# Histology and Embryology

**Lecturers:**

Aleš Hampl, D.V.M., Ph.D., Assoc. Prof., Head of the Dept.
Petr Vaňhara, RNDr., Ph.D., Assoc. Prof.

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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?

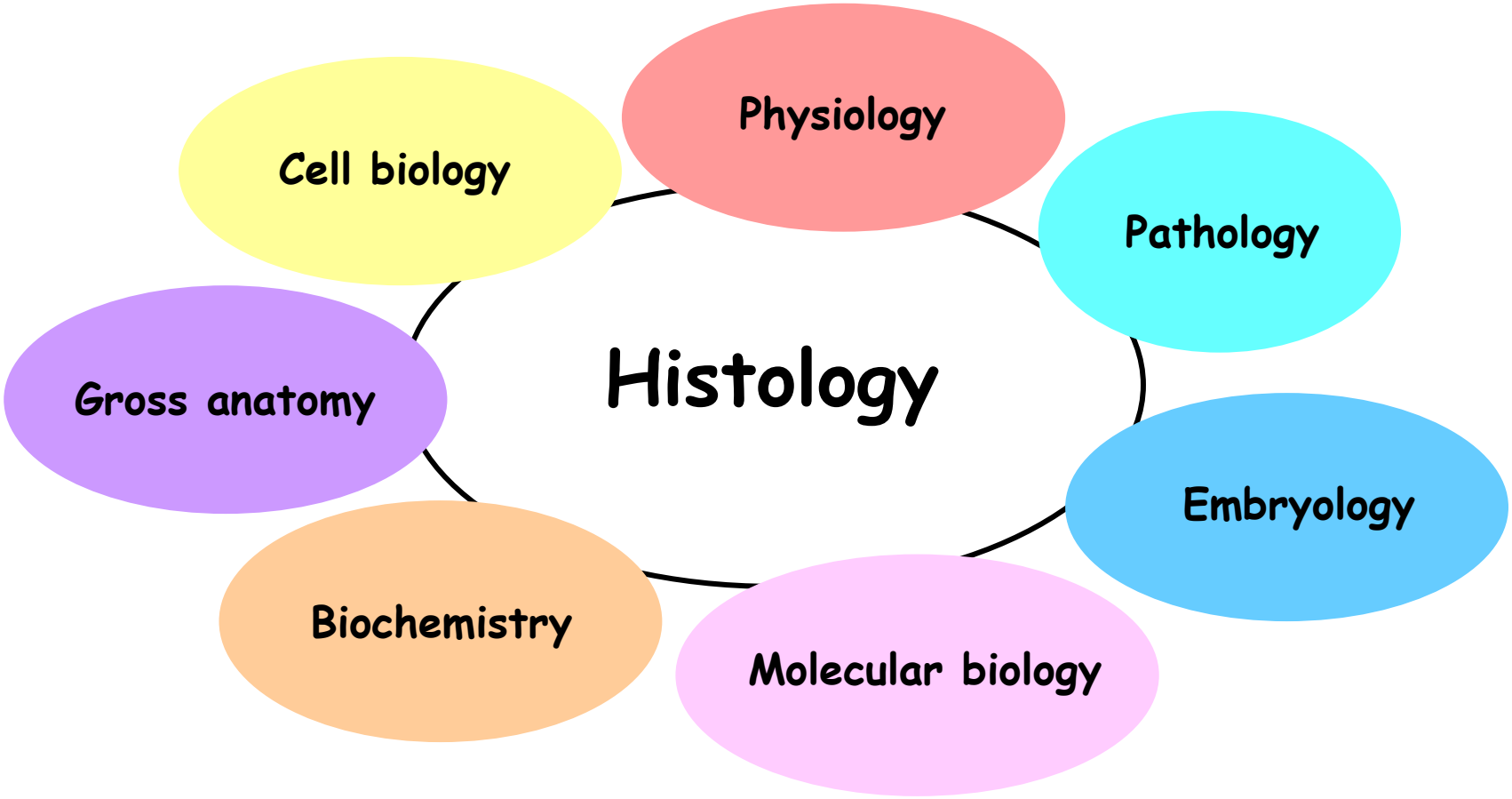
### Microscopic anatomy

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

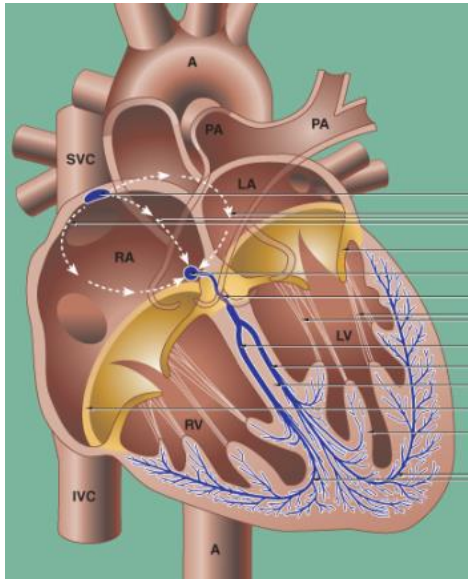
**Bohemian** physiologist

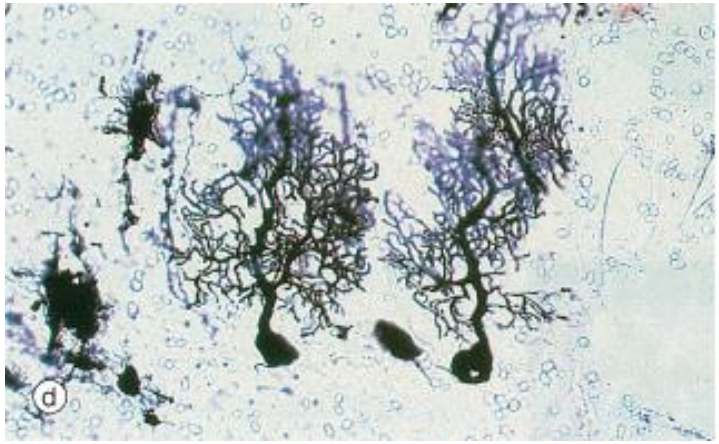
**Schwann + Schleiden – 1839 – cell theory**

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

- Introduced the term **plasma**

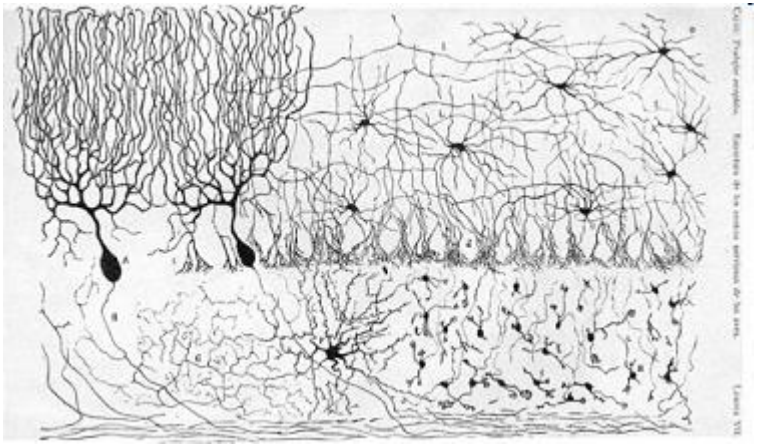
- Found **Purkinje fibers** of the heart →
- Found **Purkinje cells** of the cerebellar cortex

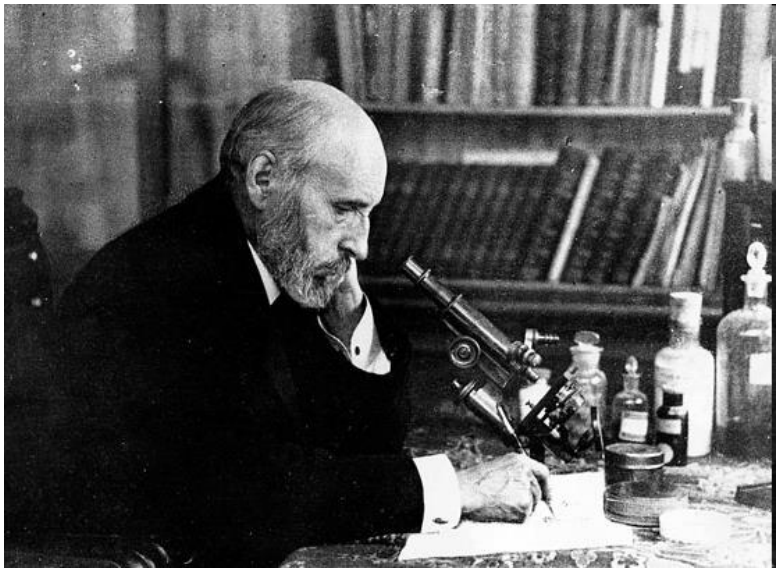


# Santiago Ramón Y Cajal
# 1852 - 1934

Spanish physician and anatomist





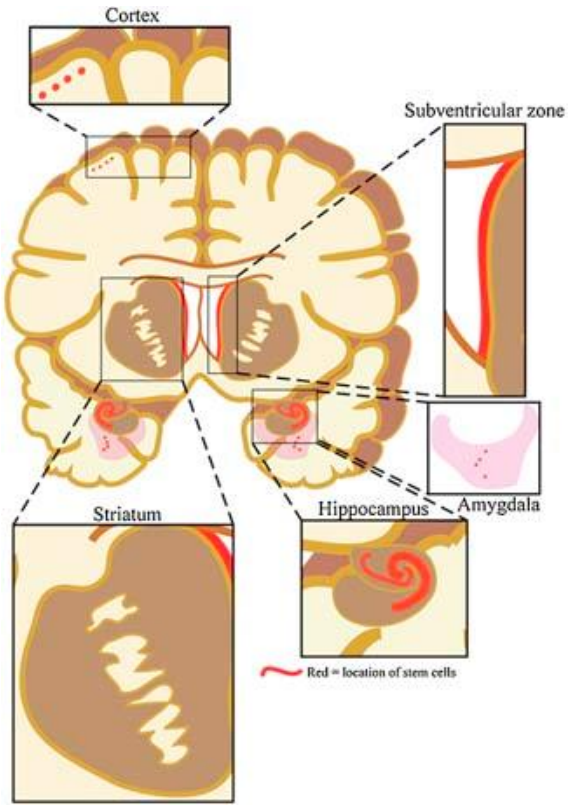
He established the neuron as the primary structural and functional unit of the nervous system.
Nobel Prize in 1906

"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

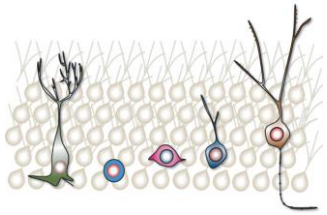
**(since early 1990s)**

**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

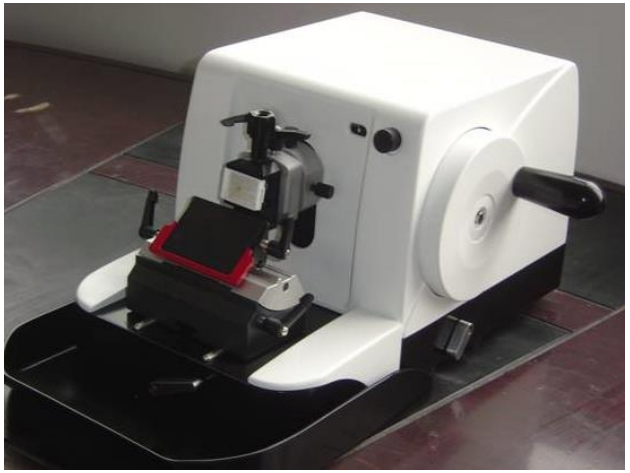
# Methodologies to study cells and tissues 2

## 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"

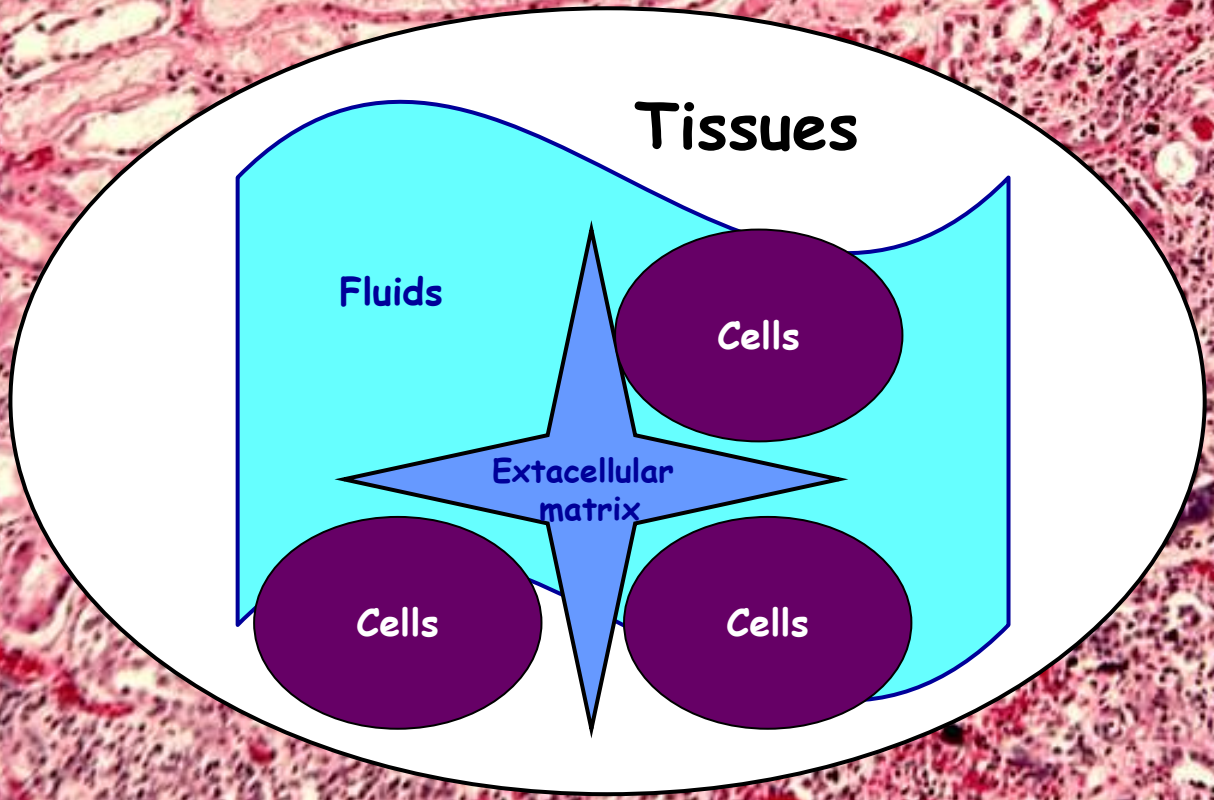
**Chemical stains** (H+E, Azan, van Gieson, …)

**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

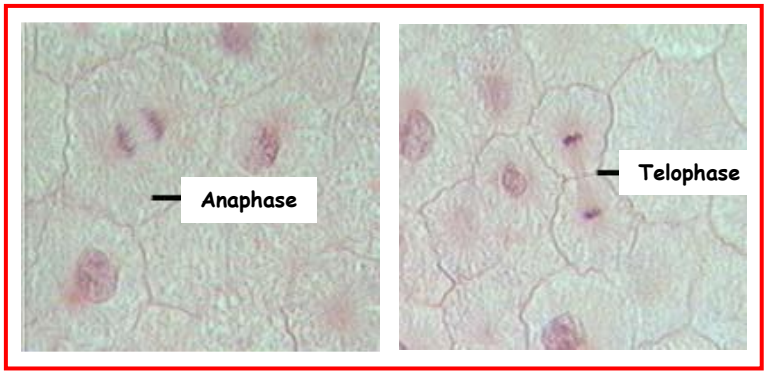
Cell can develop only from preexisting cells
„Omnis cellula e cellula"

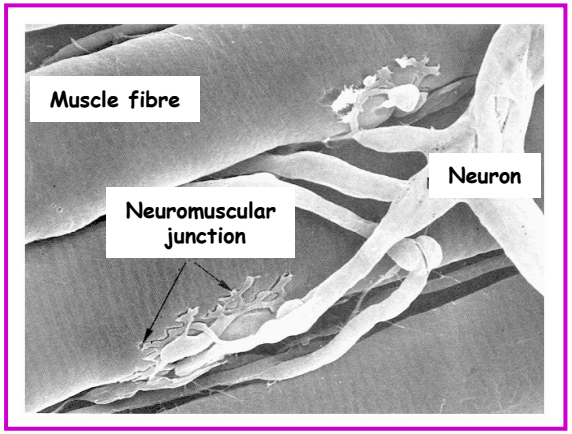
# Cell is unifying theme/element of life

(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)

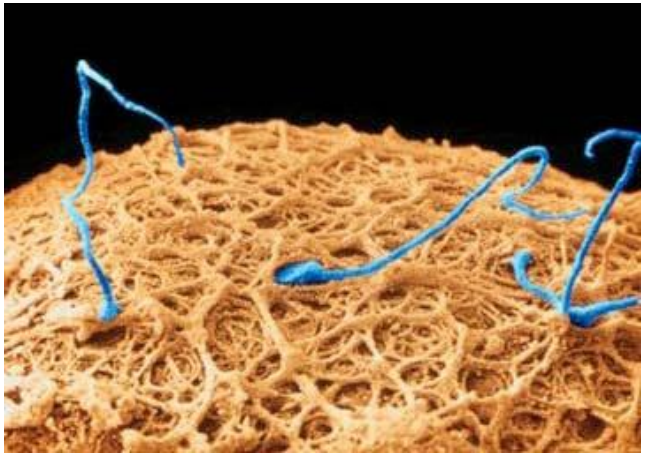


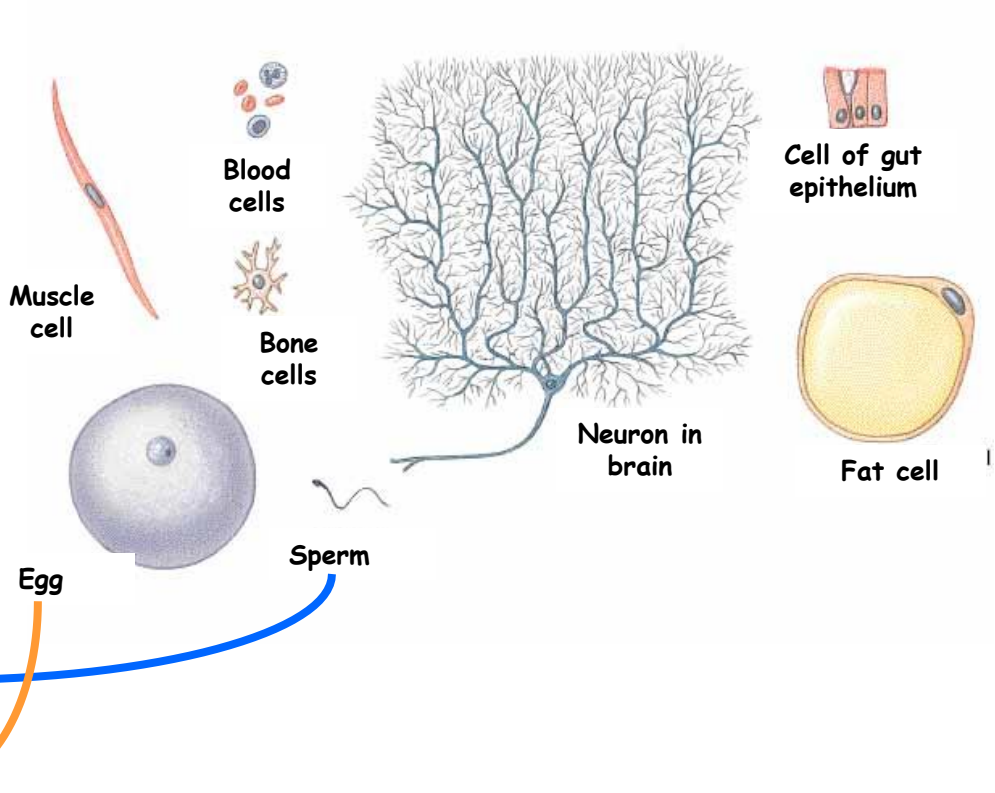



Despite of their common scheme, structural and functional diversity is a typical feature of all eukaryotic cell types

# 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



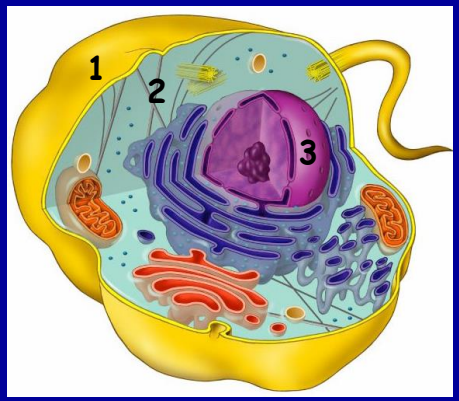


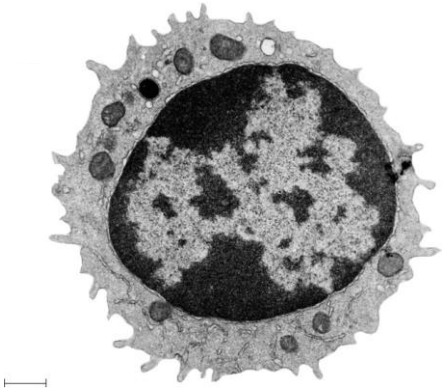
# No cell is exactly like all others, but cells do have many common structural and functional features.

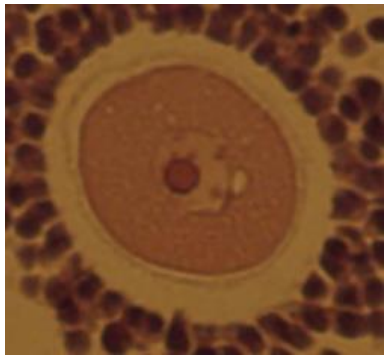
**Keep in mind that not all cells contain all the structures we will discuss !**

All cells have 3 major parts:

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





# Cellular organization is based on COMPARTMENTALIZATION

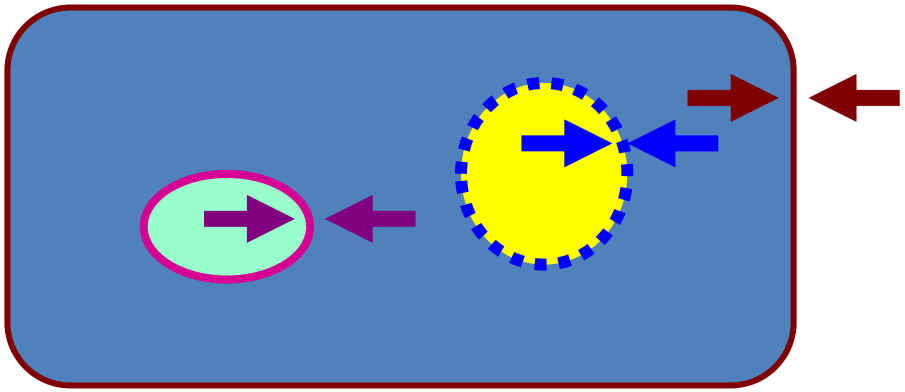
**Specialized functions can be carried out in different locations**

**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.

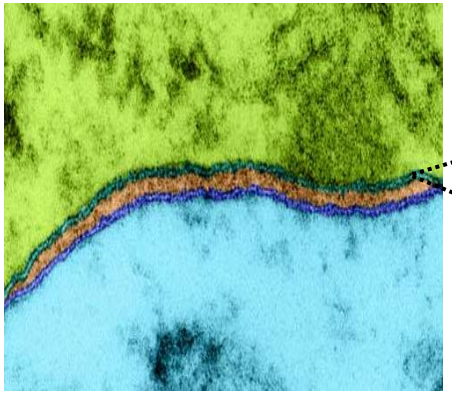
**Amplification X Reduction** of selected compartments

**Specialization of cells** for different functions

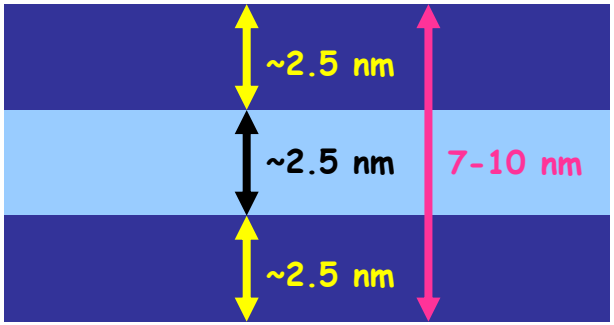
**Cell differentiation**

**Rough ER in secretory cells**
**Mitochondria in cardiac musle cells**

# Biological membrane structure 1



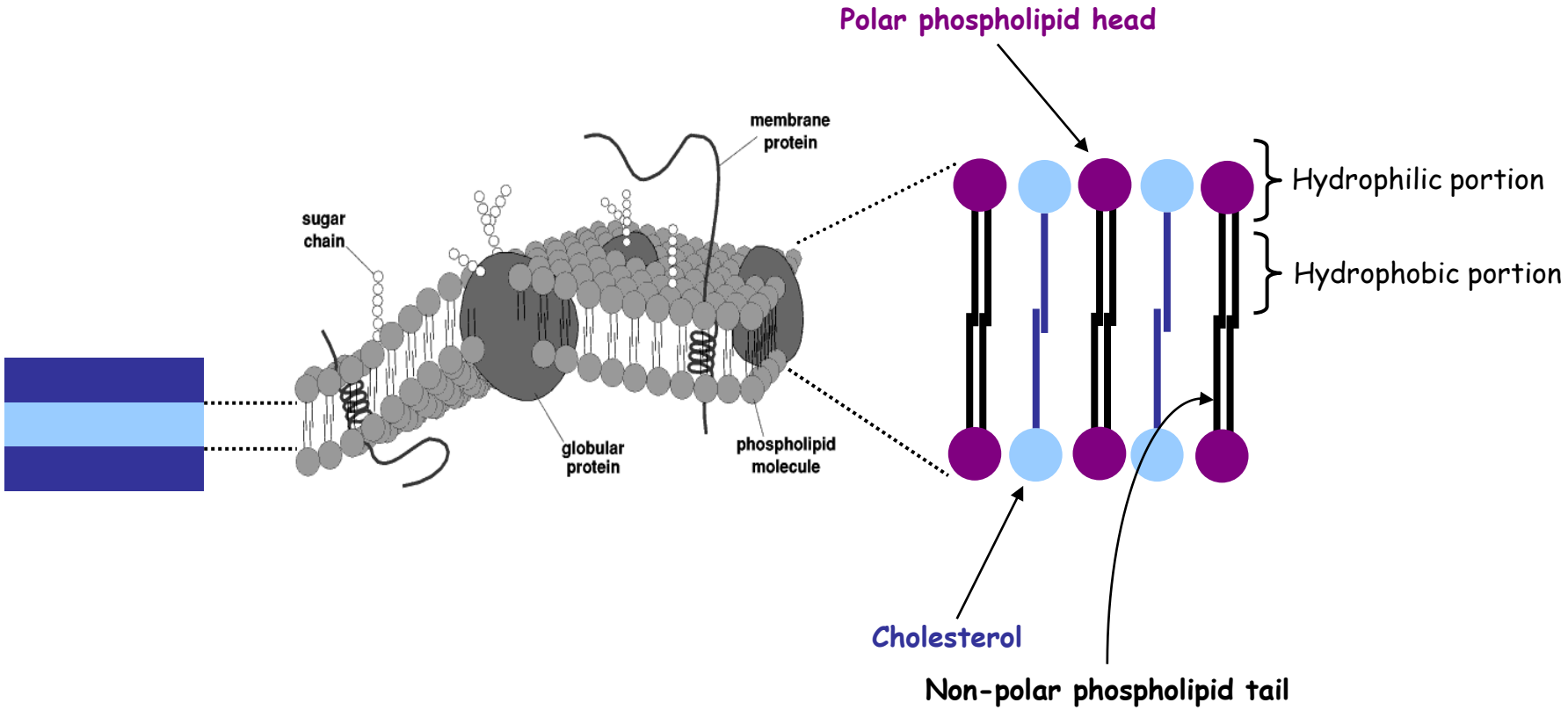
Cell membranes seen
in electron microscope
(pseudocolored)




**Unit membrane**
common to all membranes

# Biological membrane structure 2

**Fluid mosaic** - A bilayer of lipids with mobile globular proteins



# Membrane structure 3

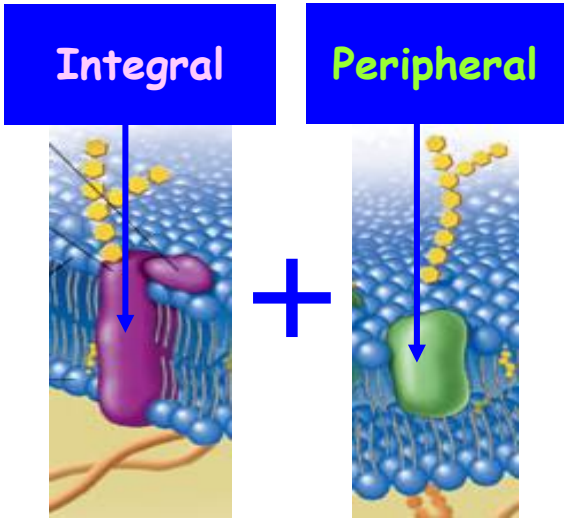
## Membrane lipids

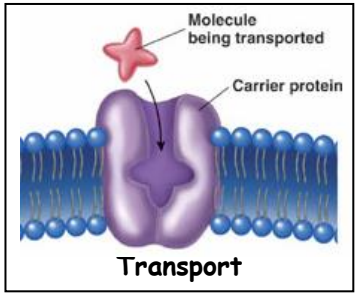
Make up 90-99% of molecules in membrane (in numbers).

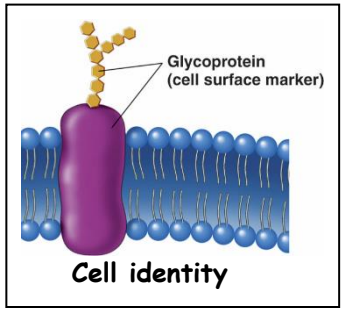
- **Phospholipids** - 75% of lipids
- **Cholesterol** - 20%
- **Glycolipids** - 5% - only on cytoplasmic membrane - GLYCOCALYX

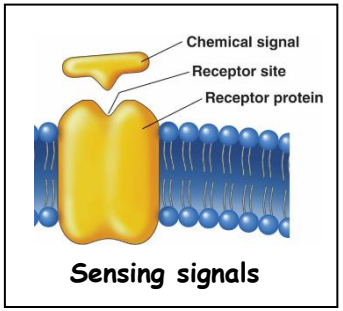
## Membrane proteins

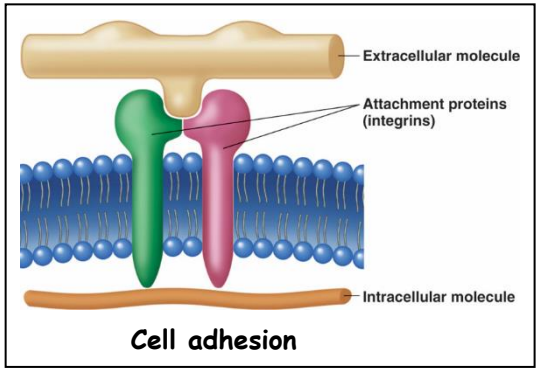
Constitute 1-10% of total molecules but 50% of the weight because of their larger size.

