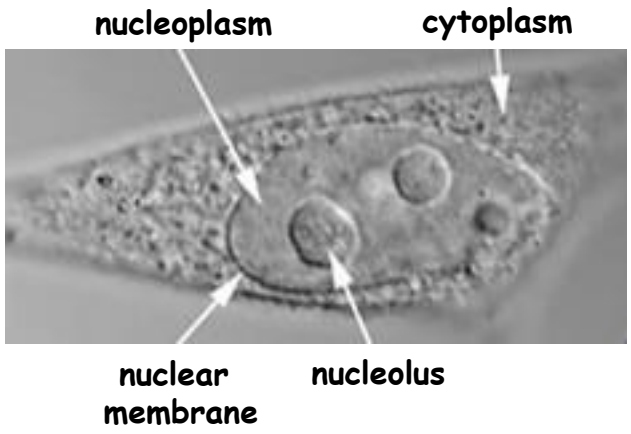


Nucleus 5
Nucleolus

non-membrane-bounded structure

Main functions

Synthesis of rRNA
Assembly of ribosomes



Pars granulosa
Assembly of ribosomes

Pars fibrosa
Primary transcripts of rRNA

Nucleolar-organizing regions of DNA

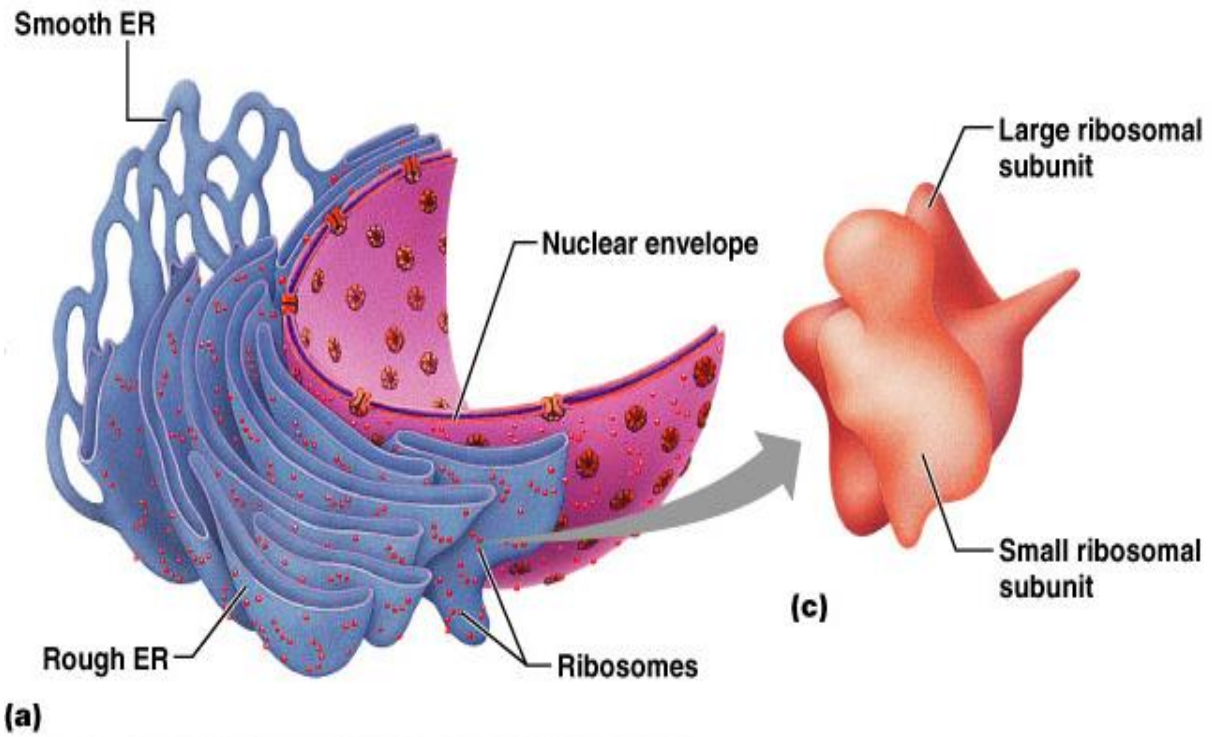
on five chromosomes in human cells
(chrs. 13, 14, 15, 21, 22)

Endoplasmic reticulum 1

„within cell“ „net“

Majority of the membrane within cells.

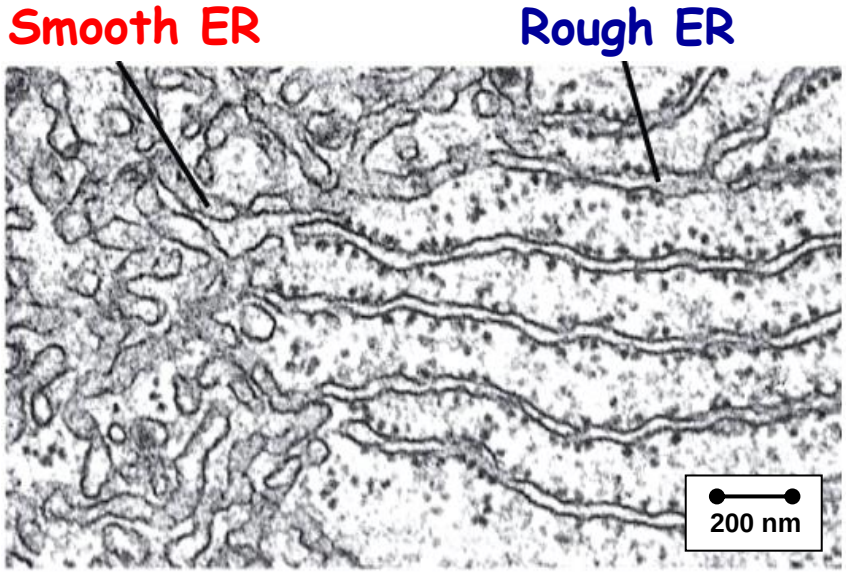
Interconnected tubuli and vesicles → Cisterns

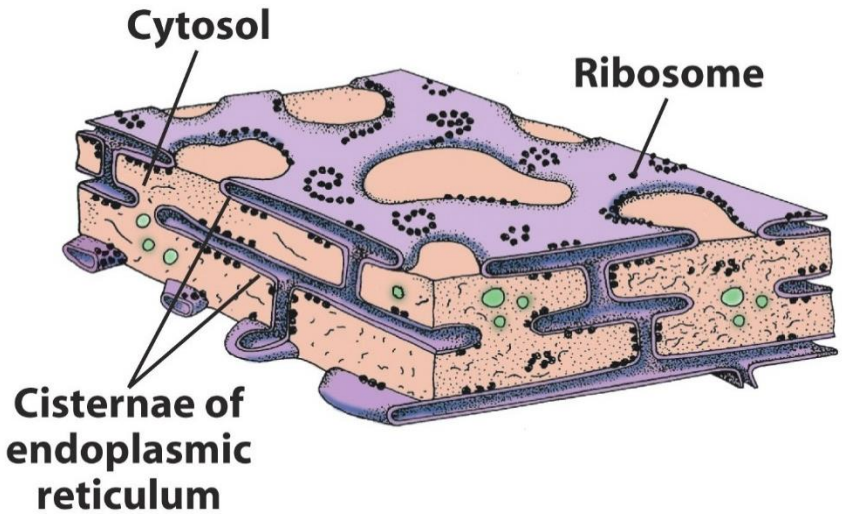


Endoplasmic reticulum 2

NO attached ribosomes → **No** protein-synthesis functions!
Manufactures phospholipids and cholesterol

- **Liver** – lipid and cholesterol metabolism, breakdown of glycogen and, along with the kidneys, detoxification of drugs
- **Testes** – synthesis of steroid-based hormones (testosterone)
- **Intestinal cells** – absorption, synthesis, and transport of lipids
- **Skeletal and cardiac muscle** – storage and release of calcium (sarcoplasmic reticulum)





External surface **has ribosomes attached**

- Manufactures all secreted proteins
- Synthesizes integral membrane proteins
- Modifies proteins

Ribosomes

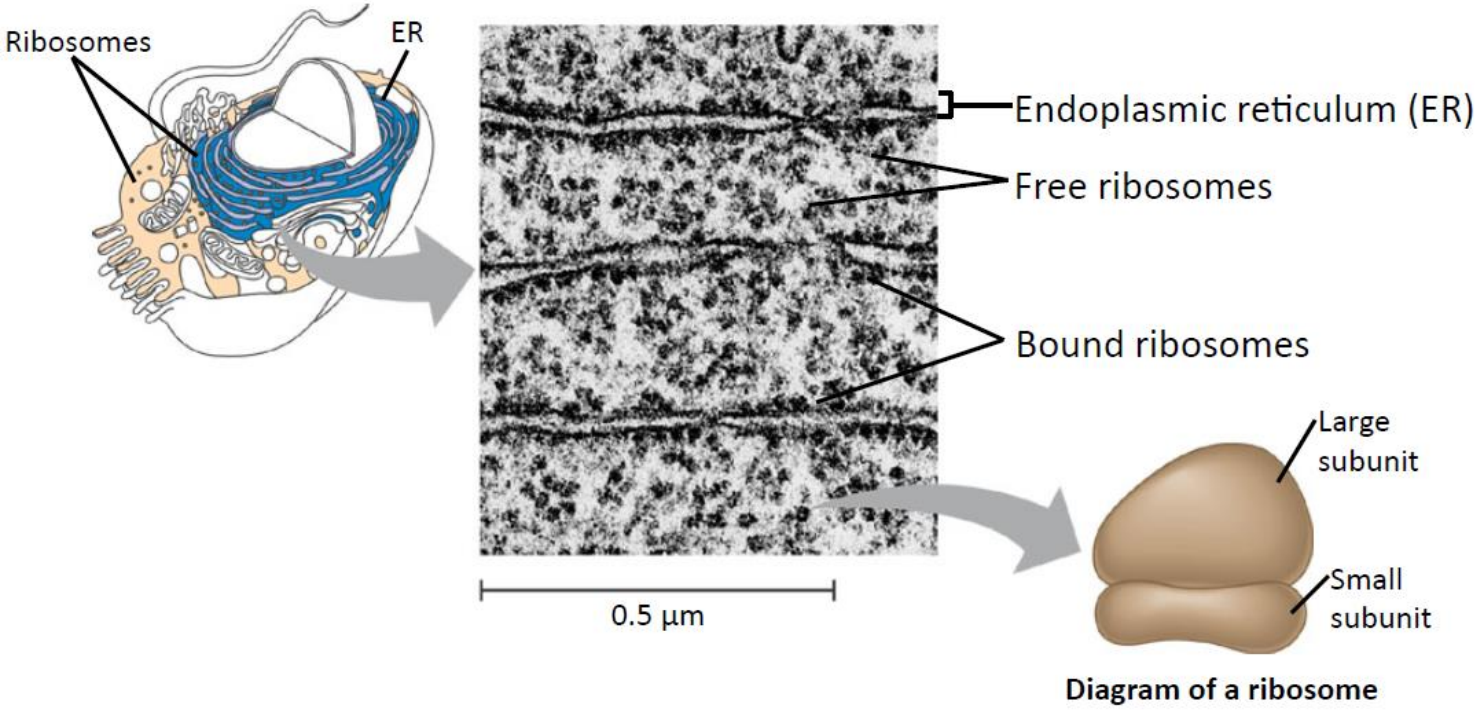
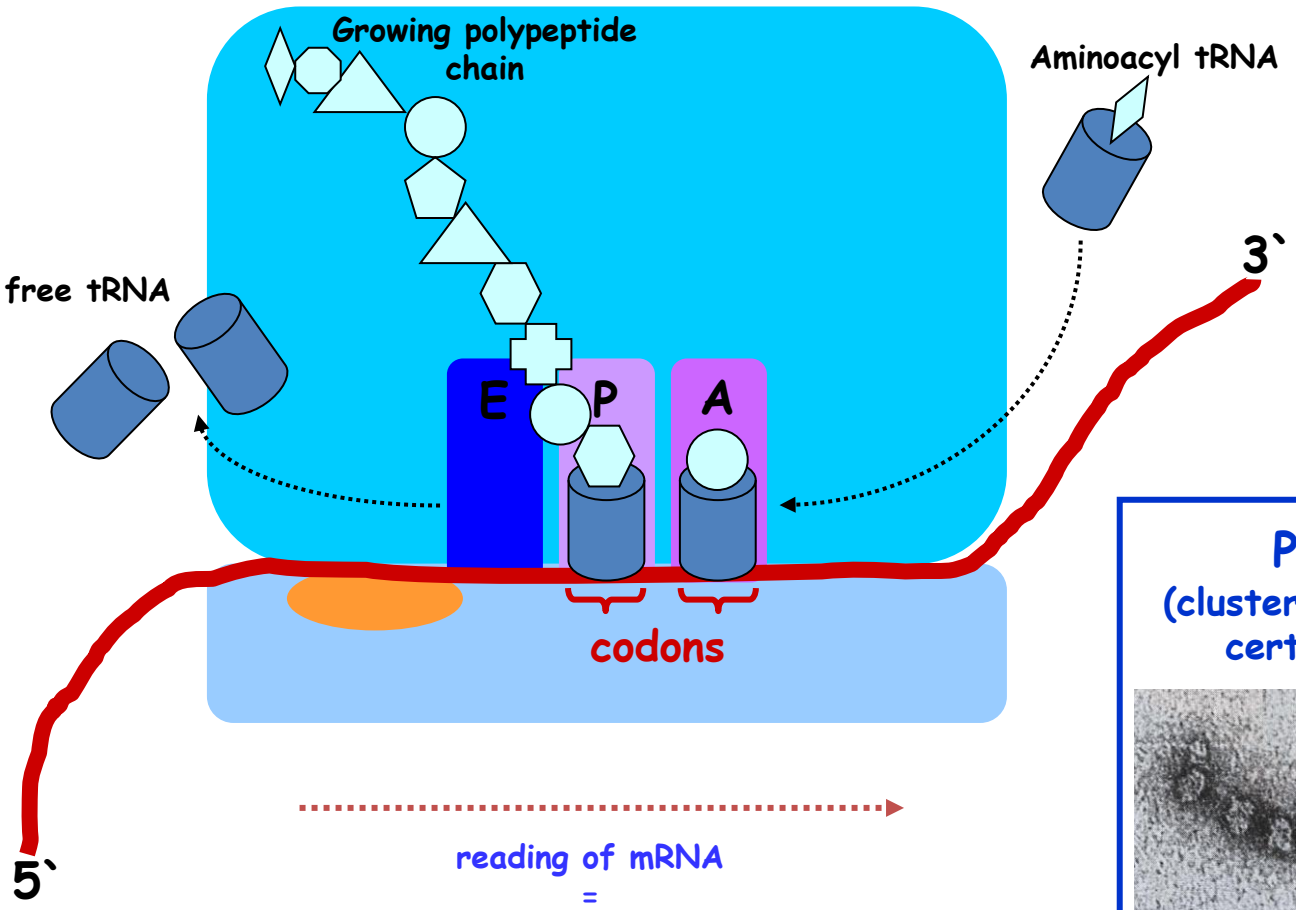


Diagram of a ribosome

Ribosomes - Translation



Beginning of translation

Met-tRNA

3` UAC 5`

mRNA 5` — AUG — 3`

START kodon

End of translation

mRNA 5` — UAG — 3`

mRNA 5` — UAA — 3`

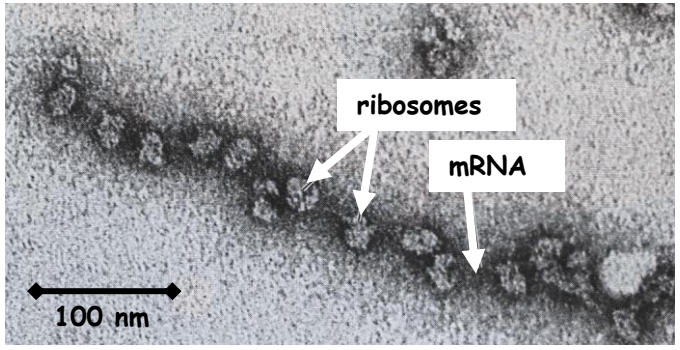
mRNA 5` — UGA — 3`

STOP kodony

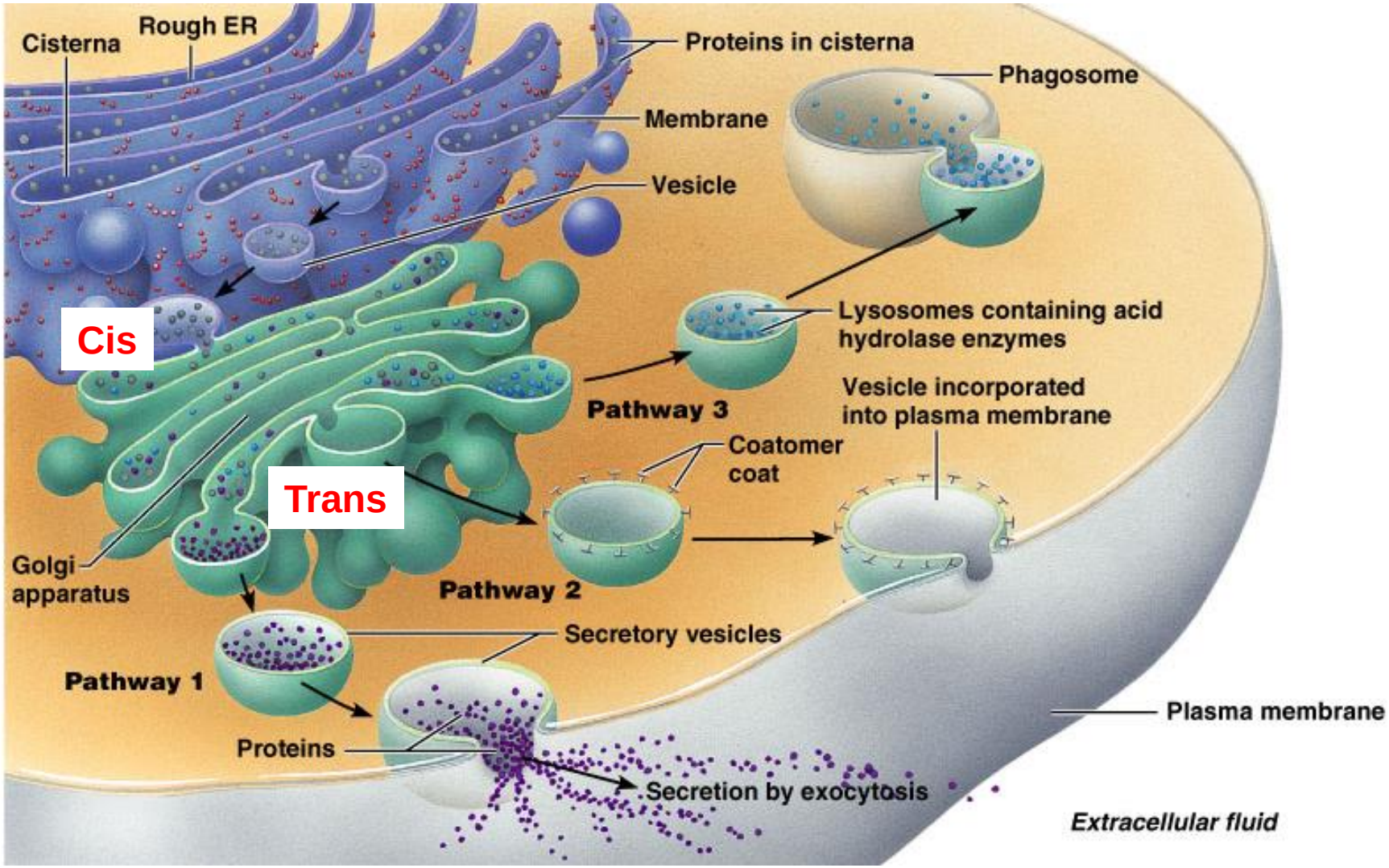
bind „release factor"

POLYRIBOSOME

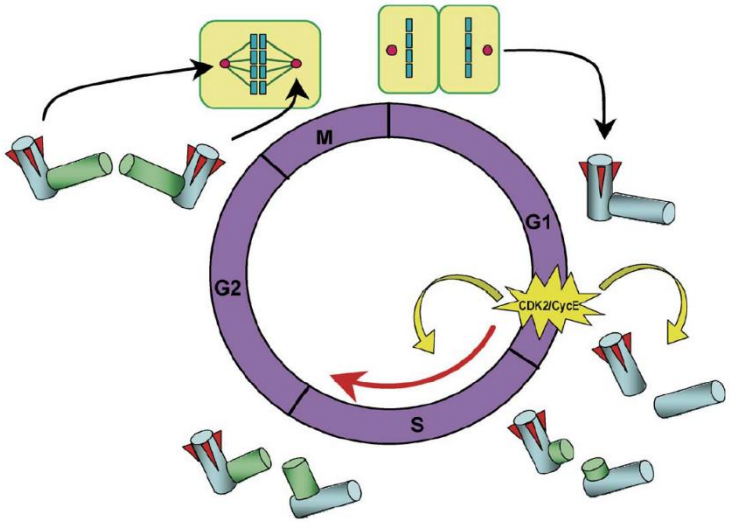
(cluster of ribosomes translating certain segment of mRNA)

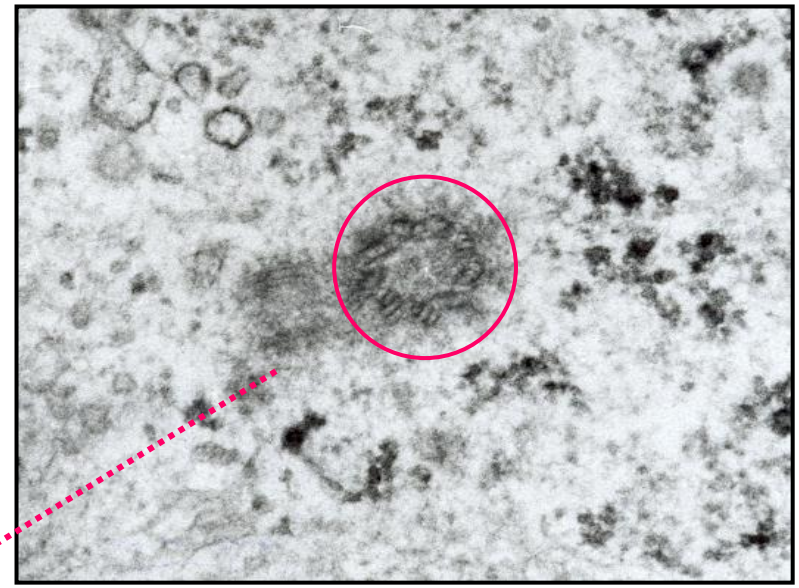


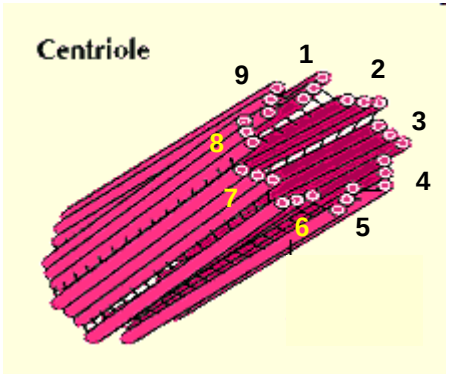
Golgi apparatus – Transgolgi pathway



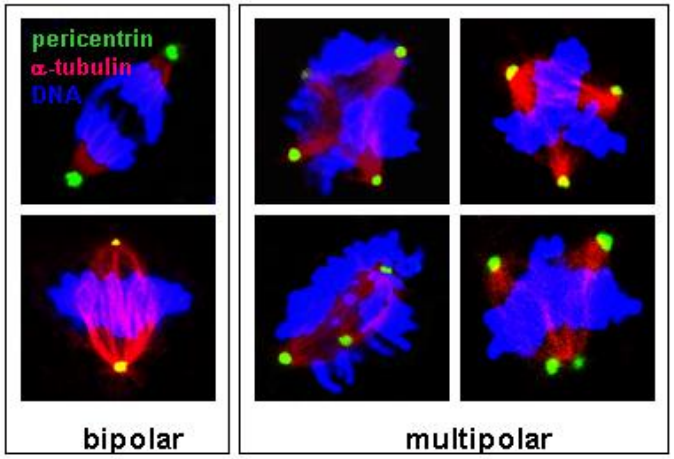
Centrosome



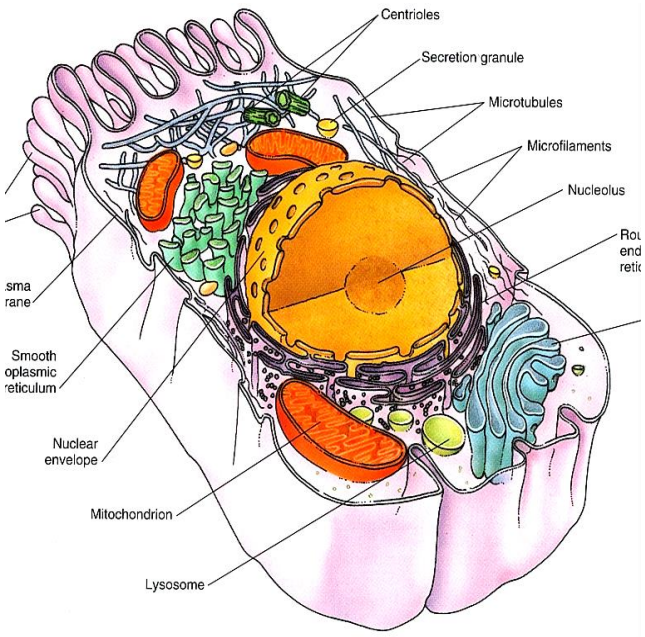


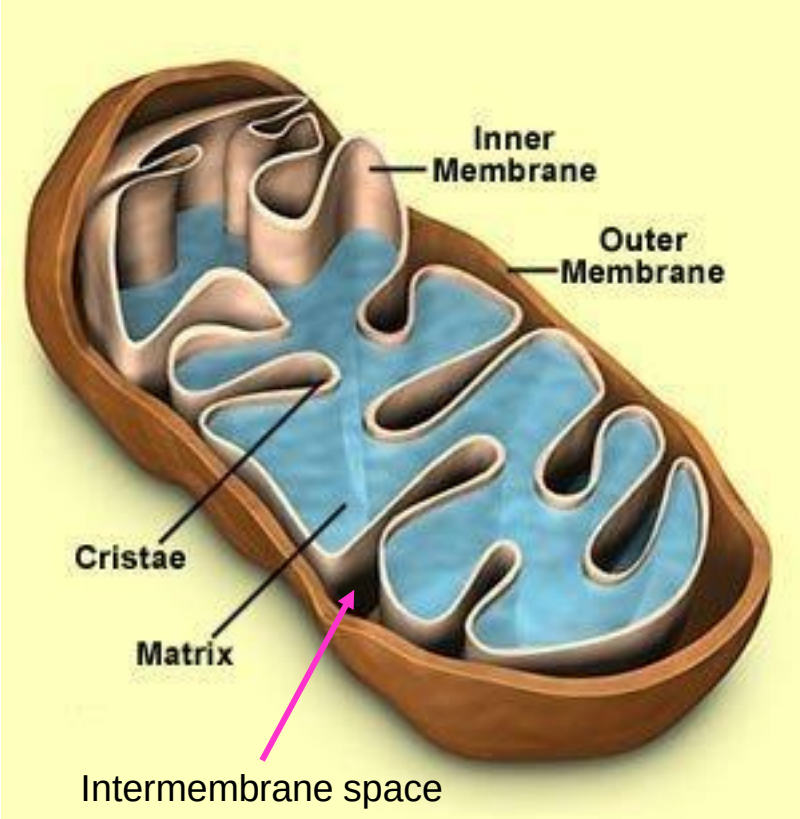


Diameter – 0.2 μm
Length - 0.5 μm



Mitochondria 1

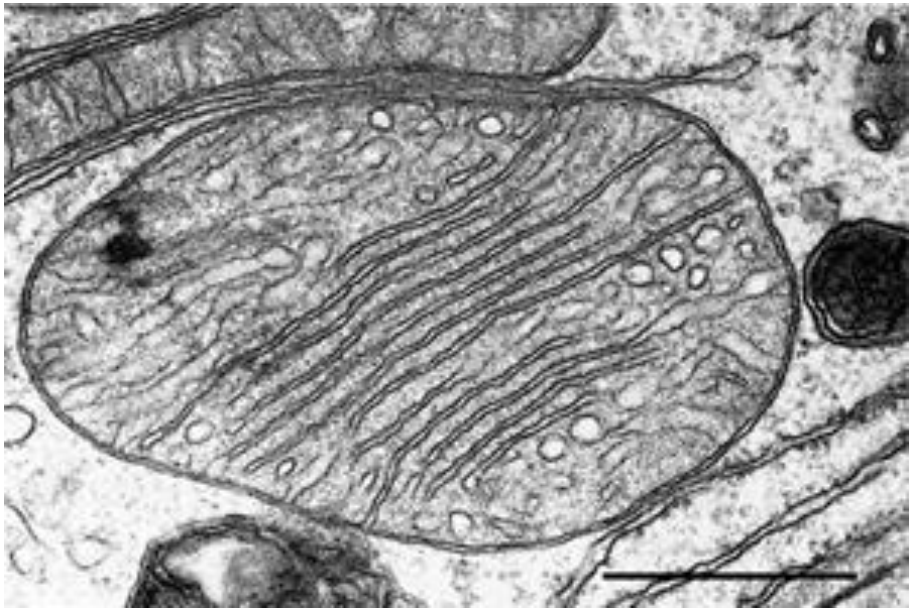




- all cells except erythrocytes
- double membrane
- diameter cca 0,5 μm
- length up to 50 (100) μm
- oxidative metabolism (glucose – ATP + CO_2 + H_20)
- cytochrome c – activation of apoptotic pathway
- origin in oocyte
- mtDNA (circular)
- brown fat thermogenesis

