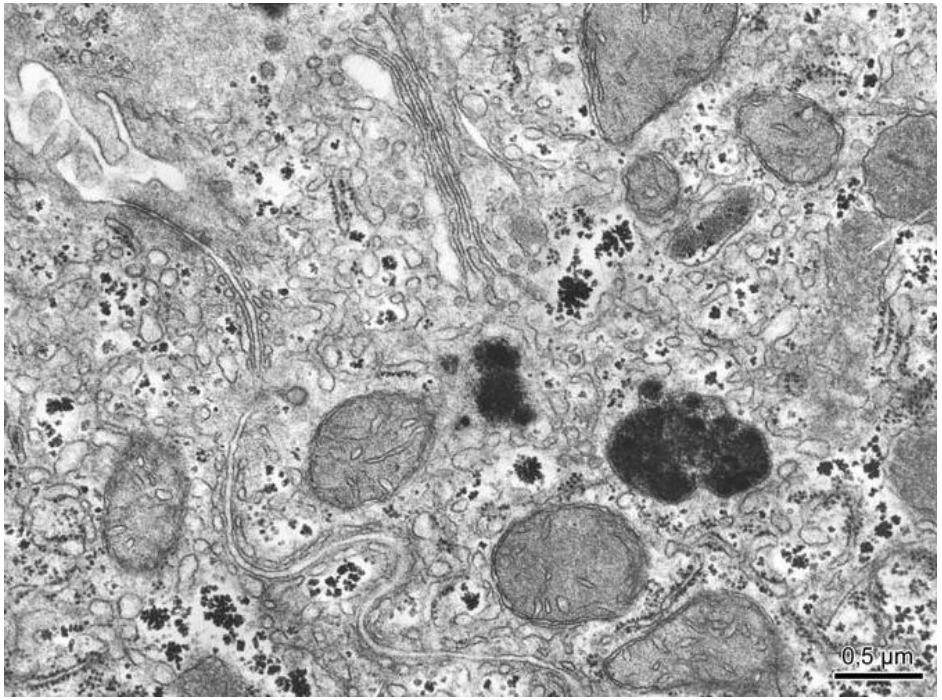
Úvod do cytologie

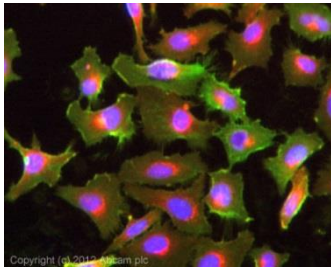
Cytologie

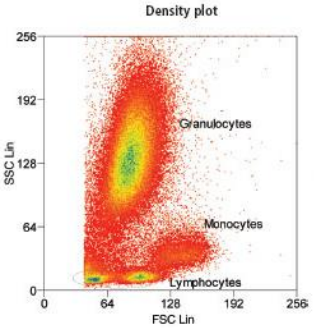
Ultrastruktura buňky (morfologie)

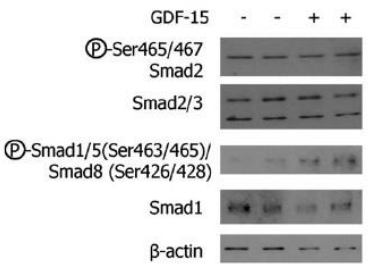
Molekulární a buněčná biologie

→ Funkční morfologie



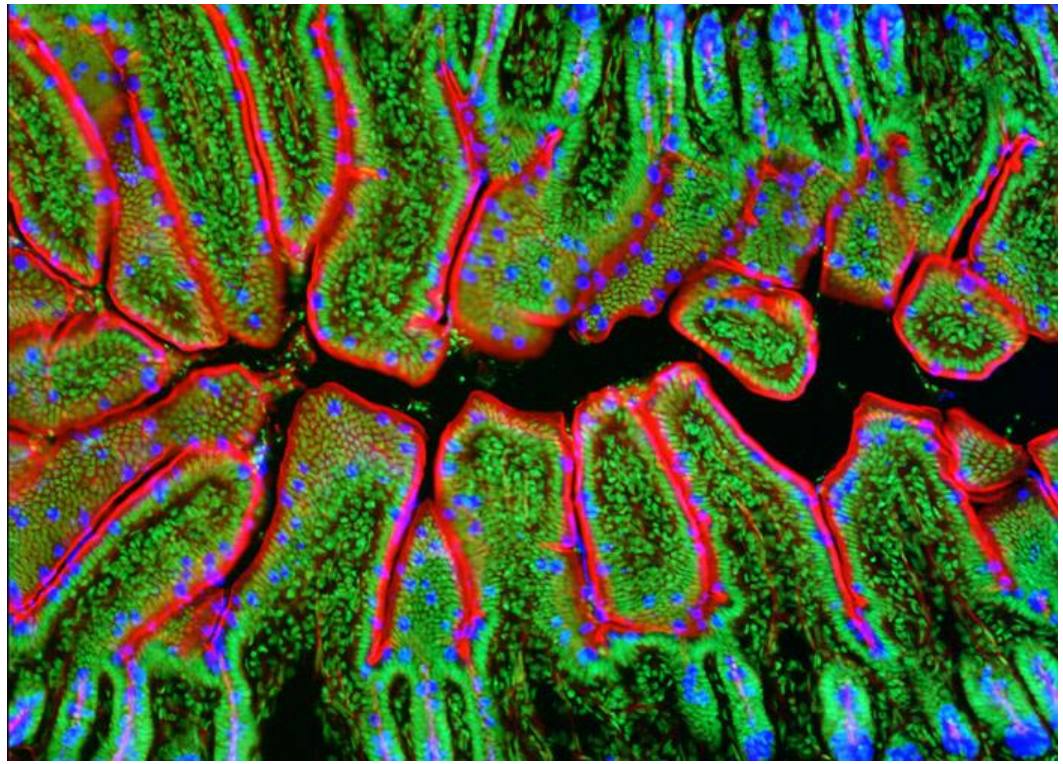


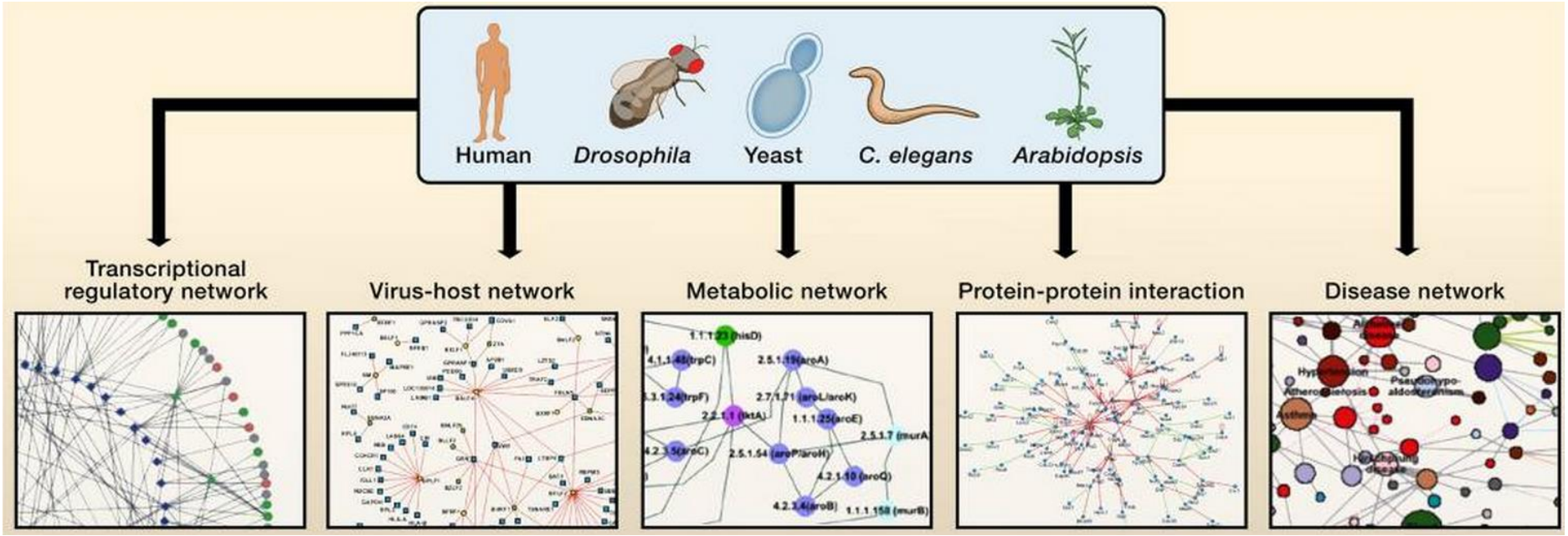


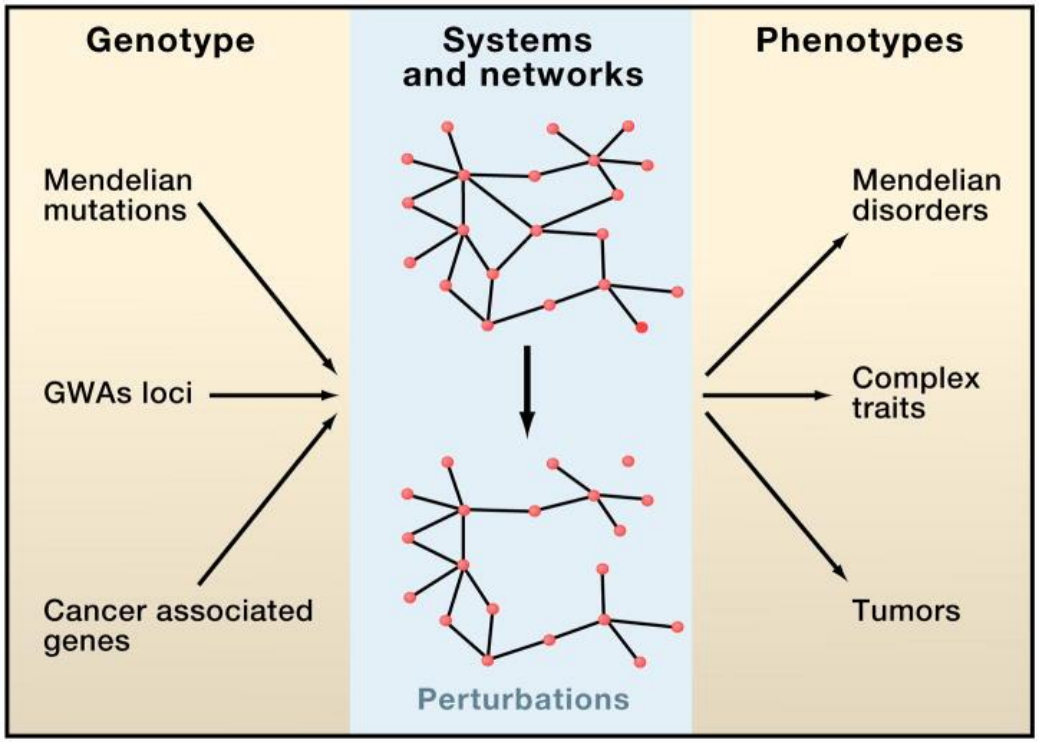


Buňka

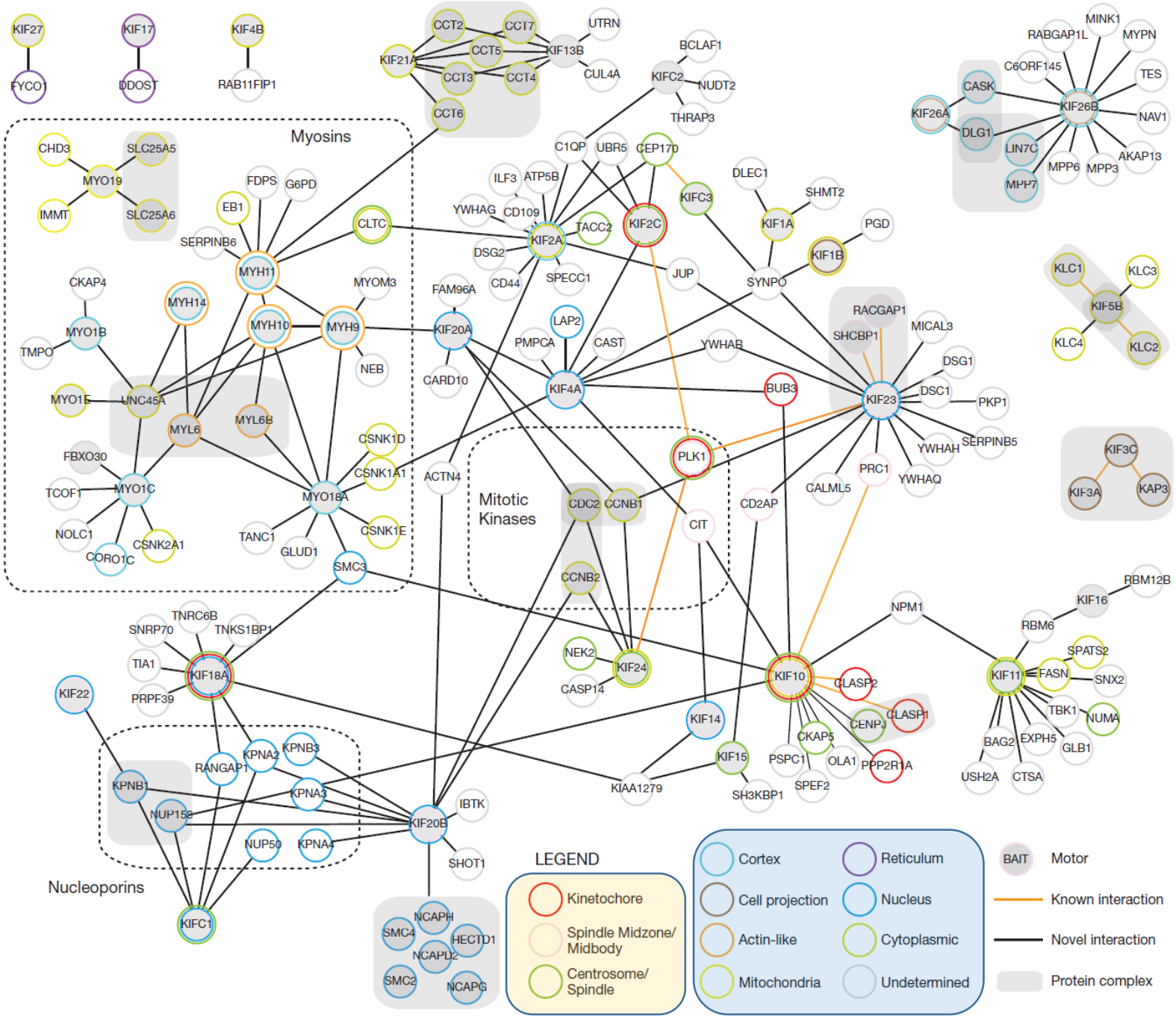
- Základní strukturní a funkční jednotky všech mnohobuněčných organismů
- Konkrétní molekulární funkce (děje) můžeme přiřadit konkrétním buněčným strukturám (doménám, kompartmentům)
- Popis







Vidal et al. Cell. 2011 March 18; 144(6): 986–998.
doi: 10.1016/j.cell.2011.02.016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CCT4
CUL4A
CCT6
BCLAF1
KIFC2
NUDT2
THRAP3
MINK1
RABGAP1L
MYPN
C6ORF145
TES
CASK
KIF26A
KIF26B
NAV1
DLG1
LIN7C
AKAP13
MPP6
MPP3
MPP7
Myosins
CHD3
SLC25A5
MYO19
IMMT
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EB1
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CLTC
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UBR5
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MYH9
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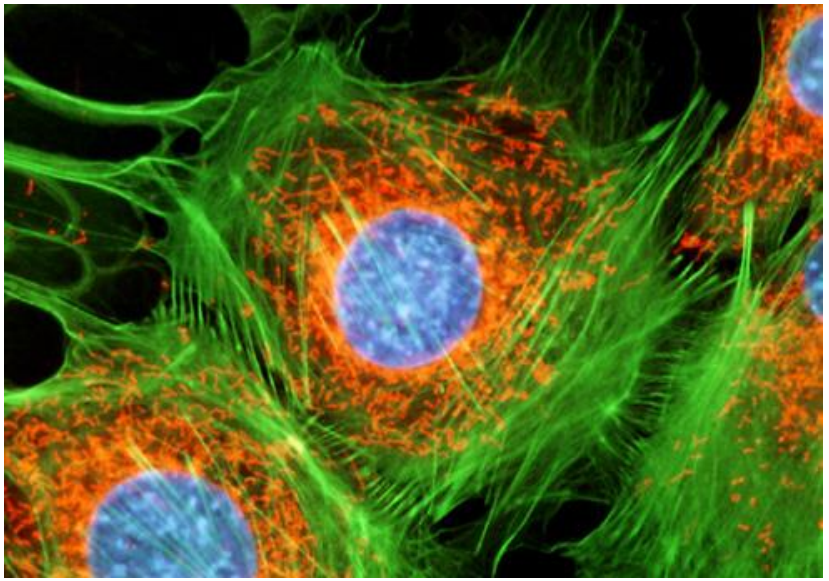
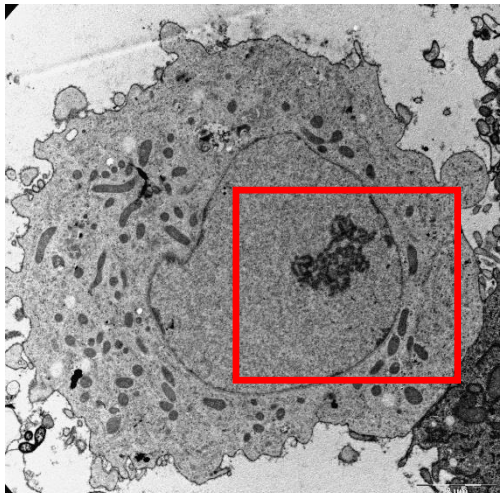
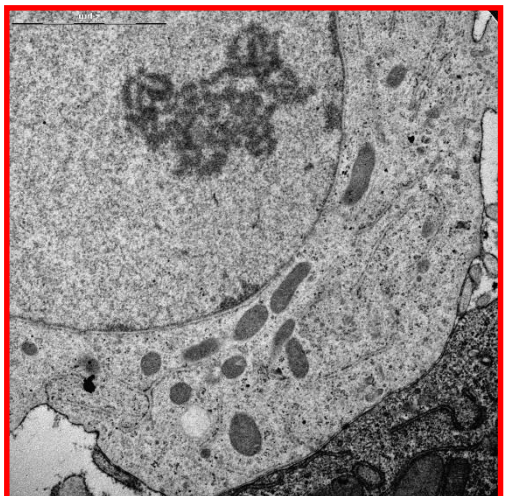
SHOT1
Nucleoporins
KIFC1
NCAPH
SMC4
HECTD1
NCAPD2
SMC2
NCAPG
LEGEND
Kinetochore
Spindle Midzone/
Midbody
Centrosome/
Spindle
Cortex
Reticulum
Cell projection
Nucleus
Actin-like
Cytoplasmic
Mitochondria
Undetermined
BAIT
Motor
Known interaction
Novel interaction
Protein complex