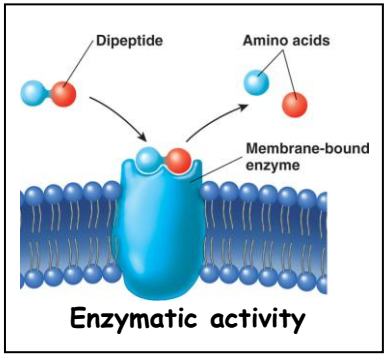


# Organelles

Specialized internal structures with specialized functions

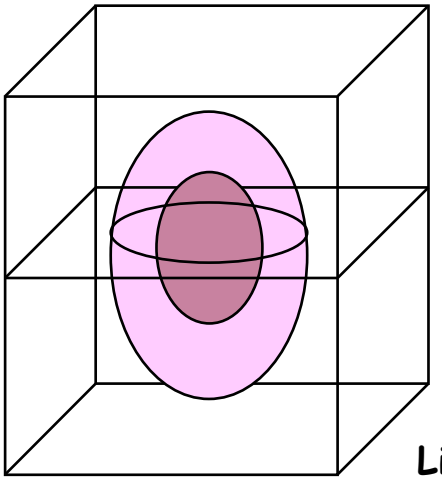
## Membranous

- 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

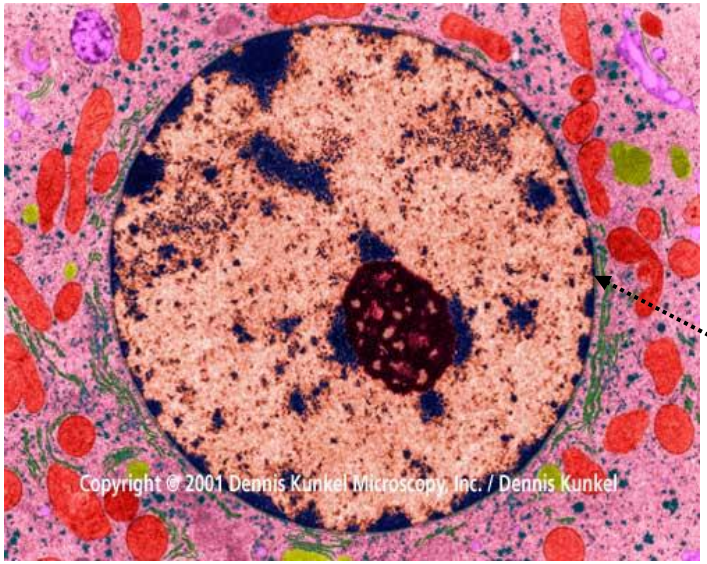


# Nucleus 1
# Envelop-bounded structure

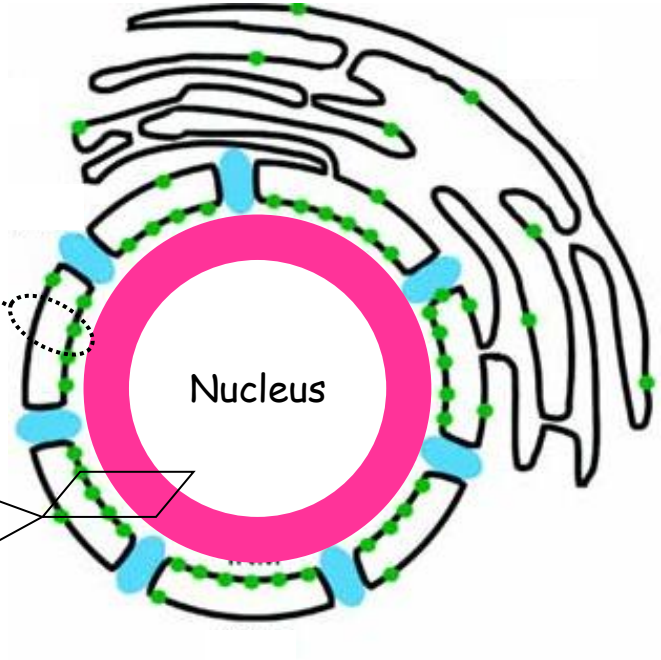
Mostly:

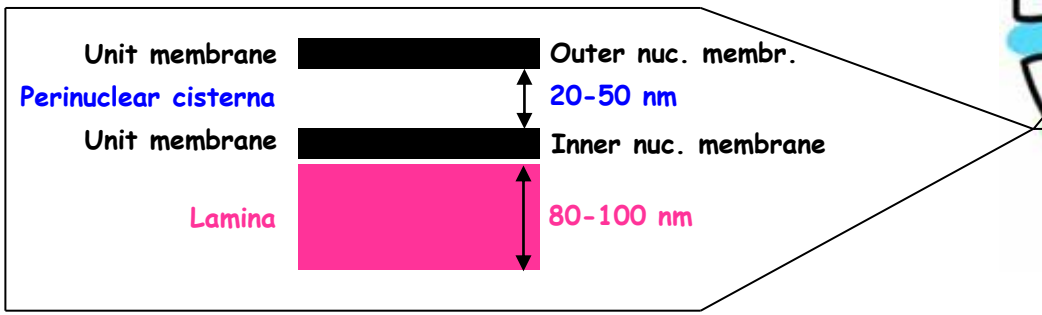
- Spheherical (5-10 μm) (lobular, twisted, disk-shaped,...)
- Located centrally
- One per cell (osteoclast more, erythrocyte none)

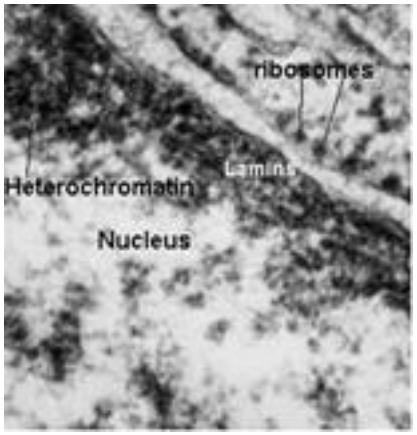
**Liver cell nucleus**



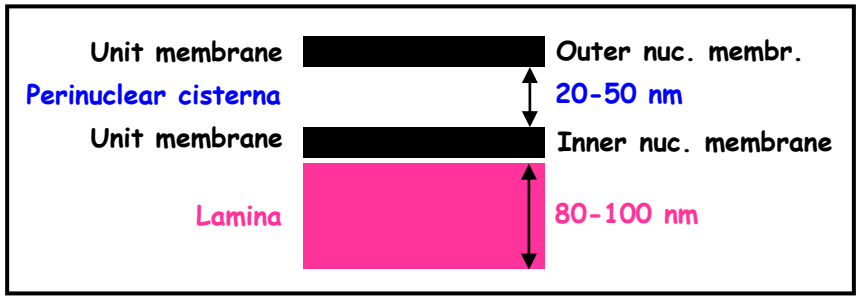

Nuclear envelope

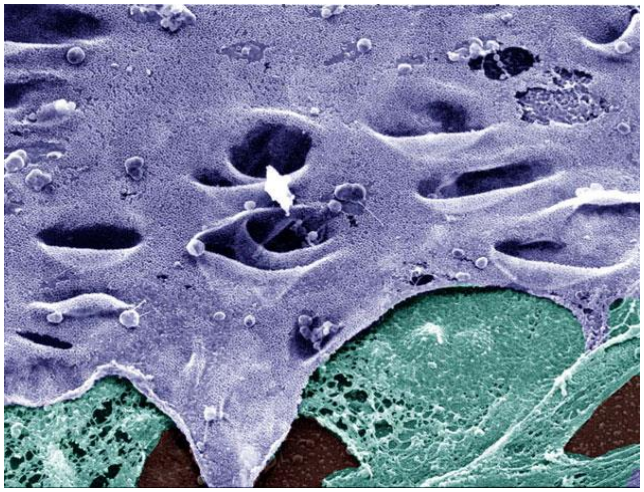


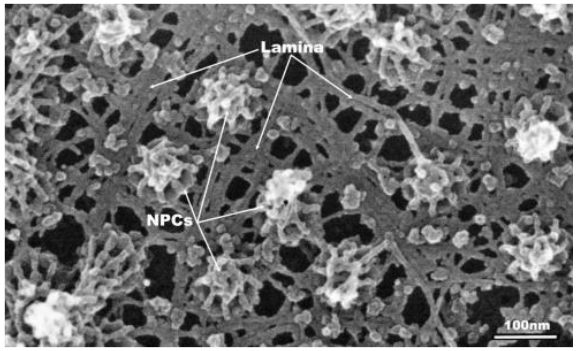



# Nucleus 2
## Continuation on nuclear envelop

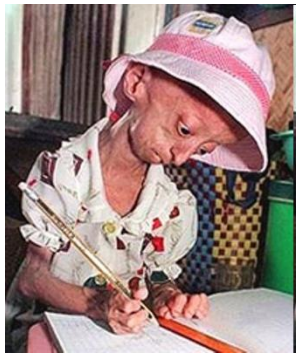


**Lamins:**
- Intermadiate filament proteins (A, B, C)
- Form meshwork inside of INM, some extend into nucleoplasm
- Nuclear strength and architecture
- Anchorage sites for chromatin
- DNA replication and mRNA transcription
- Involved in apoptosis



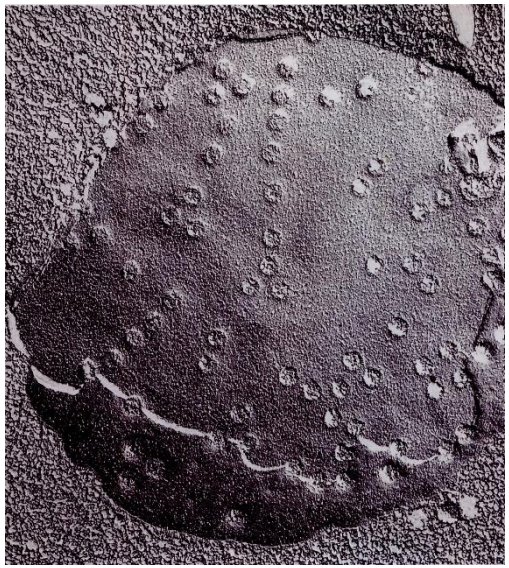

**Laminopathies**
- Human diseases (at least 13 known)
- Mutations in lamin genes (almost 200 mutations known)
- Deregulated gene expression
- Premature aging

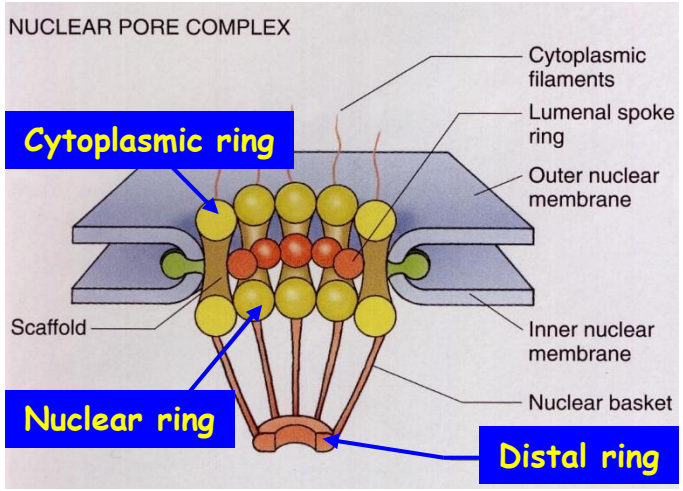


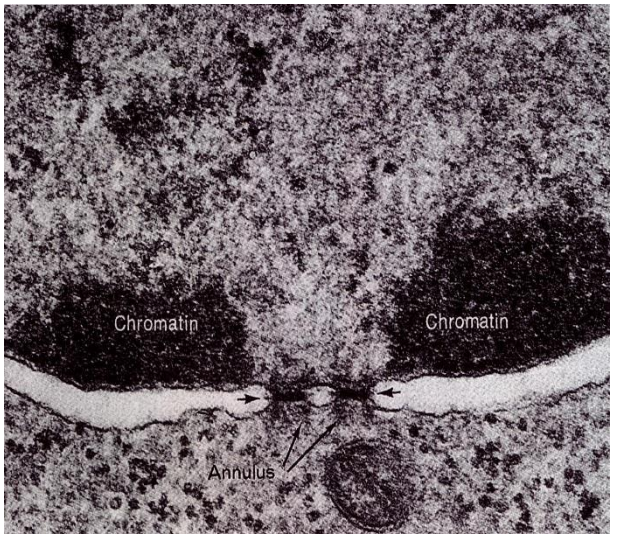
**Hutchinson-Gilford progeria**

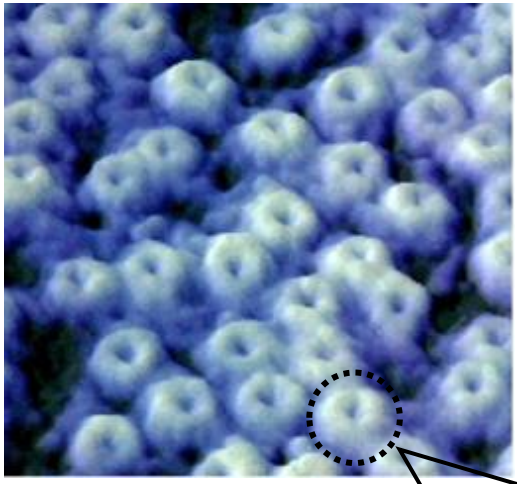
Rare - 1-4 per 8 milion of newborns
Missense mutation in A-type lamin

# Nucleus 3
## Nuclear pore complex





Diameter ~ 100 – 125 nm

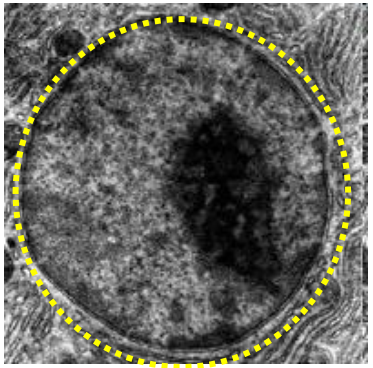
Three rings (8 subunits each)

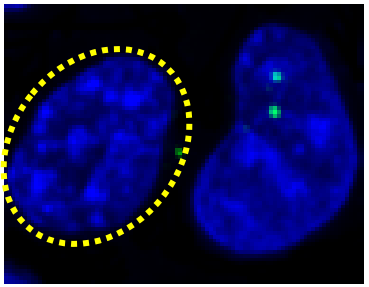
Inner filamentous basket

**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





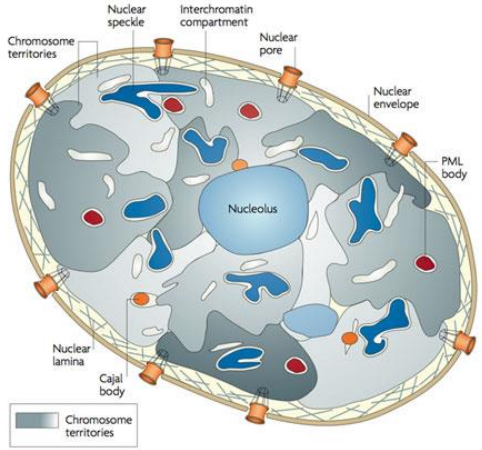
## Interphase nucleus

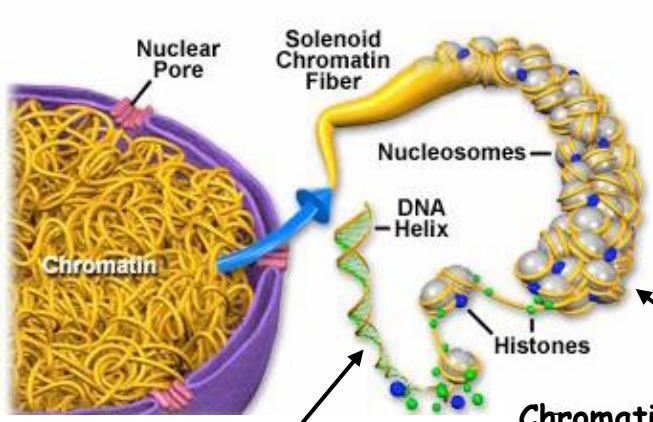
### Heterochromatin

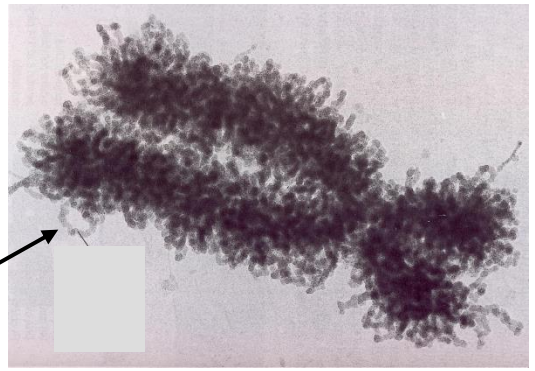
Feulgen positive – dark in light microscope
Dark/dense granular in TEM
Transcriptionally inactive

### Euchromatin

Invisible in light microscope
Relaxed uncoiled chromosomes
Transcriptionally active

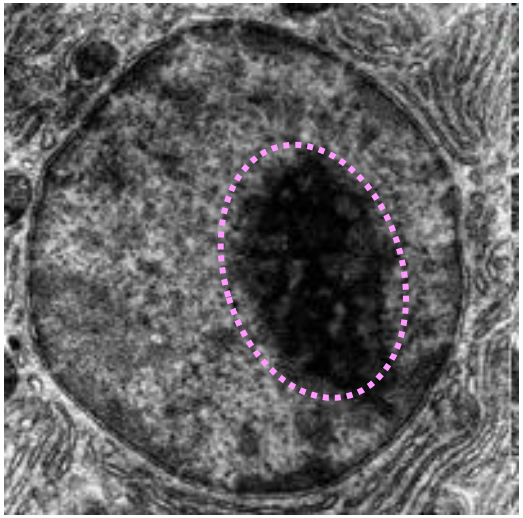


2 nm
DNA double helix

30 nm
Chromatin fiber of packed nucleosomes

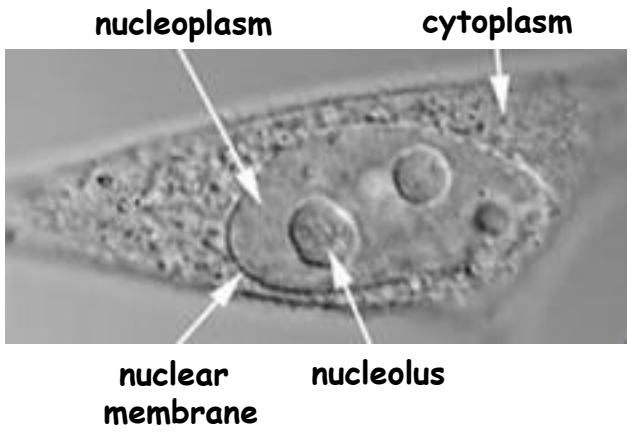


# Nucleus 5
# Nucleolus

**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**

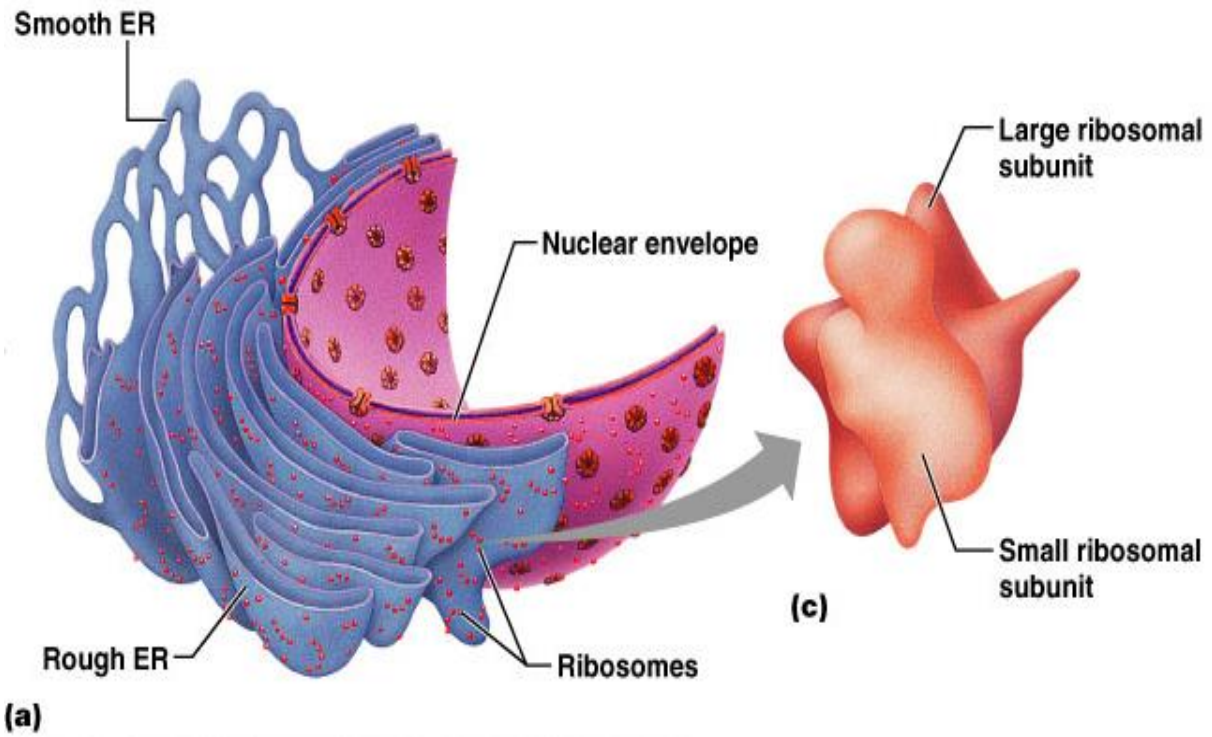
on five chromosomes in human cells
(chrs. 13, 14, 15, 21, 22)

# Endoplasmic reticulum 1

„within cell“ „net“

Majority of the membrane within cells.

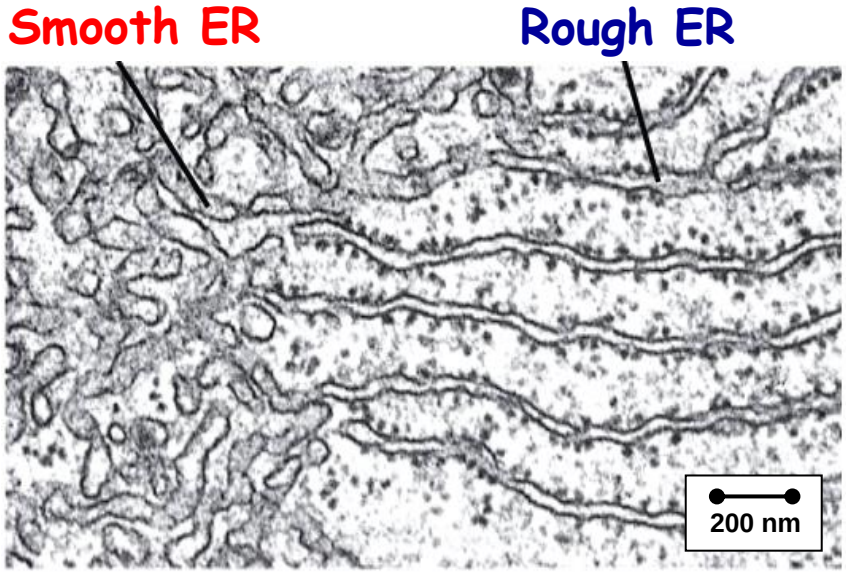
Interconnected tubuli and vesicles → Cisterns

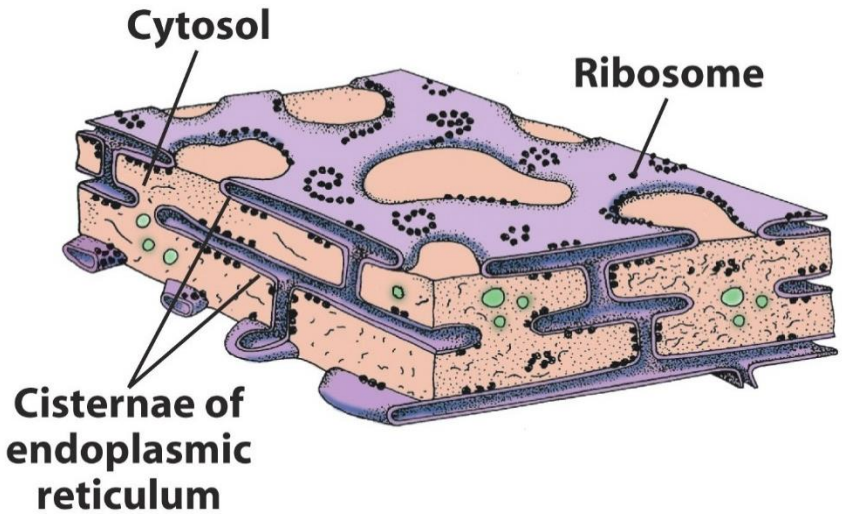


# Endoplasmic reticulum 2

**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

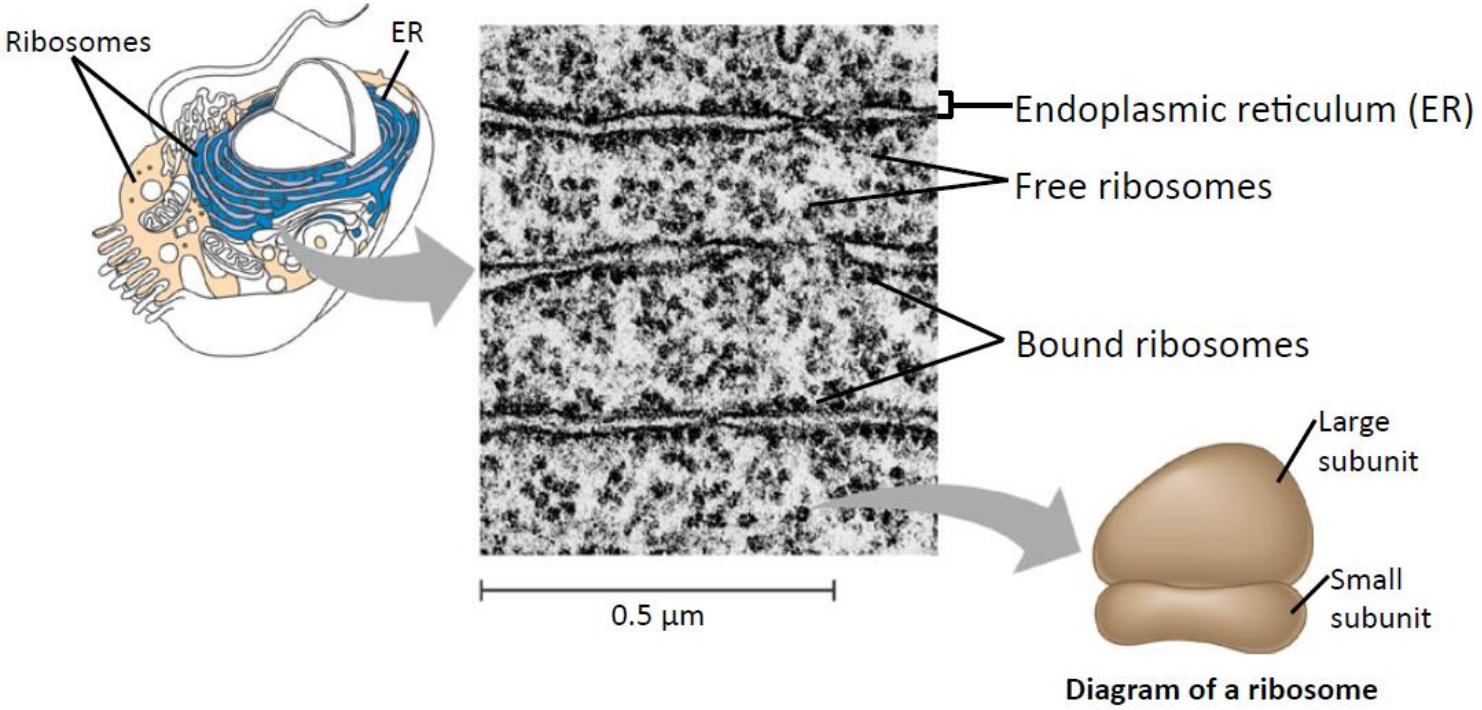
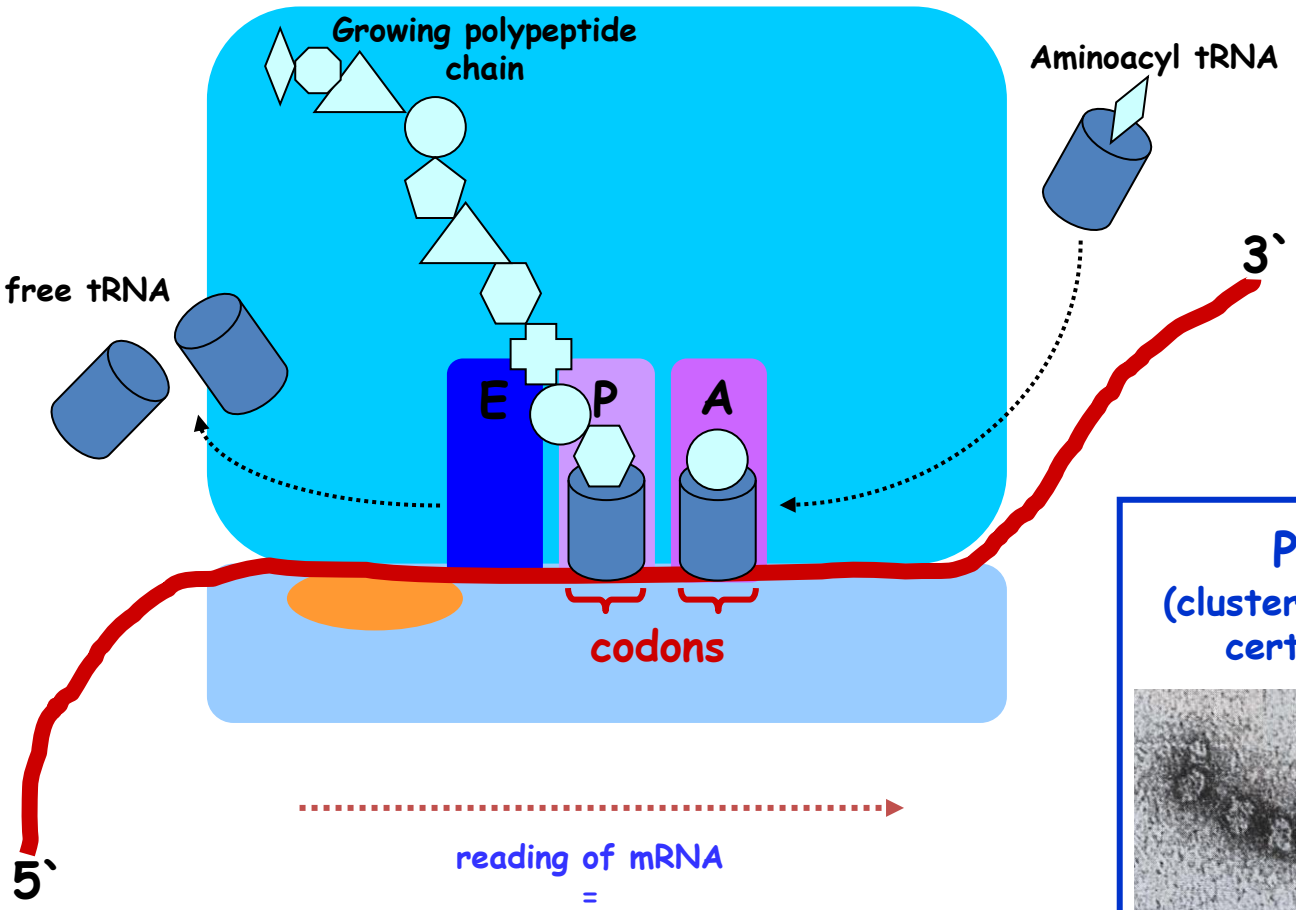



