Histologie a Embryologie

Přednášející:

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Přednáška 1

Úvod

- Předmět a význam histologie, její členění.
- Hraniční oblasti histologie.
- Historie, současnost a budoucnost histologie.

Cytologie

- Buňka: definice, obecná stavba, kompartmentalizace.
- Buněčné jádro: ultrastruktura a funkční význam, chromosomy, jadérko.
- Endoplasmatické retikulum
- Golgiho aparát
- Centrosom
- Mitochondrie
- Lyzosomy + Peroxisomy
- Cytoplasmatické inkluze
- Cytoskelet
- Buněčné povrchy
- Buněčný cyklus, dělení buněk, diferenciace buněk

Histologie

Mikroskopická a submikroskopická struktura těla

(buňky, mezibuněčná hmota, tekutiny)

Cytologie

Struktura buňky
a její vztah k funkci.

Obecná histologie

Jaké jsou základní typy tkání?
Jaké jsou jejich funkce?
Jakými buněčnými typy jsou tvořeny?

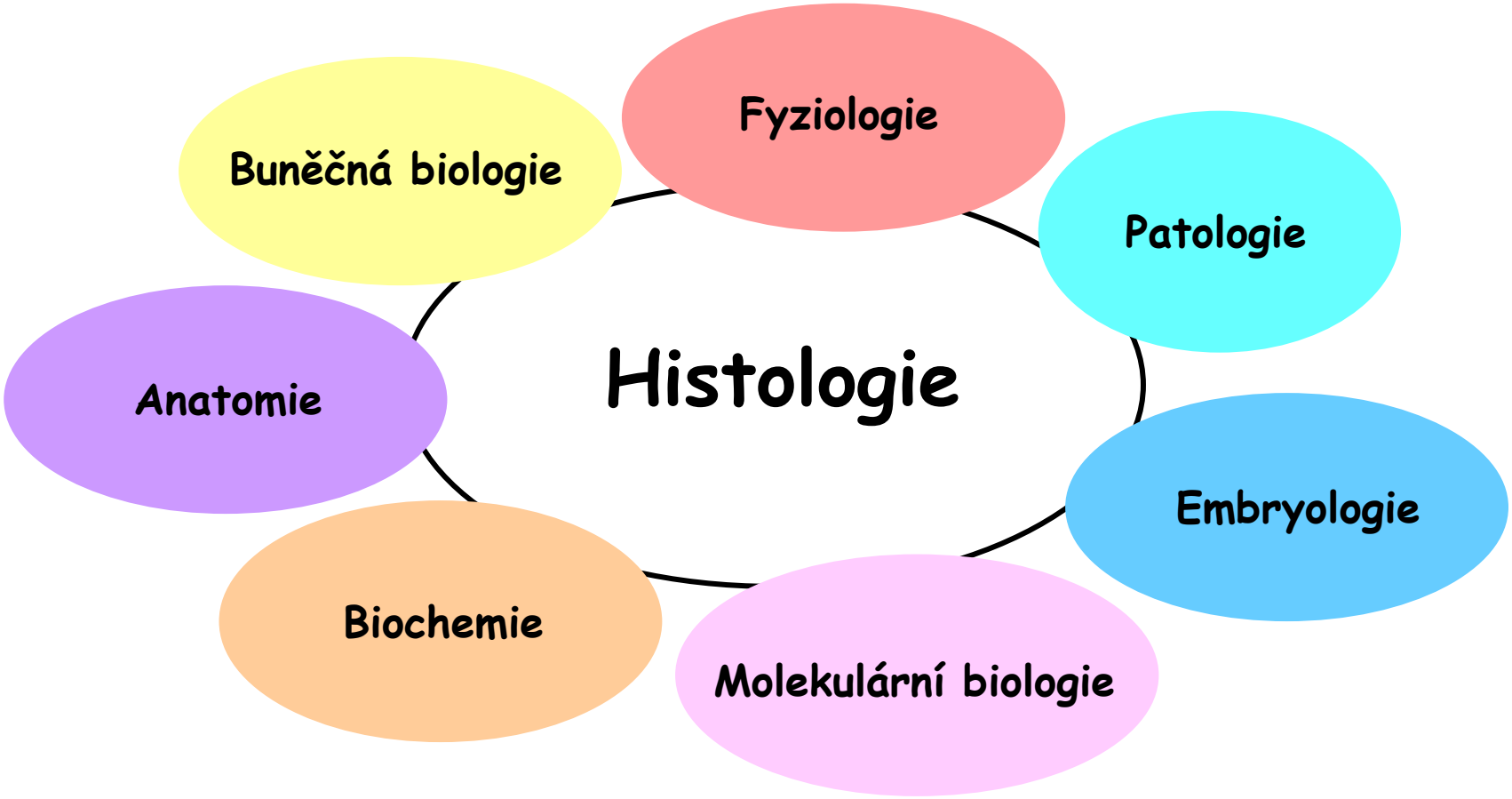
Mikroskopická anatomie

Složení a struktura orgánových systémů & individuálních orgánů

Jaké typy tkání a jak jsou organizovány?
Jaké speciální buněčné typy?
Které speciální struktury? (např. tubuly)
Jak to celé funguje?

Toto vše je odrazem hierarchické struktury mnohobuněčných organismů

Histologie není statickou disciplínou, která se zabývá výhradně strukturou !!!



Mysleme „histologicky“

Spojme si histologii s akcí a pohybem

Studium histologie se poprvé stalo povinným v roce 1893
na John's Hopkins Medical School !

Mnoho velkých histologů byli Němci, protože vyráběli kvalitní mikroskopy.

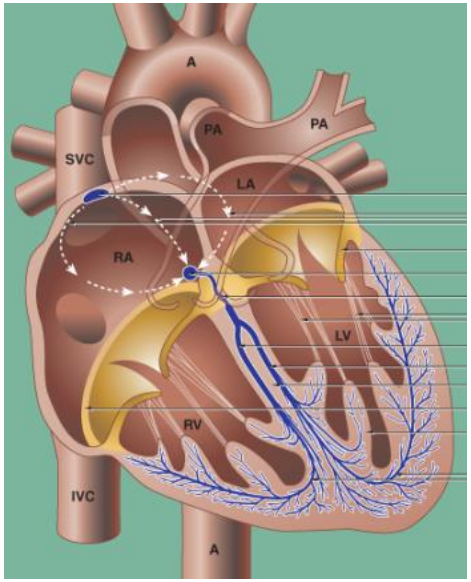
Eponymously theirs…..

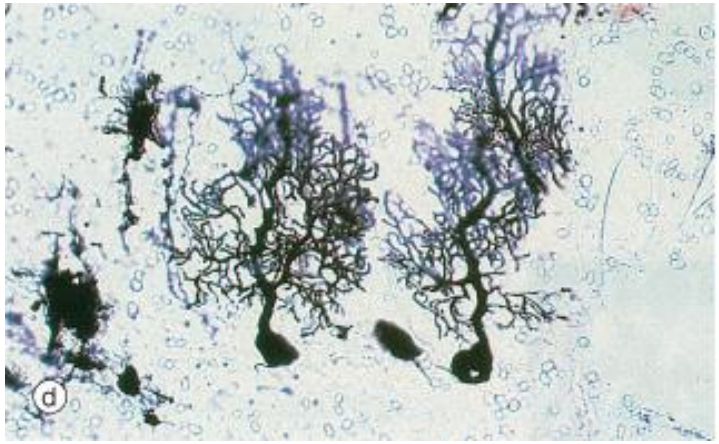
Jan Evangelista Purkyně
1787 - 1869

Český fyziolog

Schwann + Schleiden – 1839 – buněčná teorie

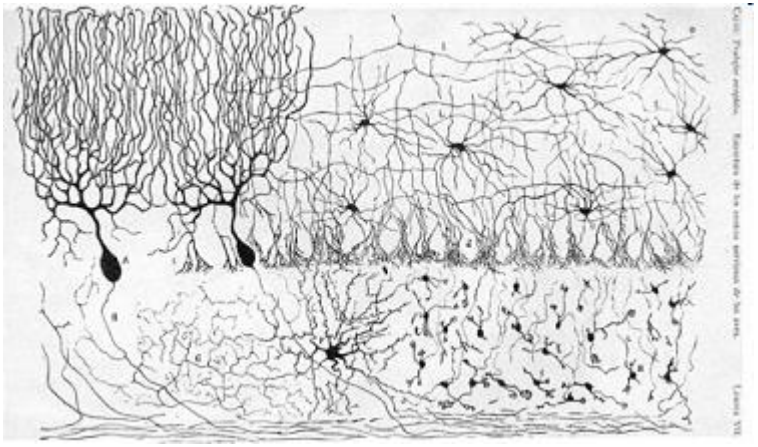
- Pionýr histologických technik
  Poprvé použil přístroj podobný současnému **mikrotomu**
- Zavedl termín **plasma**
- Popsal **Purkyňova vlákna** v srdci
- Popsal **Purkyňovy buňky** v kůře mozečku

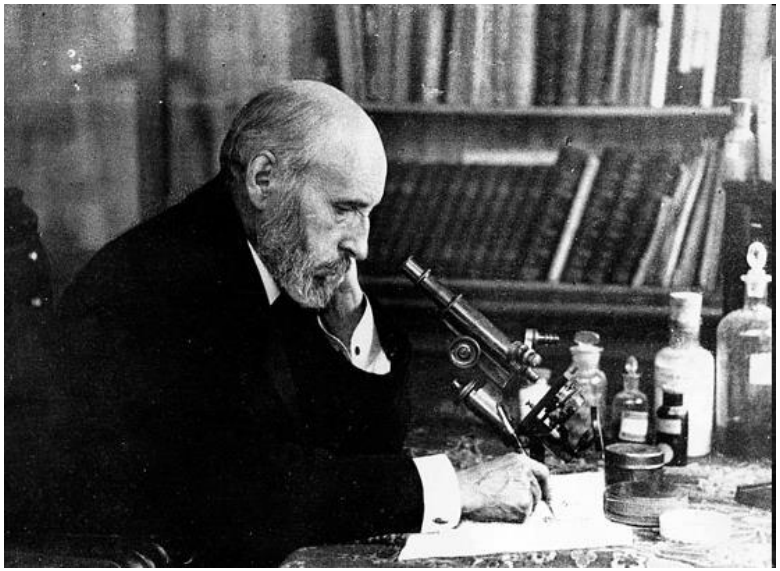




Santiago Ramón Y Cajal
1852 - 1934

Španělský lékař a anatom





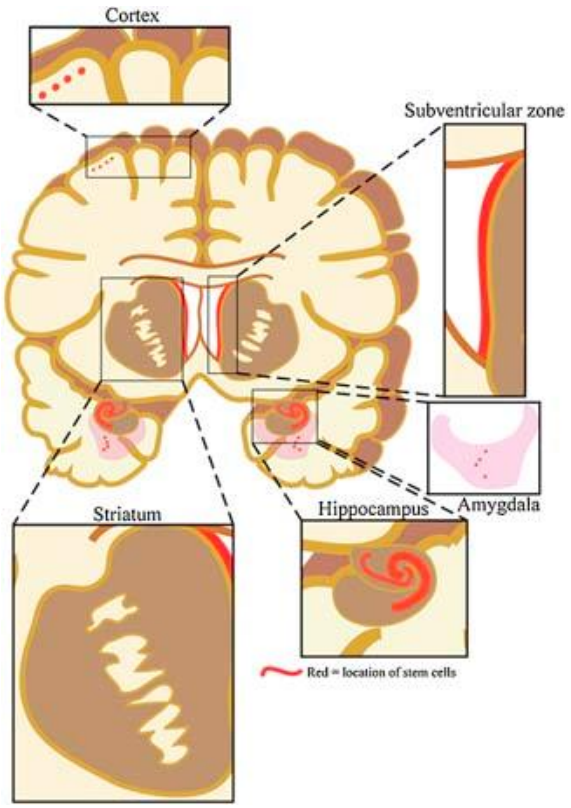
Poprvé popsal neuron jako primární strukturální a funkční jednotku nervové tkáně.
Nobelova cena v roce 1906

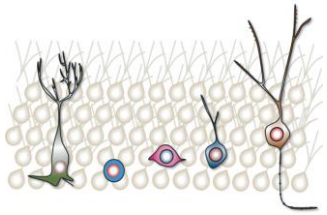
"Once the development was ended, the founts of growth and regeneration of the axons and dendrites dried up irrevocably. In the adult centers, the nerve paths are something fixed, ended, and immutable. Everything may die, nothing may be regenerated. It is for the science of the future to change, if possible,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

Neočekávané objevy

(od časných 90-tých let)

Existence multipotentních sebeobnovujících se progenitorů v postnatálním a dospělém nervovém systému





BEZPOCHYBY V:

- Subventrikulární zána laterálních komor mozku
- Subgranulární zóna v gyrus dentaus hipokampu

MOŽNÁ V:

- Kůra koncového mozku ?
- Amygdala ?

Náš pohled na organizaci centrálního nervového systému se dramaticky změnil !!!

Histologické metody studia buněk a tkání 1

Učinit pozorovatelným

Stabilizovat struktury

Fixace

Učinit objekty menšími – prostupnými pro světlo

Zalití + Příprava řezů

Zviditelnit struktury

„Barvení"

Zvětšit

Použití mikroskopů

Světelné (optické) mikroskopy

(interakce fotonů s hmotou)

Rozlišení 0.1 μm

- Pouze s viditelným světlem
- S fluorescenčním světlem
- Konfokální laserový skenovací mikr.

Elektronové mikroskopy

(interakce elektronů s hmotou)

Rolišení až 0.1 nm (v praxi 1 nm)

- Transmisní
- Skenovací

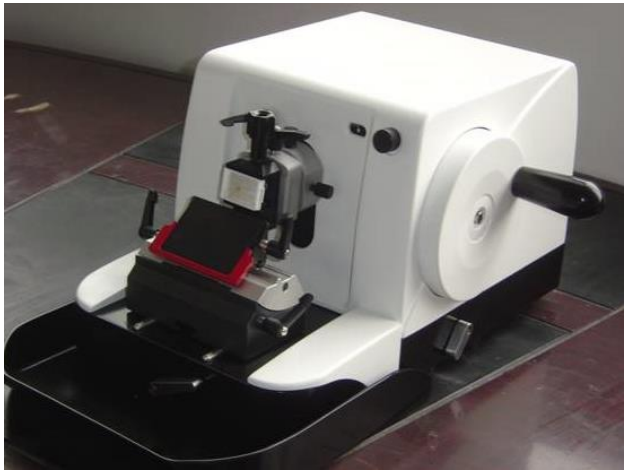
Histologické metody studia buněk a tkání 2

Fixace (denaturace)

- **Organická rozpouštědla** (etanol, metanol, aceton,…)
- **Aldehydy** (form-, paraform-, glutar-aldehyd, …)
- **Organické kyseliny** (octová, pikrová, …)
- **Soli těžkých kovů** (rtuť, chrom, osmium, …)

Zalití + Krájení (řezy)

- **Parafinový vosk**
- **Celloidin** (=nitrát celulózy)
- **Durcupan** (syntetický polymer)
- **LR White** (syntetický polymer)
- **jiné**



„Barvení"

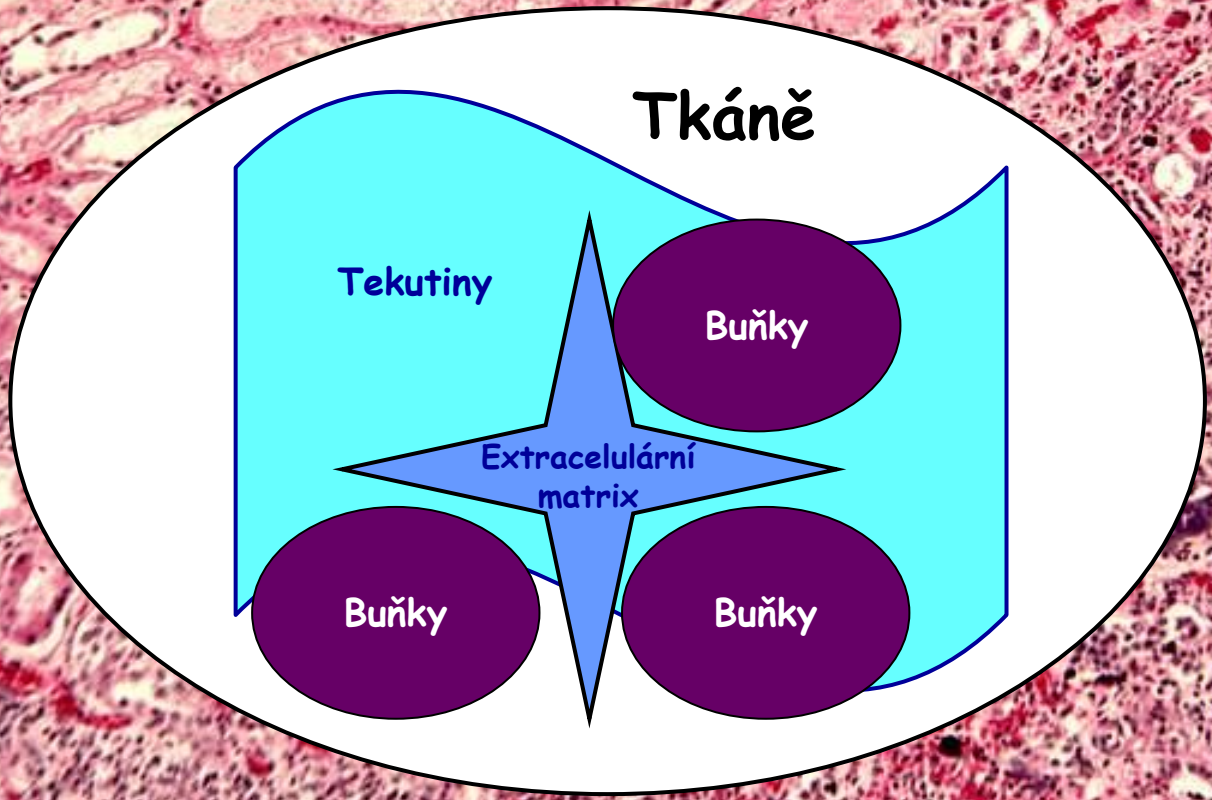
Chemická přehledná barviva (H+E, Azan, van Gieson, …)

Histochemické reakce (průkaz proteinů/enzymů, lipidů, cukrů, …)

Imunochemické reakce (značené protilátky)

Těžké kovy (pro TEM – soli uranu, olova, wolframu, …)

Pochopení komplexních systémů musí stát na pochopení struktury a funkce jejich součástí



Tekutiny
- Intersticiální tekutina
- Plazma (krev)
- Lymfa (v lymfatických cévách)
- Cerebrospinální mok
- Intracelulární tekutina (cytosol)

Vše je produktem buněk !

Živé organismy jsou tvořeny buňkami

Dlouhá cesta k tomuto odhalení:

Robert Hooke
1665

Poprvé viděl buňky korku - cell

Antonie van Leeuwenhoek
1678

Poprvé uviděl mikroskopické organismy
(bakterie, prvoky)

1839

Matthias Schleiden

Theodor Schwann

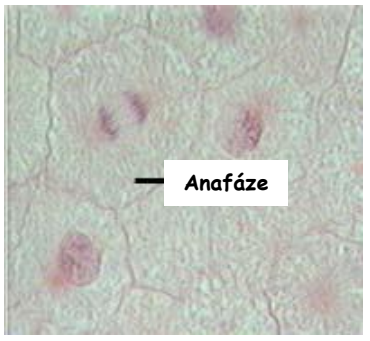
Všechny organismy jsou tvořeny jednou nebo více buňkami

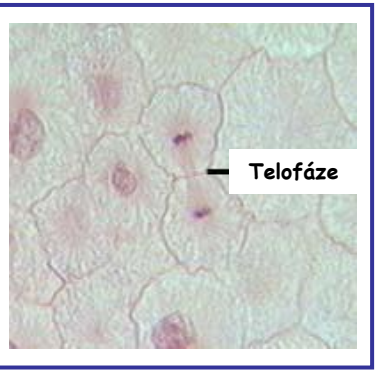
Rudolph Virchow
1855

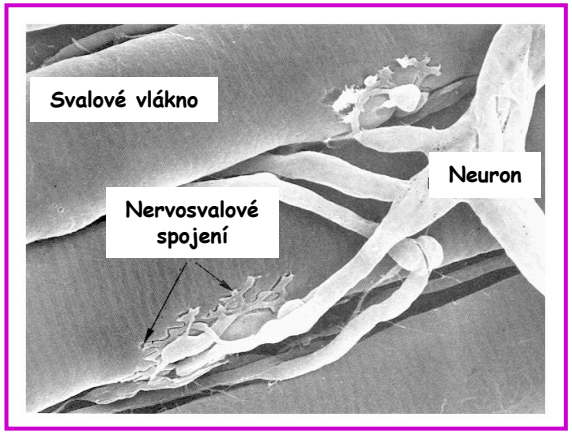
Buňka může vzniknout pouze z již existující buňky
„Omnis cellula e cellula"

Současná buněčná teorie – 6 principů na kterých stojí

- Buňka je nejmenší strukturní a funkční jednotka schopná životních procesů
- Funkce každé buňky je dána její specifickou strukturou
- Buňky jsou stavební jednotky všech mnohobuněčných organismů, všechny funkce v organismu jsou plněny buňkami
- Struktura a funkce všech organizmů je závislá na strukturálních a funkčních vlastnostech buněk, kterými jsou tvořeny
- Všechny nové buňky vznikají z buněk již existujících
- Díky kontinuitě života na zemi jsou buňky všech organizmů principiálně stejné (univerzální genetický kód a jeho exprese)



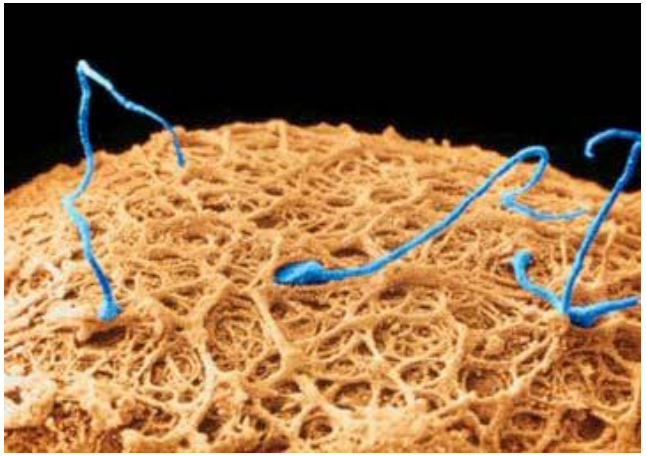


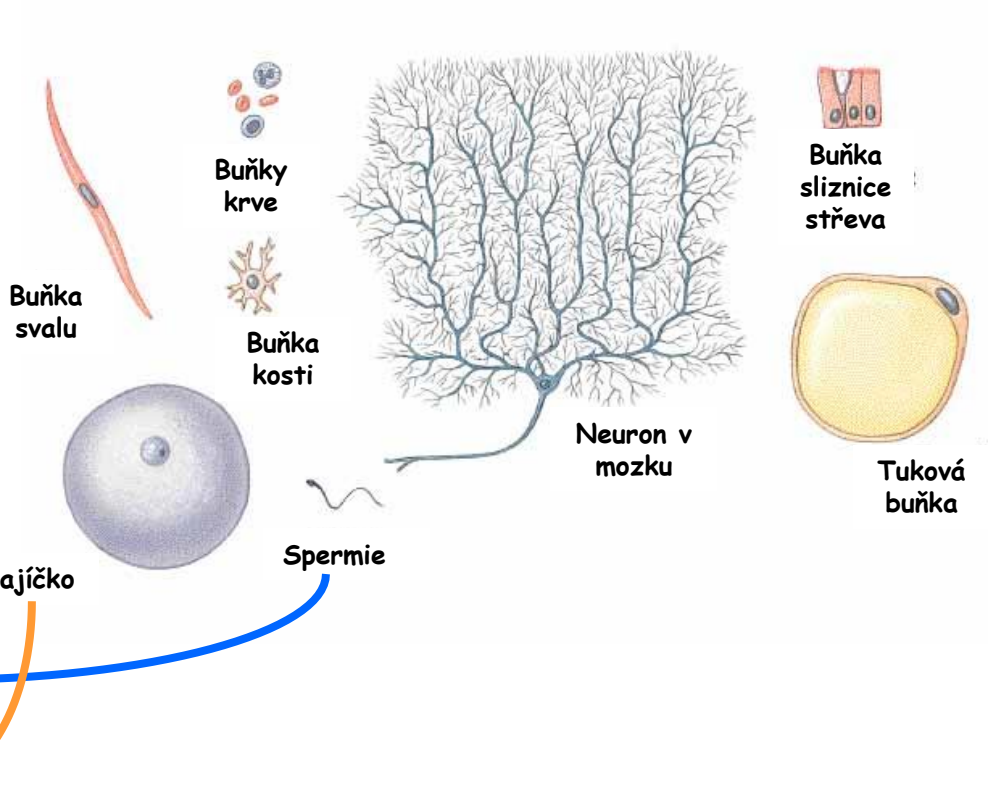


Přes jednotné organizační schéma,
je typickou vlastností eukaryontních buněk
jejich strukturální a funkční diverzita

Také buňky člověka jsou strukturálně a funkčně extrémně rozmanité

Tato různorodost je předpokladem pro schopnost buněk plnit v organismu člověka specializované funkce



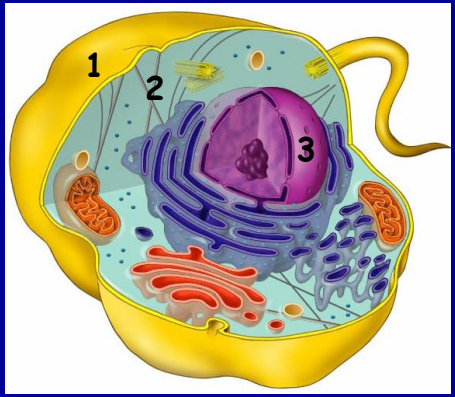


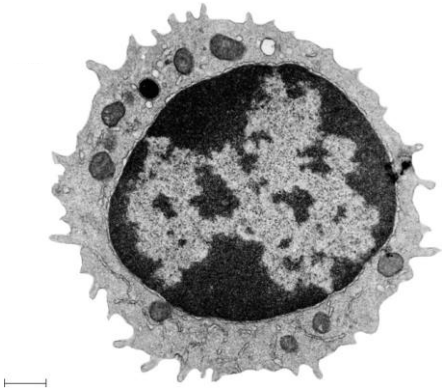
Žádná buňka není zcela stejná jako buňky ostatní, všechny buňky ale mají společné strukturální a funkční znaky.

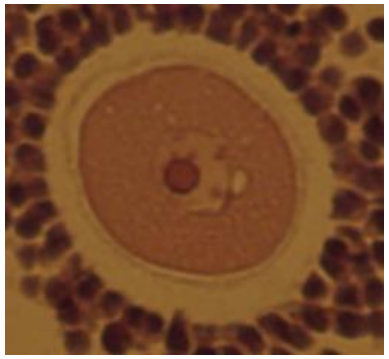
Ne všechny buňky obsahují všechny komponenty, o kterých budeme mluvit !

Buňky mají 3 hlavní součásti:

1. Plazmatickou membránu
2. Cytoplazmu
3. Jádro (eukaryontní b.)







Organizace buňky je postavena na KOMPARTMENTALIZACI

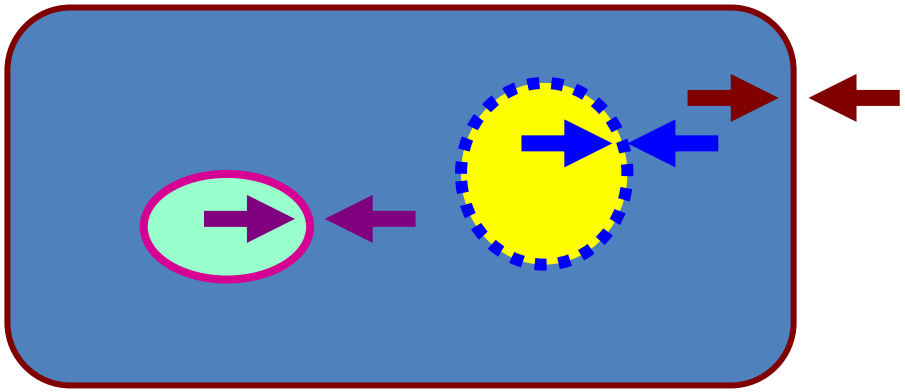
Specializované funkce se mohou plnit v různých sektorech buňky

Membrány tvoří hranice mezi jednotlivými kompartmenty

Unikátní proteinové a lipidové komponenty a unikátní funkce

Unikátní kontrola pohybu molekul

Unikátní složení obklopeného prostoru



Kompartmenty & Membrány

Mnoho malých kompartmentů je lepší

Větší plocha membrány na obklopený objem → Více plochy pro:
- **regulaci**
- **výměnu živin**
- **odstranění odpadních látek**

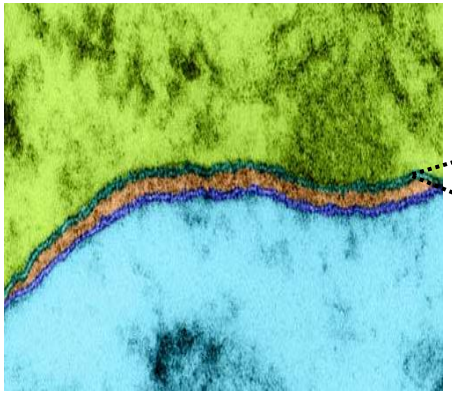
Plocha povrchu je proporcionální se **čtvercem poloměru** (r^2).
Objem je proporcionální se **třetí mocninou poloměru** (r^3).

Zmnožení X Redukce vybraných kompartmentů → **Specializace buněk** pro různé funkce

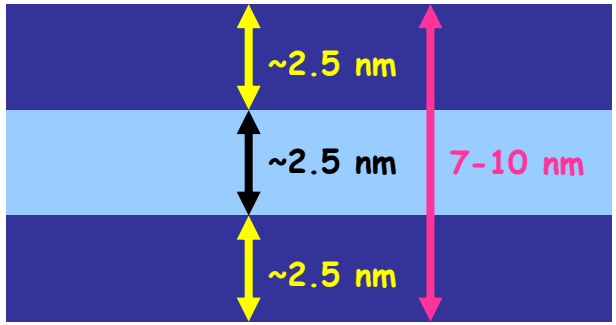
Diferenciace buněk

Drsné ER v sekrečních buňkách
Mitochondrie v buňkách srdeční svaloviny

Struktura biologické membrány 1



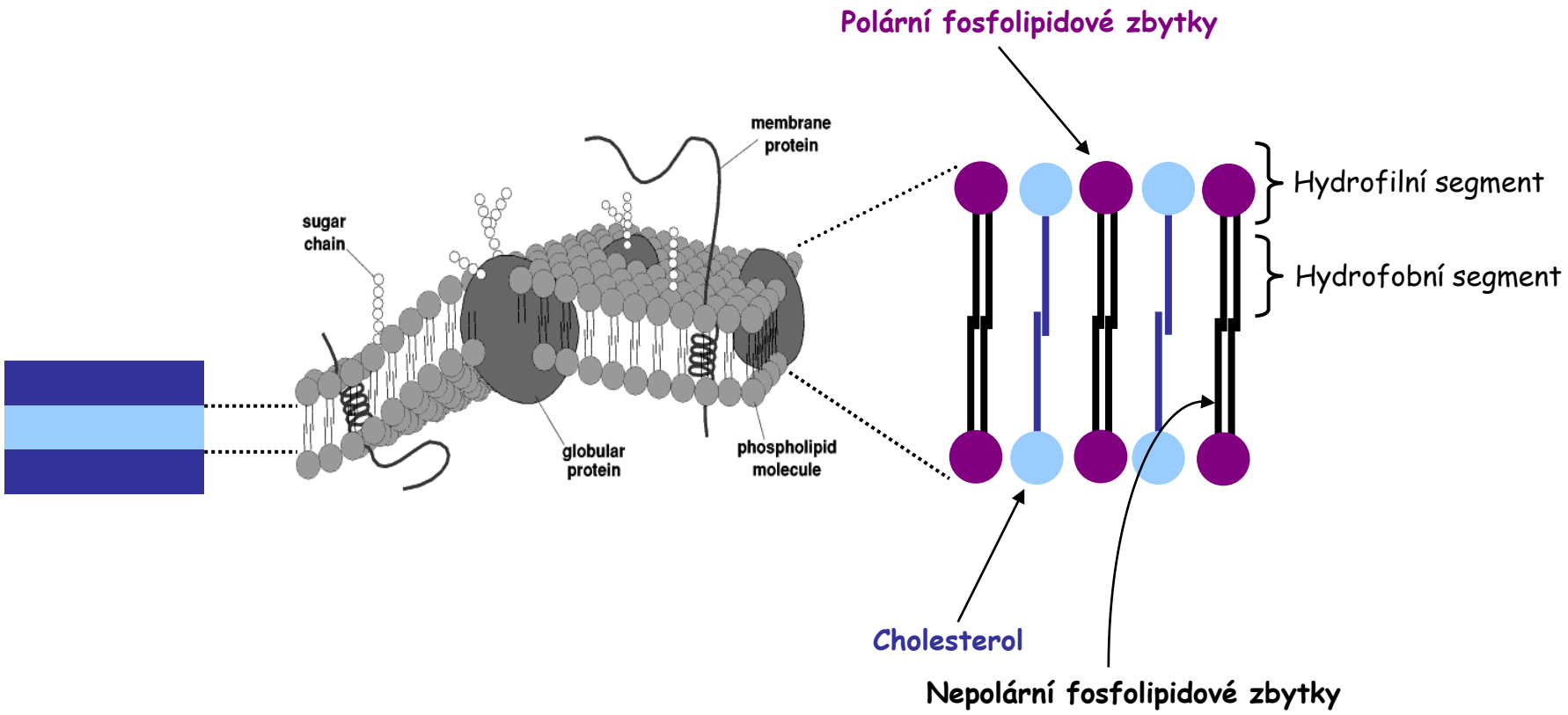
Buněčné membrány viděné elektronovým mikroskopem
(pseudokolorováno)



Membránová jednotka
společná všem membránám

Struktura biologické membrány 2

Fluidní mosaika – Dvojvrstva lipidů s mobilními globulárními proteiny



Struktura biologické membrány 3

Membránové lipidy

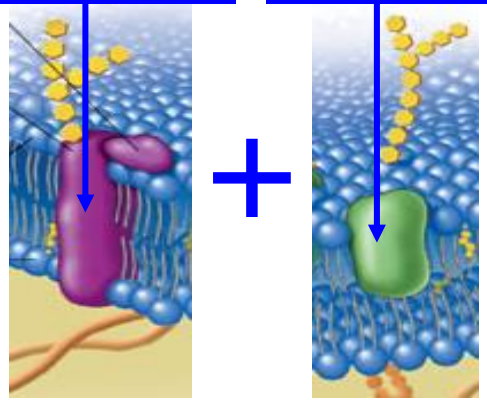
Představují 90-99% molekul v membráně (v počtech).