Ultrastruktura buňky

- **Jádro (karyoplazma)**
- **Cytoplazma**
  - **Organely**
  - **Inkluze**
  - **Cytoplazmatická matrix**



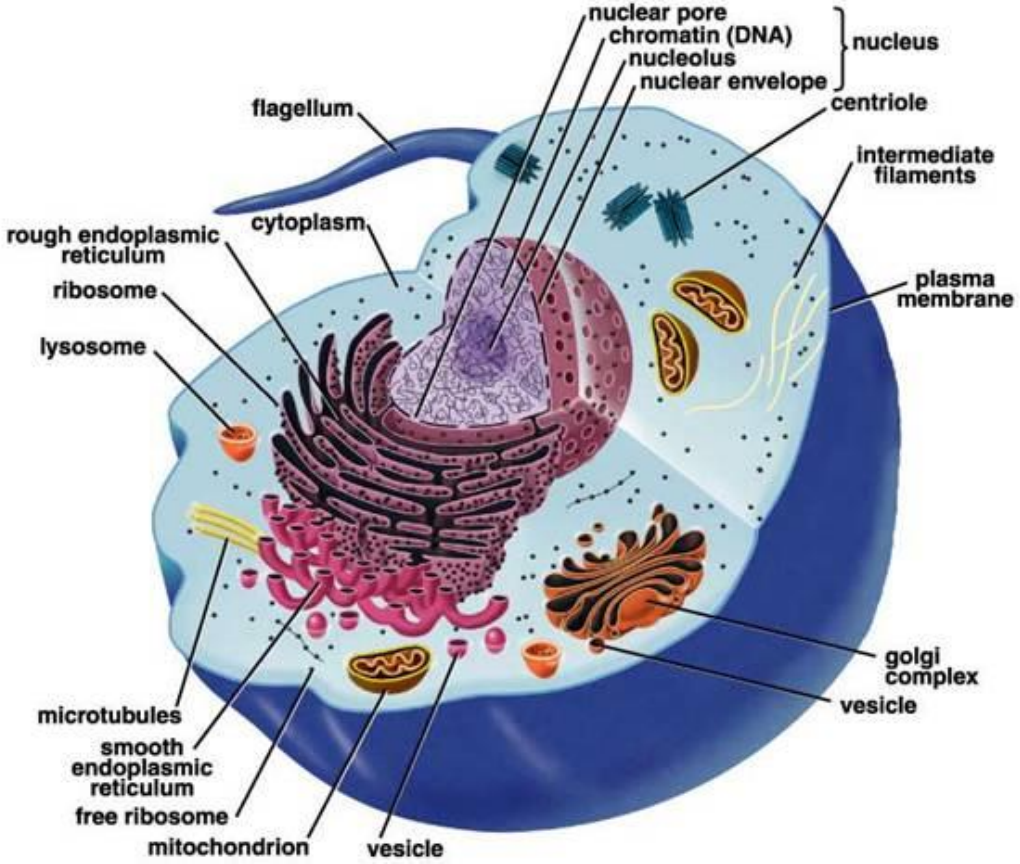




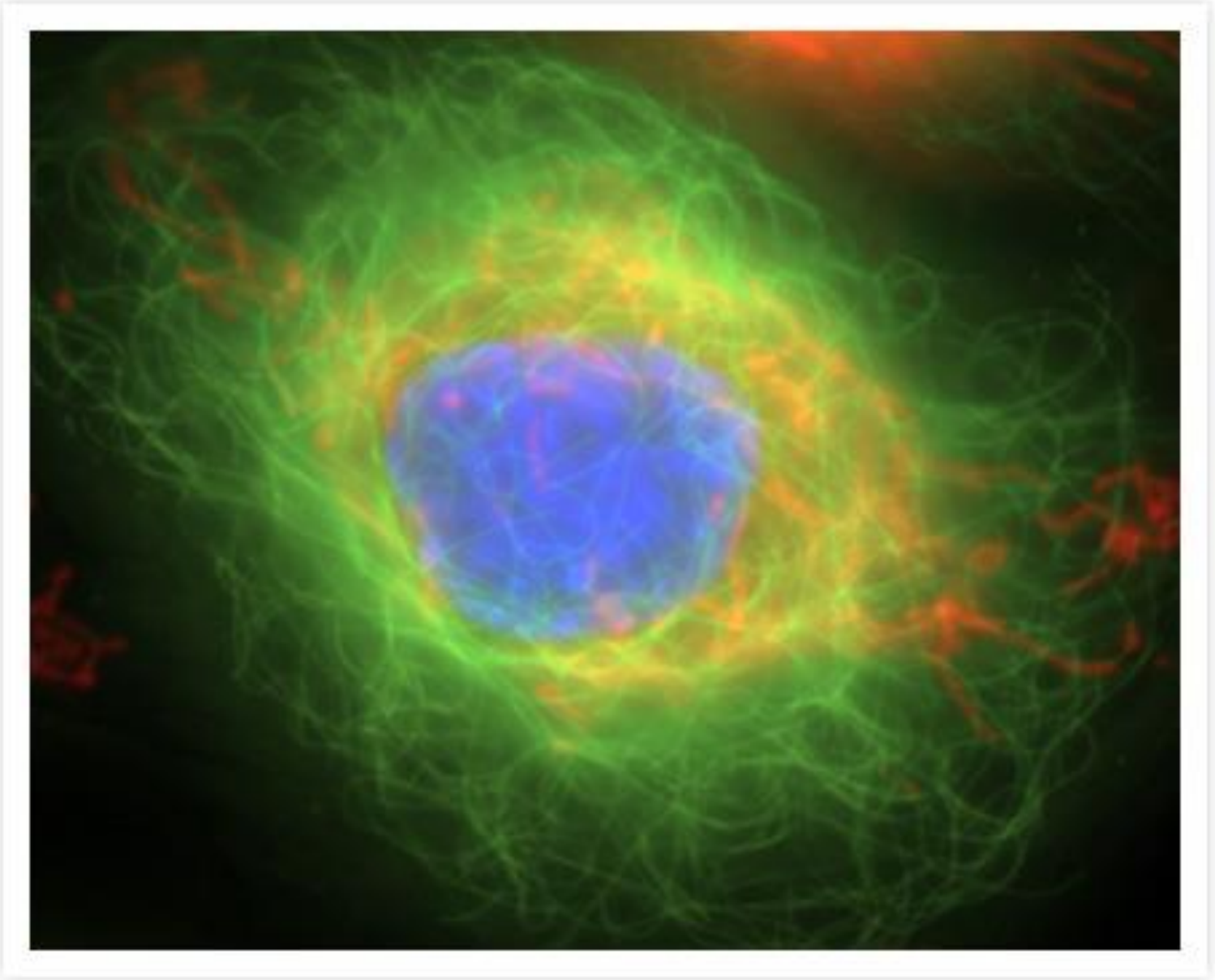
Organely

- **Membránové organely**
  - Plazmatická membrána
  - Endoplazmatické retikulum
  - Golgiho aparát
  - Endosomy
  - Lysosomy
  - Transportní váčky
  - Mitochondrie
  - Peroxisomy

- **Organely bez membrány**
  - Cytoskelet
  - Centrioly
  - Ribosomy

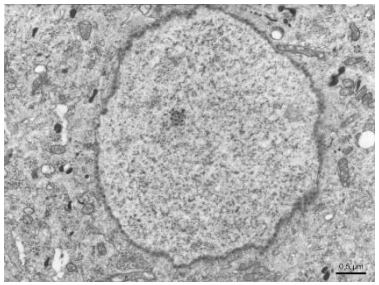


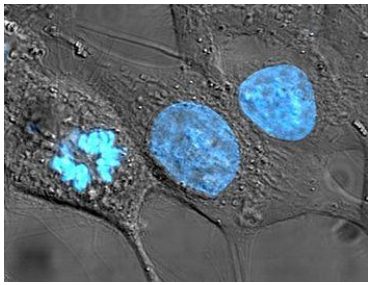
Jádro



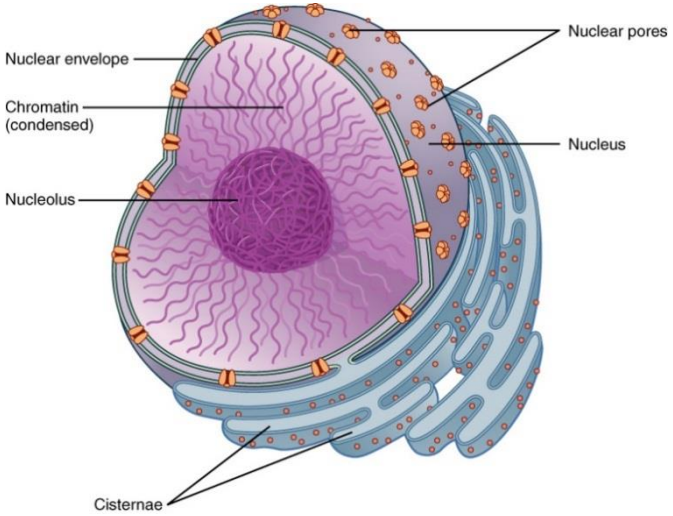
Jádro

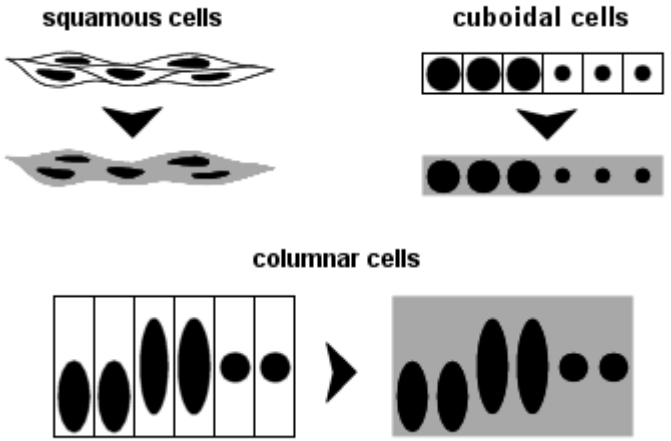
- Morfologie závisí na buněčném cyklu a transkripční aktivitě buňky
- Tvar jádra přibližně kopíruje tvar buňky





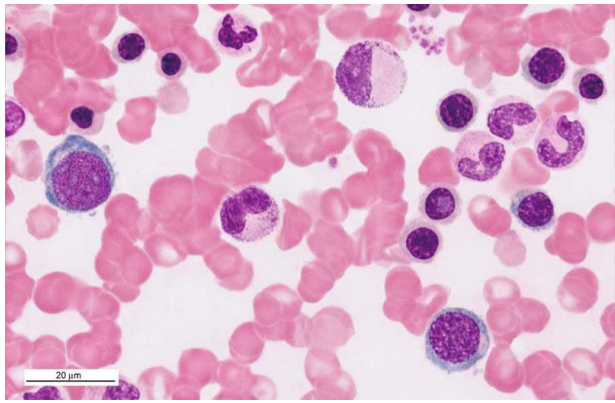
  - Chromatin
  - Jadérko (nucleolus)
  - Jaderná membrána
  - Nukleoplazma

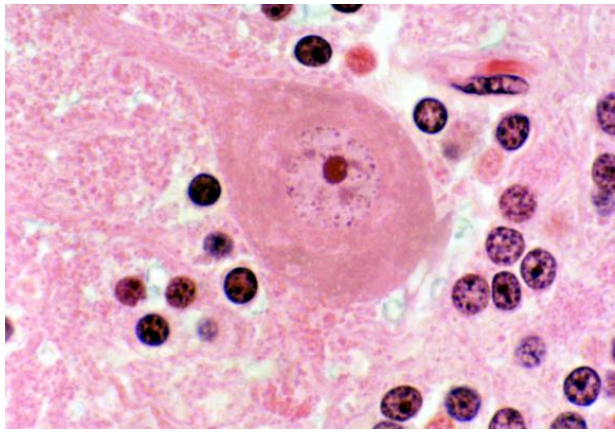


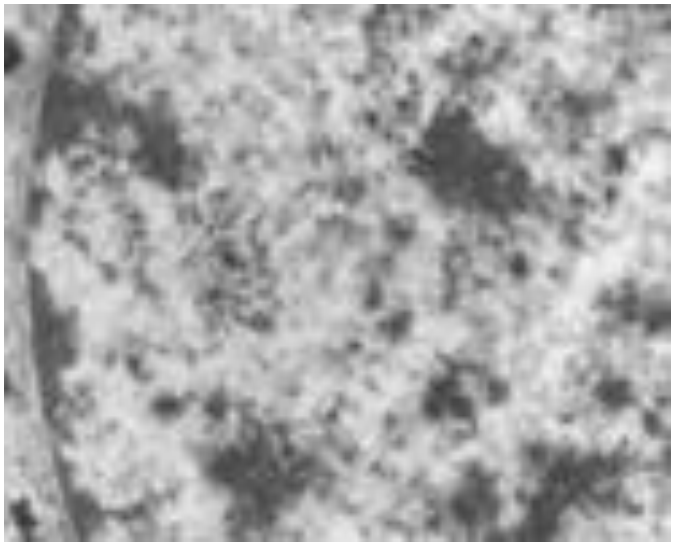


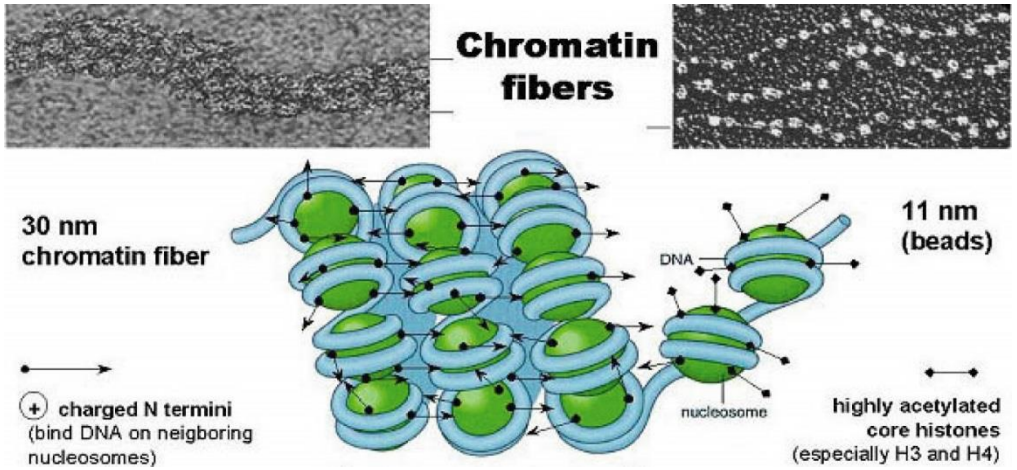
Chromatin a chromosomy

- Komplex DNA a proteinů
- Zodpovědný za bazofilii buněčného jádra
- DNA – 1,8m, 3×10^9bp, 20 000 strukturních genů (1,5%), nekódující RNA, regulační DNA sekvence, LINE, SINE, introny…
- Složitá organizace
- Heterochromatin, euchromatin
- Karyotyp 46XX/XY