**Diagram of a ribosome**

# 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`

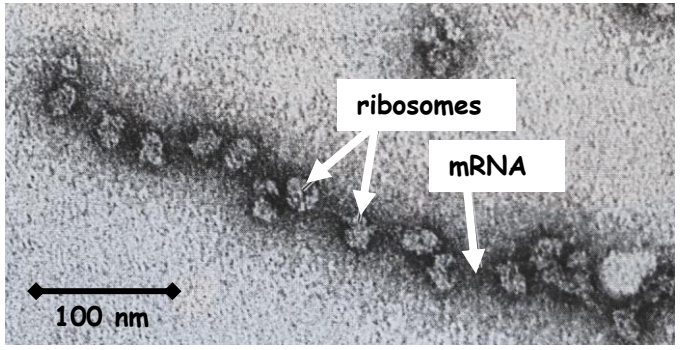
mRNA 5` — UGA — 3`

STOP kodony

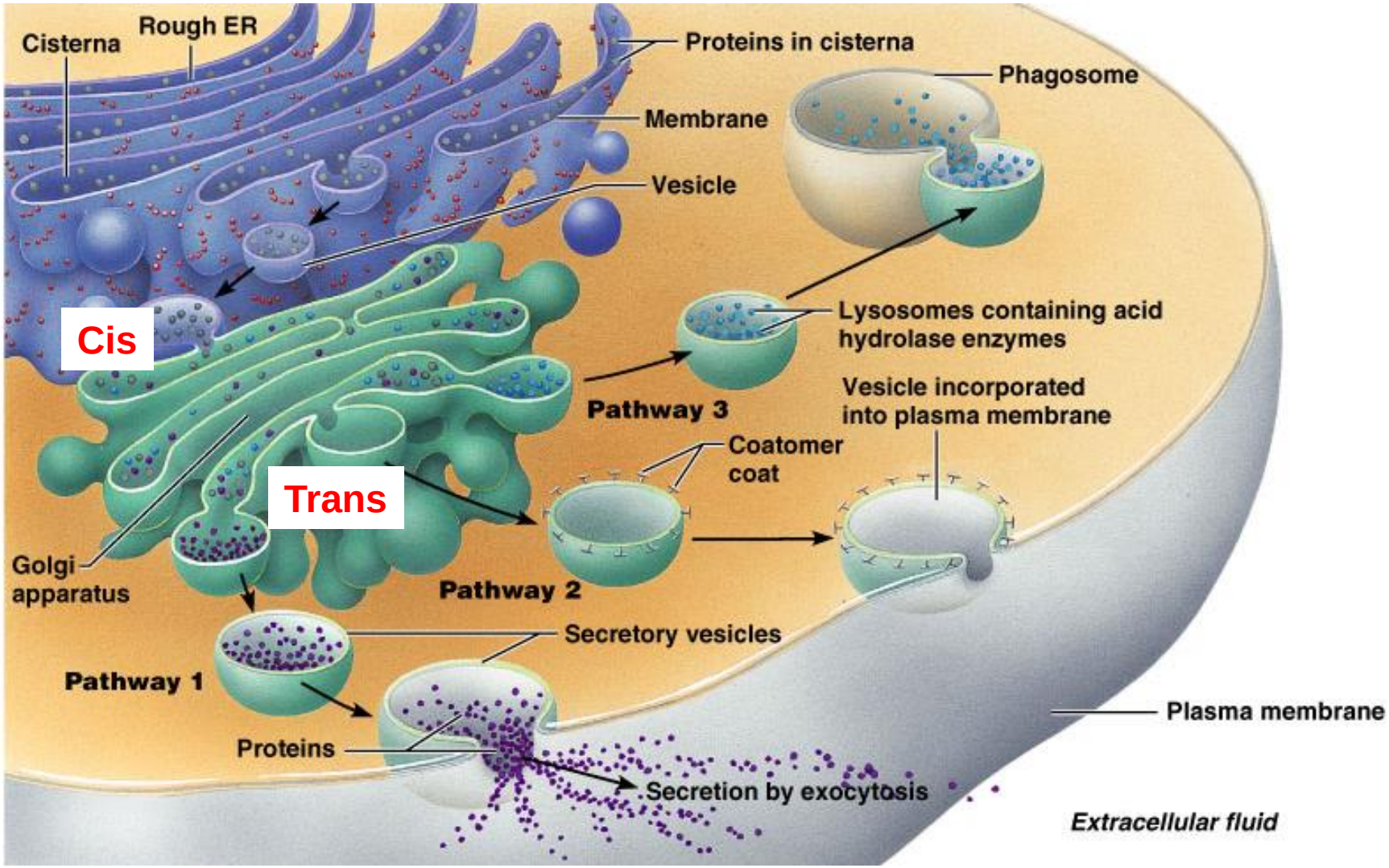
bind „release factor"

## POLYRIBOSOME

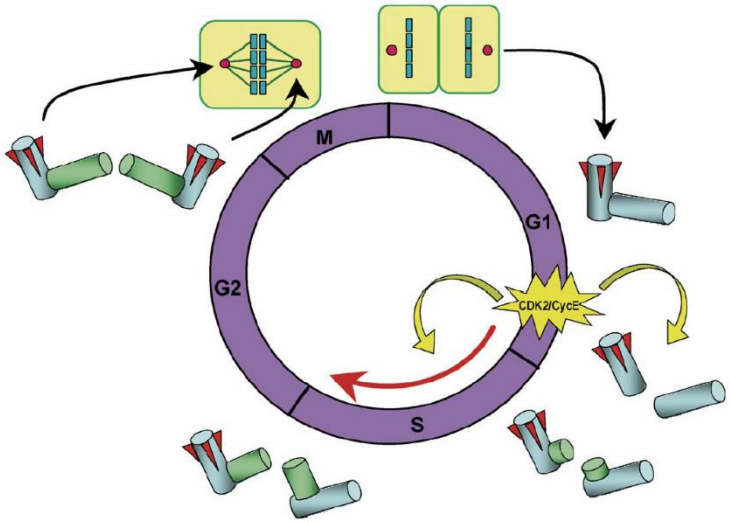
(cluster of ribosomes translating certain segment of mRNA)

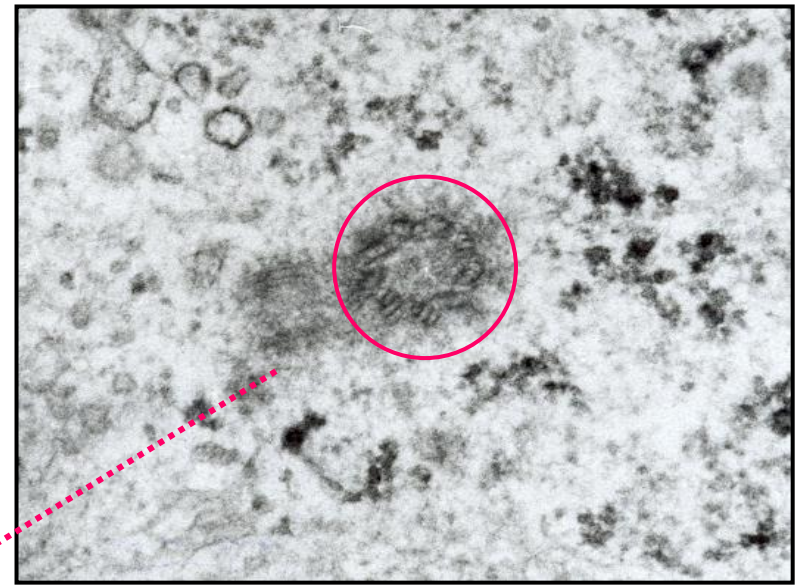


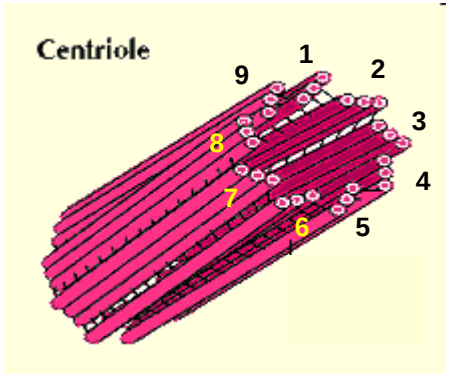
# Golgi apparatus – Transgolgi pathway



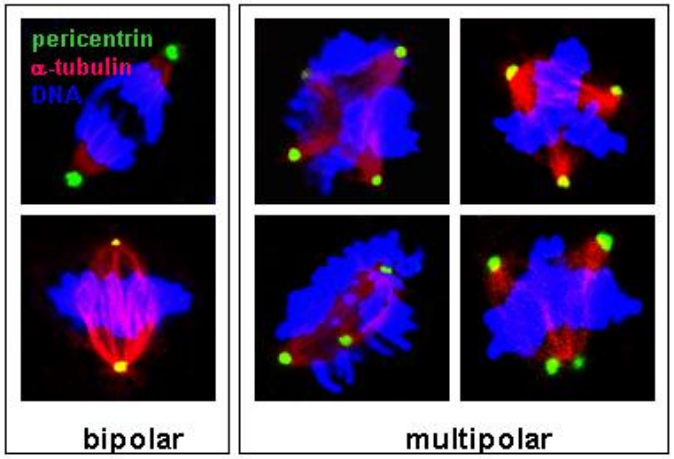
# Centrosome



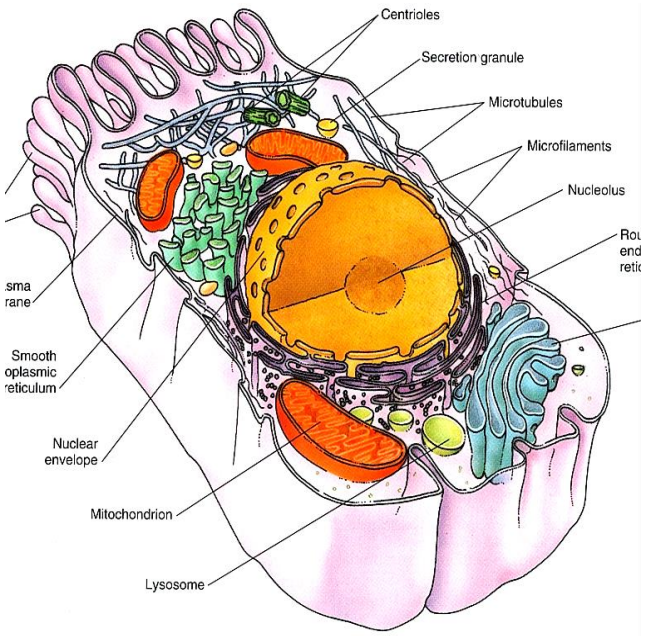



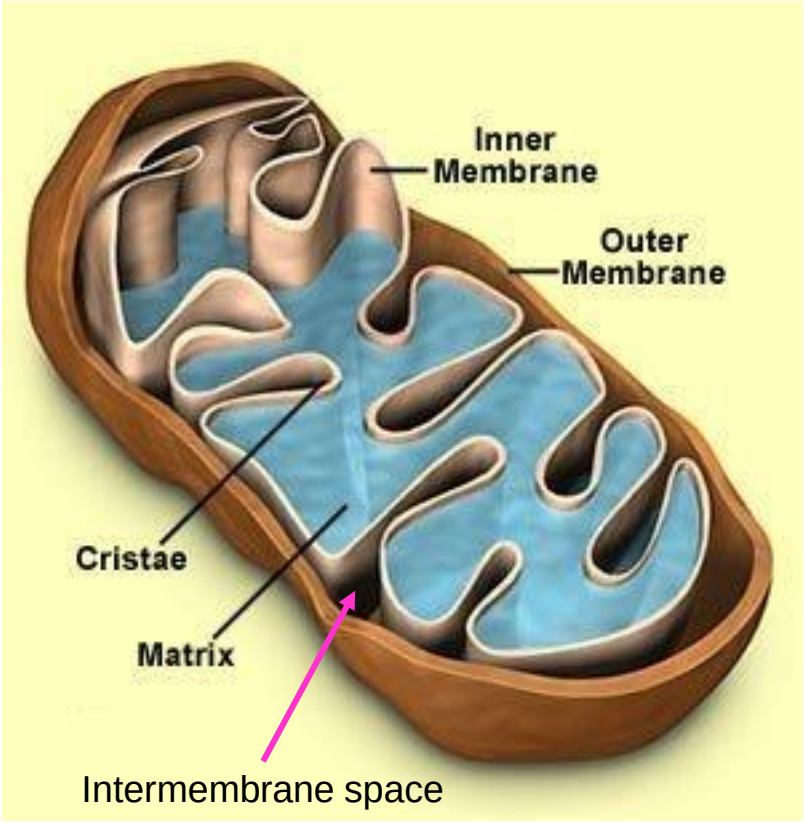



Diameter – 0.2 μm
Length - 0.5 μm



# Mitochondria 1

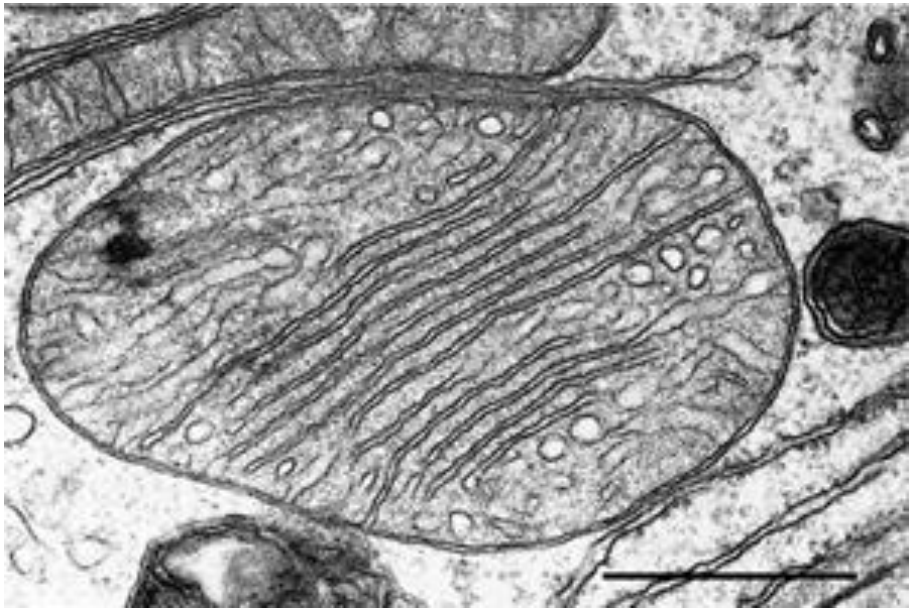



- all cells except erythrocytes
- double membrane
- diameter cca 0,5 μm
- length up to 50 (100) μm
- oxidative metabolism (glucose – ATP + $CO_2$ + $H_20$)
- cytochrome c – activation of apoptotic pathway
- origin in oocyte
- mtDNA (circular)
- brown fat  thermogenesis

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

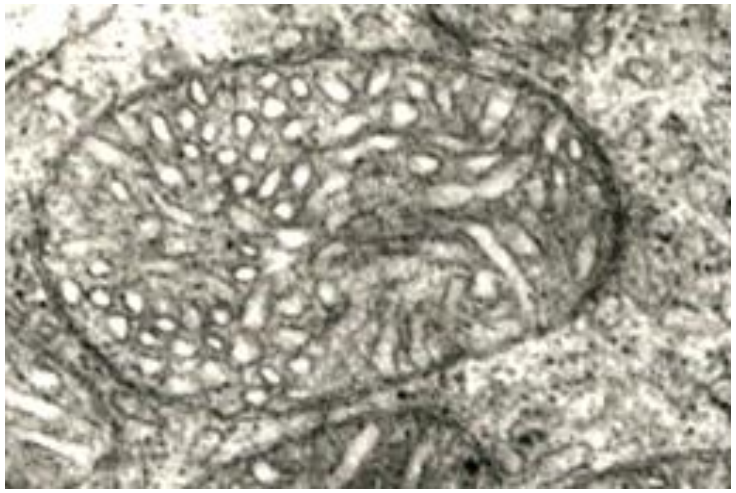
# Mitochondria 2



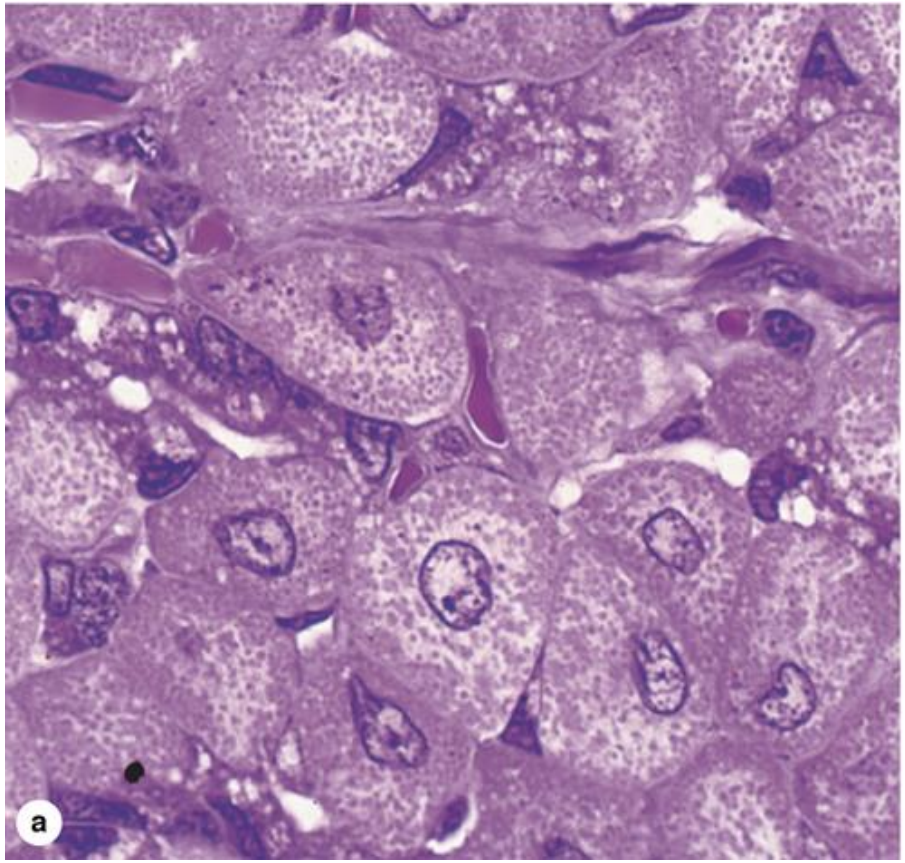
# Mitochondria 3

with crists

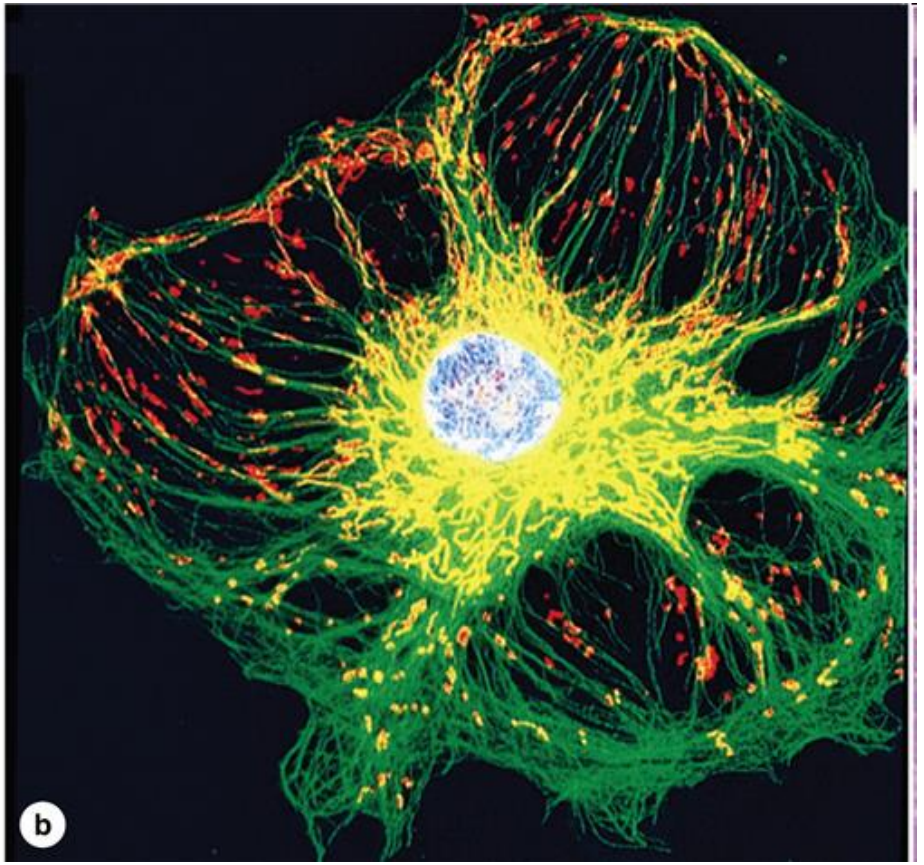
with tubuli (in steroid producing cells)



# Mitochondria 4




mitochondrial eosinophilia




mitochondria
microtubuli

# Lysosomes 1

## endosome-lysosome system

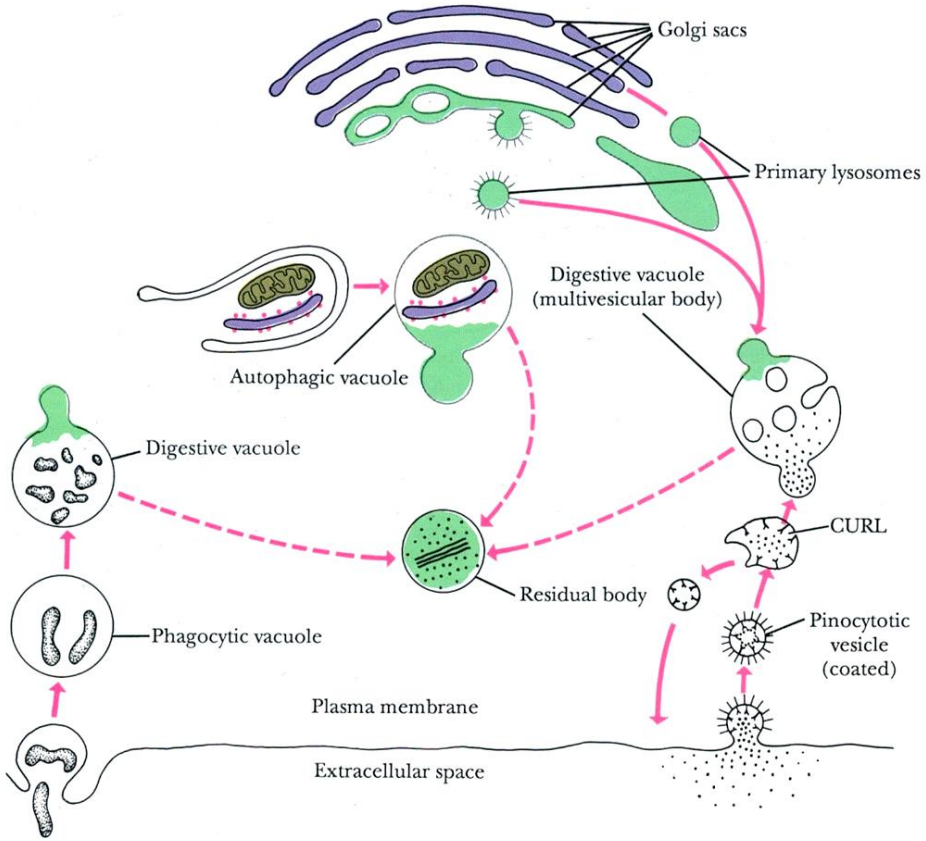
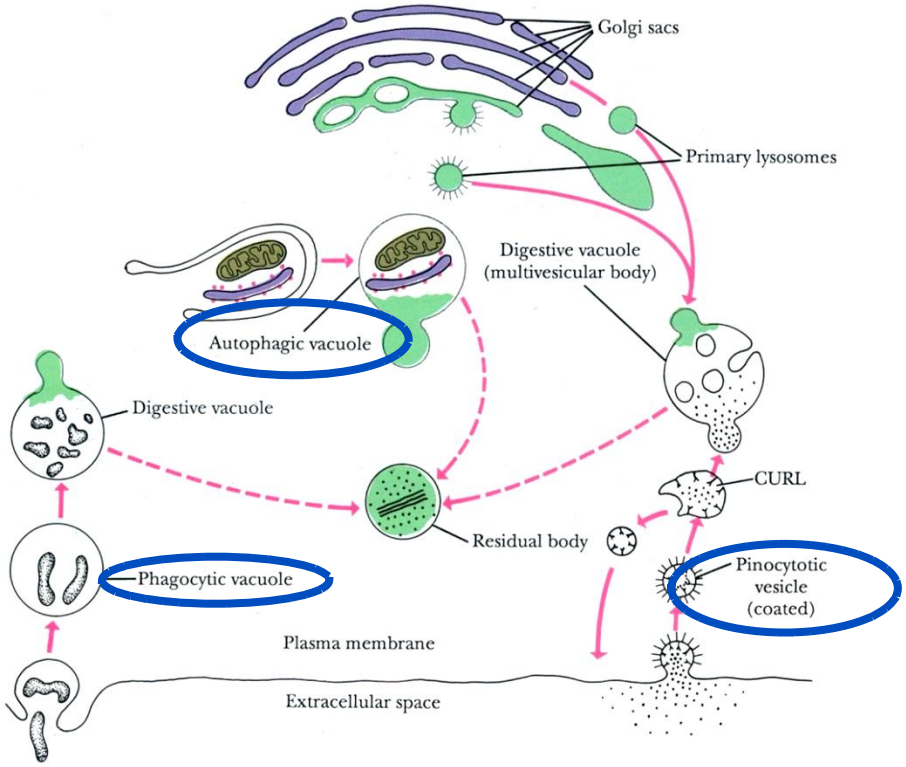



**Figure 2.17.** Origins of primarily lysosomes from the Golgi and trans-Golgi network. Primary lysosomes fuse with and discharge hydrolytic enzymes into autophagic, pinocytotic (or endosome), and phagocytic vacuoles to form secondary lysosomes (digestive vacuoles). Residual bodies contain undigested 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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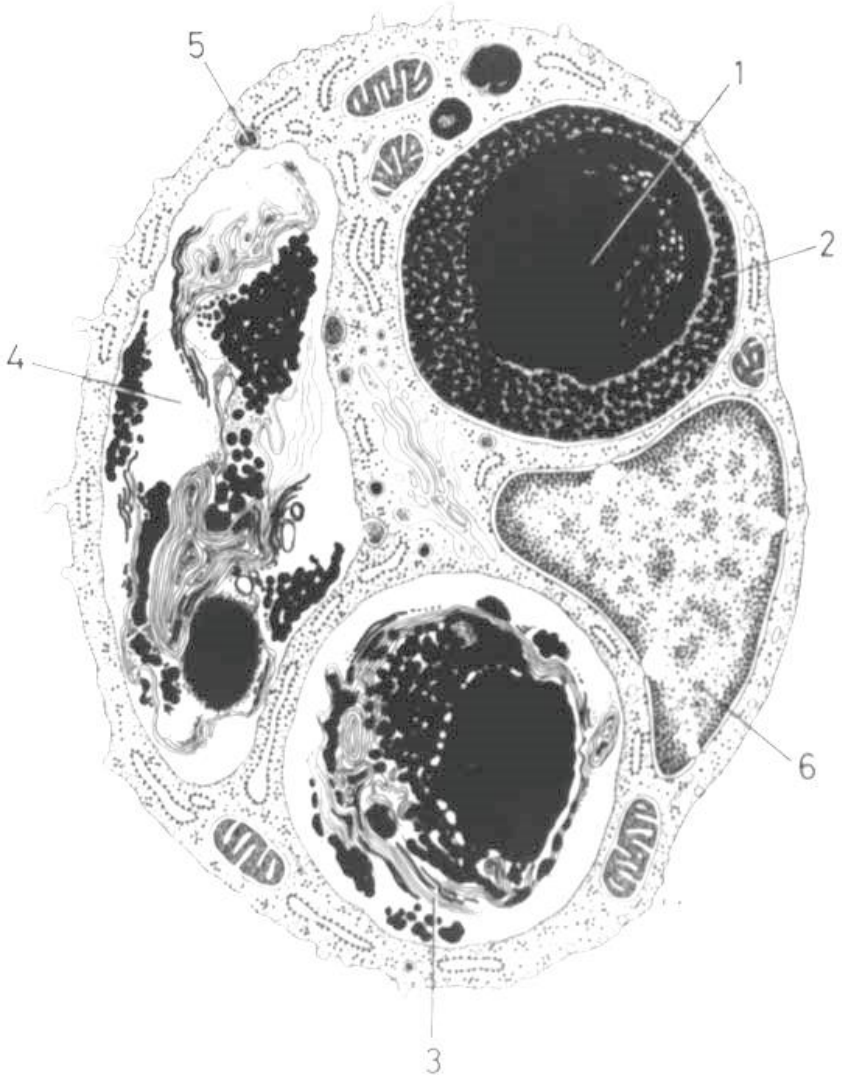
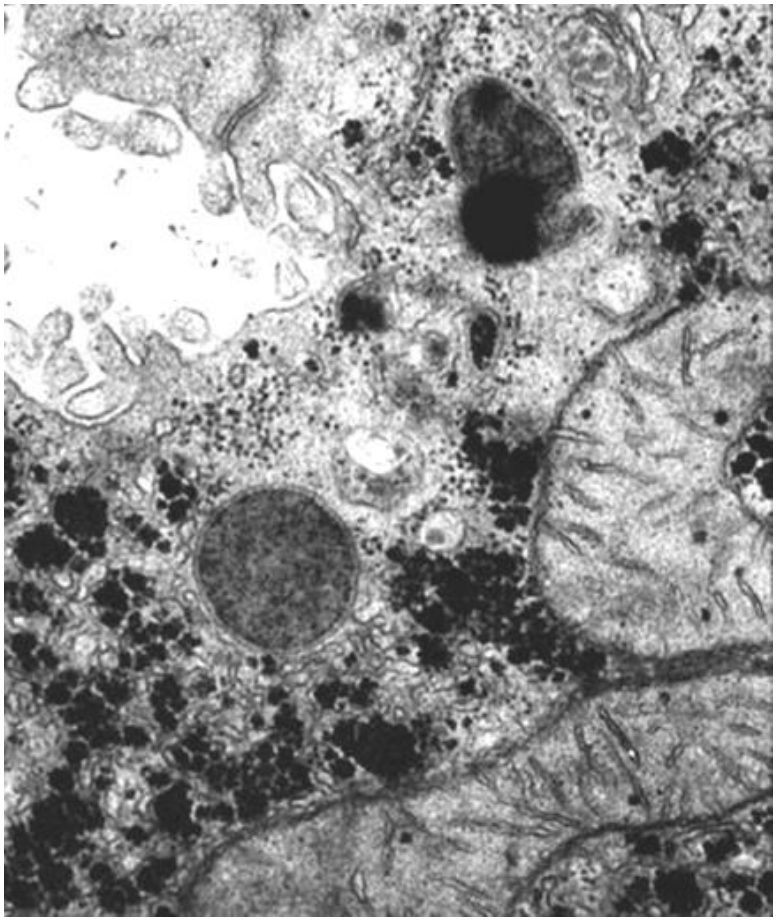
- primary lysosomes
- secondary lysosomes (fagolysosomes)
- residual bodies (lipofuscin)