- both membranes with low fluidity
- both membranes equipped with many protein molecules
- growth and divission of mitochondria

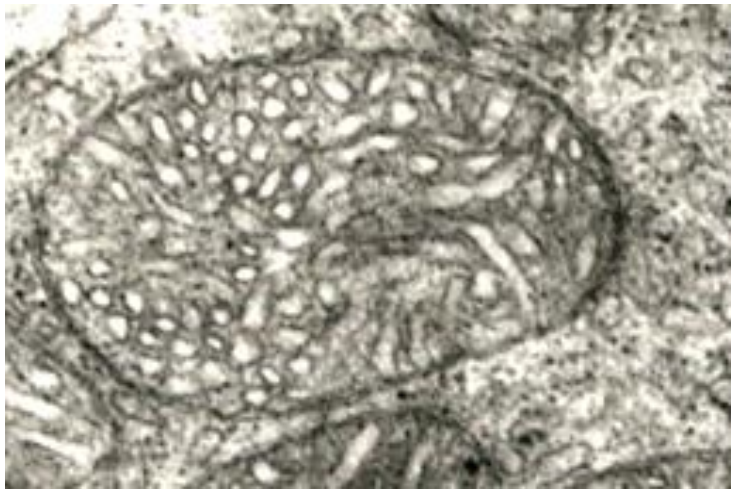
Mitochondria 2



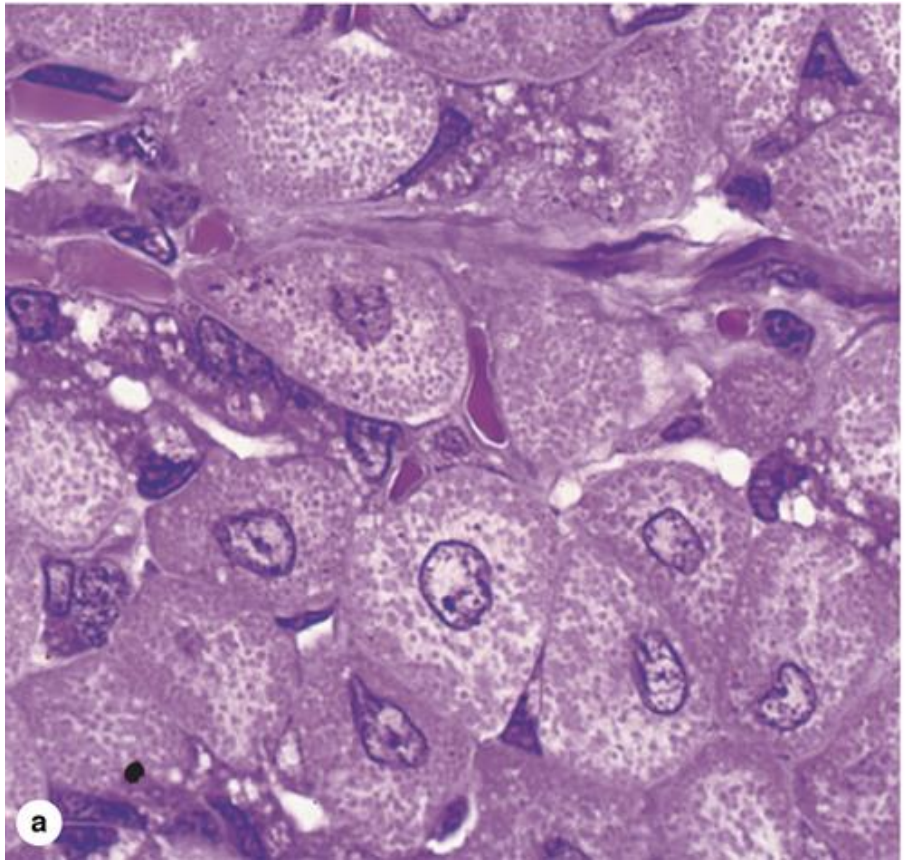
Mitochondria 3

with crists

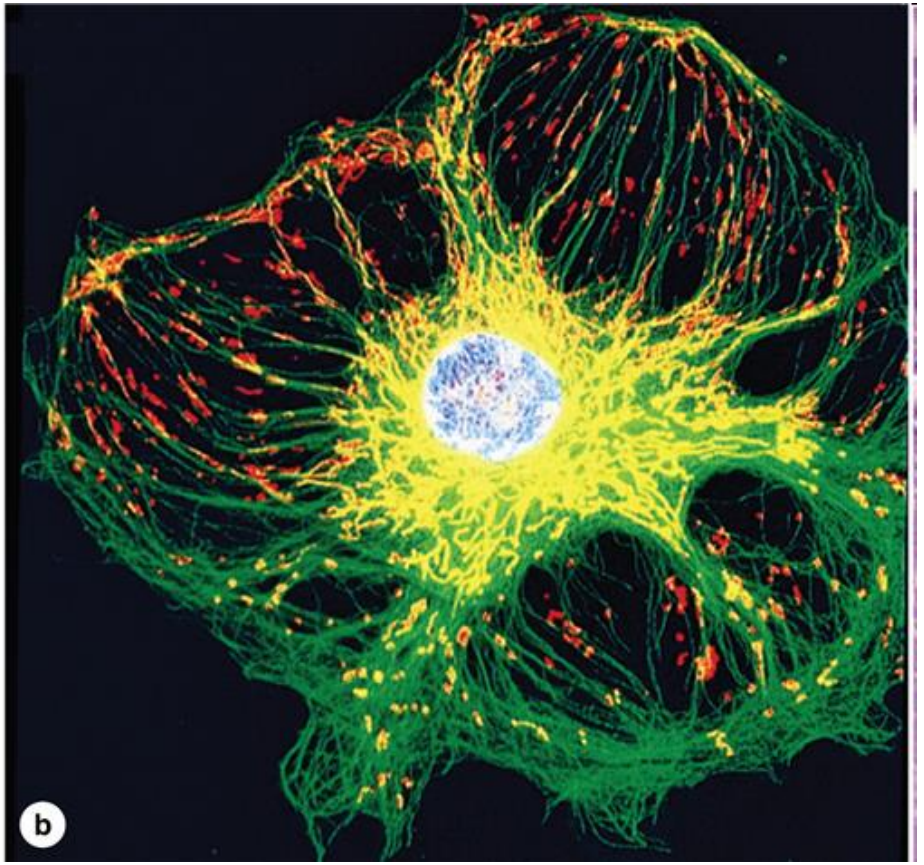
with tubuli (in steroid producing cells)



Mitochondria 4



mitochondrial eosinophilia



mitochondria
microtubuli

Lysosomes 1

endosome-lysosome system

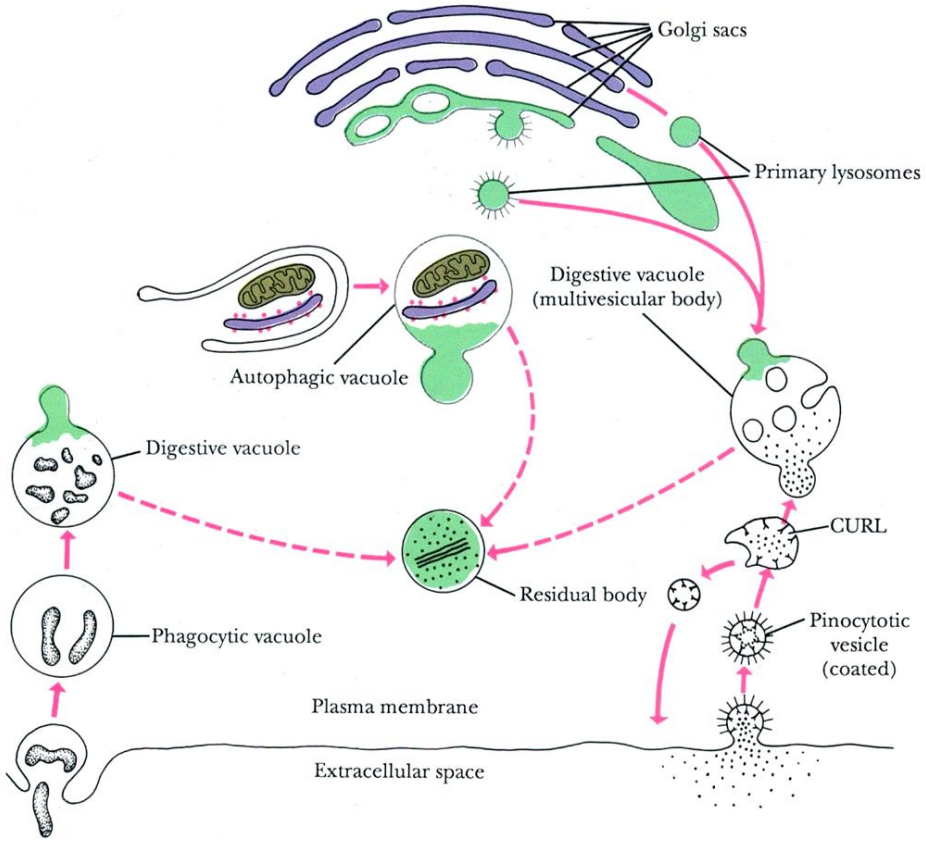
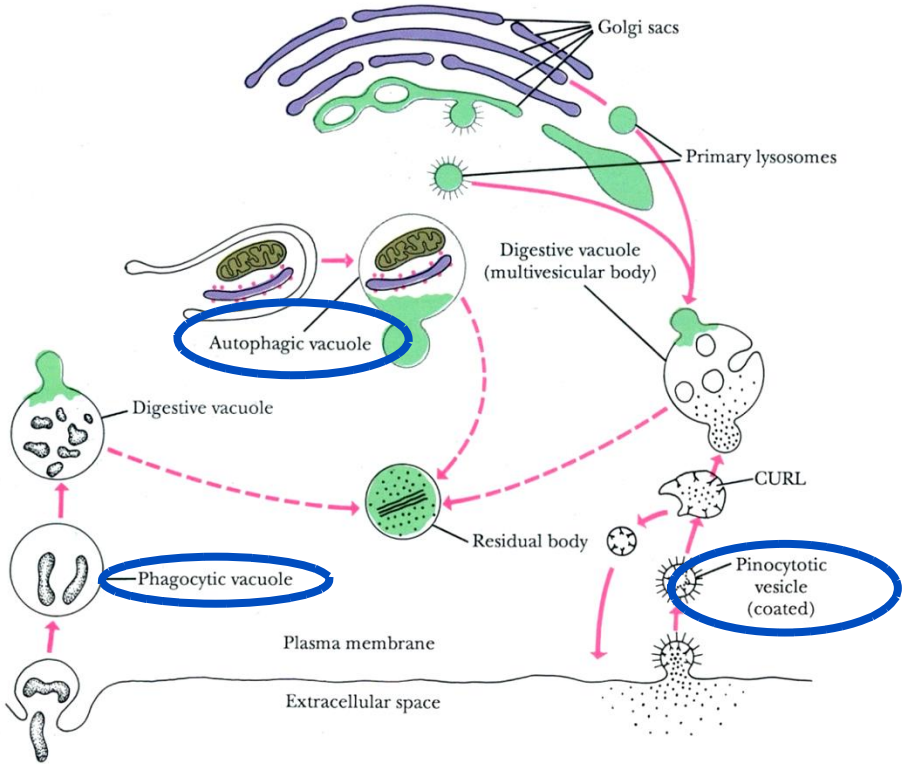


Figure 2.17. Origins of primarily lysosomes from the Golgi and trans-Golgi network. Primary lysosomes fuse with and discharge hydrolytic enzymes into autophagic, pinocytotic (or endosome), and phagocytic vacuoles to form secondary lysosomes (digestive vacuoles). Residual bodies contain undigested residue. Endosomes fuse to form a compartment where uncoupling of the ligands and surface receptors occurs (CURL, see text for explanation). The compartment containing the free ligands subsequently fuses with the lysosome; the receptors remain bound to the membrane of vesicles which is partitioned off from the CURL and recycle to the plasma membrane. (Modified from Novikoff AB, Holtzman E: *Cells and Organelles,* 2nd ed. New York, Holt, Rinehart and Winston, 1976.)

- in all cells except for erythrocytes
- vesicles about 0,05 – 0,5 μm
- membrane-bound
- highly acidic internal space (cca pH 5)
- hydrolytic enzymes inside (min. 50 types)
- tagging by mannose-6-fosphate

Lysosomes 2

primary x secondary



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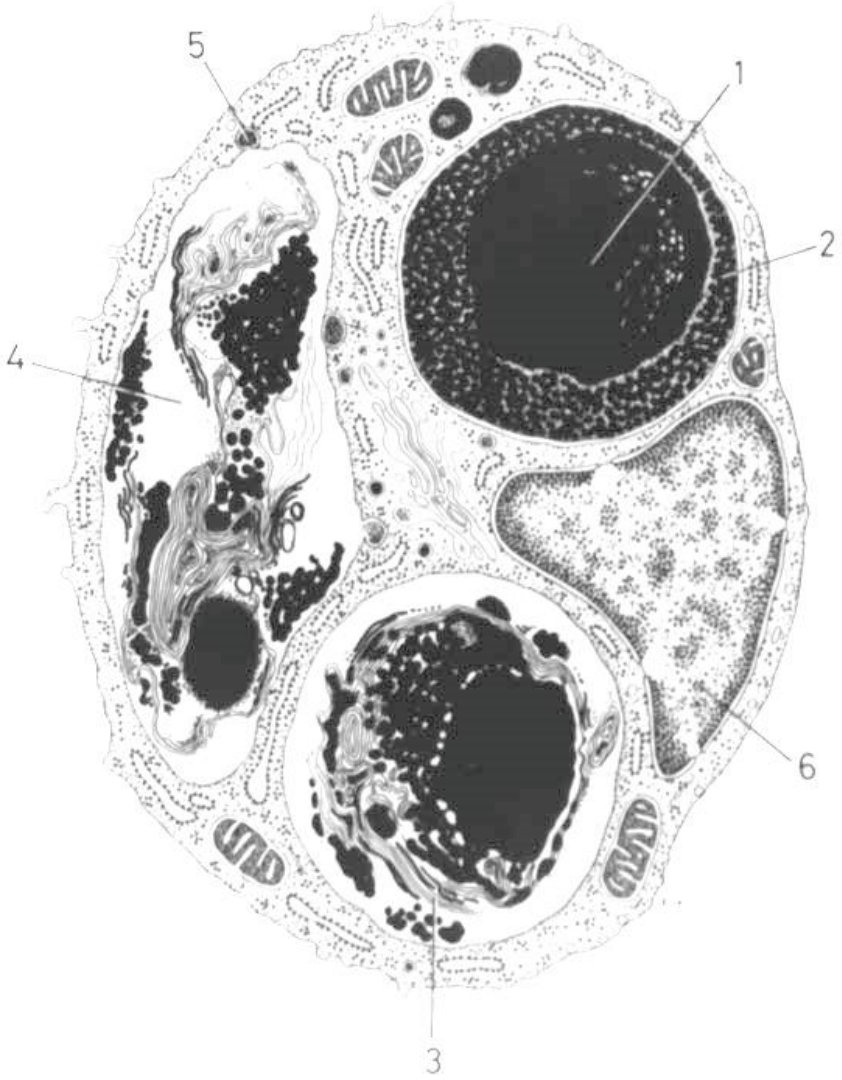
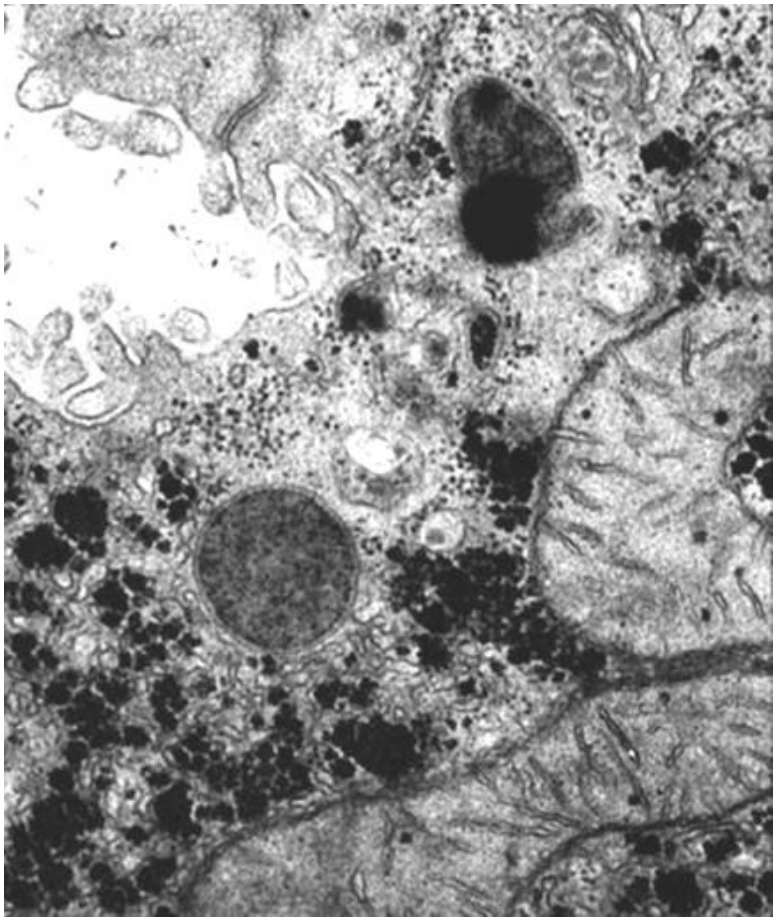
- primary lysosomes
- secondary lysosomes (fagolysosomes)
- residual bodies (lipofuscin)

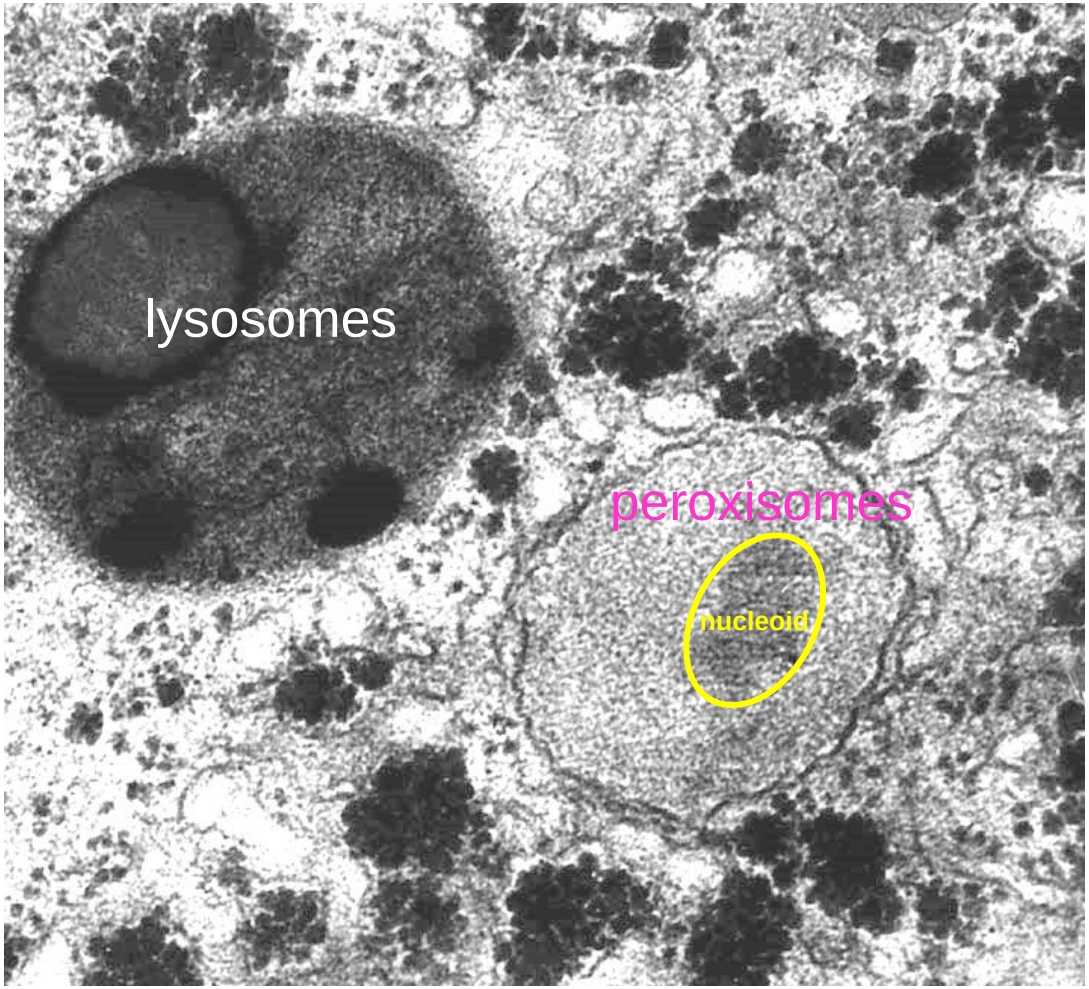
Lysosomes 3

secondary lysosomes





Peroxisomes



- structuraly similar to lysosoms
- functionally similar to mitochondria
- „nucleus “ = nucleoid
- degradation of fatty acids (H_20_2, H_2O, 0_2)
- detoxification (complement SER)
- origin: growth from ER or division

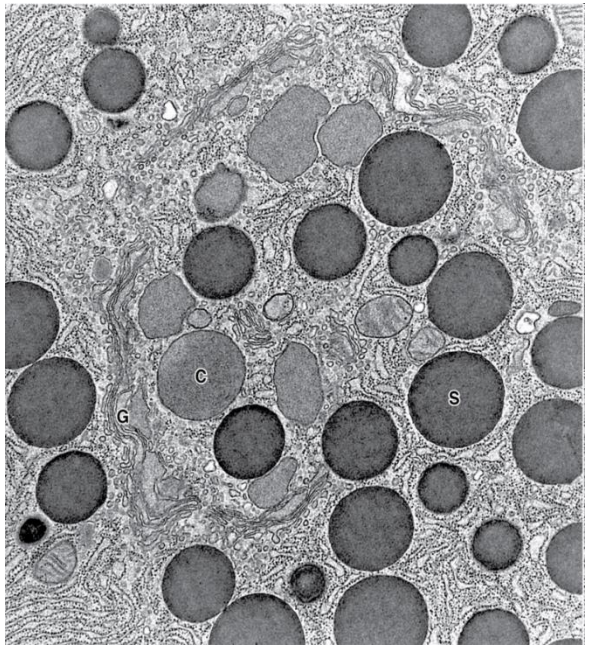
Cytoplasmic inclusions 1

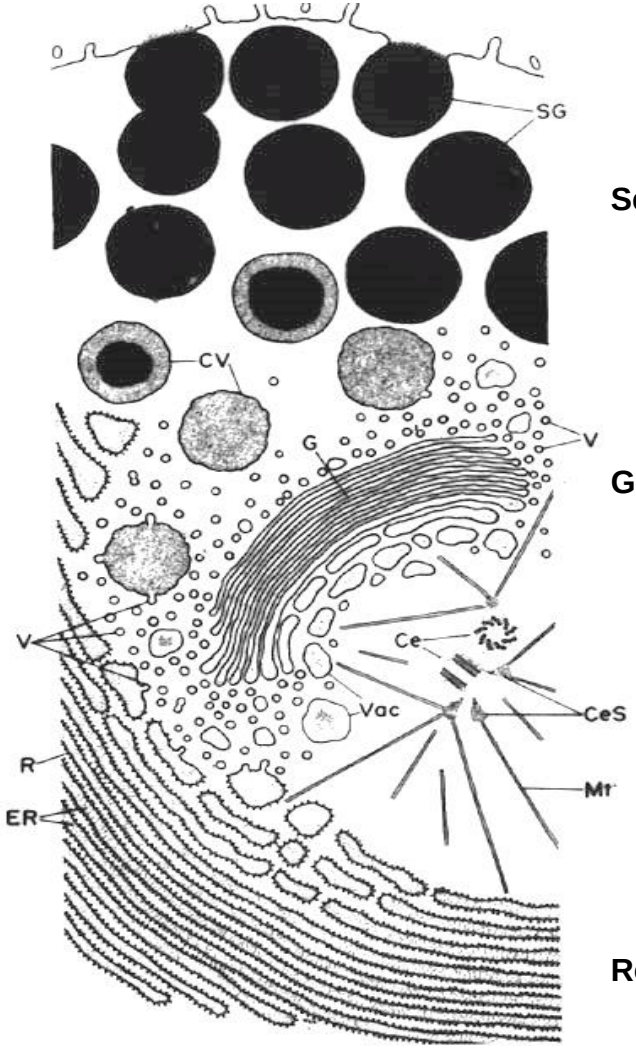
(no or only little metabolic activity on themselves)