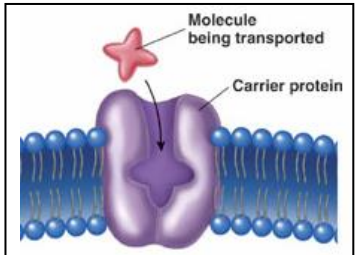
- **Fosfolipidy** - 75%
- **Cholesterol** - 20%
- **Glykolipidy** - 5% - pouze cytoplazmatická membrána - GLYCOCALYX

Membránové proteiny

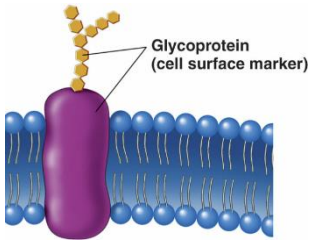
Představují 1-10% všech molekul, ale 50% hmotnosti díky jejich velikosti.

Integrální + **Periferní**

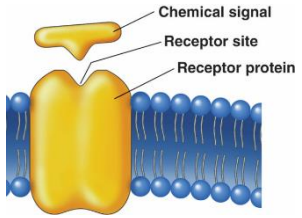




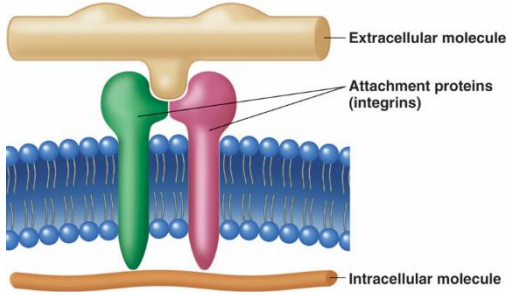
Transport



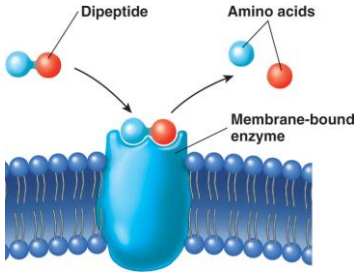
Identita buněk



Přenos signálů



Adheze buněk



Enzymatická aktivita

Organely

Specializované vnitřní struktury se specializovanými funkcemi

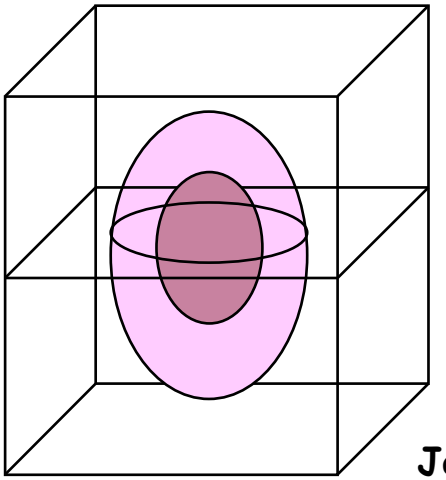
Ohraničené membránou

- Endoplasmatické retikulum
- Golgiho aparát
- Lyzosomy
- Endosomy
- Peroxisomy
- Mitochondrie

Bez membrány

- Ribosomy
- Centrosomy
- Centrioly
- Bazální tělíska

Vztah mezi strukturou buňky a její specifickou funkcí
Např.: potřeba hodně energie → hojnost mitochondrií

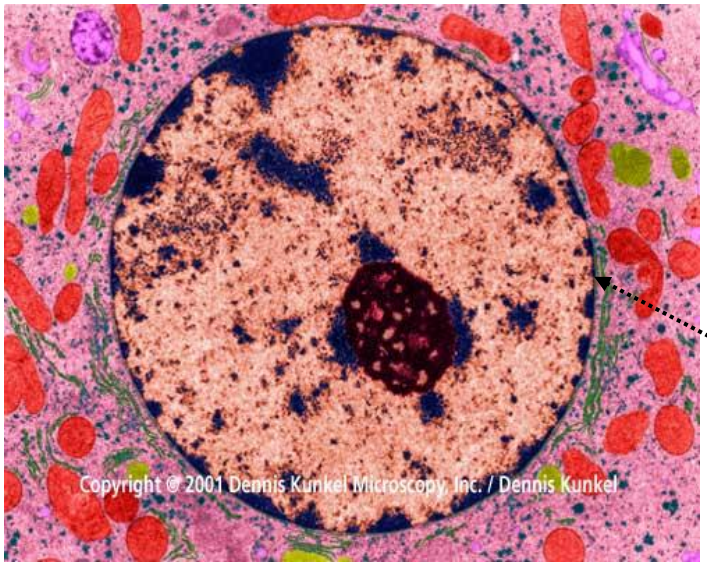


Jádro 1
obalem ohraničená struktura

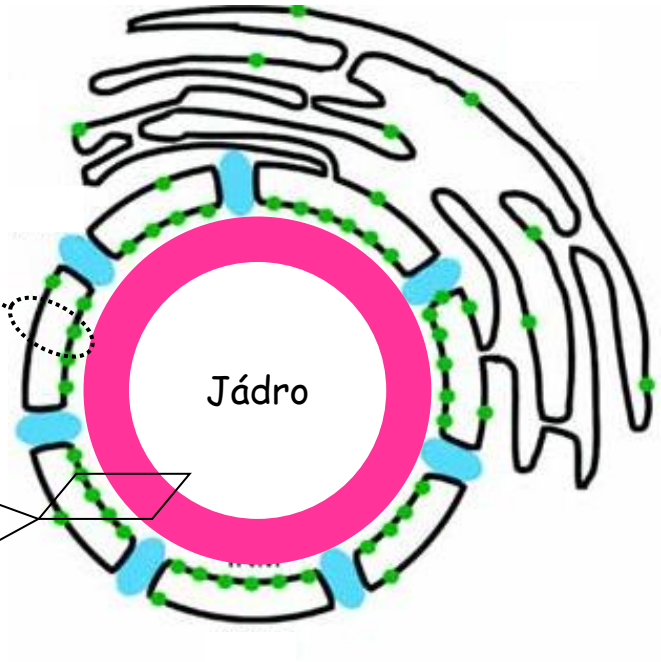
Nejčastěji:

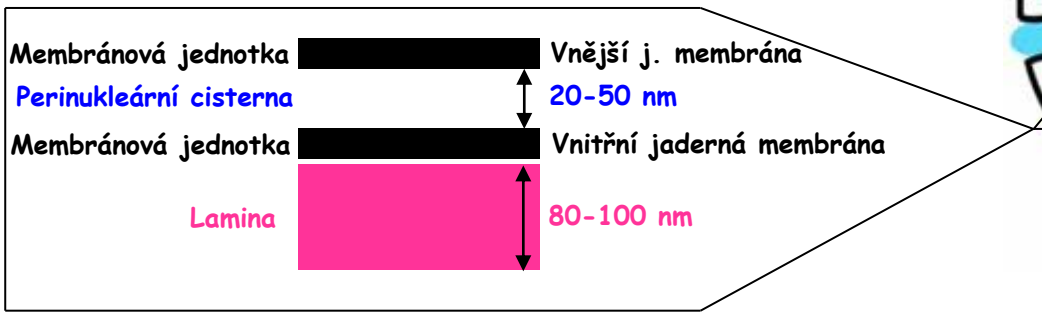
- Sférické (5-10 μm) (lobulární, prohnuté, diskovité,…)
- Uloženo centrálně
- Jedno v buňce (osteoklast více, erytrocyt žádné)

Jádro jaterní buňky

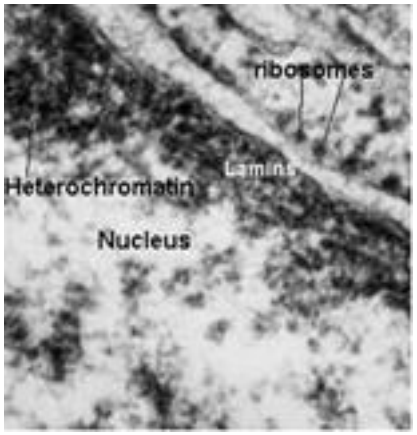


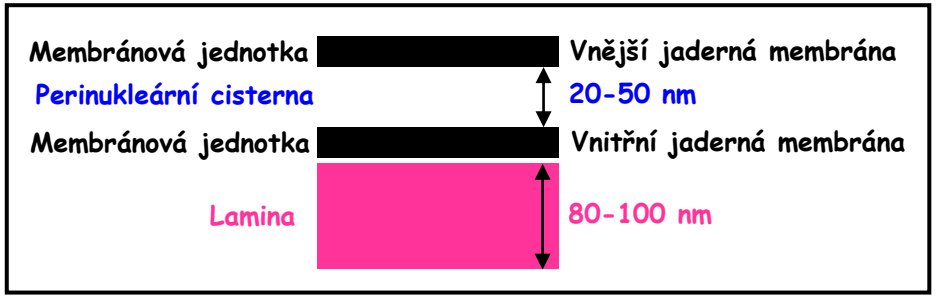
Jaderný obal

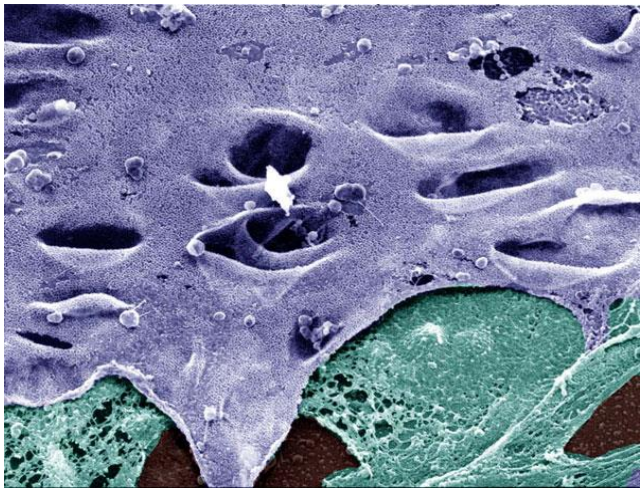




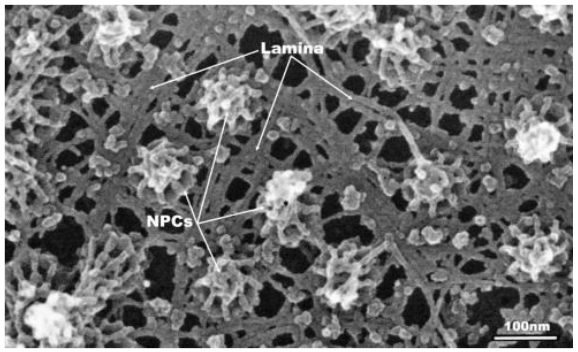
Jádro 2
Jaderný obal - pokračování



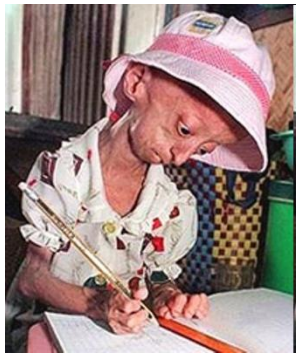




Laminy:
- Intermediární filamenta - proteiny (A, B, C)
- Tvoří síť na vnitřní straně vnitřní jad. membrány, pronikají i do nukleoplazmy
- Udržují pevnost a architekturu jádra
- Ukotvují chromatin
- Regulují replikaci DNA a tranksripci rRNA
- Účastní se regulace apoptózy



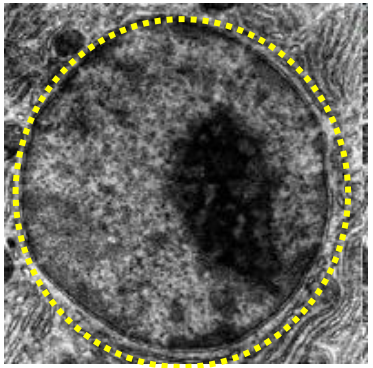
Laminopatie
- Lidské choroby (nejméně 13 známých)
- Mutace v genech pro laminy (popsáno asi 200 mutací)
- Deregulace exprese genů
- Předčasné stárnutí

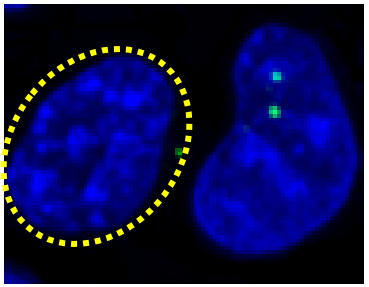


Hutchinson-Gilford progerie

Vzácná - 1-4 na 8 milionů porodů
Missense mutace v laminu typu A

Jádro 4
Chromatin





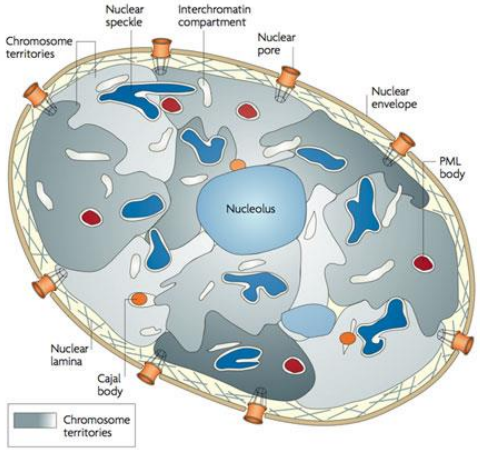
Interfázové jádro

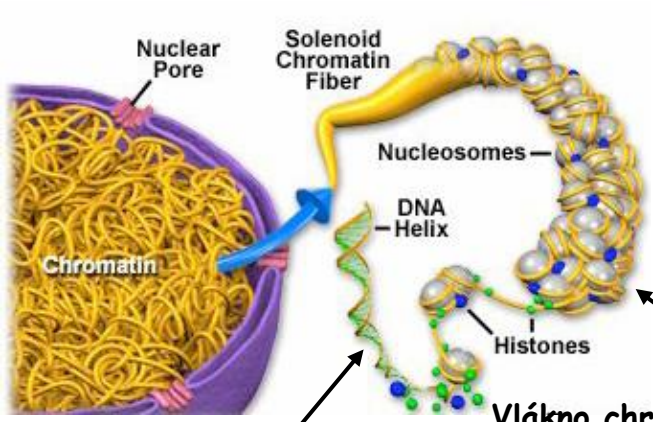
Heterochromatin

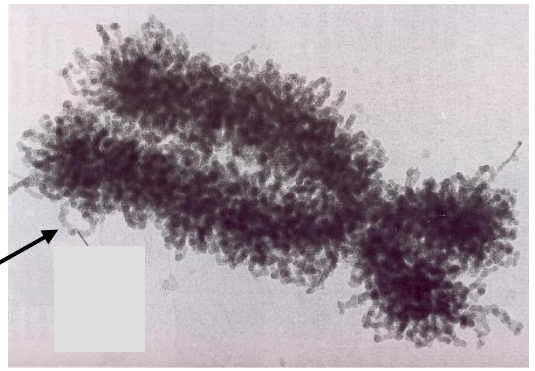
Feulgen positivní – tmavé ve světelném mikr.
Tmavé/denzní granula v TEM
Transkripčně inaktivní

Euchromatin

Světlejší ve světelném mikroskopu
Relaxované chromosomy
Transkripčně aktivní

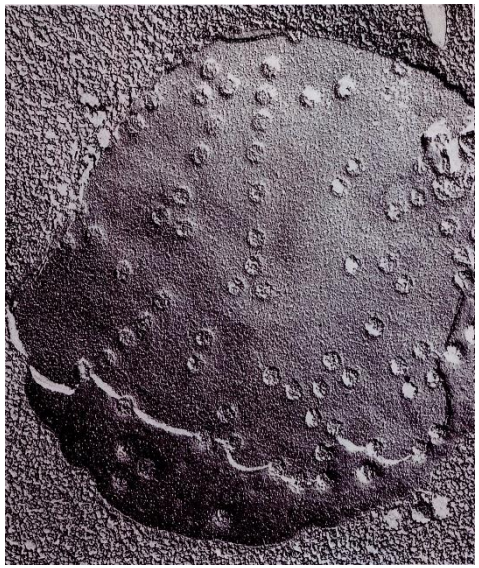




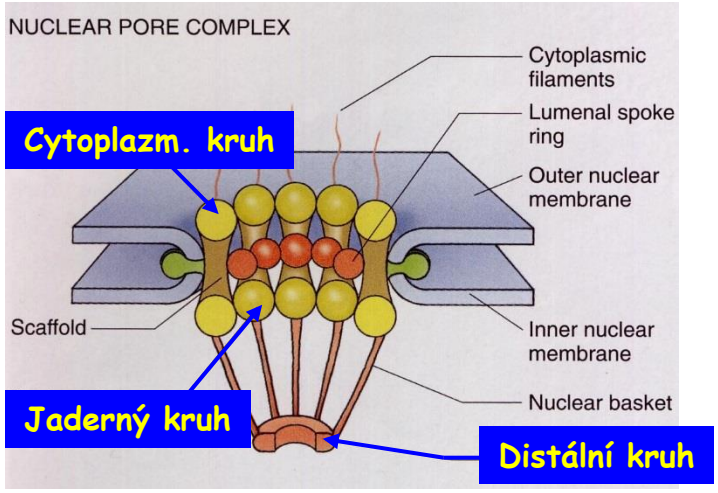


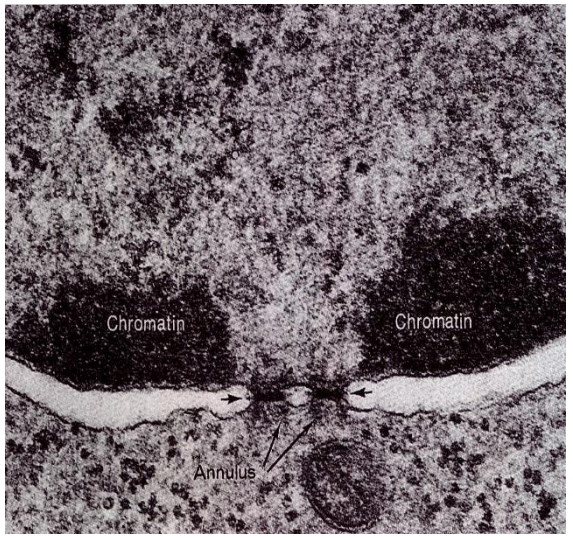
2 nm
Dvojšroubovice DNA

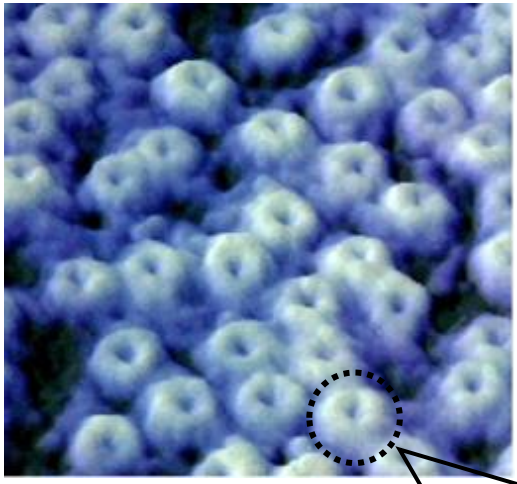
30 nm
Vlákno chromatinu – seskládané nukleosomy



Jádro 3
Komplex jaderného póru







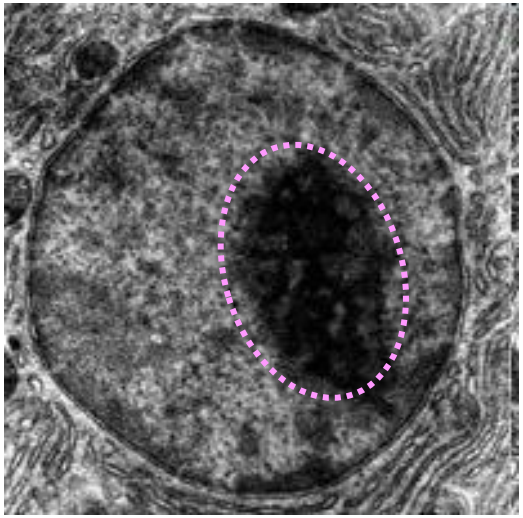
Průměr ~ 100 – 125 nm

Tři kruhy (každý 8 podjednotek)

Vnitřní vláknitý košík

Transport jadernými póry
(Nukleocytoplazmatický přesun)

- Proteiny, RNA, podjednotky ribosomů
- Oboustranný
- Vyžaduje jaderné lokalizační/exportní signály
- Podporován importiny/exportiny
- Regulován Ran GTPázami

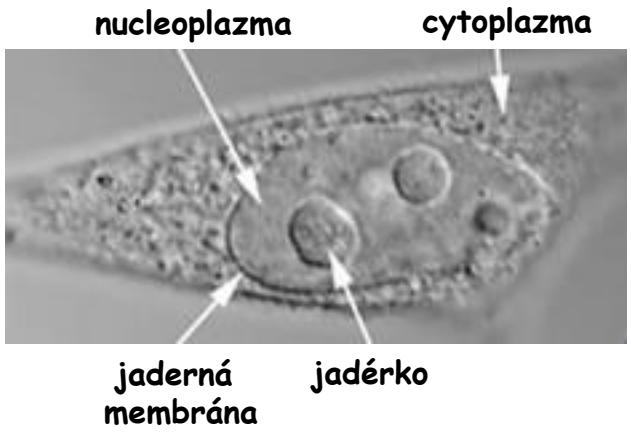


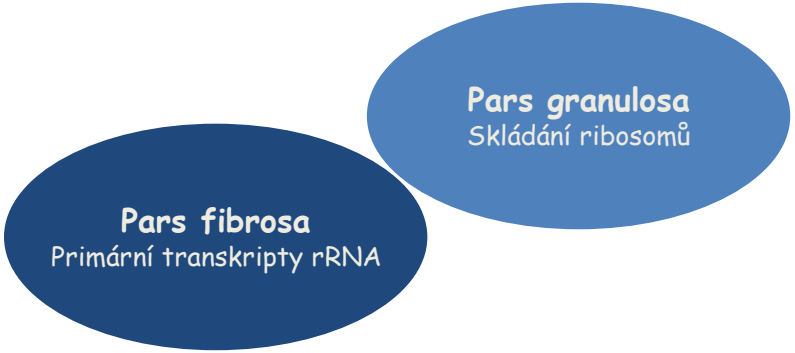
Jádro 5
Jadérko

Není ohraničeno membránou

Hlavní funkce

Syntéza RNA
Skládání ribosomů





NOR – nukleolární organizátor (na DNA)

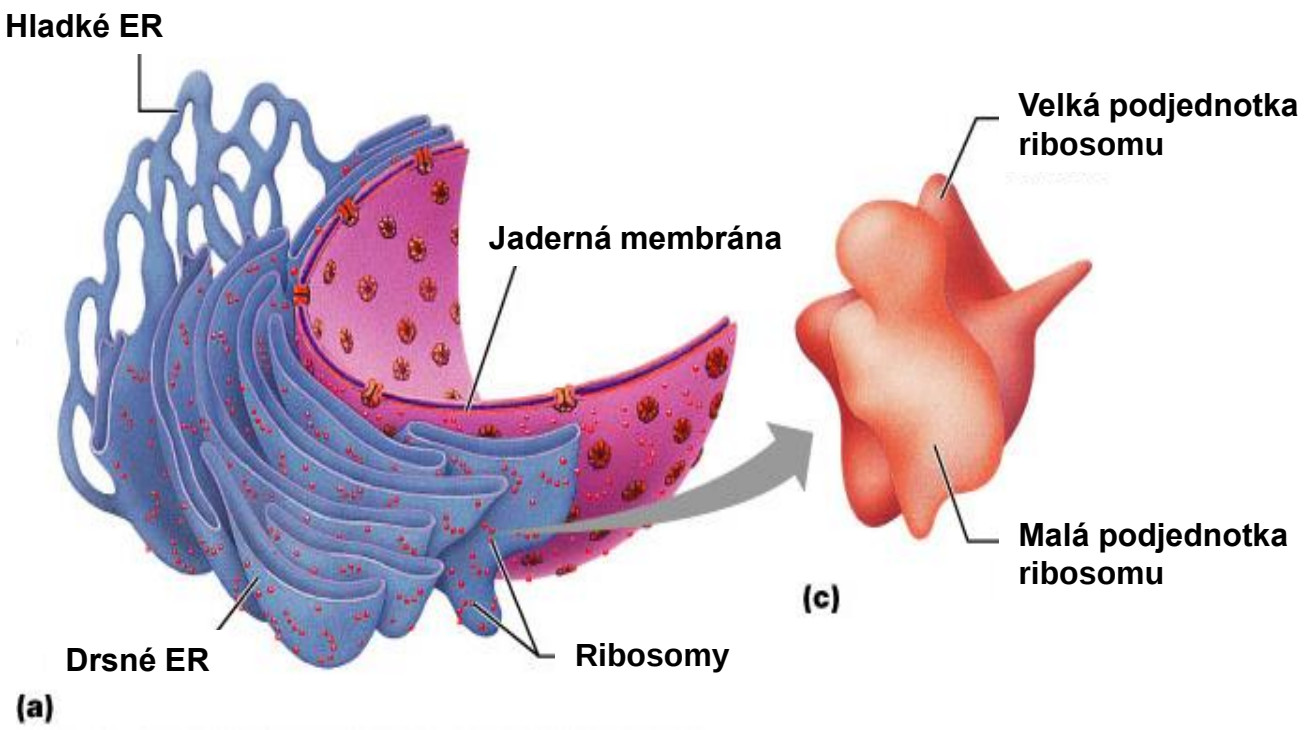
V lidských buňkách na 5-ti chomosomech
(chr. 13, 14, 15, 21, 22)

Endoplasmatické retikulum 1

„uvnitř buňky“ „síť“

Většina membrán uvnitř buňky.

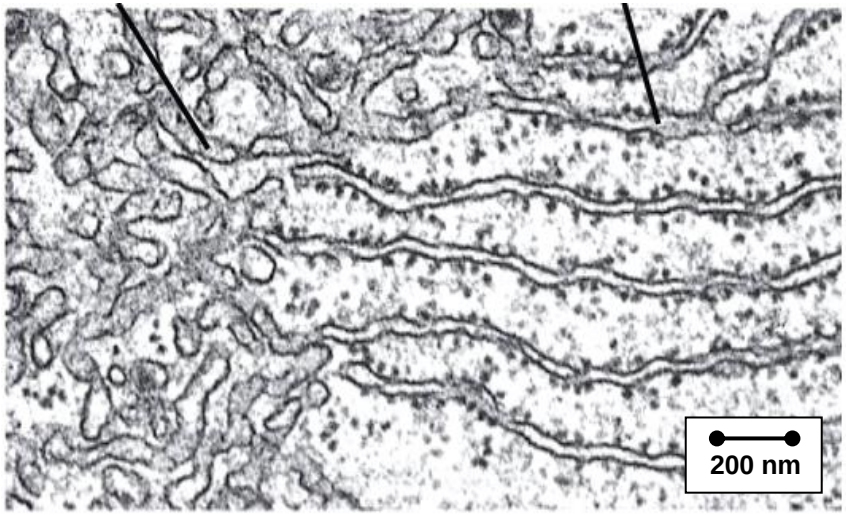
Vzájemně propojené kanálky a váčky → Cisterny

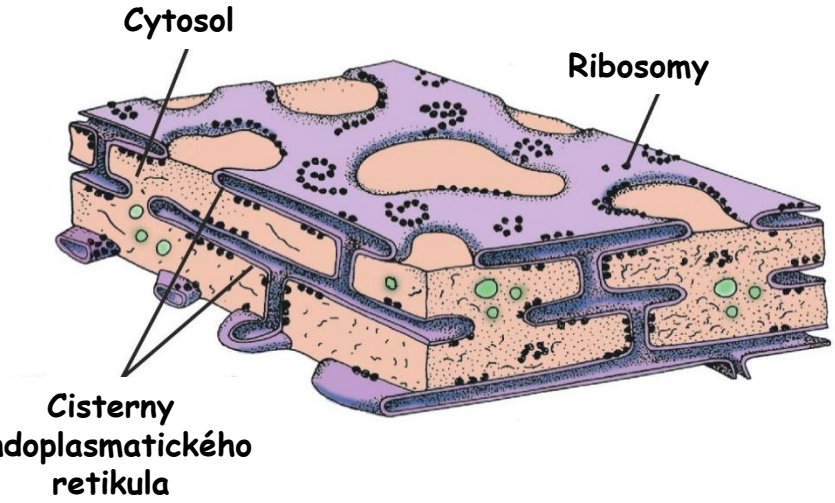


Endoplasmatické retikulum 1

Bez ribosomů → Nemá proteosyntetickou funkci !
Syntetizuje fosfolipidy a cholesterol
- **Játra** – metabolismus lipidů a cholesterolu, degradace glykogenu, detoxifikace (spolu s ledvinami)
- **Varlata** – syntéza steroidních hormonů (testosteron)
- **Buňky střeva** – absorbce, syntéza, a transport lipidů
- **Kosterní a srdeční svalovina** – ukládání a uvolňování vápníku (sarkoplasmatické retikulum)

Hladké ER **Drsné ER**





- Syntéza všech sekretovaných proteinů
- Syntéza integrálních proteinů membrán
- Modifikace proteinů

Ribosomy

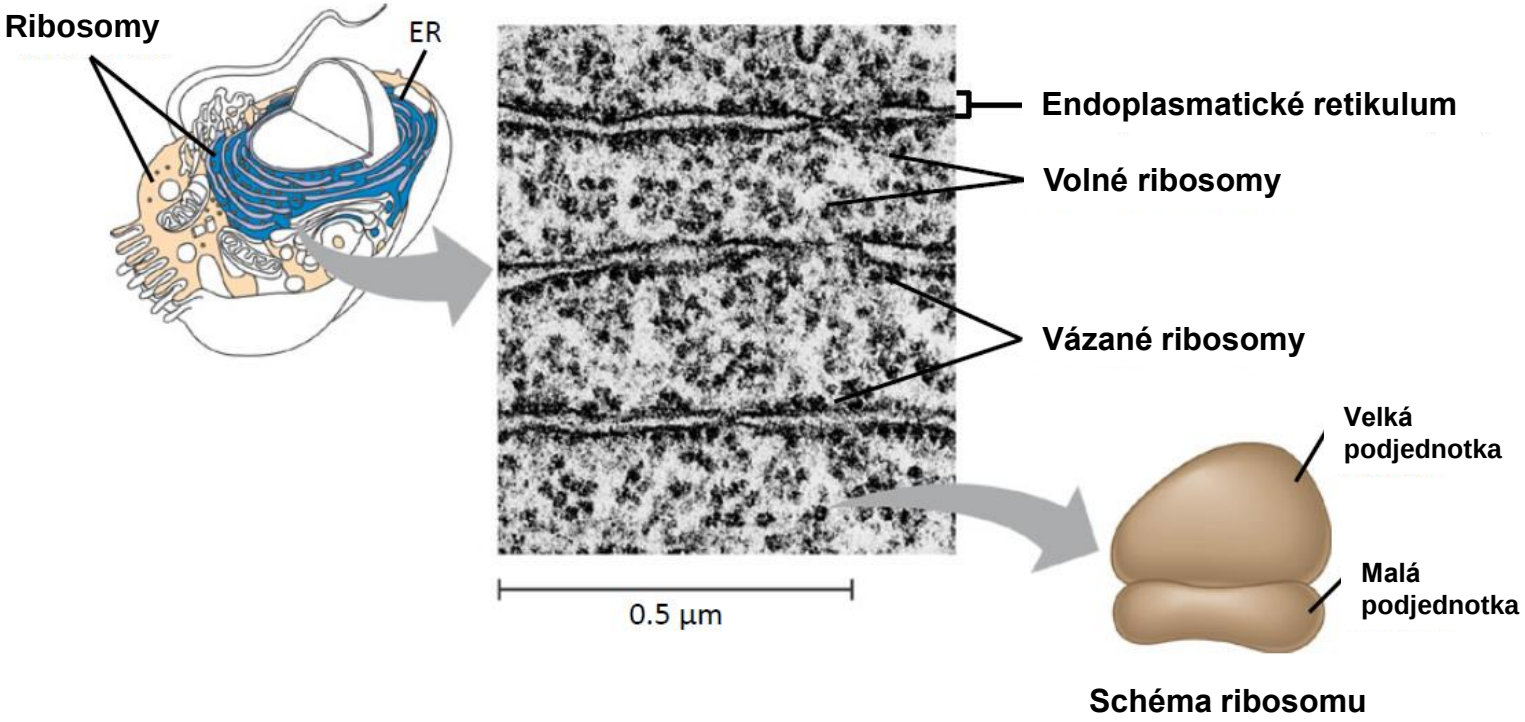
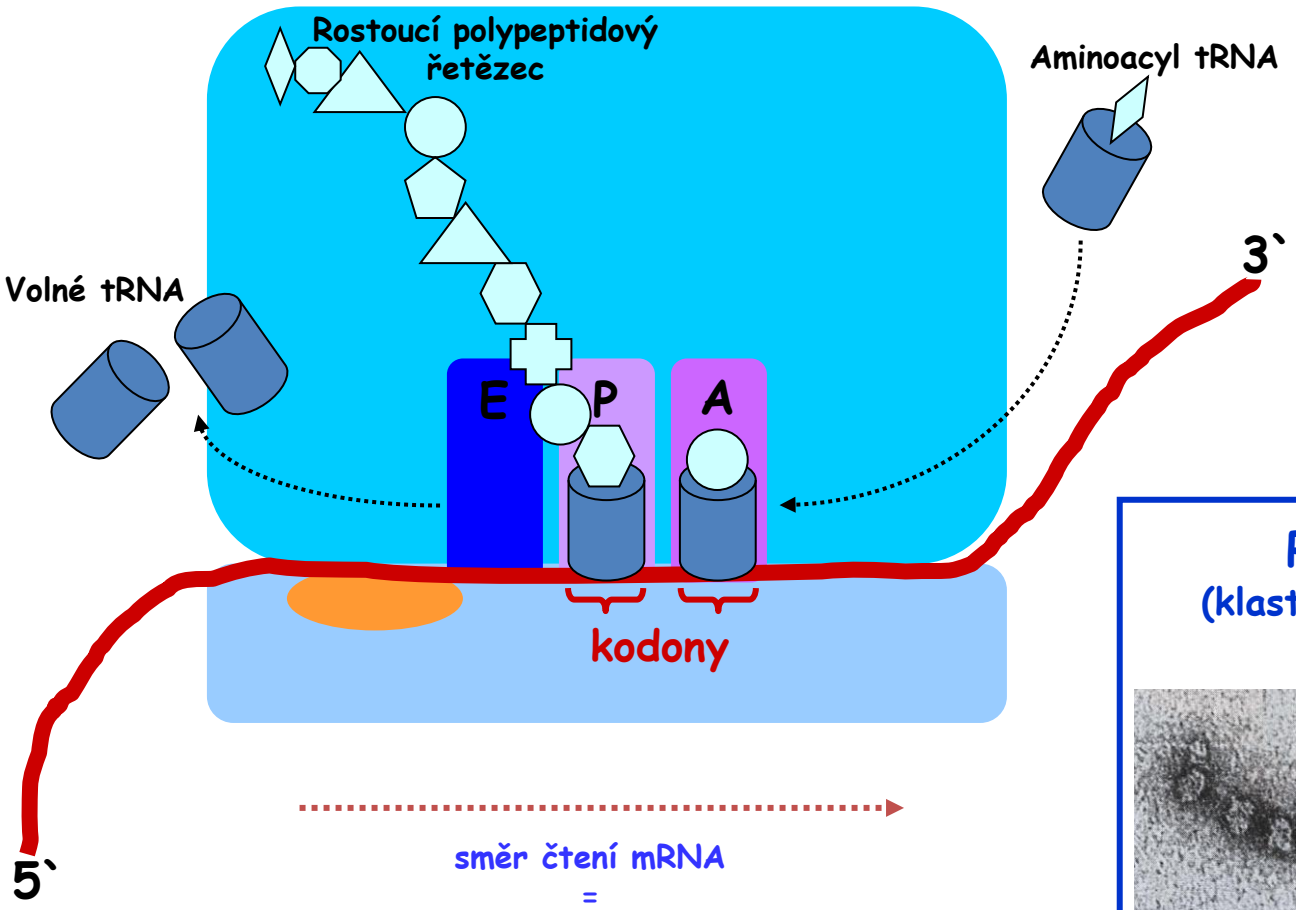