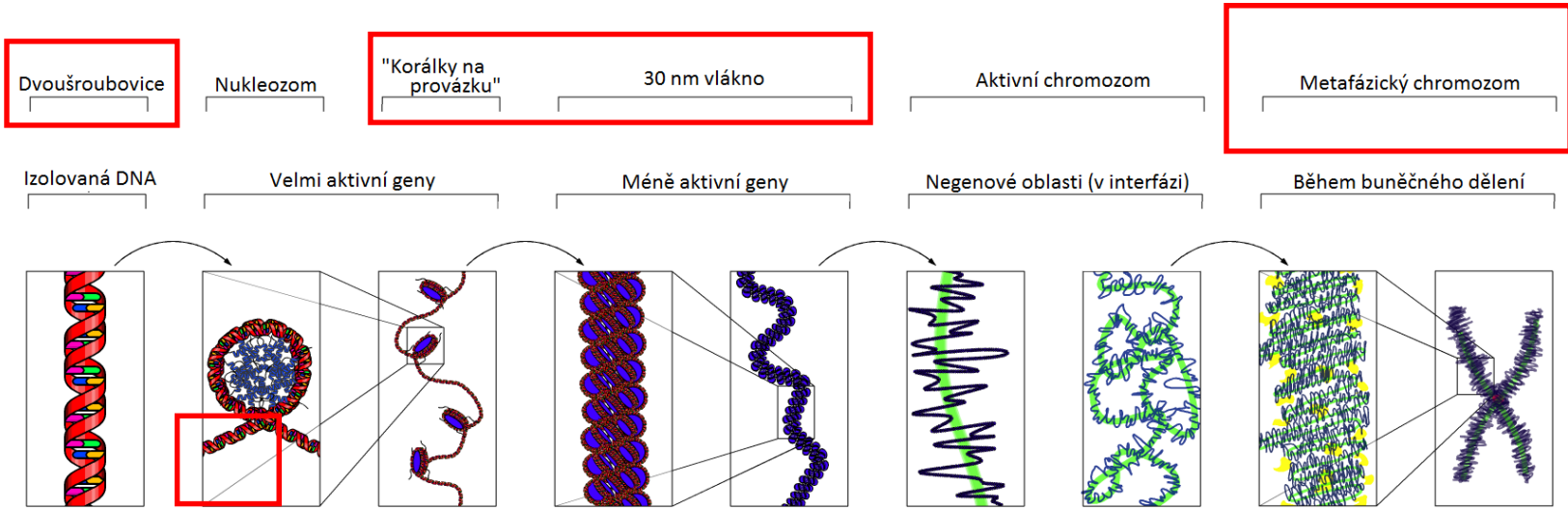


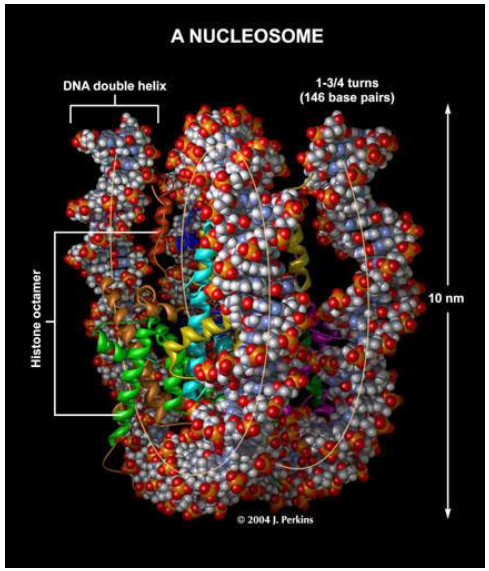


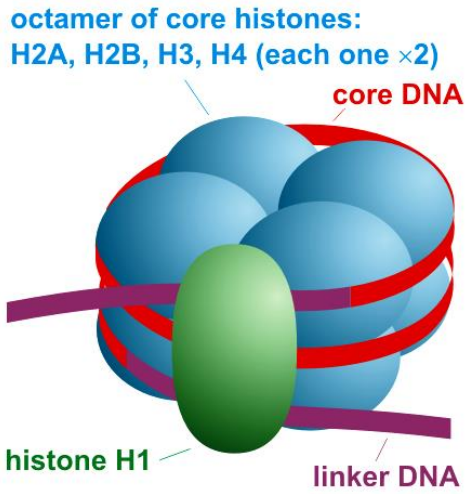


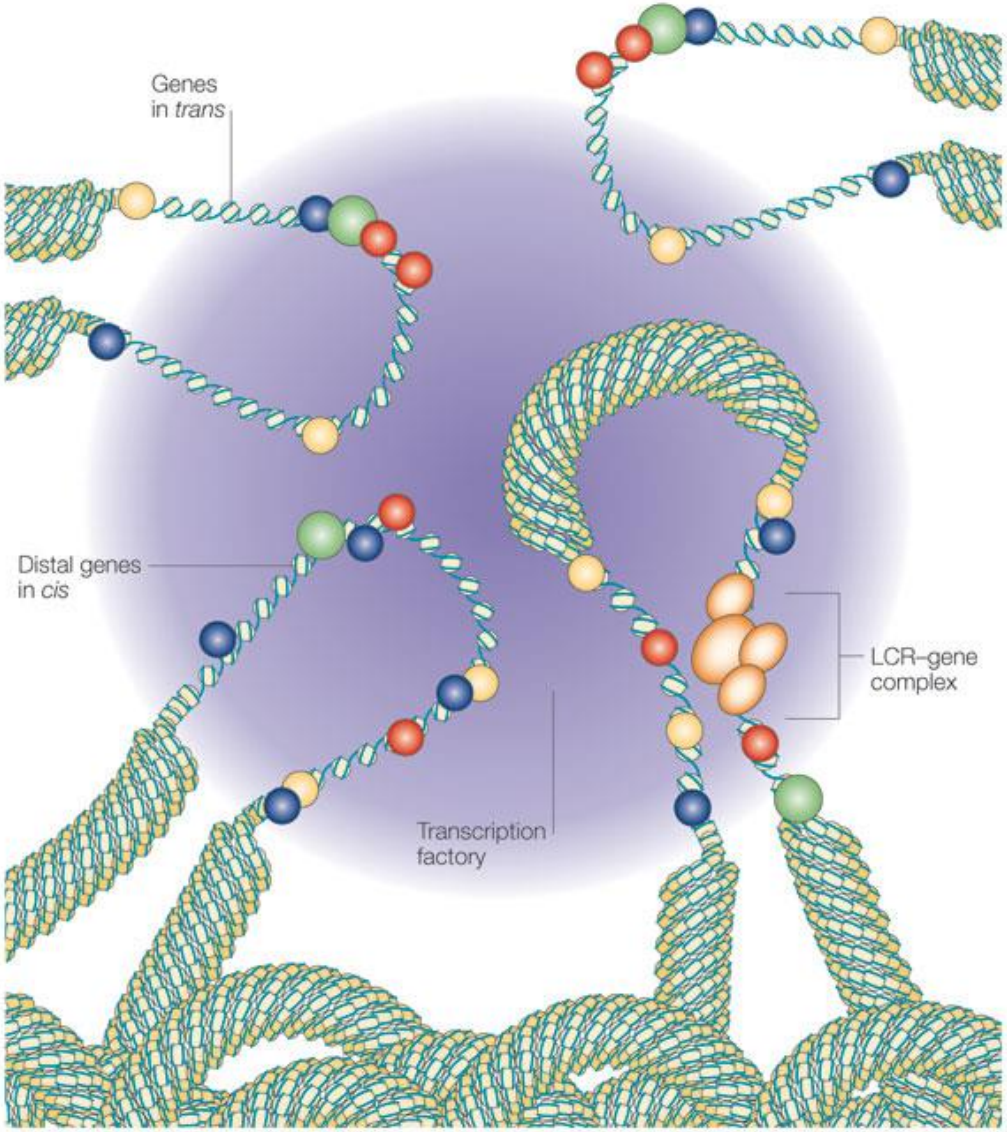


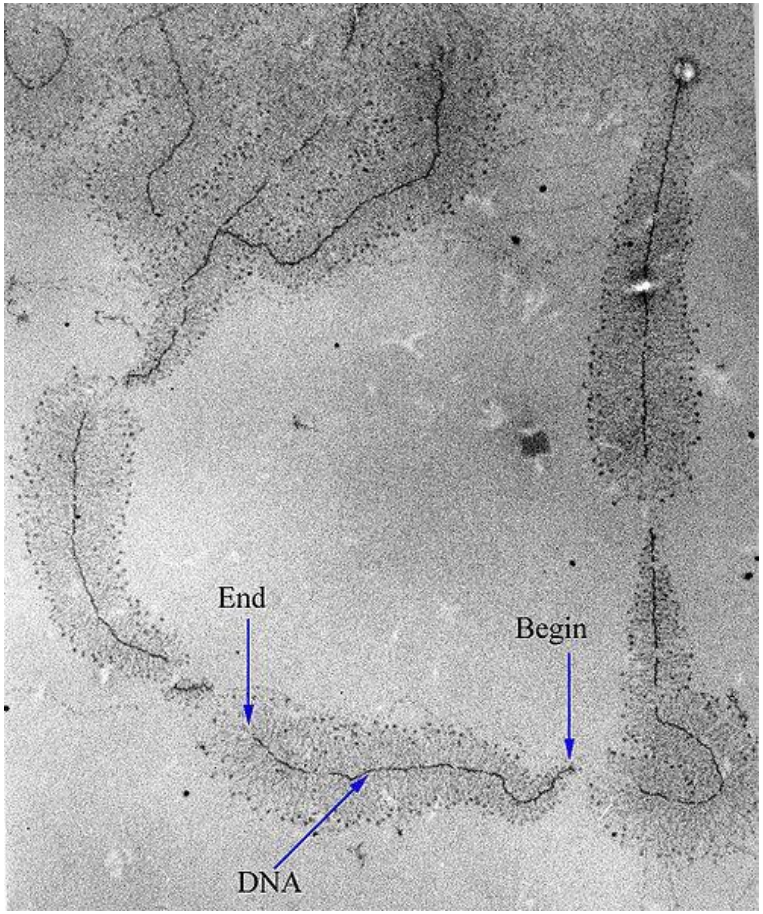
Organizace chromatinu





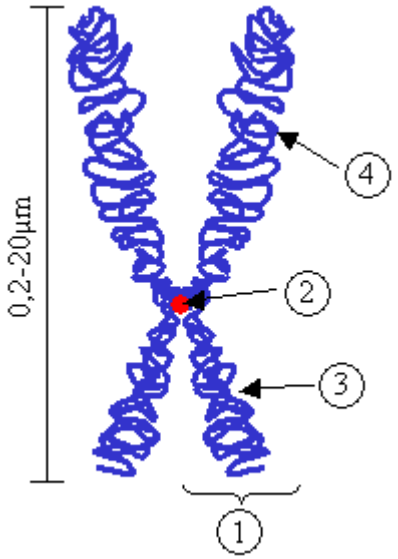


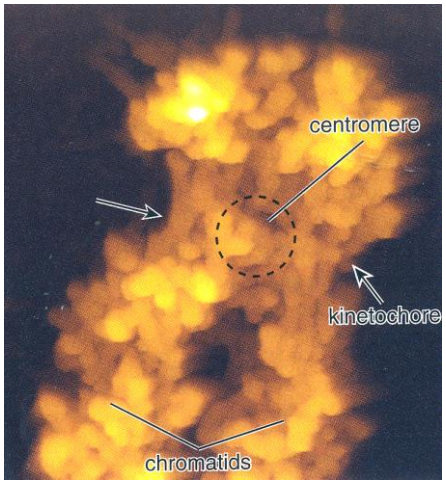


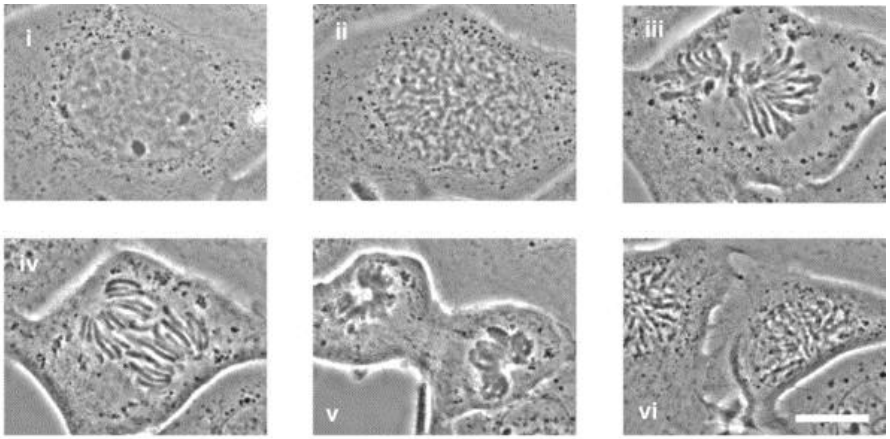


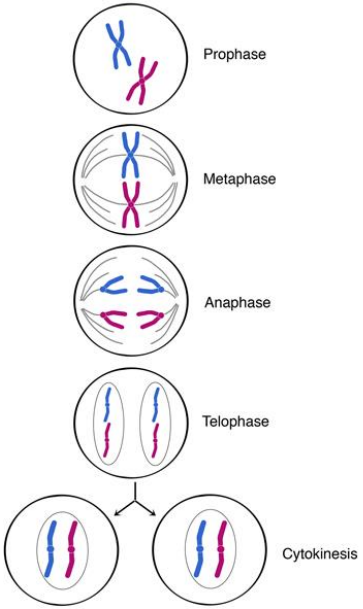
Chromosomy

- Kondenzovaná vlákna chromatinu
- Centromera
- Telomery
- Chromatidy



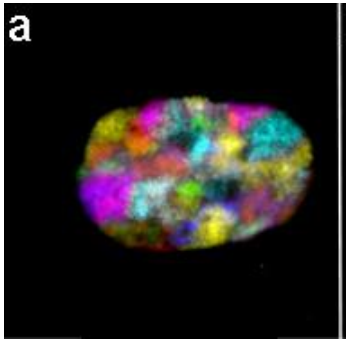


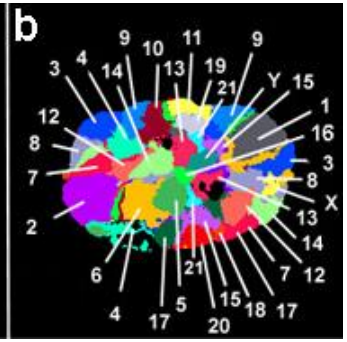


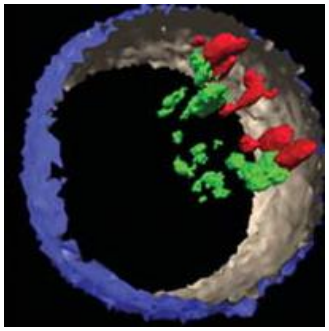


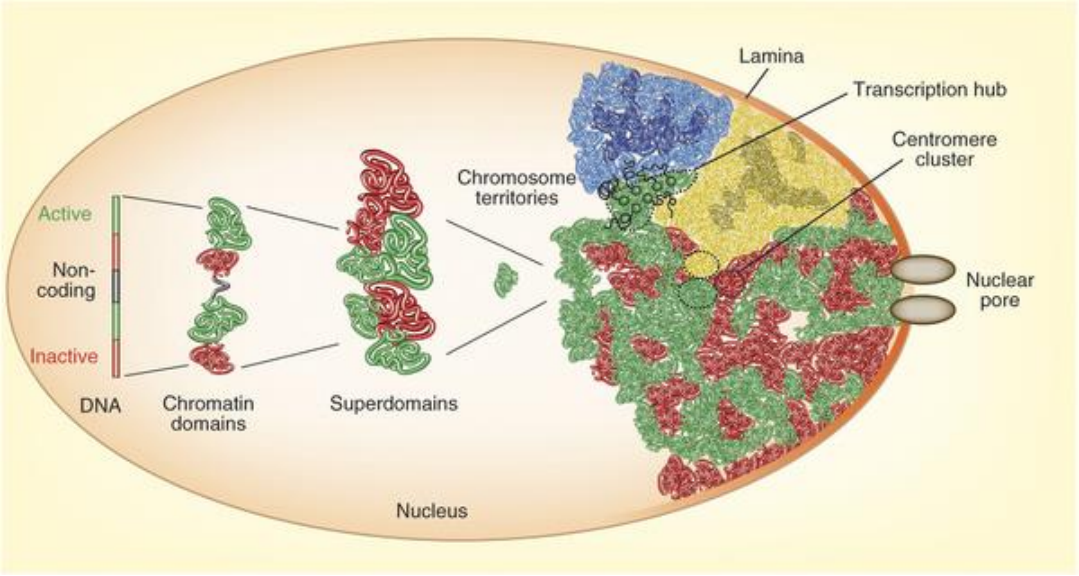
Chromosomová teritoria

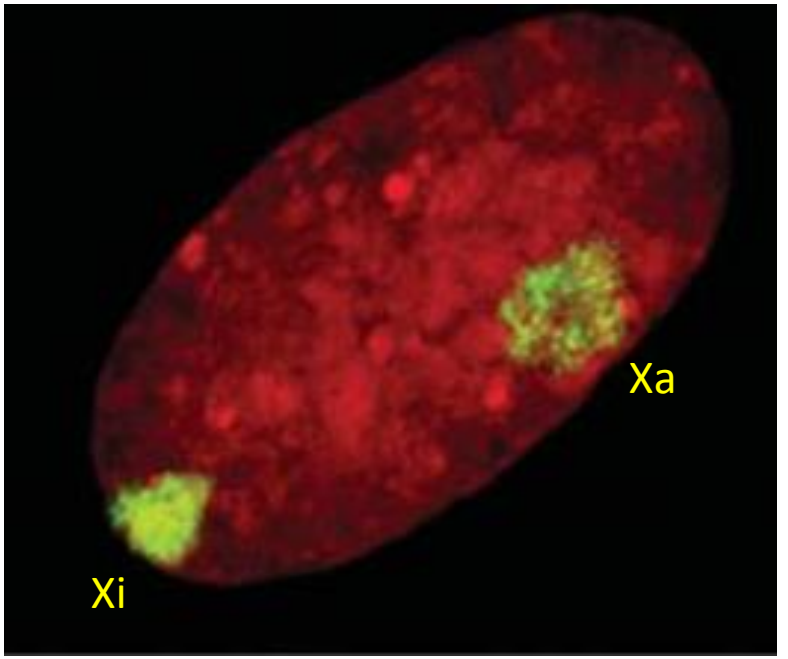
- Interfázní chromosomy jsou nenáhodně uspořádány
- Organizace transkripčně aktivních oblastí, chromatinu
- Regulace transkripce, organizace jadérka…