- **secretory granules**
- **storage compounds**: sugars (glycogen), lipids
- **crystals** (proteins)
- **pigments**: endogenous (autogenic and hematogenic) + exogenous

Cytoplasmic inclusions 2

Secretory granules





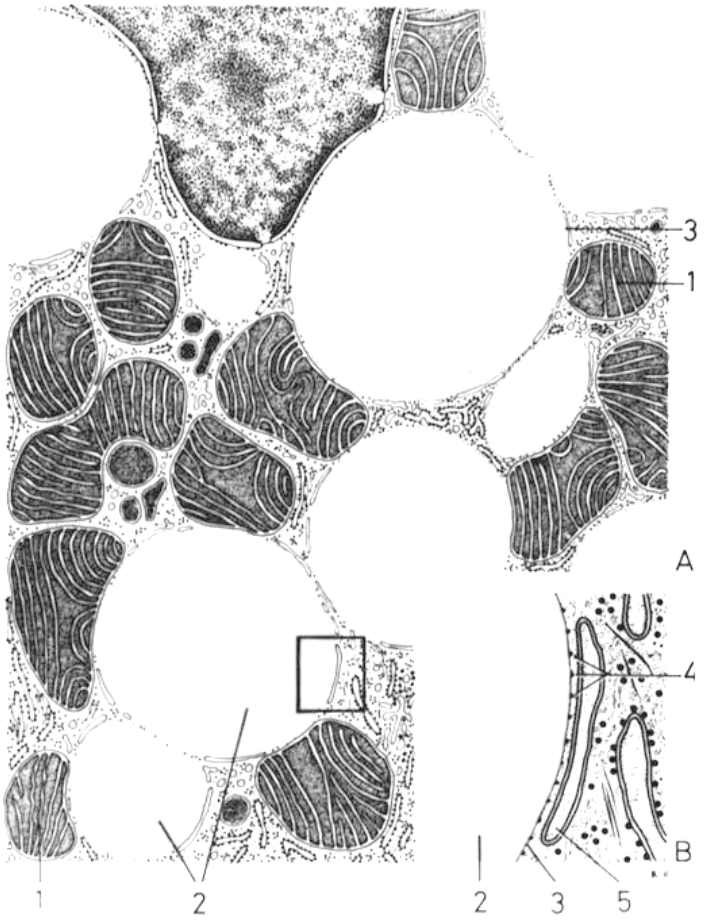
Secretory granules

Golgi apparatus

Rough ER

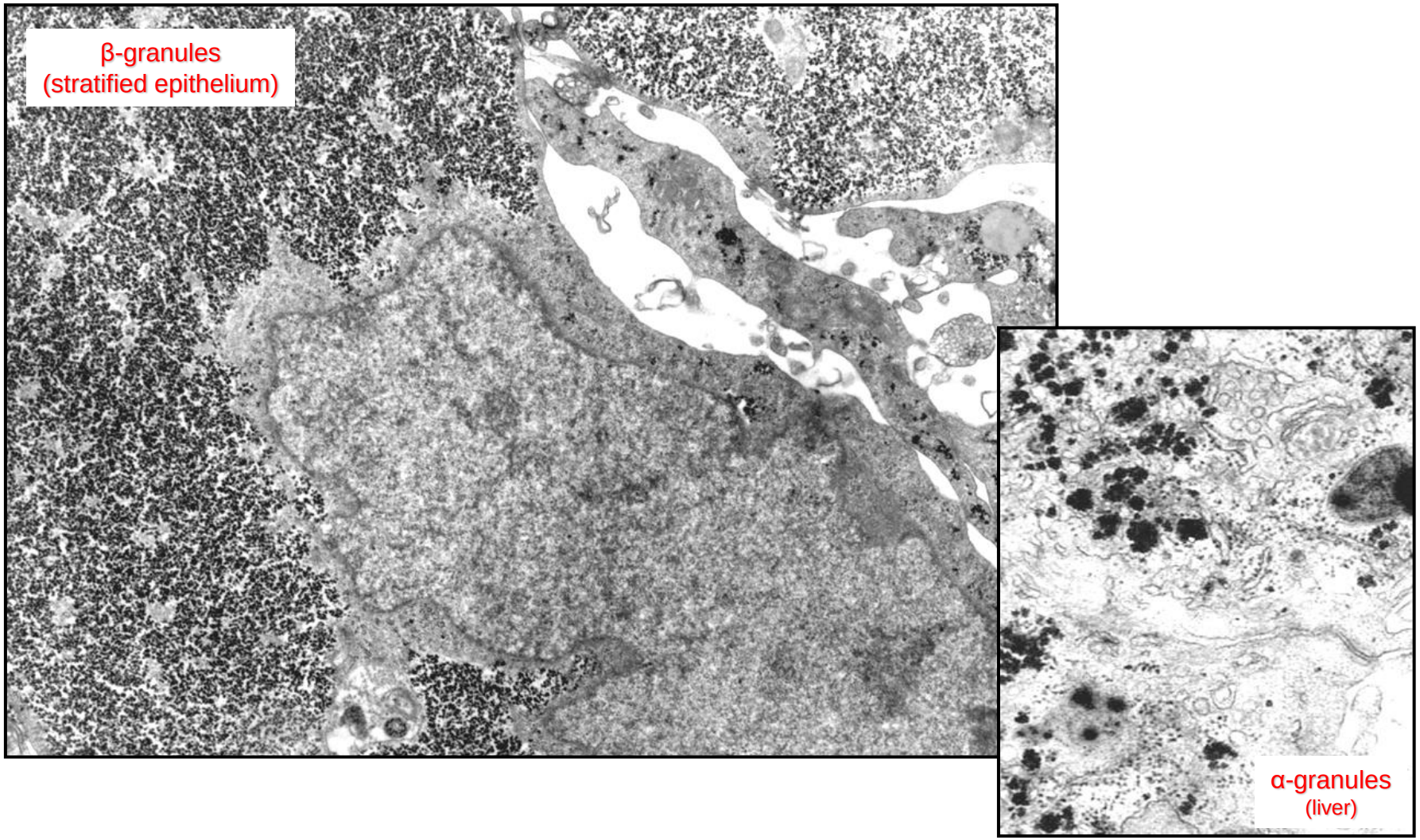
Cytoplasmic inclusions 3

Lipid inclusions



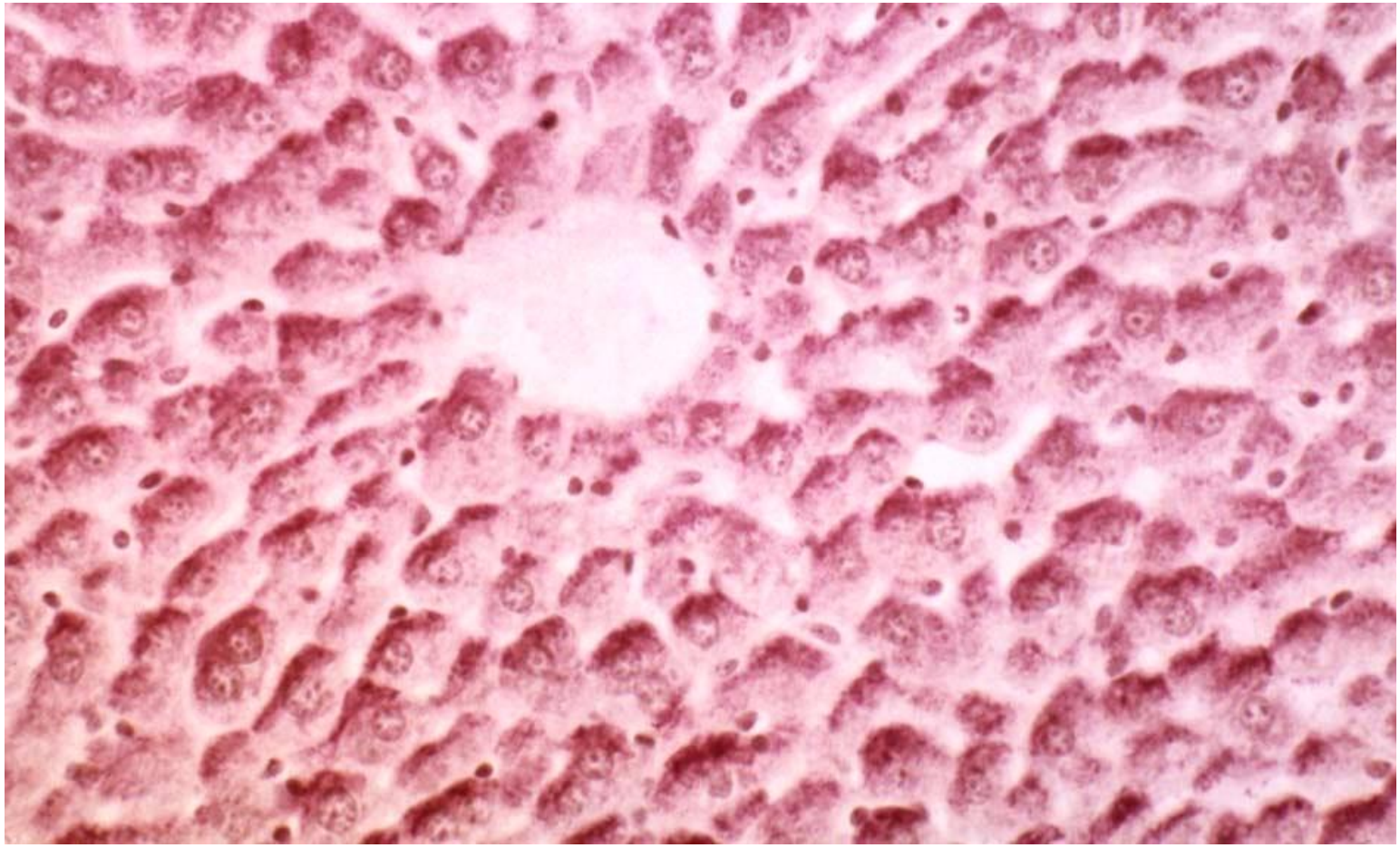
Cytoplasmic inclusions 4

Glycogen



Cytoplasmic inclusions 5

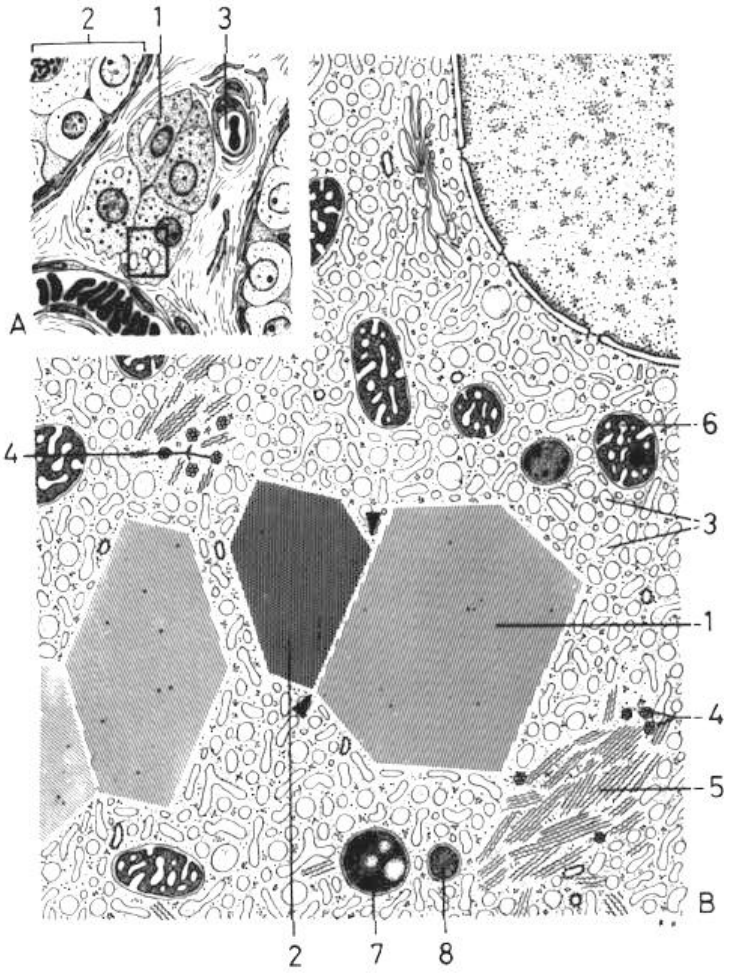
Glycogen

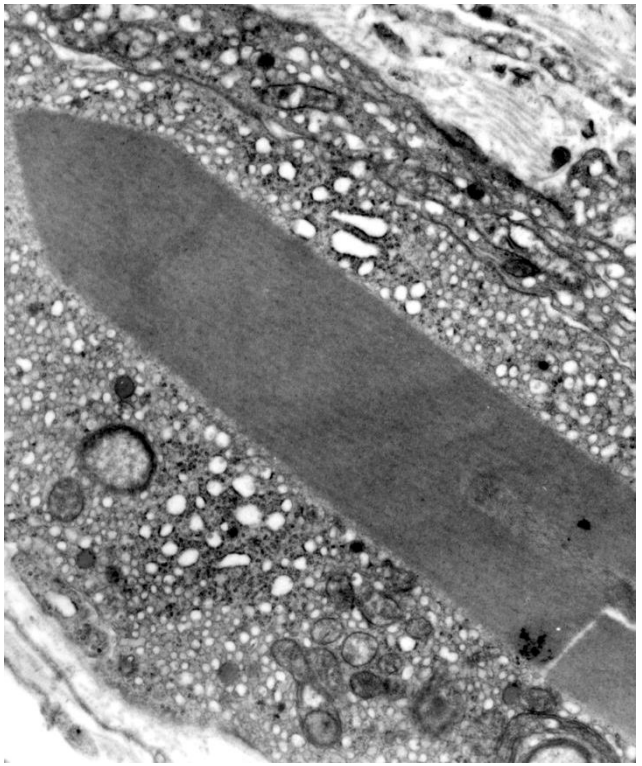


Glycogen in liver cells (light microscope; PAS reaction)

Cytoplasmic inclusions 6

Crystals



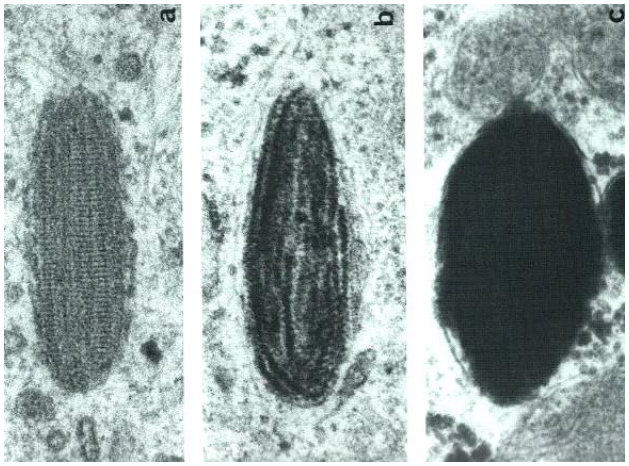


Protein inclusions in Leydig cells

Cytoplasmic inclusions 7

Pigments (colour inclusions): Exogenous x Endogenous

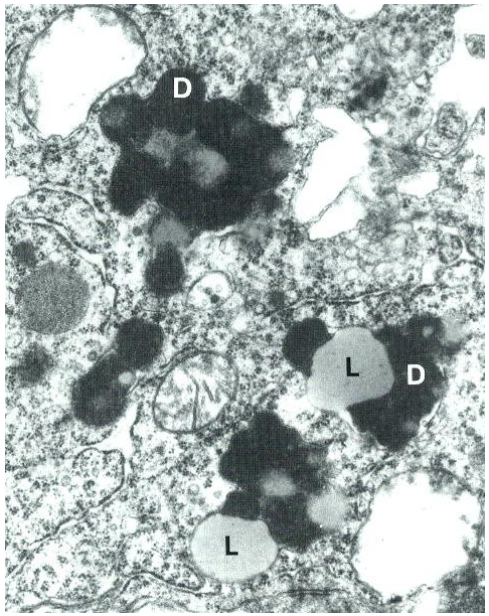
- **Autogenous**
  Specific functions – **melanin**



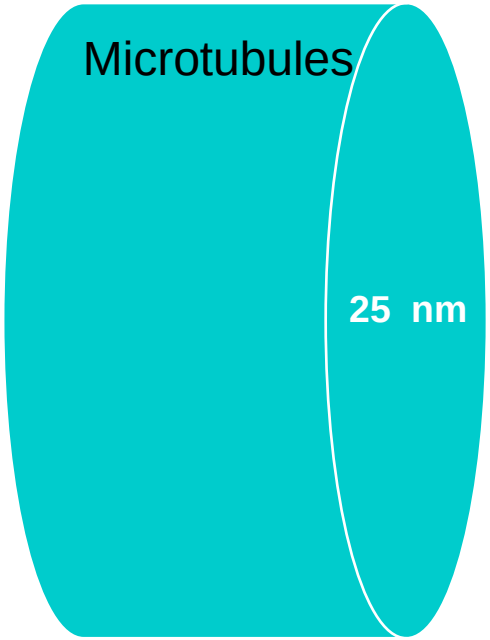
- **Hematogenous**
  Hemoglobin decomposition – **hemosiderin**, **biliverdin**, **bilirubin**

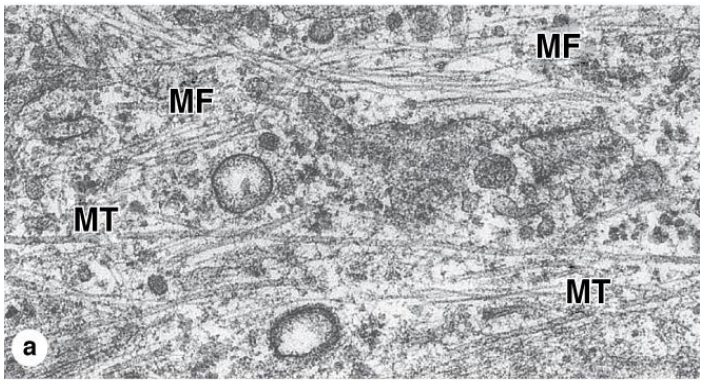
Pigment in aged cells

lipofuscin – accumulation of residual bodies in long-lived cells (neurones, kardiomyocytes)

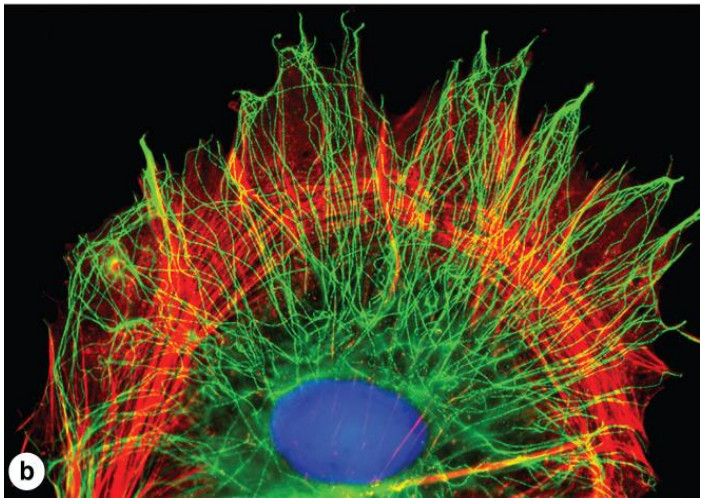


Cytoskeleton 1



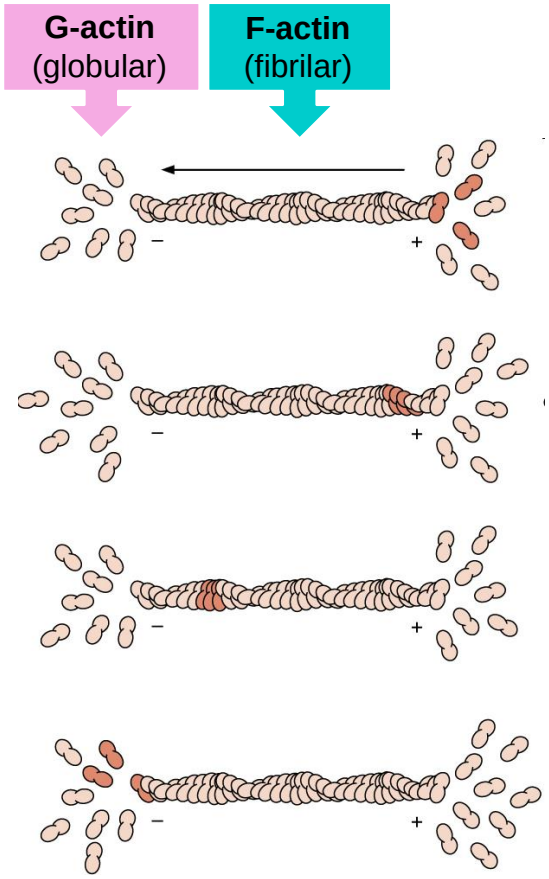


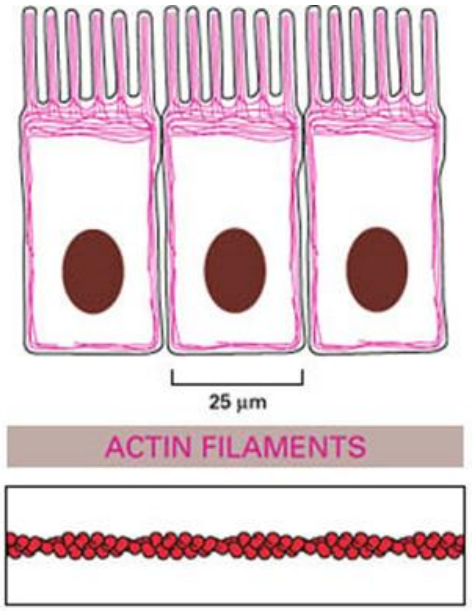
microtubules
microfilaments - actin



Cytoskeleton 2

Microfilaments (actin)

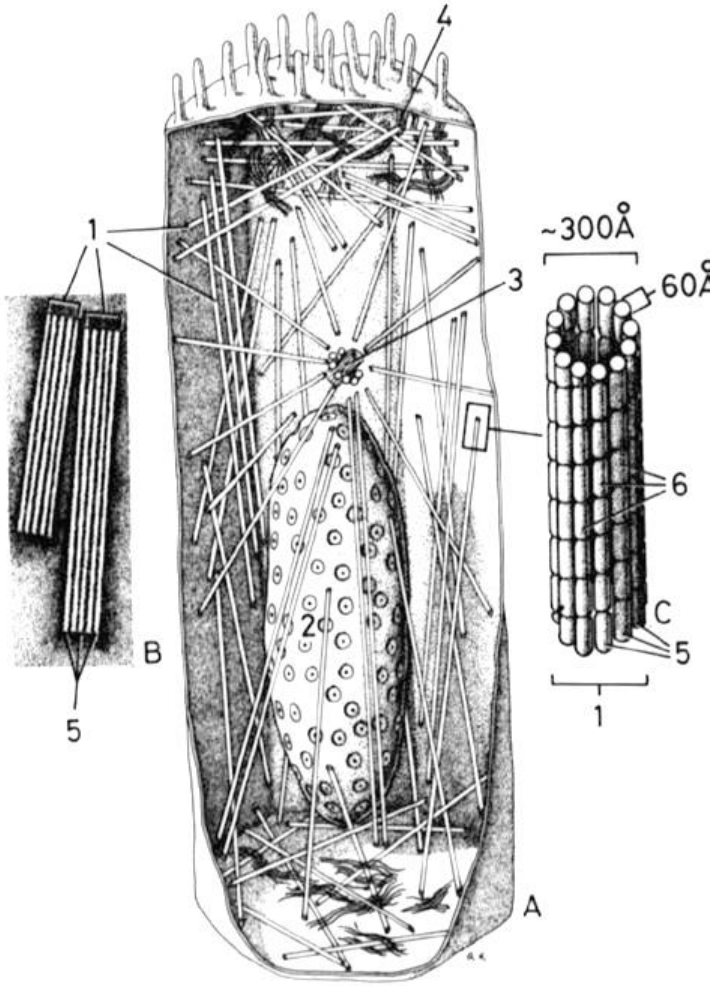


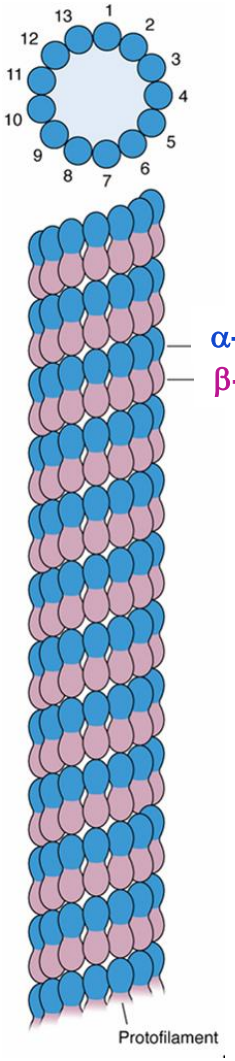


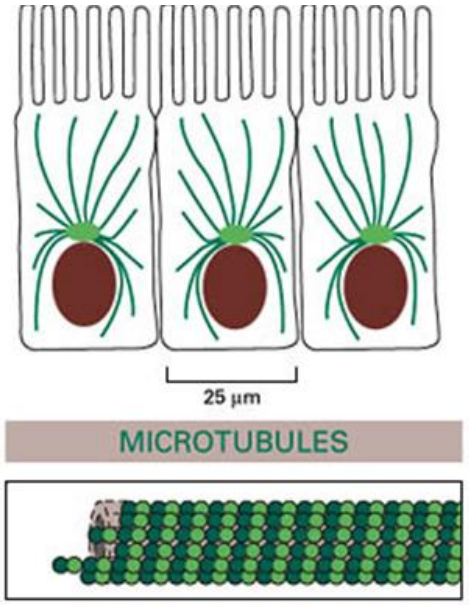
- actin isoformes (α, β, γ)
- fast polymerisation and depolymerisation
- polarisation (+ a – ends)
- stabilisation by associated proteins (tropomyosin – myofibrils)
- crosslinking by associated proteins (fimbrin, filamin, …)
- anchoring to cell membrane (vinculin, tallin, …)
- cortical actin – membrane skeleton
- myosin motors *(analogous to dynein + kinesin on microtubuli)*