Schéma ribosomu

Ribosomy - Translace



směr čtení mRNA
=
směr pohybu ribosomů po mRNA

Začátek translace

Met-tRNA

3`UAC 5`

mRNA 5` — AUG — 3`

START kodon

Konec translace

mRNA 5` — UAG — 3`

mRNA 5` — UAA — 3`

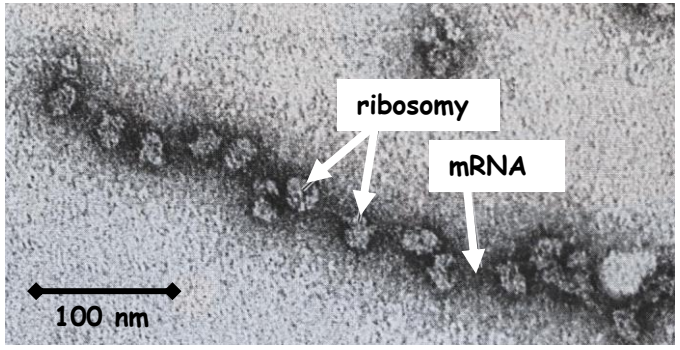
mRNA 5` — UGA — 3`

STOP kodony

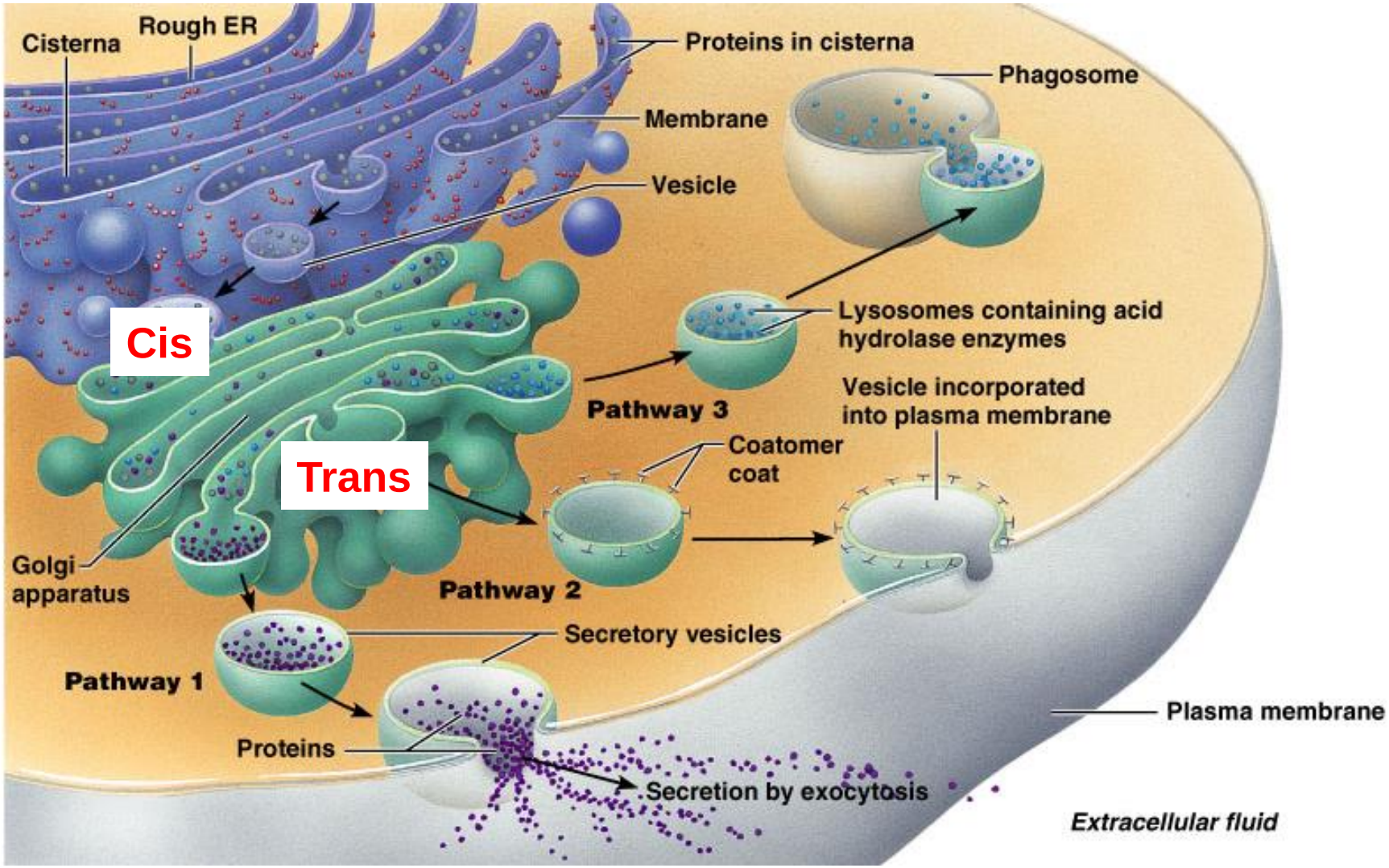
váží „uvolňující faktor"

POLYRIBOSOM

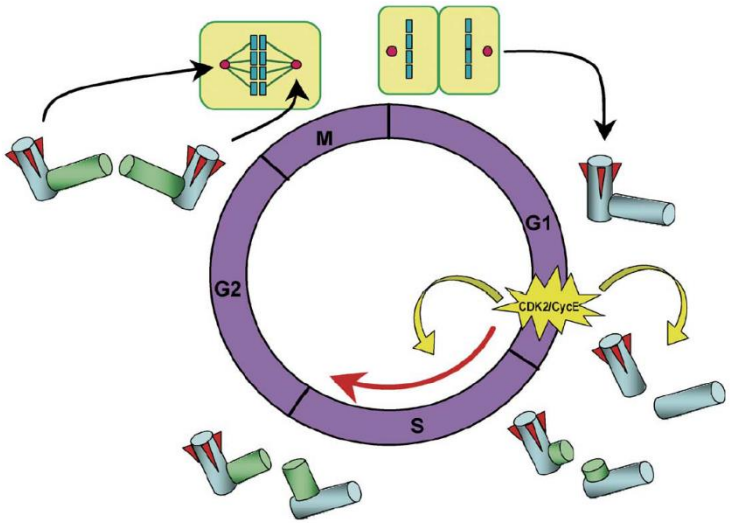
(klastr ribosomů překládající určitý úsek mRNA)

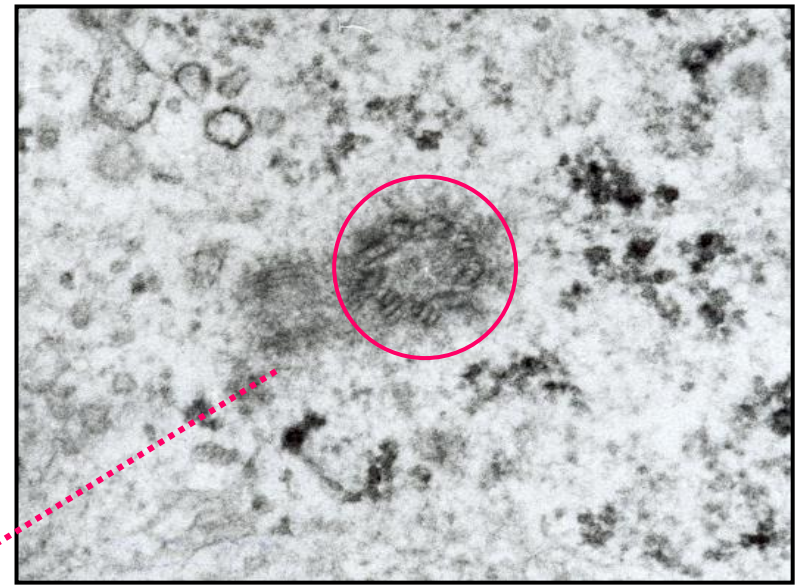


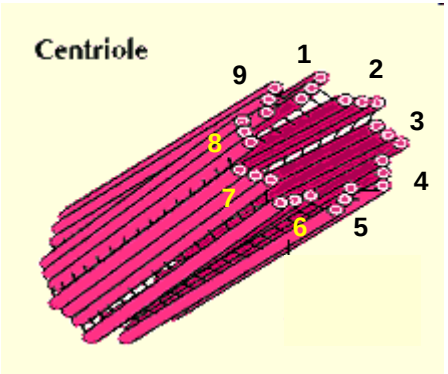
Golgiho aparát



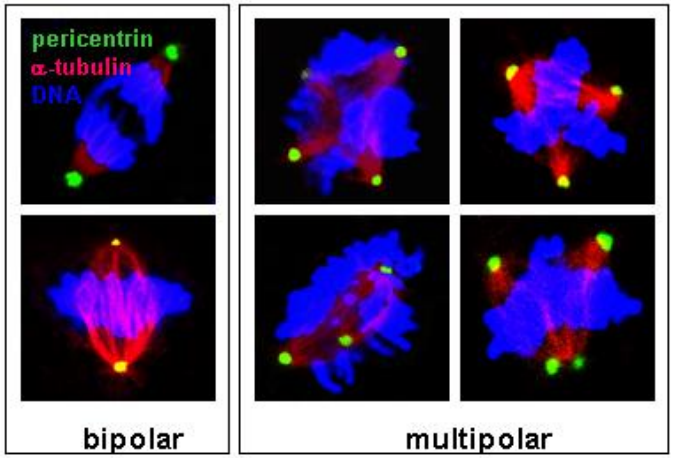
Centrosom



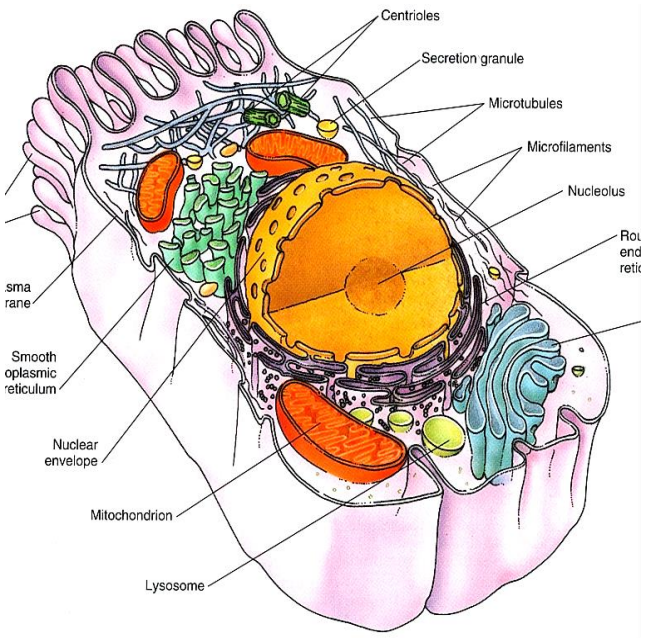


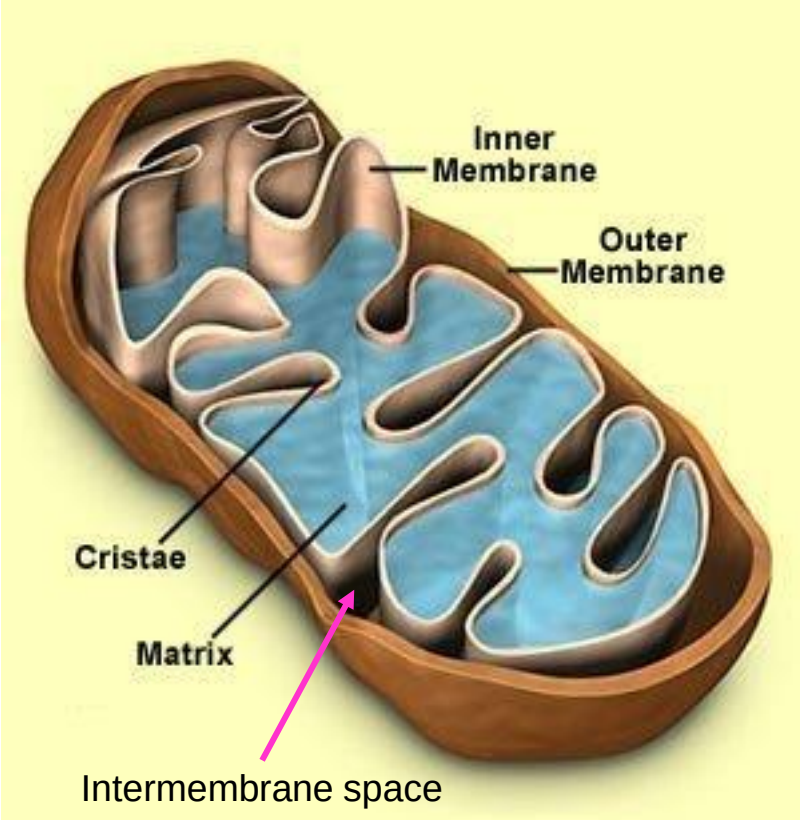


Průměr – 0.2 μm
Délka - 0.5 μm



Mitochondria 1

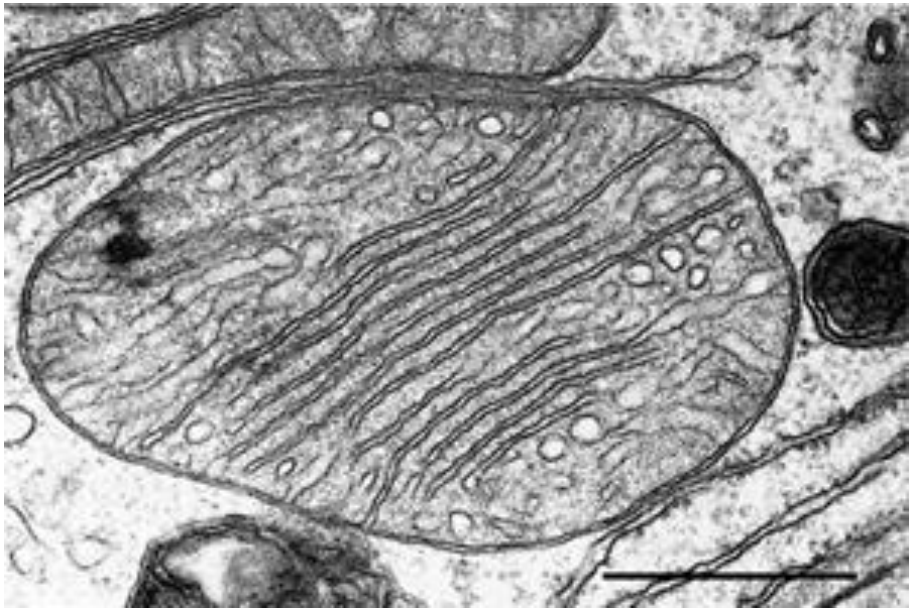




- all cells except erythrocytes
- double membrane
- diameter cca 0,5 μm
- length up to 50 (100) μm
- oxidative metabolism (glucose – ATP + CO_2 + H_20)
- cytochrome c – activation of apoptotic pathway
- origin in oocyte
- mtDNA (circular)
- brown fat thermogenesis

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

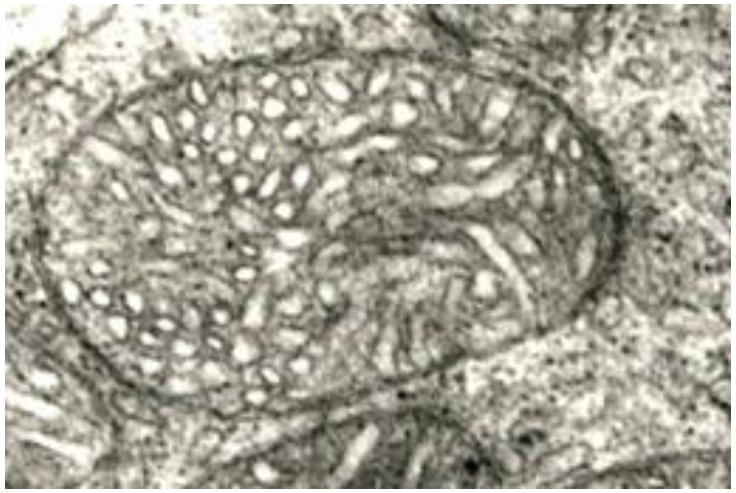
Mitochondria 2



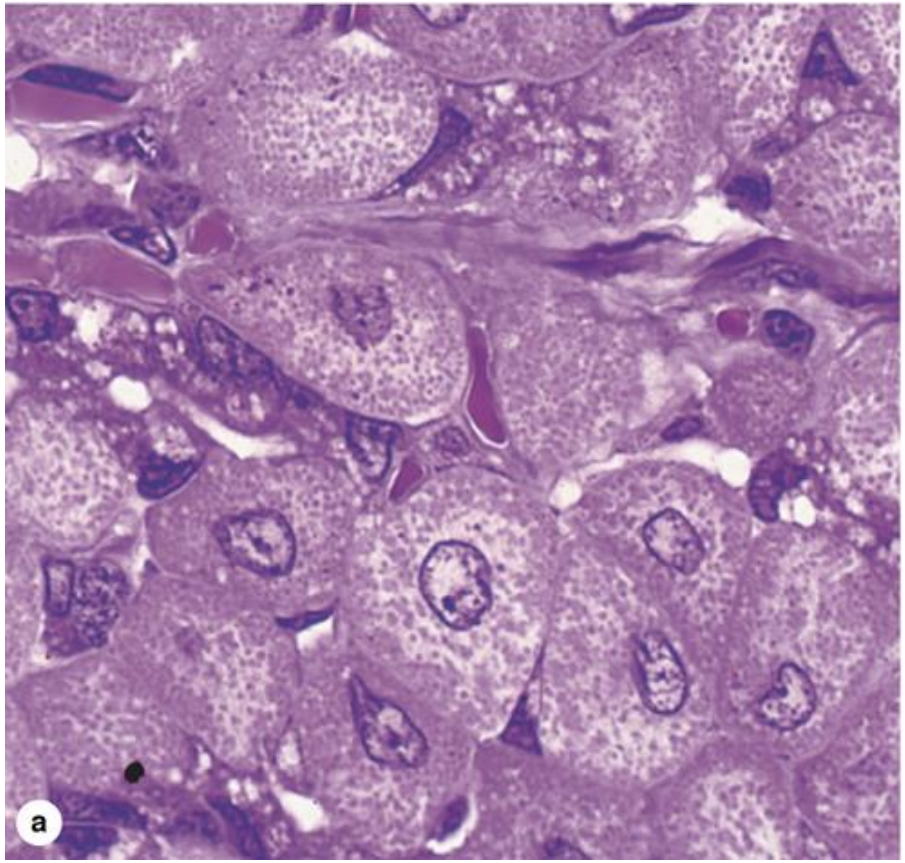
Mitochondria 3

with crists

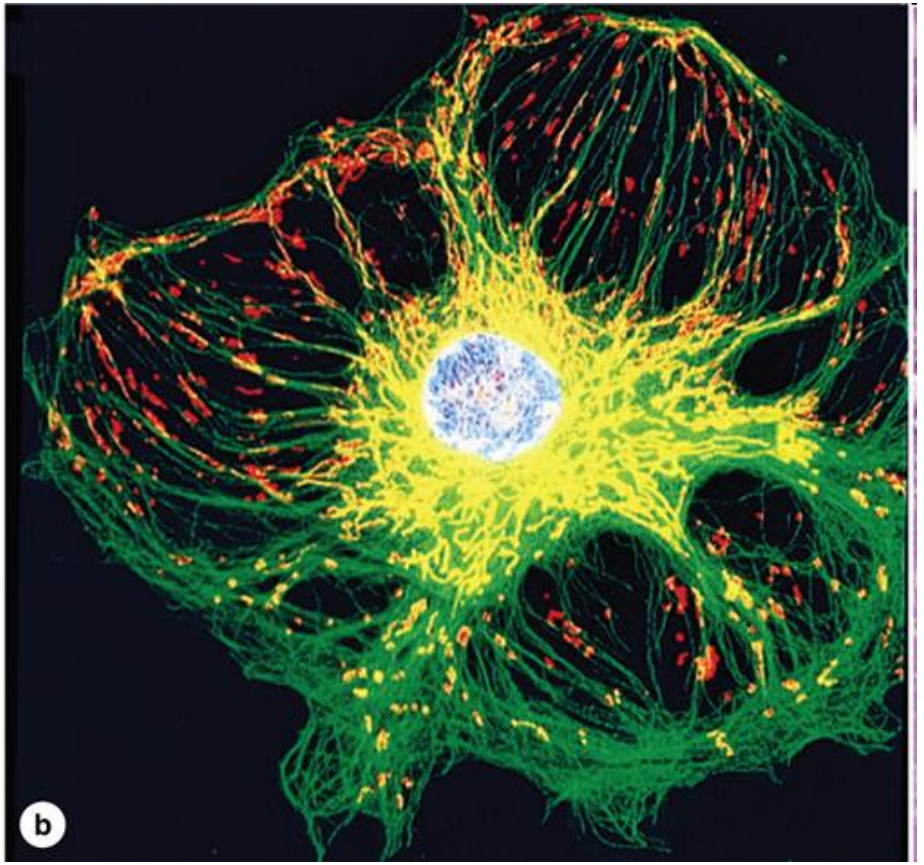
with tubuli (in steroid producing cells)



Mitochondria 4



mitochondrial eosinophilia



mitochondria
microtubuli

Lysosomes 1

endosome-lysosome system

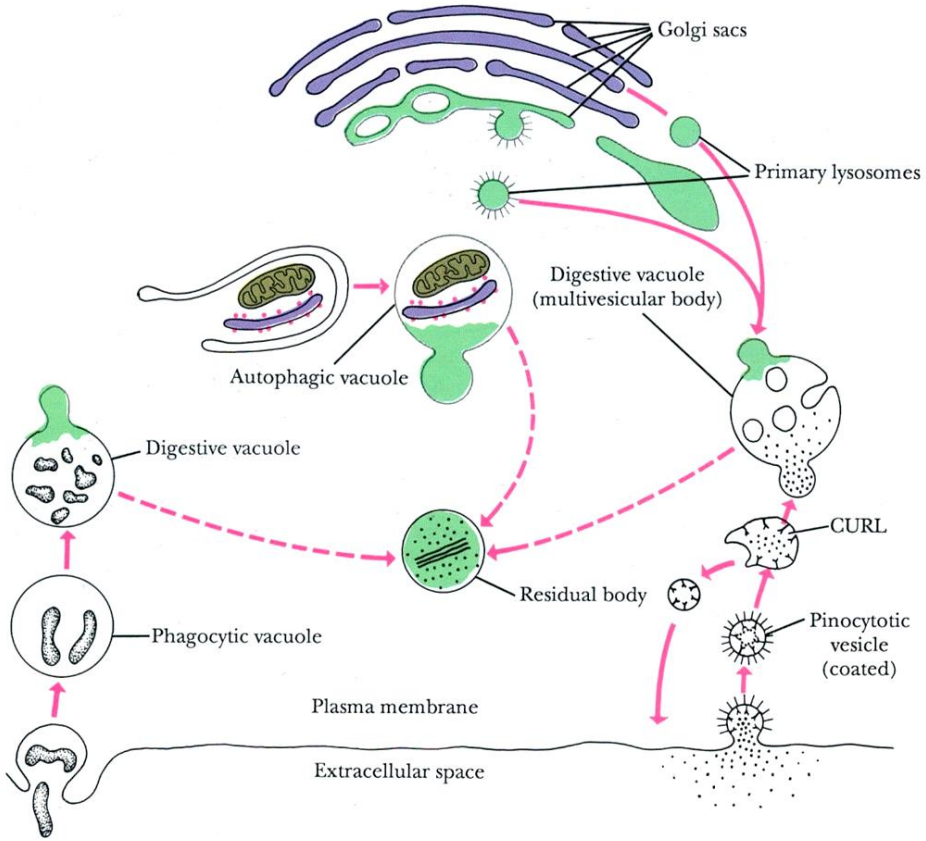
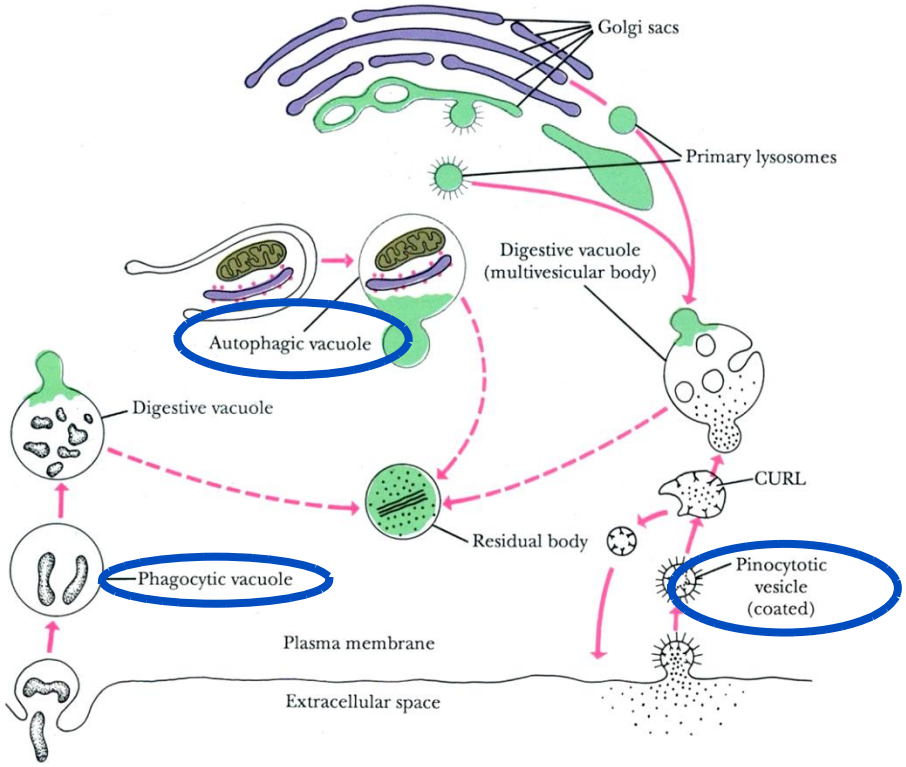


Figure 2.17. Origins of primarily lysosomes from the Golgi and trans-Golgi network. Primary lysosomes fuse with and discharge hydrolytic enzymes into autophagic, pinocytotic (or endosome), and phagocytic vacuoles to form secondary lysosomes (digestive vacuoles). Residual bodies contain undigested residue.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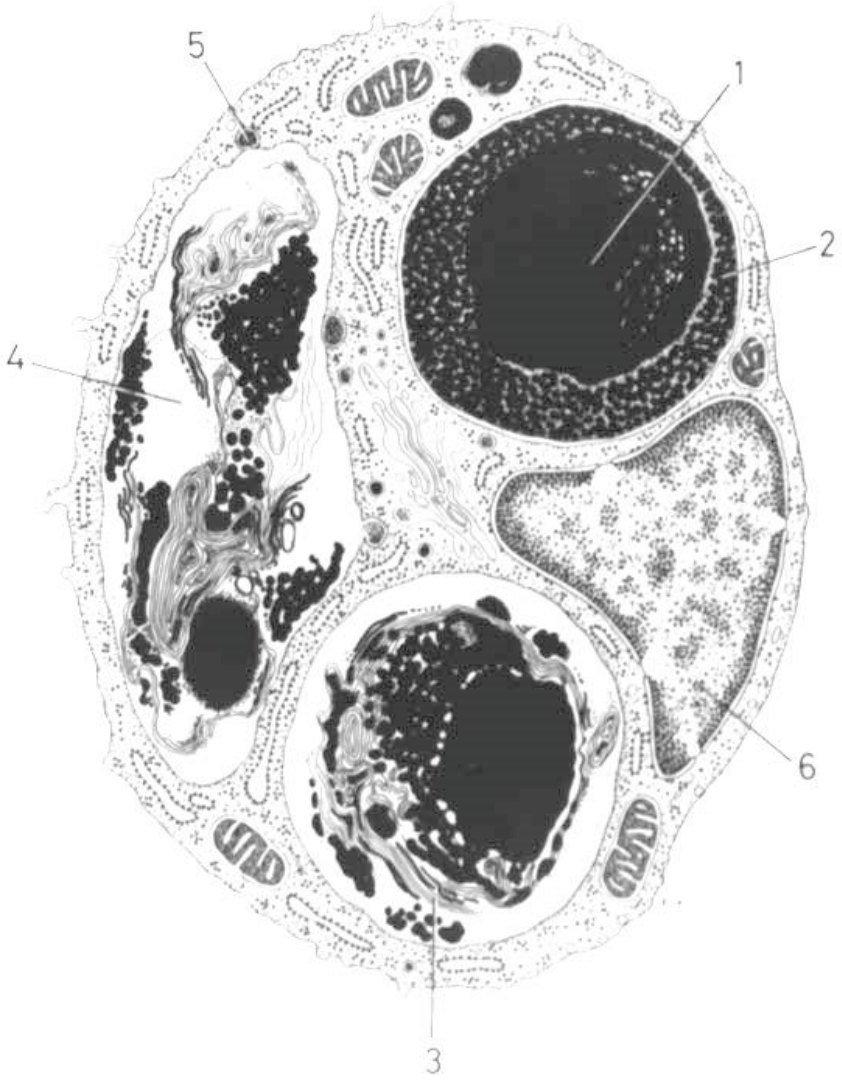
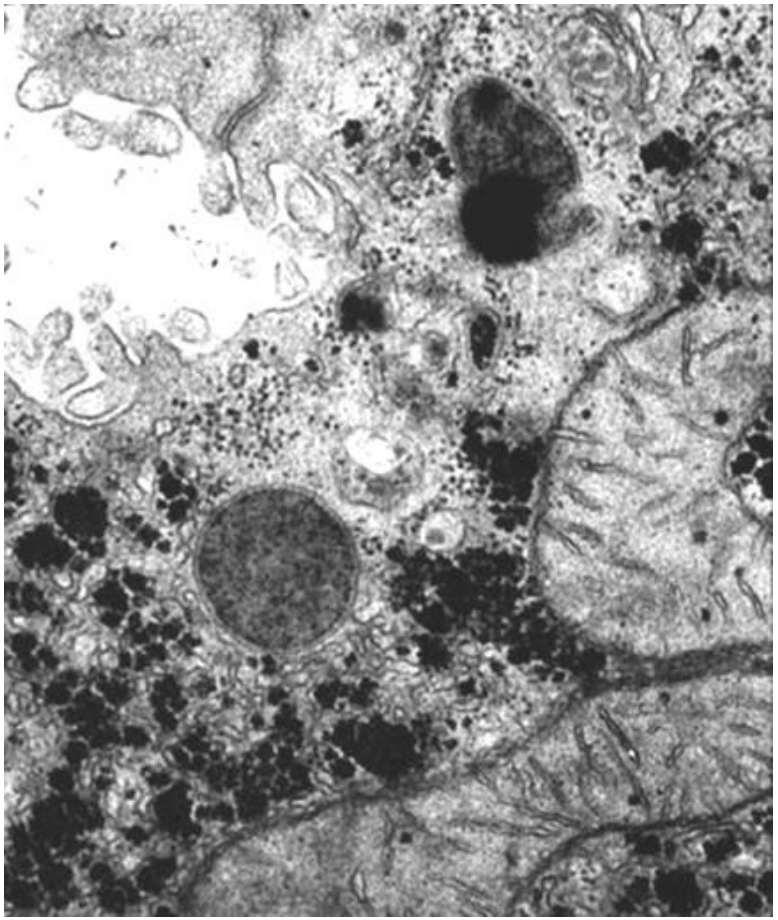
- primary lysosomes
- secondary lysosomes (fagolysosomes)
- residual bodies (lipofuscin)