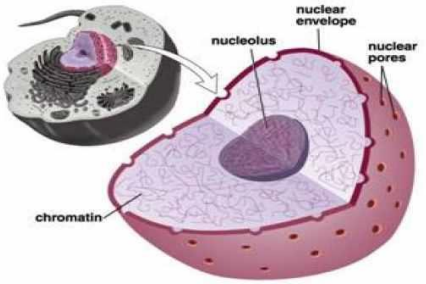




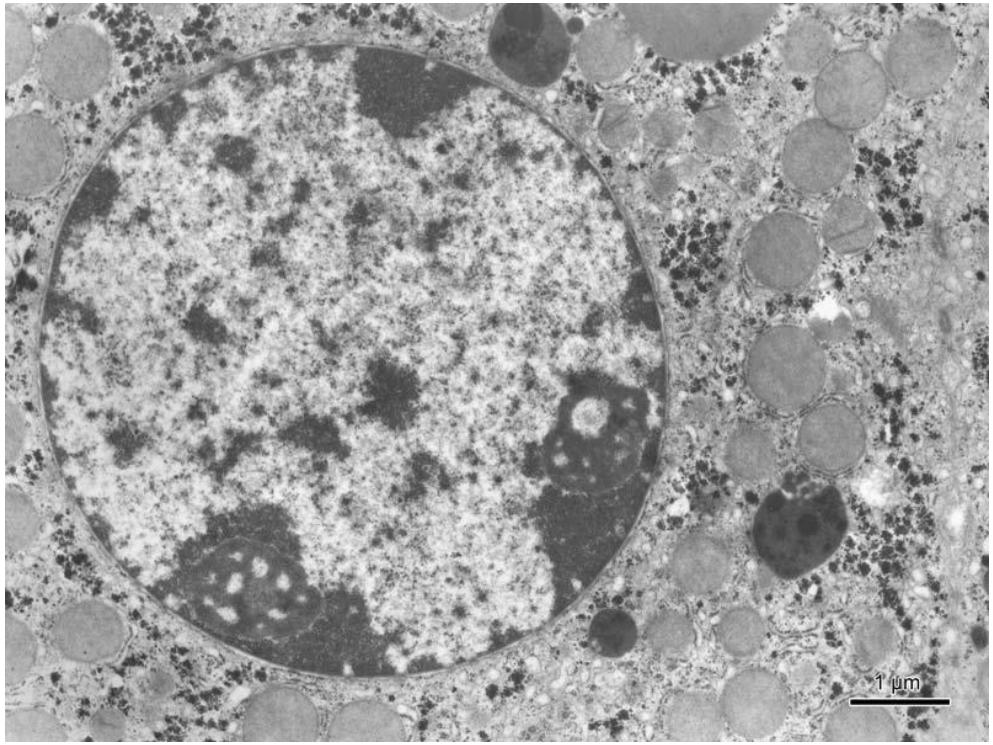




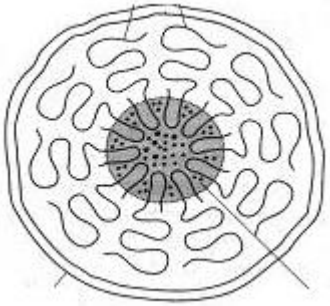
Jadérko



- Nápadná oblast v buněčném jádře, dominantní u proteosynteticky aktivních buněk
- Asociace s chromozomy
- Buněčný cyklus
- Syntéza rRNA a sestavování ribozomů

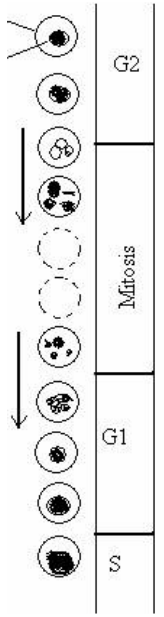


Chromozomy s geny pro rRNA



Jaderný obal

Jadérko



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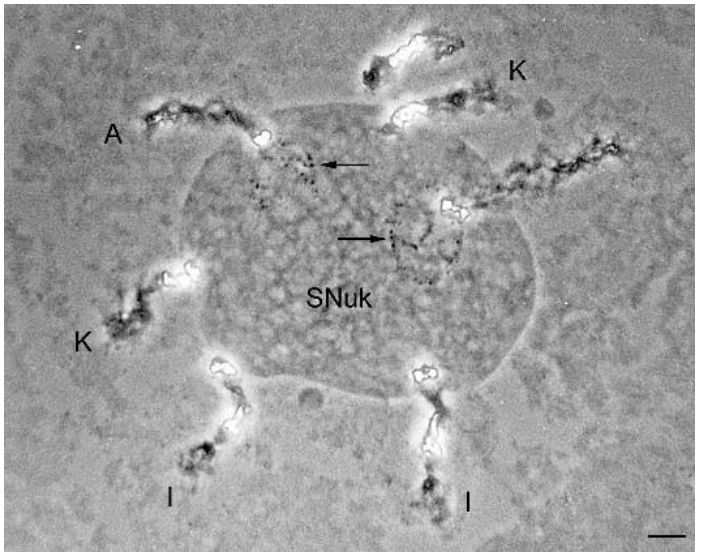


- **Fibrilární centra**

  Obsahují chromozomální DNA (13,14,15,21,22) – geny kódující rRNA, RNA pol I, transkripční faktory)

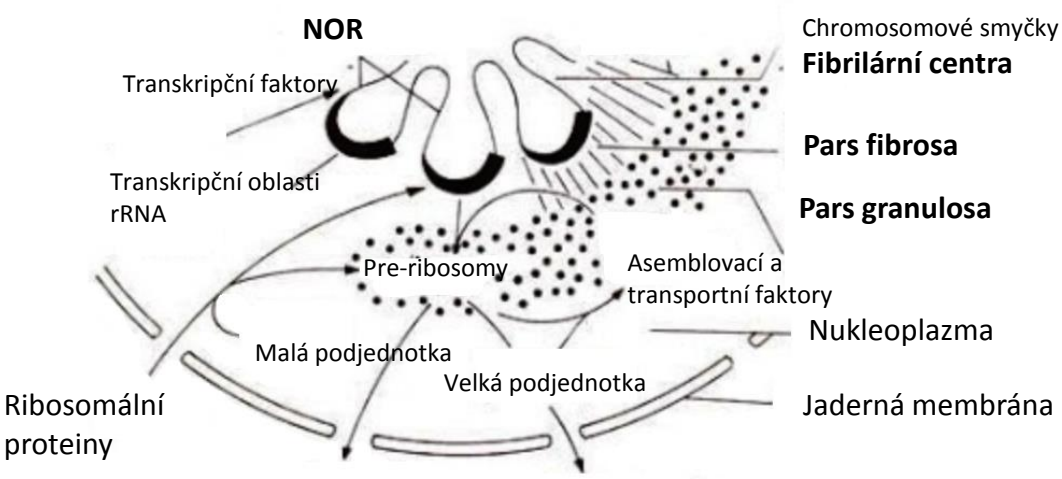
- **Pars fibrosa**

  Aktuálně transkribované ribozomální geny rRNA

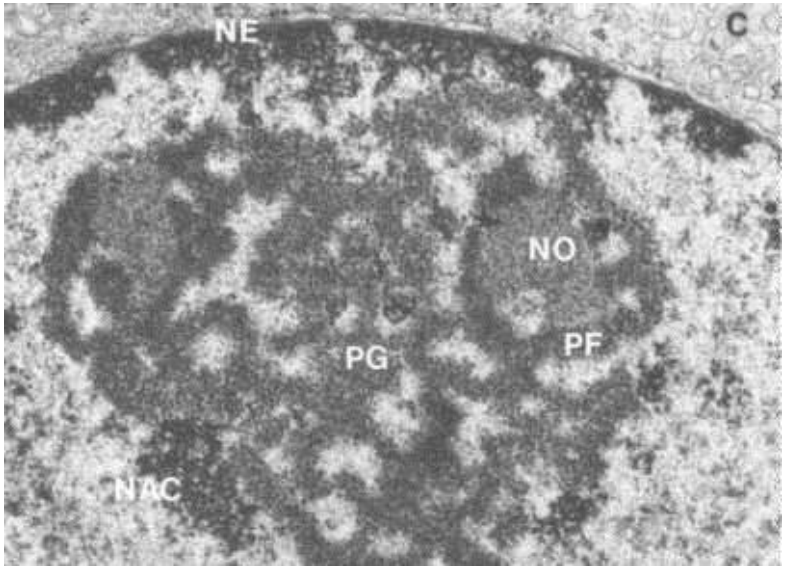
- **Pars granulosa**

  Sestavování ribozomů

- **Perinukleolární chromatin** (asociovaný s jadérkem)

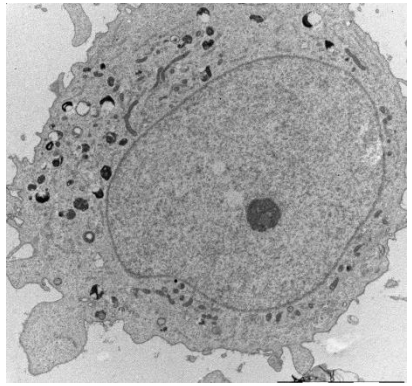


Sestavení ribozomových podjednotek s mRNP

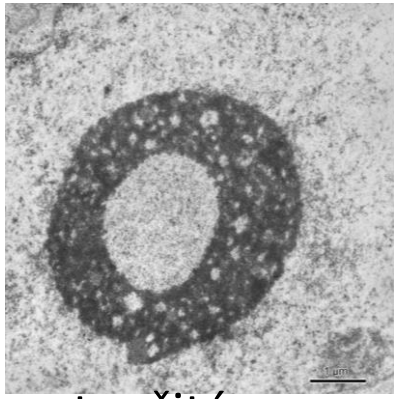


Jadérko

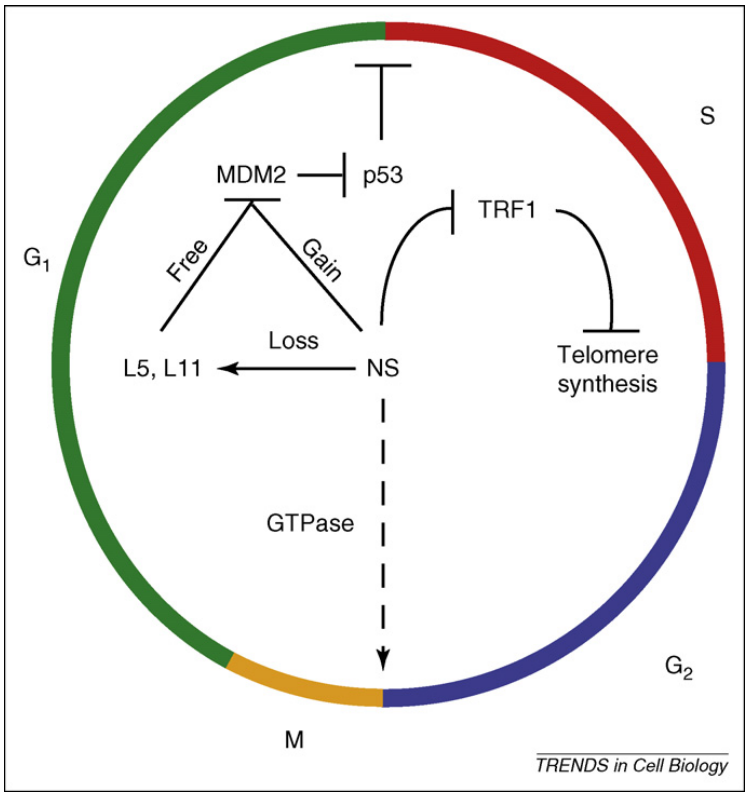
- Variabilní morfologie – souvisí s aktivitou
- Buněčný cyklus
- Jaderný – cytoplazmatický shuttling
- Komplexní role
- Nucleostemin