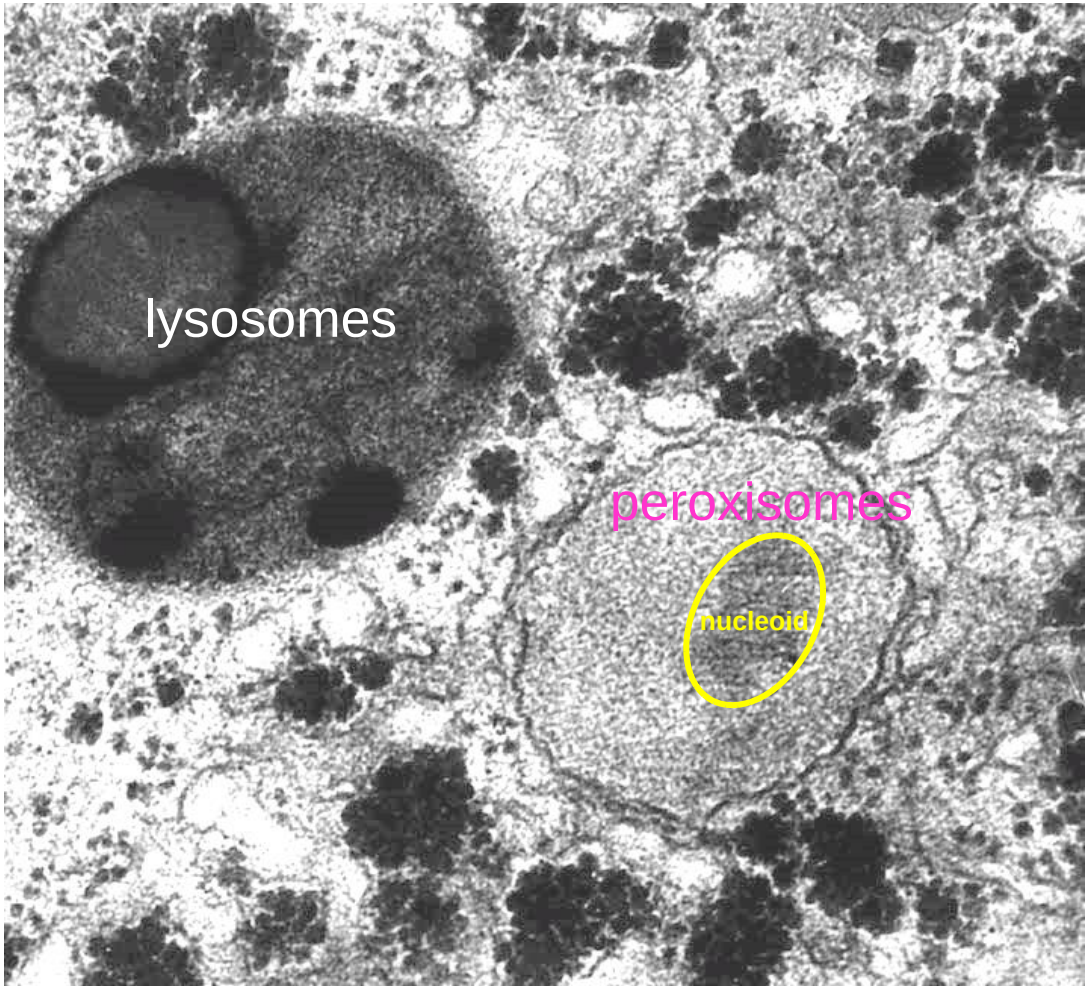
# Lysosomes 3

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

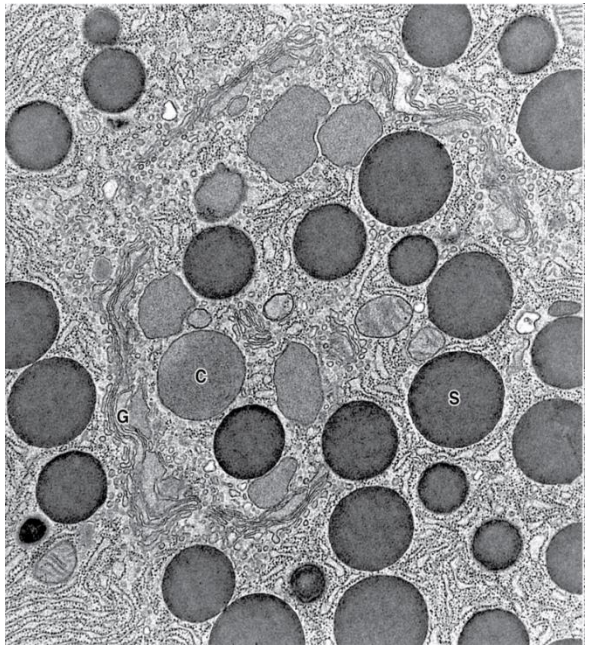
# Cytoplasmic inclusions 1

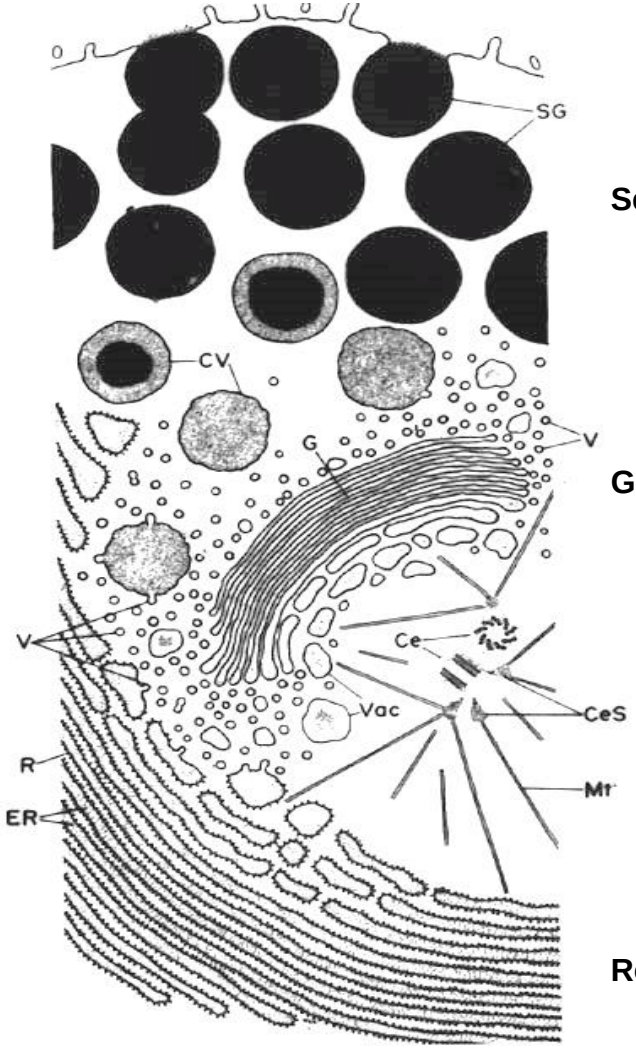
**(no or only little metabolic activity on themselves)**

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

# Cytoplasmic inclusions 2

## Secretory granules



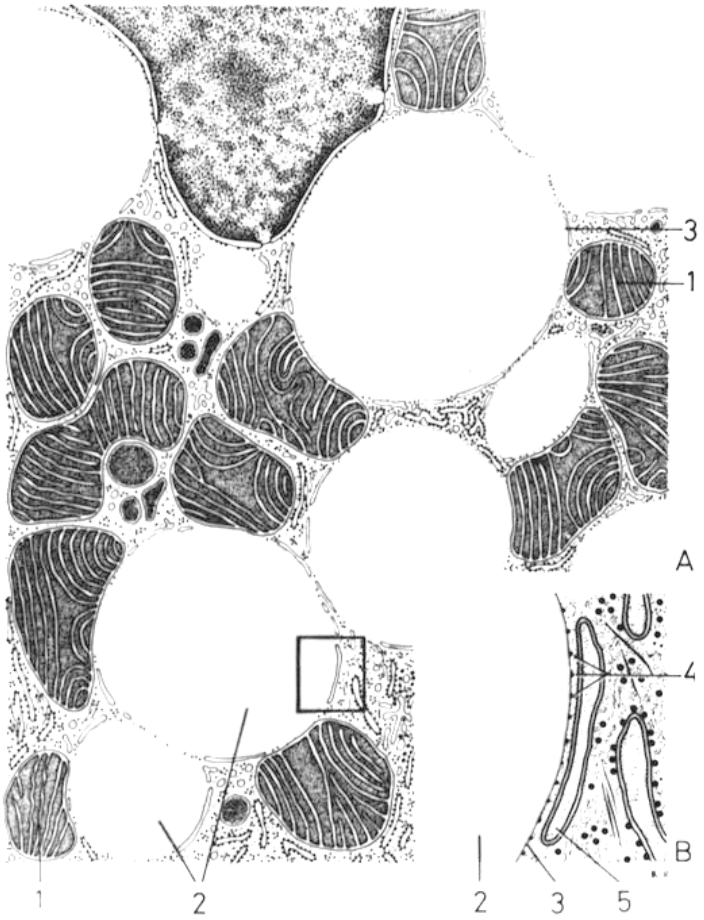

Secretory granules

Golgi apparatus

Rough ER

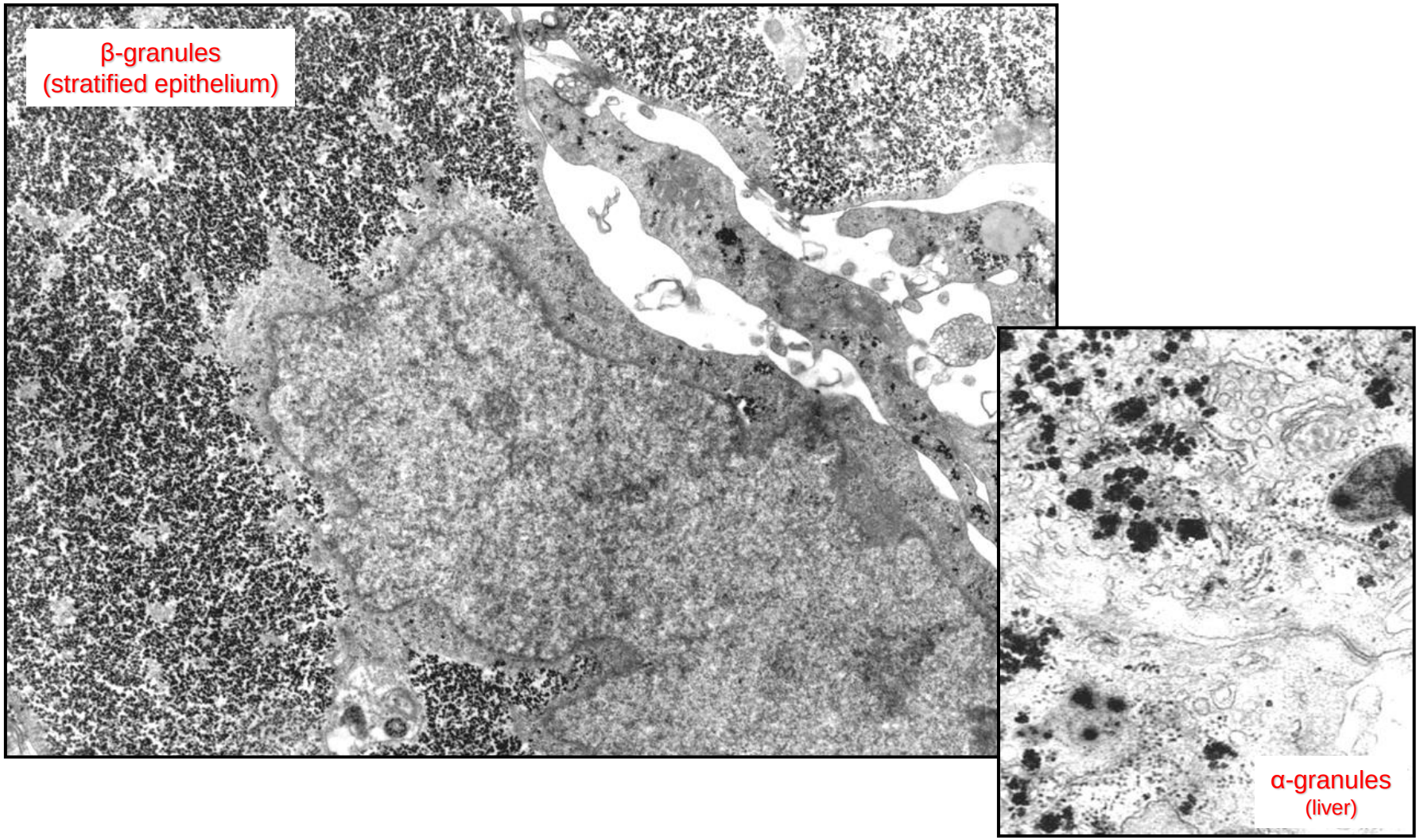
# Cytoplasmic inclusions 3

## Lipid inclusions



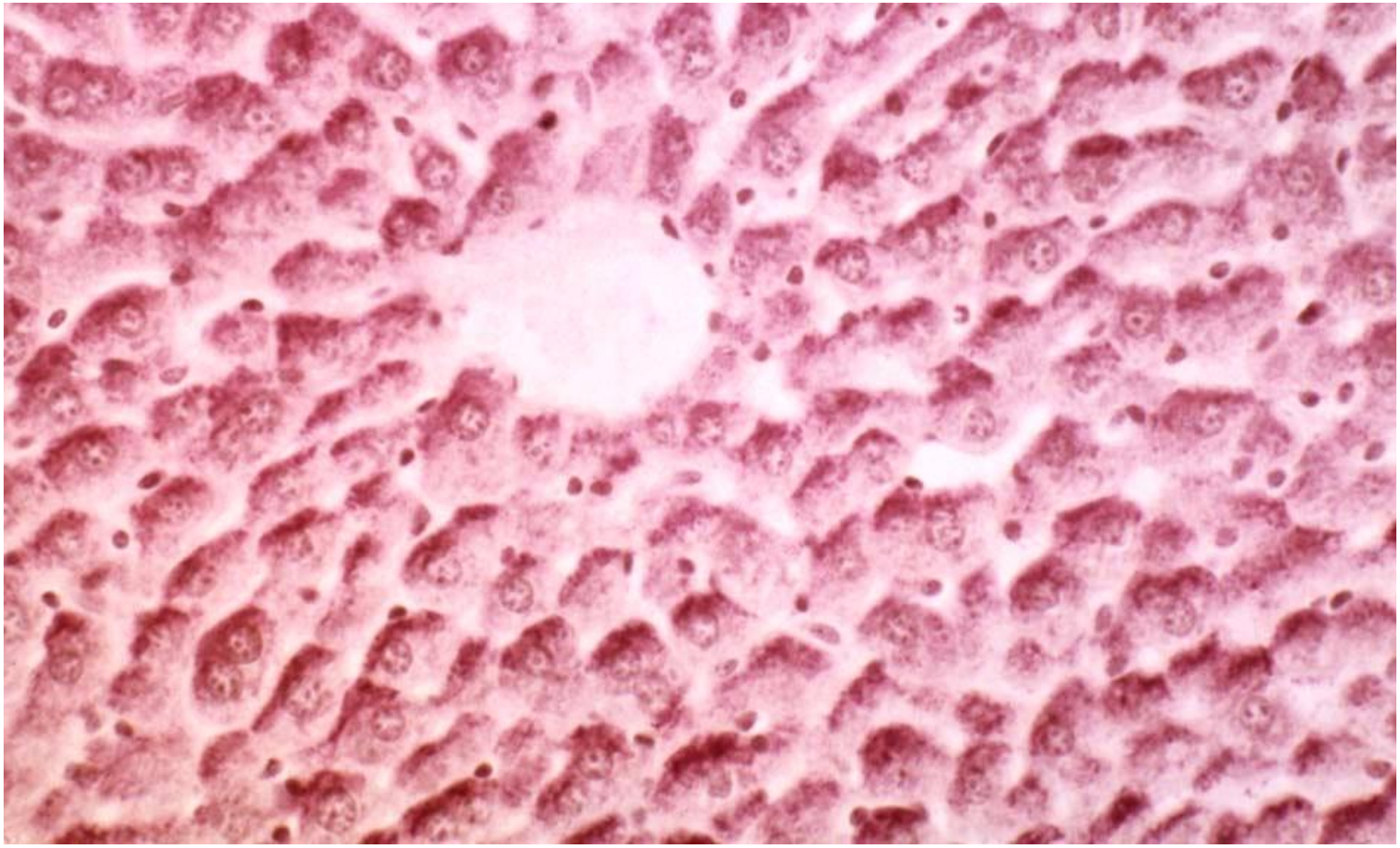

# Cytoplasmic inclusions 4

**Glycogen**



# Cytoplasmic inclusions 5

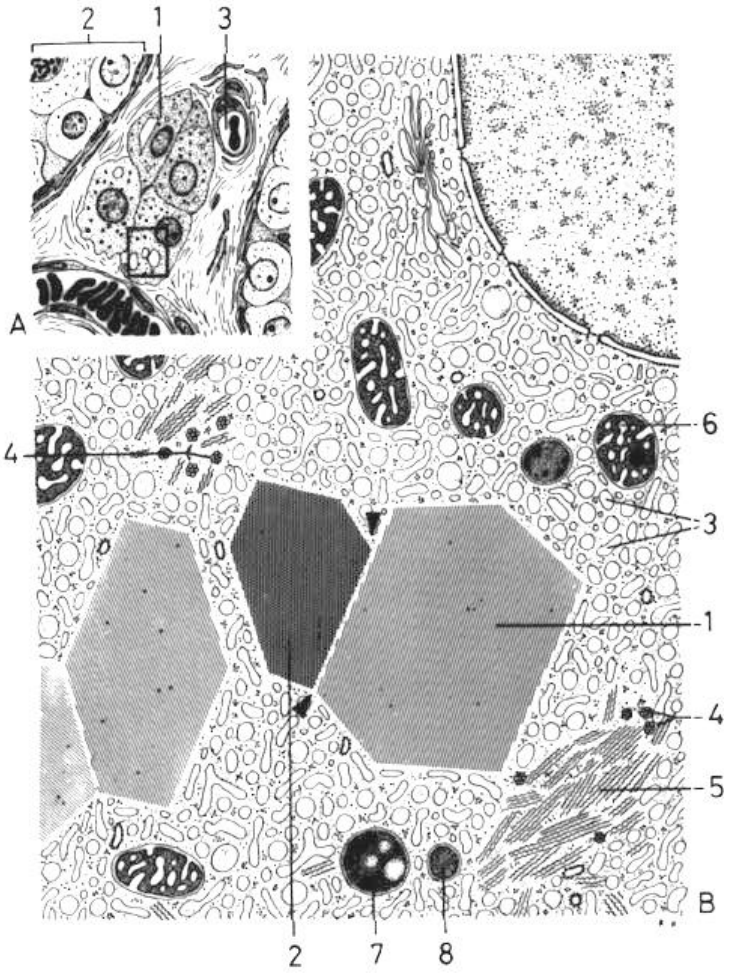
## Glycogen

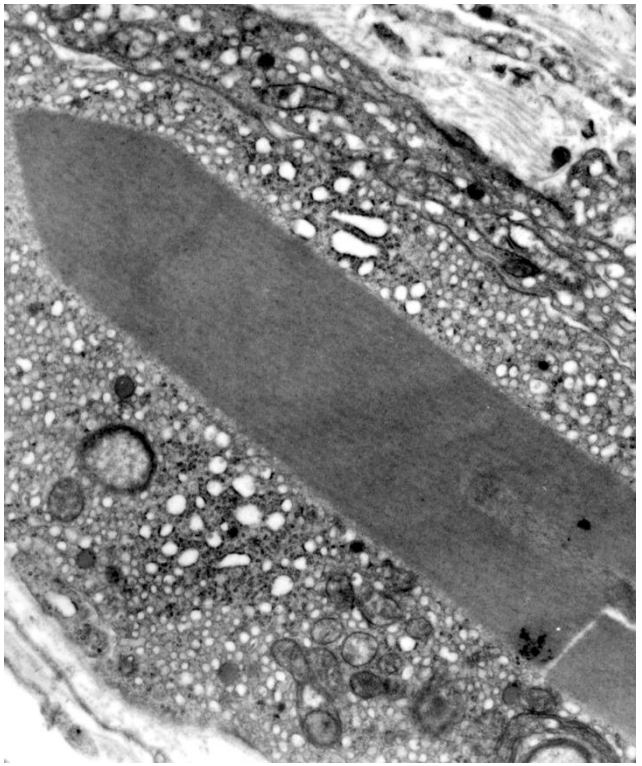


Glycogen in liver cells (light microscope; PAS reaction)

# Cytoplasmic inclusions 6

## Crystals



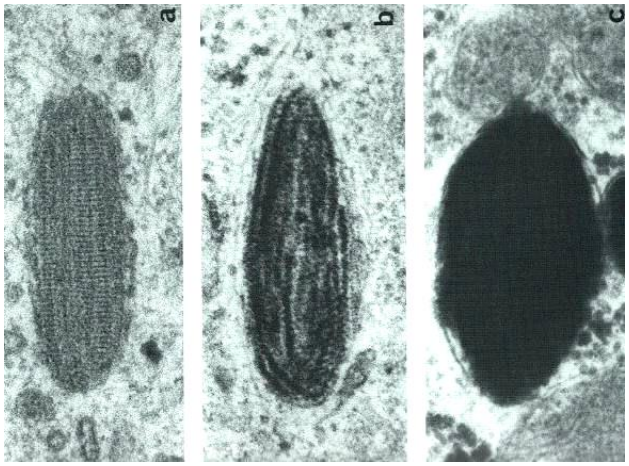



Protein inclusions in Leydig cells

# Cytoplasmic inclusions 7

## Pigments (colour inclusions): Exogenous x Endogenous

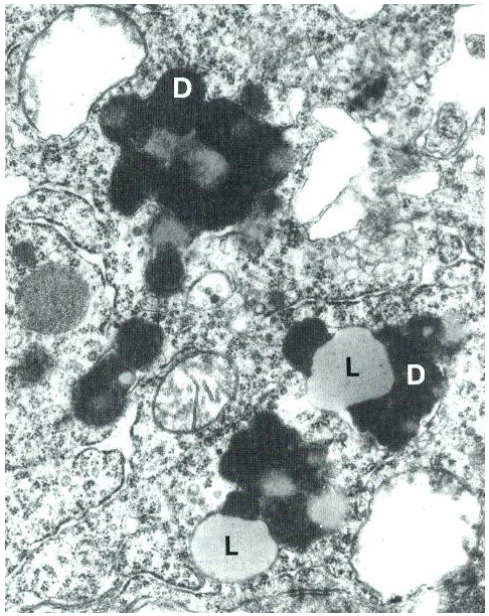
- **Autogenous**
  Specific functions – **melanin**



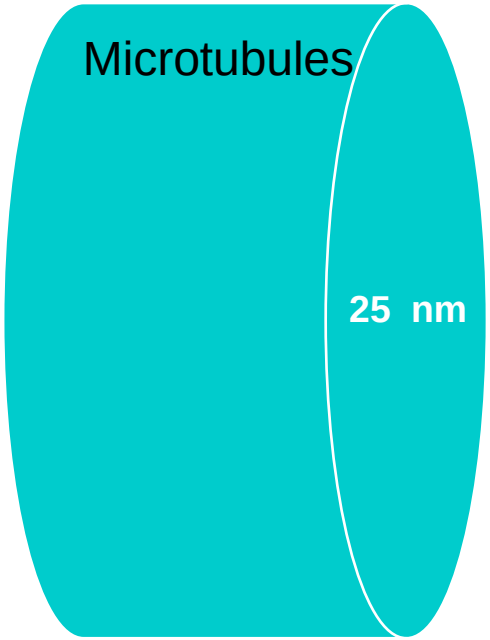

- **Hematogenous**
  Hemoglobin decomposition – **hemosiderin**, **biliverdin**, **bilirubin**

Pigment in aged cells

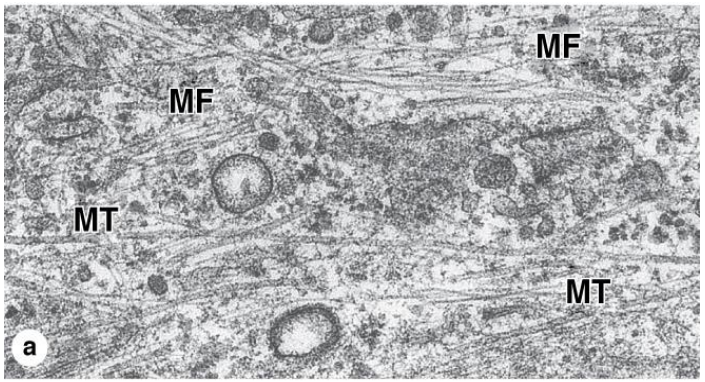
**lipofuscin** – accumulation of residual bodies in long-lived cells (neurones, kardiomyocytes)



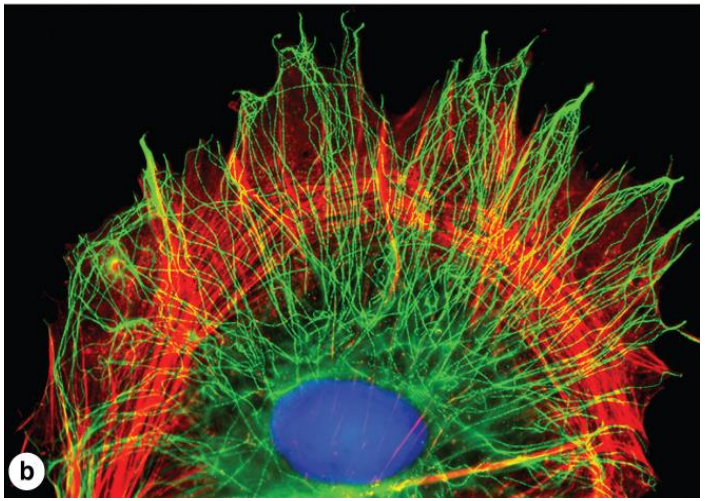
# Cytoskeleton 1





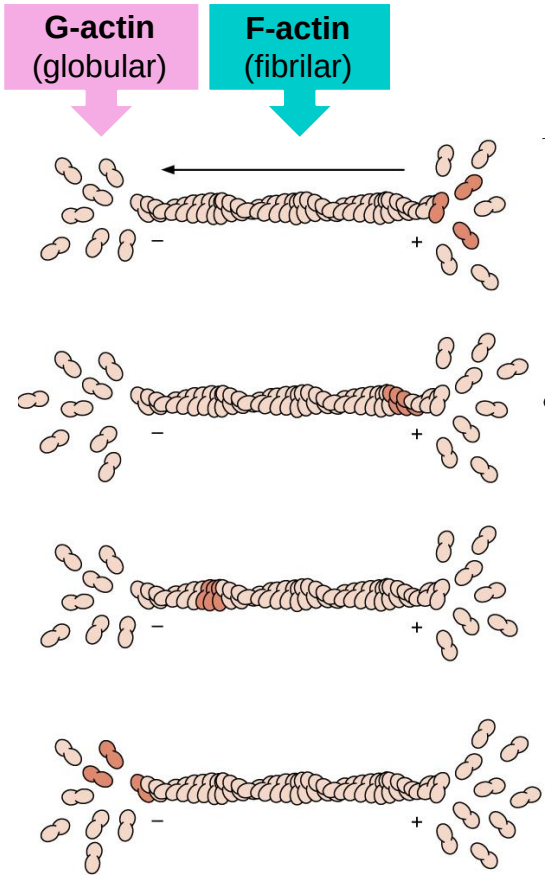



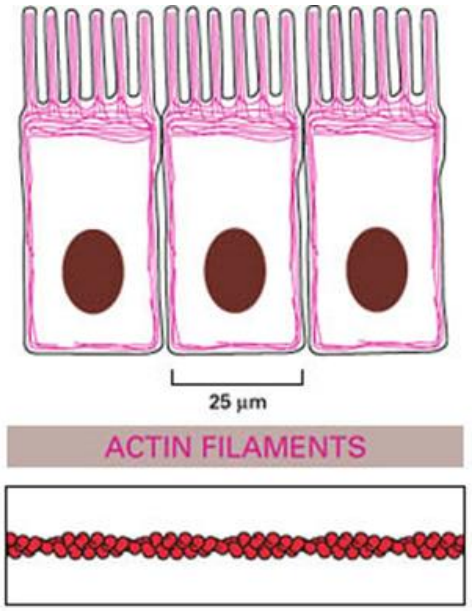

microtubules
microfilaments - actin



# Cytoskeleton 2

## Microfilaments (actin)

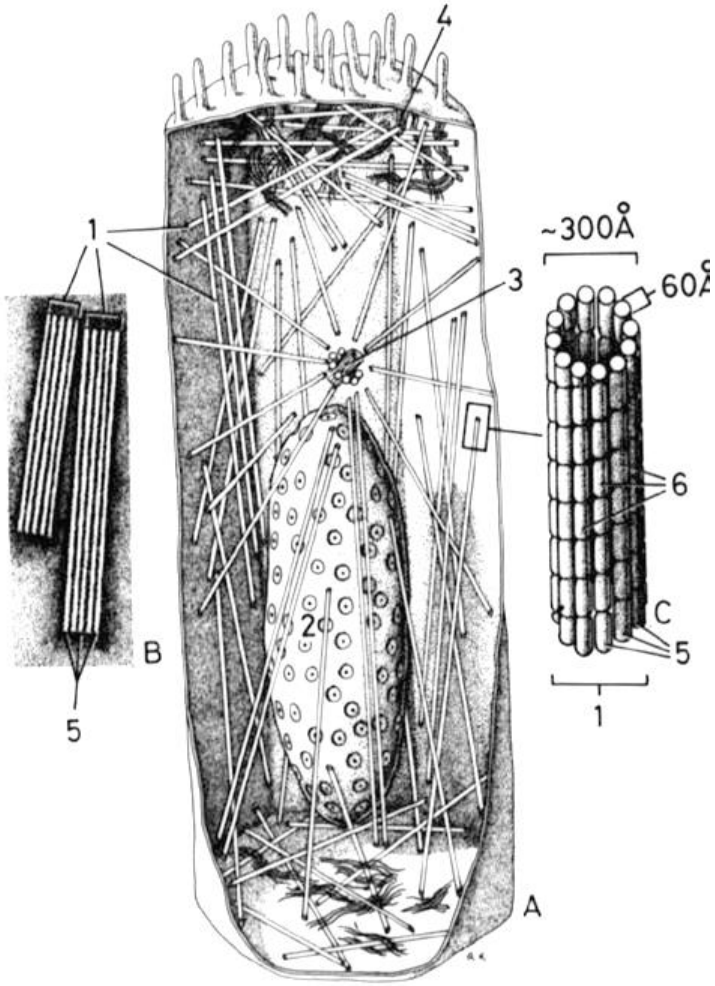


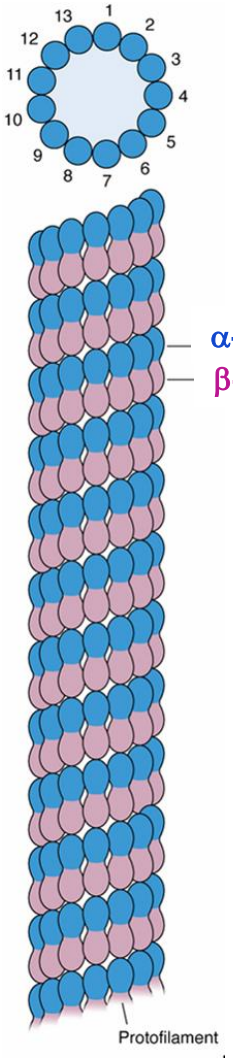



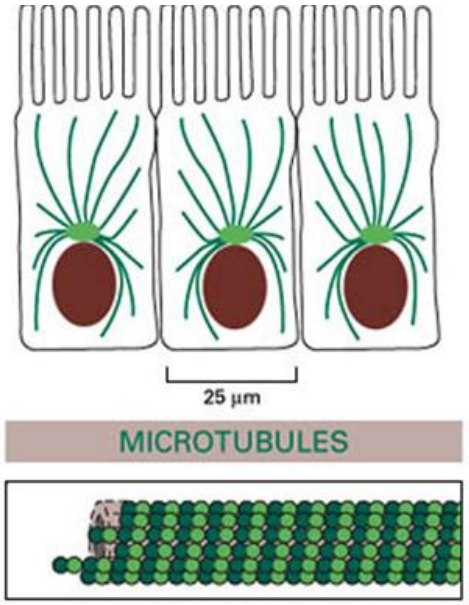

- actin isoformes (α, β, γ)
- fast polymerisation and depolymerisation
- polarisation (+ a – ends)
- stabilisation by associated proteins (tropomyosin – myofibrils)
- crosslinking by associated proteins (fimbrin, filamin, …)
- anchoring to cell membrane (vinculin, tallin, …)
- cortical actin – membrane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