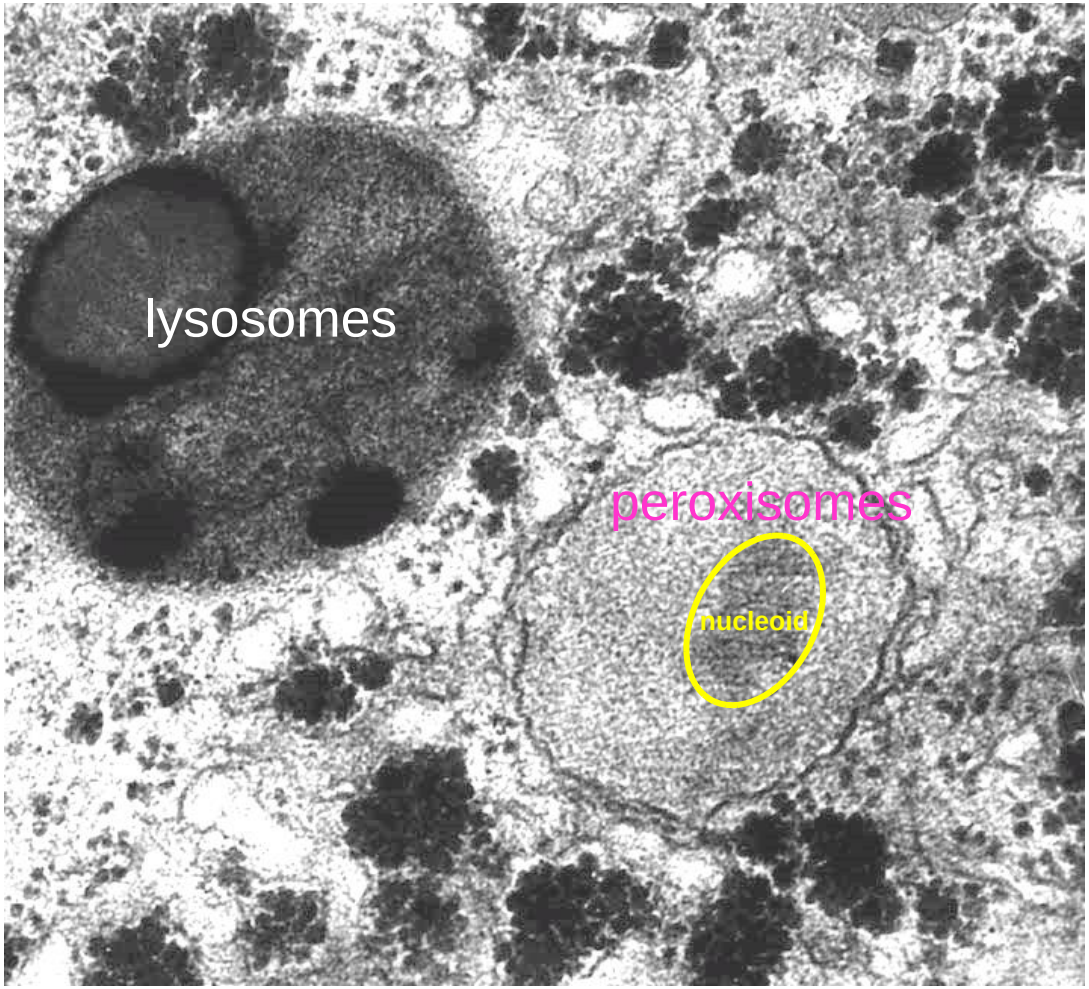
Lysosomes 3

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

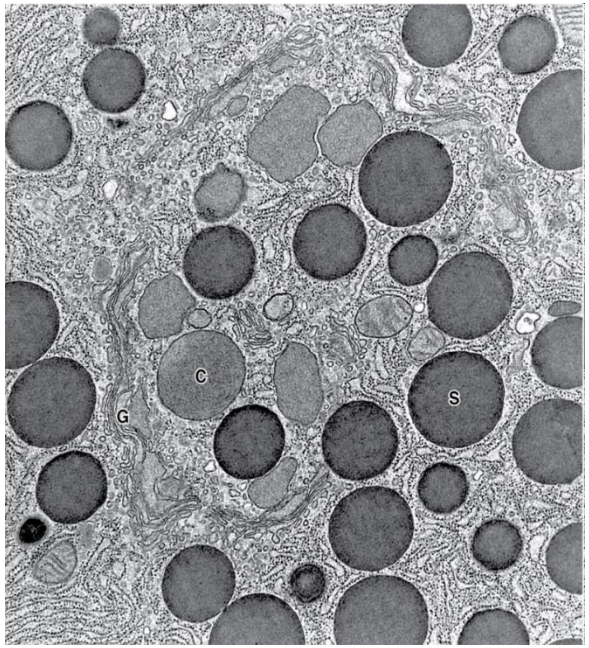
Cytoplasmic inclusions 1

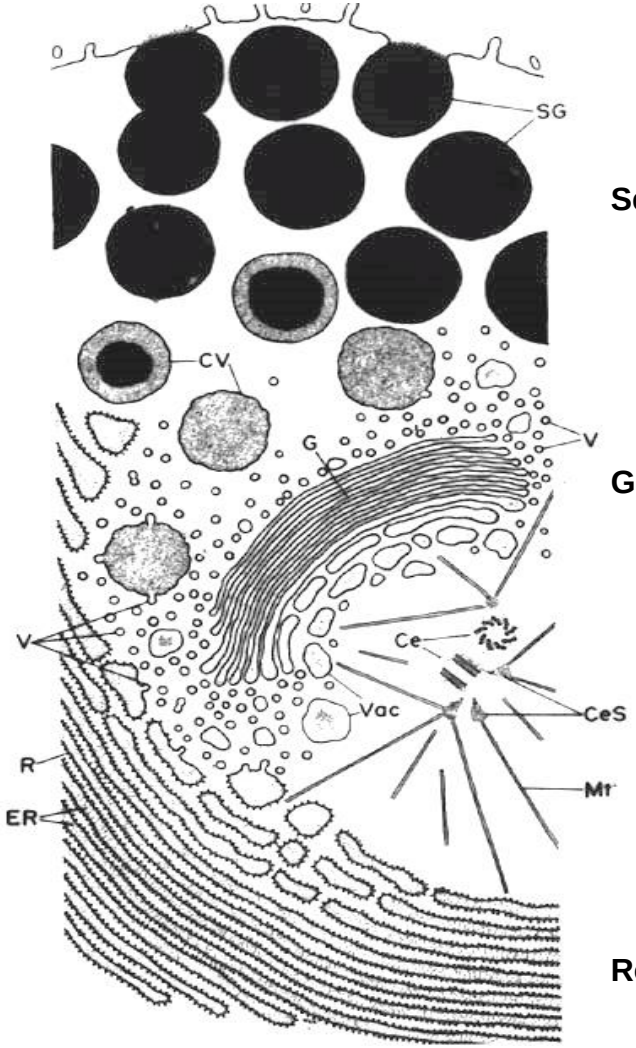
(no or only little metabolic activity on themselves)

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

Cytoplasmic inclusions 2

Secretory granules





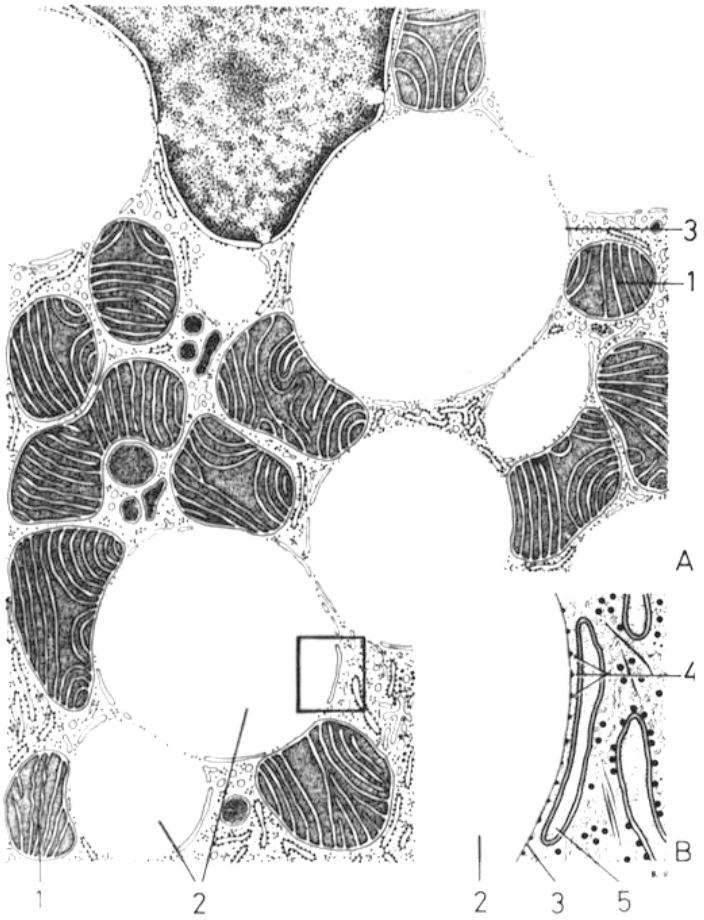
Secretory granules

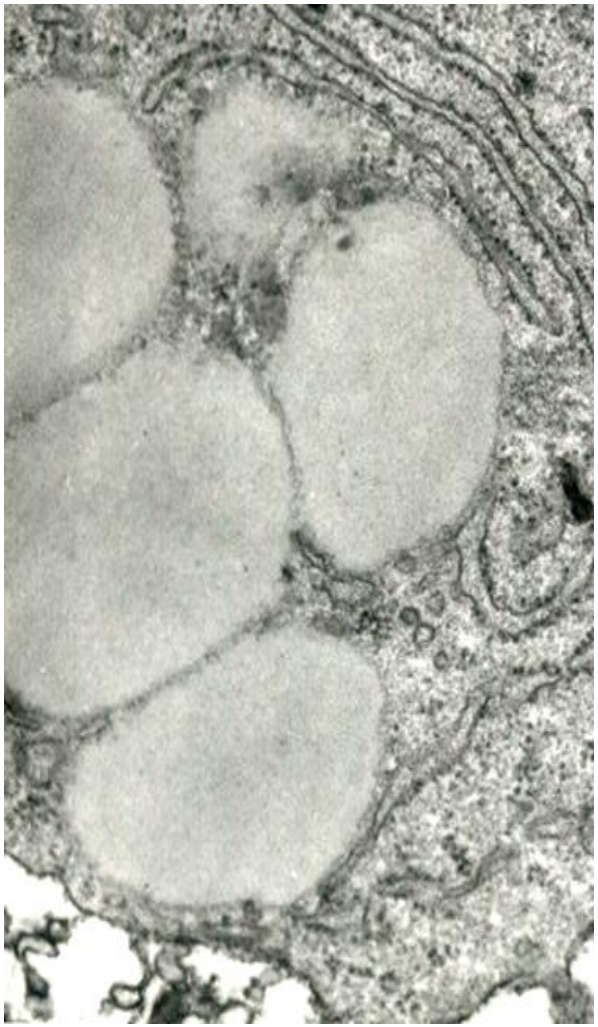
Golgi apparatus

Rough ER

Cytoplasmic inclusions 3

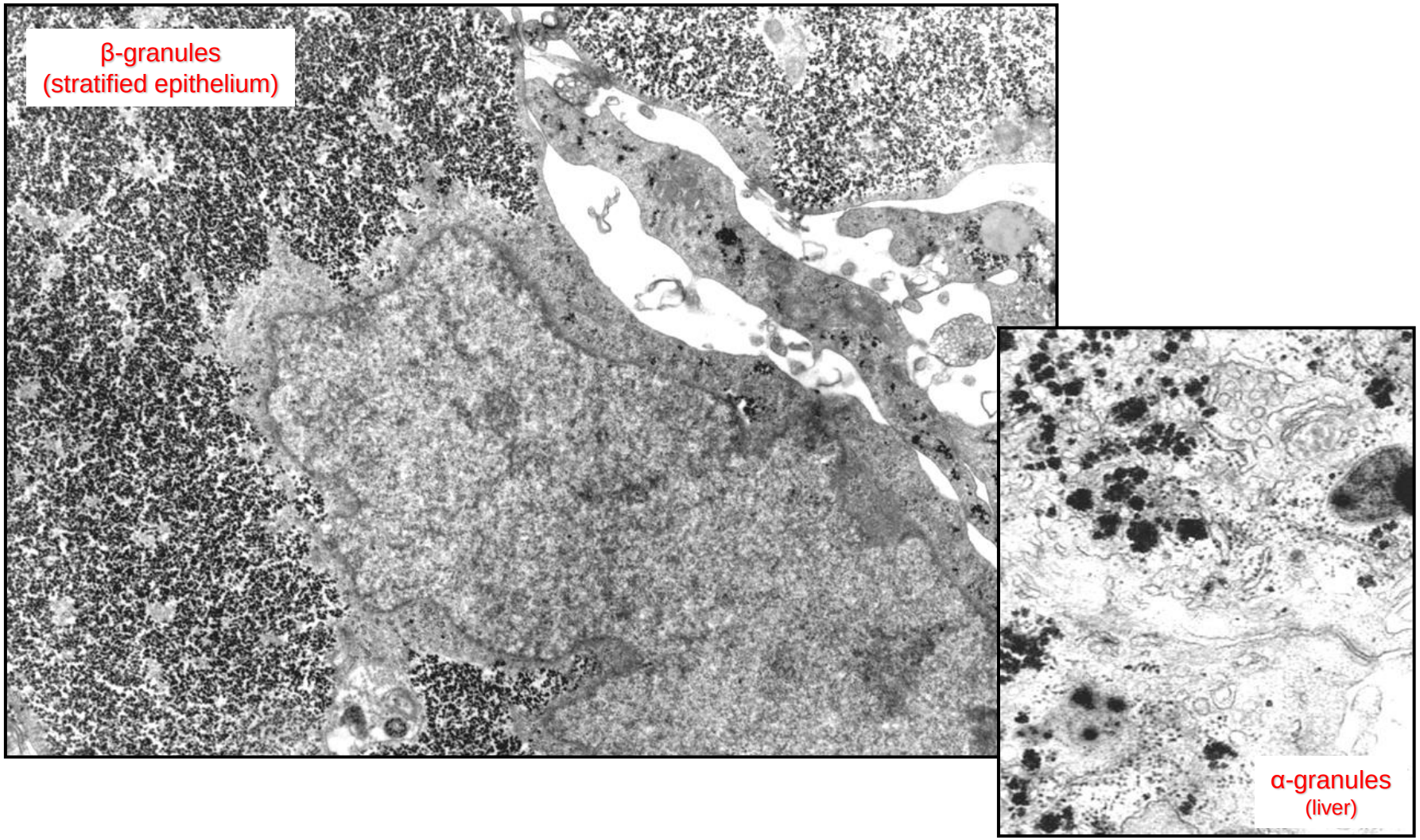
Lipid inclusions





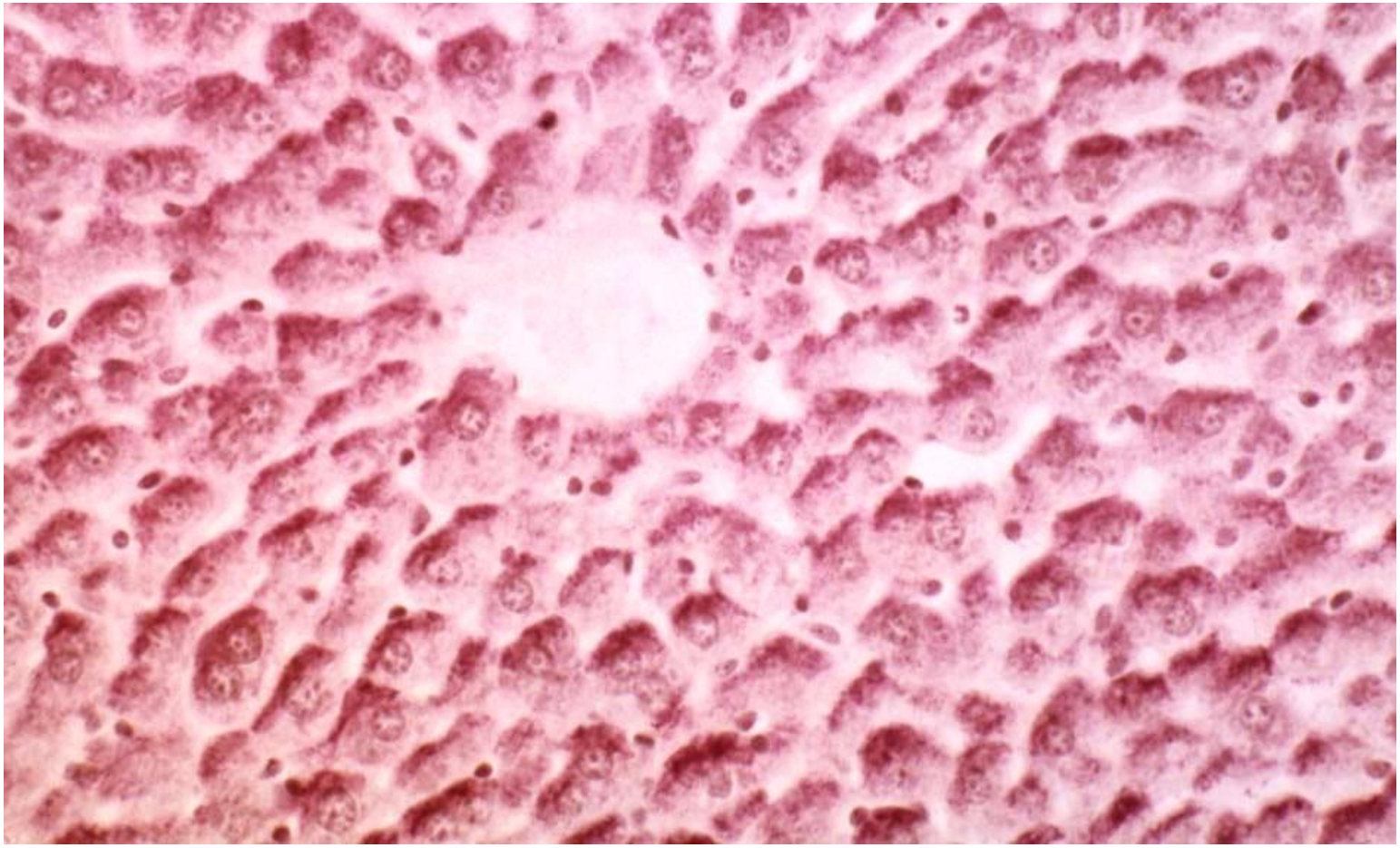
Cytoplasmic inclusions 4

Glycogen



Cytoplasmic inclusions 5

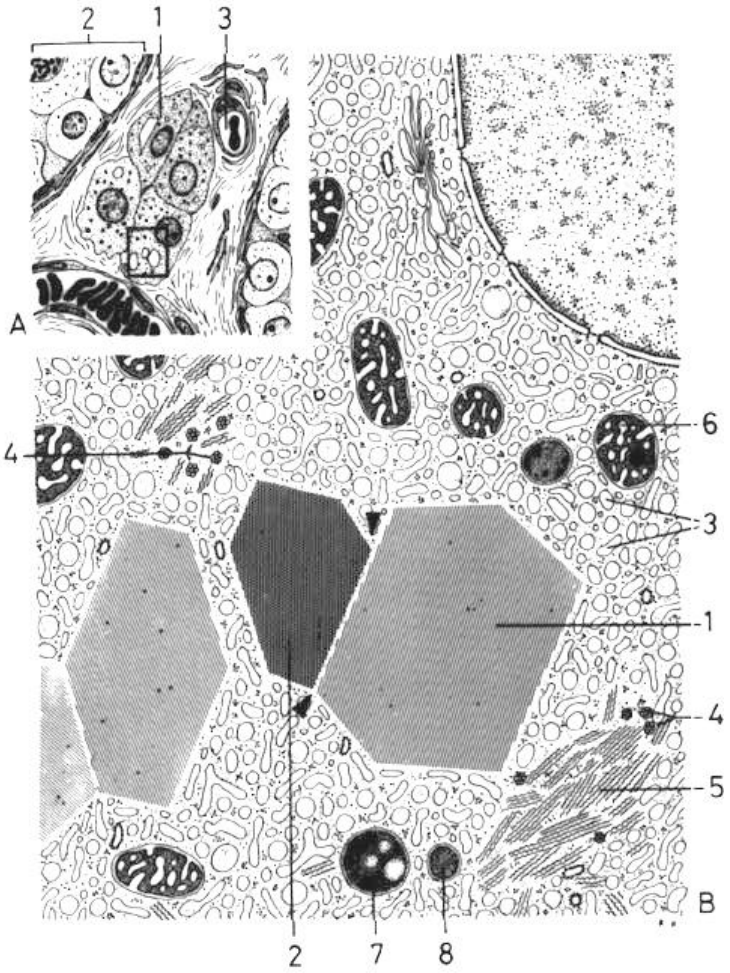
Glycogen

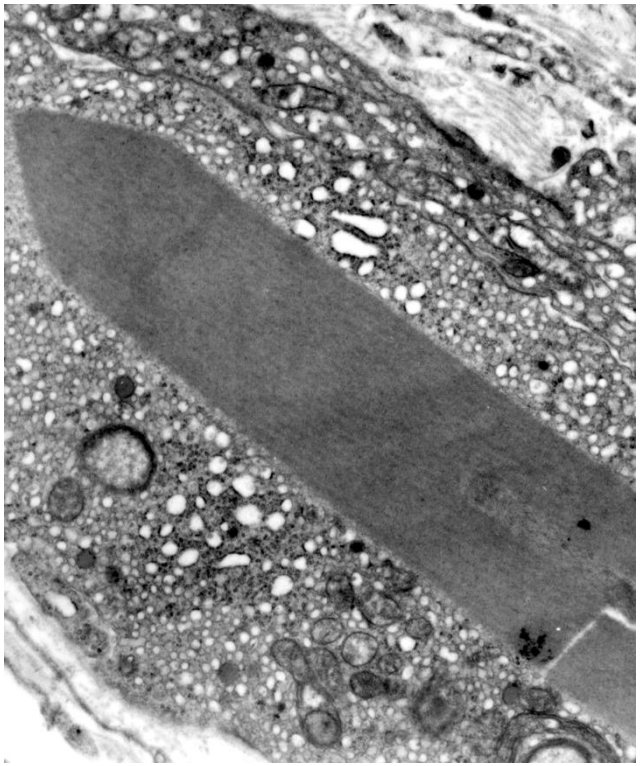


Glycogen in liver cells (light microscope; PAS reaction)

Cytoplasmic inclusions 6

Crystals



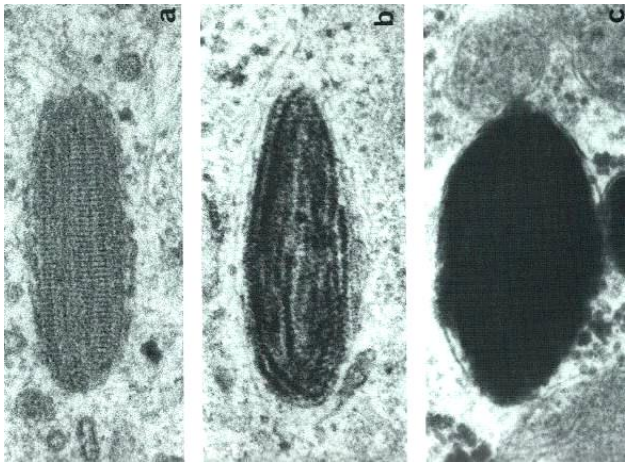


Protein inclusions in Leydig cells

Cytoplasmic inclusions 7

Pigments (colour inclusions): Exogenous x Endogenous

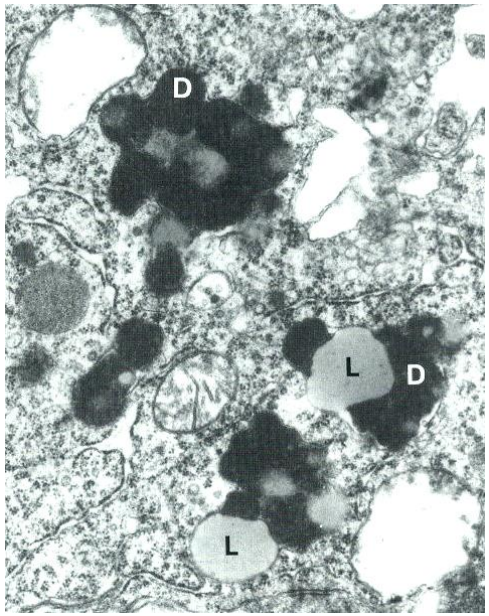
- **Autogenous**
  Specific functions – **melanin**



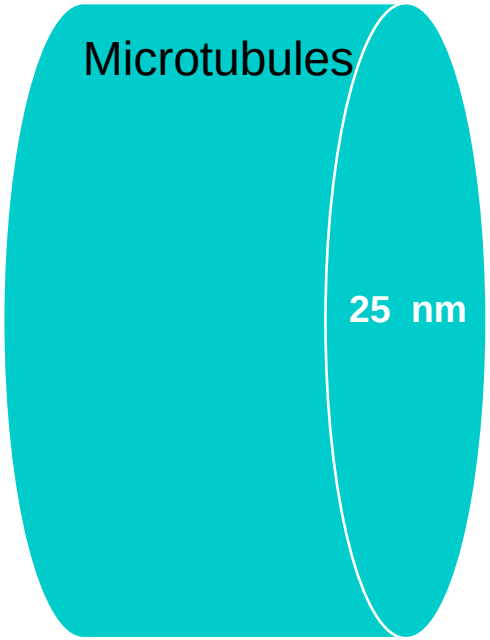
- **Hematogenous**
  Hemoglobin decomposition – **hemosiderin**, **biliverdin**, **bilirubin**

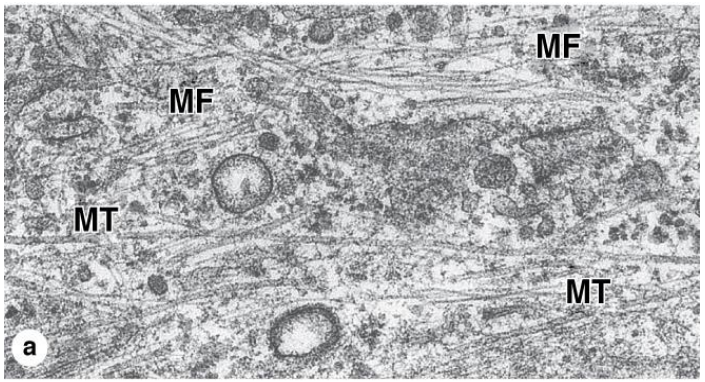
Pigment in aged cells

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

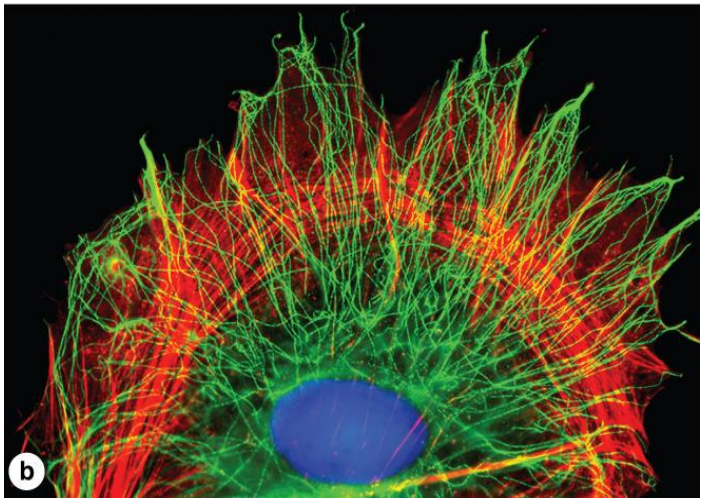


Cytoskeleton 1



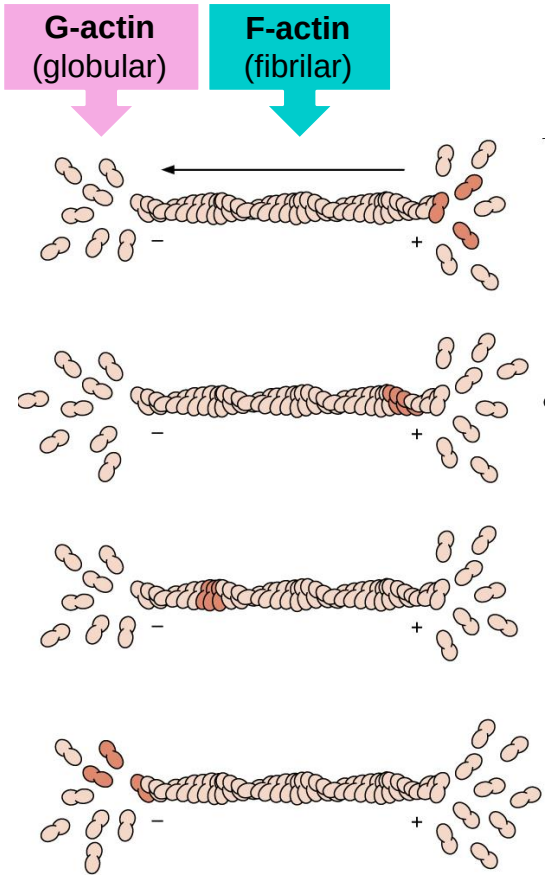


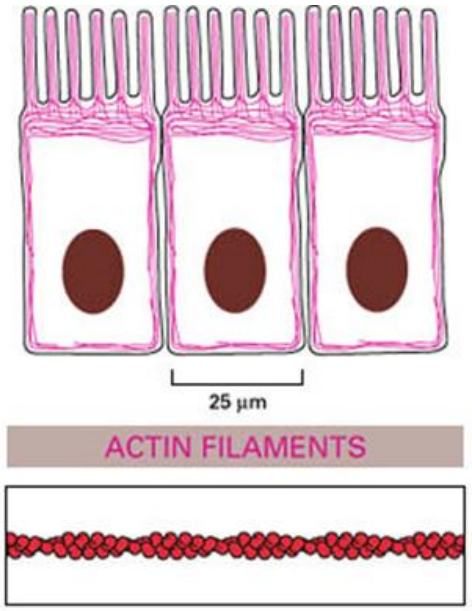
microtubules
microfilaments - actin



Cytoskeleton 2

Microfilaments (actin)

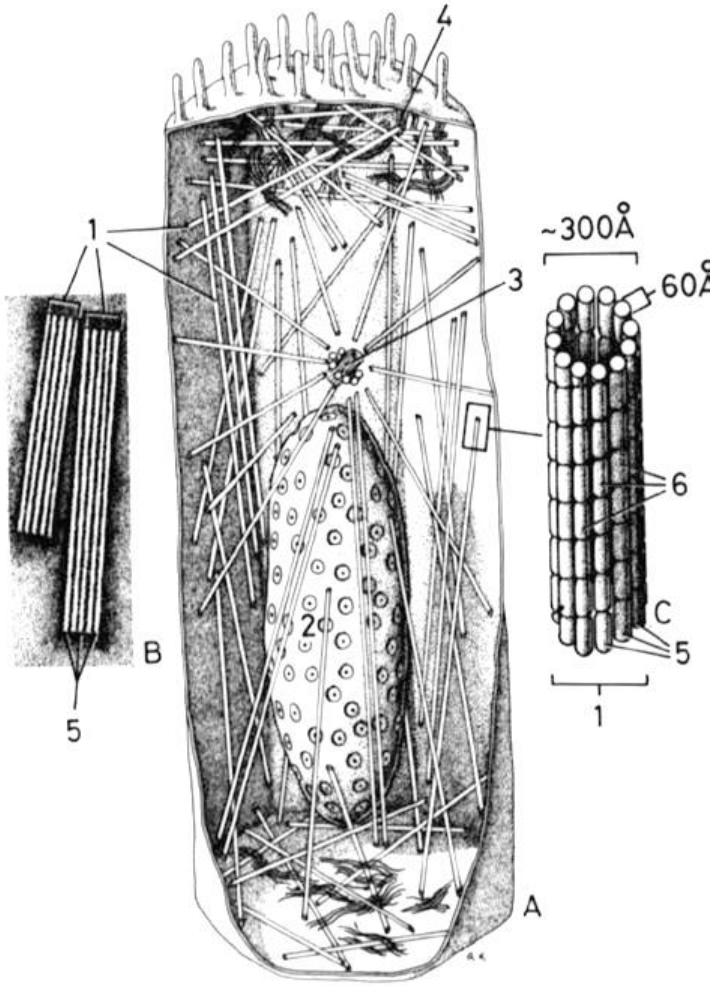


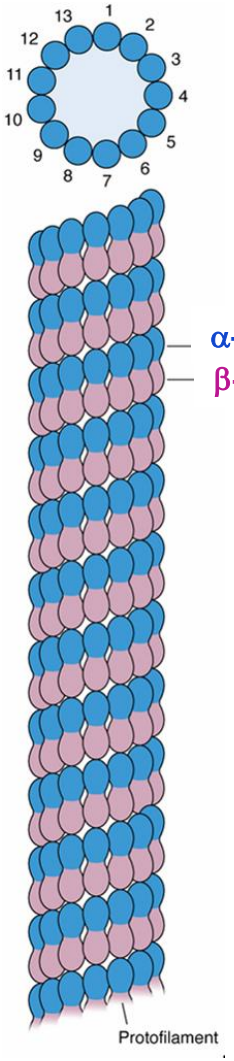


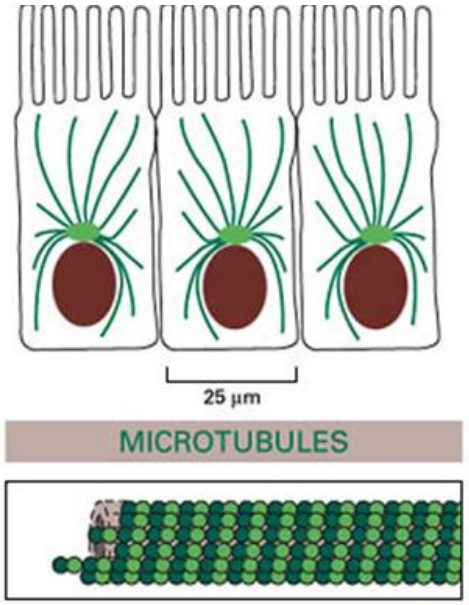
- actin isoformes (α, β, γ)
- fast polymerisation and depolymerisation
- polarisation (+ a – ends)
- stabilisation by associated proteins (tropomyosin – myofibrils)
- crosslinking by associated proteins (fimbrin, filamin, …)
- anchoring to cell membrane (vinculin, tallin, …)
- cortical actin – membrane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