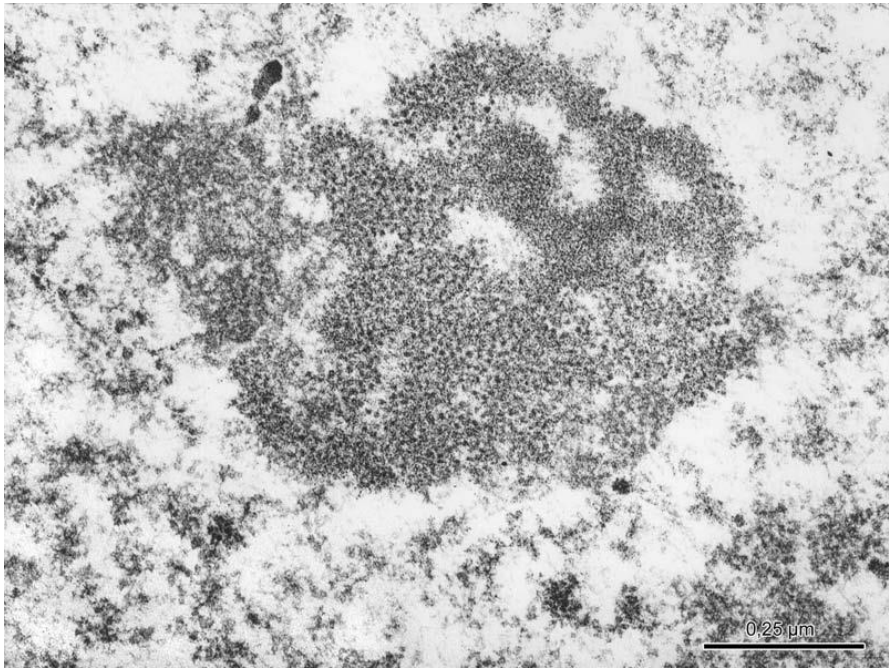


kompaktní



prstenčité

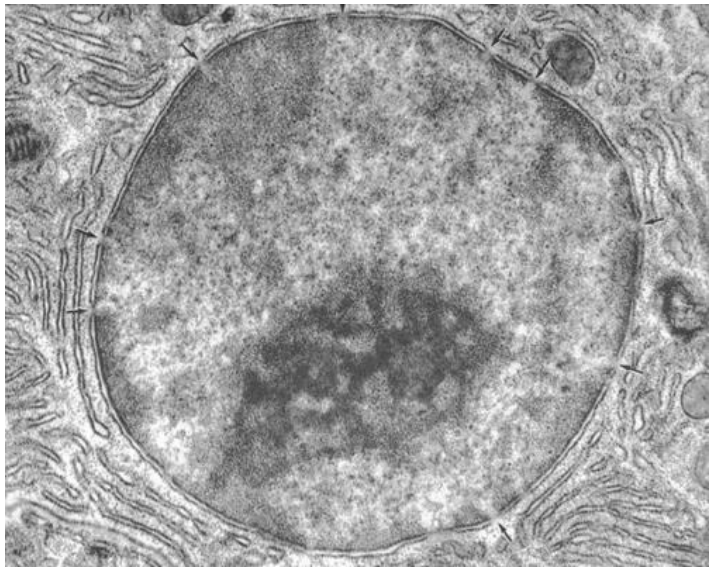


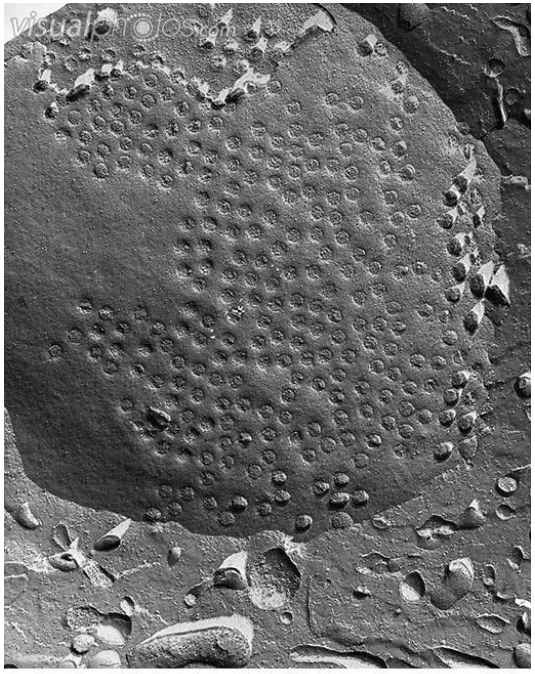


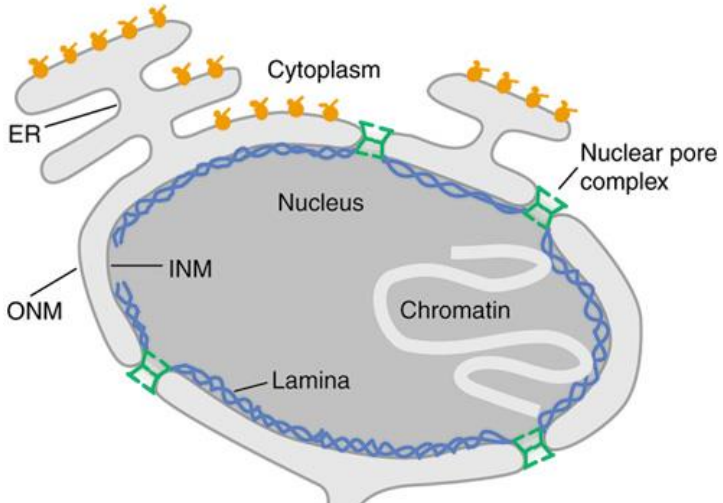
retikulární

Jaderná membrána

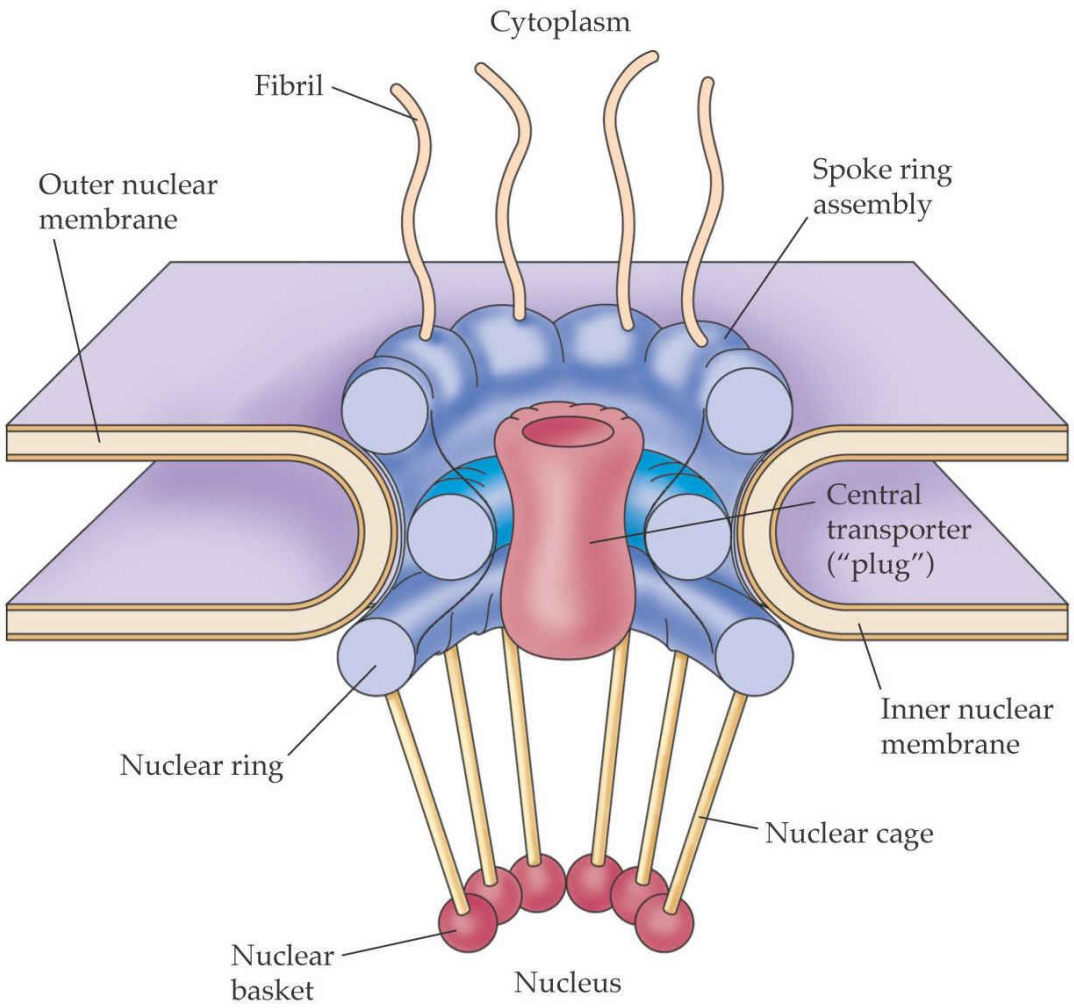
- Kontrolovaná permeabilita
- Dvě lipidové dvouvrstvy a **perinukleární prostor** (40-70nm)
- Vnější membrána kontinuální s ER
- Vnitřní – rigidní, intermediární filamenta – jaderná lamina (→ lamin)
- Jaderné póry, 60-70nm (→ nucleoporiny)
- Jaderný lokalizační signál (→ importin)



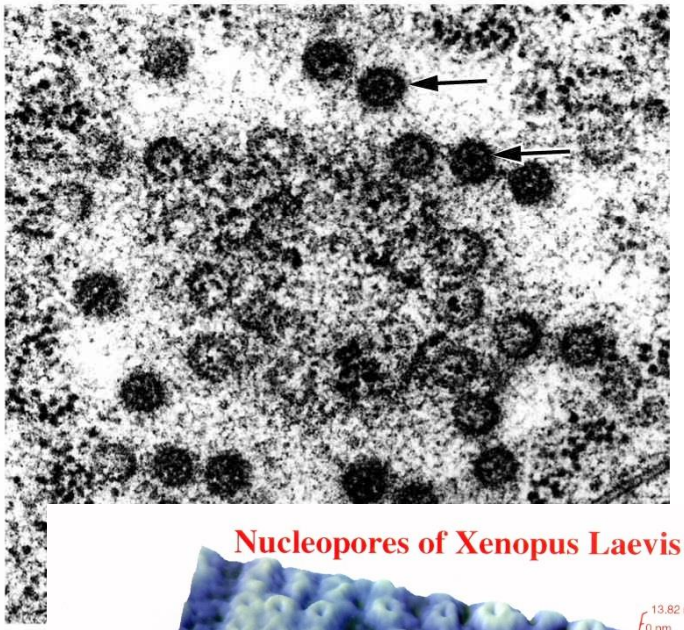


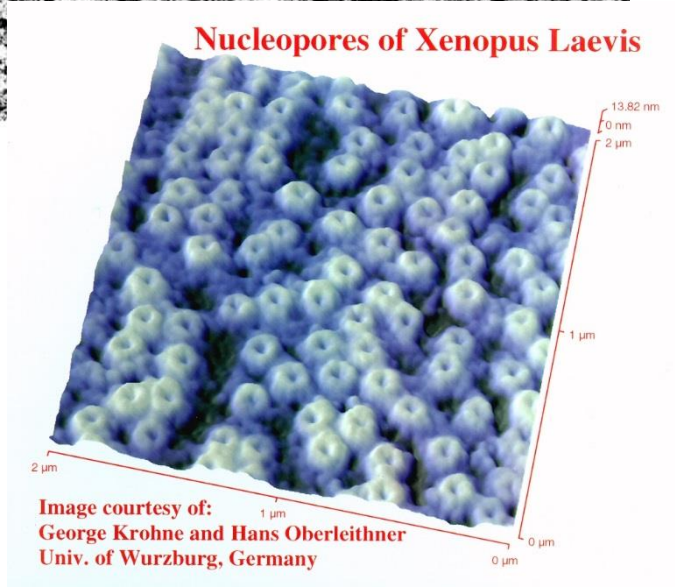


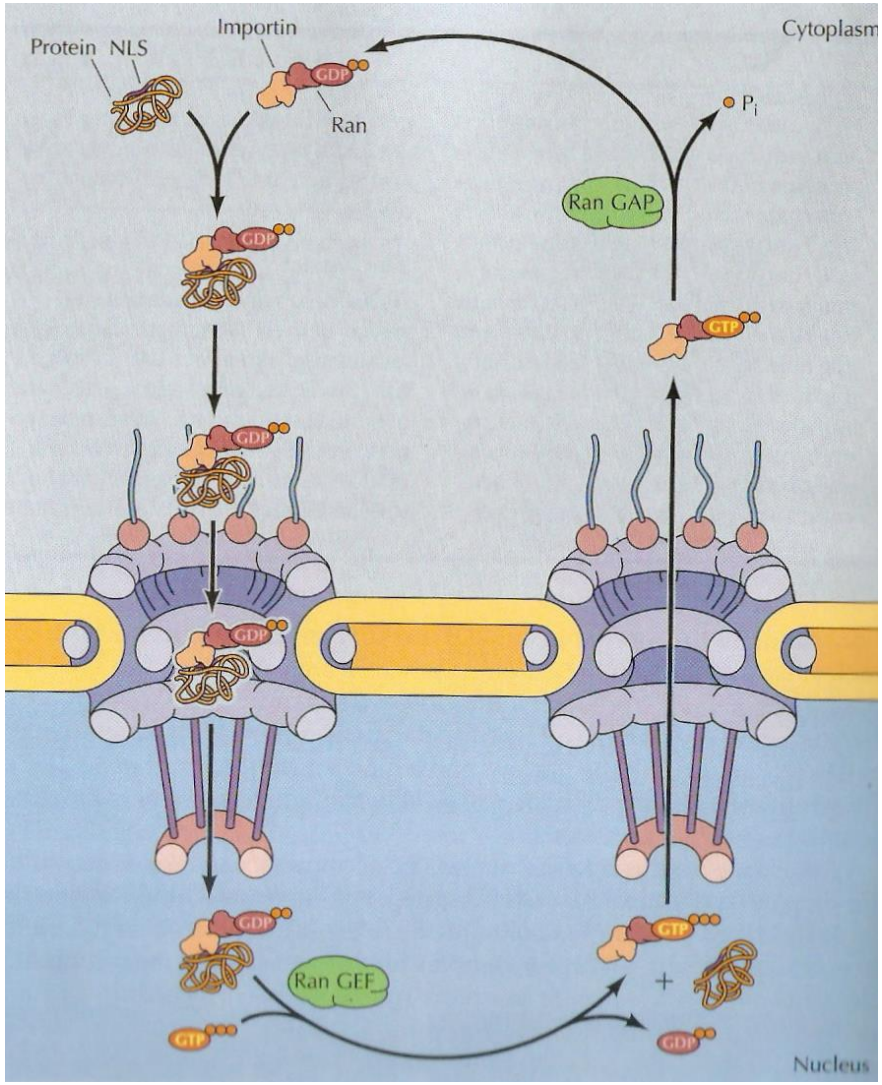
(A)

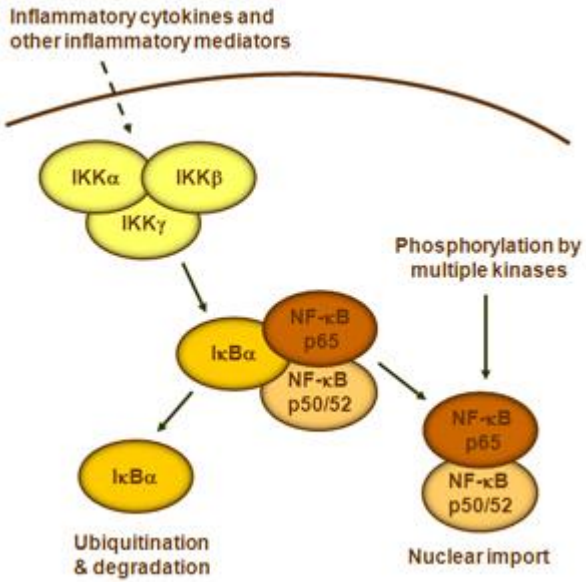

Cytoplasm
Fibril
Outer nuclear membrane
Spoke ring assembly
Central transporter ("plug")
Inner nuclear membrane
Nuclear ring
Nuclear cage
Nuclear basket
Nucleus

(B)

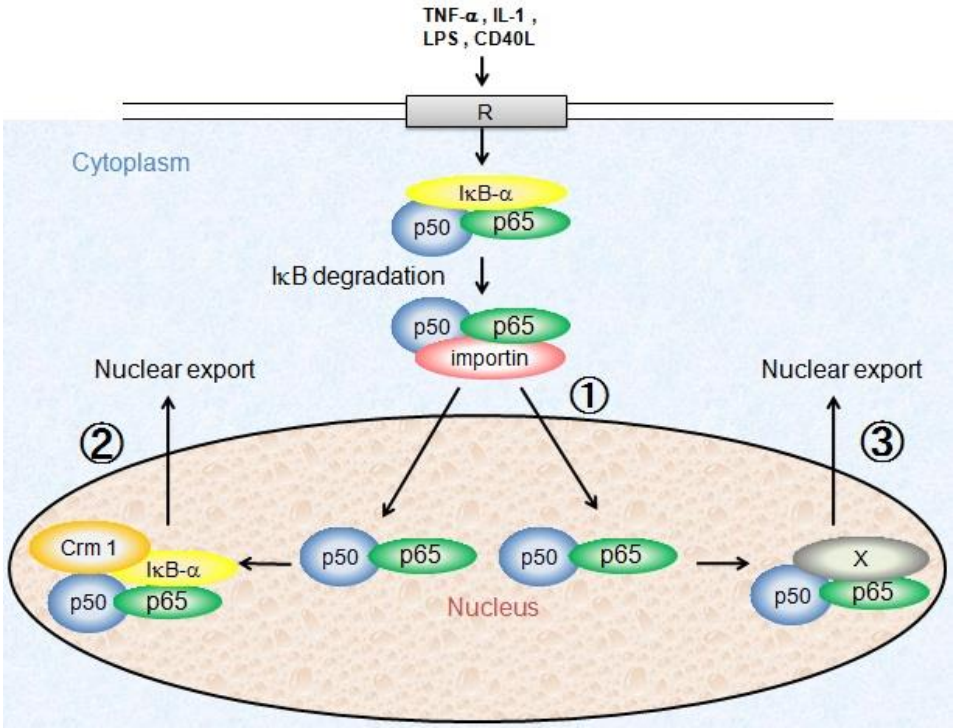



Nucleopores of Xenopus Laevis
13.82 nm
0 nm
2 µm
1 µm
0 µm
2 µm
1 µm
Image courtesy of:
George Krohne and Hans Oberleithner
Univ. of Wurzburg, Germany