# Cytoskeleton 3

## Microtubules



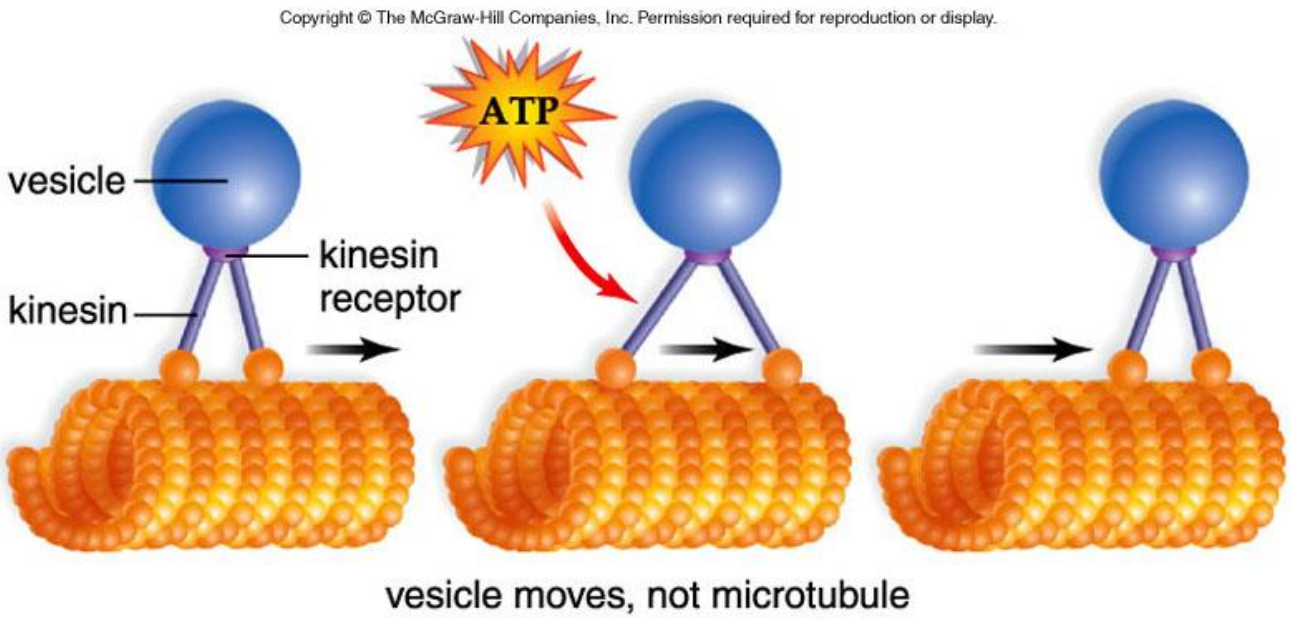




- hollow tubes
- α-tubulin + β-tubulin – dimers
- fast polymerisation and depolymerisation
- polarisation (+ a – ends)
- MAP (proteins associated with microtubuli)
- MTOC – microtubules organizing centre (centrosome; γ-tubulin)
- mechanical support
- intracellular transport
- mitotic spindle
- cilia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

# Cytoskeleton 4

## Microtubules - motors

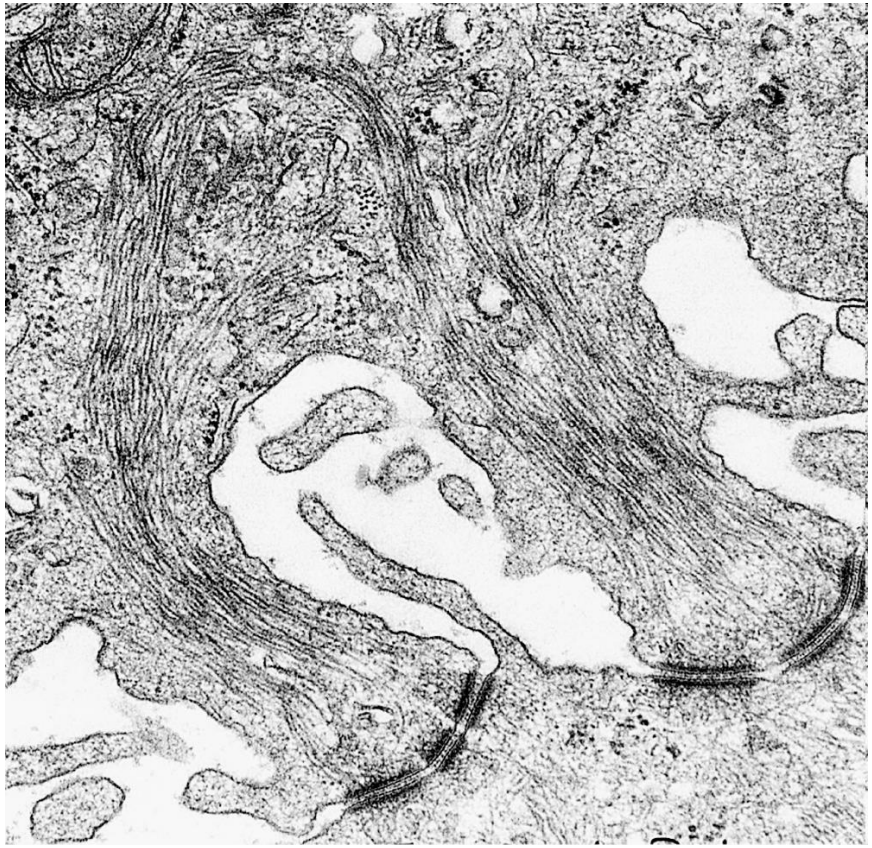



**Kinesins**
- move towards „plus“ end of microtubuli
- transport from centrosome

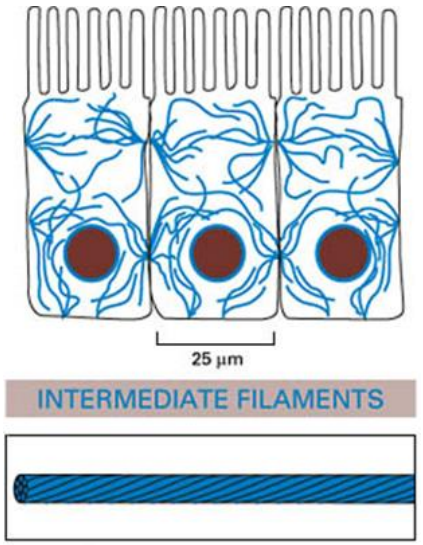
**Dyneins**
- move towards „minus“ end microtubuli
- transport towards centrosome
- axonal transport – long distance

# 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

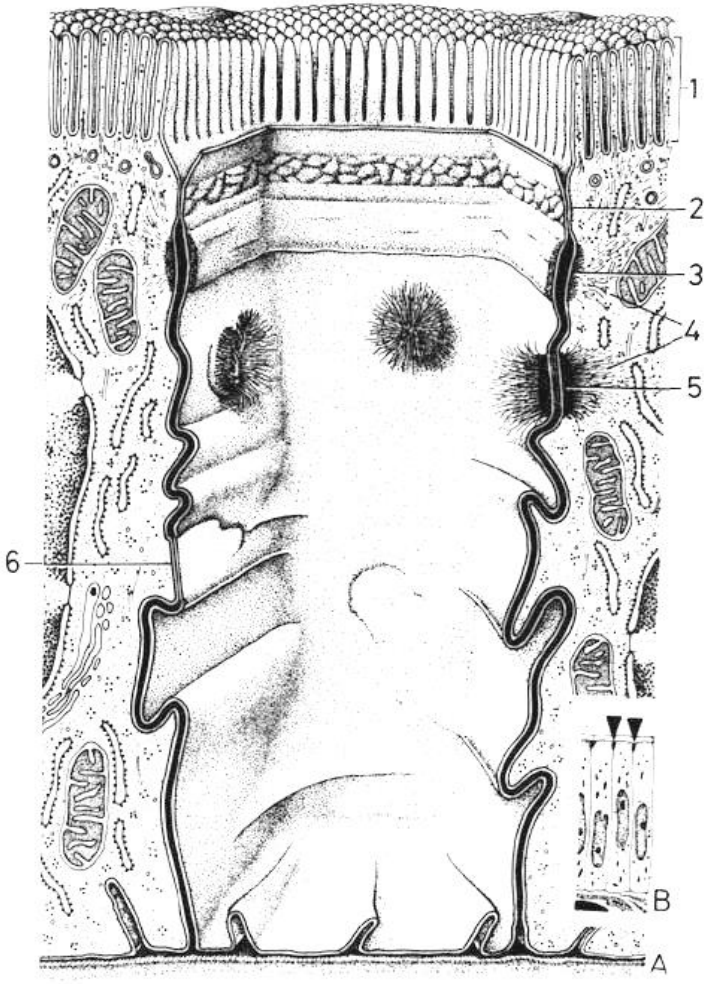
Cell-to-cell junction:

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

## Basal

- focal adhesions
- hemidesmosomes
- basal labyrinth

free surface

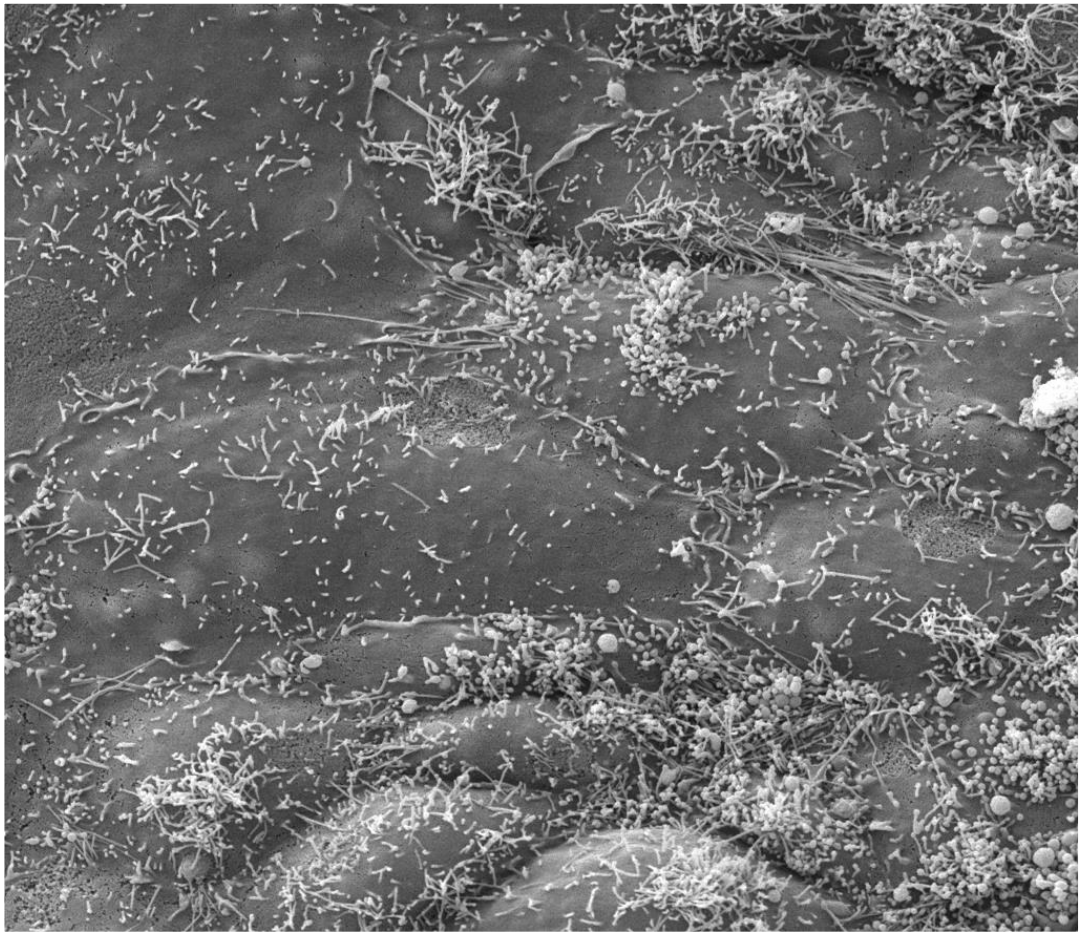



lateral surface

basal surface

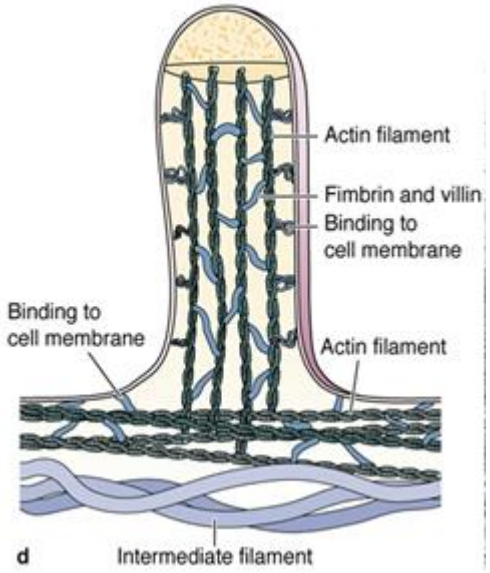
# Cell surfaces 2

## Microvilli



Free surface of cultured human embryonic stem cells

# Cell surfaces 3



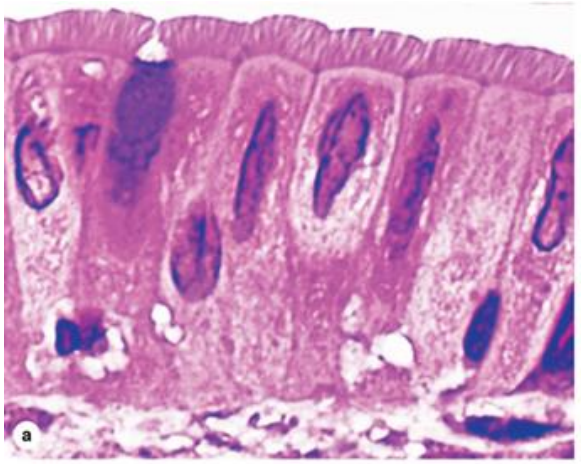

## Microvilli

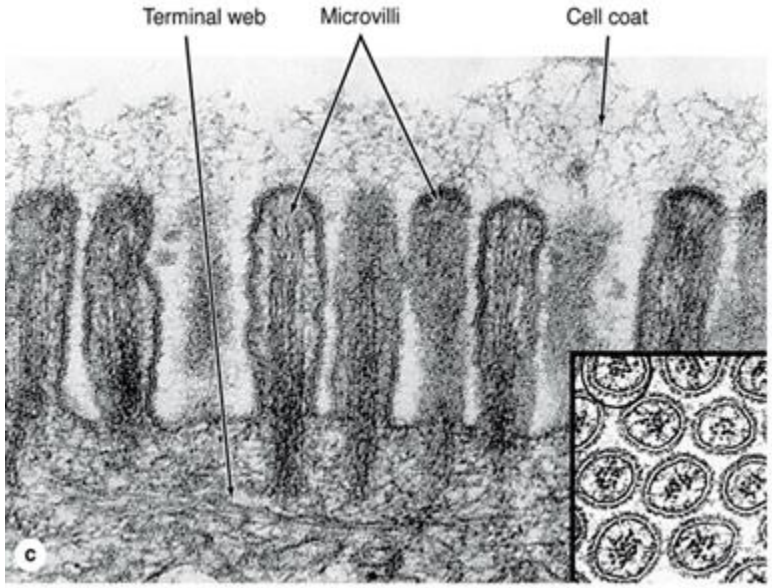
**Thickness about 0,1 μm**
**Length about 1-6 μm**

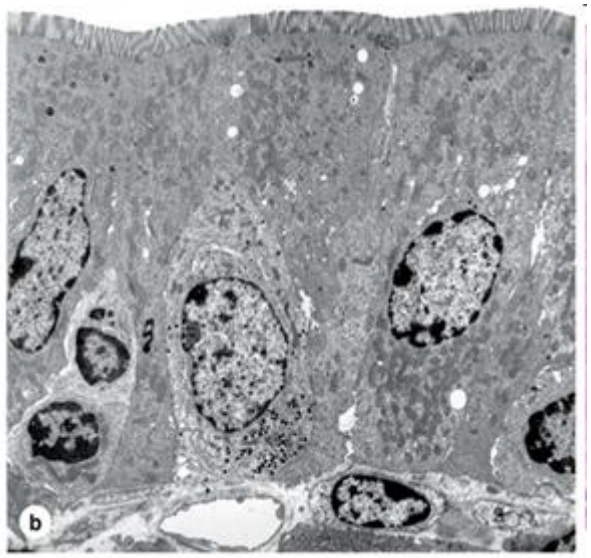
**Actin filaments in microvilli**

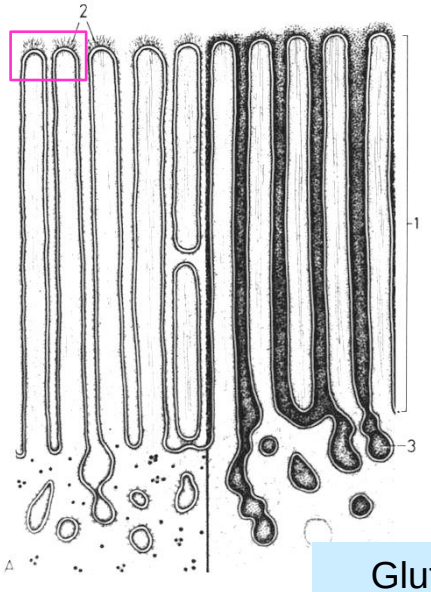
- 20 in microvilli of epithelial cells
- several hundreds in stereocilia of hair cells

Regularly organised microvilli
= striated border + brush border



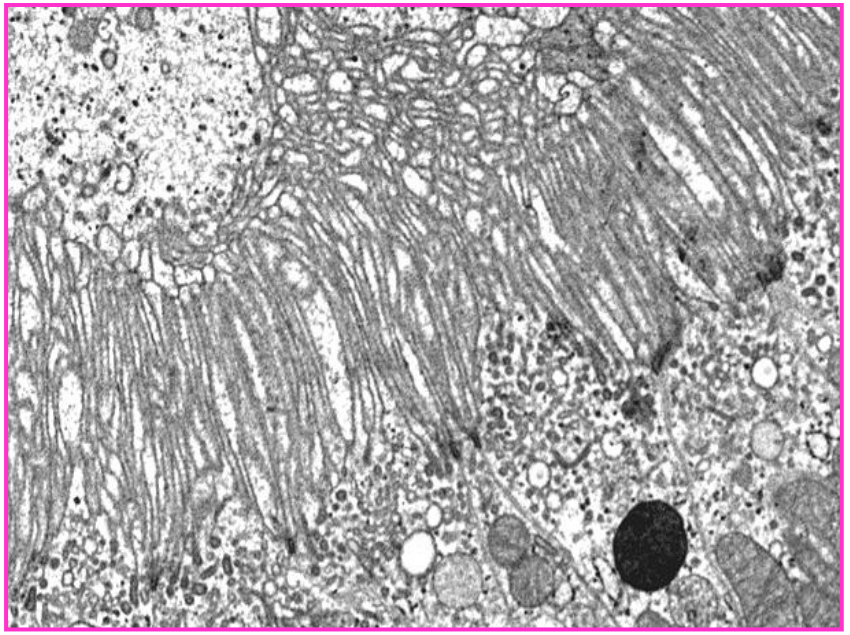



# Cell surfaces 4

## Microvilli

Gluten – Celiac disease

**striated border**
(tops of enterocytes)



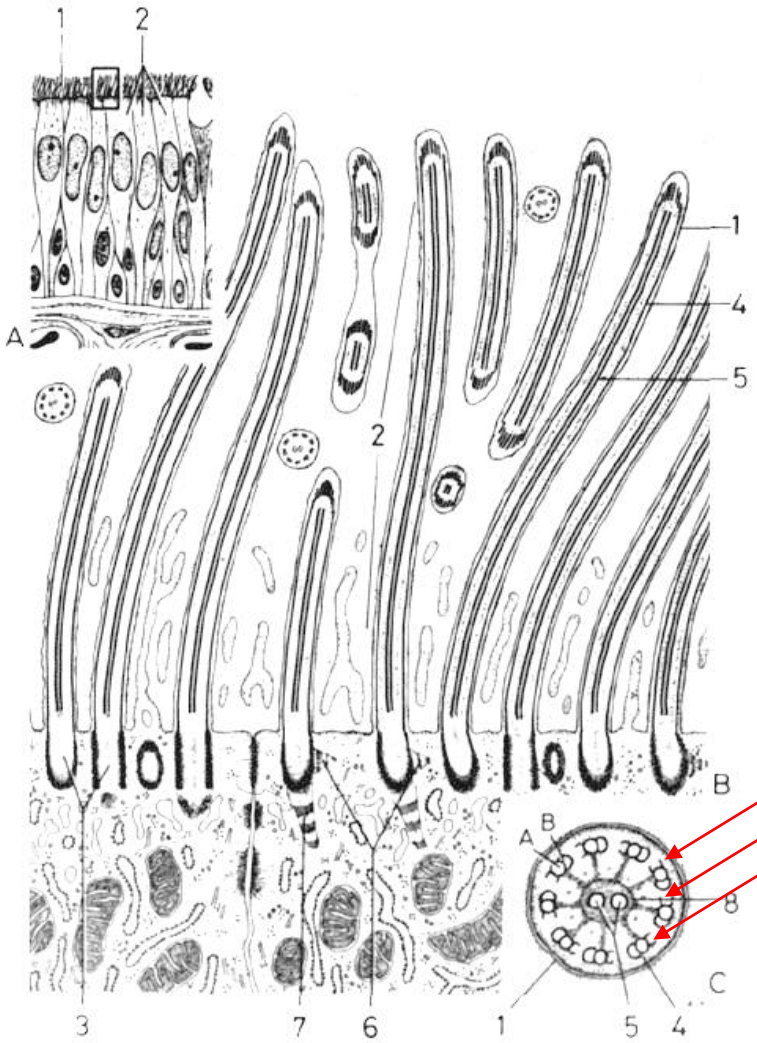
**brush border**
(proximal tibuli of kidney)