Cytoskeleton 3

Microtubules



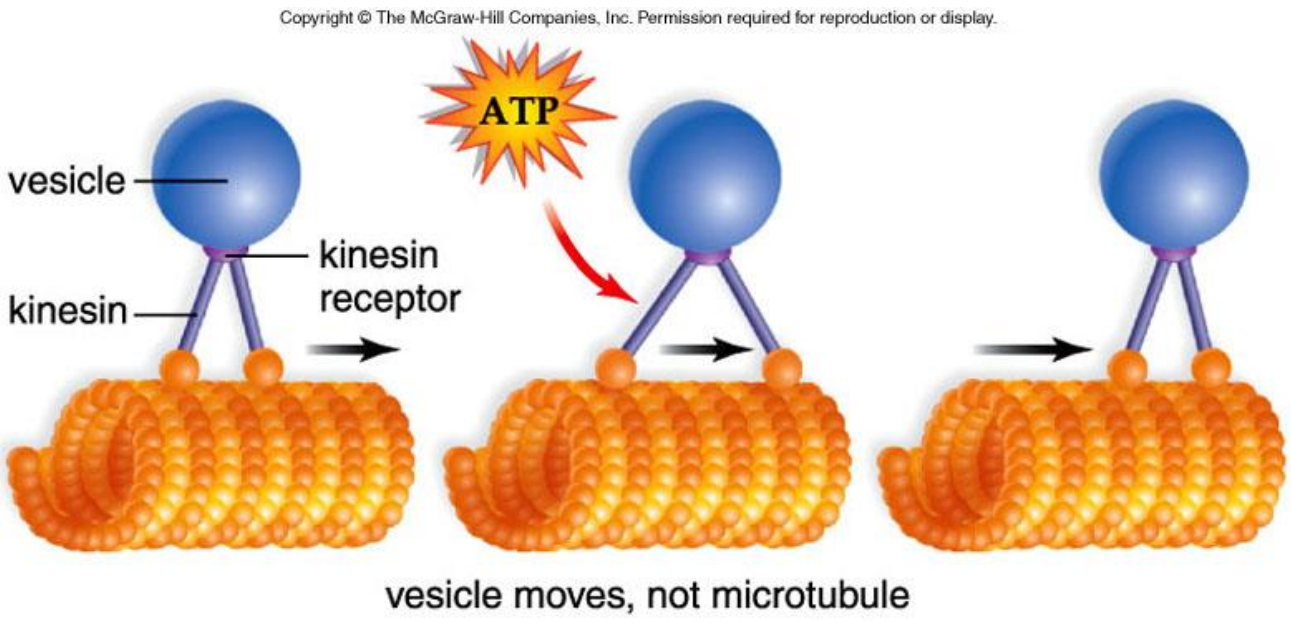




- hollow tubes
- α-tubulin + β-tubulin – dimers
- fast polymerisation and depolymerisation
- polarisation (+ a – ends)
- MAP (proteins associated with microtubuli)
- MTOC – microtubules organizing centre (centrosome; γ-tubulin)
- mechanical support
- intracellular transport
- mitotic spindle
- cilia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

Cytoskeleton 4

Microtubules - motors

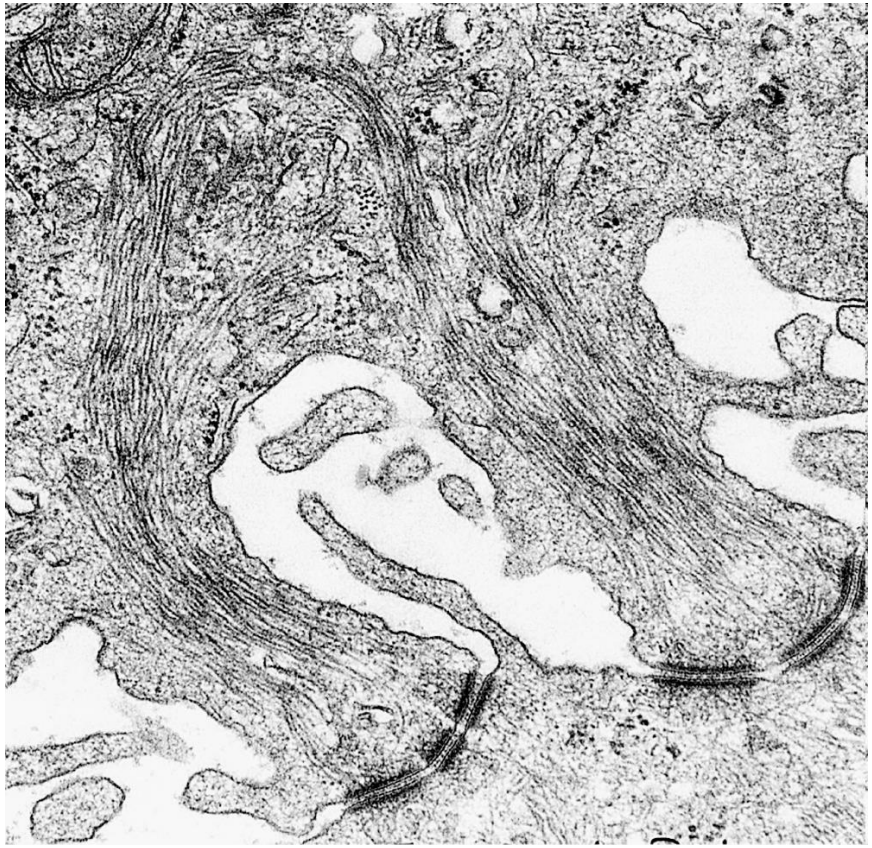


Kinesins
- move towards „plus“ end of microtubuli
- transport from centrosome

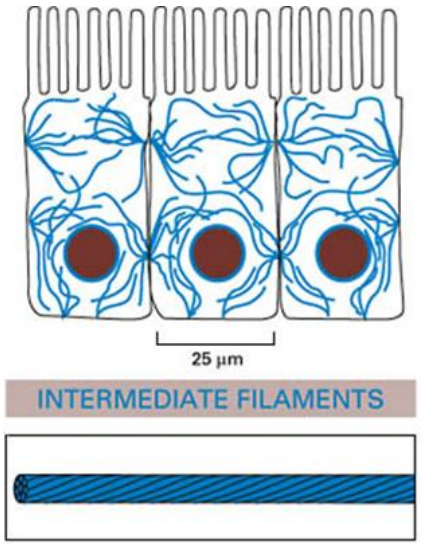
Dyneins
- move towards „minus“ end microtubuli
- transport towards centrosome
- axonal transport – long distance

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

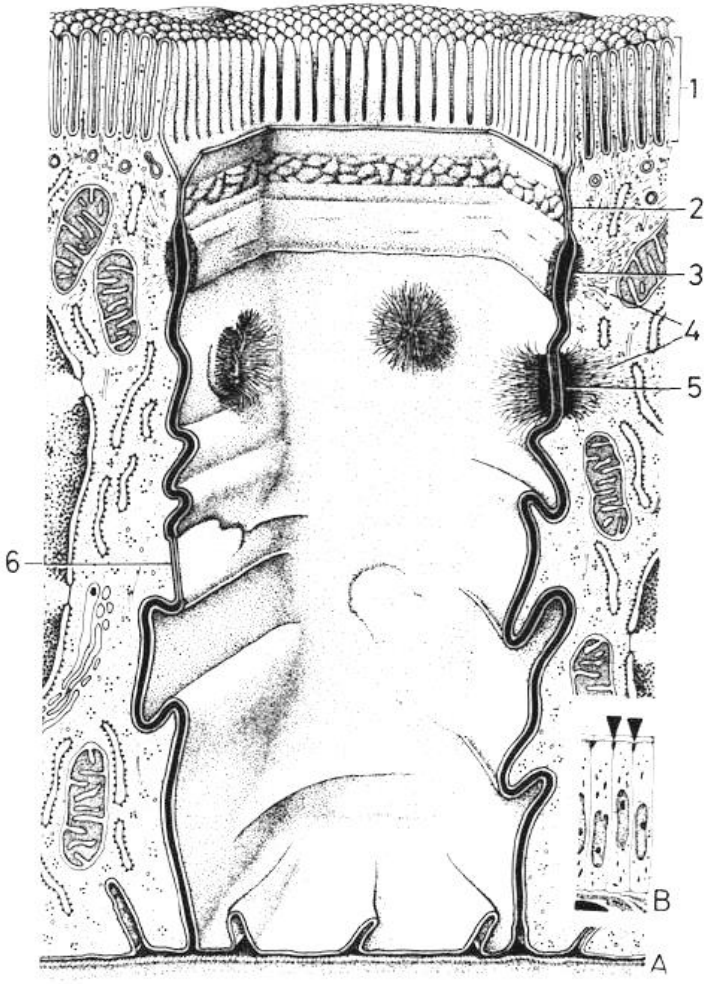
Cell-to-cell junction:

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

Basal

- focal adhesions
- hemidesmosomes
- basal labyrinth

free surface

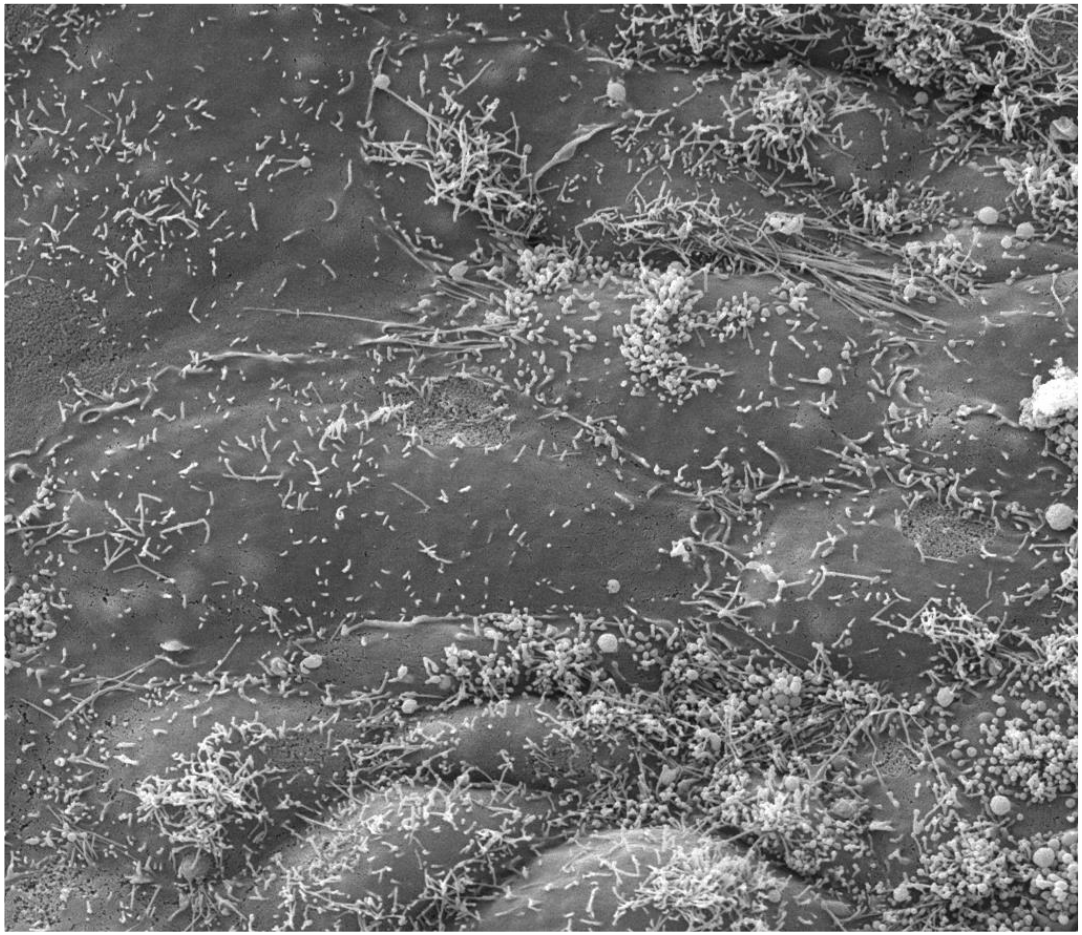


lateral surface

basal surface

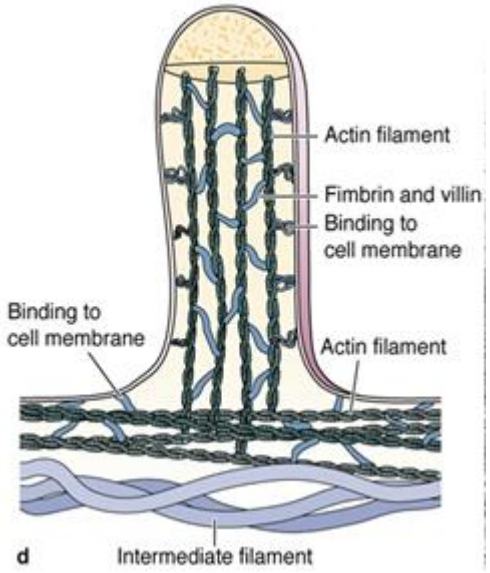
Cell surfaces 2

Microvilli



Free surface of cultured human embryonic stem cells

Cell surfaces 3



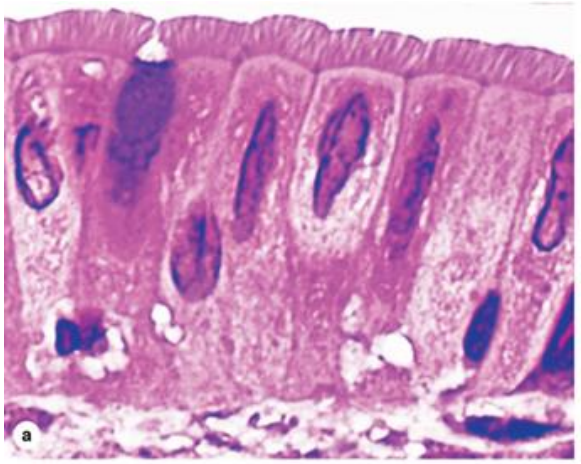
Mikroklky

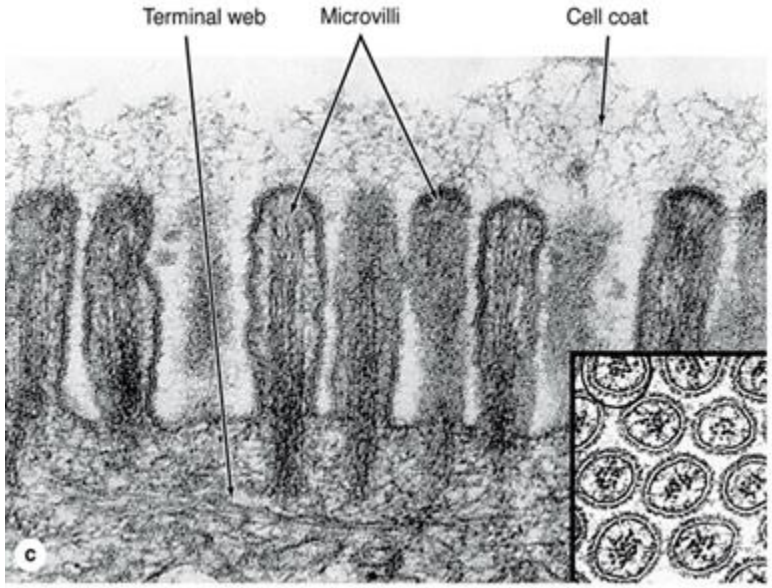
Thickness about 0,1 μm
Length about 1-6 μm

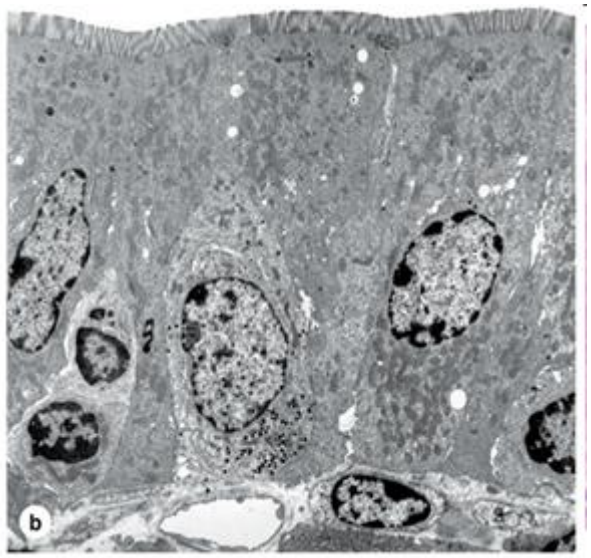
Actin filaments in microvilli

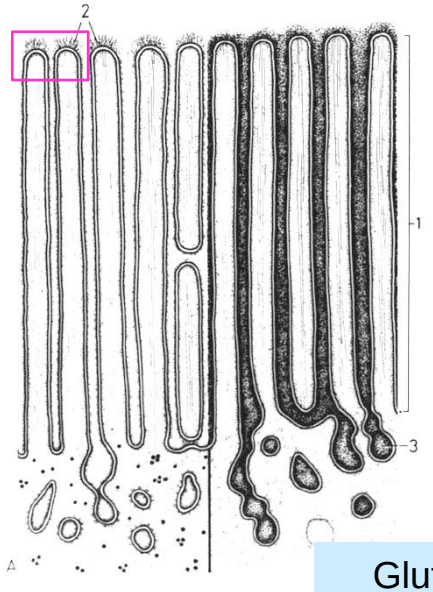
- 20 in microvilli of epithelial cells
- several hundreds in stereocilia of hair cells

Regularly organised microvilli
= striated border + brush border





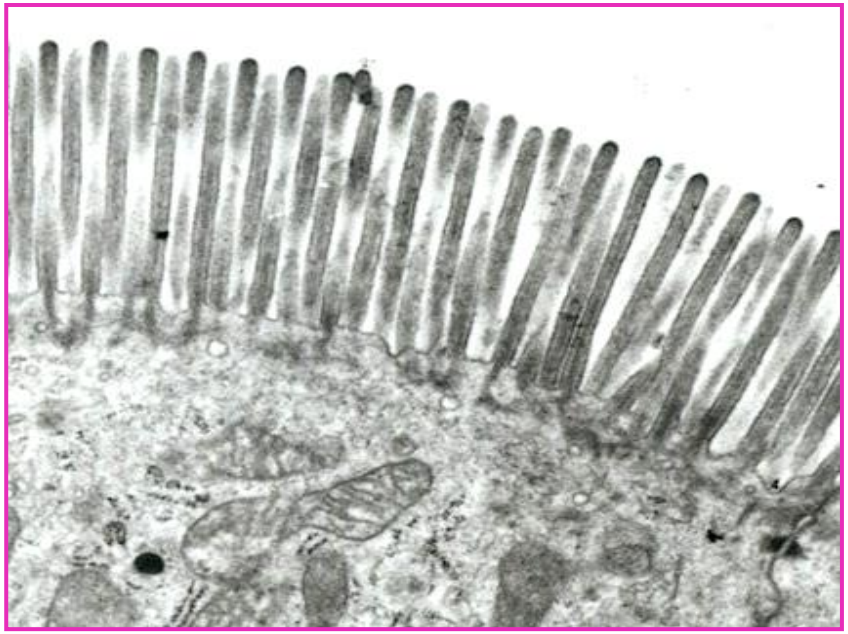




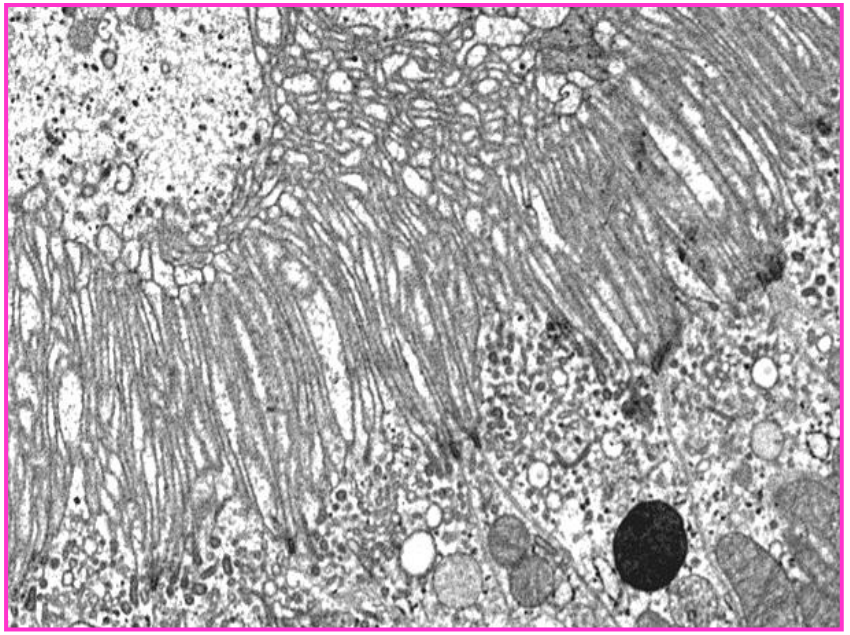
Cell surfaces 4

Mikroklky

Gluten – Celiac disease



žíhaná kutikula
(tops of enterocytes)



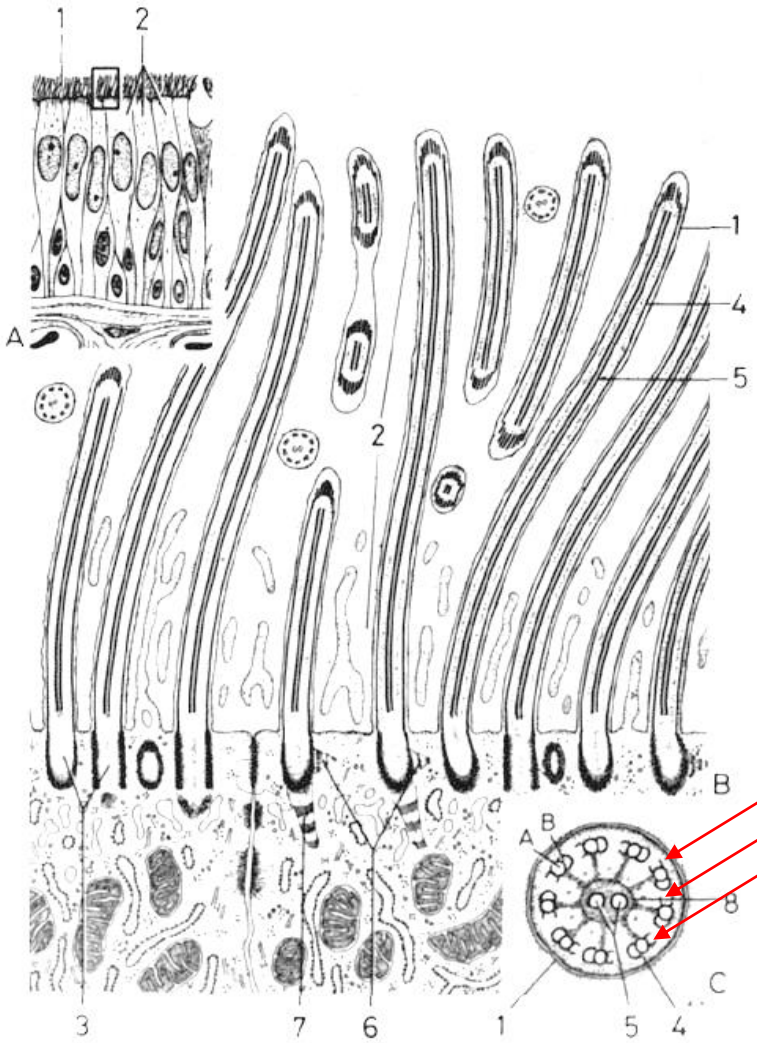
kartáčový lem
(proximal tibuli of kidney)

Cell surfaces 5

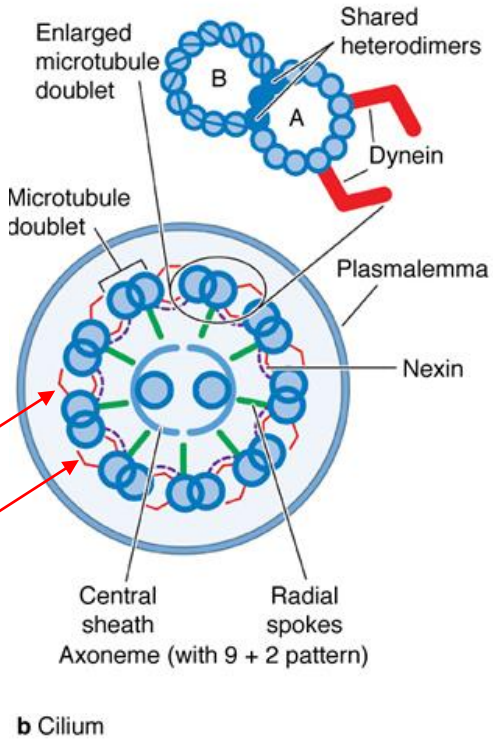
Řasinky + Bičíky

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

Axonema
20 microtubuli (9x2 + 2)



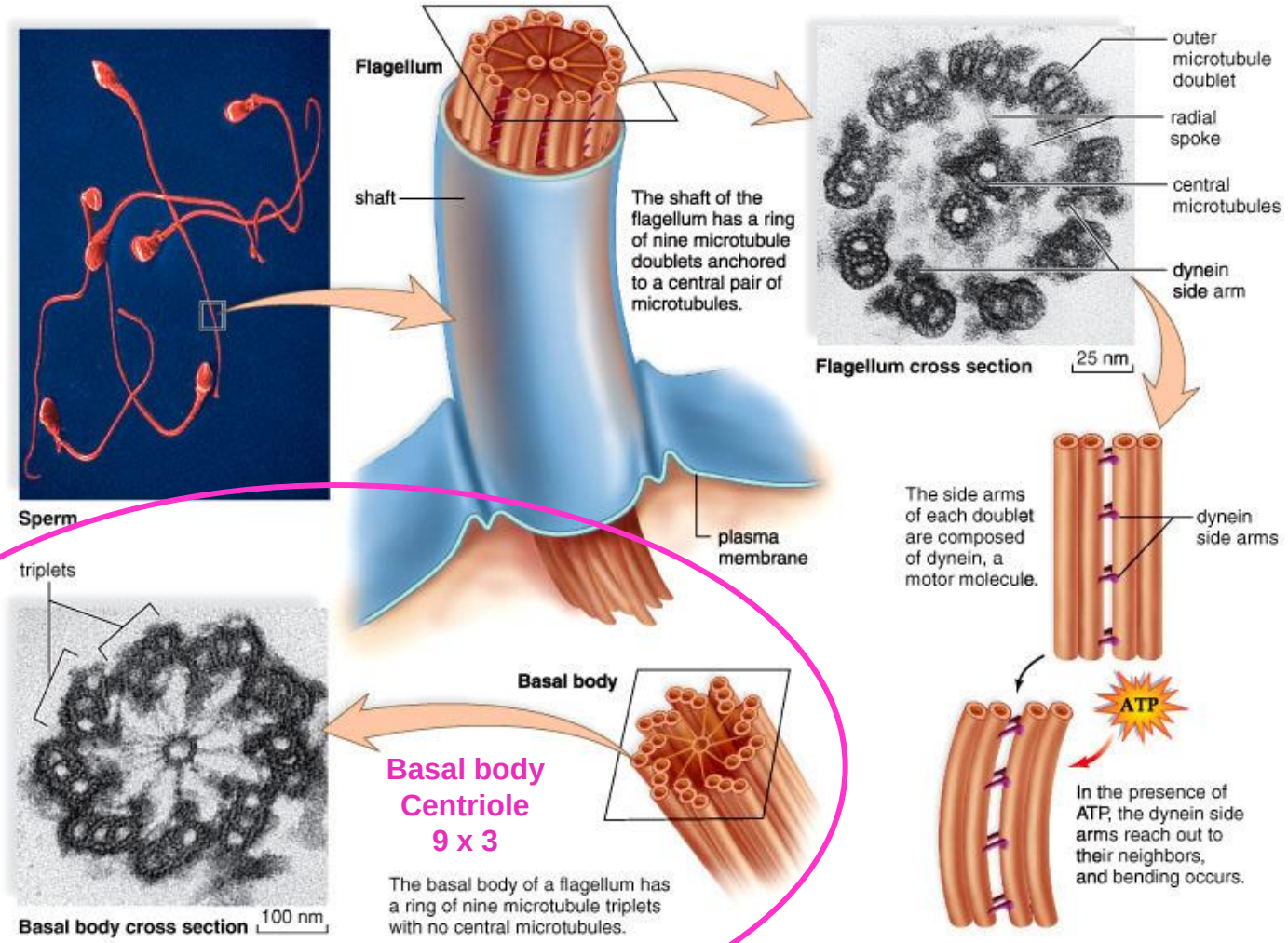
Dynein arms
(movement)