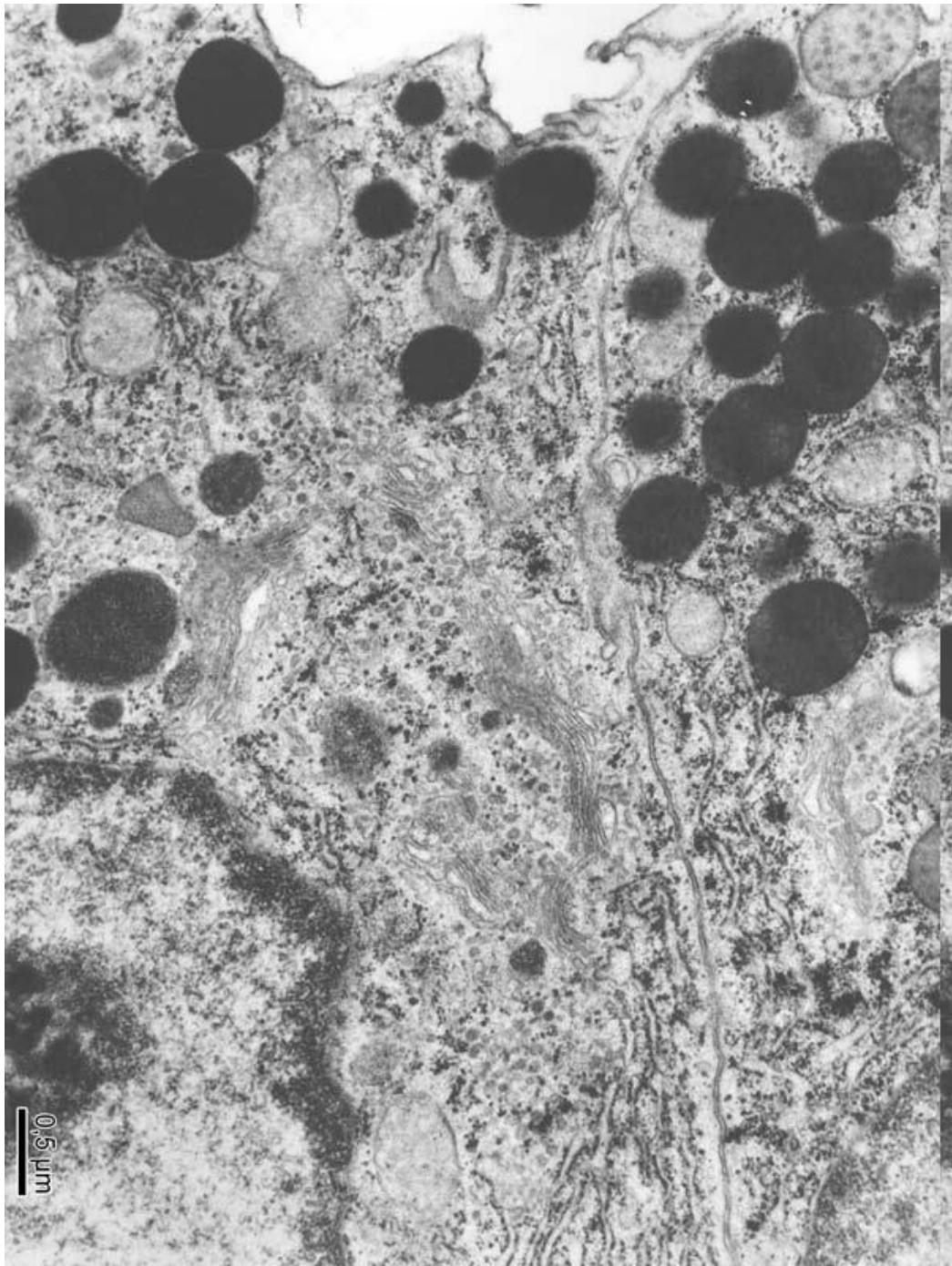


- Inflammation response
- Apoptosis
- Drug resistance
- Survival
- …



Organely x inkluze

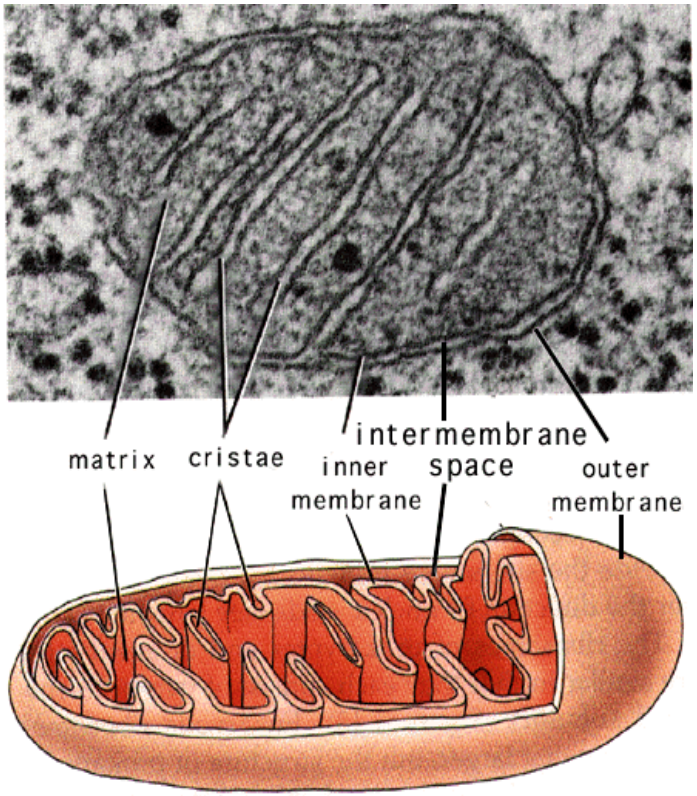
- Mitochondrie
- Endoplazmatické retikulum
  - granulární – rER /GAR/
  - agranulární – sER /AER/
- Golgiho aparát
- Lyzosomy a endosomy
- Peroxisomy
- Ribosomy (6S+40S, 70S)
- Centrioly

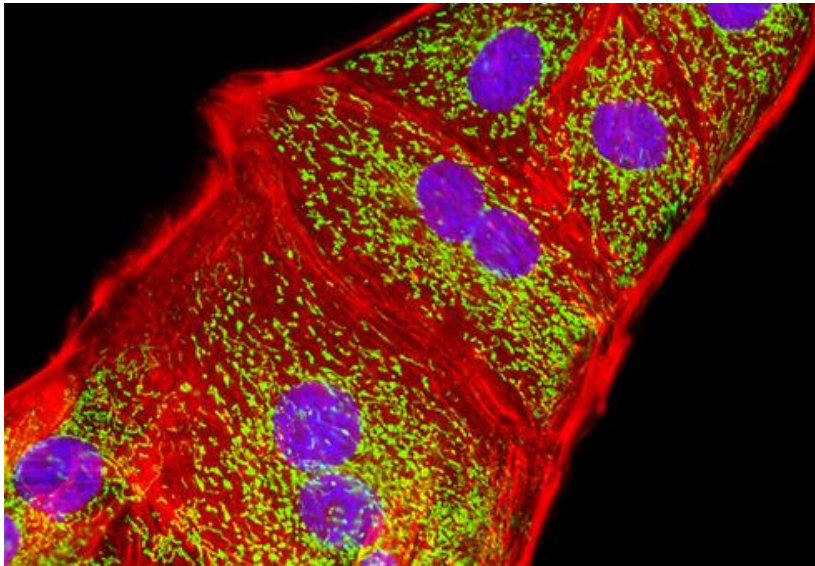


Mitochondrie

- Vnější a vnitřní membrána
- Elementární partikule (F1/ATP syntetáza)
- Matrix
- Ribozomy (50S+30S; 70S)
- Cirkulární DNA