Cytoskeleton 3

Microtubules



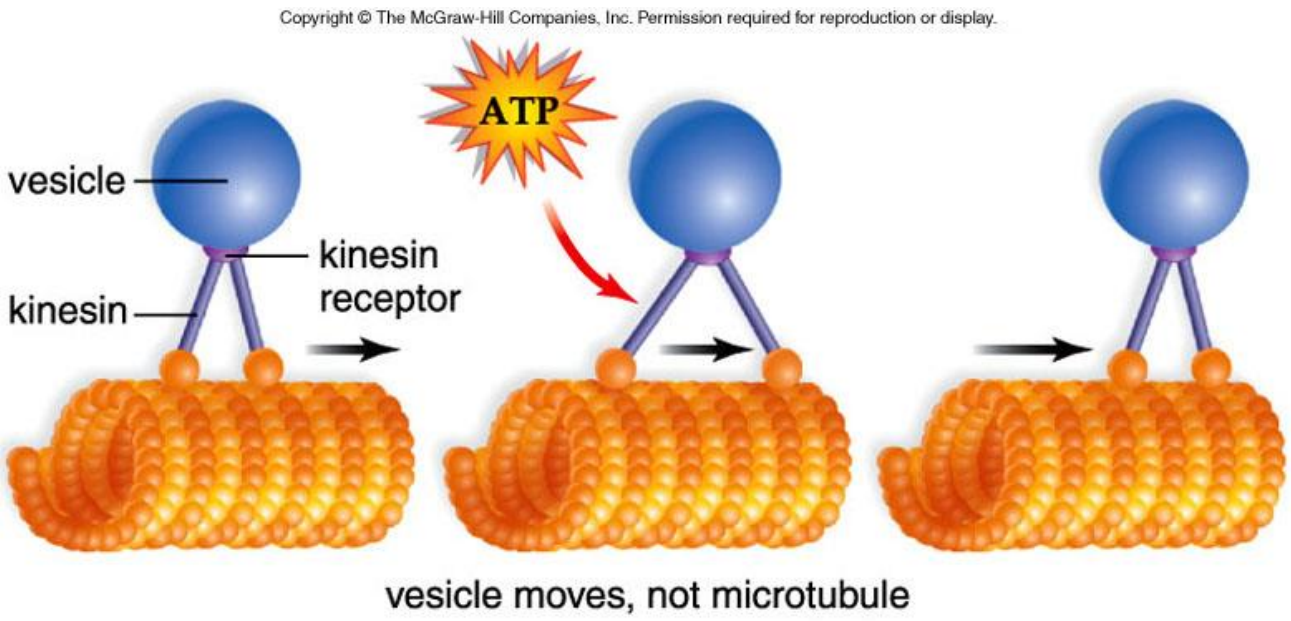




- hollow tubes
- α-tubulin + β-tubulin – dimers
- fast polymerisation and depolymerisation
- polarisation (+ a – ends)
- MAP (proteins associated with microtubuli)
- MTOC – microtubules organizing centre (centrosome; γ-tubulin)
- mechanical support
- intracellular transport
- mitotic spindle
- cilia and flagella
- mitotic poisons (colchicin, taxol, …)

Cytoskeleton 4

Microtubules - motors

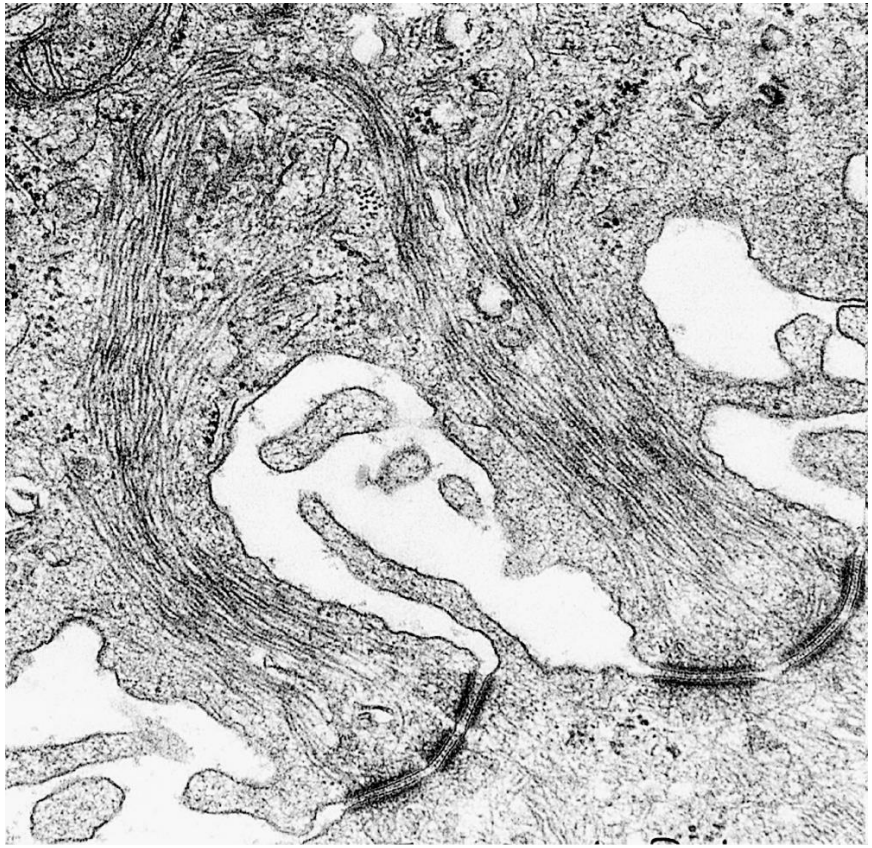


Kinesins
- move towards „plus“ end of microtubuli
- transport from centrosome

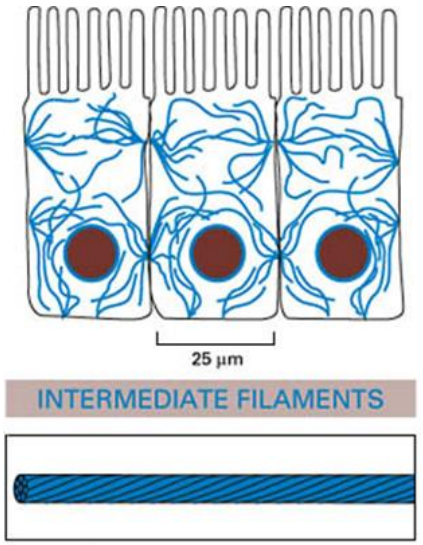
Dyneins
- move towards „minus“ end microtubuli
- transport towards centrosome
- axonal transport – long distance

Cytoskeleton 5

Intermediate filaments



Cytokeratin intermediate filaments in stratum basale of epidermis



- „chemically“ highly heterogenou group
- common composition (tetramers) “thread like“
- more stable than actin and tubulin structures
- cell type specific:

Cytokeratins (epithelia)

Vimentin (cells of mesenchymal origin)

Desmin (muscle cells)

Neurofilaments (neurons)

Glial fibrial acidic protein (neuroglia)

Lamins (nuclear envelope)

Cell surfaces 1

Free

- **microvilli** (*irregular*, *regular* – striated border, brush border)
- **cilia**

Lateral

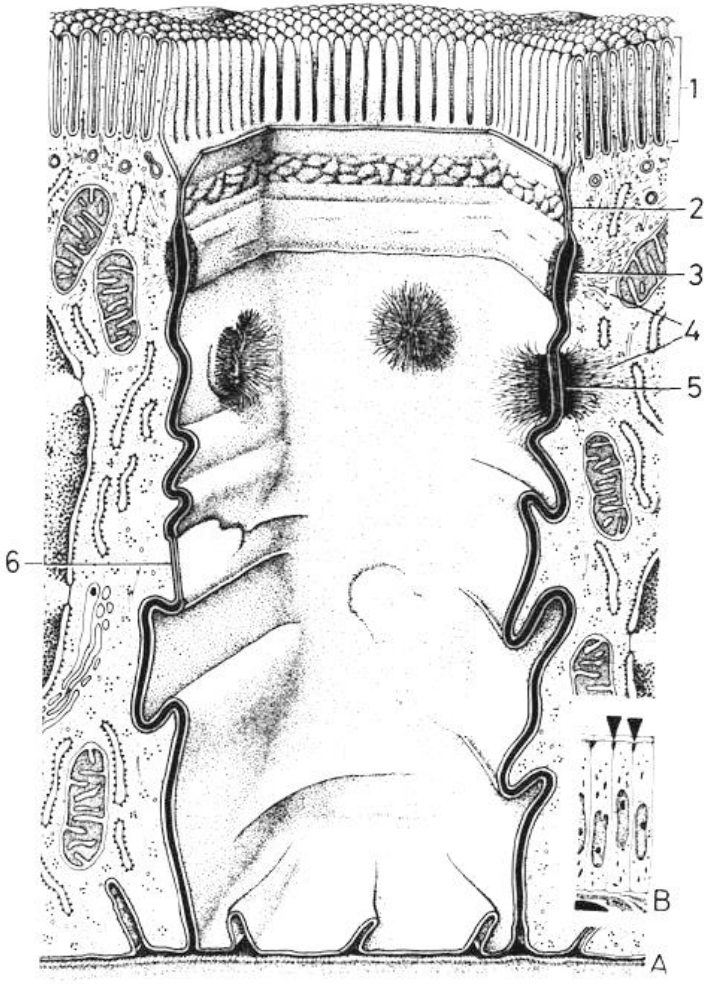
Cell-to-cell junction:

- *sealing:* tight junction=zonula occludens
- *adhesion:* zonula adherens, desmosom
- *communication:* nexus (Gap junction)

Basal

- focal adhesions
- hemidesmosomes
- basal labyrinth

free surface

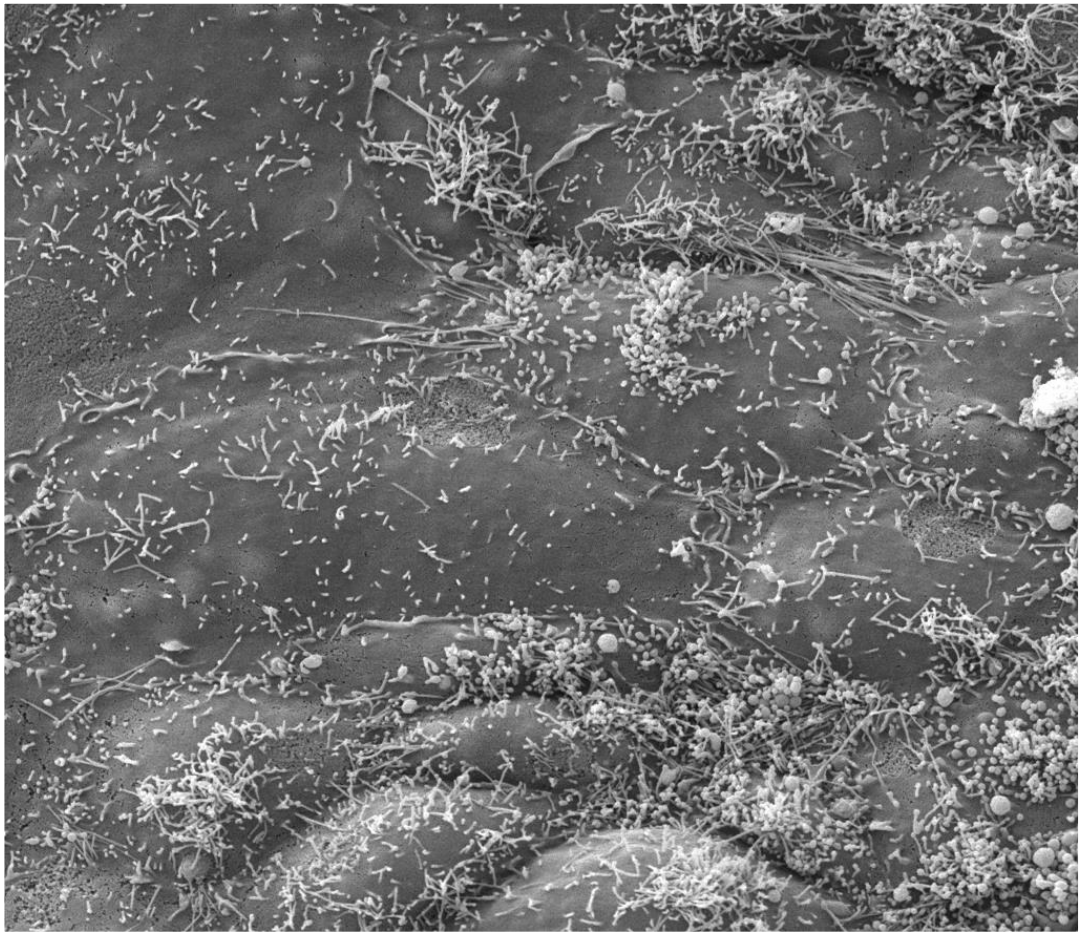


lateral surface

basal surface

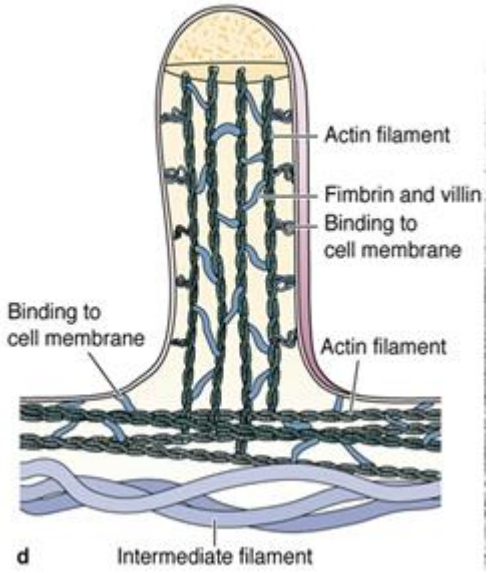
Cell surfaces 2

Microvilli



Free surface of cultured human embryonic stem cells

Cell surfaces 3



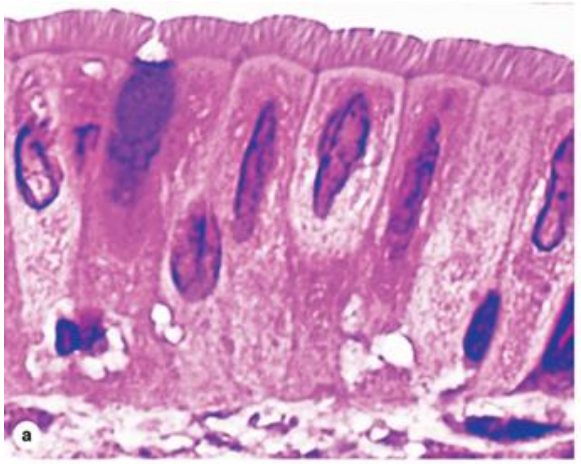
Microvilli

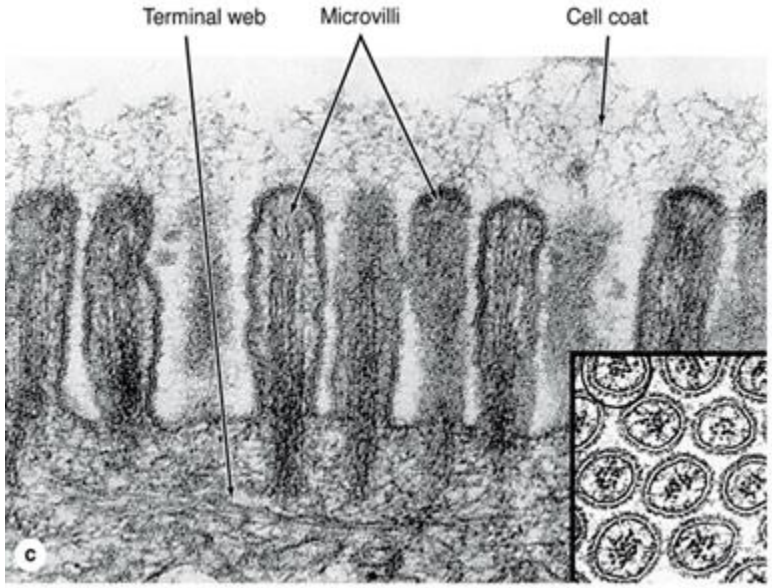
Thickness about 0,1 μm
Length about 1-6 μm

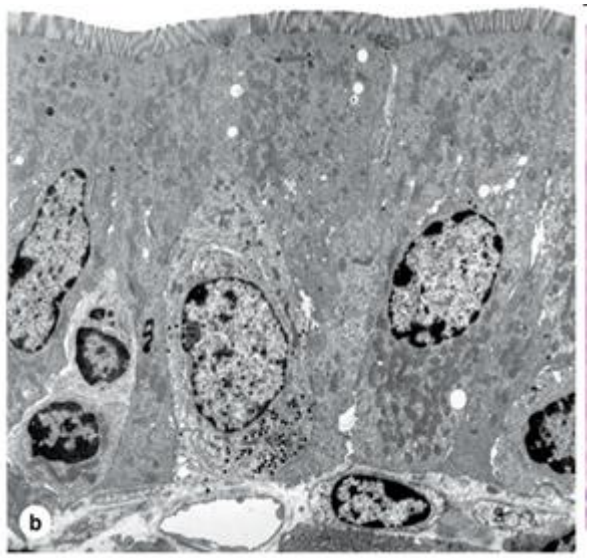
Actin filaments in microvilli

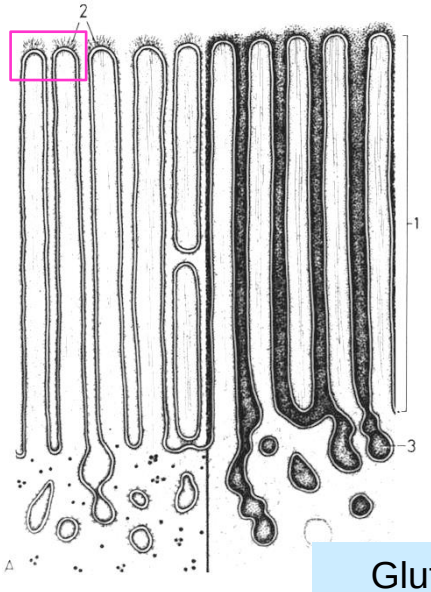
- 20 in microvilli of epithelial cells
- several hundreds in stereocilia of hair cells

Regularly organised microvilli
= striated border + brush border







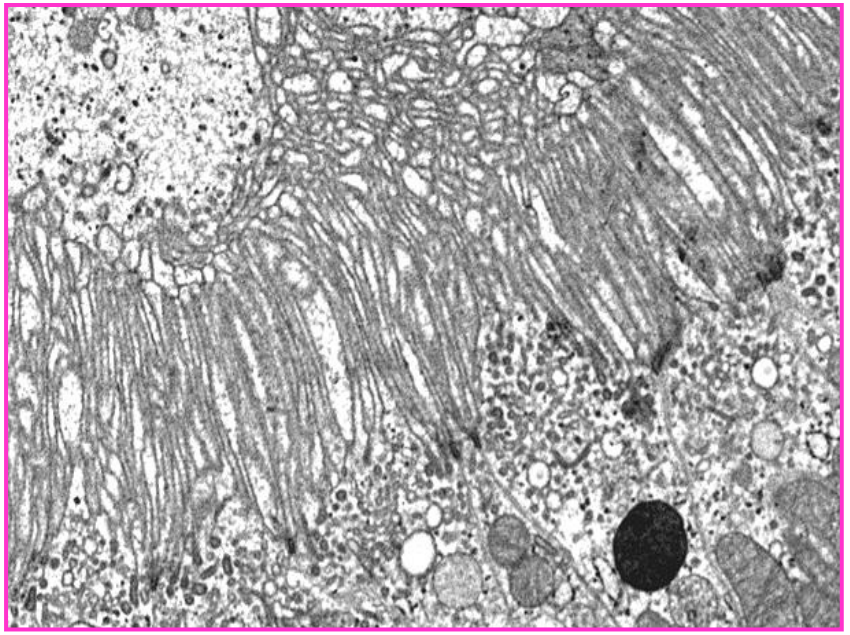


Cell surfaces 4

Microvilli

Gluten – Celiac disease

striated border
(tops of enterocytes)



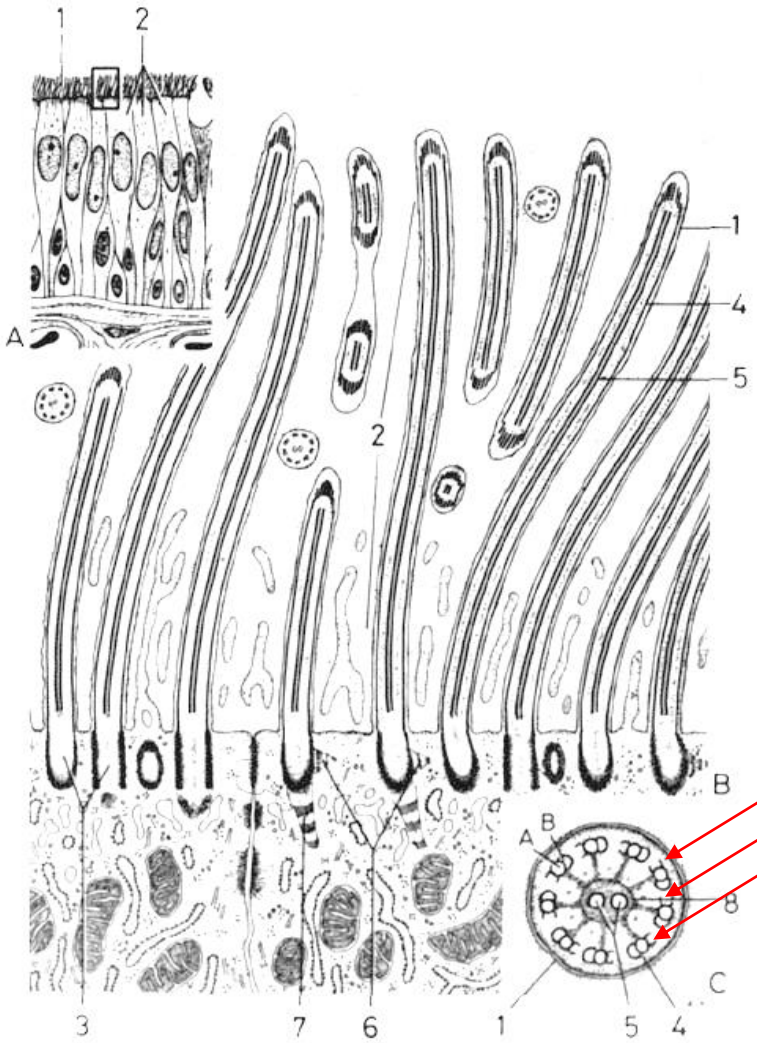
brush border
(proximal tibuli of kidney)

Cell surfaces 5

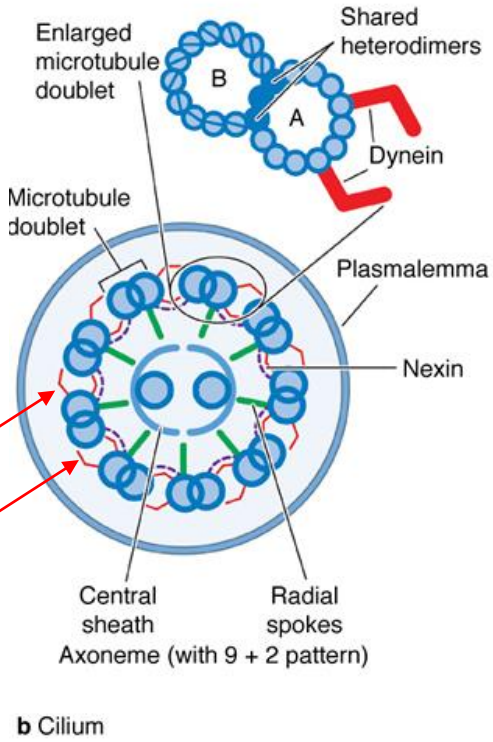
Cilia + Flagella

Thickness about 0,25 μm
Length about 7-10 μm

Axonema
20 microtubuli (9x2 + 2)