b Cilium

Cell surfaces 6

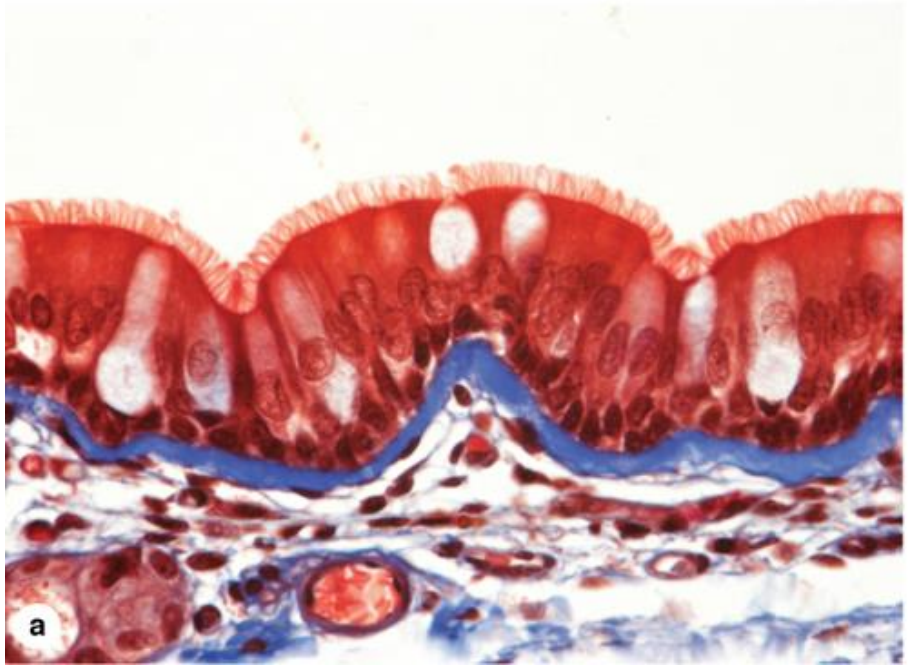
Řasinky + Bičíky



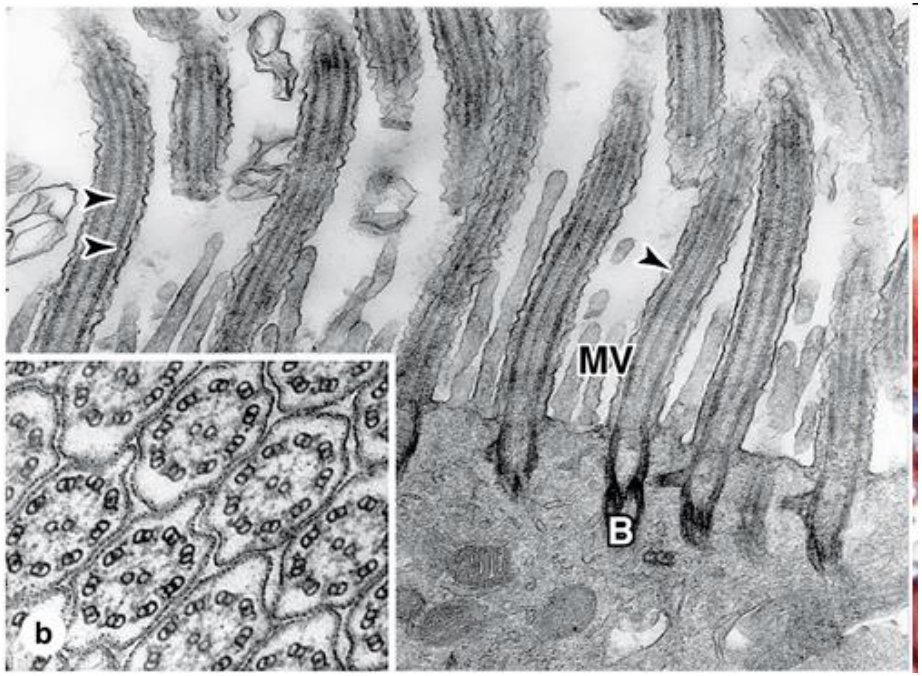
Cell surfaces 7

Řasinky + Bičíky

in light microscope

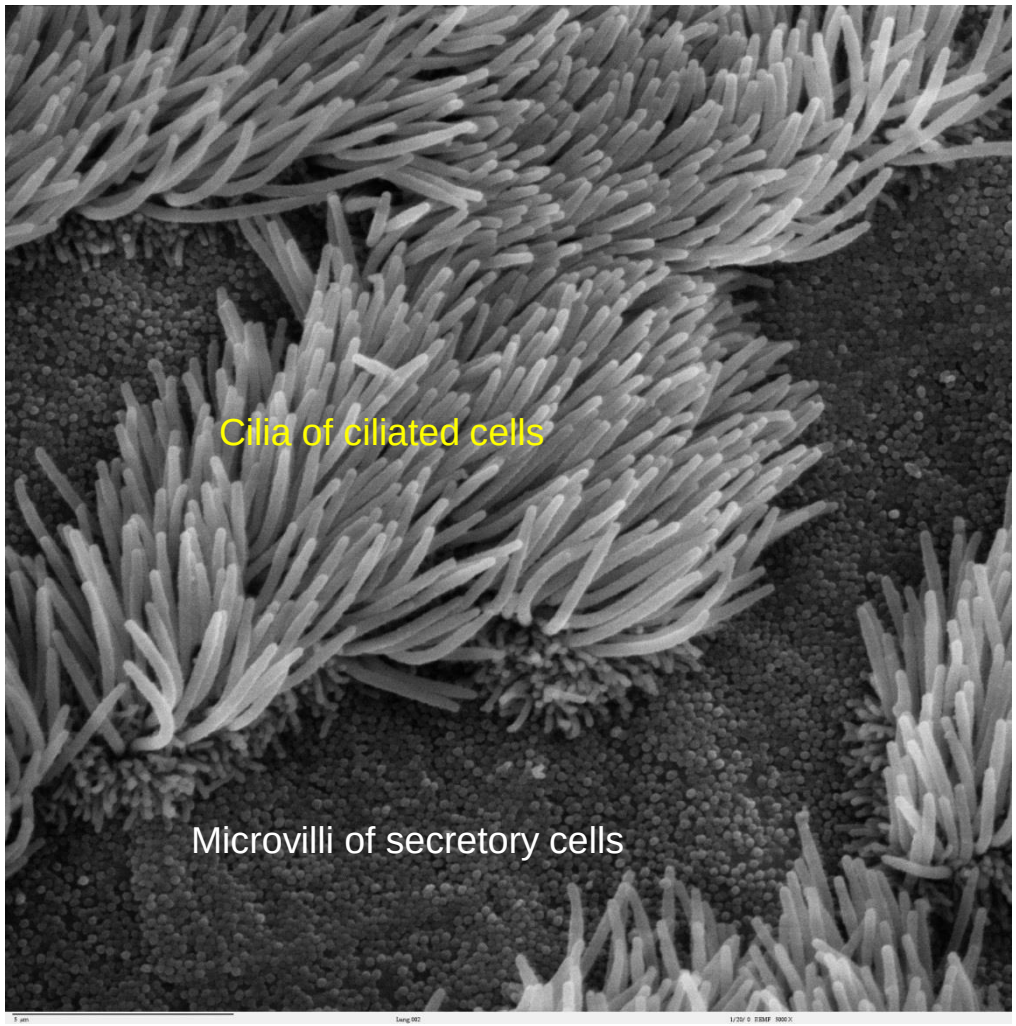


in electron microscope

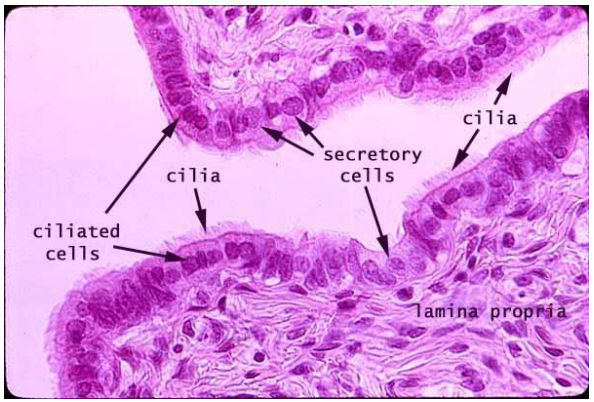


Cell surfaces 8

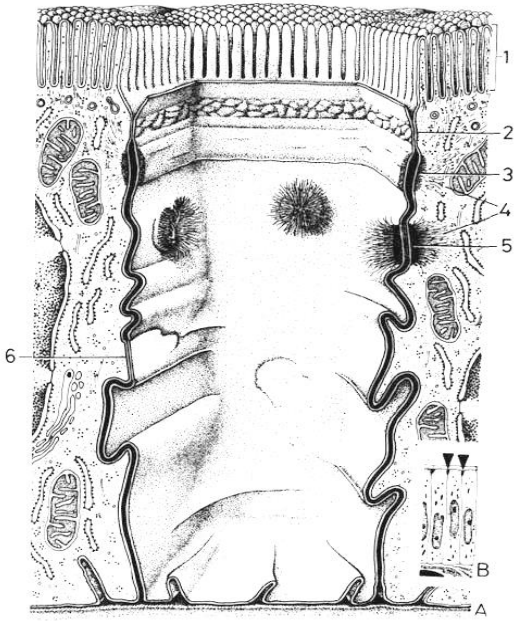
Řasinky + Bičíky



oviduct

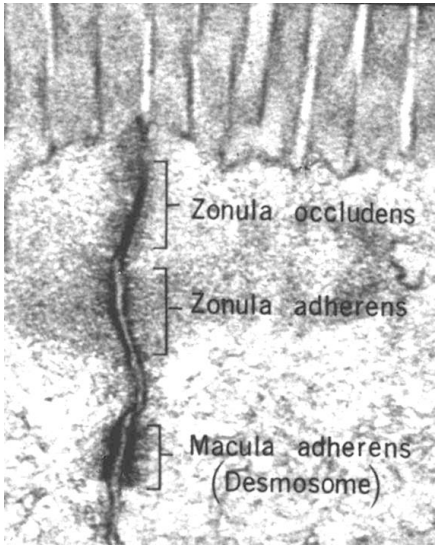


Adhesions and Junctions 1



lateral surface

Basal surface



spojovací komplex

Adheze

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

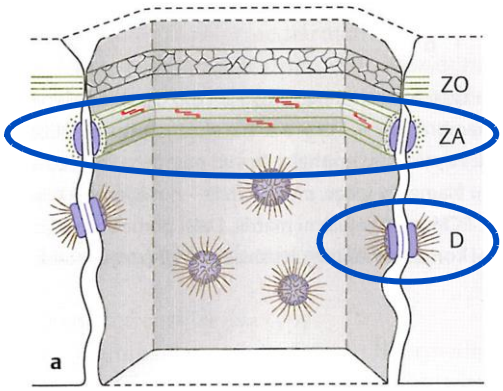
Těsnění

- **Zonula occludens** (tight junction)

Komunikace

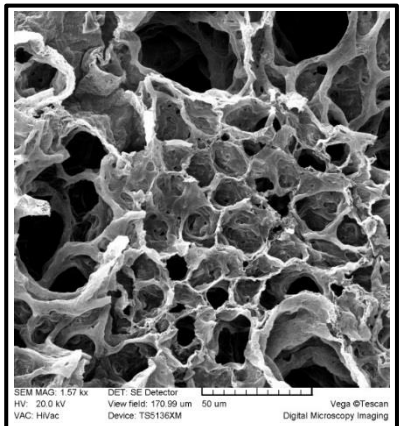
- **Gap junction** (nexus)

Adhesions and Junctions 2

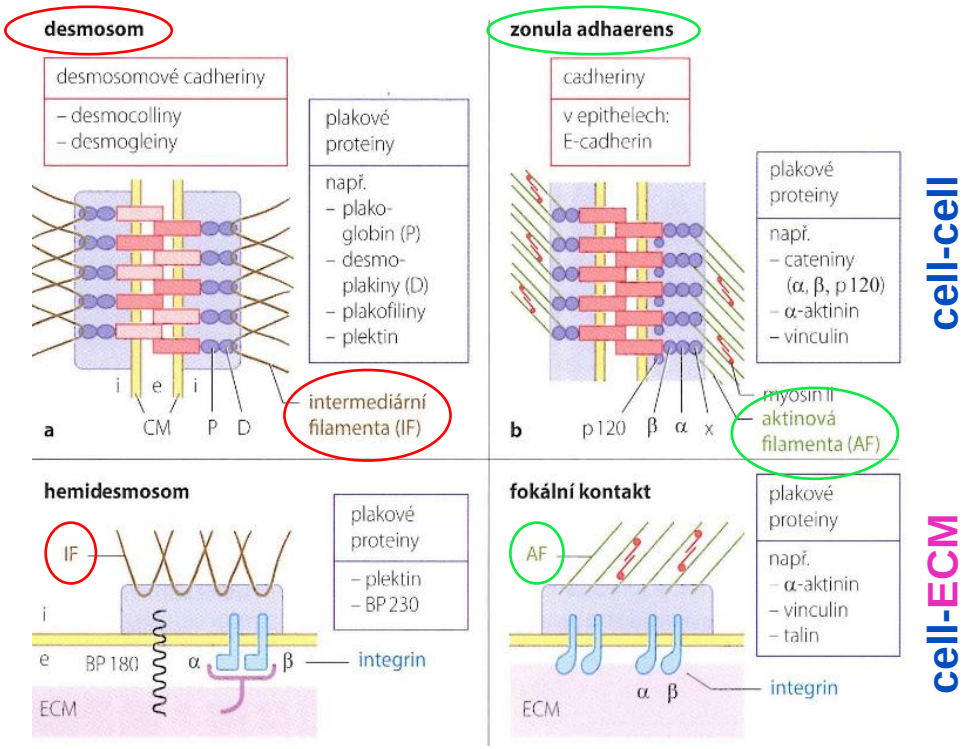


Adhesion

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

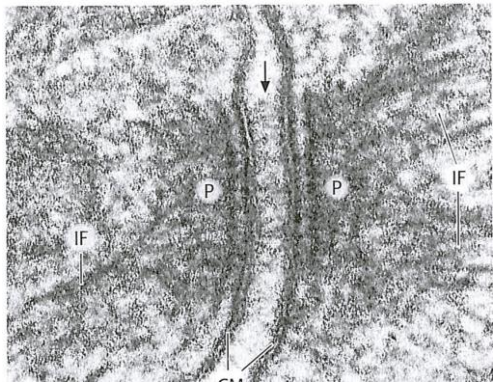


Lung ECM - alveolar region

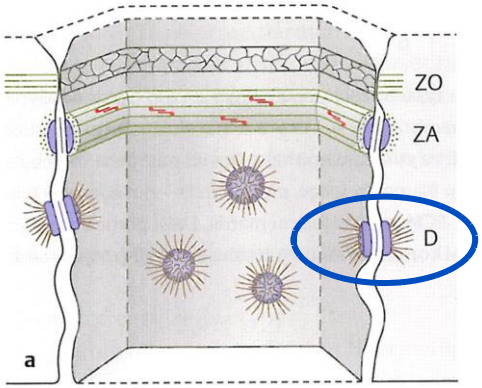


Unified composition

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



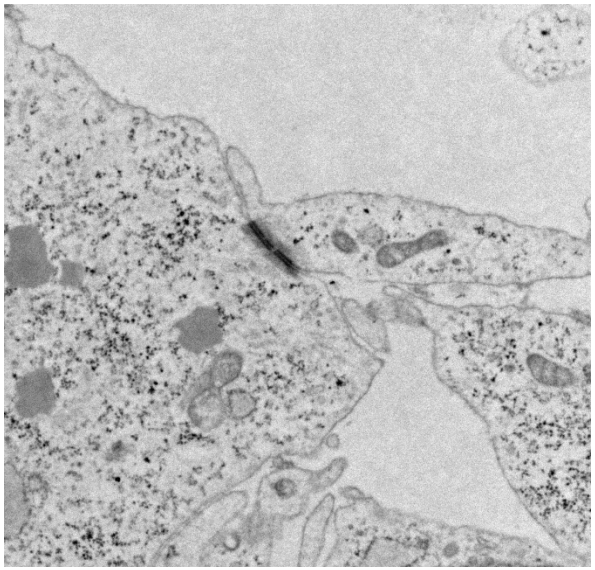
Adhesions and Junctions 3

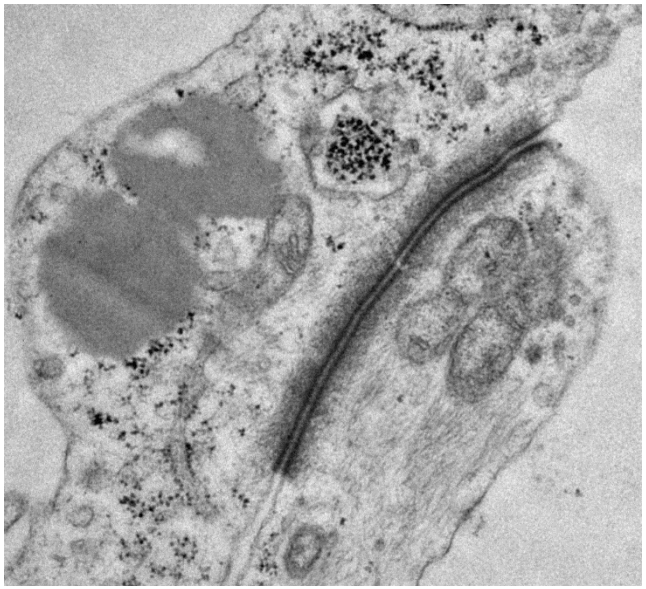


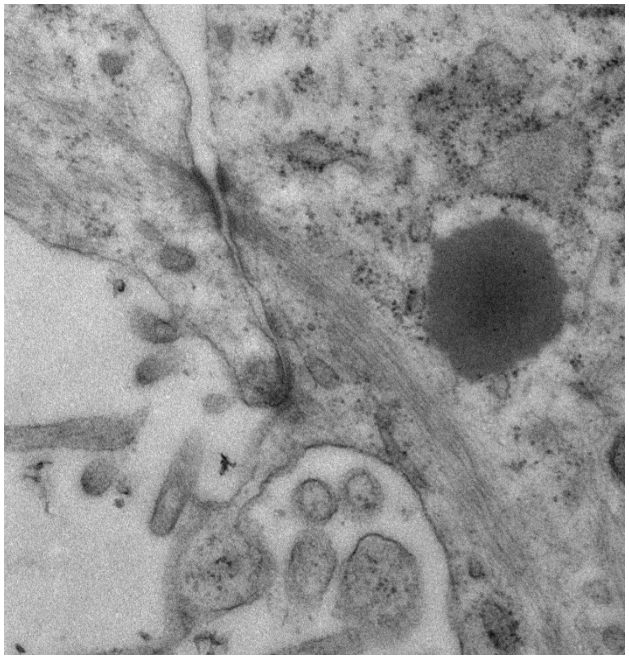
Adhesion

- **Macula adherens** (desmosome)

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



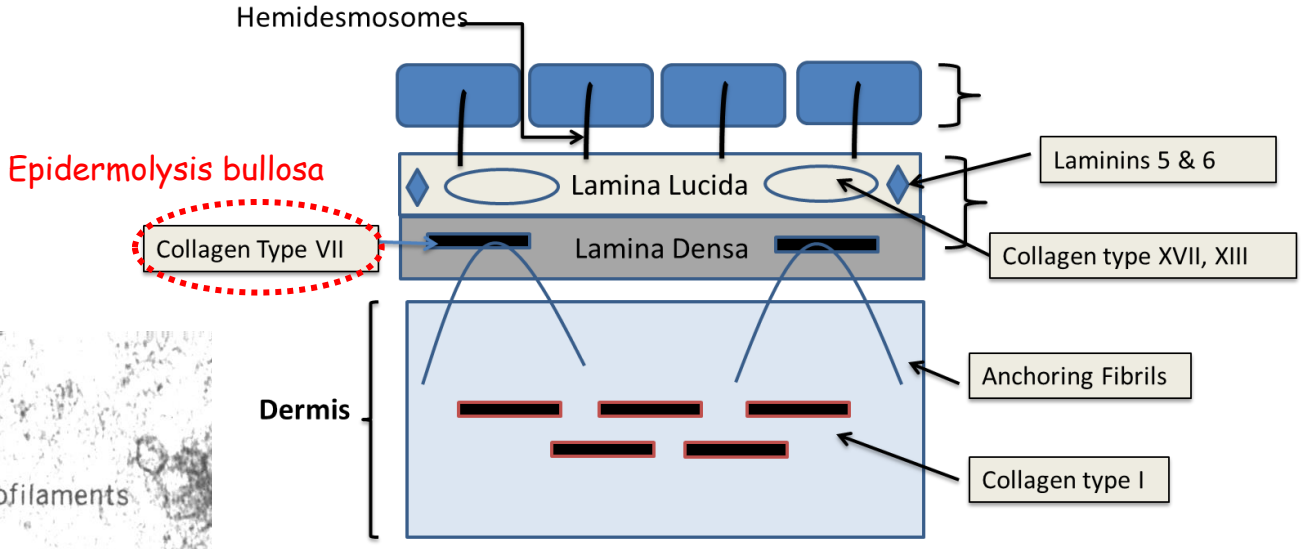


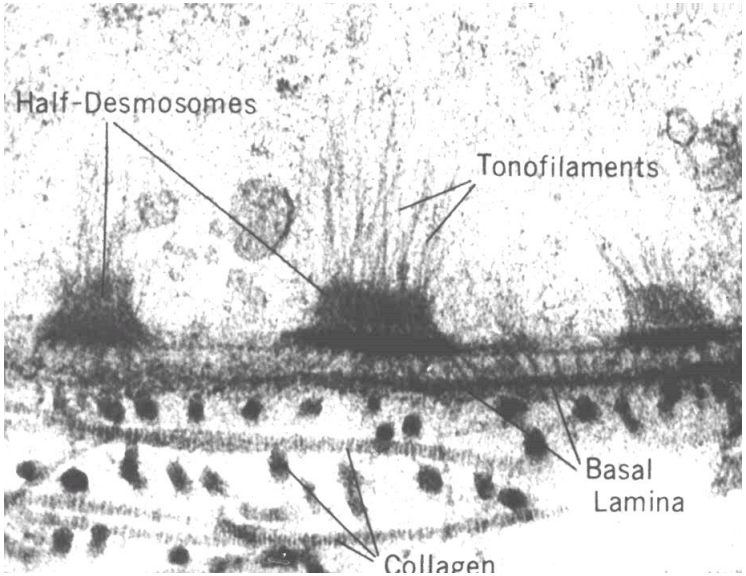


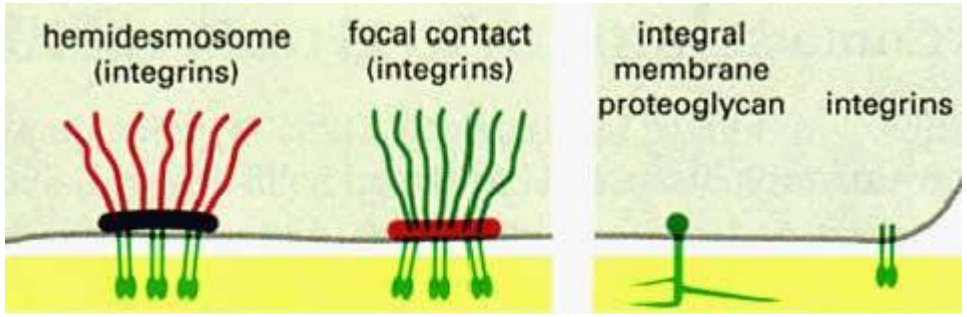
Adhesions and Junctions 4

Adhesion

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

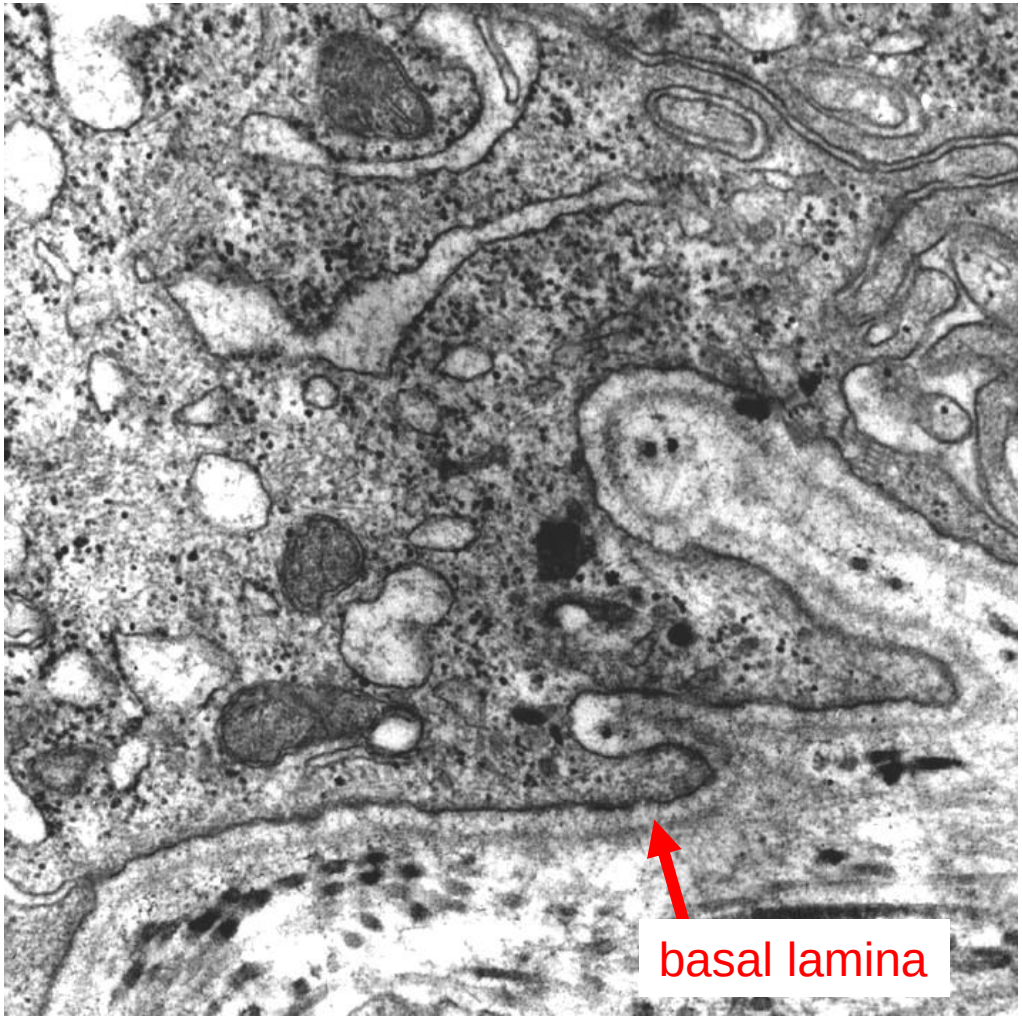






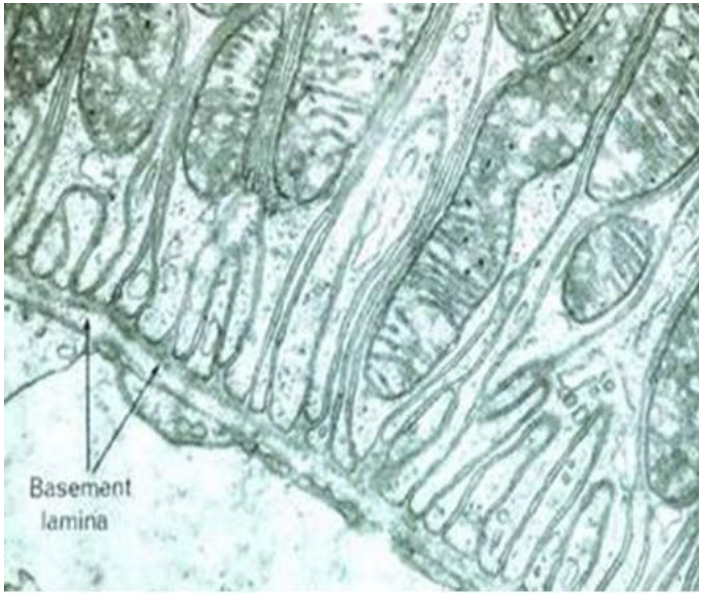
Adhesions and Junctions 5

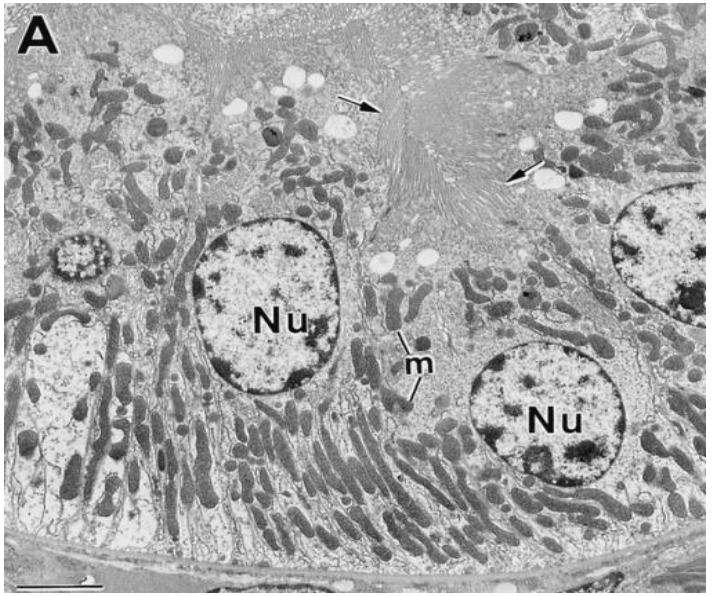
- **Focal adhesion**



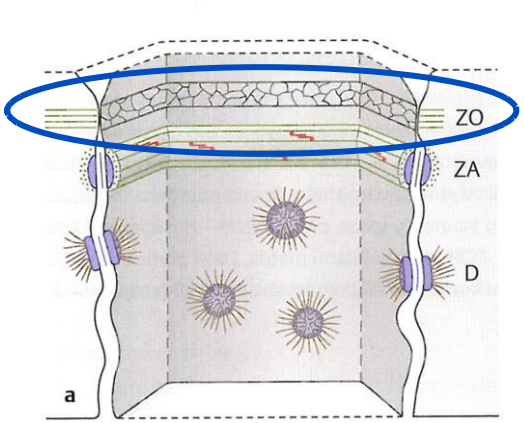
Adhesions and Junctions 6

Basal labyrinth



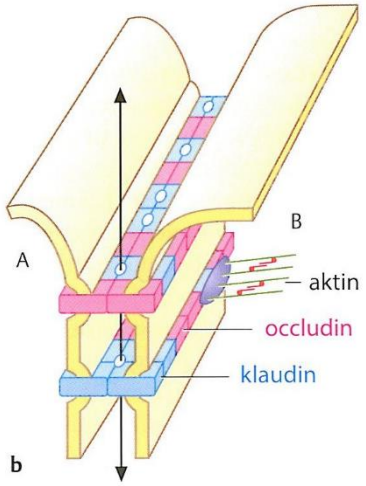


Adhesions and Junctions 7

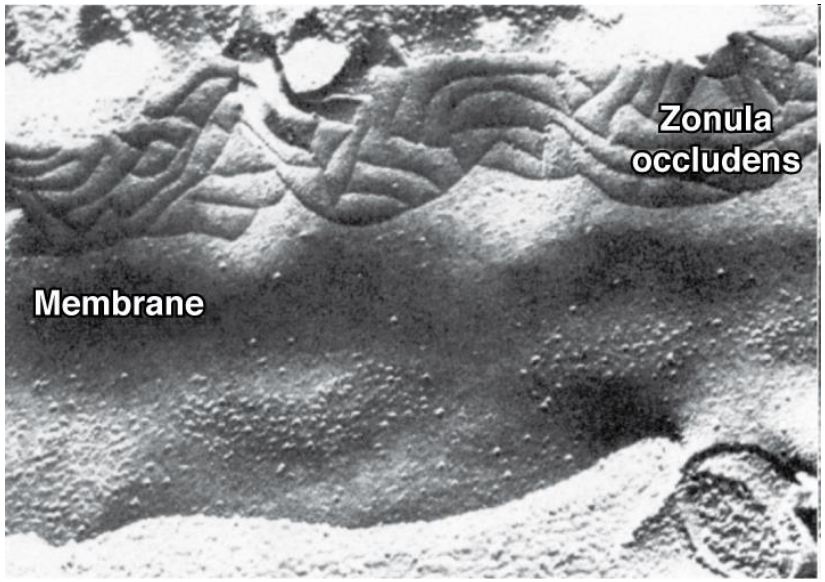


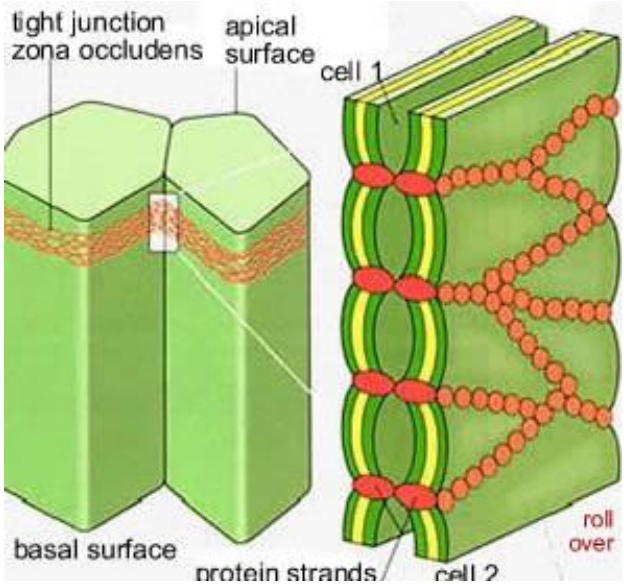
Sealing

- **Zonula occludens** (tight junction)

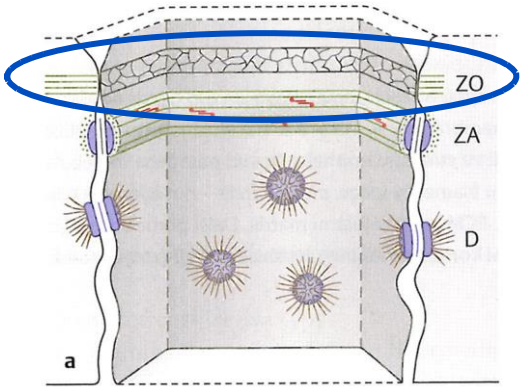


Damage by:
Clostridium perfringens
Helicobacter pylori (ZO-1)



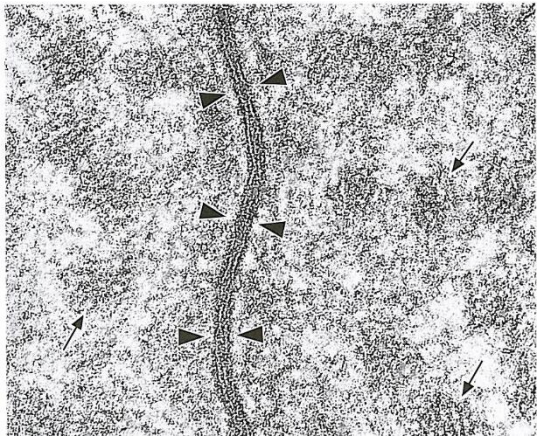


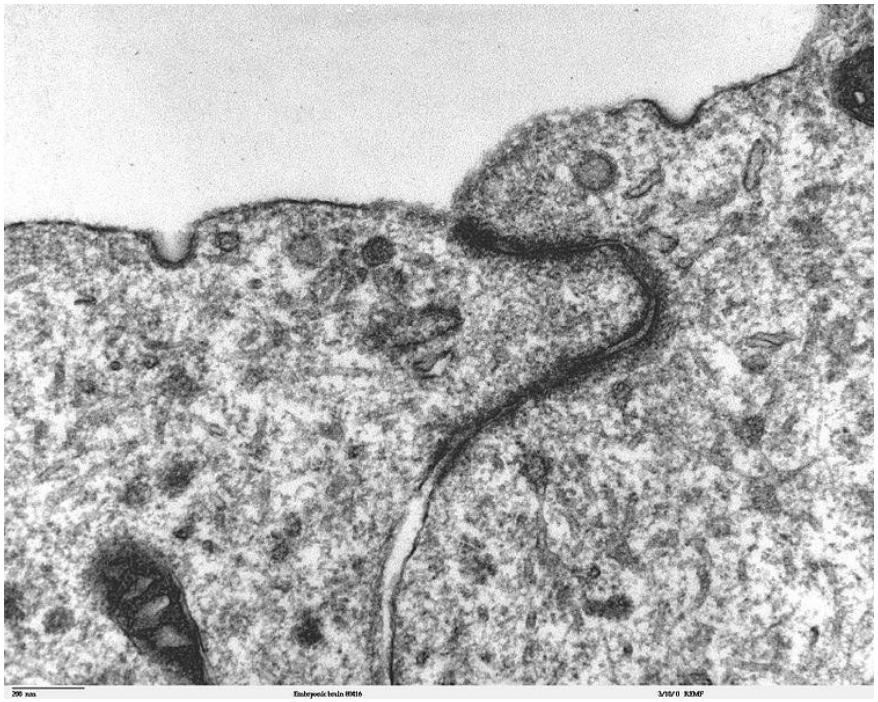
Adhesions and Junctions 8

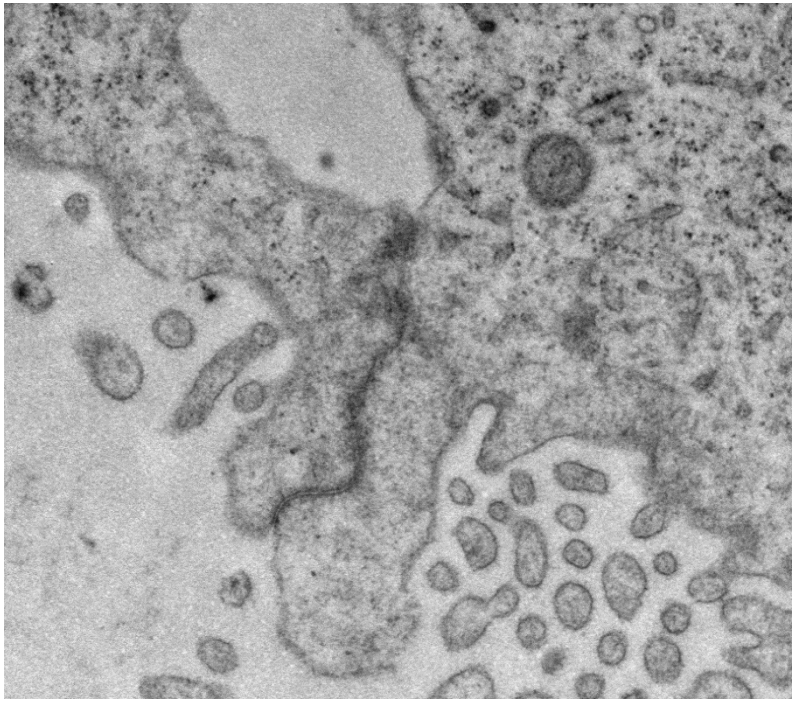


Sealing

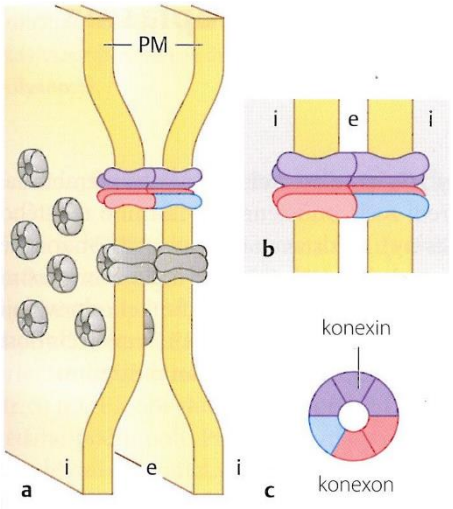
- **Zonula occludens** (tight junction)