- ATP syntéza – oxidativní fosforylace
- Apoptóza
- Metabolismus

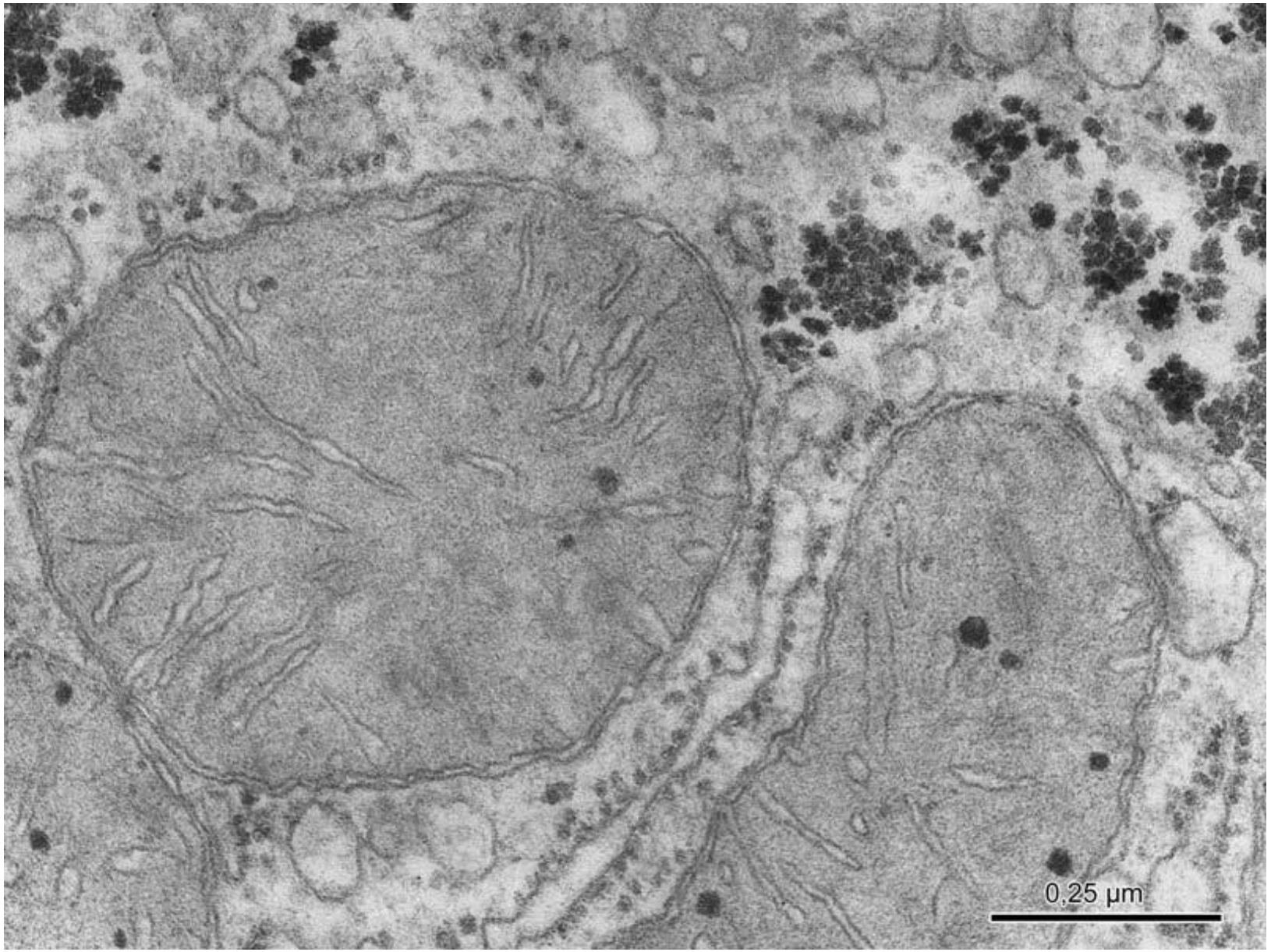




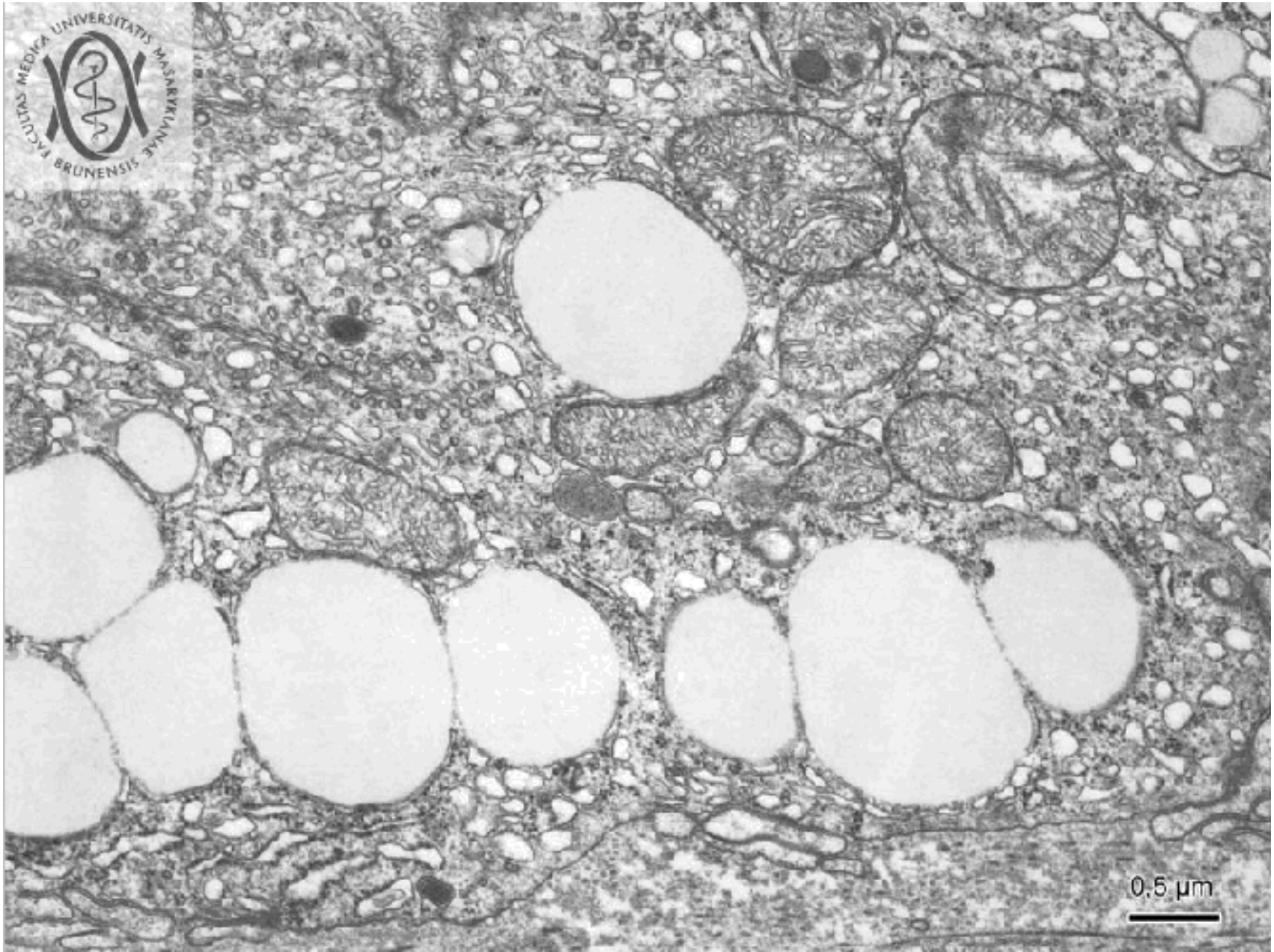
Tloušťka: 0.5-1 µm

Délka:1-10 µm

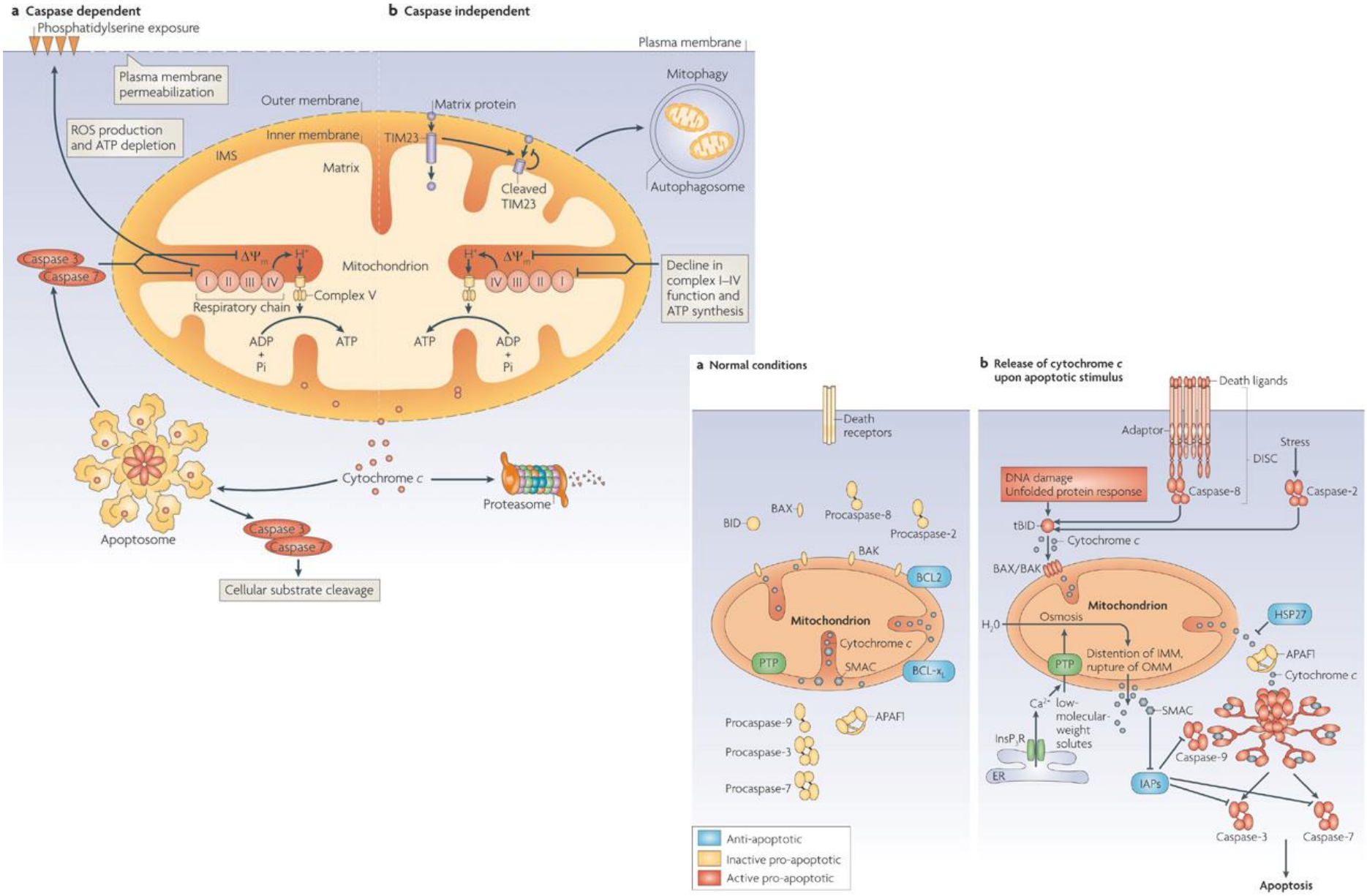
Mitochondrie



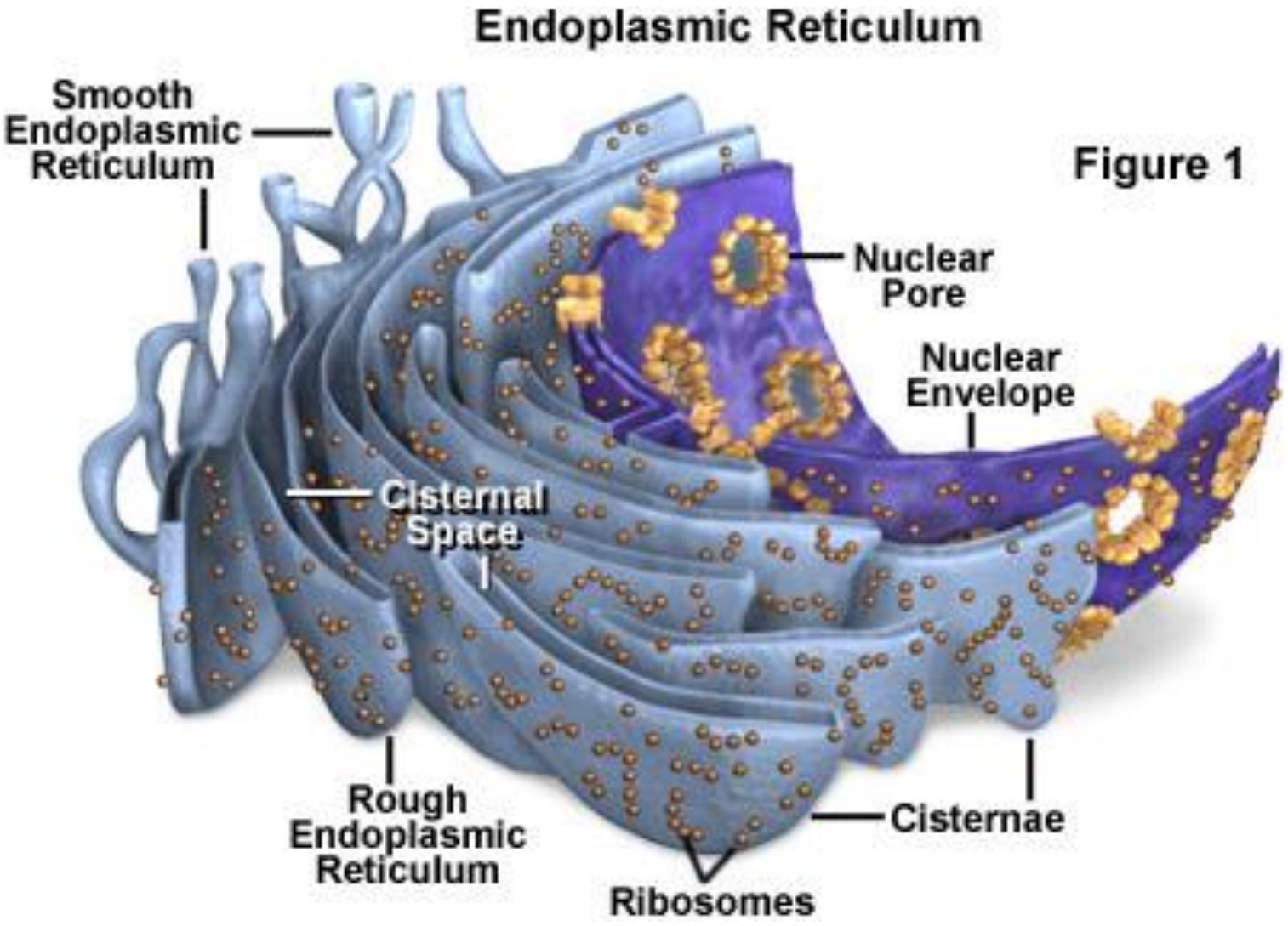
Mitochondrie



- Integrita mitochondriálních membrán je pro buňku kritická

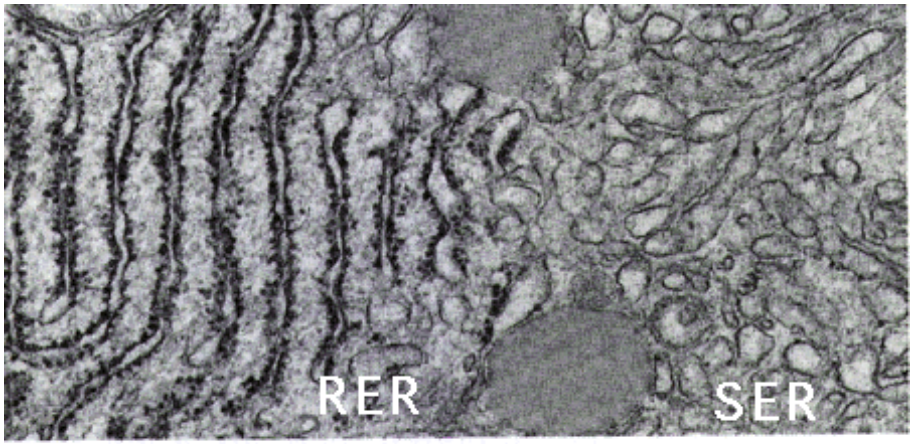


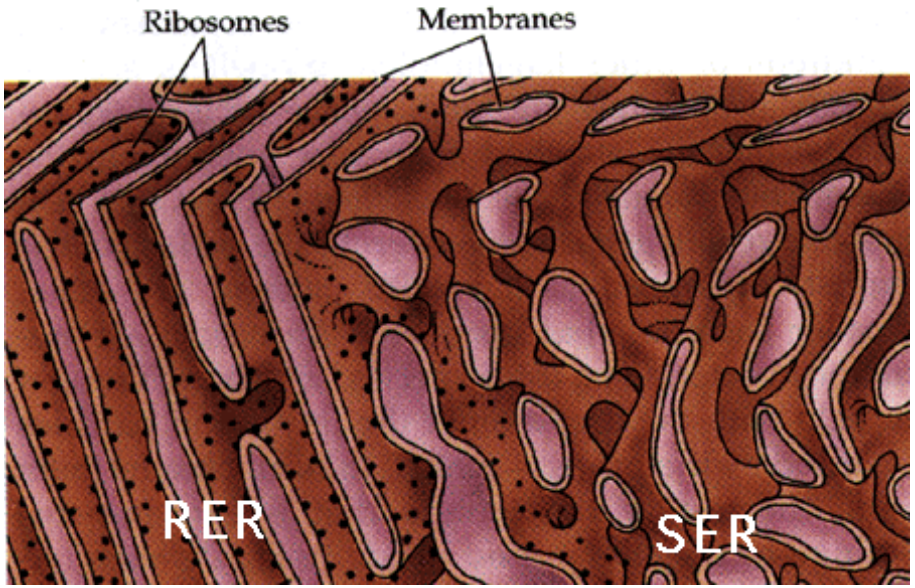
Endoplazmatické retikulum



GER a AER

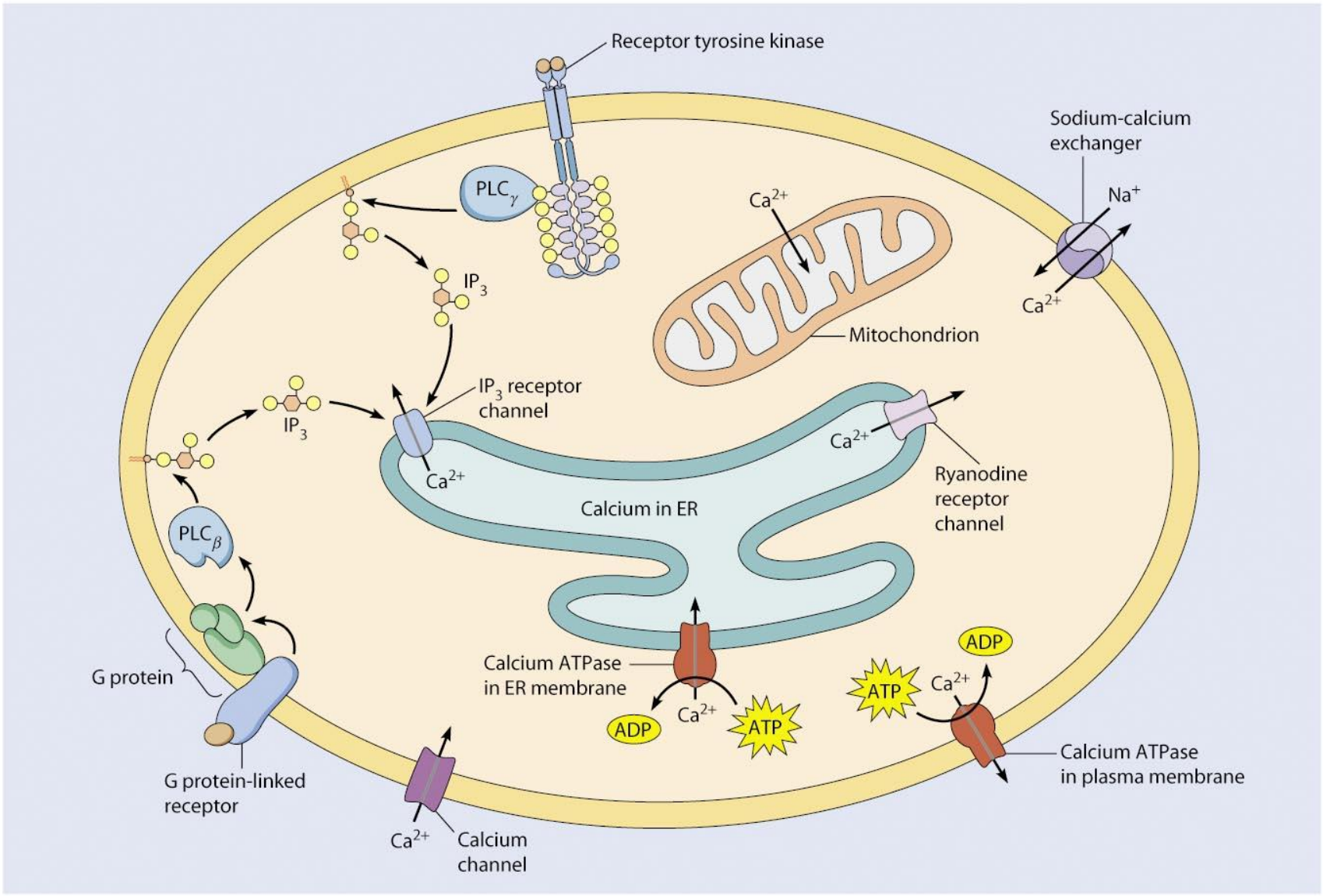
- GER
  - proteosyntéza a export
- AER
  - lipidový a cholesterolový metabolismus (syntéza steroidních hormonů)
  - syntéza membrán
  - detoxikace určitých látek a toxinů
  - metabolismus glykogenu

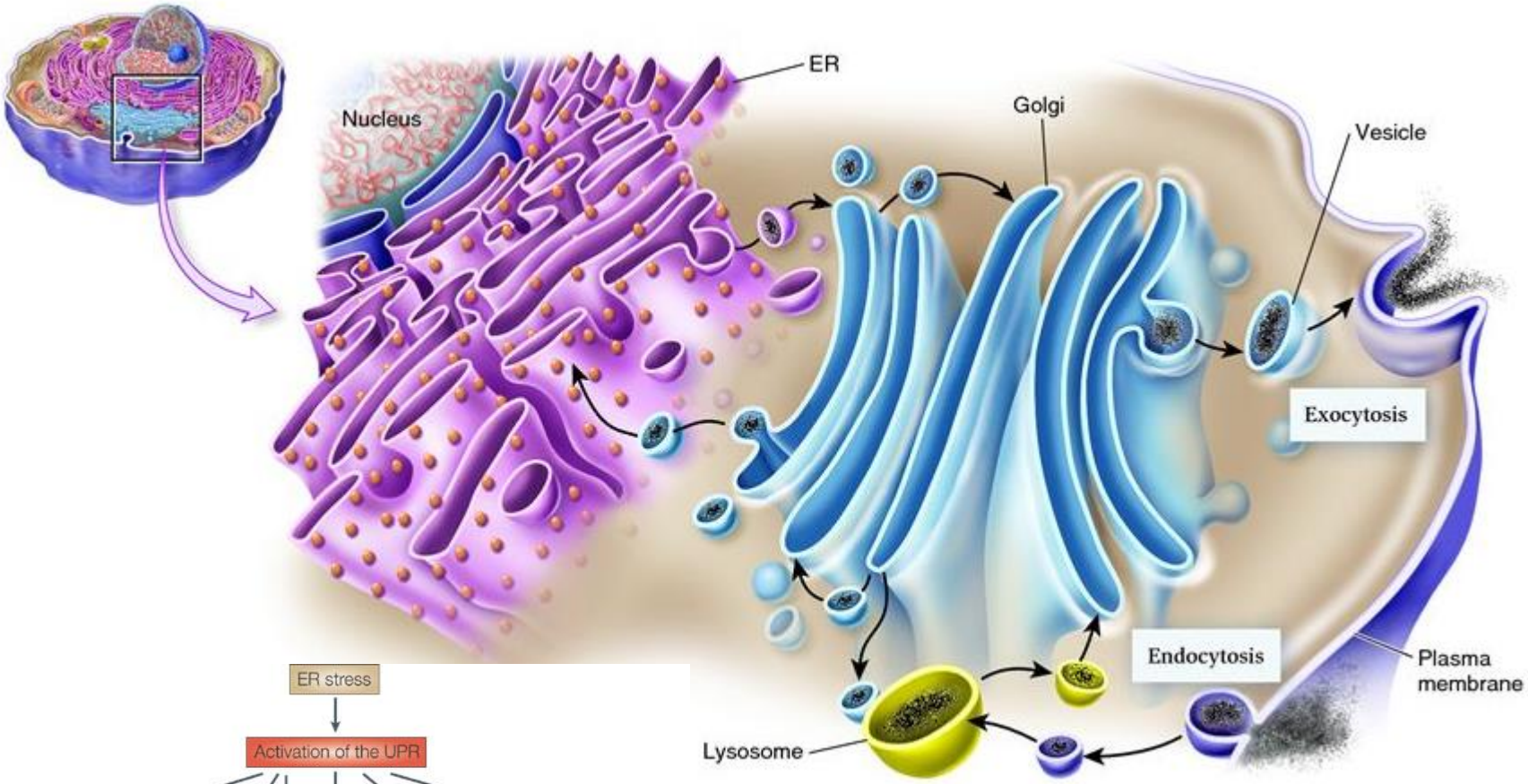


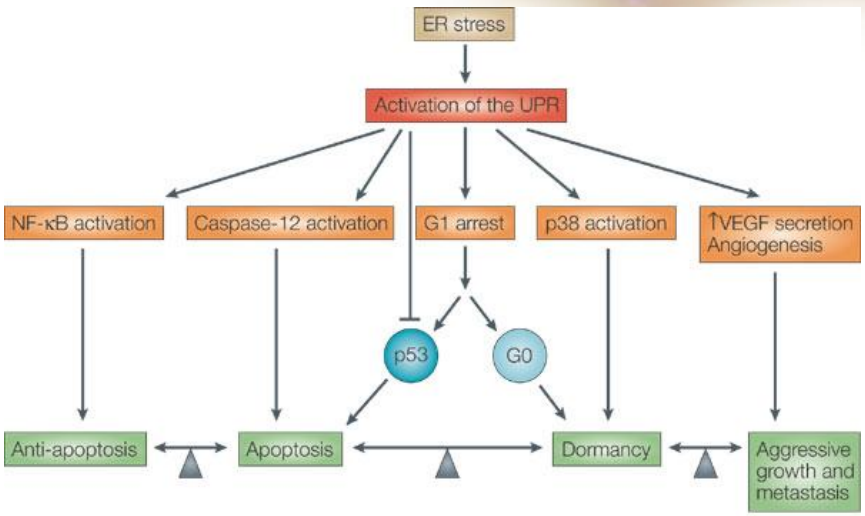


cisterny **síť tubulů a váčků**

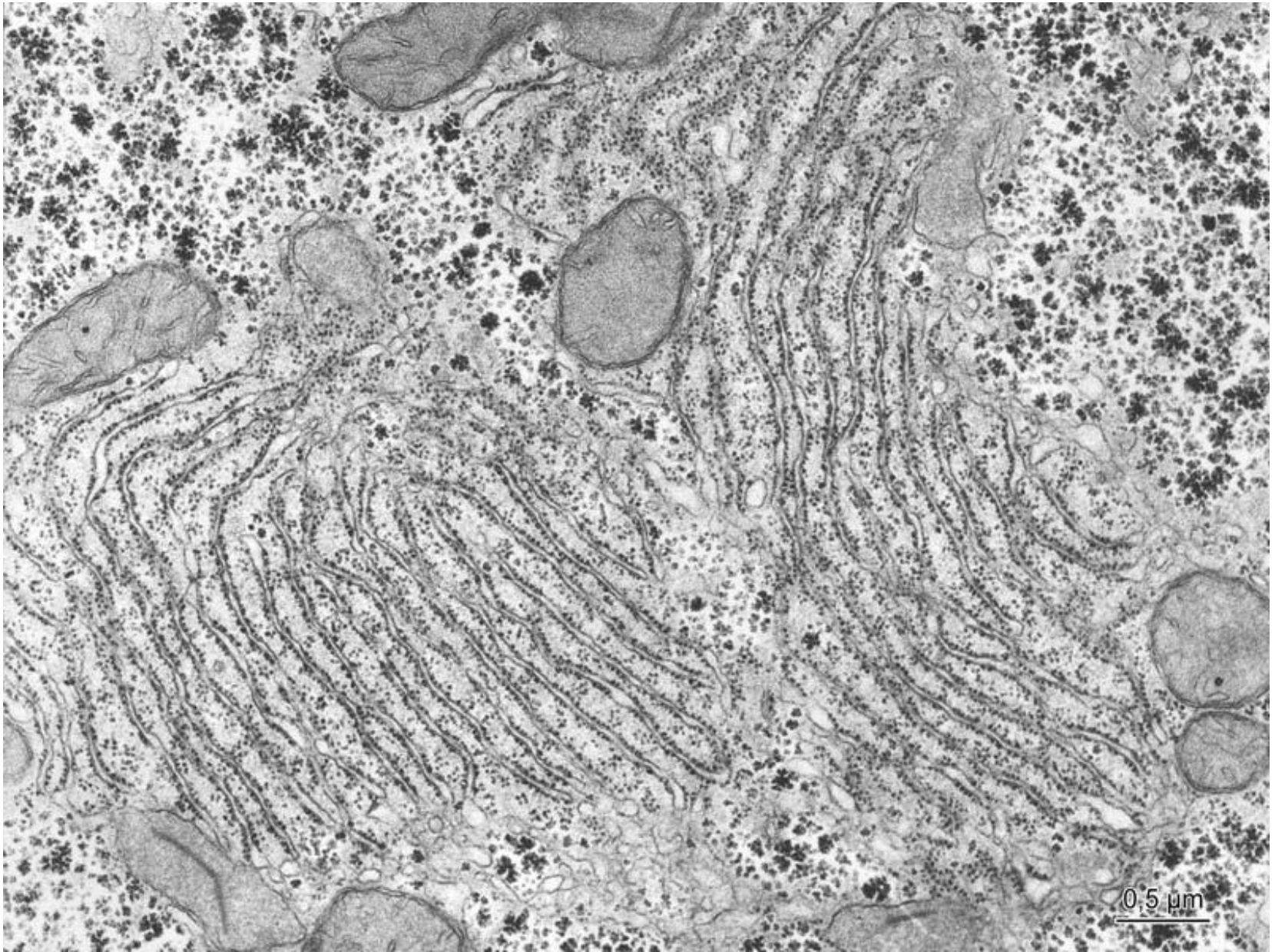
Ca^{++} zásobárna (pool)