# Cell surfaces 5

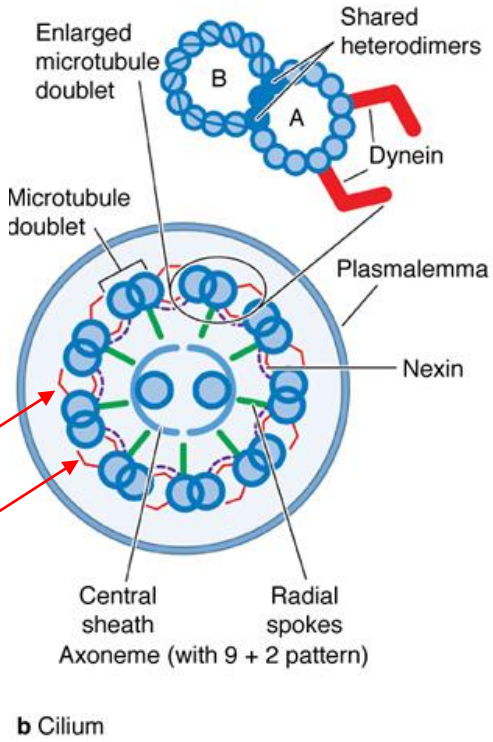
## Cilia + Flagella

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

**Axonema**
20 microtubuli (9x2 + 2)




**Dynein arms**
(movement)

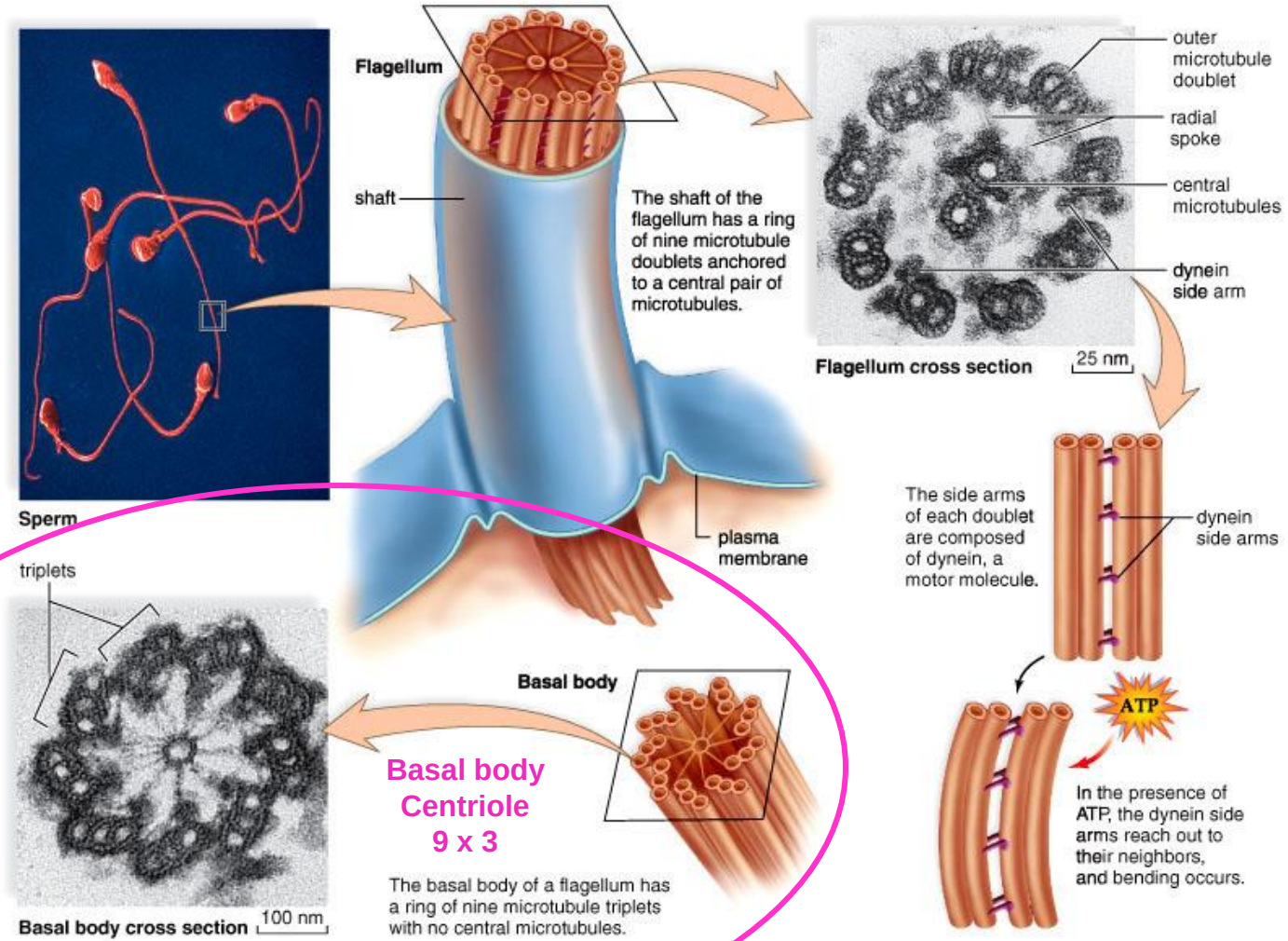



**b** Cilium

# Cell surfaces 6

## Cilia + Flagella

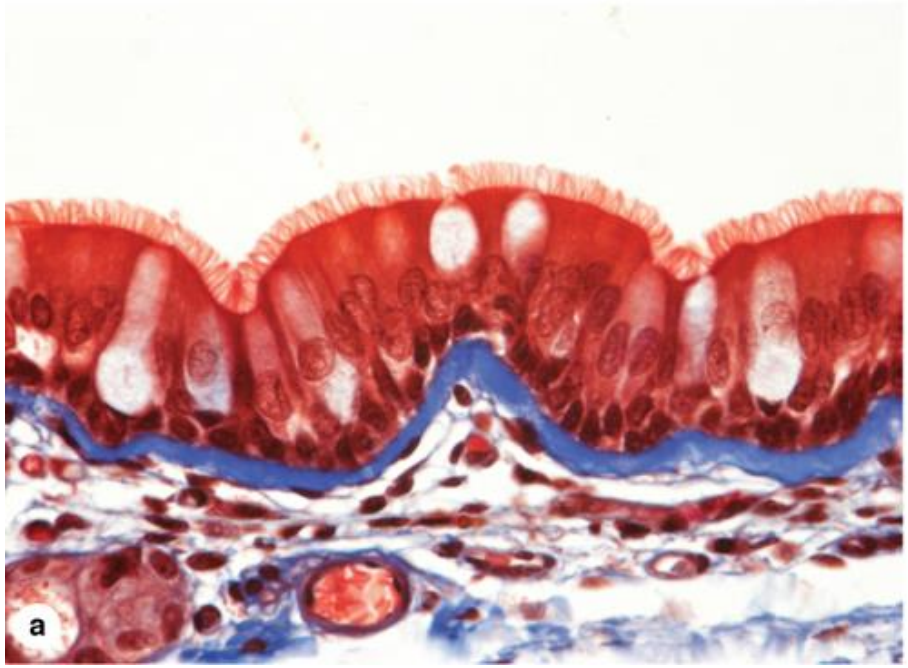




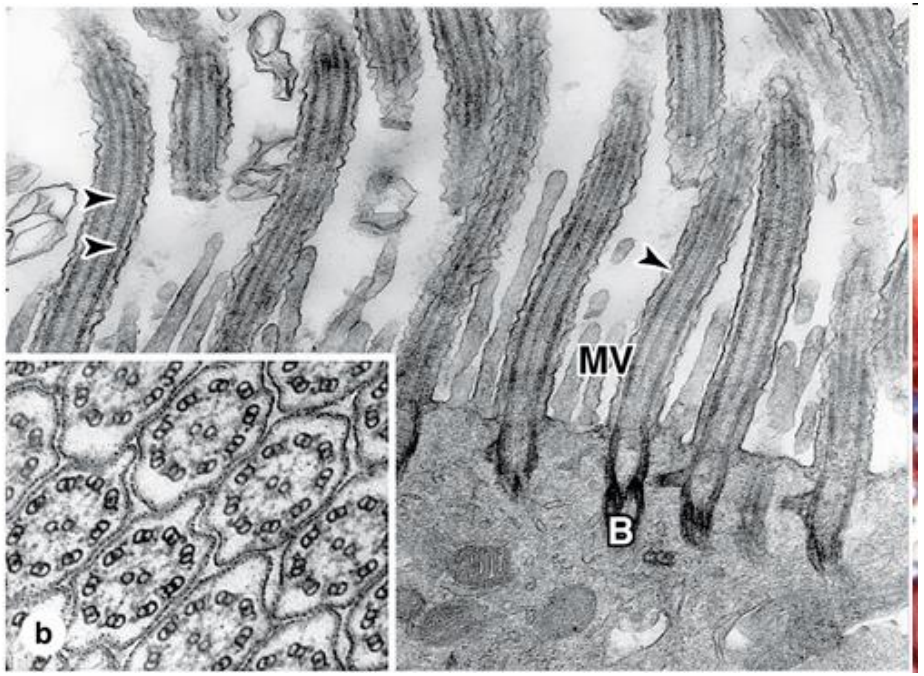
# Cell surfaces 7

**Cilia + Flagella**

in light microscope

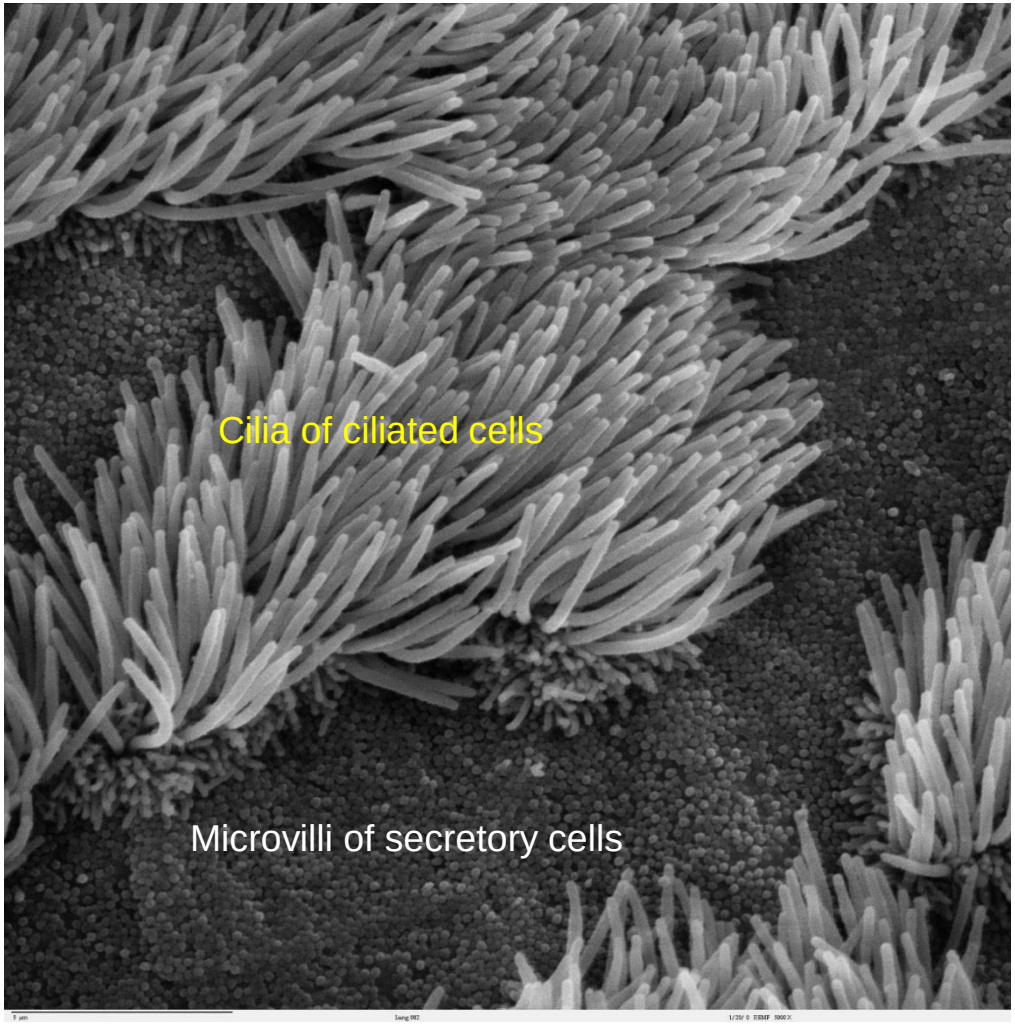



in electron microscope

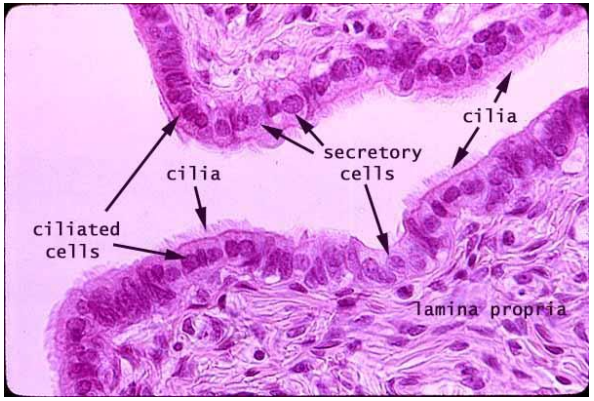


# Cell surfaces 8

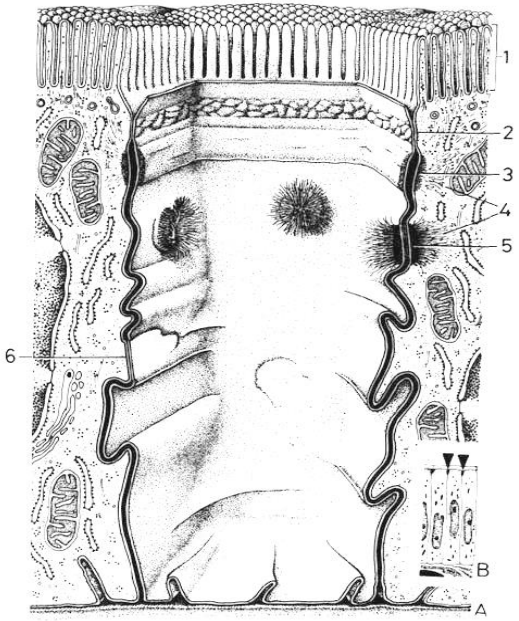
## Cilia + Flagella




oviduct

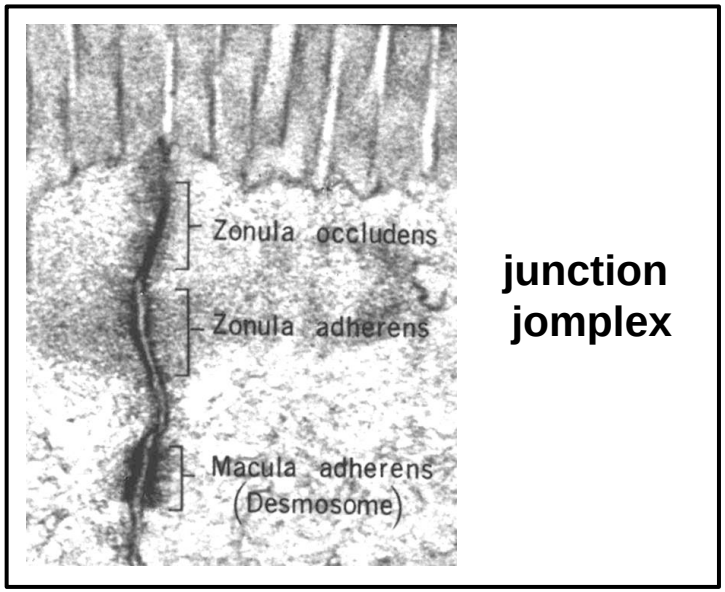


# Adhesions and Junctions 1




**lateral surface**

**Basal surface**




**junction jomplex**

## Adhesion

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

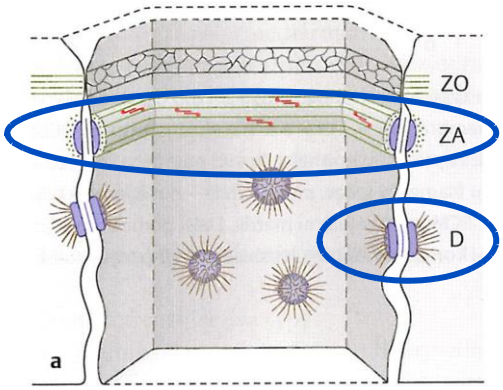
## Sealing

- **Zonula occludens** (tight junction)

## Communication

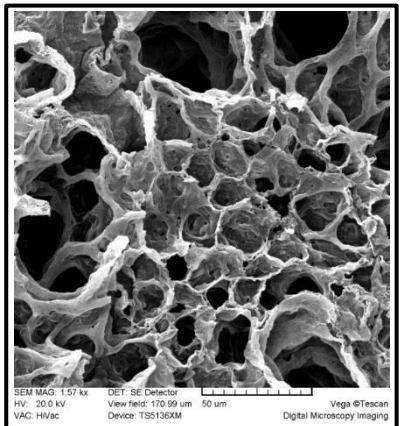
- **Gap junction** (nexus)

# Adhesions and Junctions 2

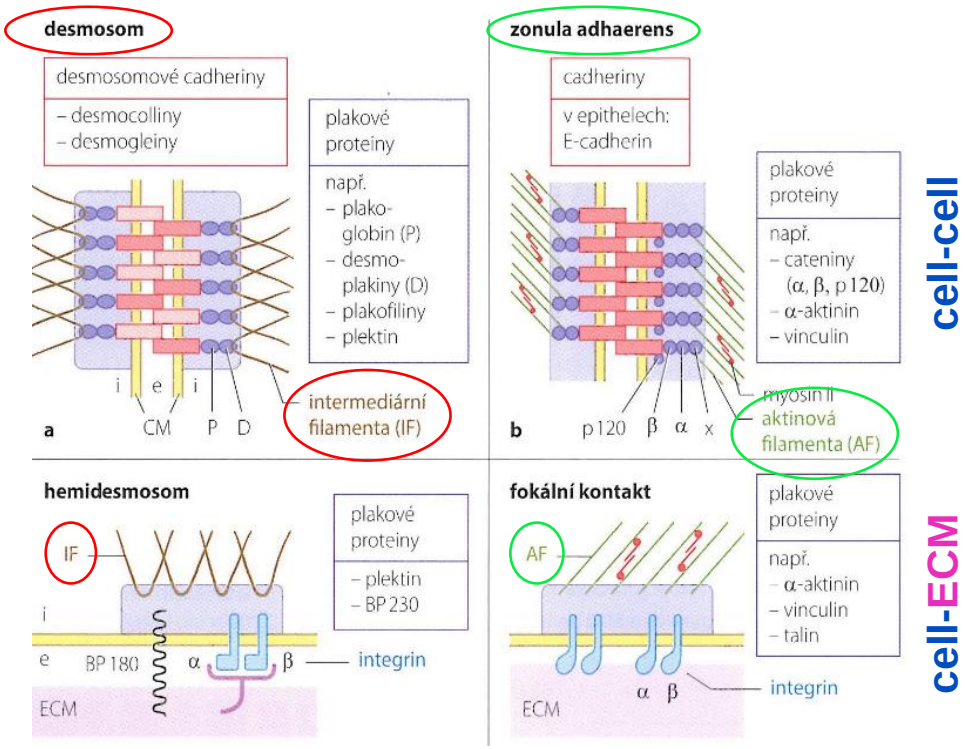



## Adhesion

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

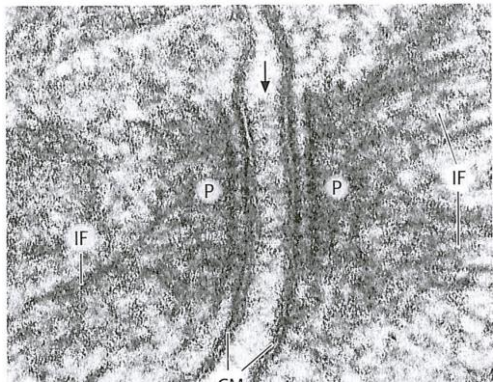


Lung ECM - alveolar region

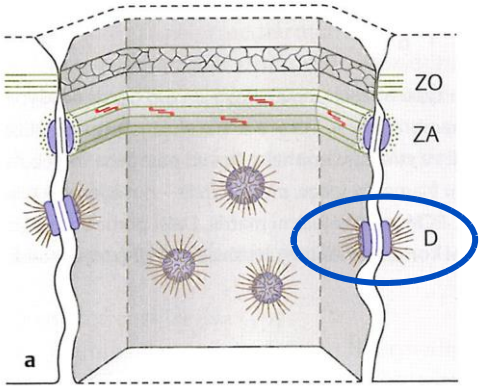



## Unified composition

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



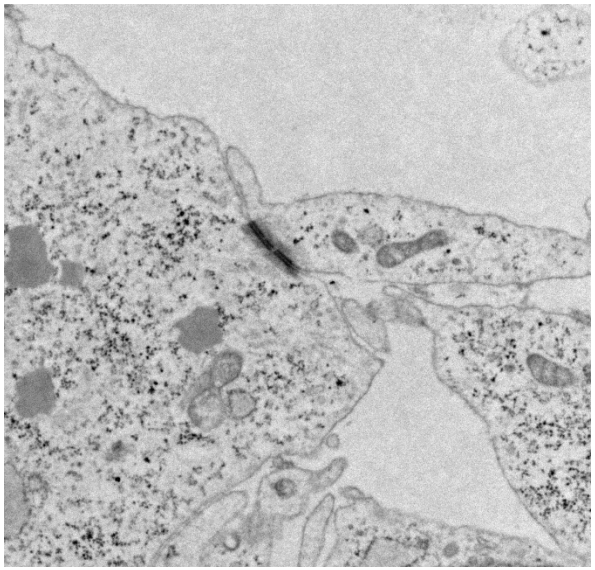
# Adhesions and Junctions 3

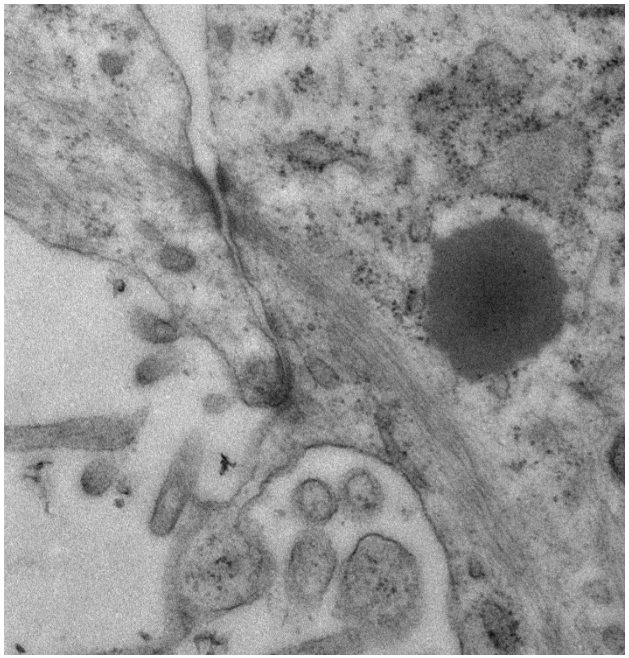



## Adhesion

- **Macula adherens** (desmosome)

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

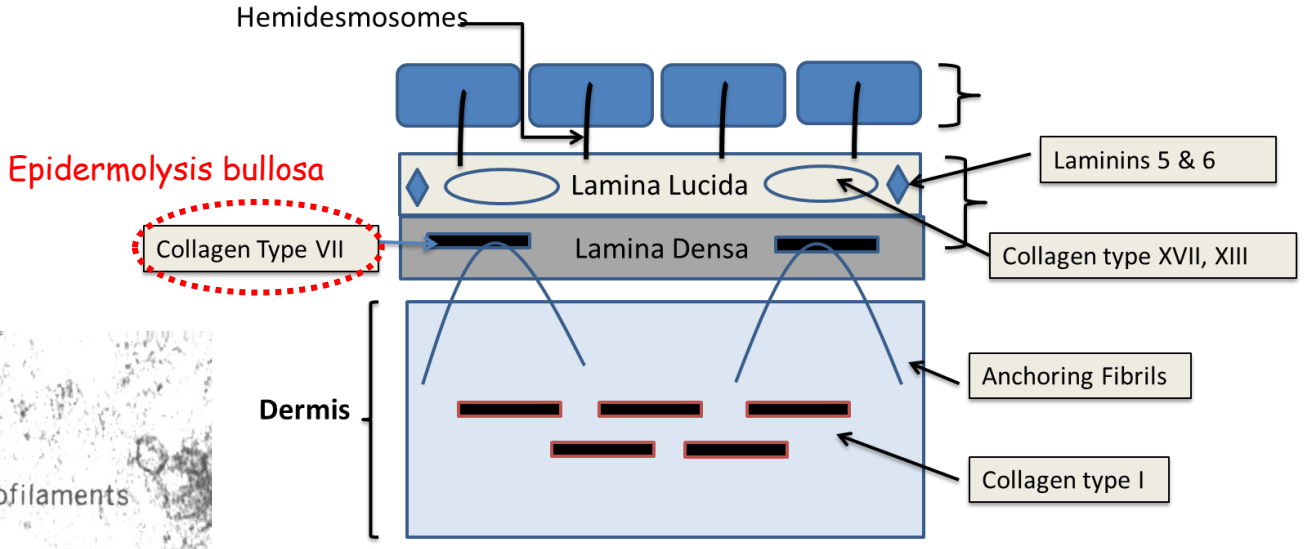


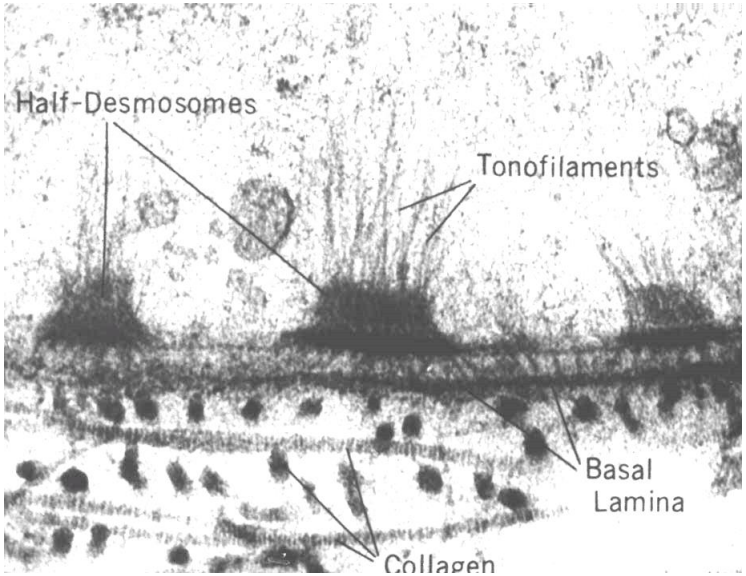


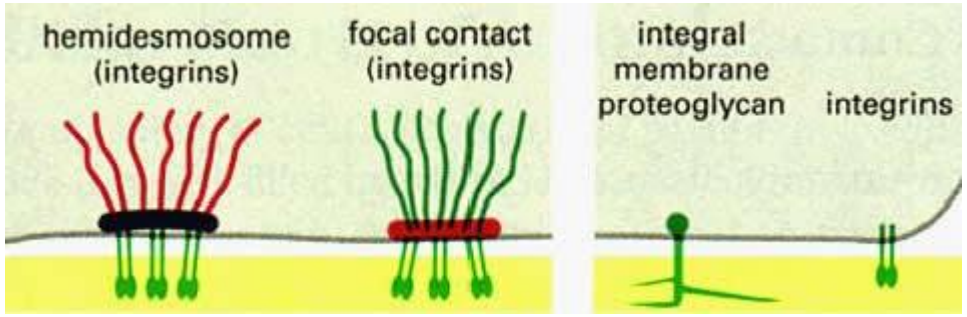
# Adhesions and Junctions 4

## Adhesion

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

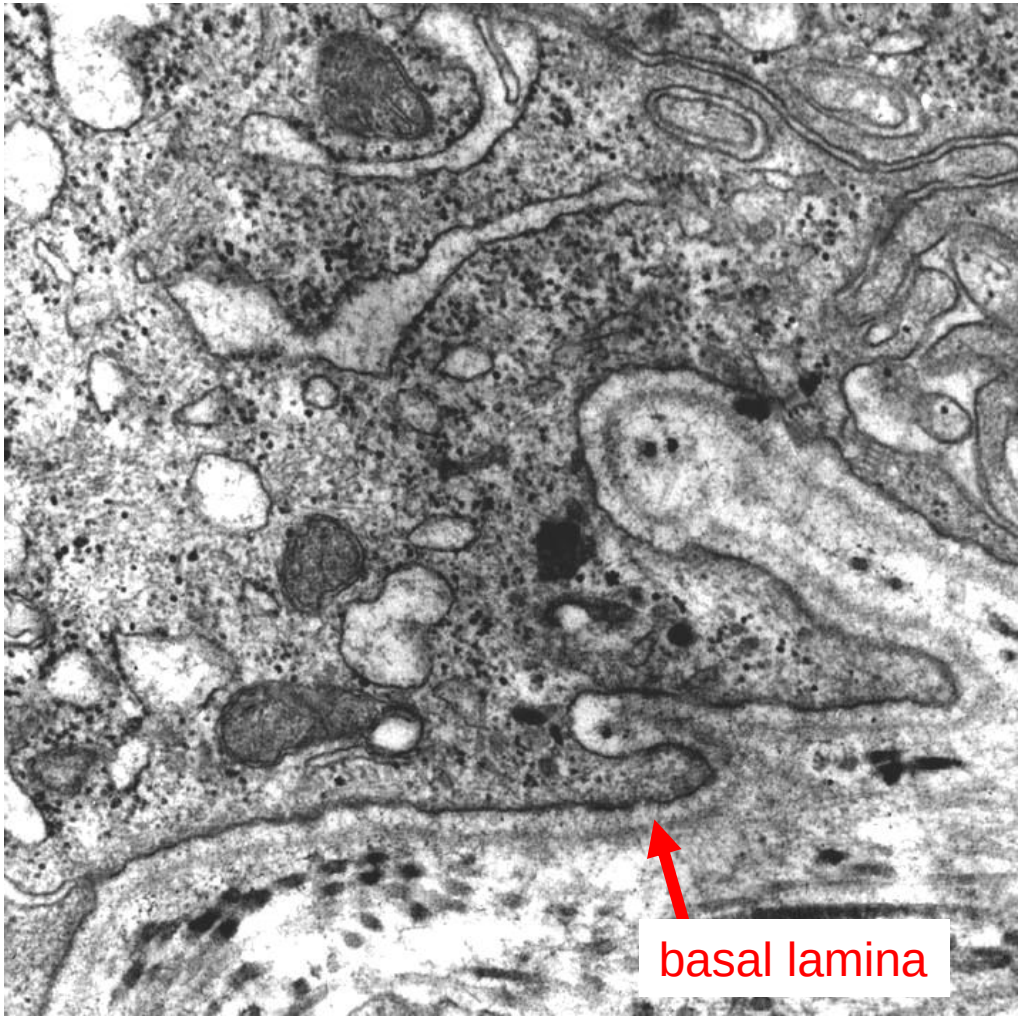


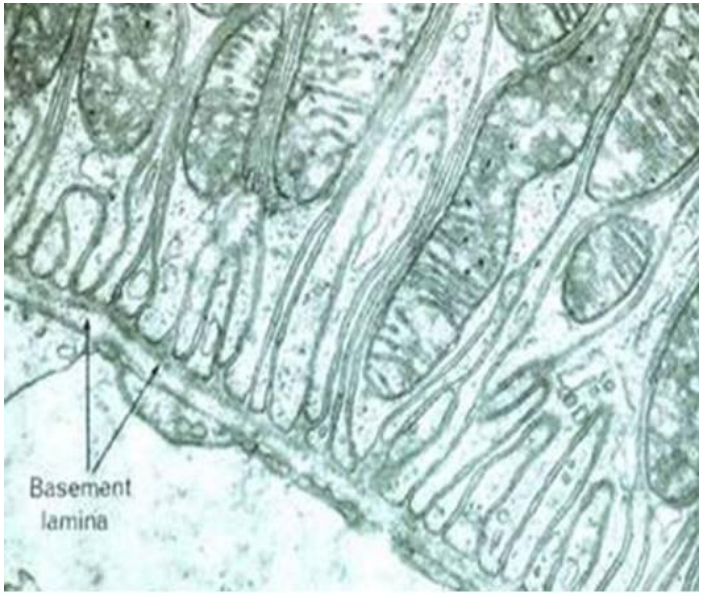
# Adhesions and Junctions 5

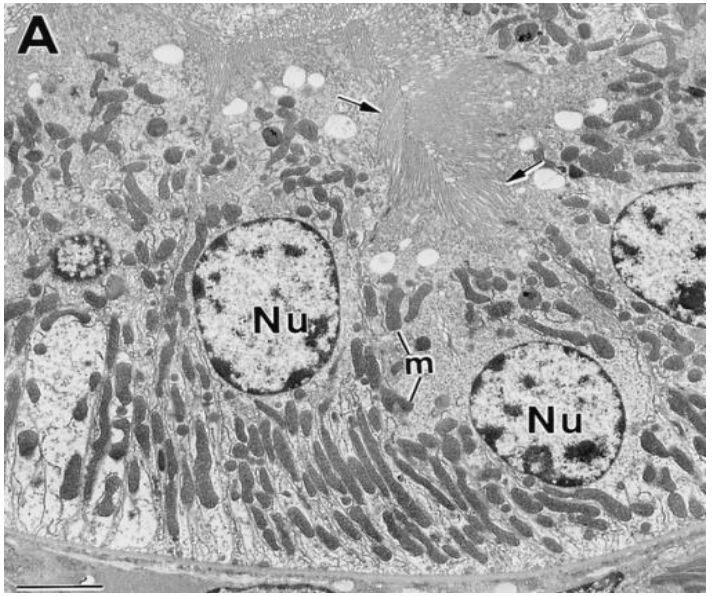
- **Focal adhesion**



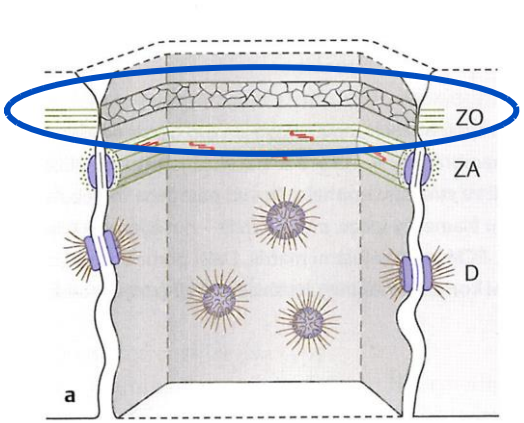
# Adhesions and Junctions 6

## Basal labyrinth



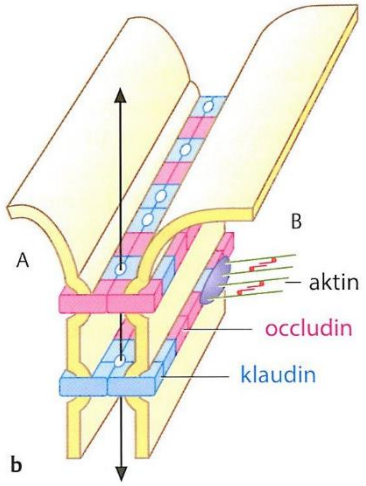



# Adhesions and Junctions 7

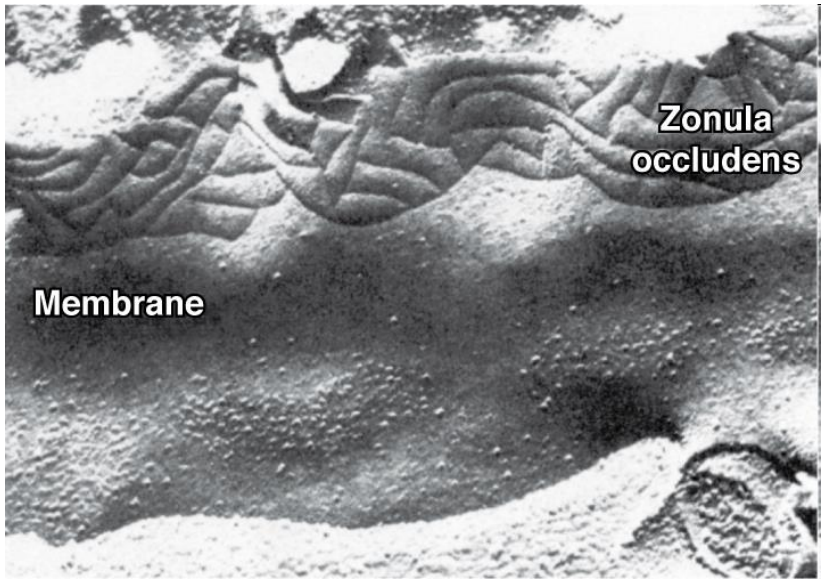


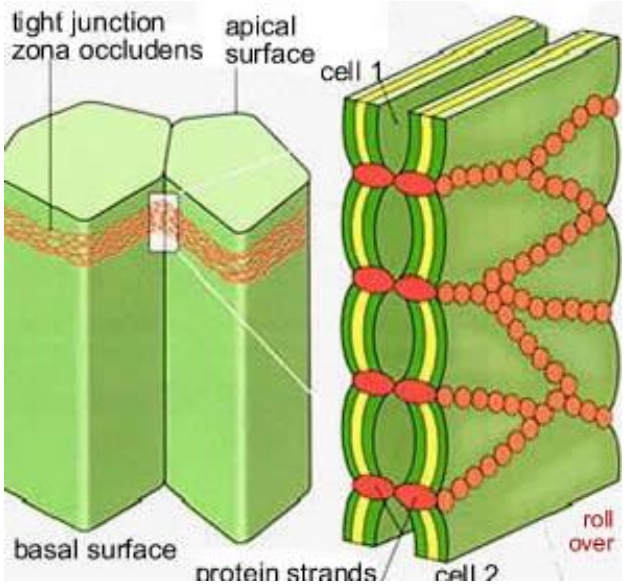

## Sealing

- **Zonula occludens** (tight junction)

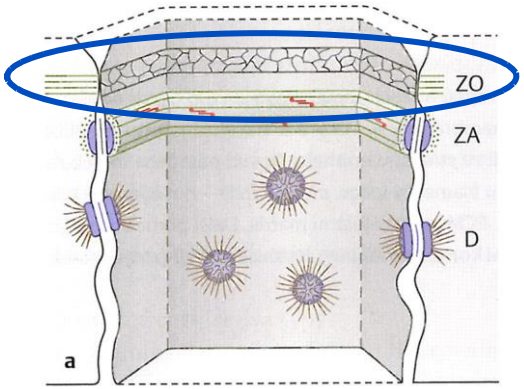



**Damage by:**
Clostridium perfringens
Helicobacter pylori (ZO-1)



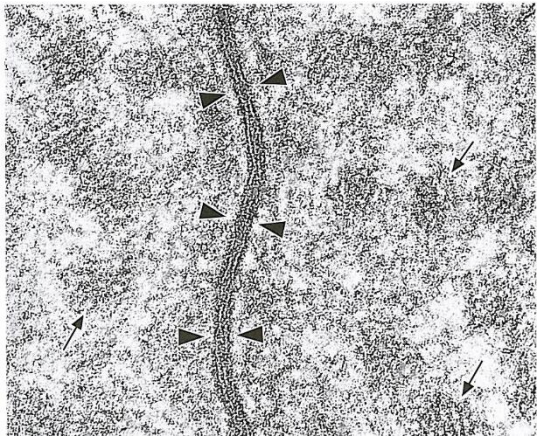



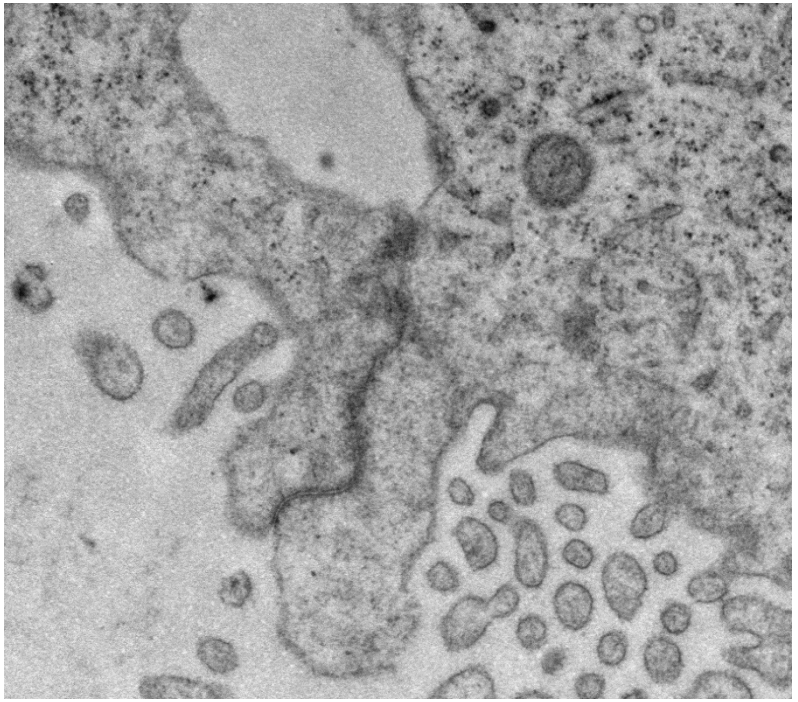
# Adhesions and Junctions 8



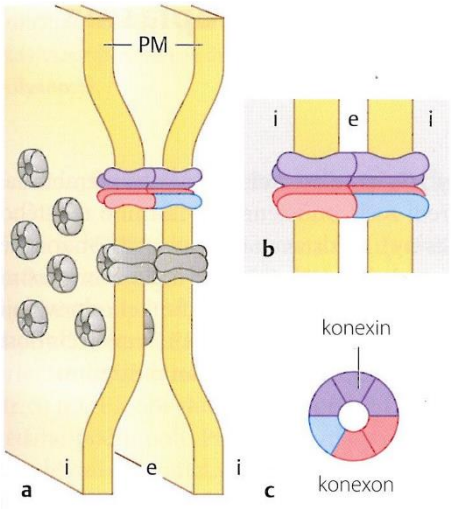

## Sealing

- **Zonula occludens** (tight junction)