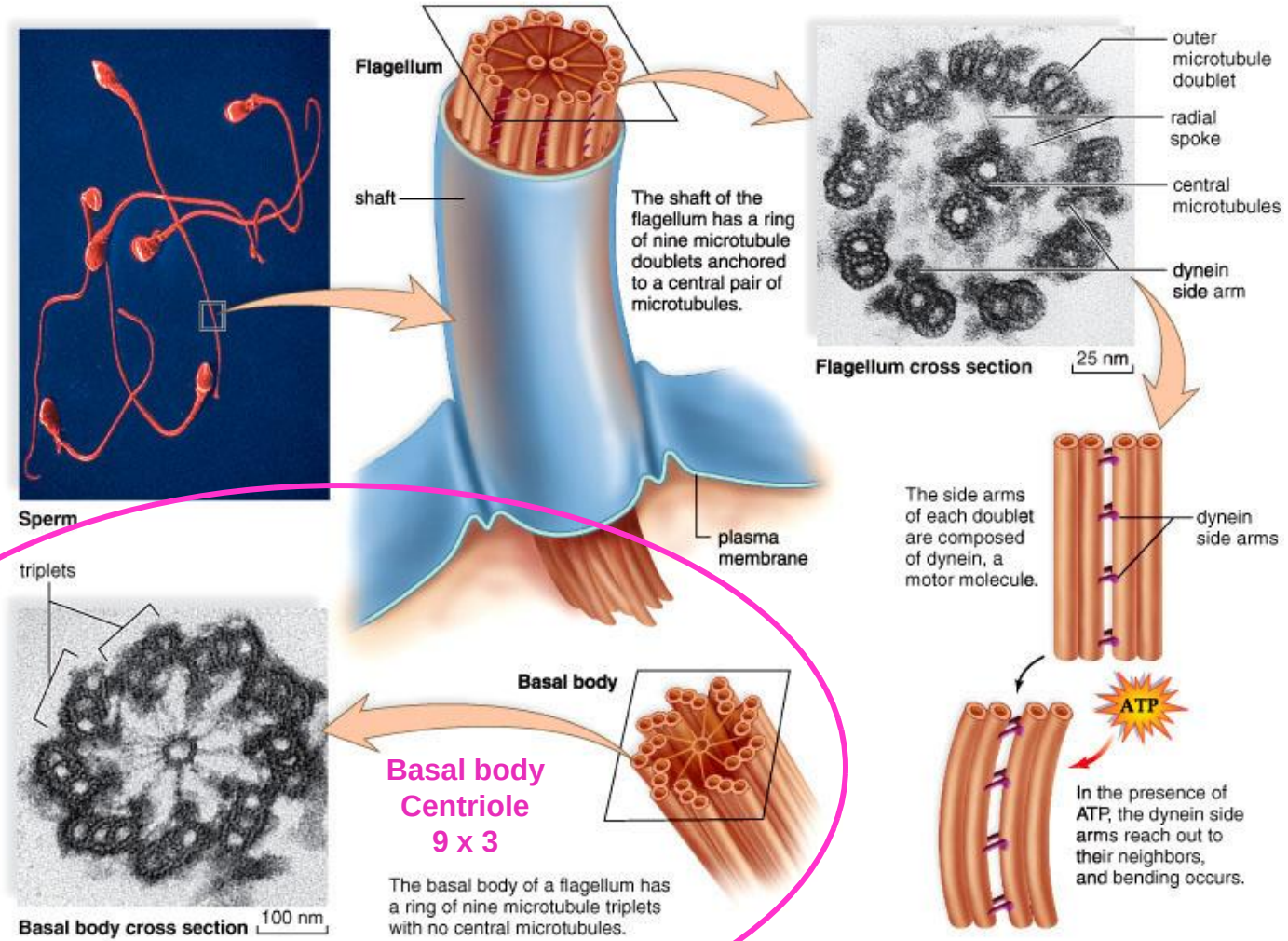
Dynein arms
(movement)



b Cilium

Cell surfaces 6

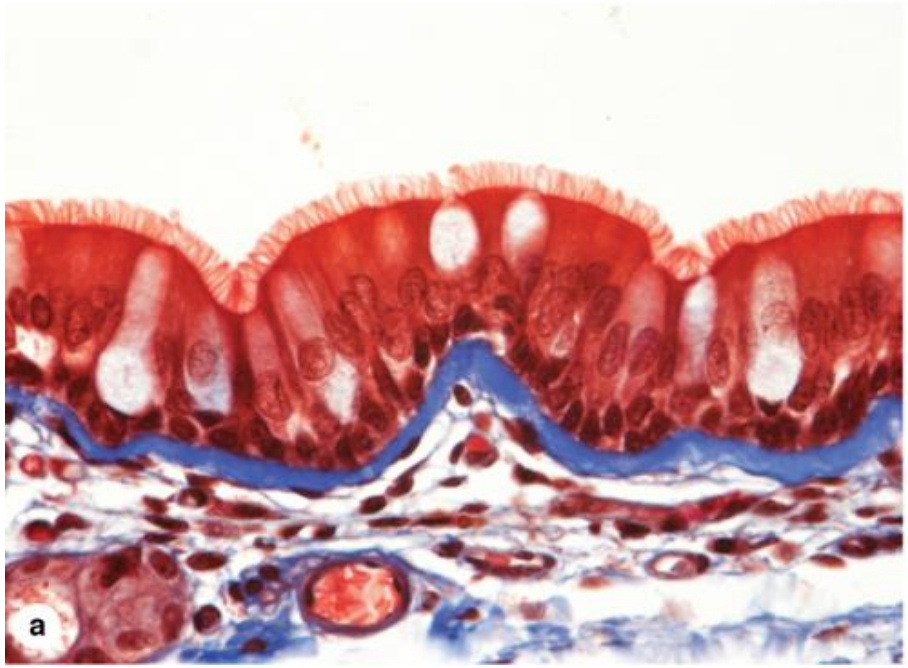
Cilia + Flagella



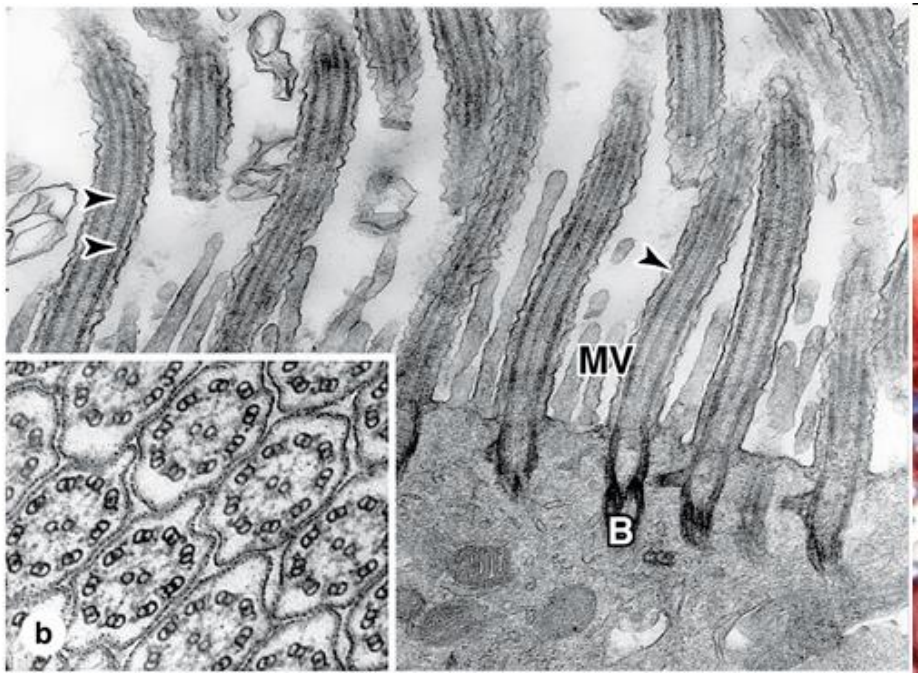
Cell surfaces 7

Cilia + Flagella

in light microscope

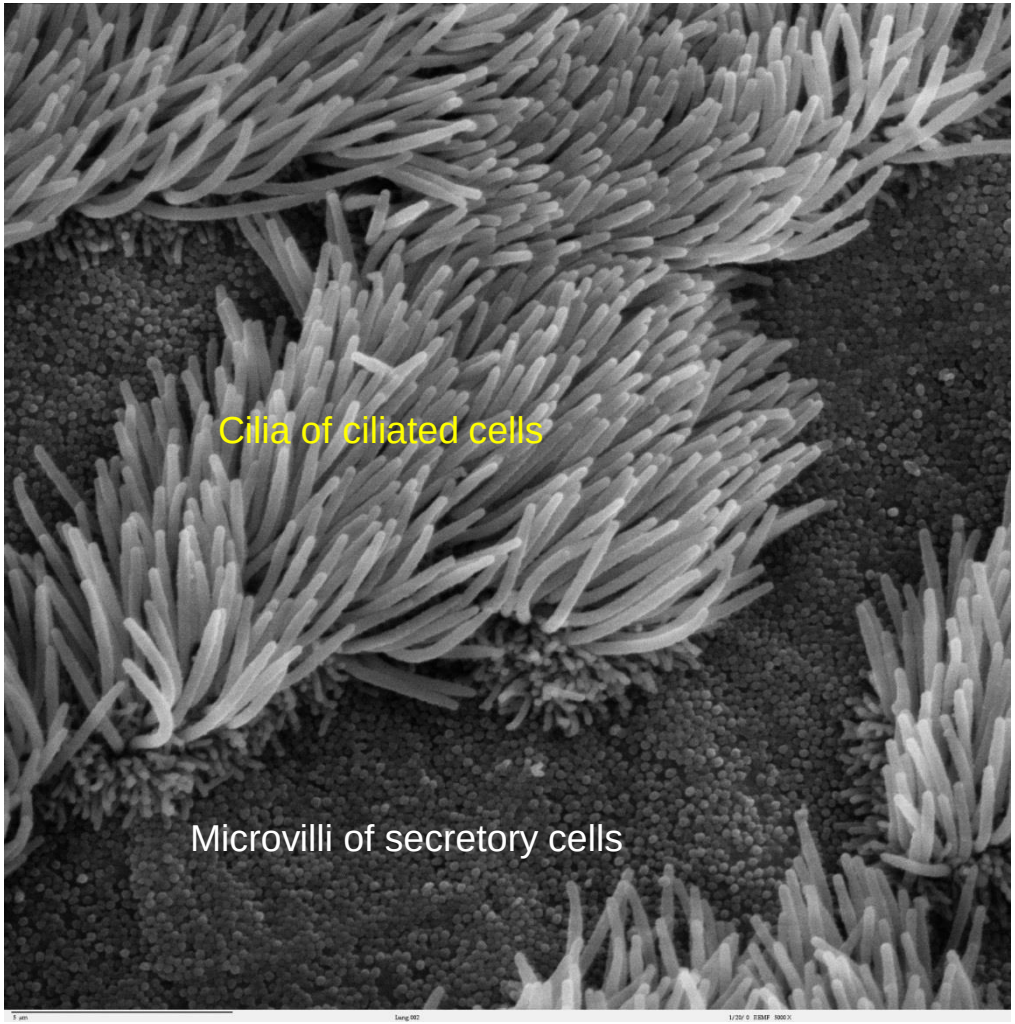


in electron microscope

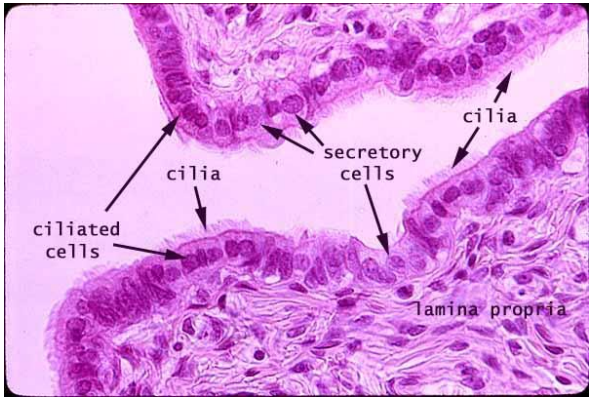


Cell surfaces 8

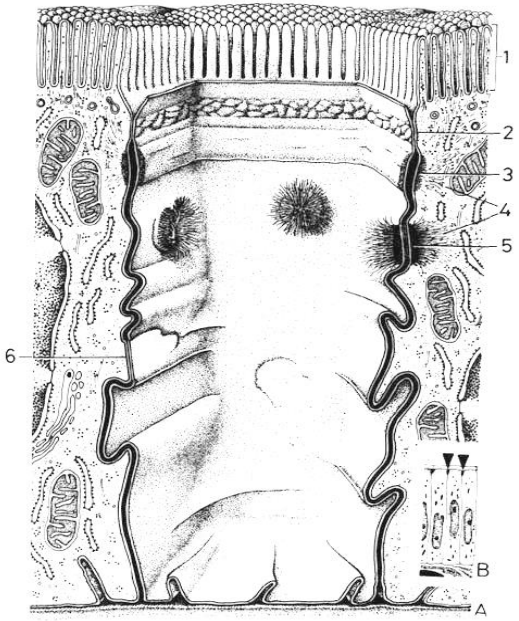
Cilia + Flagella



oviduct

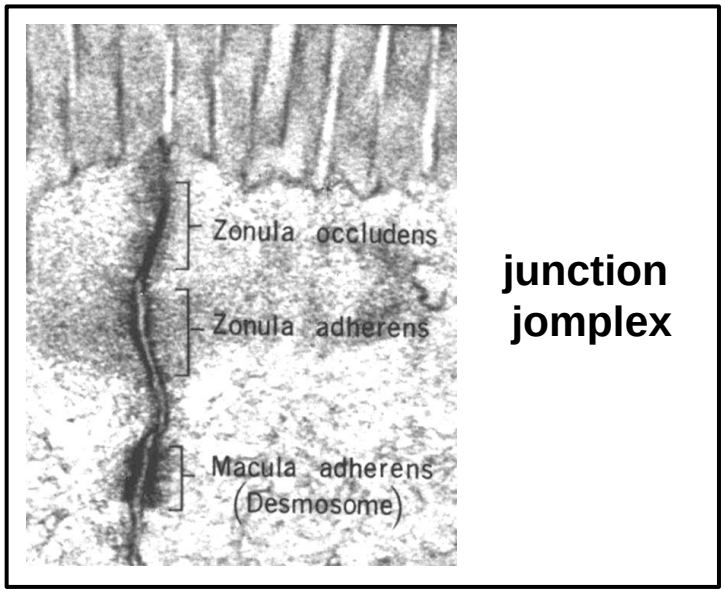


Adhesions and Junctions 1



lateral surface

Basal surface



junction jomplex

Adhesion

- **Macula adherens** (desmosome)
- **Zonula adherens**
- **Hemidesmosome**
- **Focal adhesion**

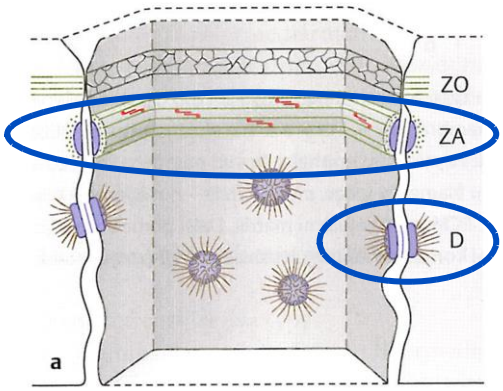
Sealing

- **Zonula occludens** (tight junction)

Communication

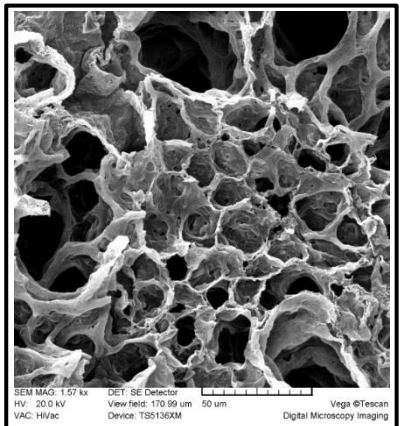
- **Gap junction** (nexus)

Adhesions and Junctions 2

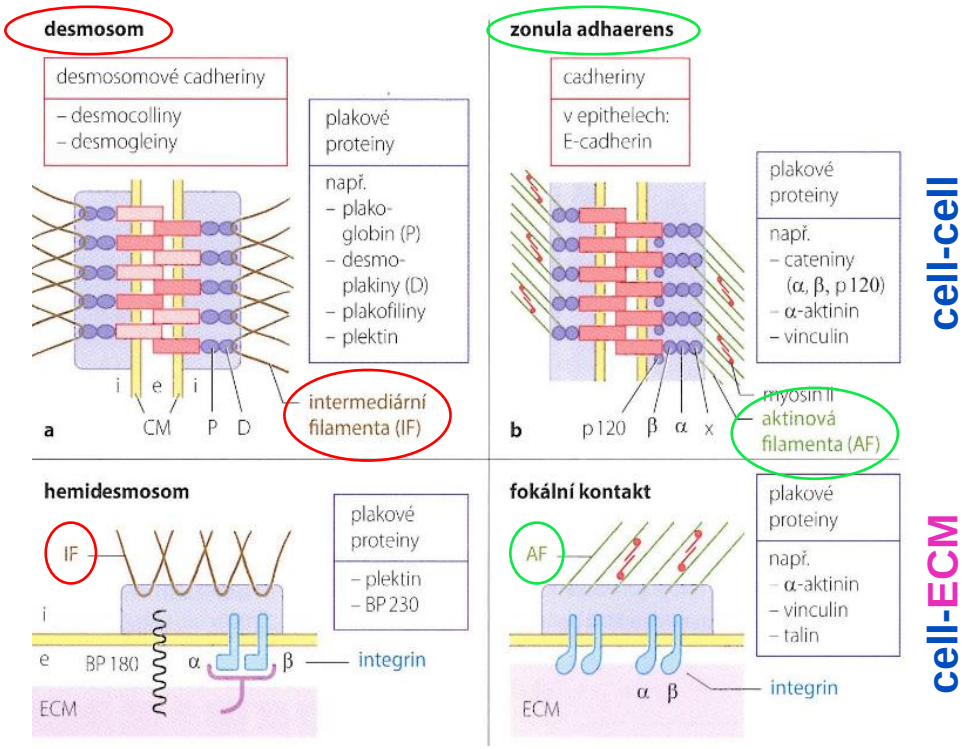


Adhesion

- **Macula adherens** (desmosom)
- **Zonula adherens**
- **Hemidesmosome**
- **Focal adhesion**

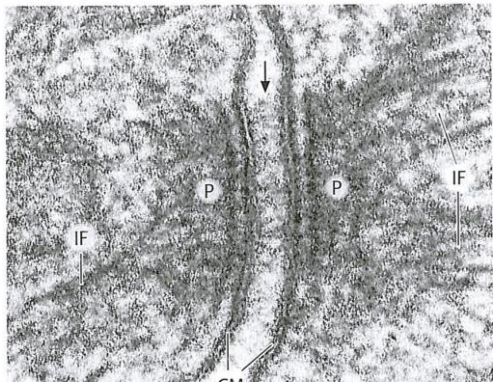


Lung ECM - alveolar region

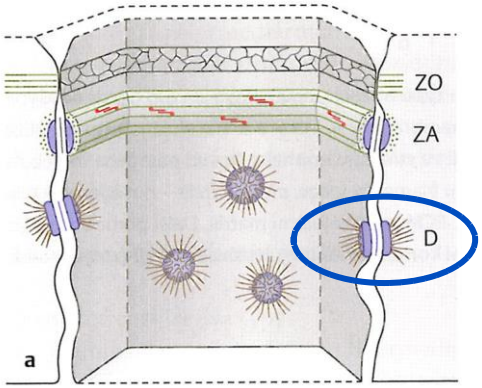


Unified composition

- **Transmembrane proteins** (cadherins+ integrins)
- **Adaptor (plak) proteins**
- **Cytoskelelal fibers**



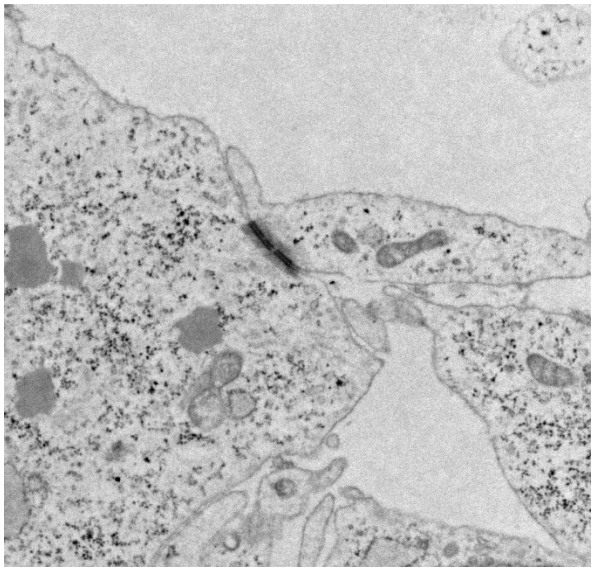
Adhesions and Junctions 3

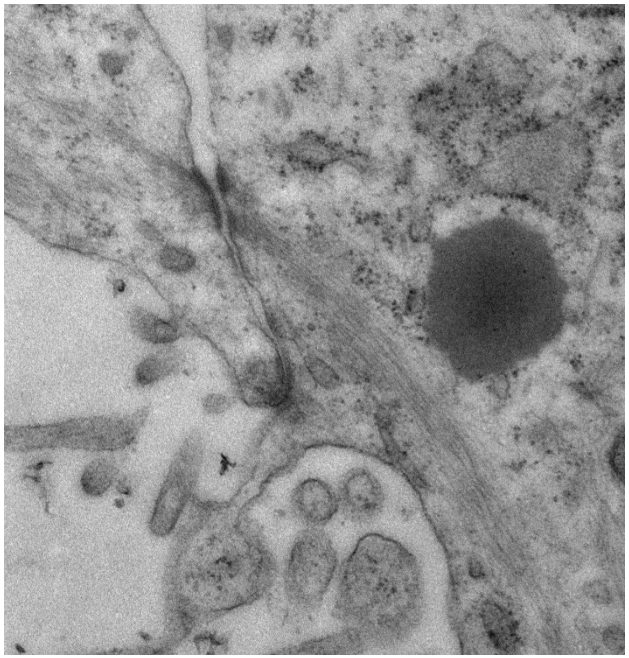


Adhesion

- **Macula adherens** (desmosome)