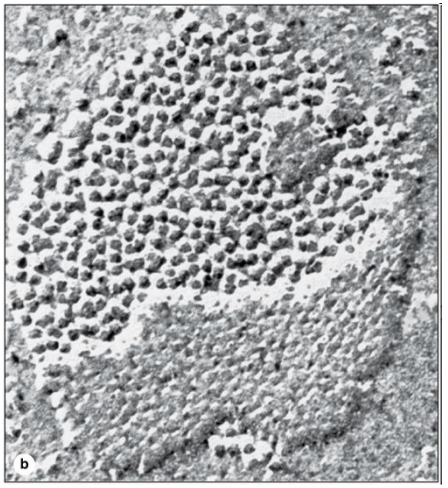
Adhesions and Junctions 9

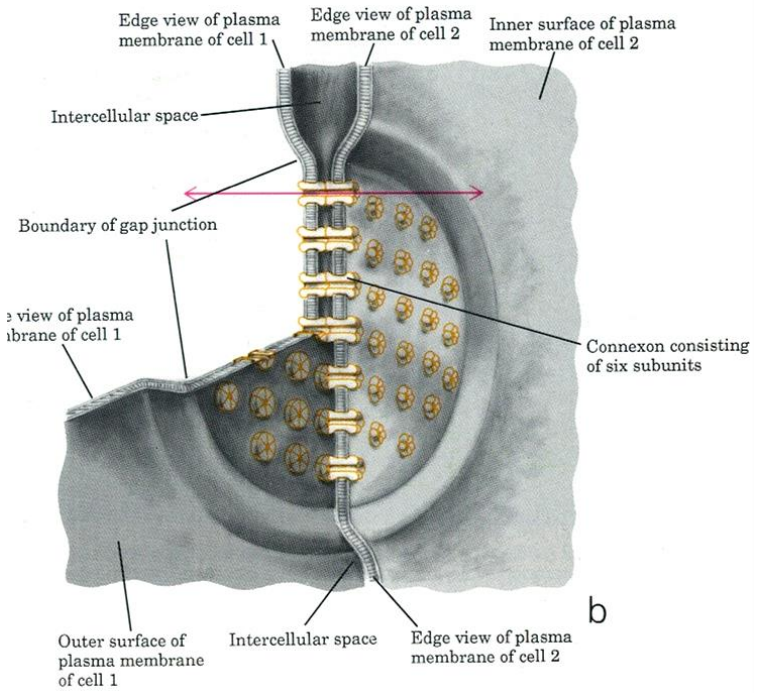


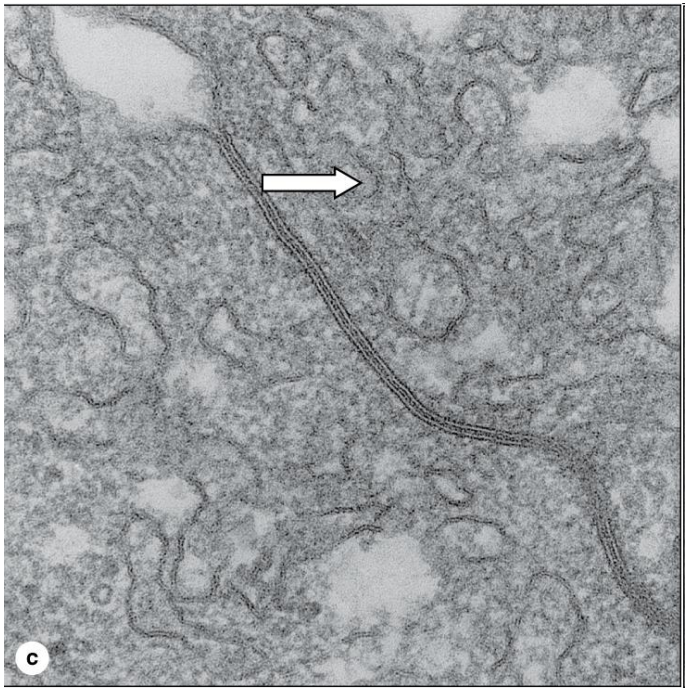
Communication

- **Gap junction** (nexus)

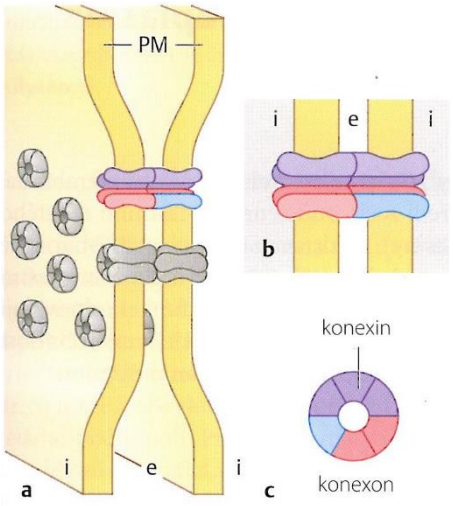
Diameter about 0,3 μm
Distance between cell membranes about 3 nm
Internal diameter of the channel about 2 nm





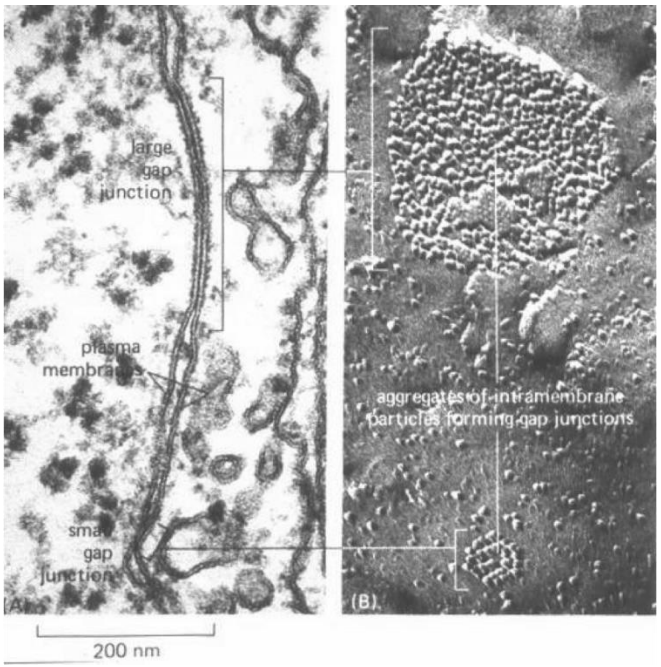


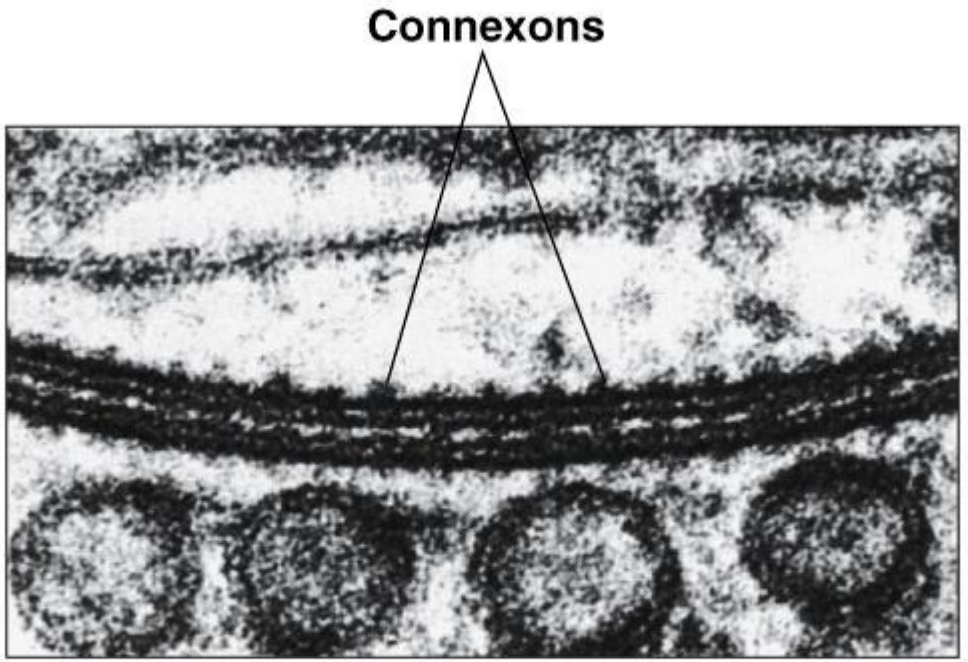
Adhesions and Junctions 10



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

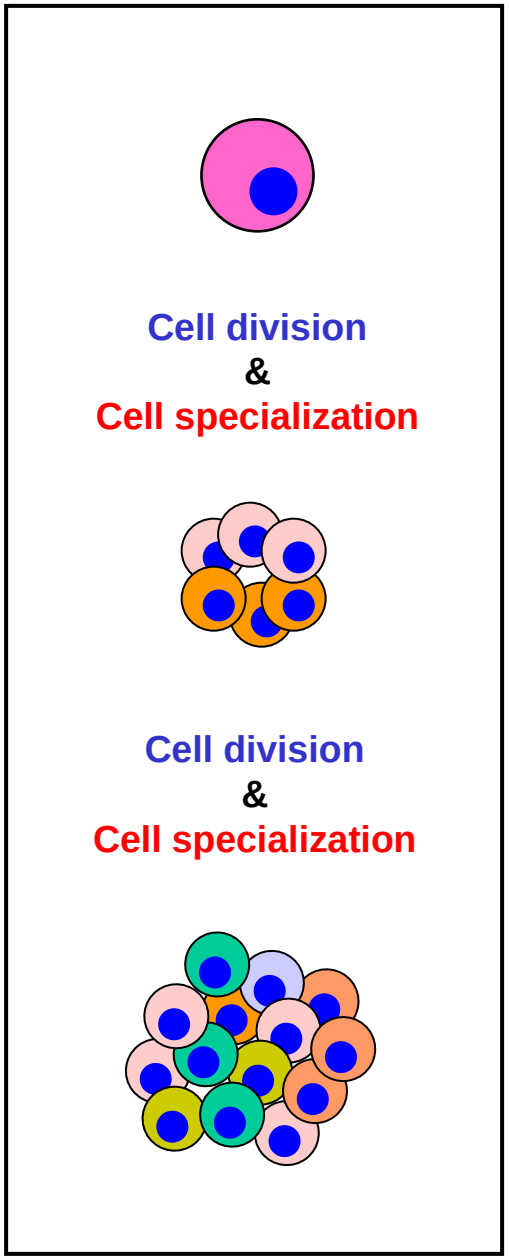
Zygote

Multicellular embryo

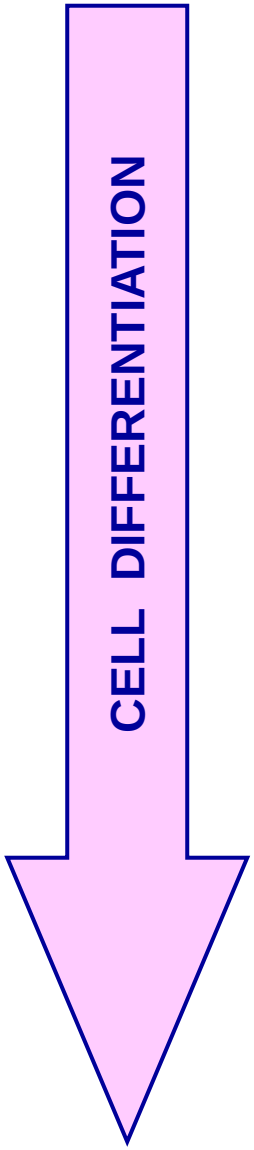
Dynamic multicellular organism

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

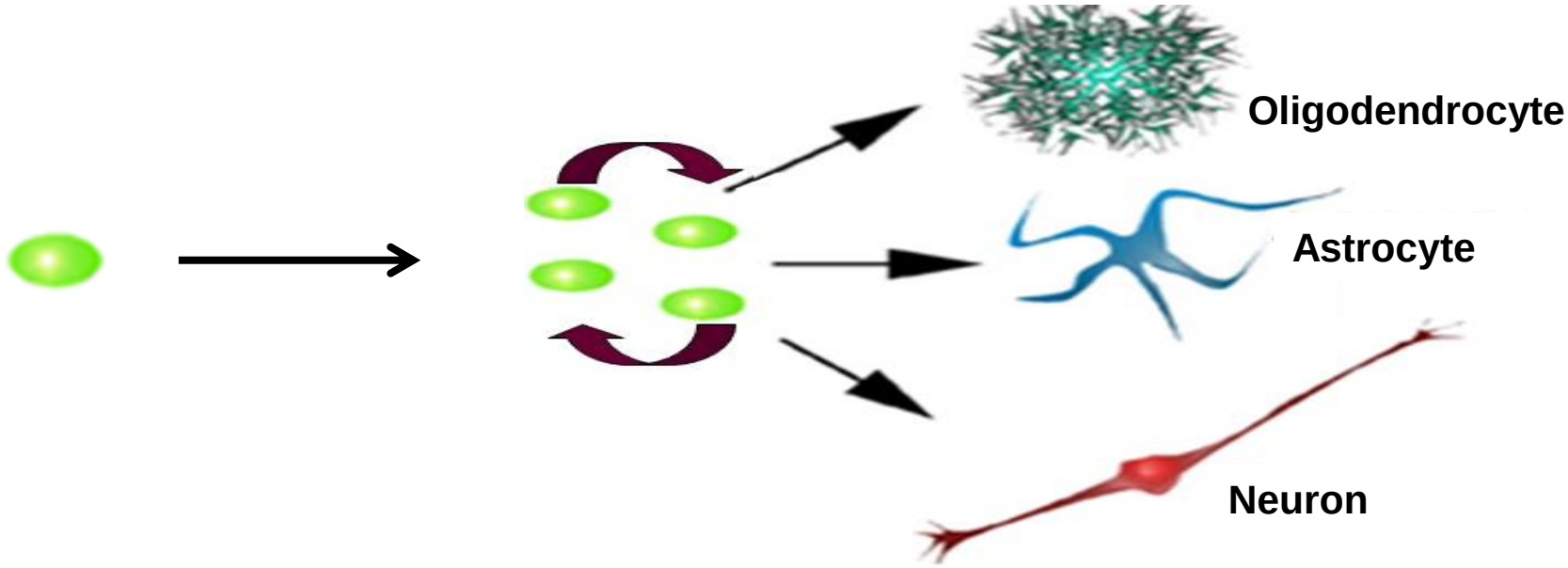
Division x Differentiation of cells 3

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

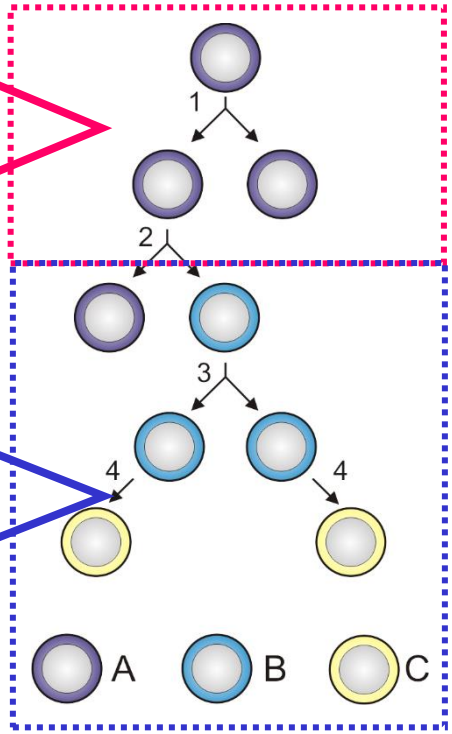
Capability to produce identical copies of itself

Self-renewal

Capability to differentite into specialized cell types

Pluripotency

1. Undifferentiated growth



2. Differentiation

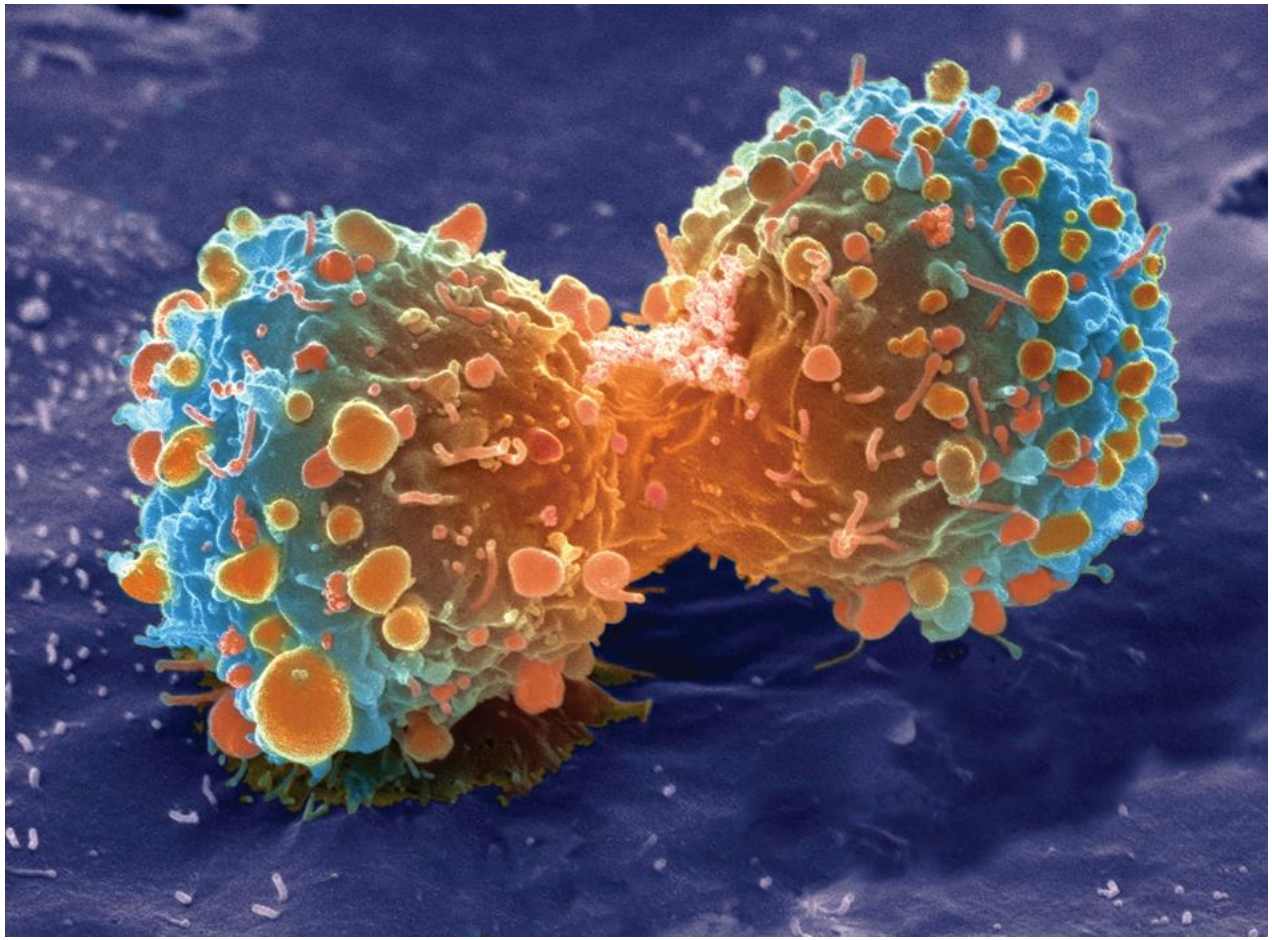
- Embryonic stem cells
- Adult stem cells
  - Fetal
  - Organ
  - Tissue
- Induced pluripotent stem cells
- Cancer stem cells

Different properties

Cell division 1

Basic concept 1

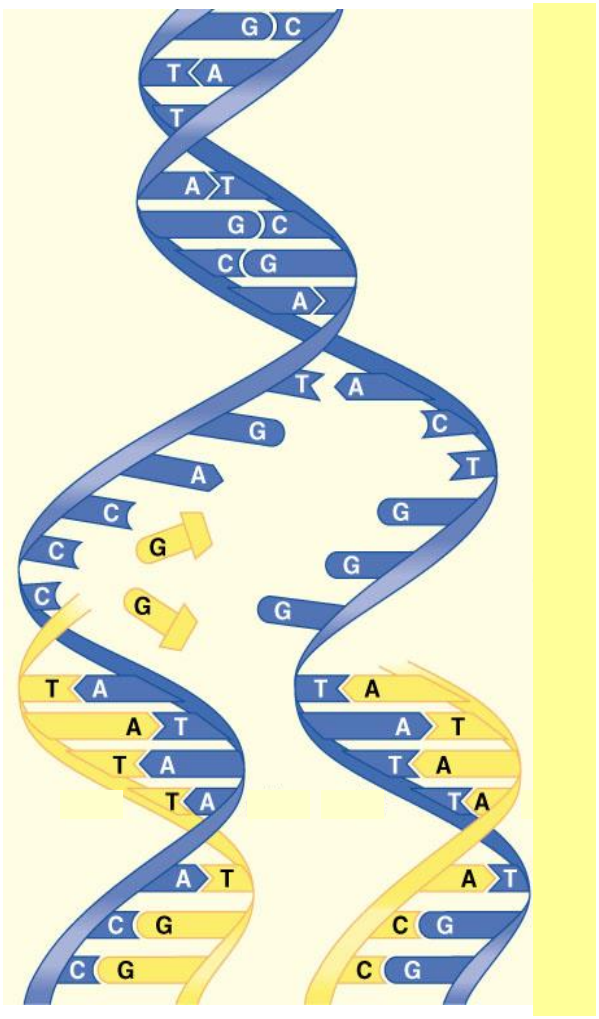
MITOSIS and CYTOKINESIS produce genetically identical cells