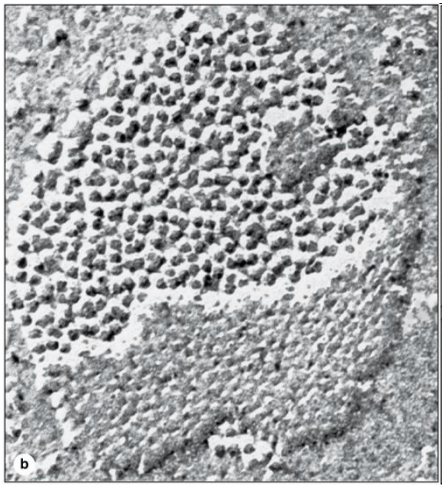
# Adhesions and Junctions 9

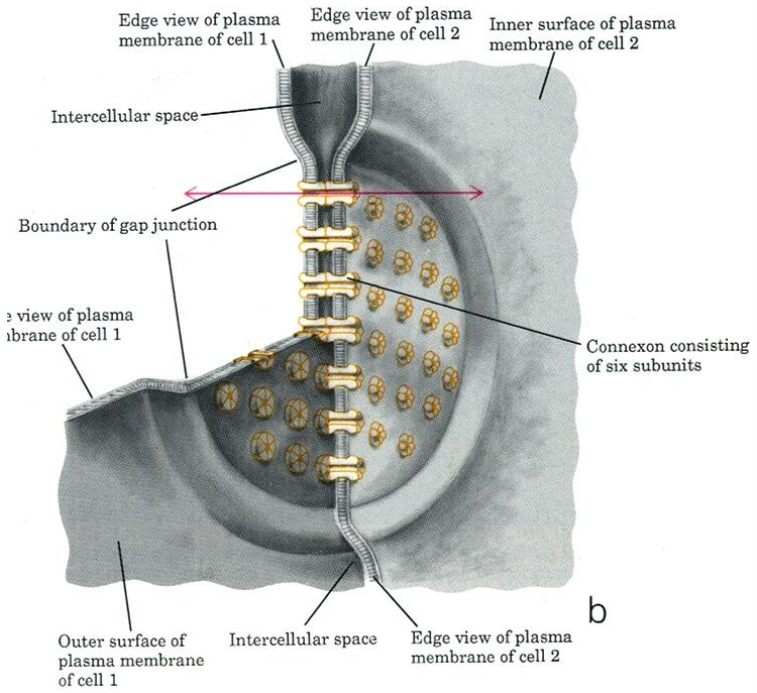


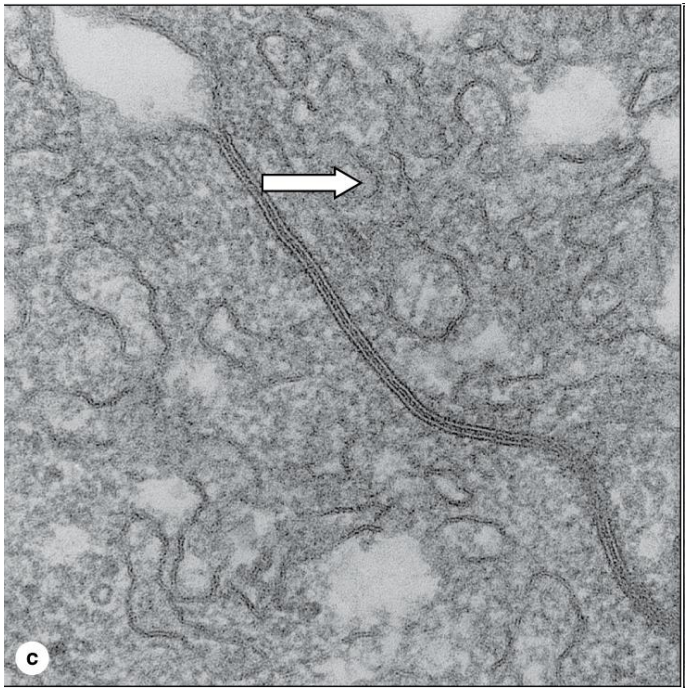

## Communication

- **Gap junction** (nexus)

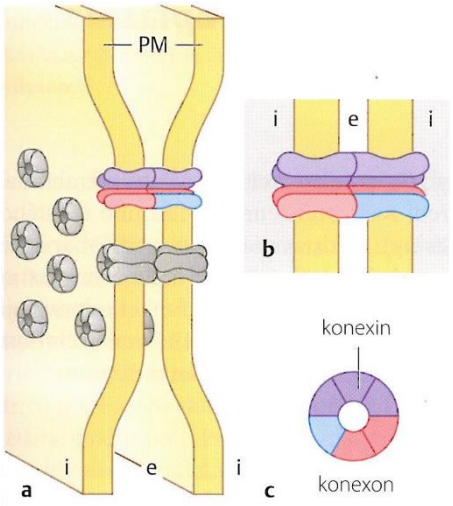
**Diameter about 0,3 μm**
**Distance between cell membranes about 3 nm**
**Internal diameter of the channel about 2 nm**



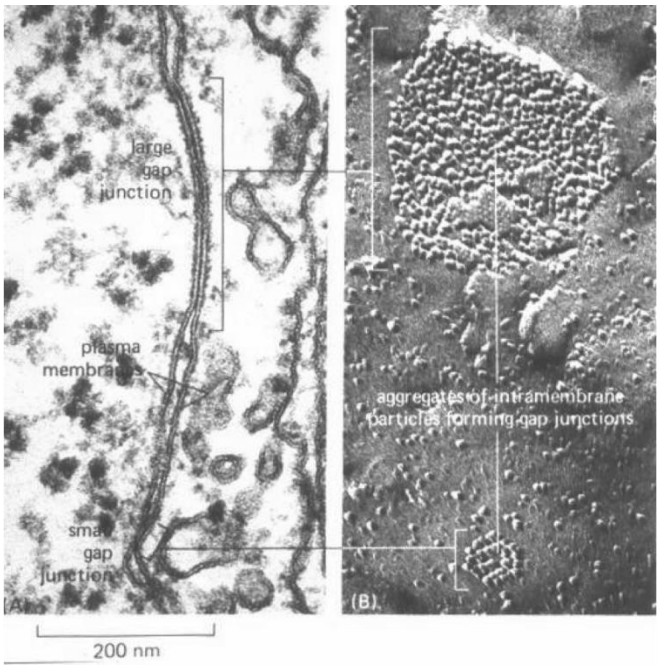



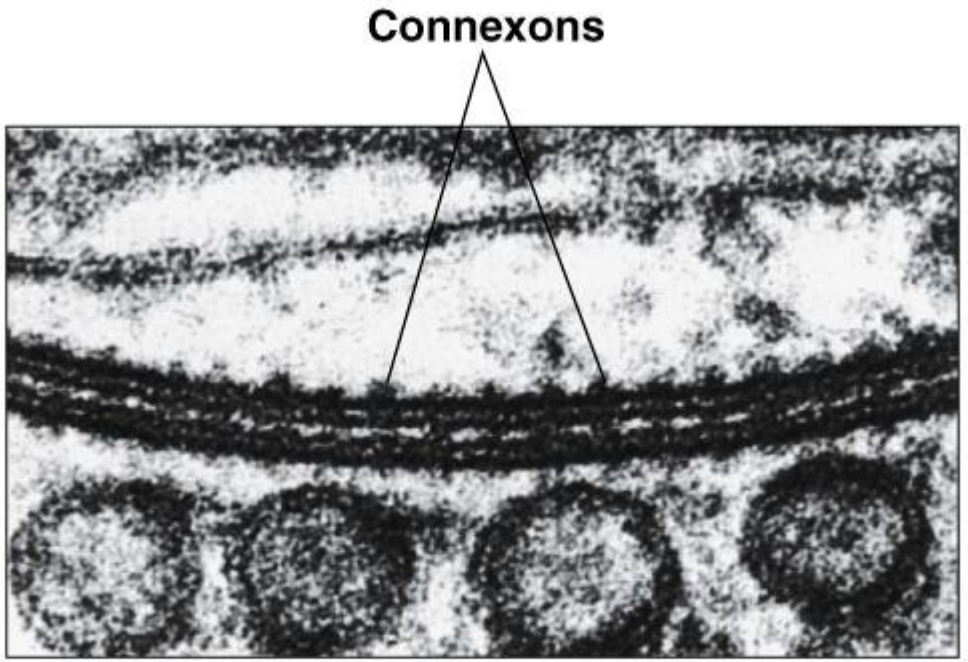
# Adhesions and Junctions 10




## 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

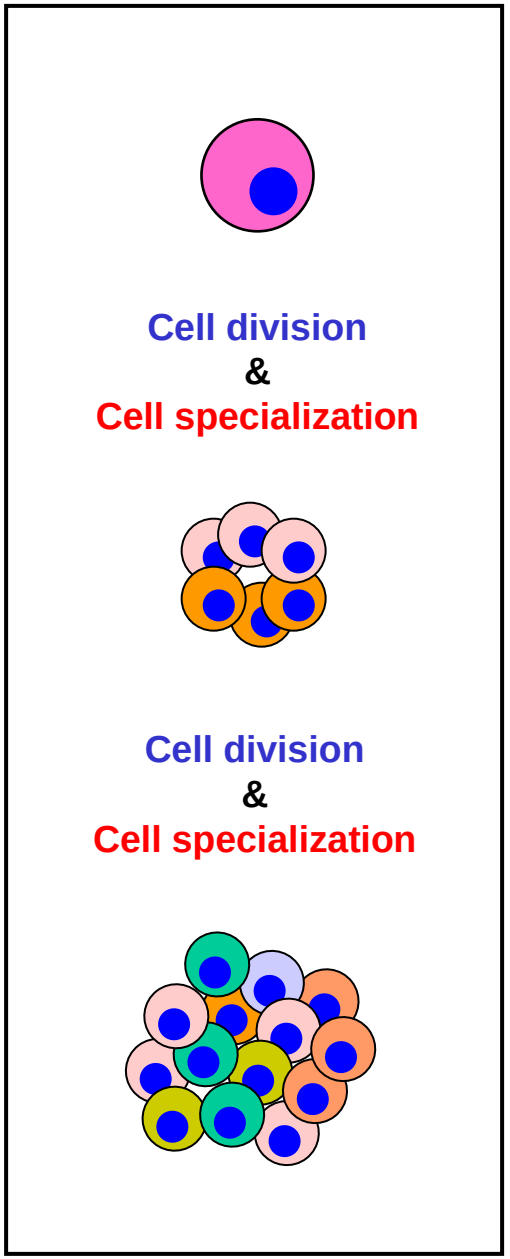
Zygote

Multicellular embryo

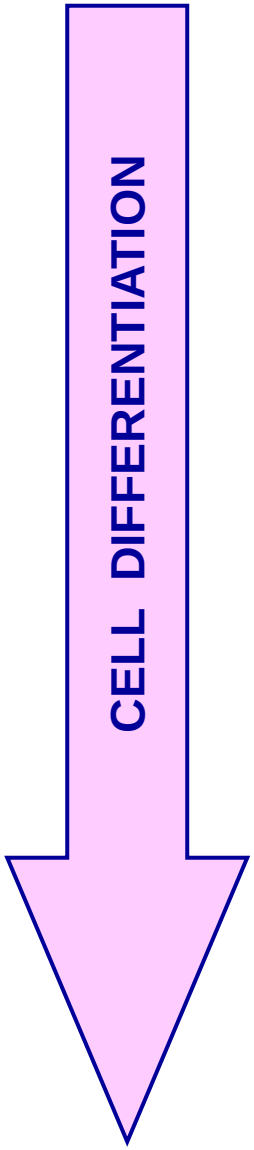
Dynamic multicellular organism

CELL DIVISION

CELL DIFFERENTIATION



# 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

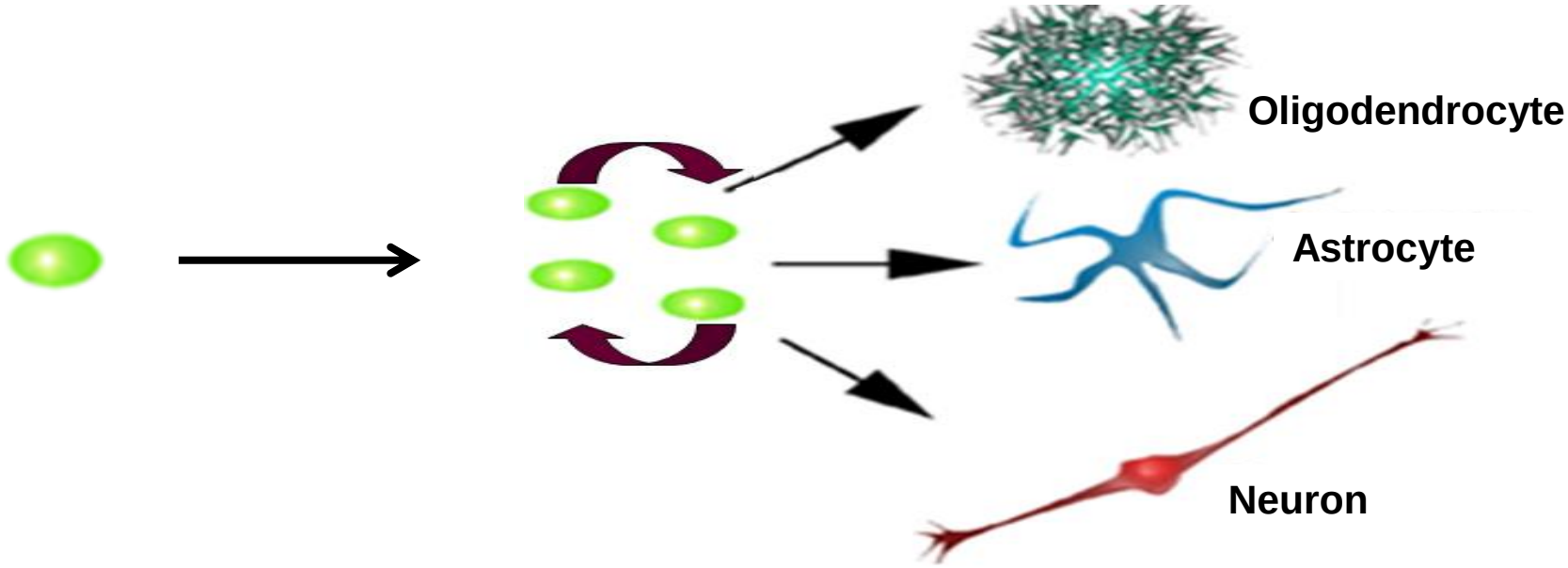
# Division x Differentiation of cells 3

## 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**

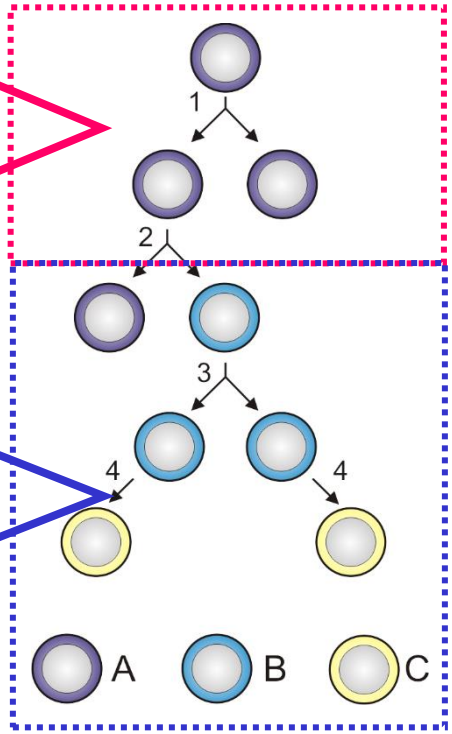
Capability to produce identical copies of itself

**Self-renewal**

Capability to differentite into specialized cell types

**Pluripotency**

**1. Undifferentiated growth**




**2. Differentiation**

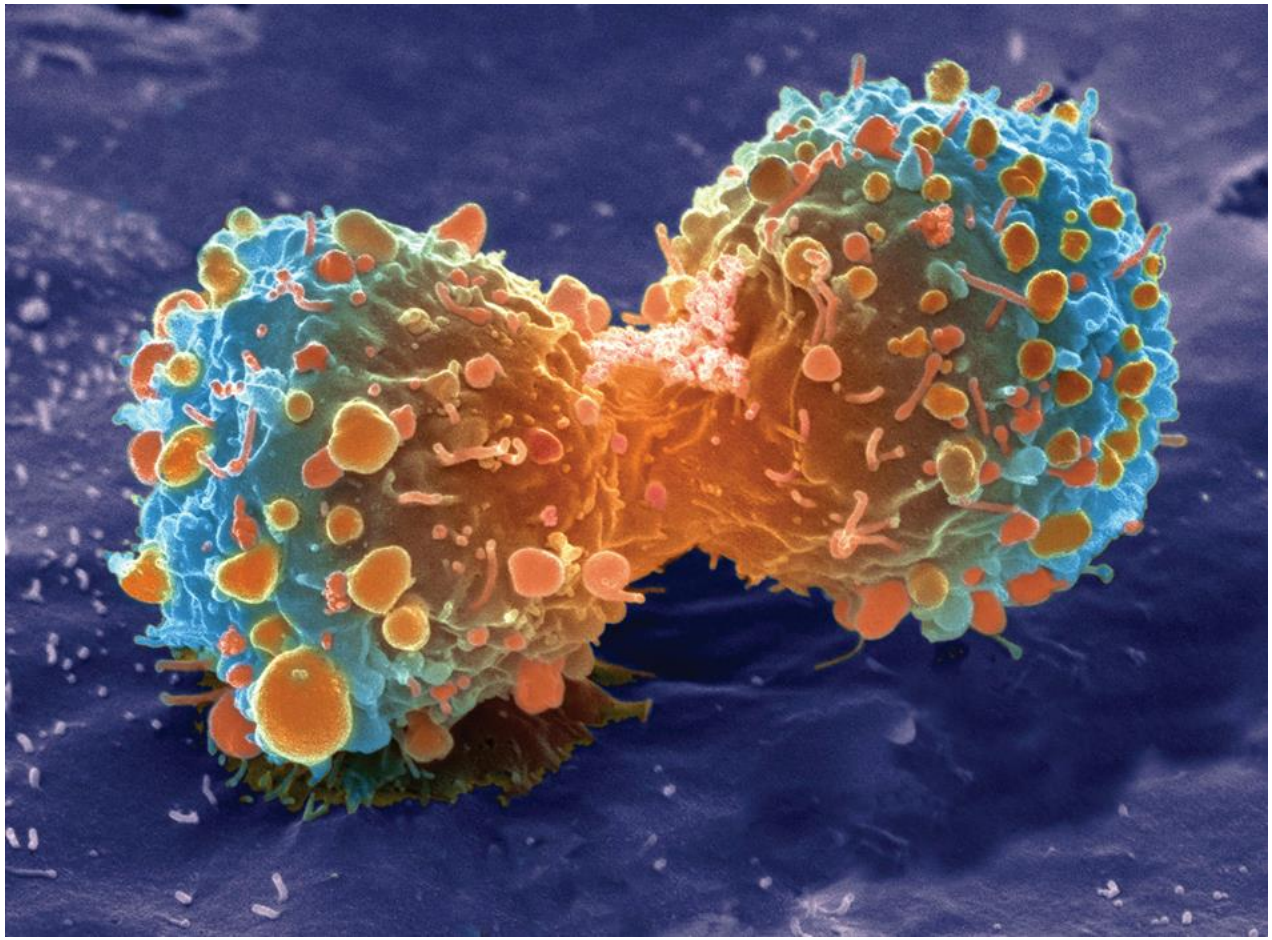
- Embryonic stem cells
- Adult stem cells
  - Fetal
  - Organ
  - Tissue
- Induced pluripotent stem cells
- Cancer stem cells

**Different properties**

# Cell division 1

## Basic concept 1

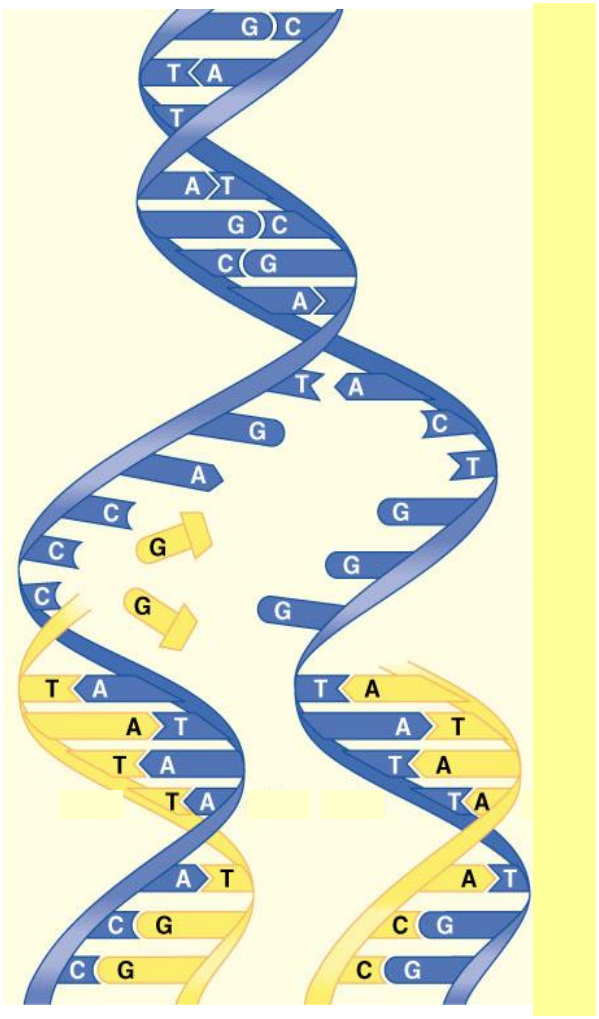
## MITOSIS and CYTOKINESIS produce genetically identical cells