Diameter about 0,3 μm
Distance between membranes about 20-40 nm

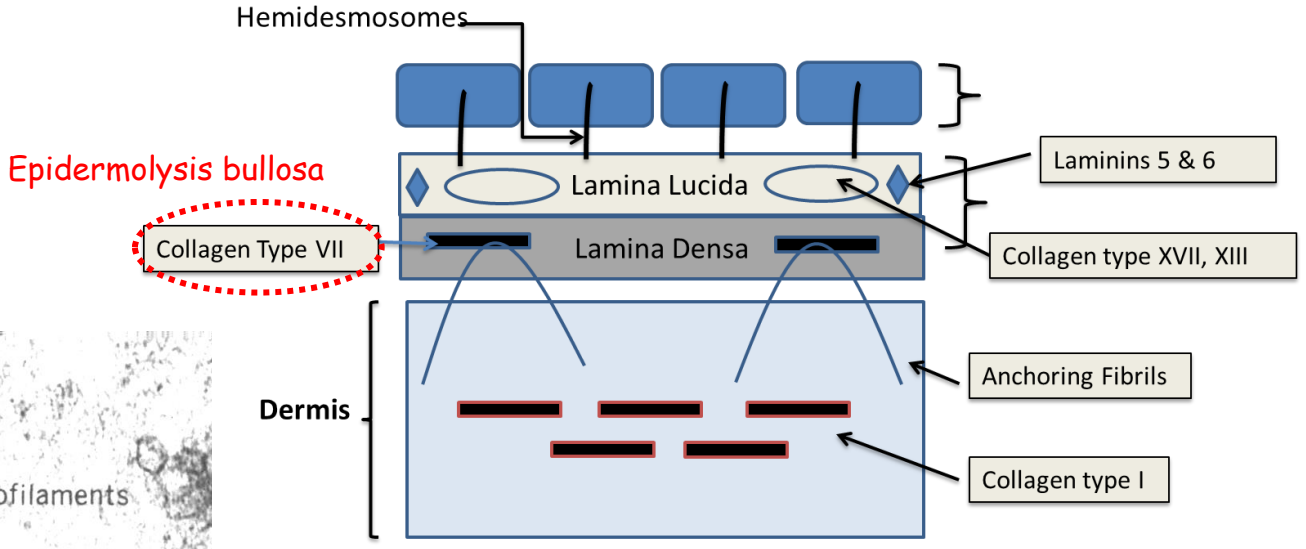


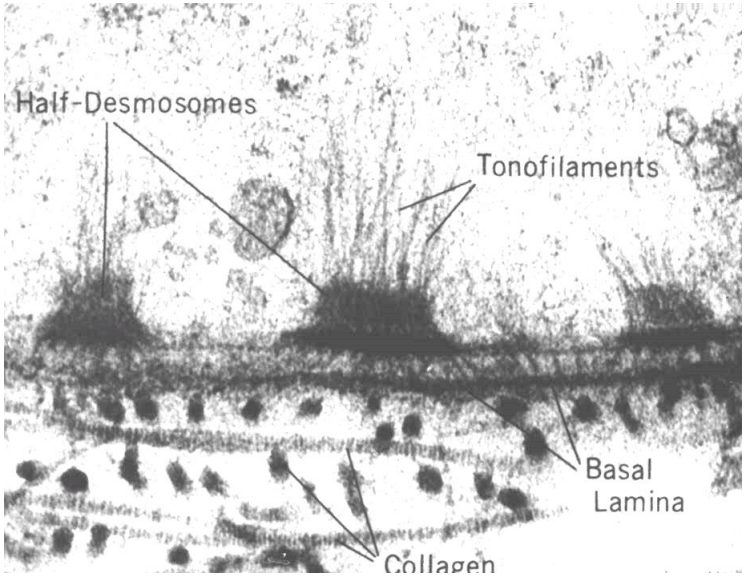


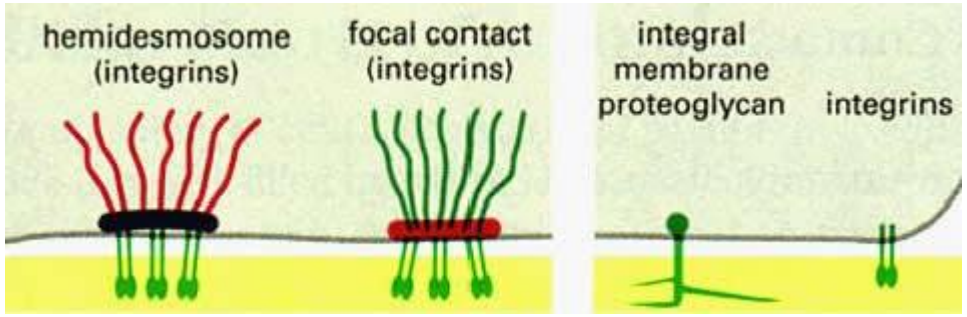
Adhesions and Junctions 4

Adhesion

- **Hemidesmosome**
- **Focal adhesion**

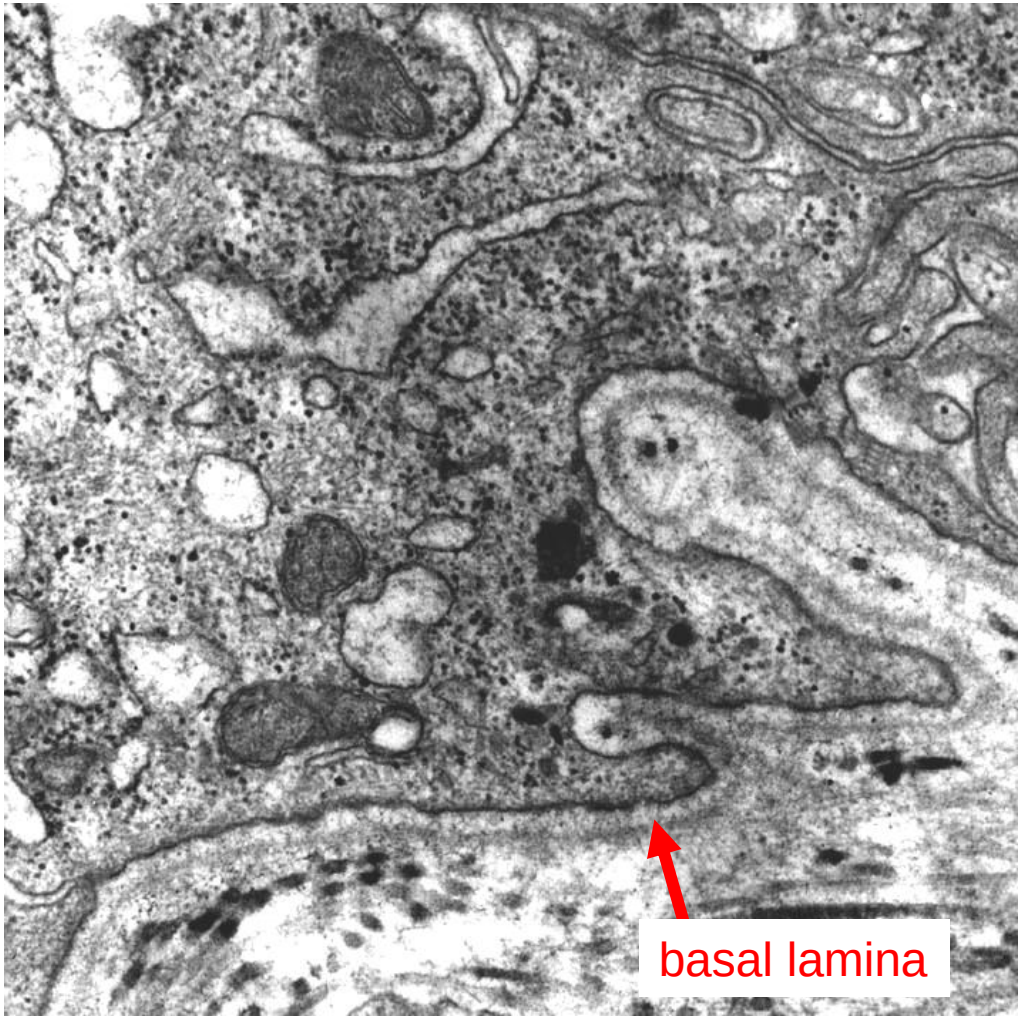






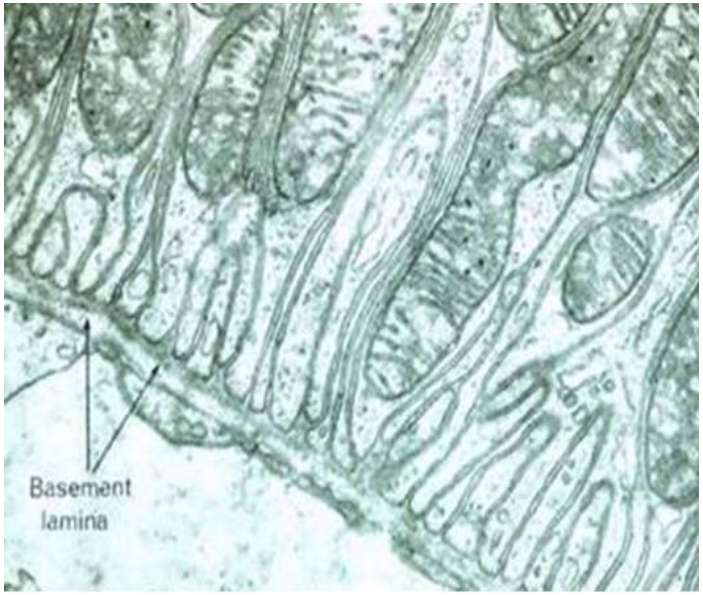
Adhesions and Junctions 5

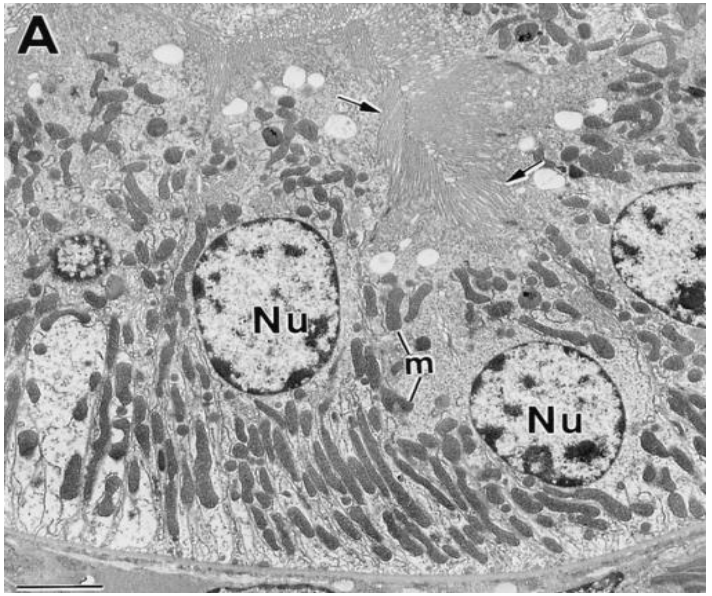
- **Focal adhesion**



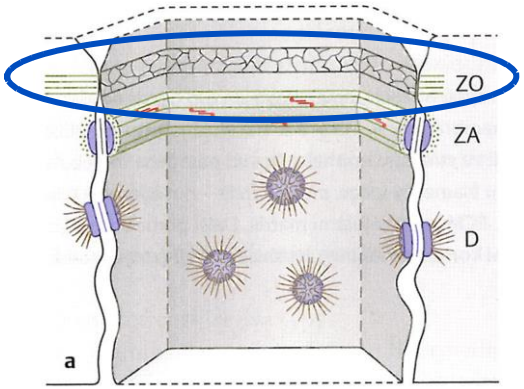
Adhesions and Junctions 6

Basal labyrinth



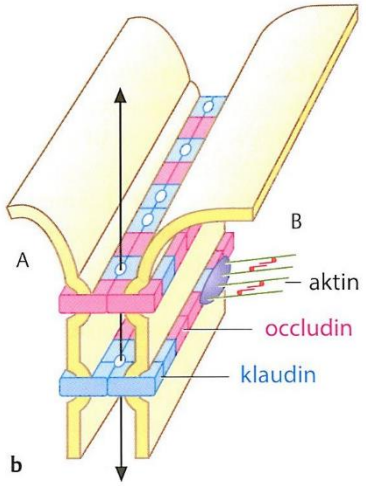


Adhesions and Junctions 7

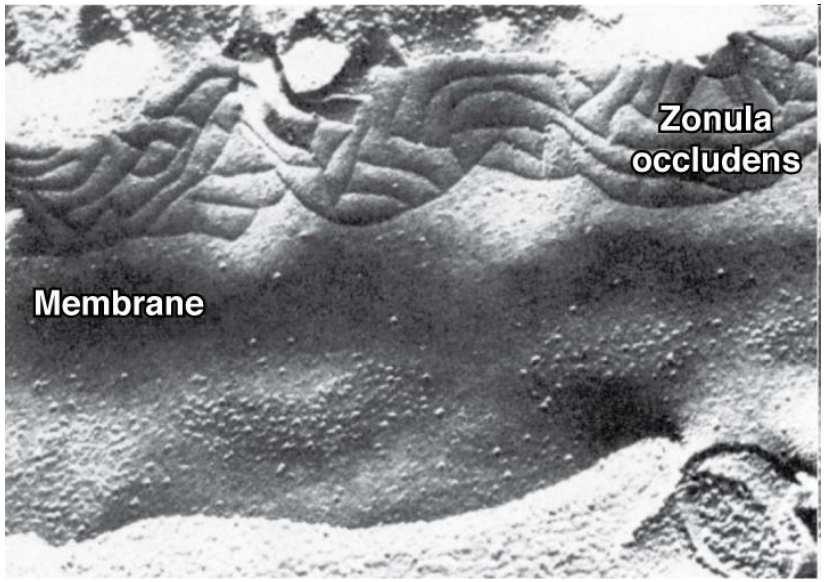


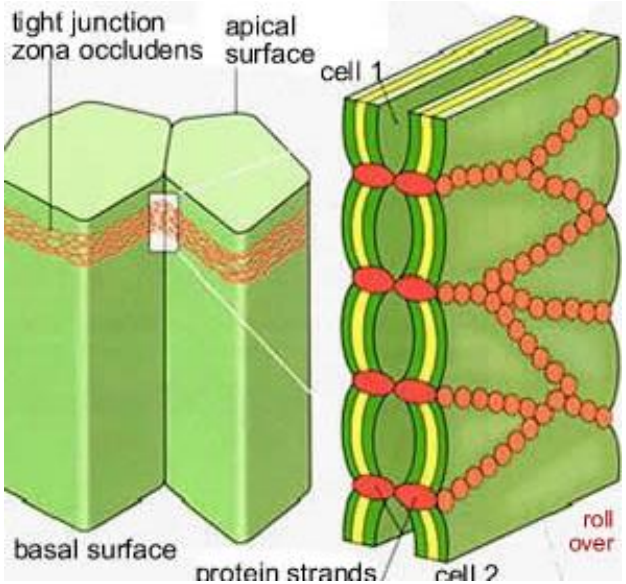
Sealing

- **Zonula occludens**
  (tight junction)

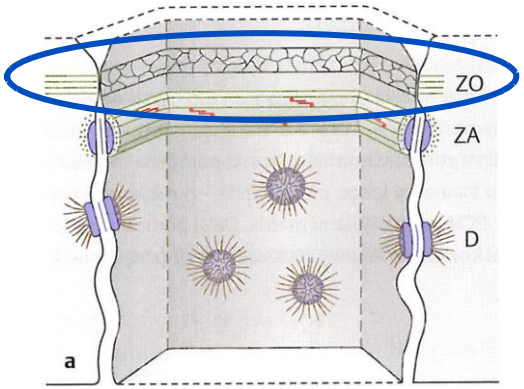


Damage by:
Clostridium perfringens
Helicobacter pylori (ZO-1)



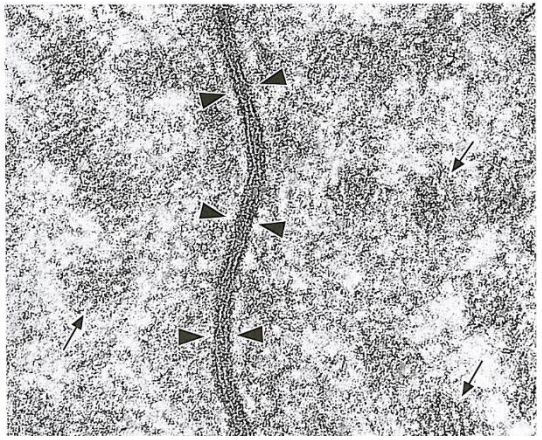


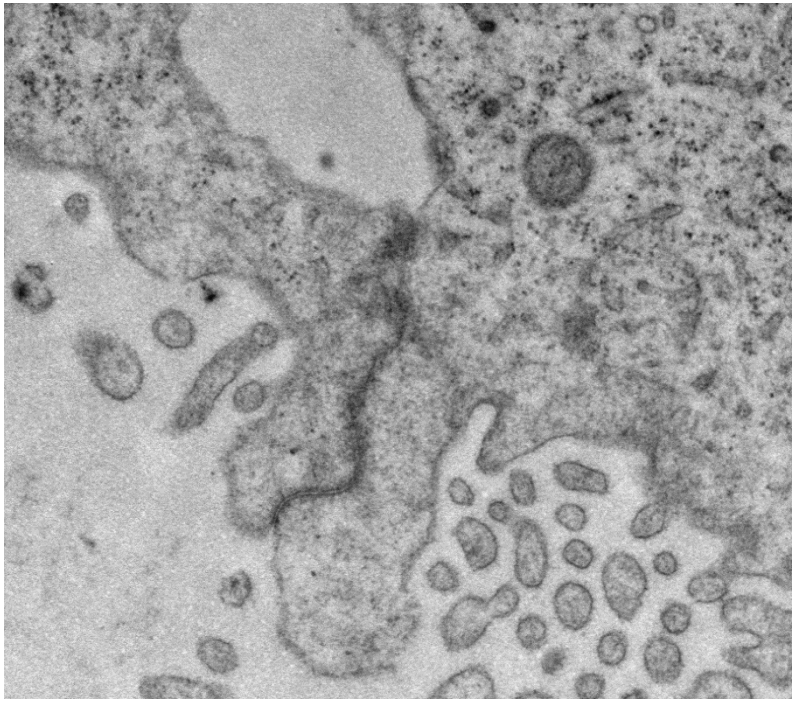
Adhesions and Junctions 8



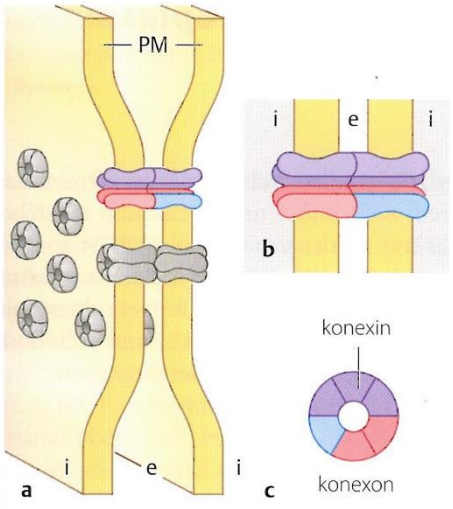
Sealing

- **Zonula occludens** (tight junction)





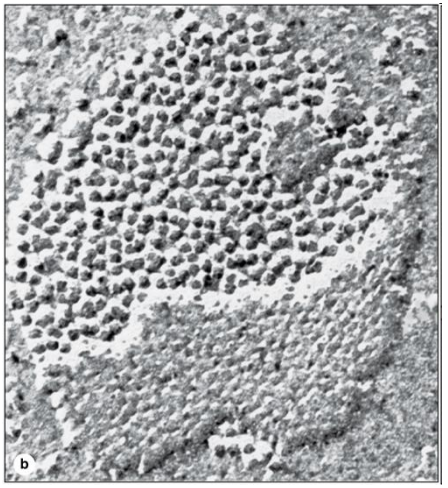
Adhesions and Junctions 9

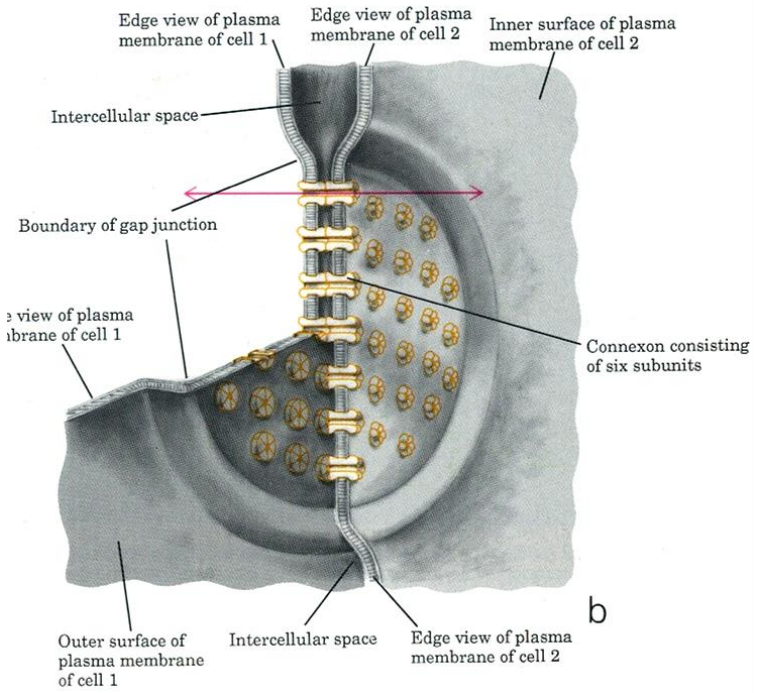


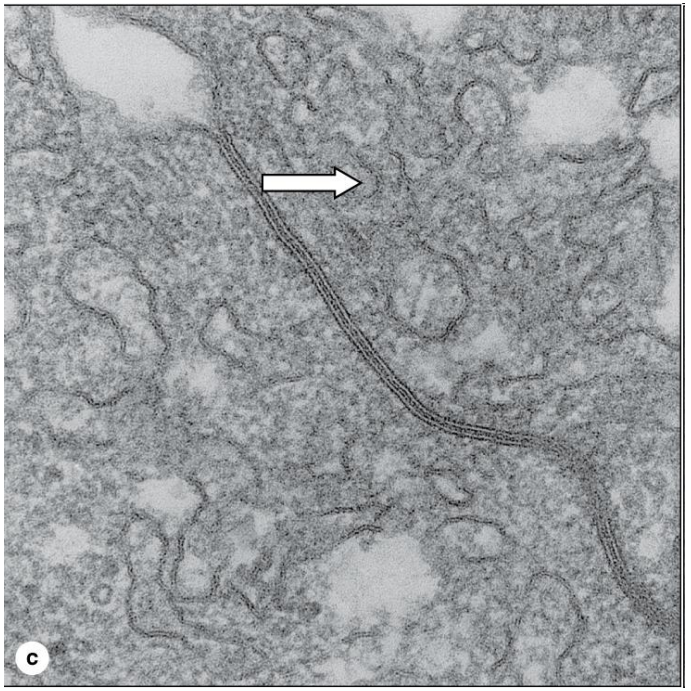
Communication

- **Gap junction** (nexus)

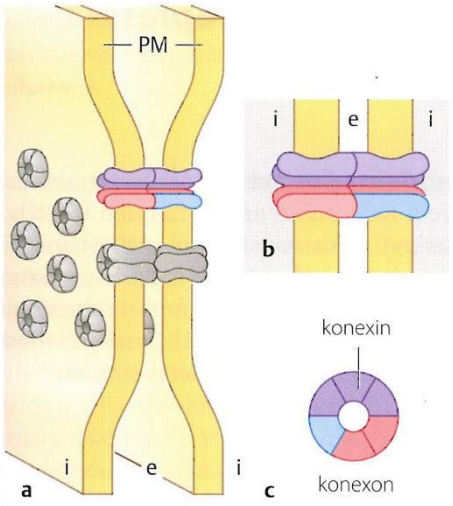
Diameter about 0,3 μm
Distance between cell membranes about 3 nm
Internal diameter of the channel about 2 nm





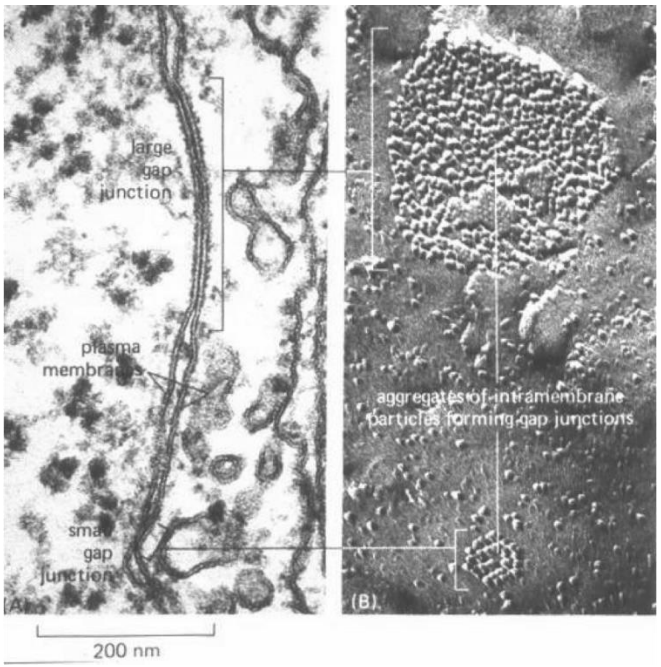


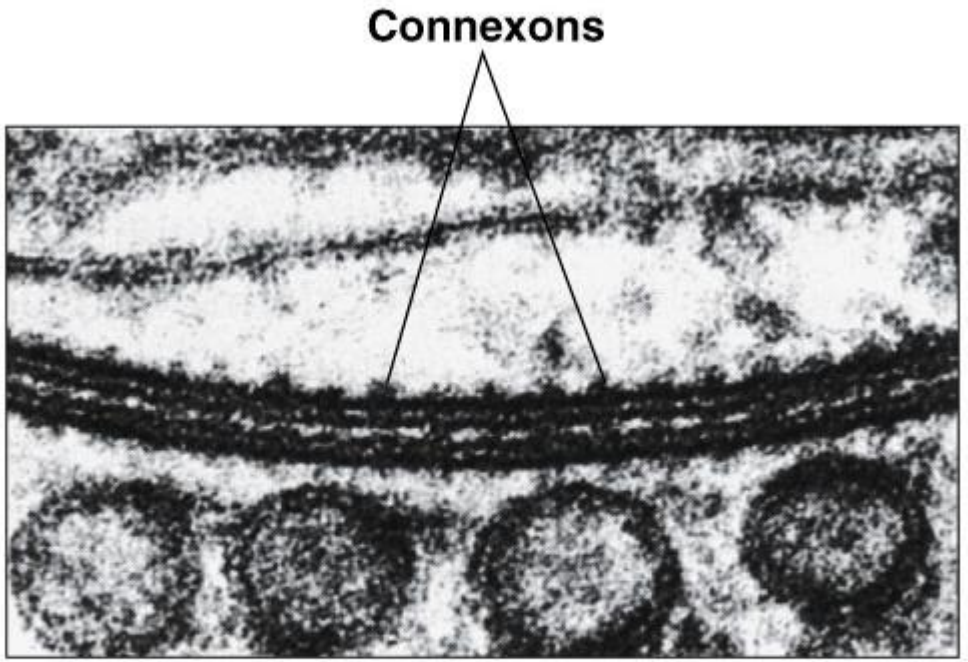
Adhesions and Junctions 10



Communication

- **Gap junction** (nexus)





(b) Electron micrograph of a gap junction

Activities of cells

- **Movement** – intracellular, amoeboid, cilia, flagella
- **Metabolism** – income, processing, outcome
- **Responsivenes**
- **Growth**
- **Differentiation**
- **Division (amplification)**

Division x Differentiation of cells 1

Zygote

↓

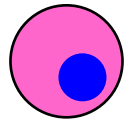
Multicellular embryo

↓

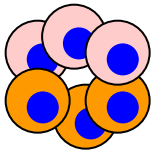
Dynamic multicellular organism

CELL DIVISION

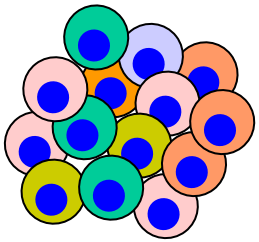
CELL DIFFERENTIATION



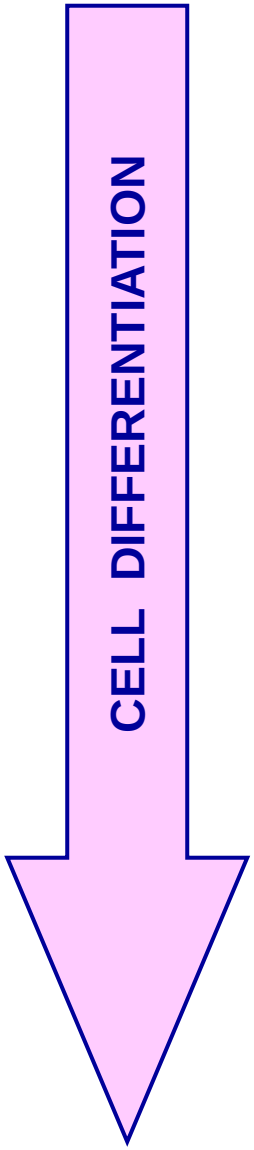
Cell division
&
Cell specialization



Cell division
&
Cell specialization



Division x Differentiation of cells 2



STABLE GENOME

↕

Genomic equivalence

(= equal amount of DNA and the same nucletide sequence in all cells of a organism – cloning)

X

VARIABLE TRANSCRiPTOME

↕

Transcription Regulators

+ other regulations:

- translation
- posttranslational modification

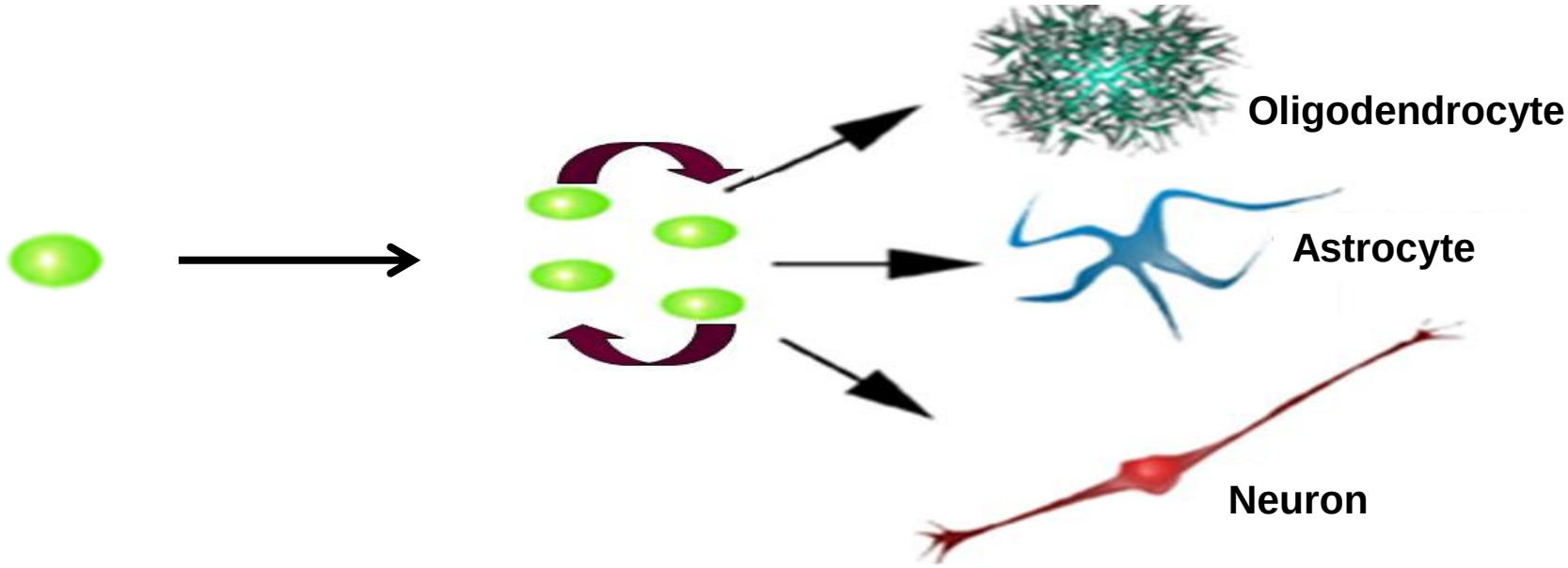
Division x Differentiation of cells 3

Tissue renewal and regeneration

Stem cells
- slowly dividing (usually)
- multipotent

Progenitor cells
- „transit amplifying cells“
- fast proliferation
- multipotent

Terminally diferentiated cells
- nondividing



Mother nature and scientists supply us with many

Stem cells generate and regenerate our body

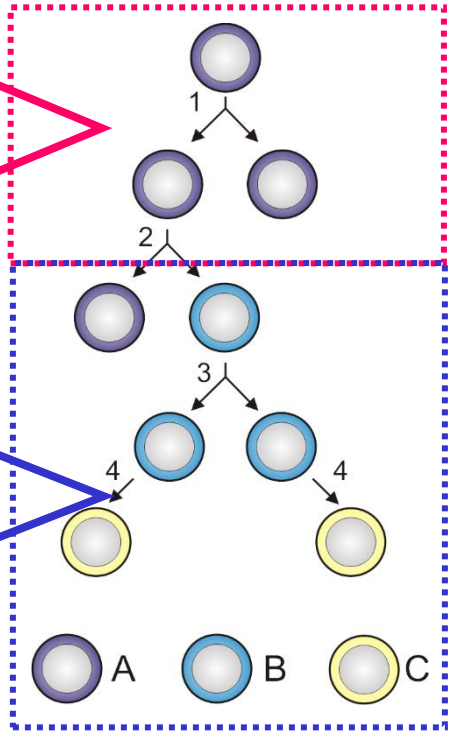
Capability to produce identical copies of itself

Self-renewal

Capability to differentite into specialized cell types

Pluripotency

1. Undifferentiated growth



2. Differentiation

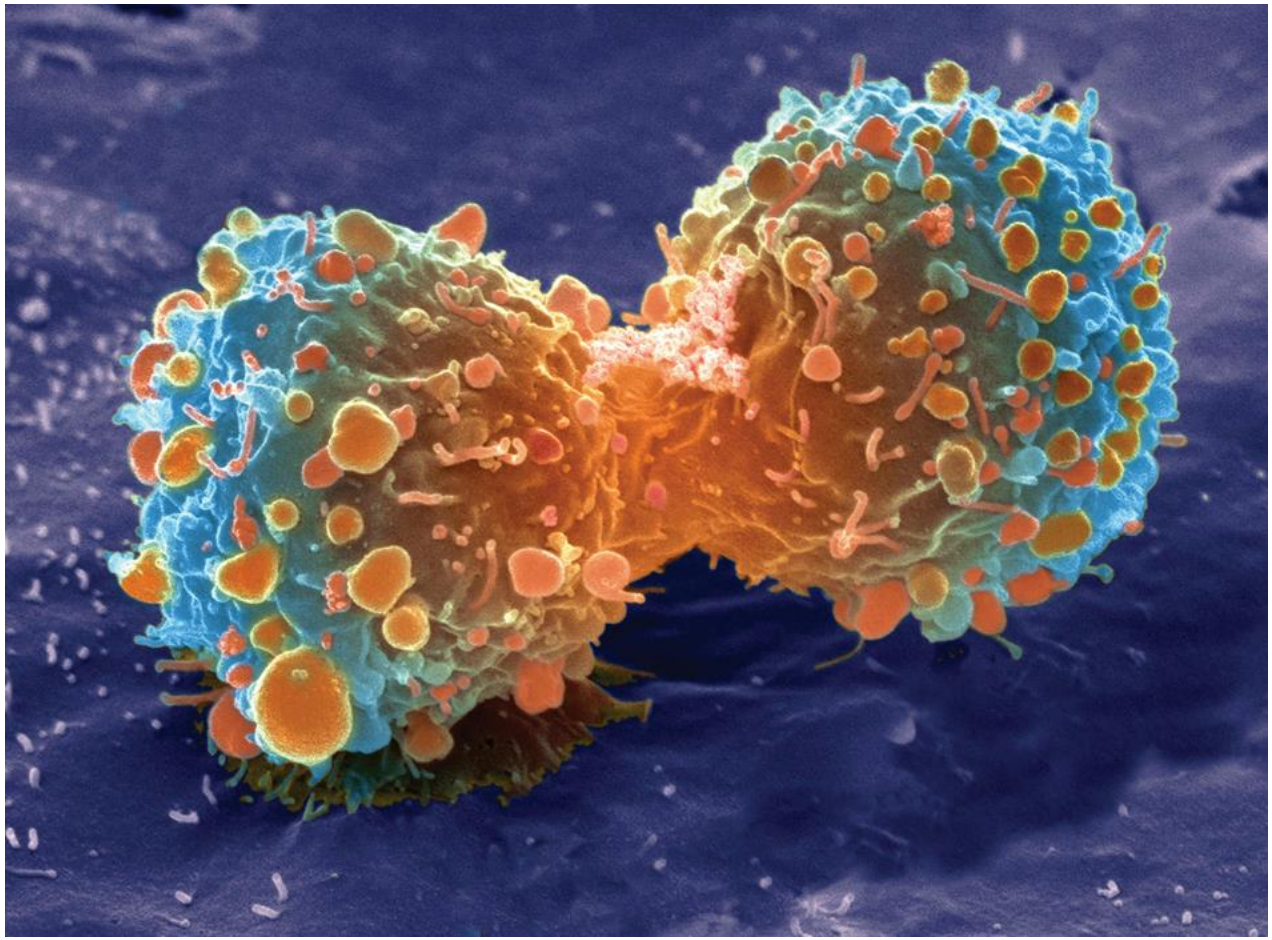
- Embryonic stem cells
- Adult stem cells
  - Fetal
  - Organ
  - Tissue
- Induced pluripotent stem cells
- Cancer stem cells

Different properties

Cell division 1

Basic concept 1

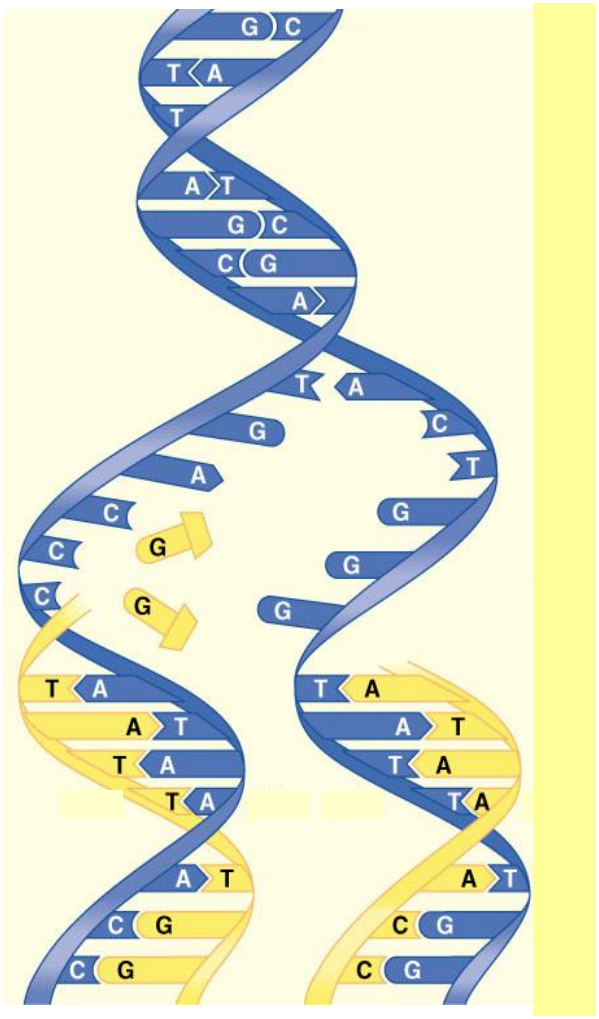
MITOSIS and CYTOKINESIS produce genetically identical cells

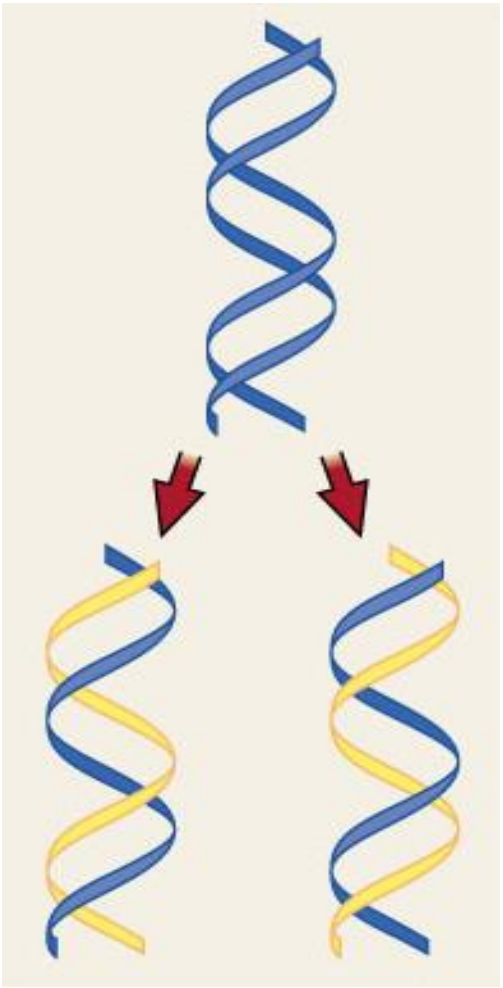


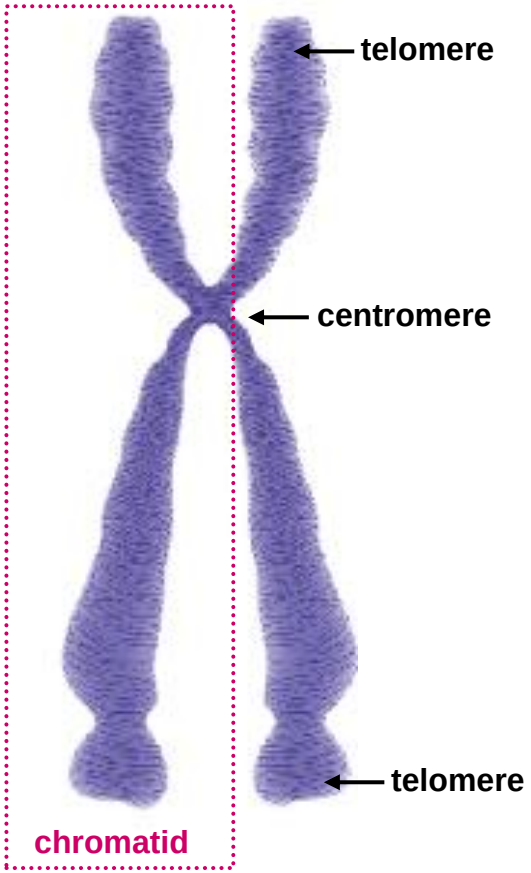
Cell division 2

STABLE (non-changing) GENOME

Due to semiconservative duplication of DNA



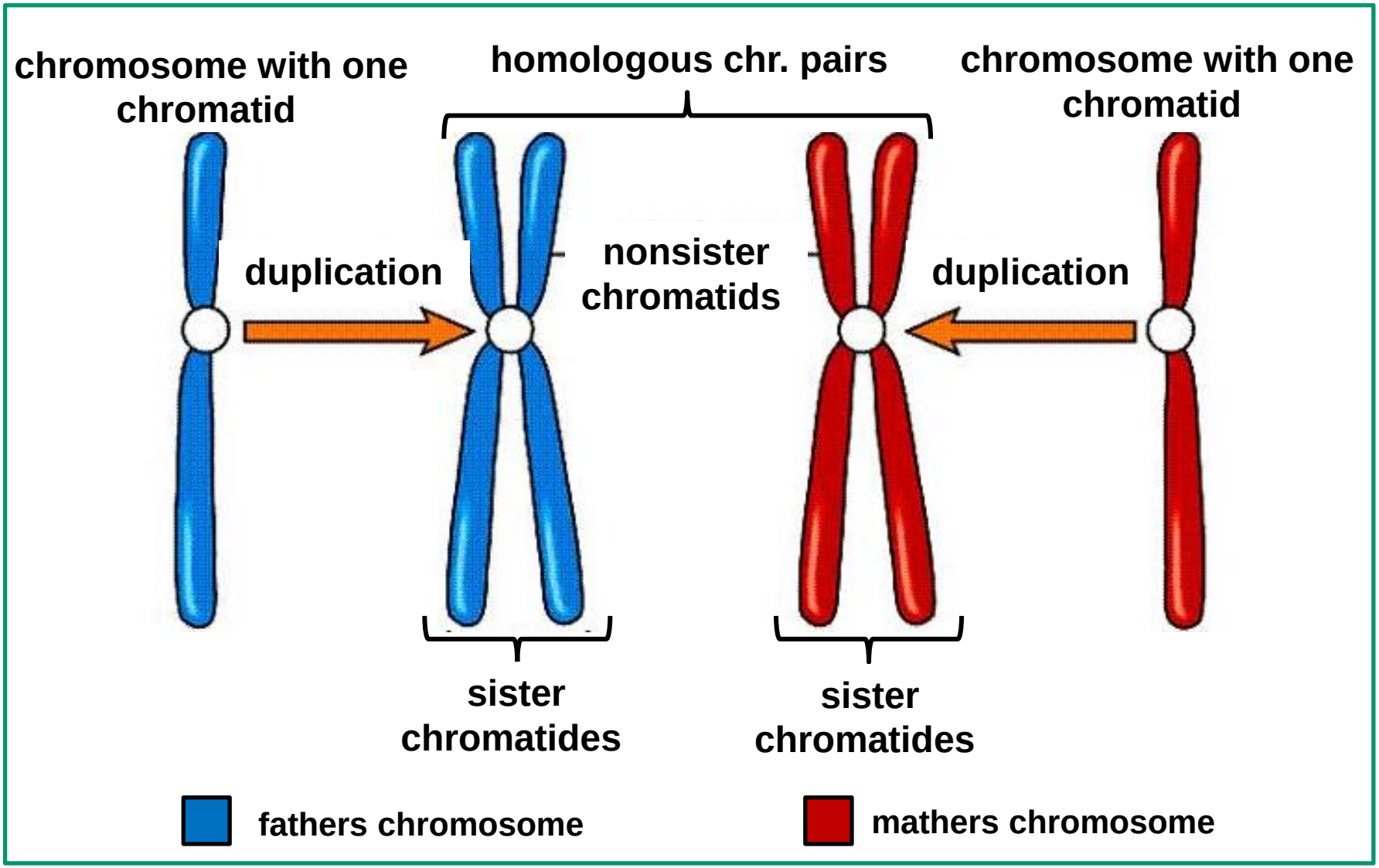




Condensed duplicated chromosome

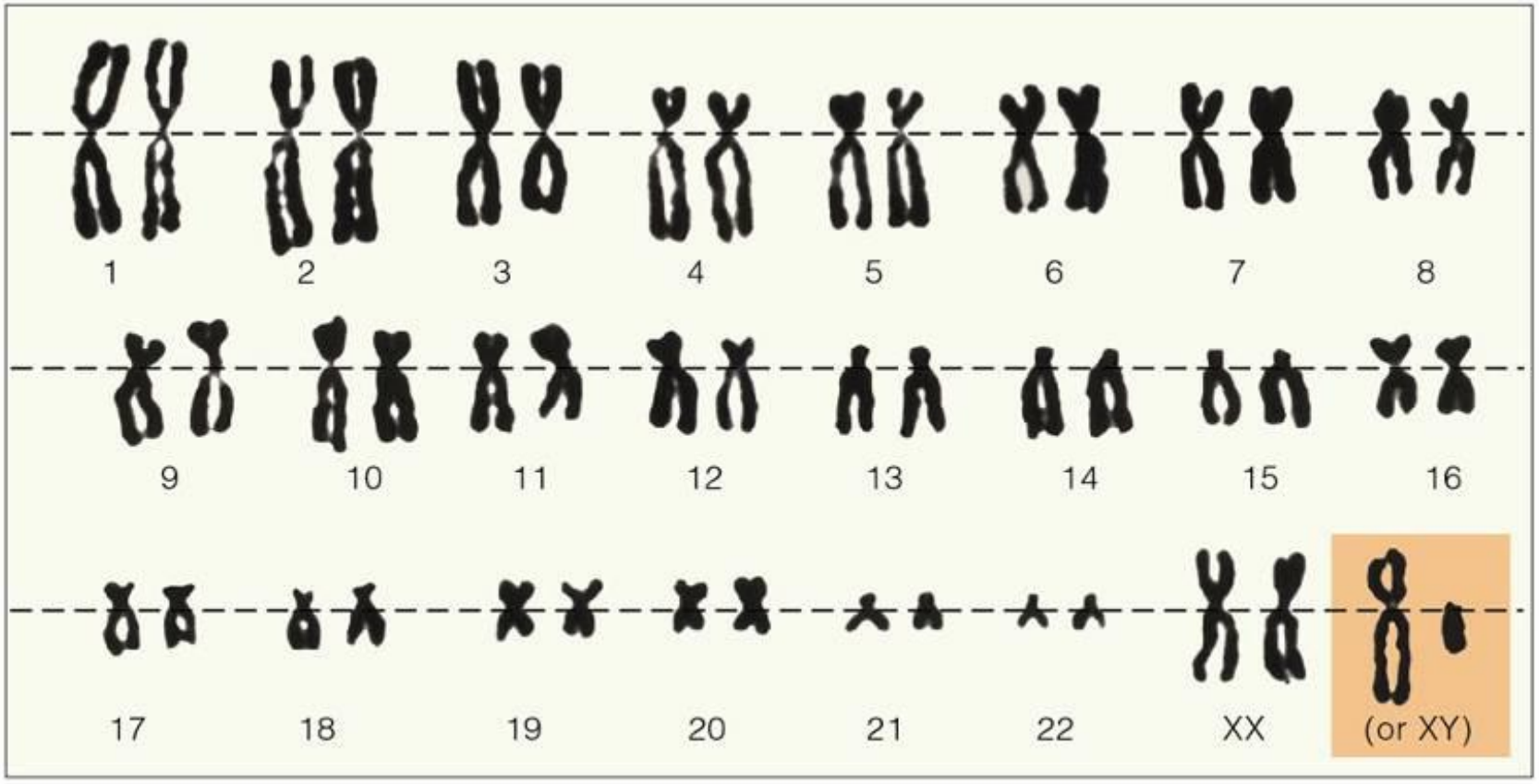
Cell division 3

Metabolism of chromosomes – Homologous chromosomes



Cell division 4

Pairs of homologous chromosomes (2N) organized into so called „KARYOTYPE“



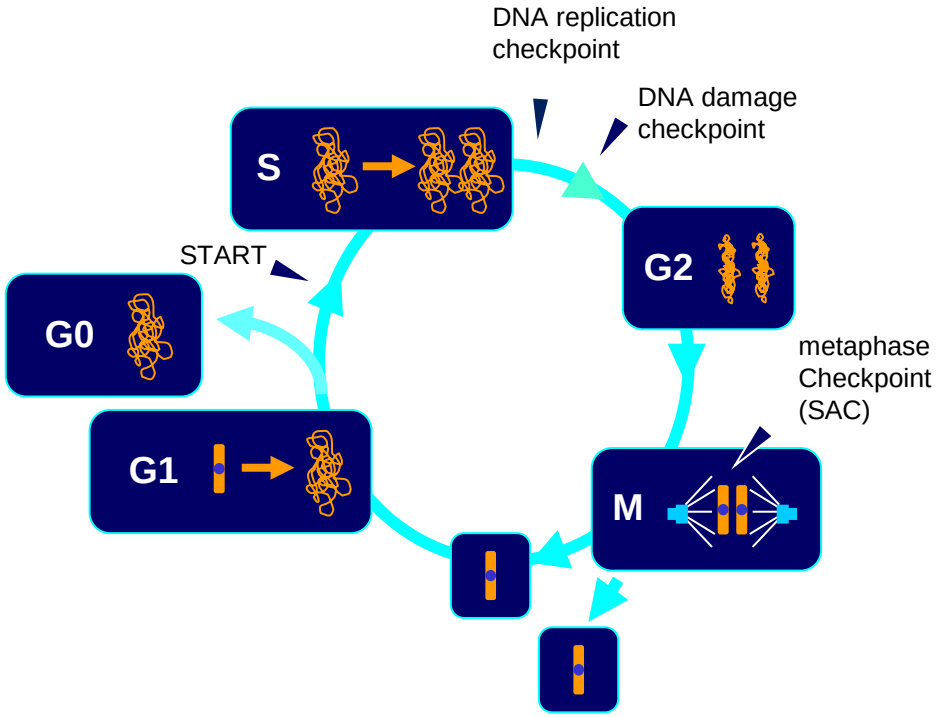
Cell division 5

Basic concept 2

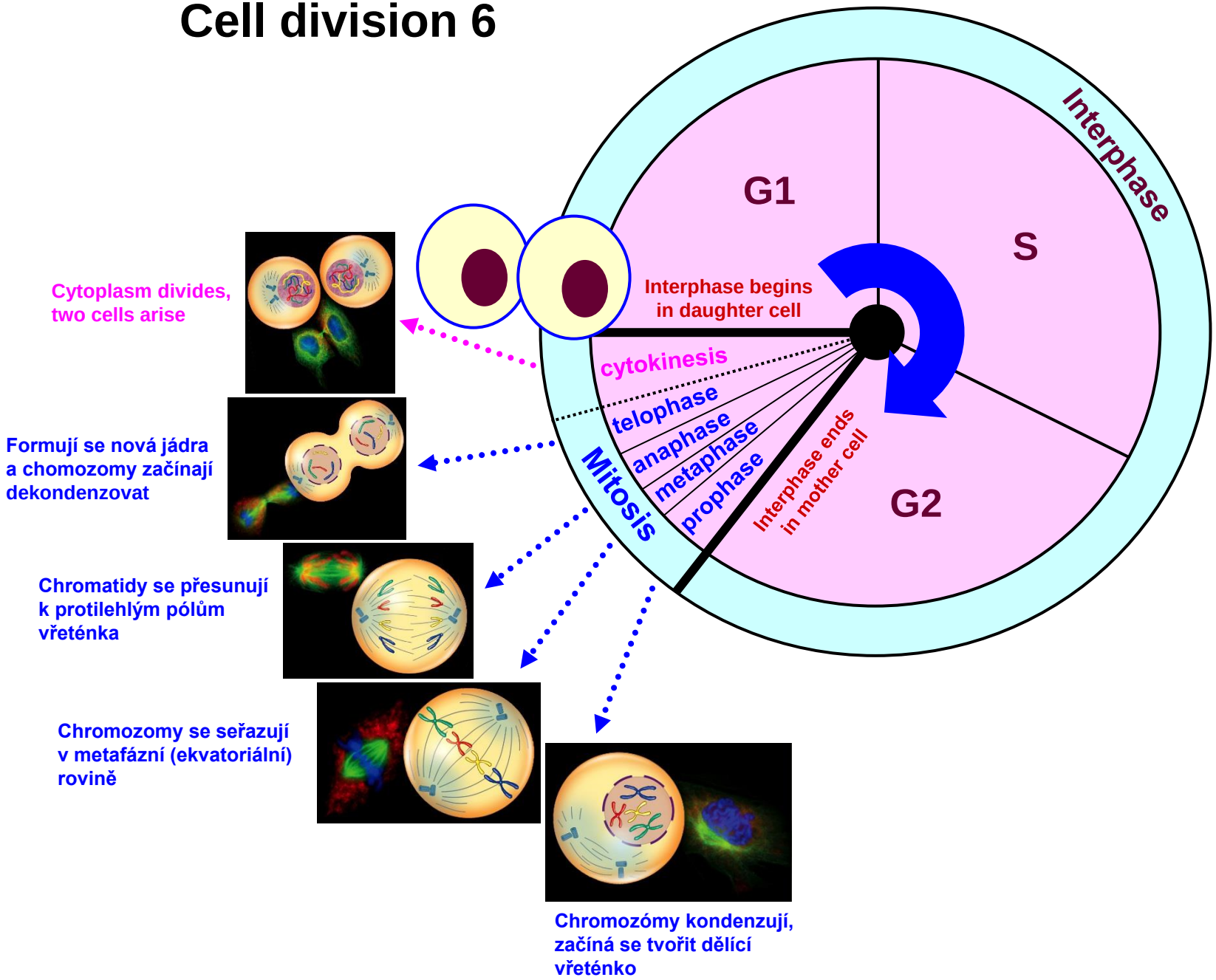
MITOSIS and CYTOKINESIS are parts of cell cycle

CELL CYCLE

- semi-modular character
- equipped with checkpoints
- among cells it is coordinated by signalling molecules