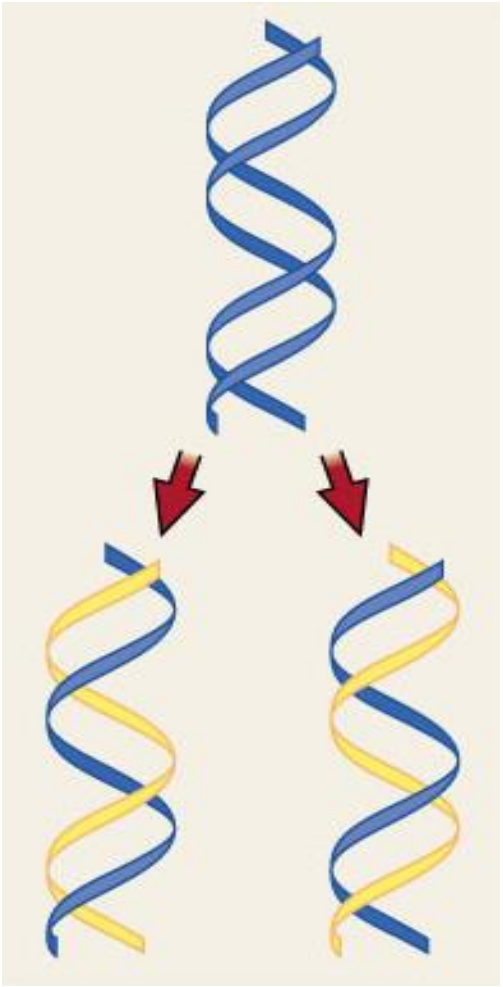


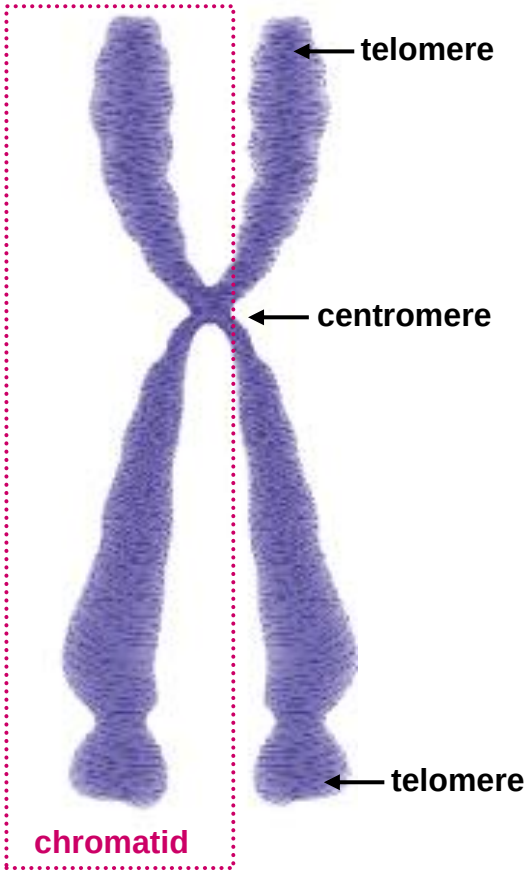
Cell division 2

STABLE (non-changing) GENOME

Due to semiconservative duplication of DNA



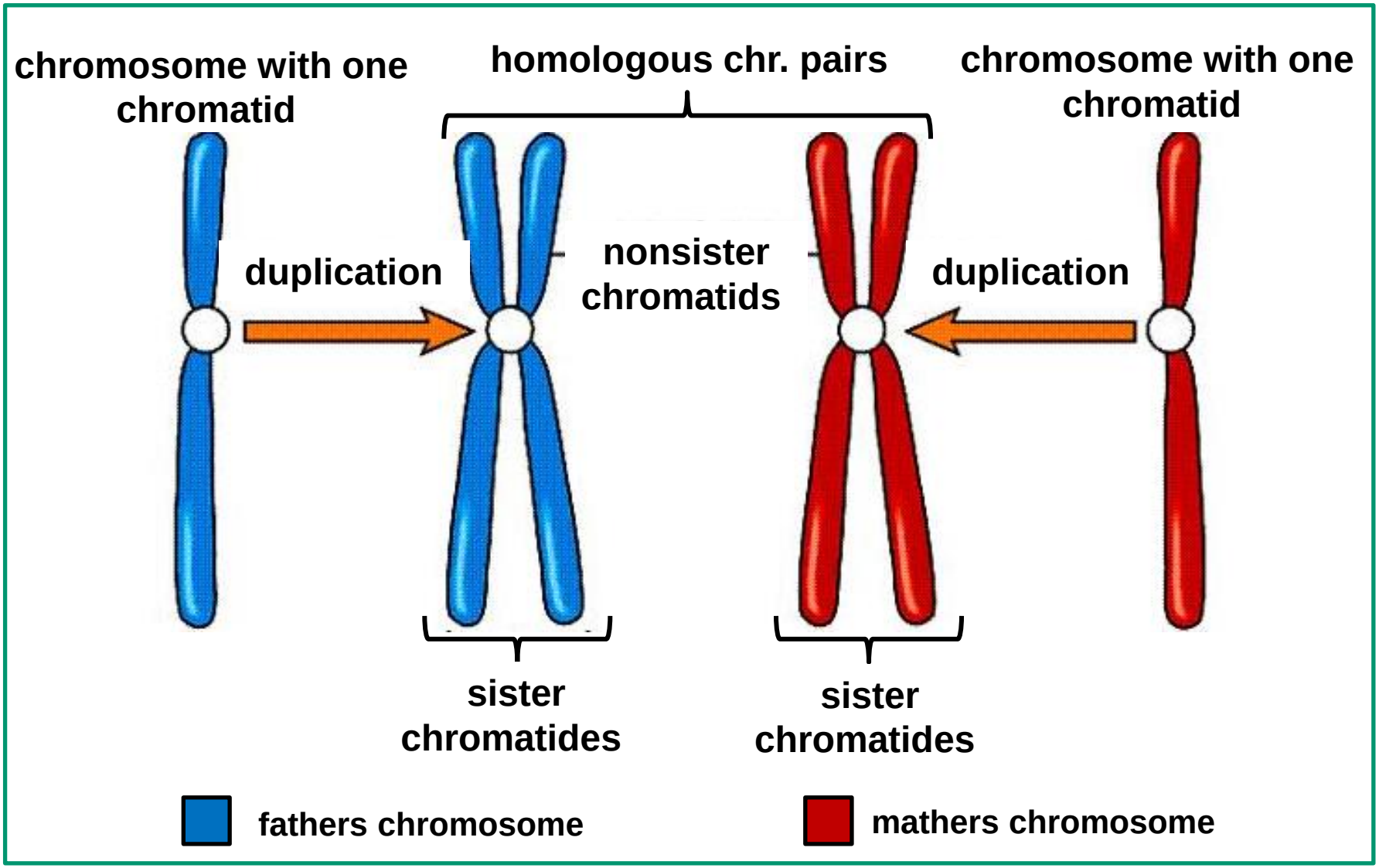




Condensed duplicated chromosome

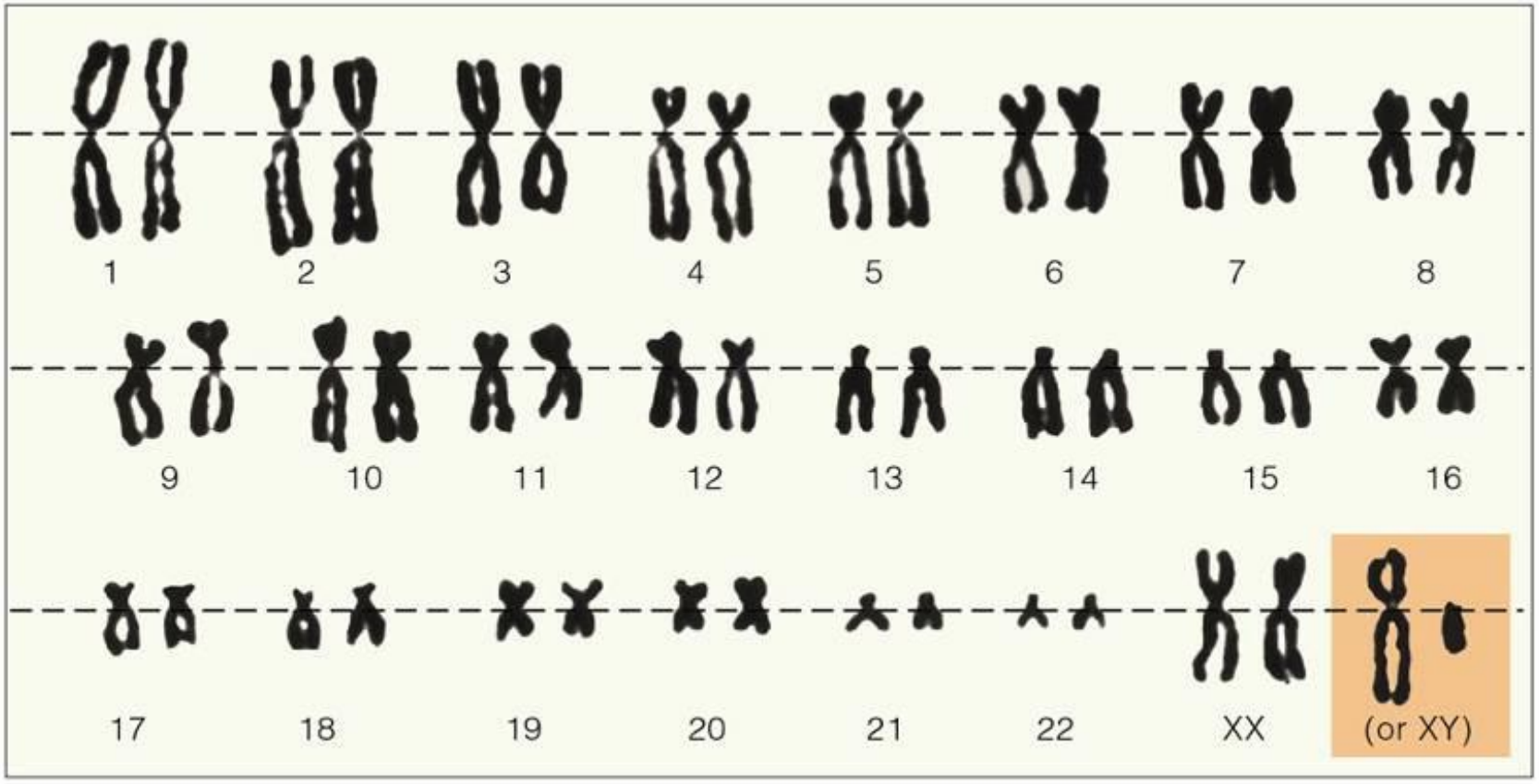
Cell division 3

Metabolism of chromosomes – Homologous chromosomes



Cell division 4

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



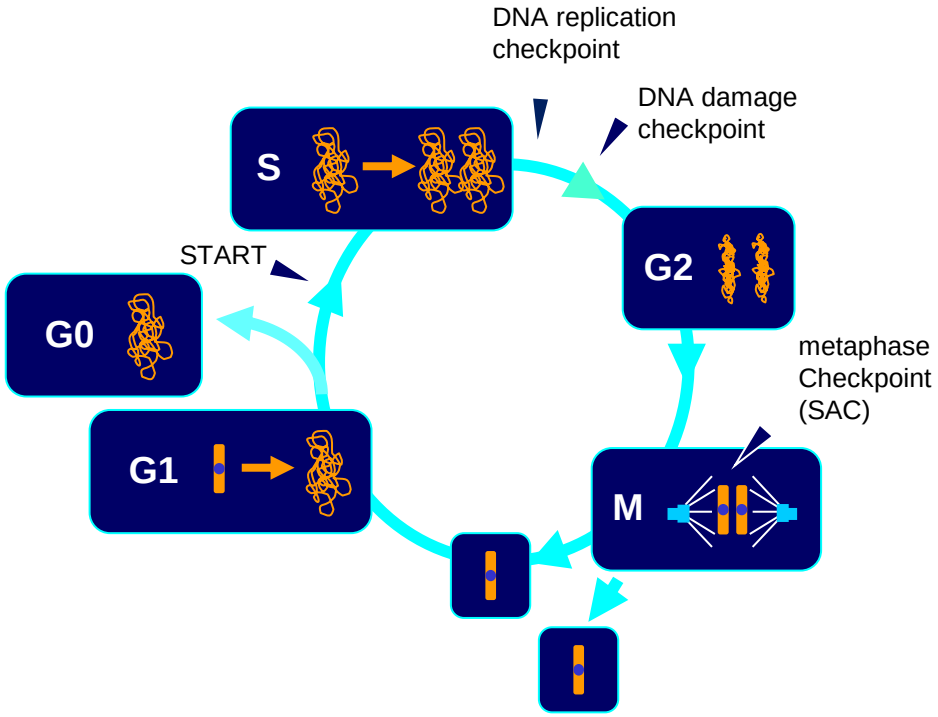
Cell division 5

Basic concept 2

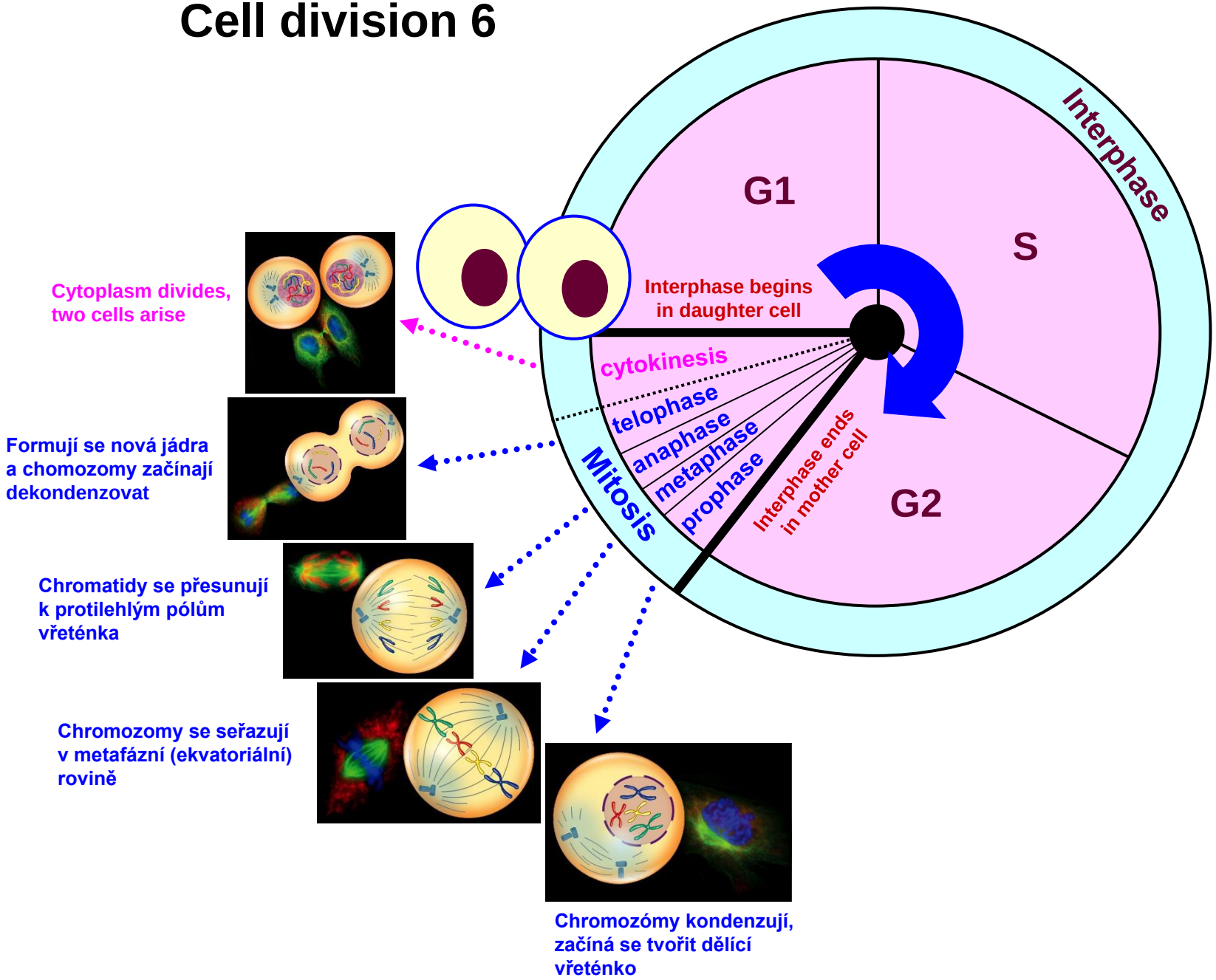
MITOSIS and CYTOKINESIS are parts of cell cycle

CELL CYCLE

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

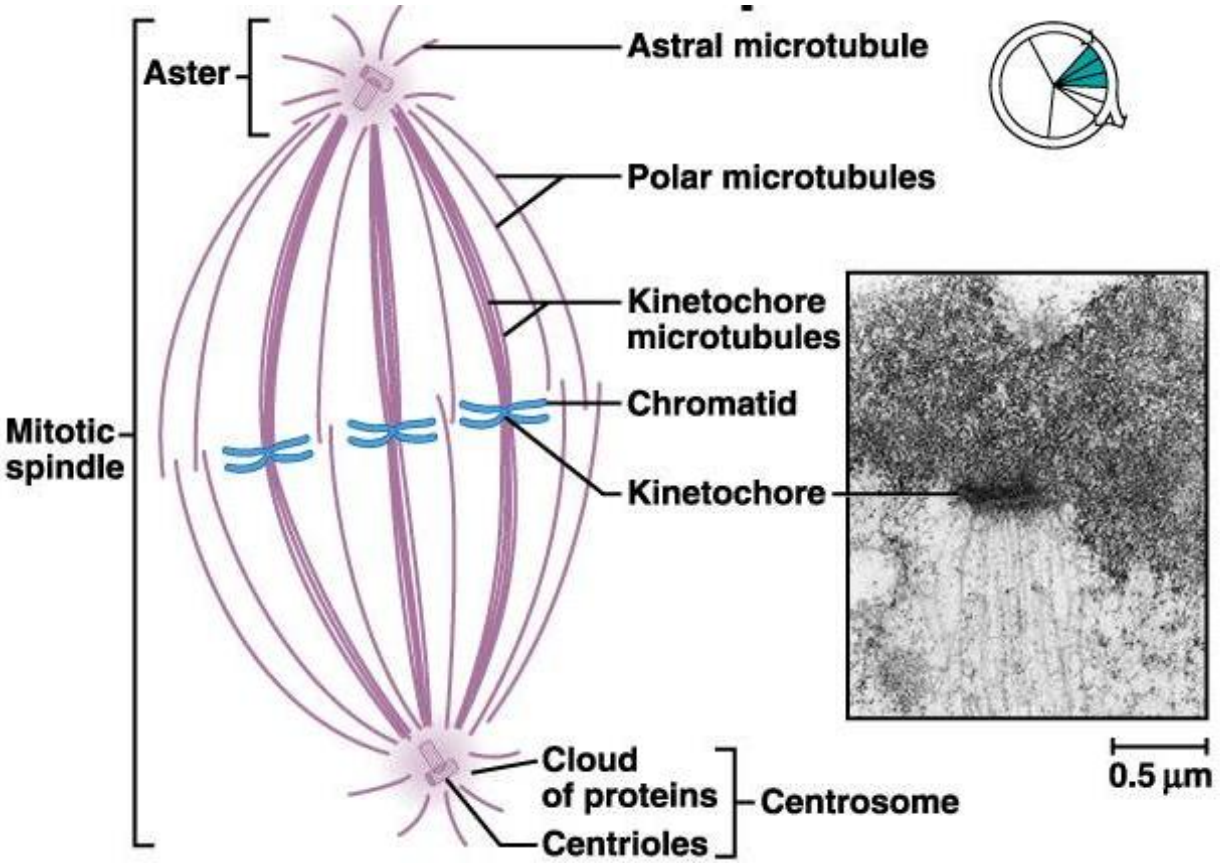


Cell division 6



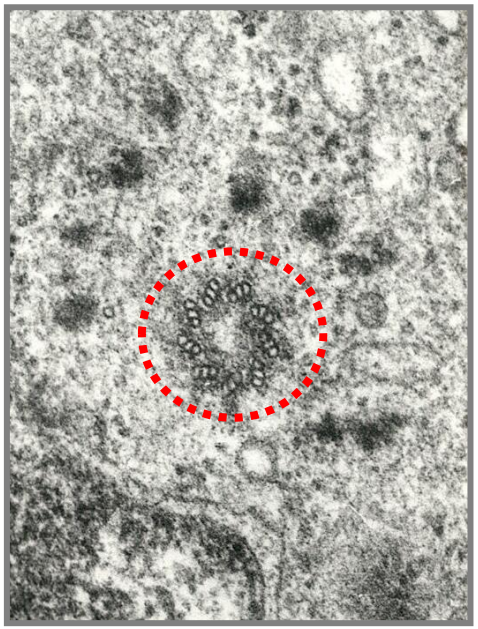
Cell division 7

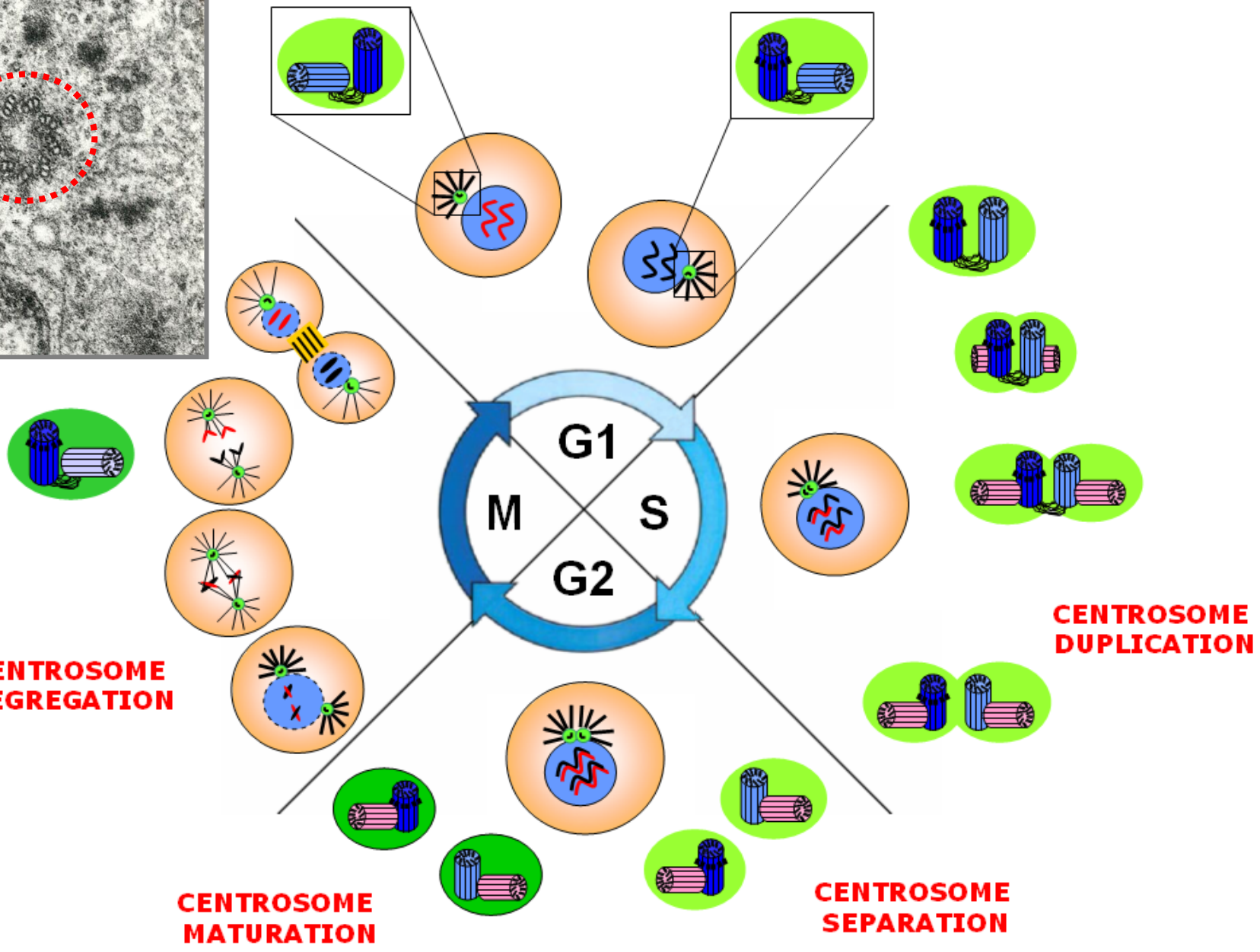
Mitotic spindle



Cell division 8

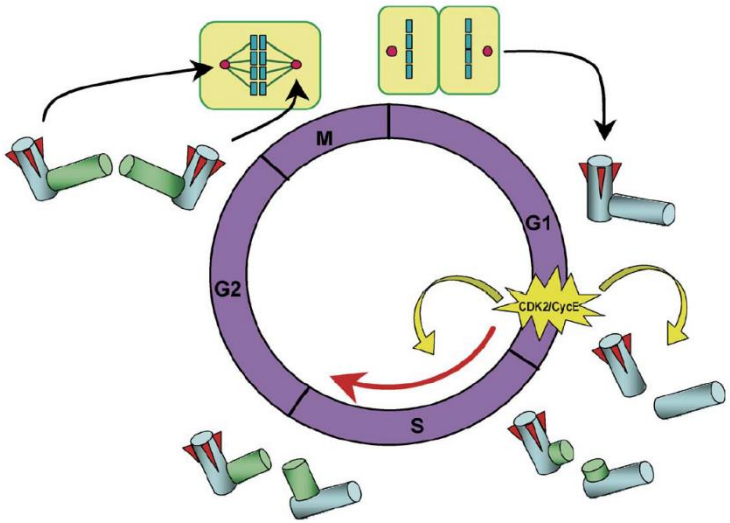
Centrosomal metabolism
Semiconservative duplication

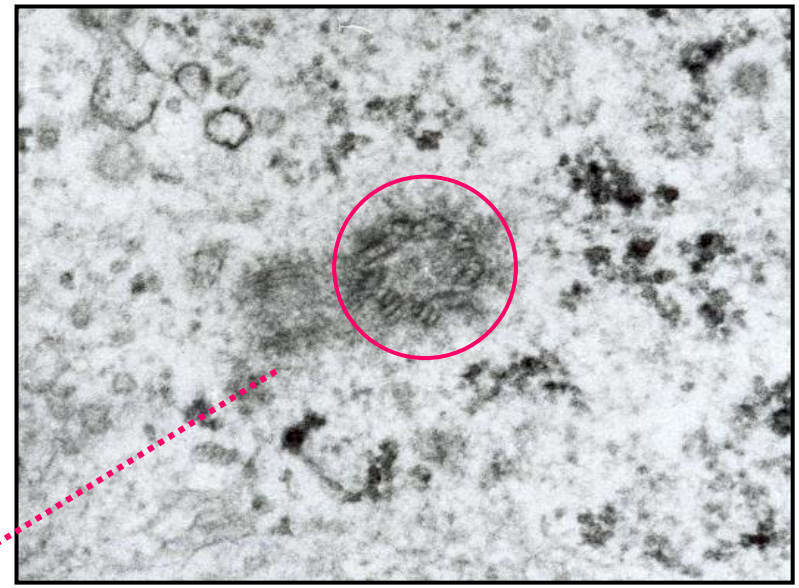


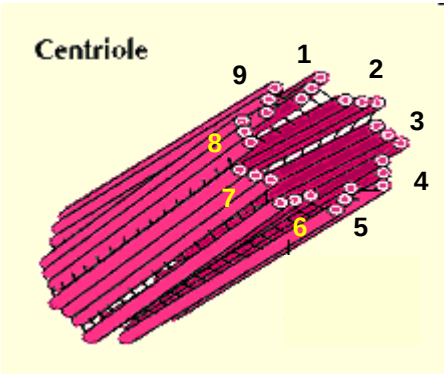


Cell division 9

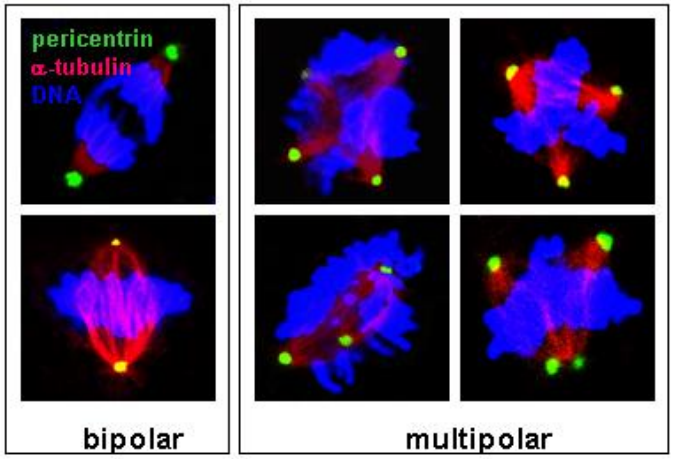
Centrosome structure







Diameter – 0.2 μm
Length - 0.5 μm



Cell division 10

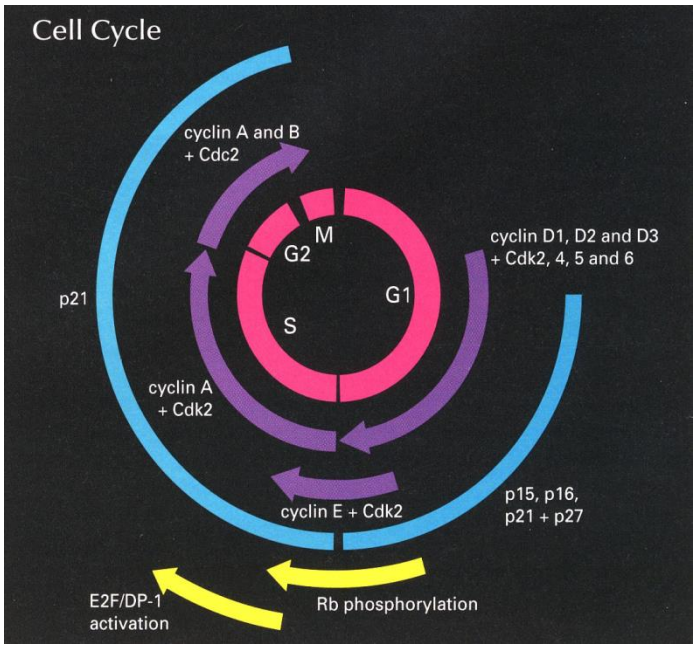
Regulation – Cyklin-Dependent Kinases (CDK) + Cyklins

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

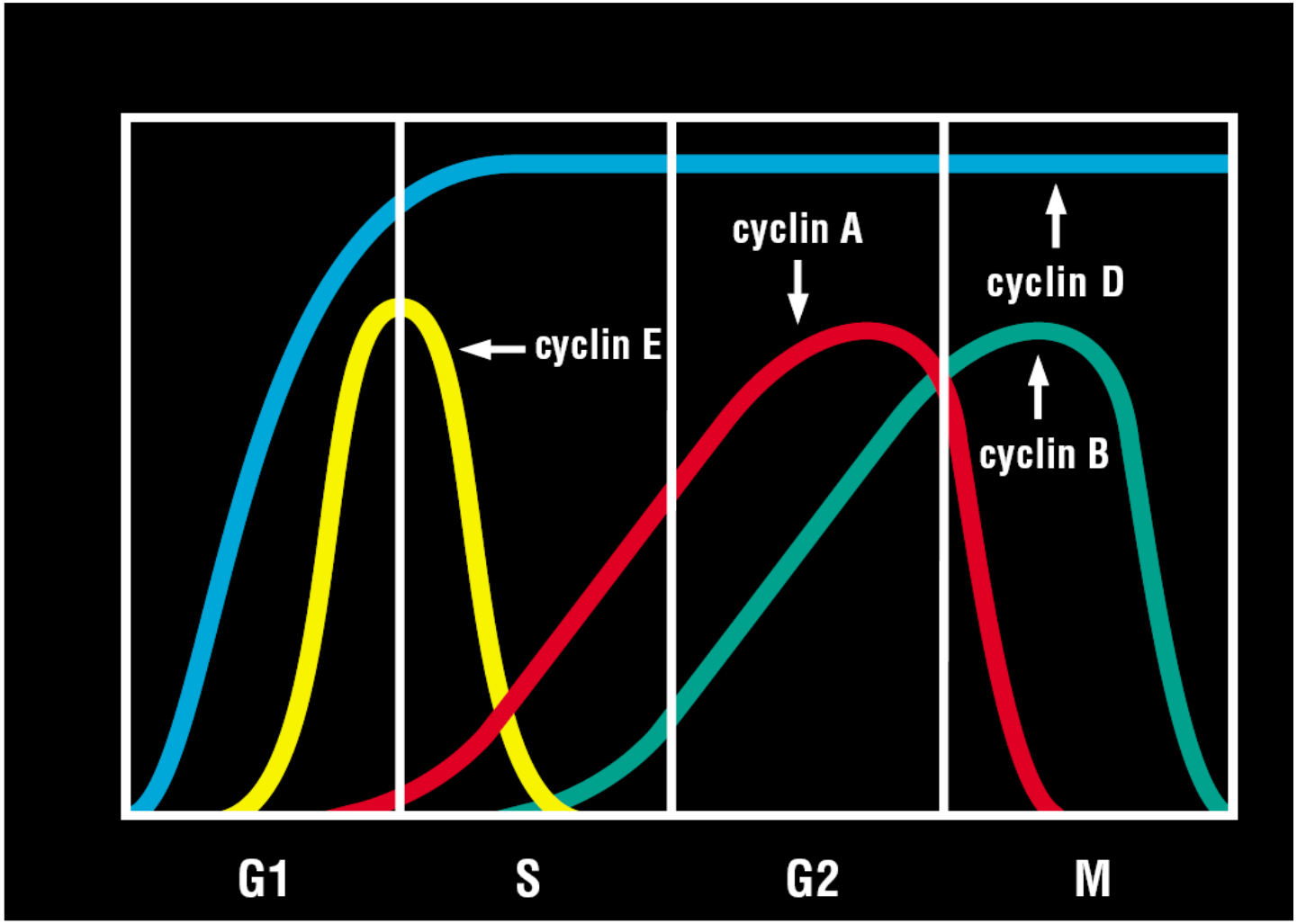
cell cycle stage	cyclin-Cdk complexes	inhibitors						
		p15	p16	p18	p19	p21	p27	p57
G1	cyclin D-Cdk4/6	+	+	+	+	+	+/–	+/–
G1/S	cyclin E-Cdk2	–	–	–	–	+	+	+
S	cyclin A-Cdk2	–	–	–	–	+	–	+
G2/M	cyclin B-Cdc2	–	–	–	–	+	–	–



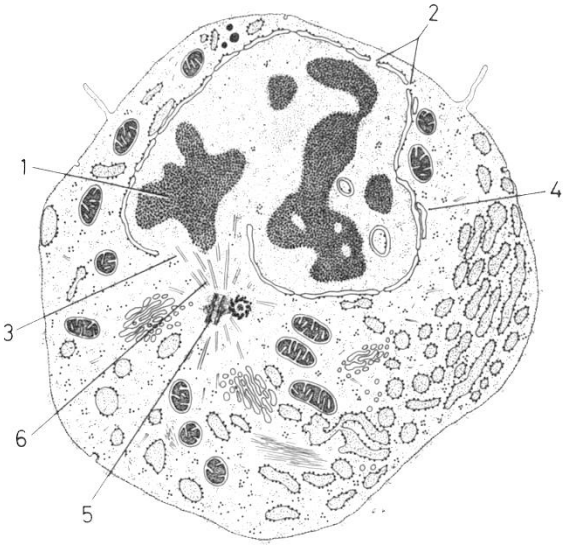
Modified from the catalogue ofSanta Cruz Biomedicals, USA

Cell division 11

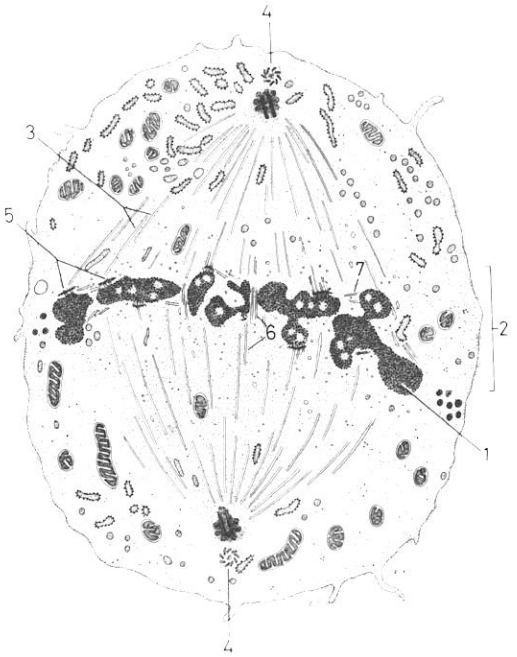
Periodicity of cyclin expression



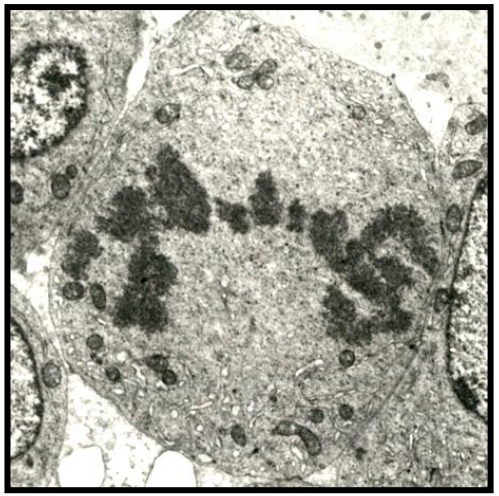
Cell division 12

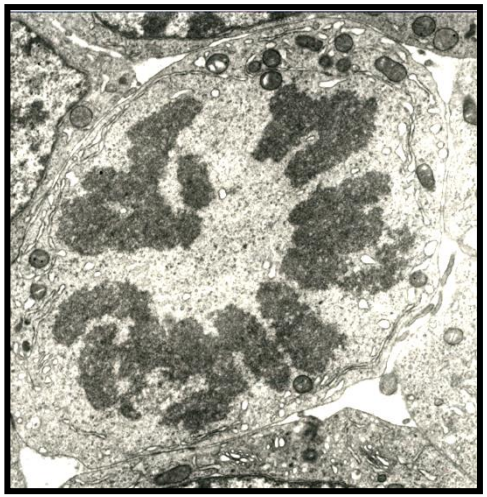


prophase

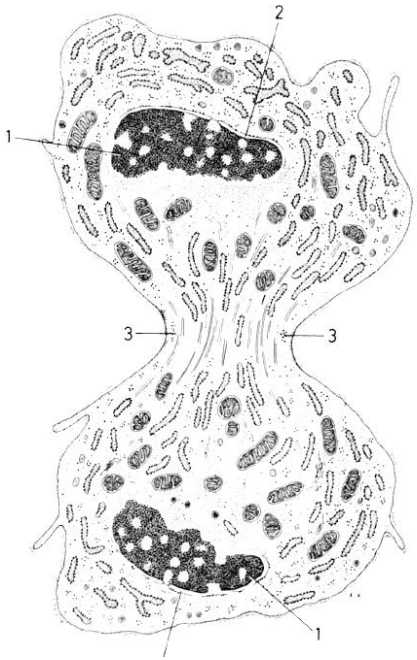


metaphase

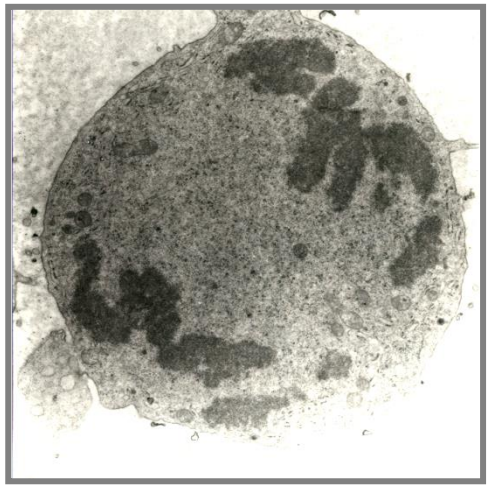


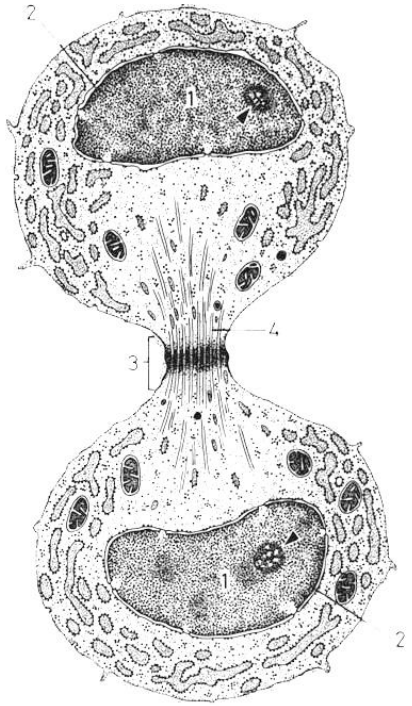


Cell division 13

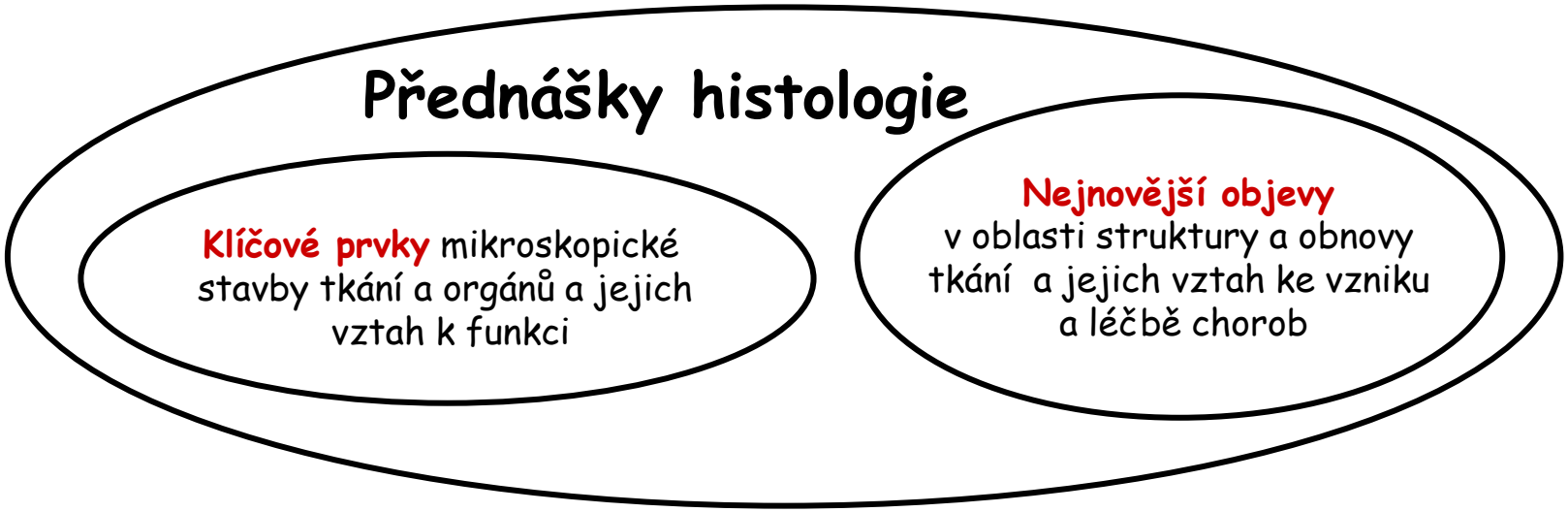


anaphase - telophase





telophase



Děkuji za pozornost !

ahampl@med.muni.cz

Budova A1 – 1. patro