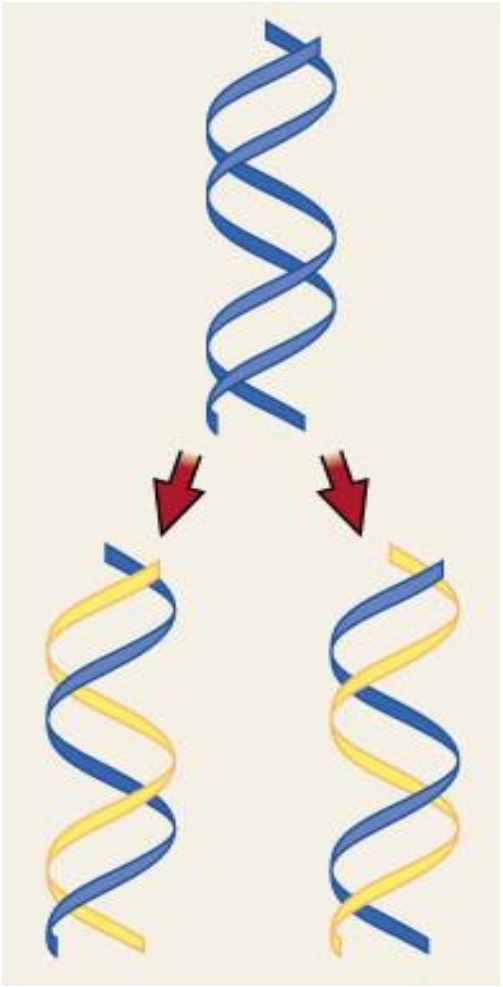


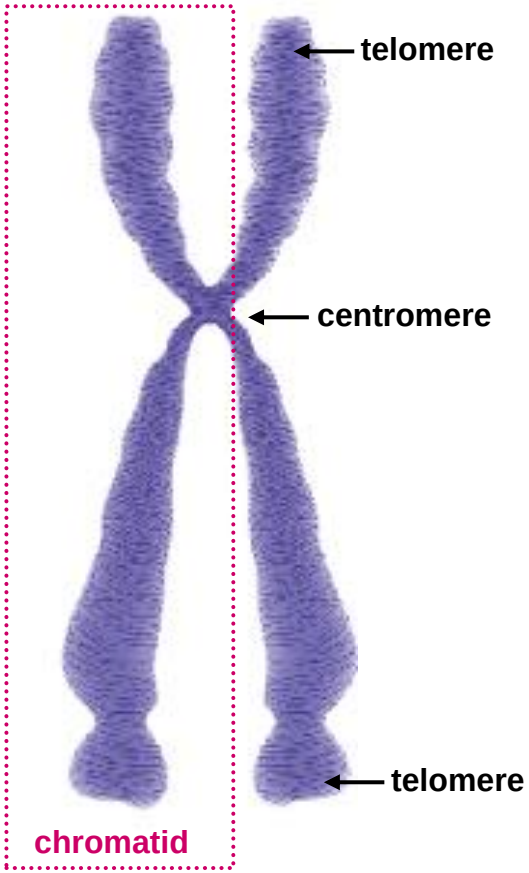
# Cell division 2

**STABLE (non-changing) GENOME**

Due to semiconservative duplication of DNA



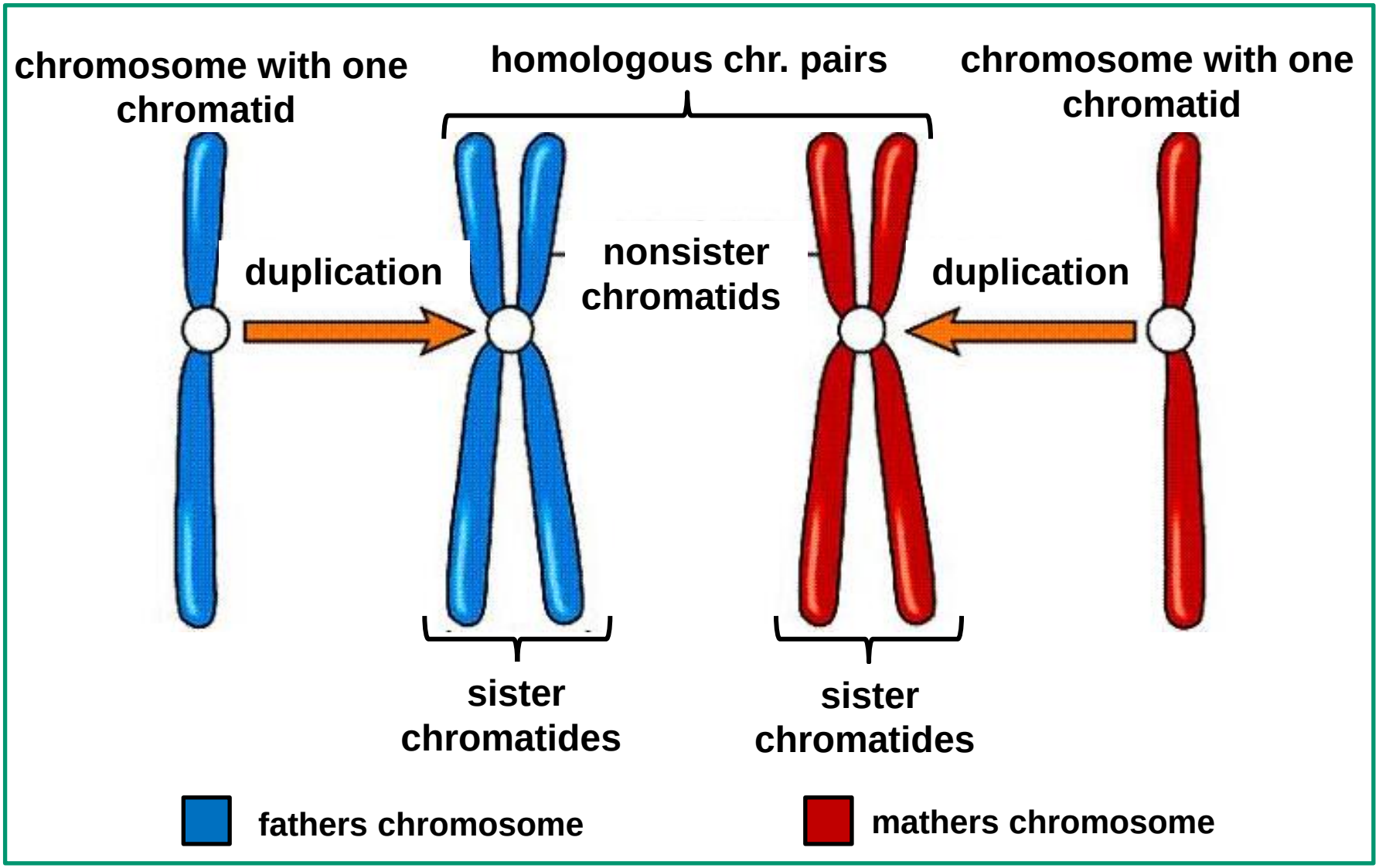





**Condensed duplicated chromosome**

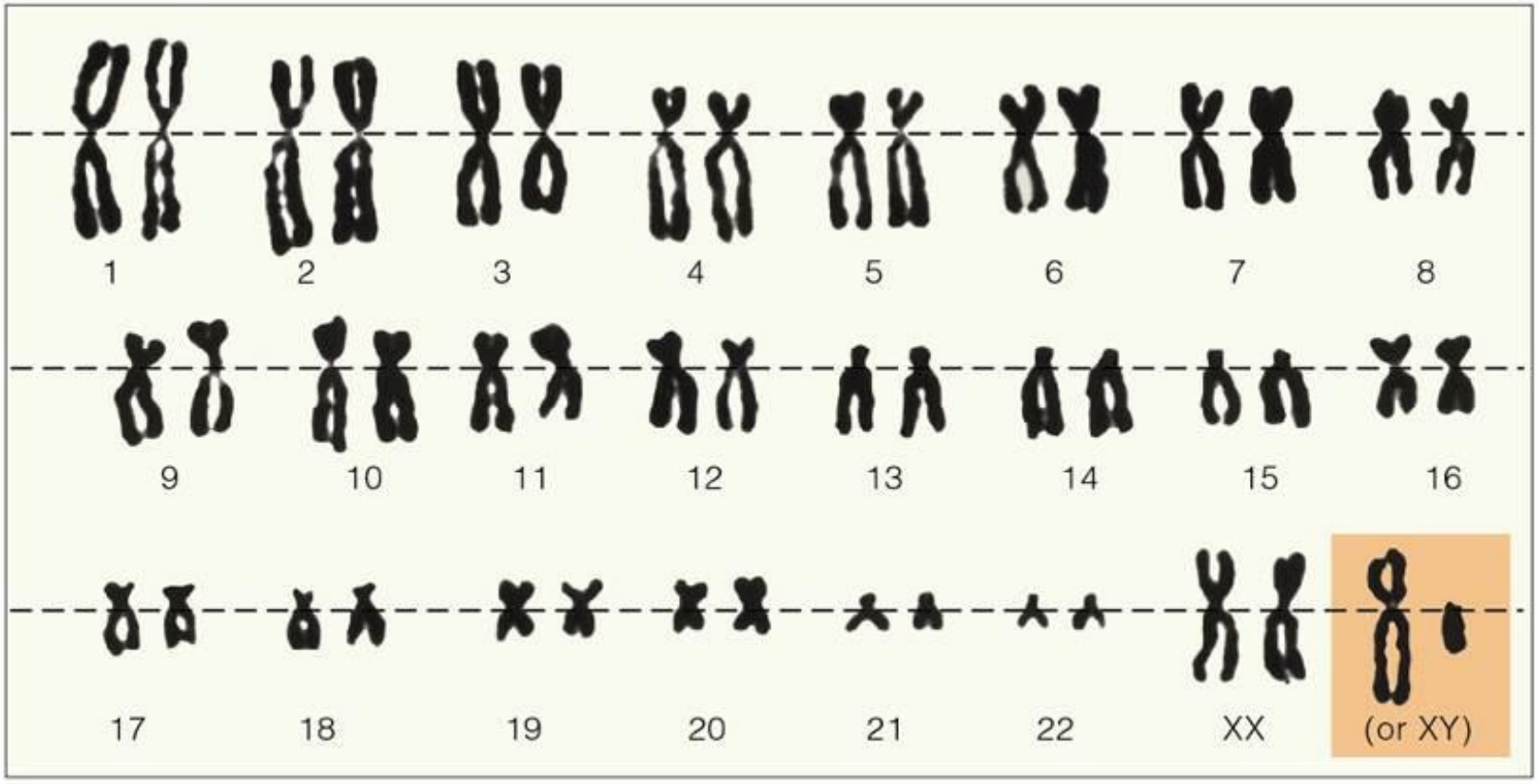
# Cell division 3

## Metabolism of chromosomes – Homologous chromosomes



# Cell division 4

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



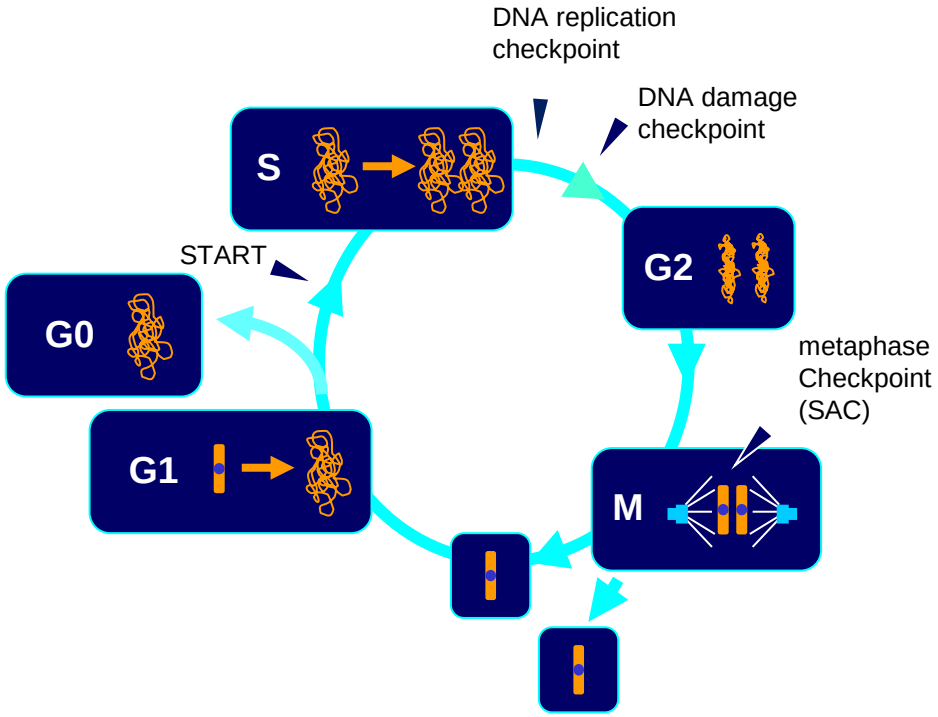
# Cell division 5

## Basic concept 2

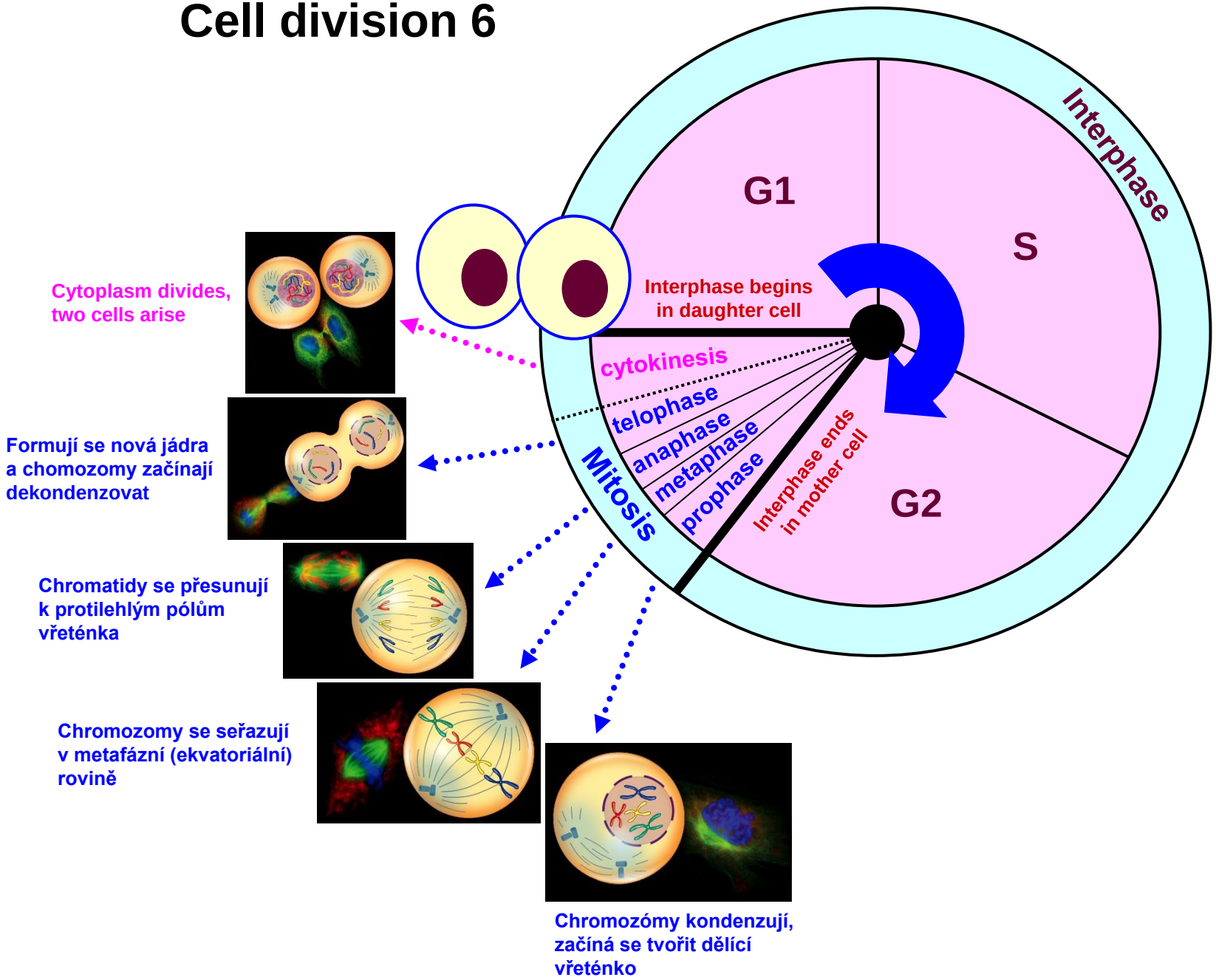
## MITOSIS and CYTOKINESIS are parts of cell cycle

**CELL CYCLE**

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

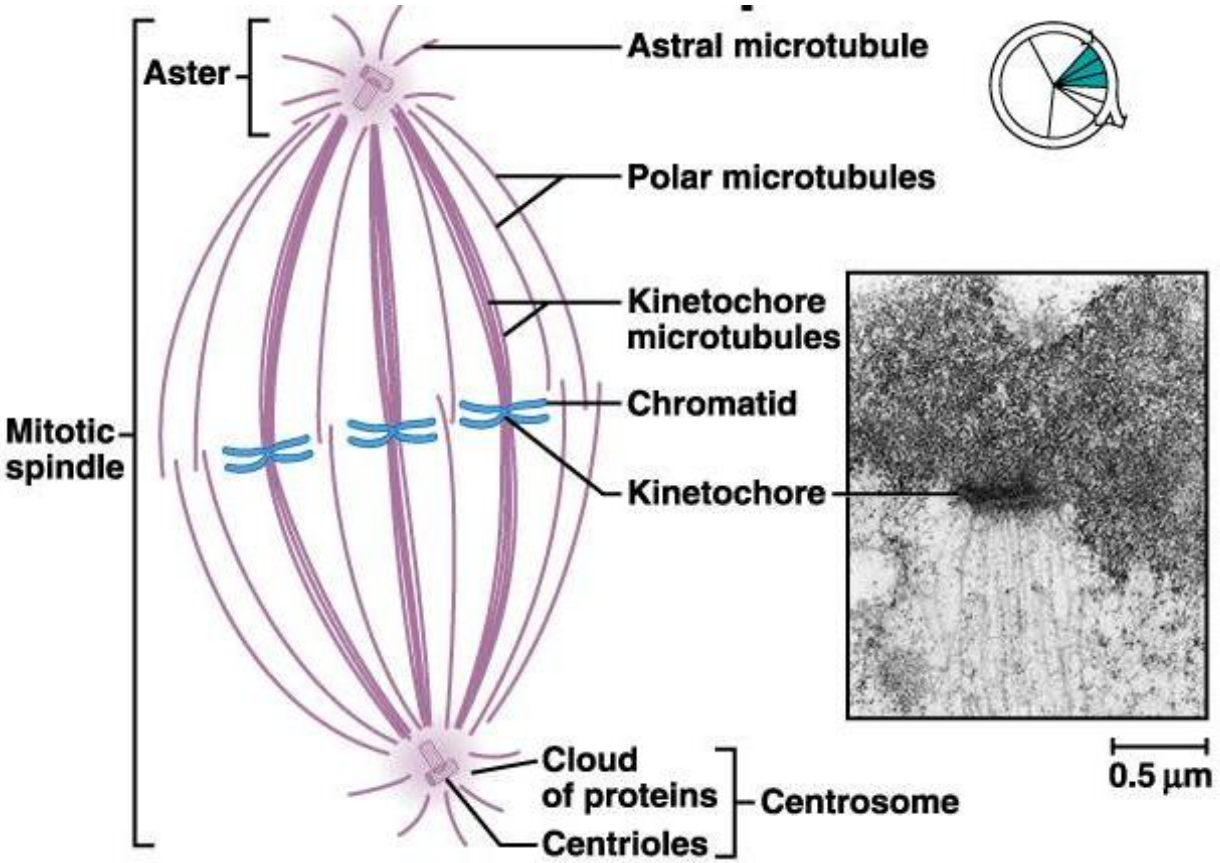


# Cell division 6



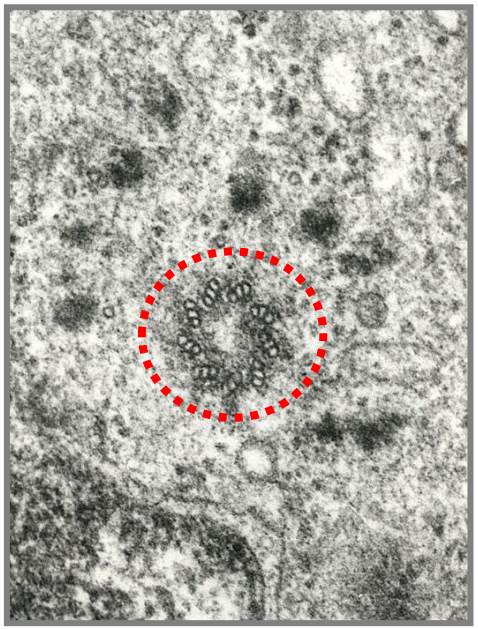
# Cell division 7

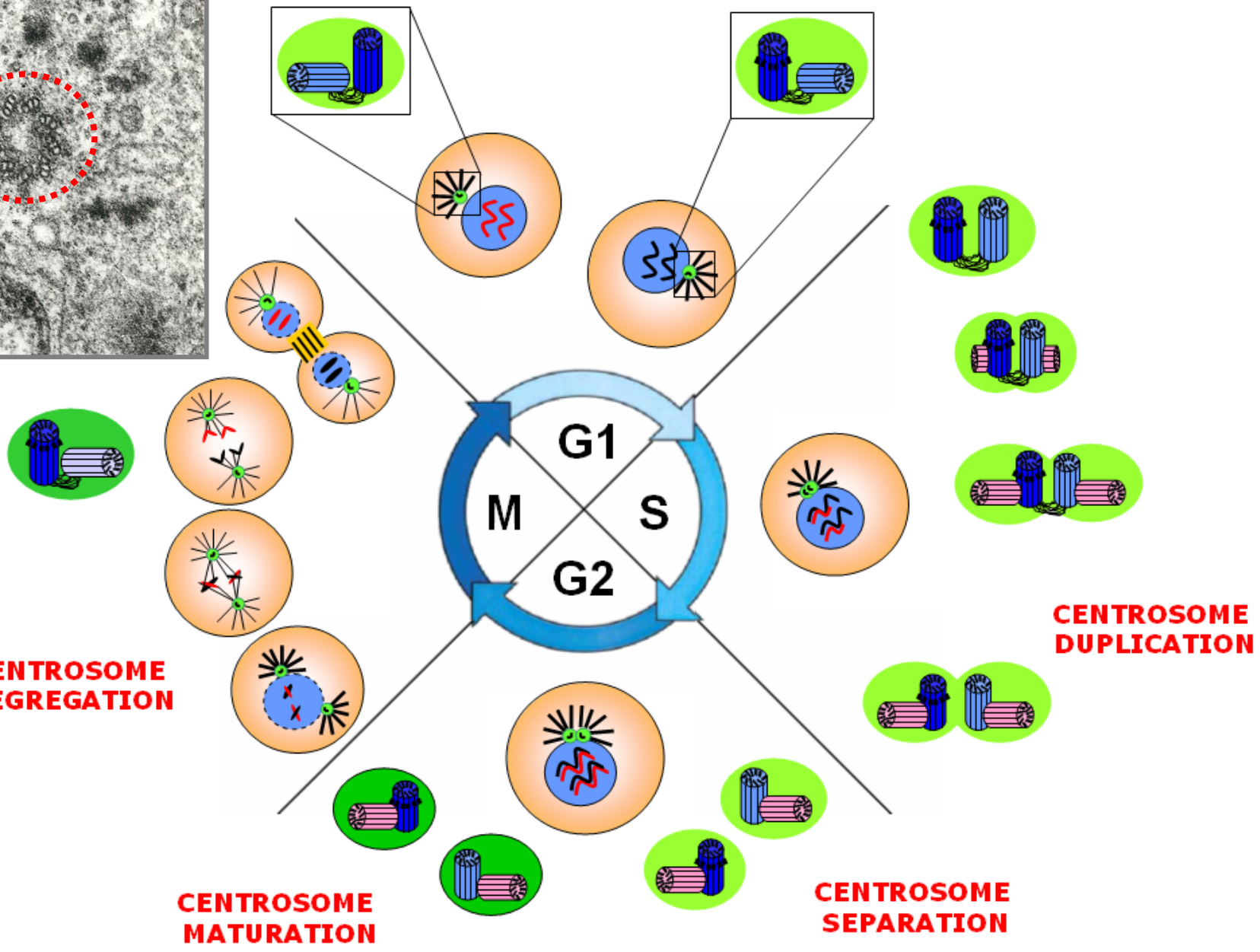
## Mitotic spindle



# Cell division 8

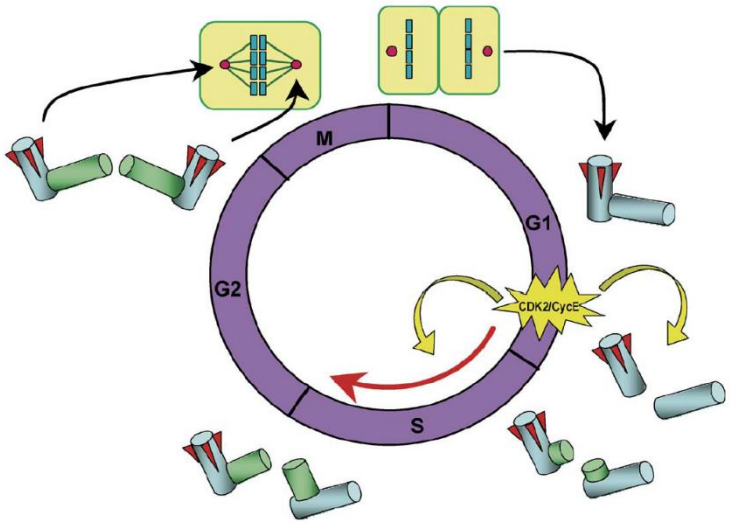
**Centrosomal metabolism**
**Semiconservative duplication**

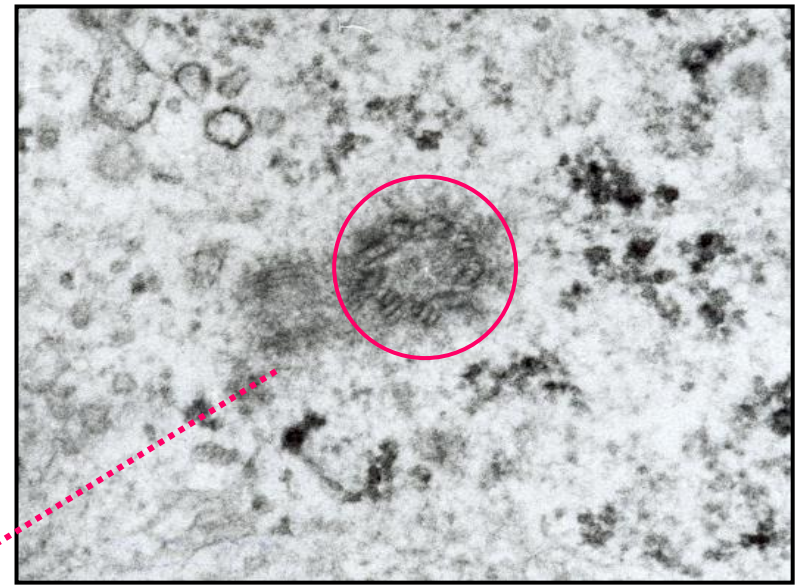


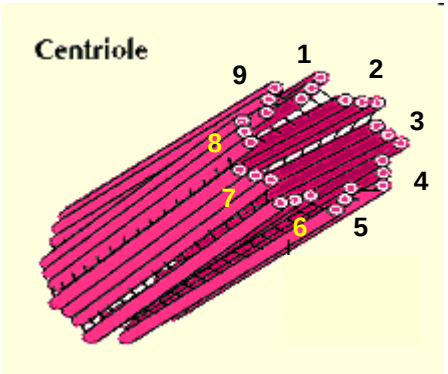


# Cell division 9

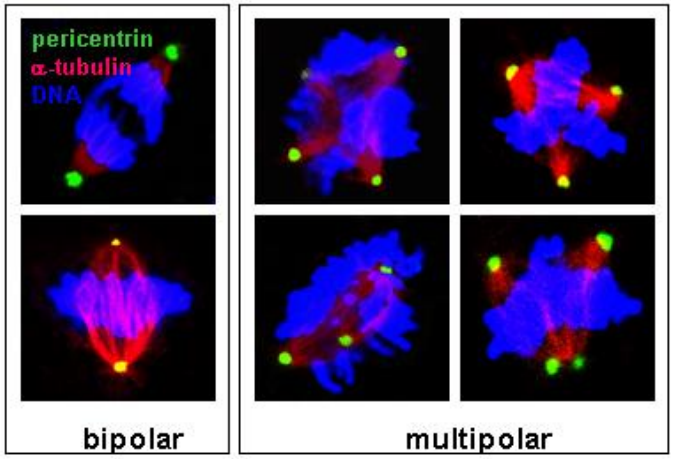
## Centrosome structure






Diameter – 0.2 μm
Length - 0.5 μm



# Cell division 10

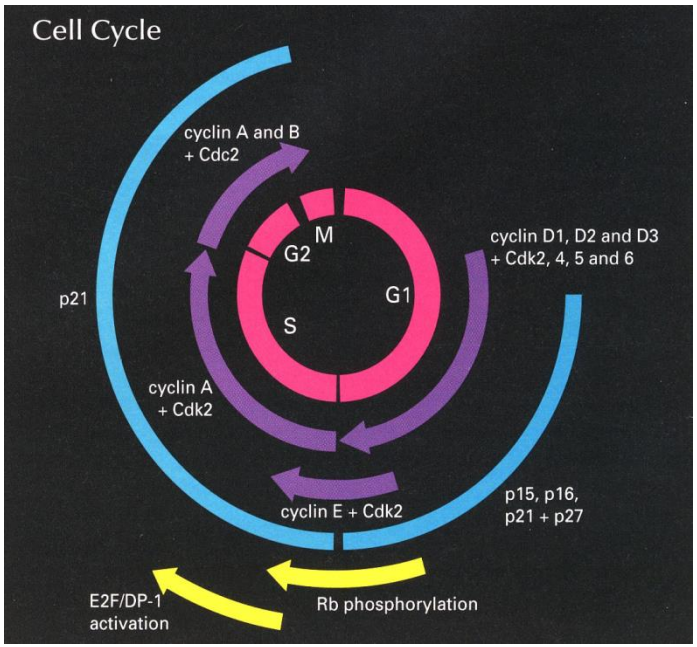
## Regulation – Cyklin-Dependent Kinases (CDK) + Cyklins

### 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

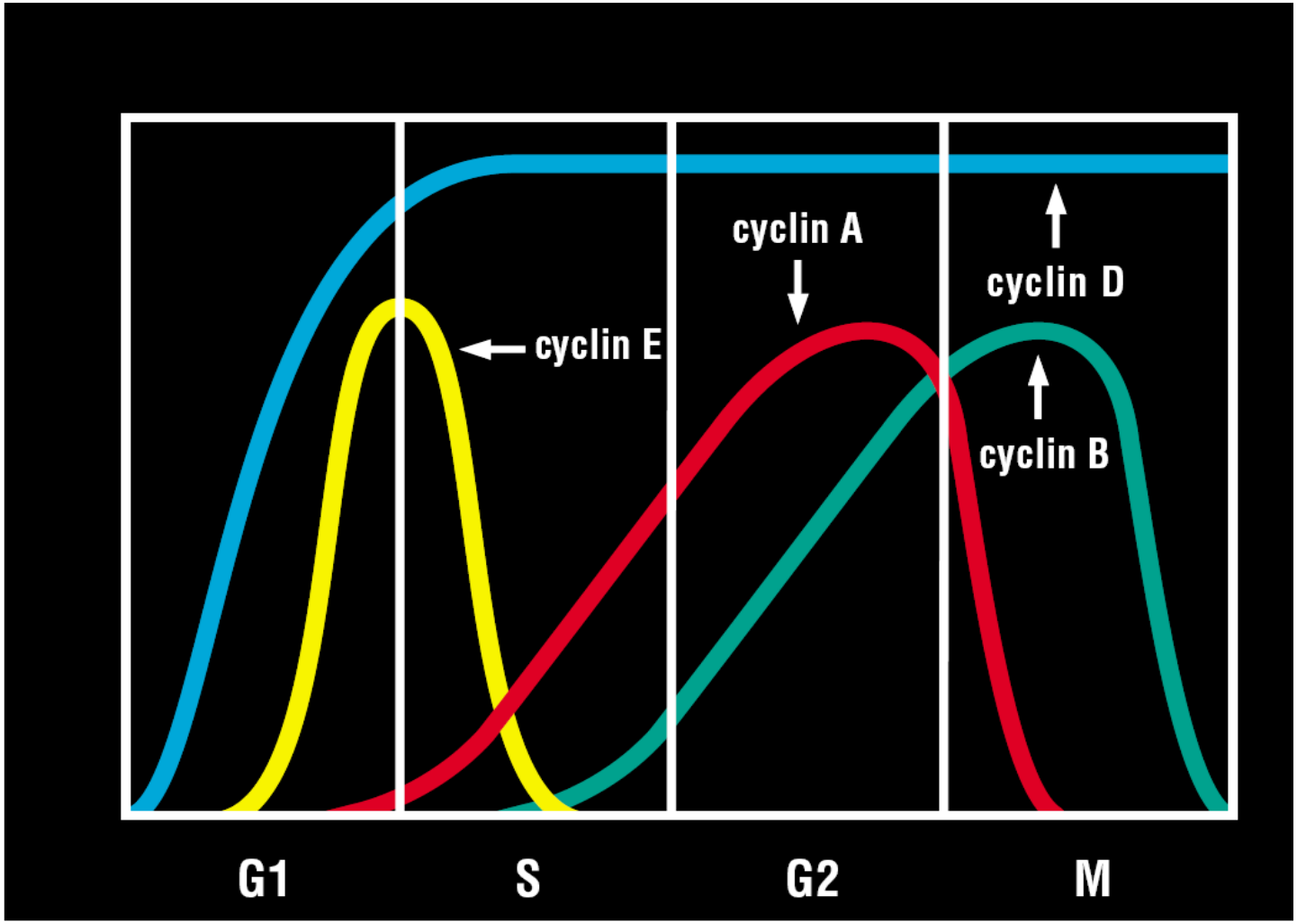
| cell cycle stage | cyclin-Cdk complexes | inhibitors | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | p15 | p16 | p18 | p19 | p21 | p27 | p57 |
| G1 | cyclin D-Cdk4/6 | + | + | + | + | + | +/– | +/– |
| G1/S | cyclin E-Cdk2 | – | – | – | – | + | + | + |
| S | cyclin A-Cdk2 | – | – | – | –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



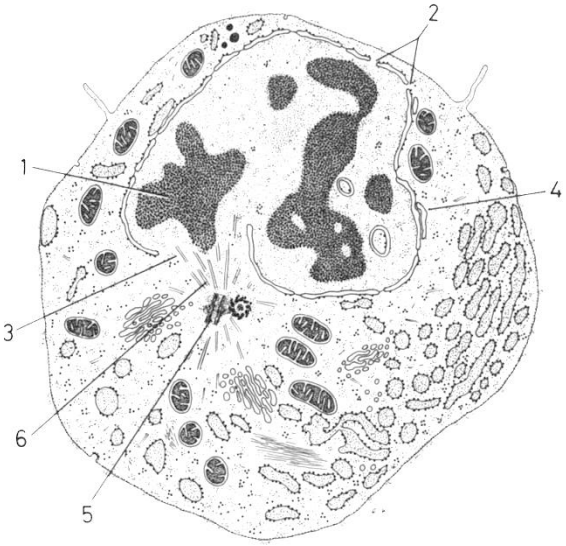

Modified from the catalogue ofSanta Cruz Biomedicals, USA

# Cell division 11

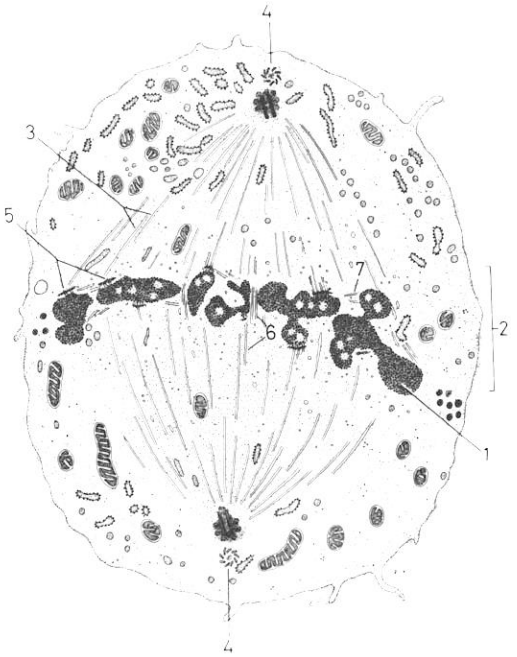
## Periodicity of cyclin expression



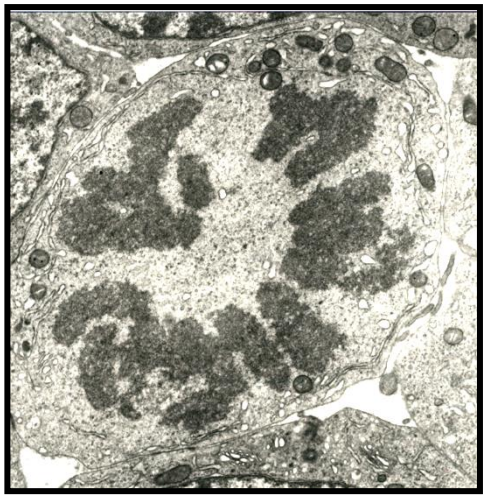
# Cell division 12



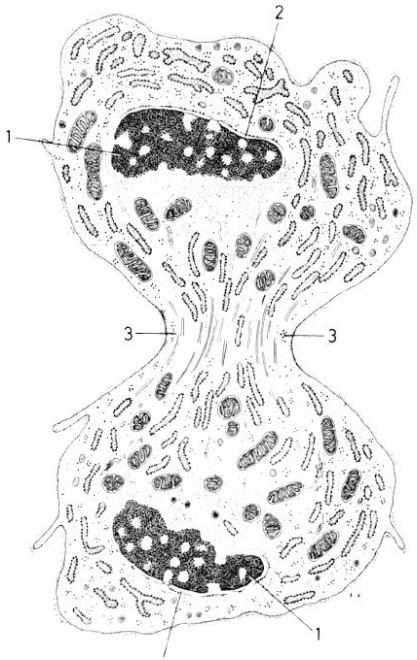

**prophase**



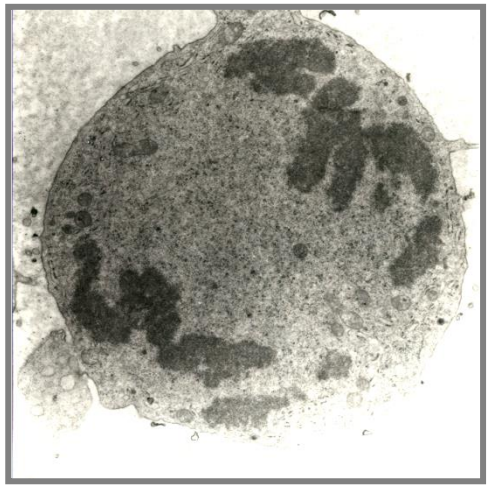

**metaphase**

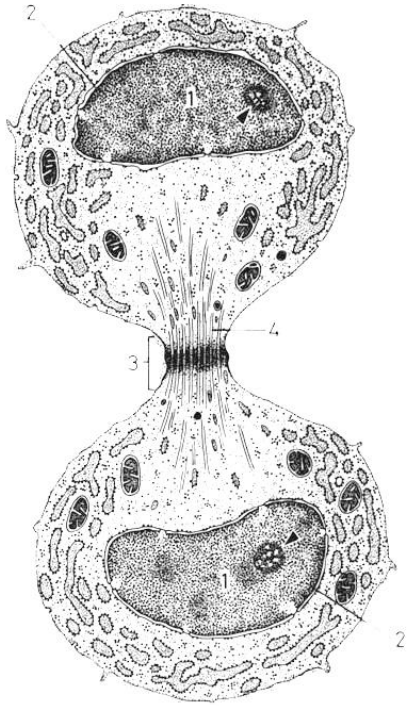


# Cell division 13

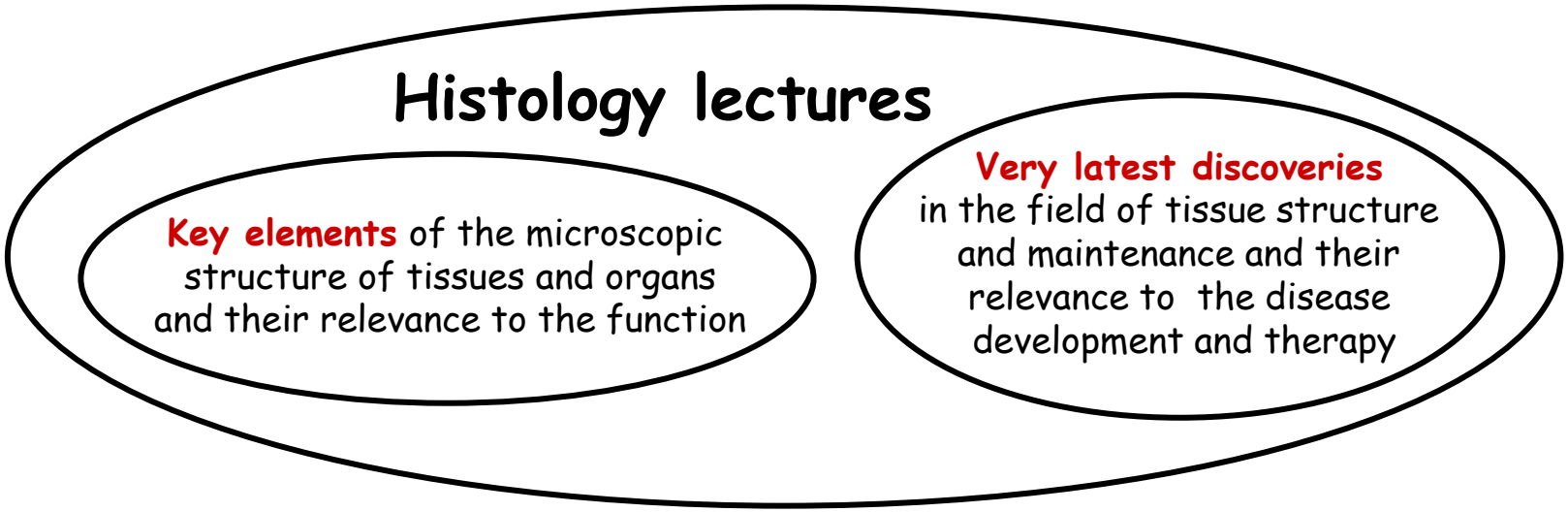



**anaphase - telophase**






**telophase**




# Thank you for your attention !

ahampl@med.muni.cz

Building A1 – 1st floor