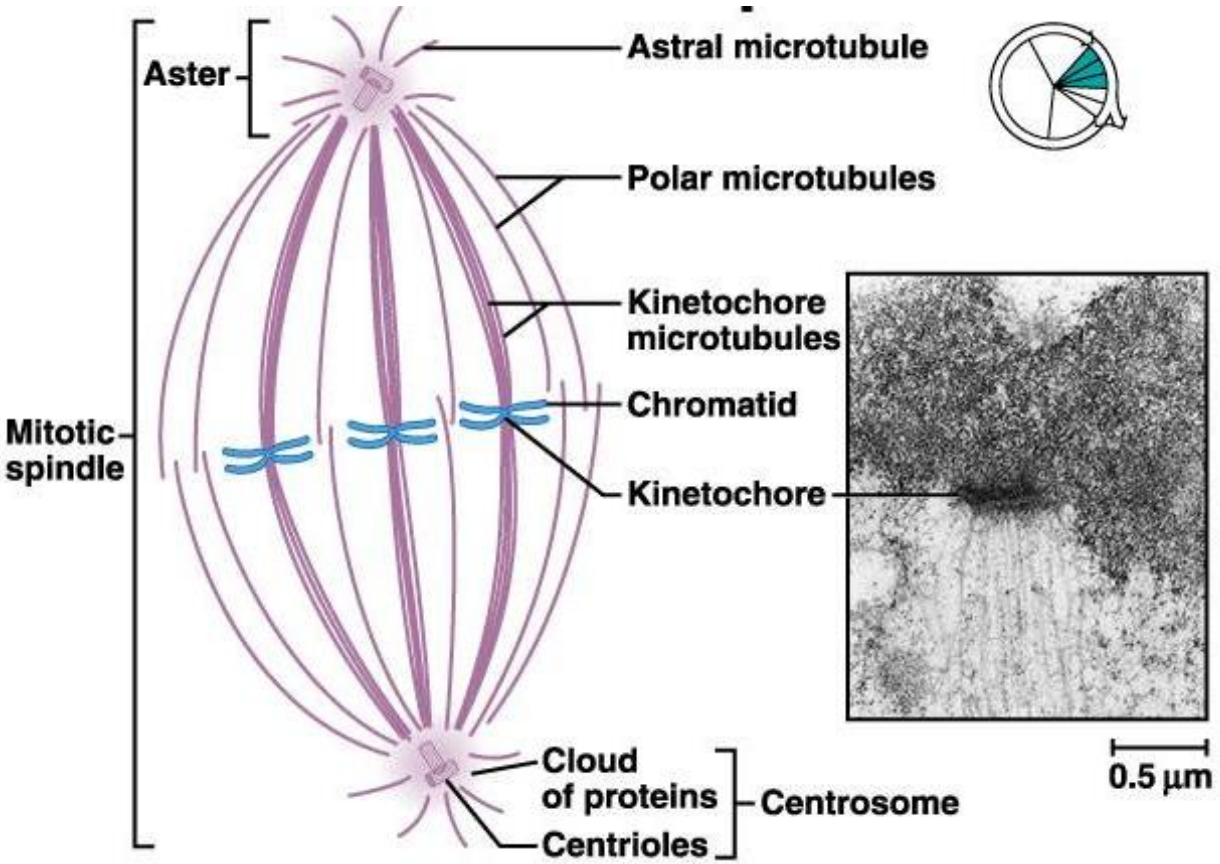


Cell division 6



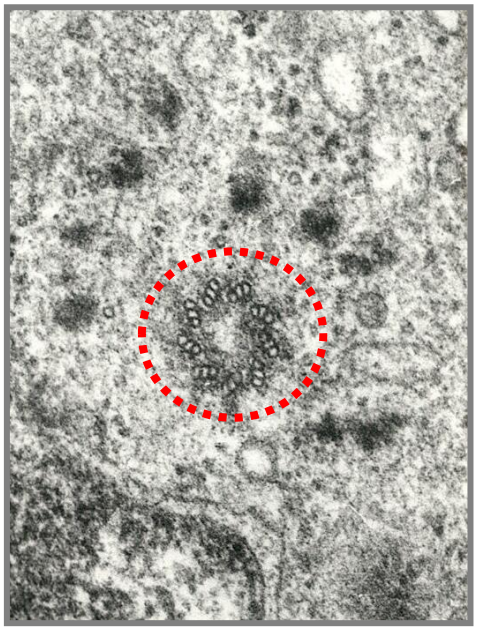
Cell division 7

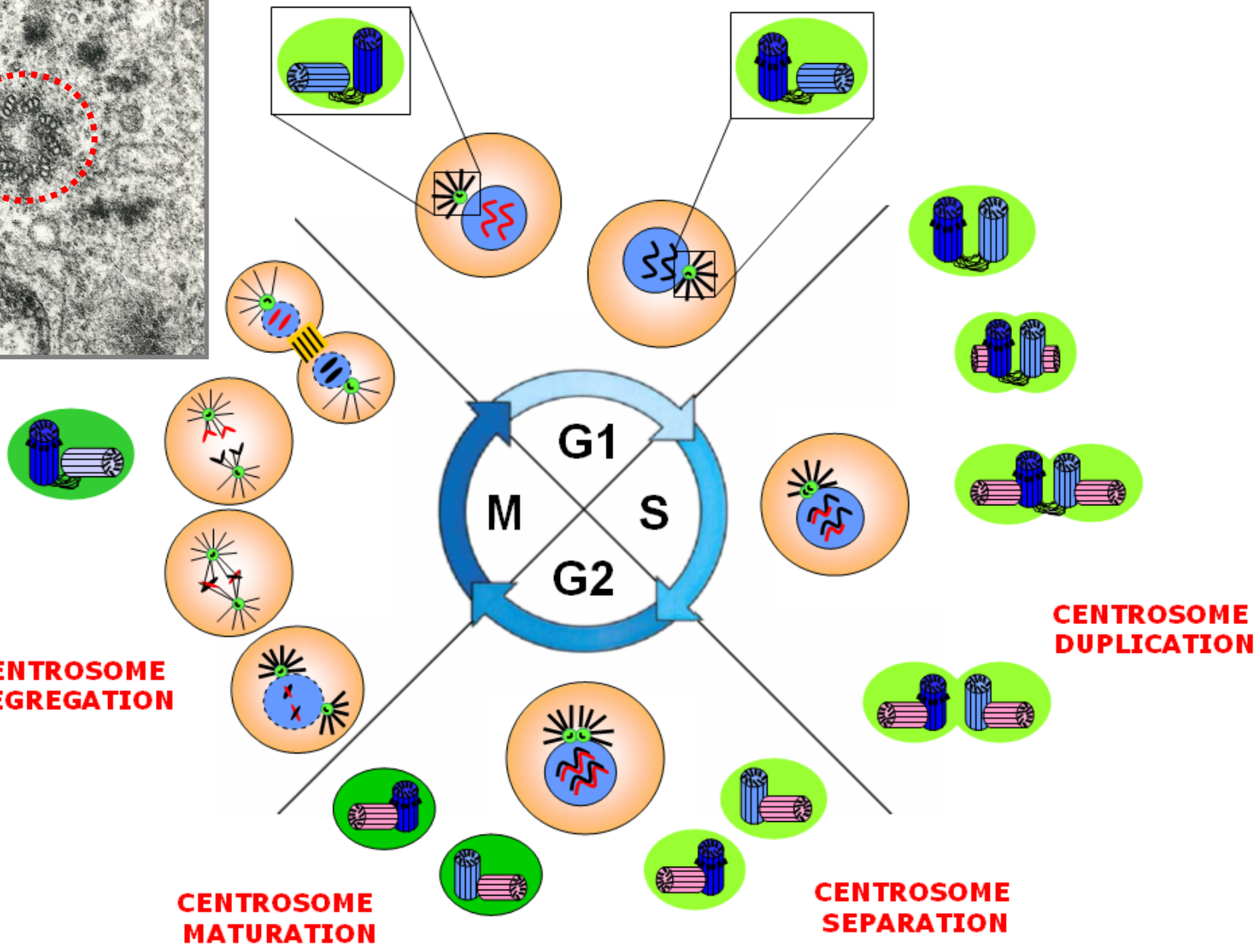
Mitotic spindle



Cell division 8

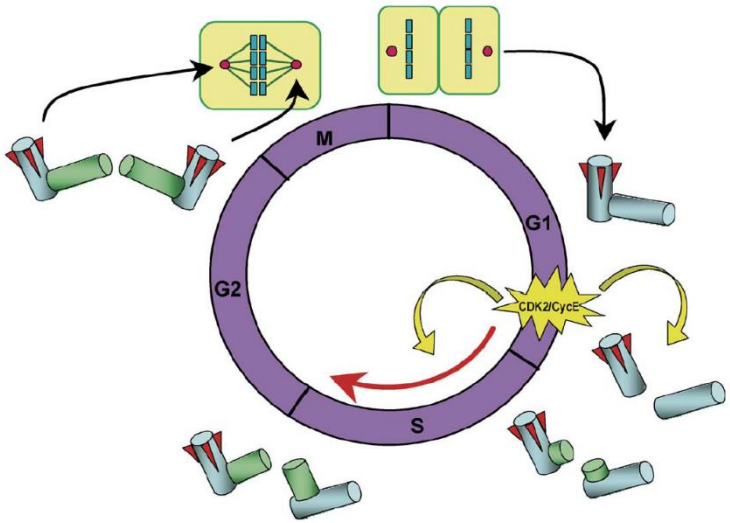
Centrosomal metabolism
Semiconservative duplication

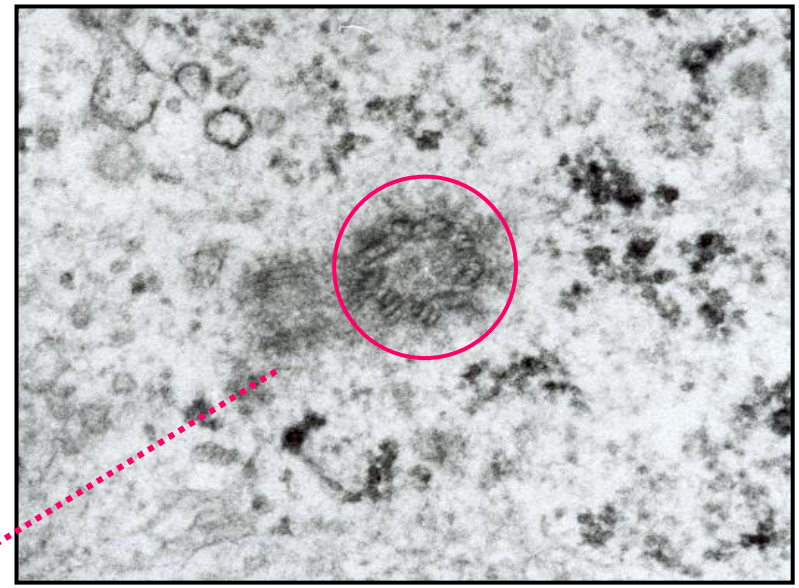


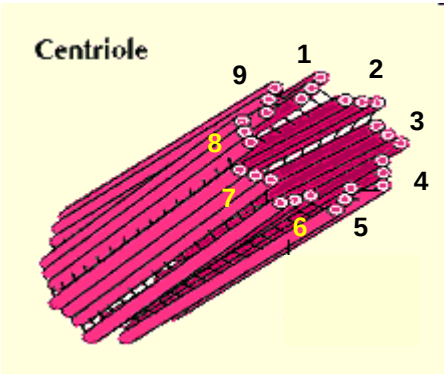


Cell division 9

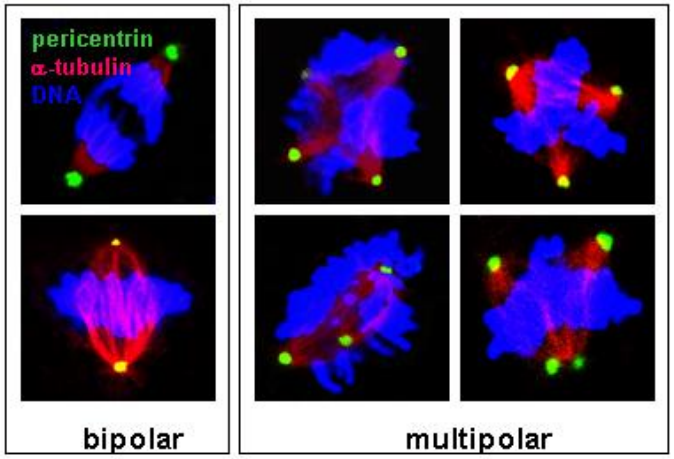
Centrosome structure







Diameter – 0.2 μm
Length - 0.5 μm



Cell division 10

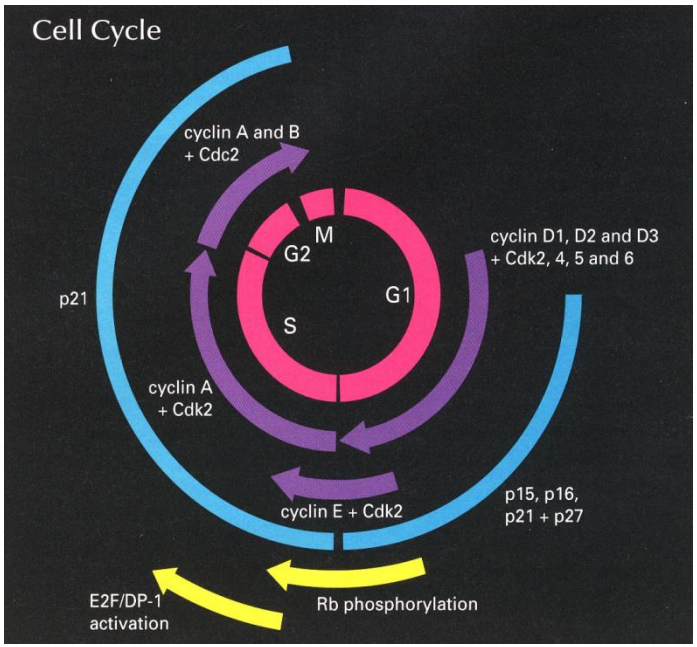
Regulation – Cyklin-Dependent Kinases (CDK) + Cyklins

Cdks and Related Proteins

kinase	PSTAIRE motif	regulatory subunits	putative substrates
Cdc2 p34	PSTAIRE	cyclin A & B	Rb, NF, histone H1
Cdk2	PSTAIRE	cyclin A, E & D	Rb, p27
Cdk3	PSTAIRE	cyclin E	E2F-1/DP-1
Cdk4	PV/ISTVRE	cyclin D1, D2, & D3	Rb
Cdk5	PISSLRE	p35	NF, Tau
Cdk6	PLSTIRE	cyclin D1, D2, & D3	Rb
Cdk7	NRTALRE	cyclin H	Cdc2, Cdk4/6
Cdk8	SACRE	cyclin C	RNA Pol II
Cdk9	PITALRE	cyclin T	Rb, MBP

Major Cyclin-Cdk Cell Cycle Complexes

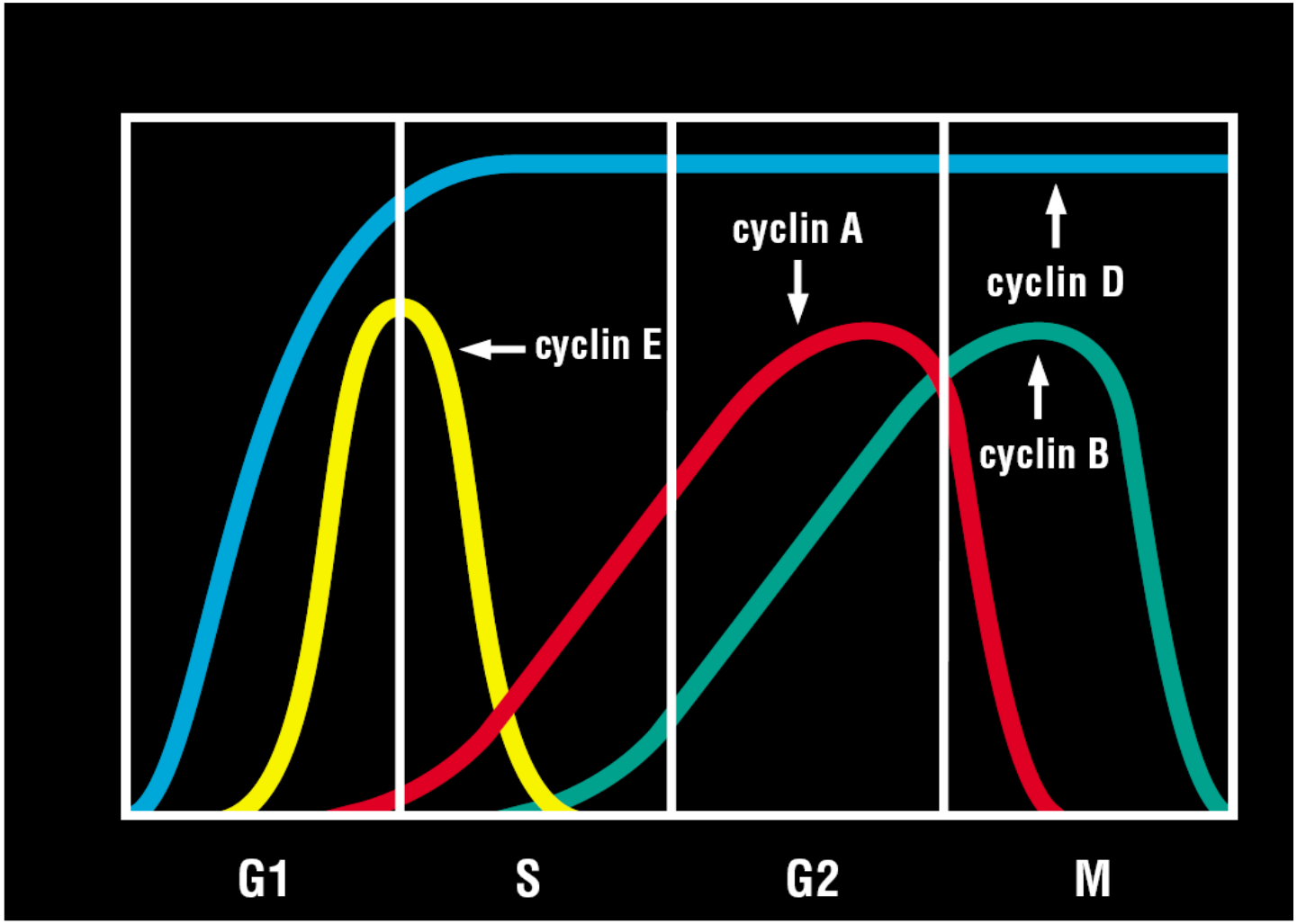
cell cycle stage	cyclin-Cdk complexes	inhibitors						
		p15	p16	p18	p19	p21	p27	p57
G1	cyclin D-Cdk4/6	+	+	+	+	+	+/–	+/–
G1/S	cyclin E-Cdk2	–	–	–	–	+	+	+
S	cyclin A-Cdk2	–	–	–	–	+	–	+
G2/M	cyclin B-Cdc2	–	–	–	–	+	–	–



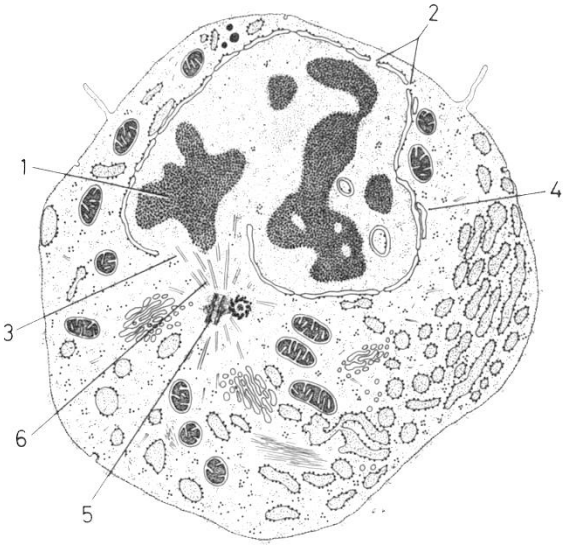
Modified from the catalogue ofSanta Cruz Biomedicals, USA

Cell division 11

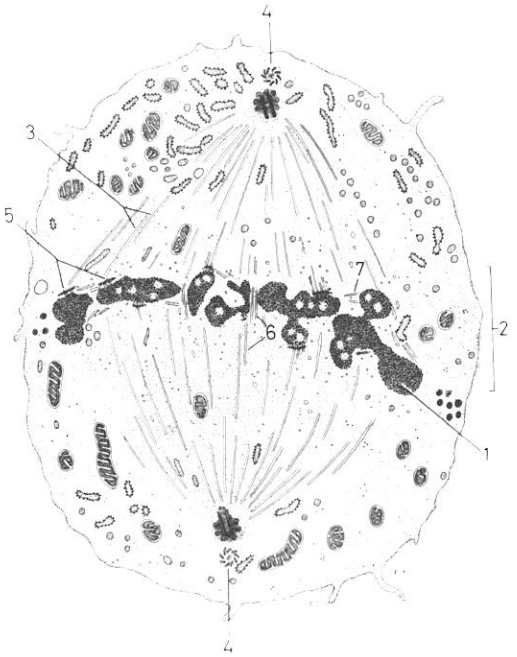
Periodicity of cyclin expression



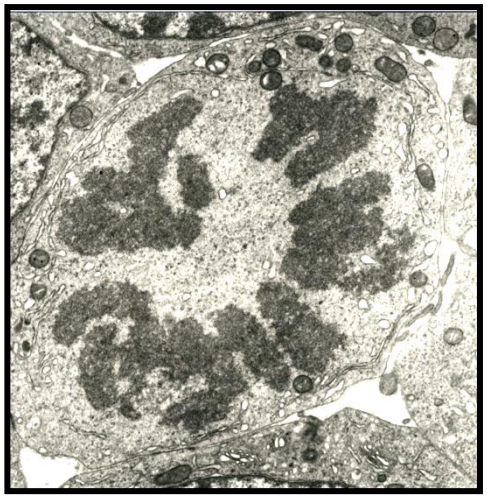
Cell division 12



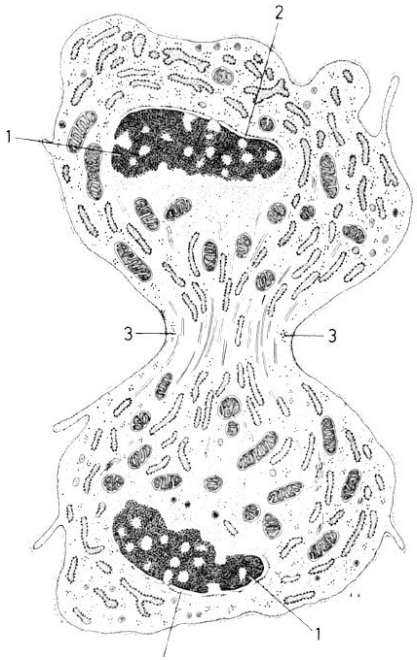
prophase



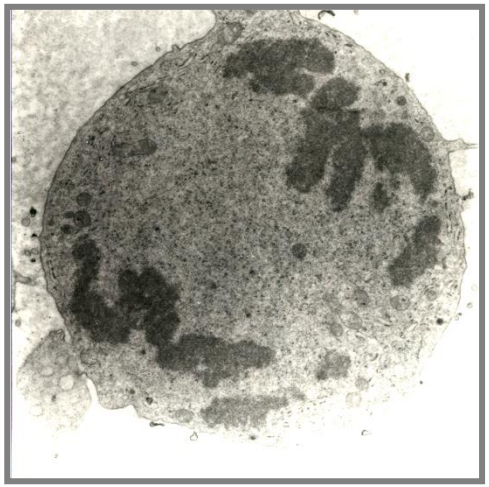
metaphase

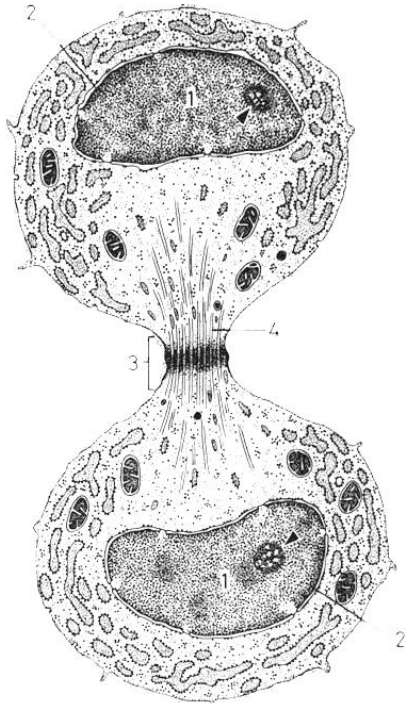


Cell division 13

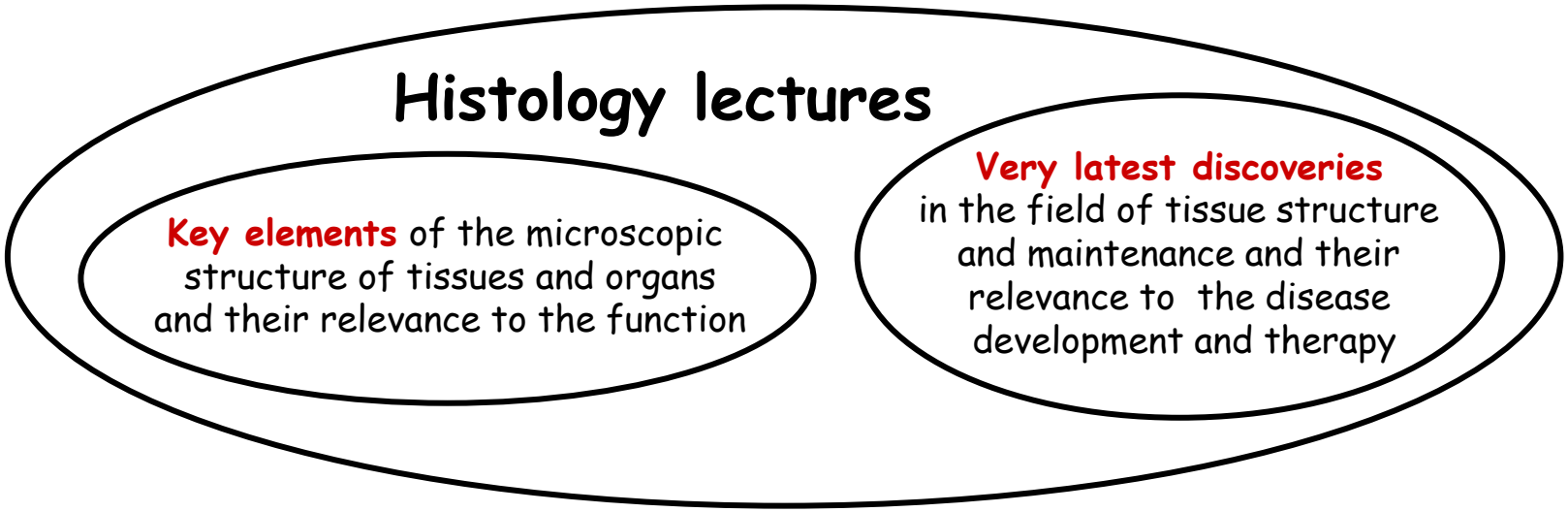


anaphase - telophase





telophase



Thank you for your attention !

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Building A1 – 1st floor