ER
Nucleus
Golgi
Vesicle
Exocytosis
Endocytosis
Plasma membrane
Lysosome

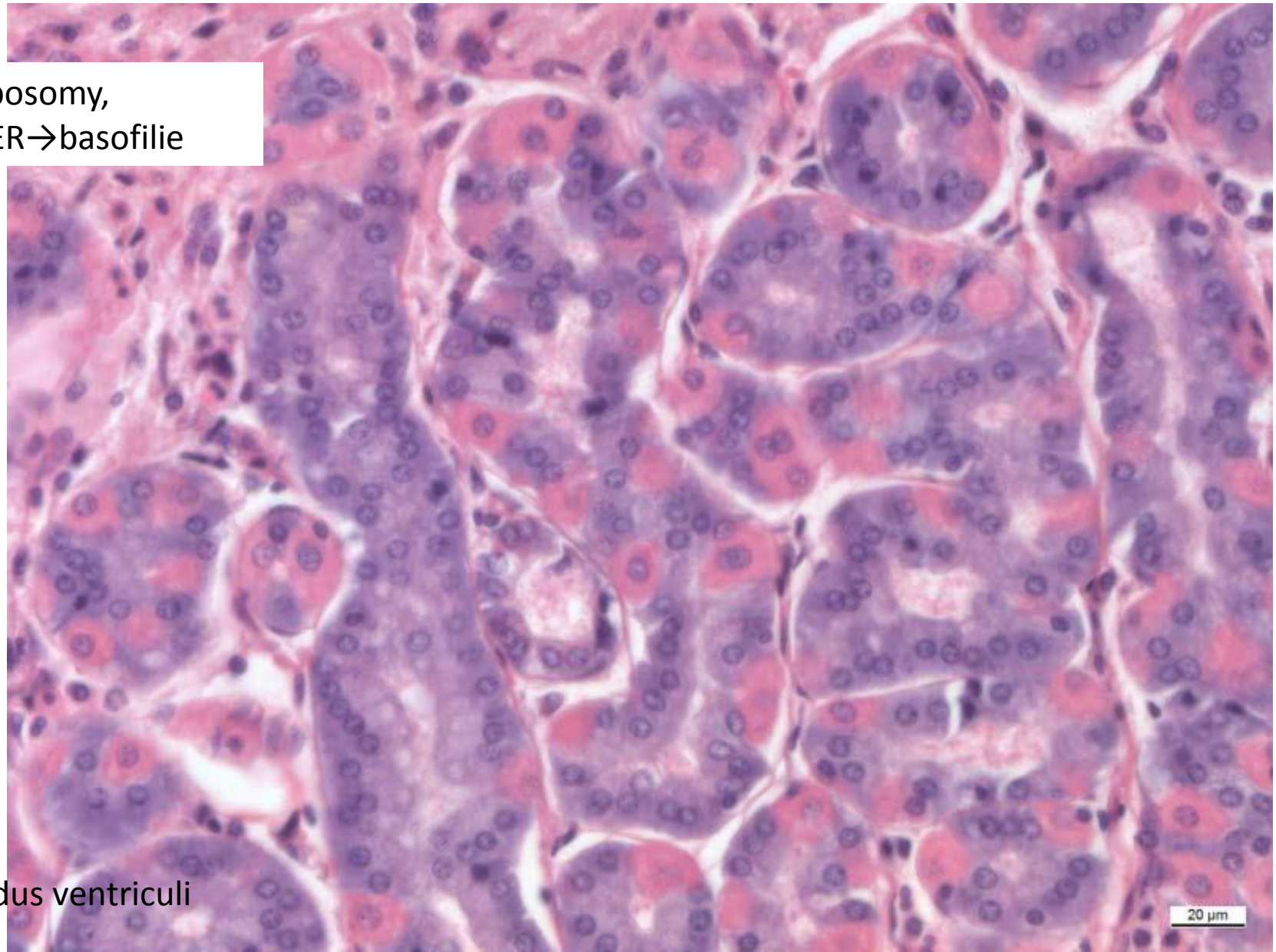

ER stress
Activation of the UPR
NF-κB activation
Caspase-12 activation
G1 arrest
p38 activation
↑VEGF secretion
Angiogenesis
p53
G0
Anti-apoptosis
Apoptosis
Dormancy
Aggressive growth and metastasis

GER a AER



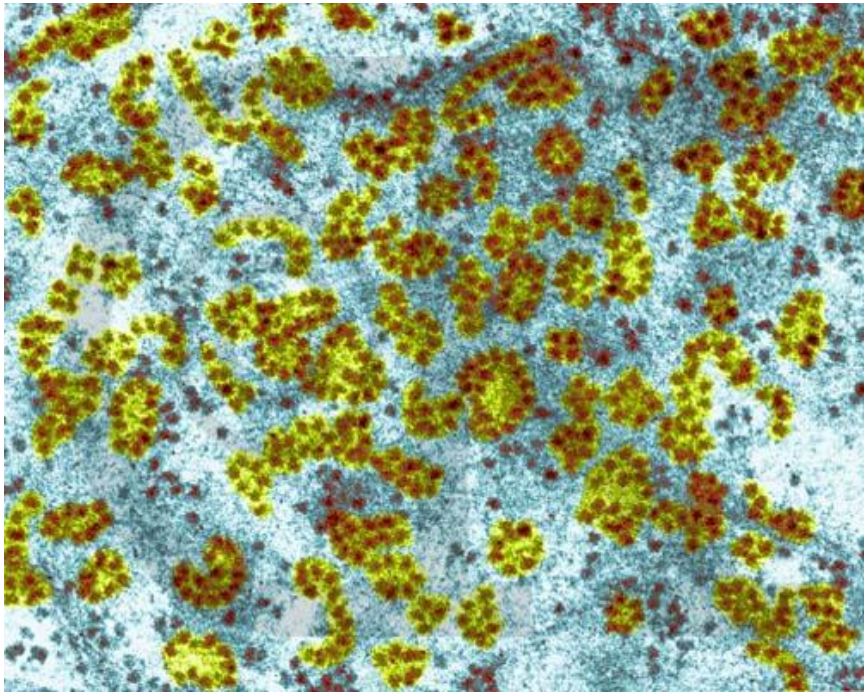
basofilní x acidofilní cytoplazma

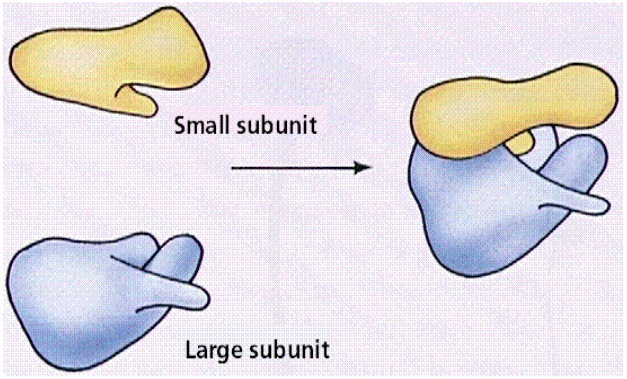
ribosomy,
GER→basofilie

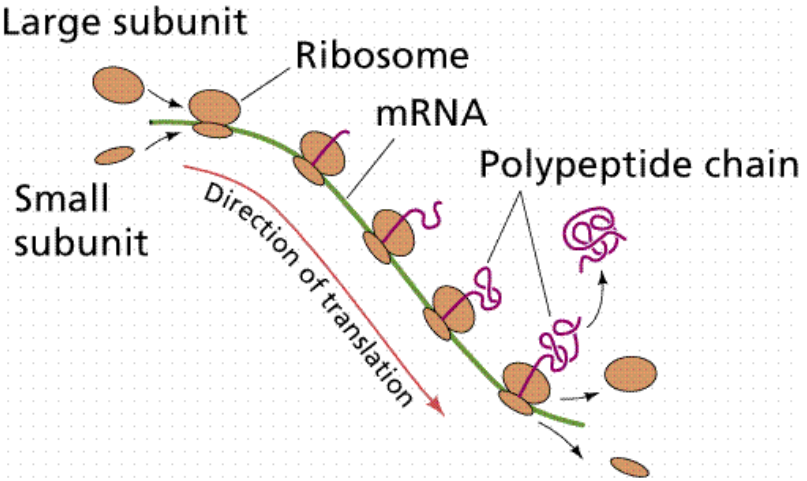


fundus ventriculi

Ribosomy

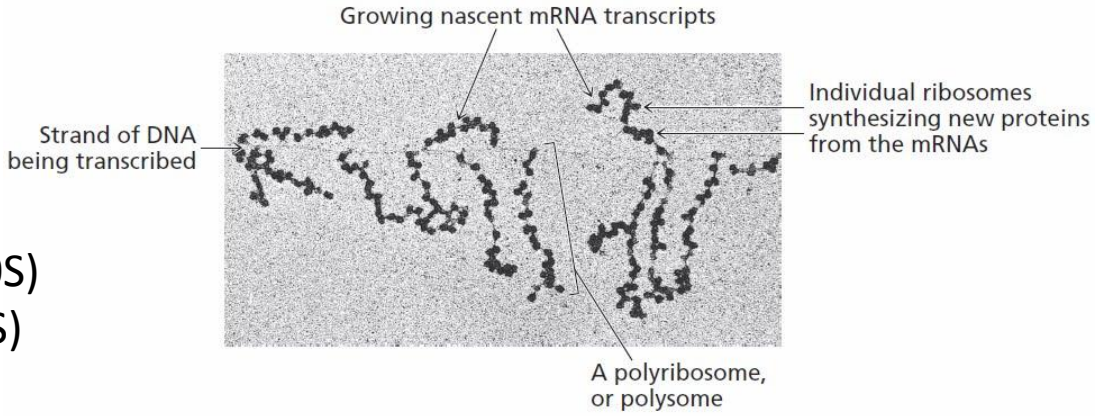






monosomy x polysomy

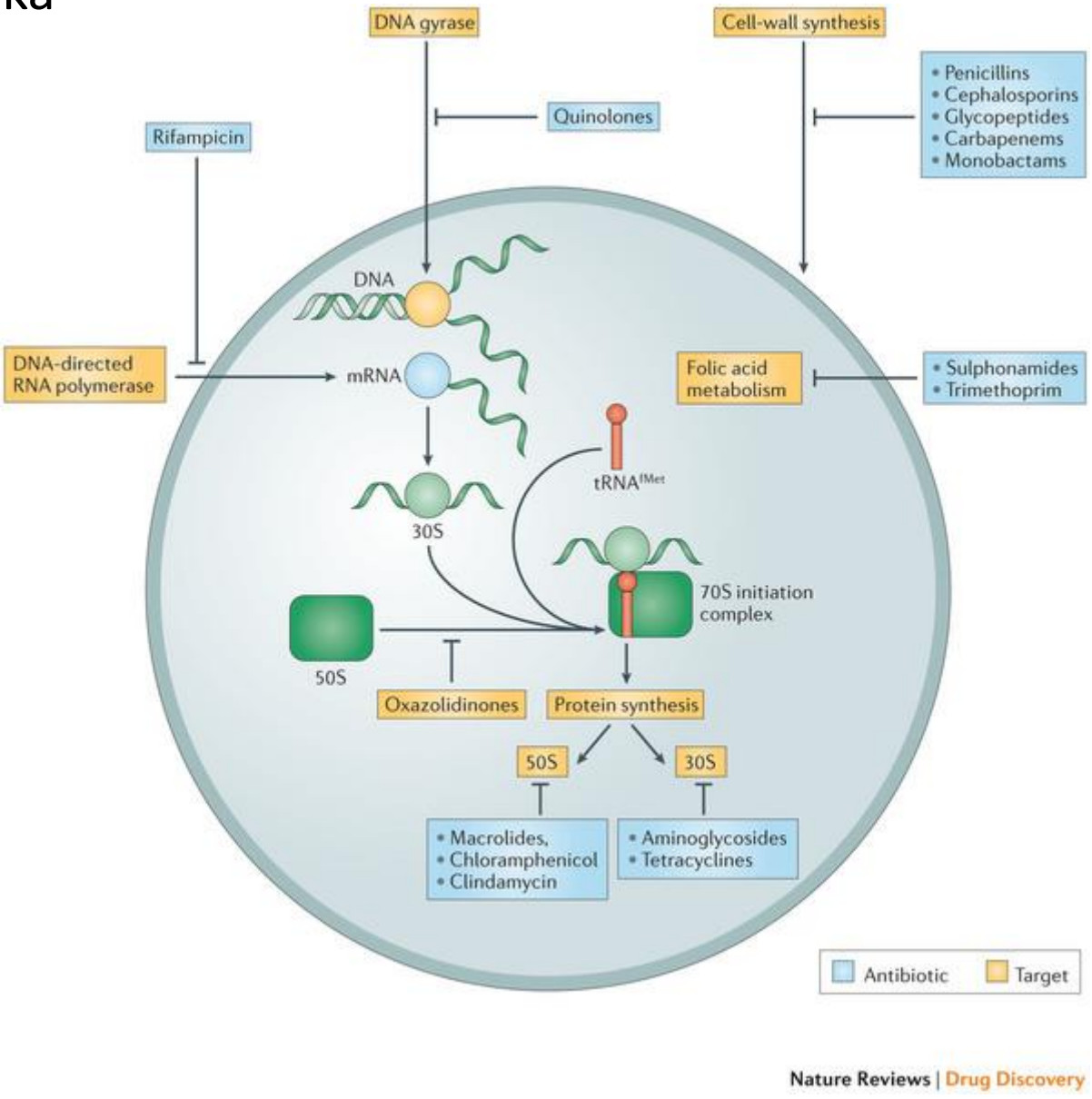
(vzhled spirál nebo roset)



Prokaryotické ribosomy (70S; 30S+50S)
Eukaryotické ribosomy (80S; 40S+60S)

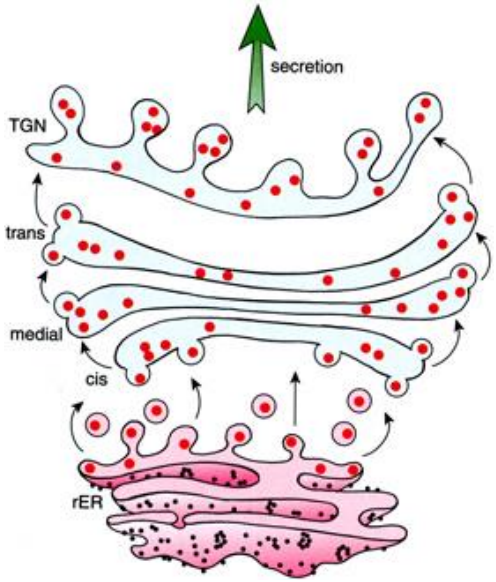
Moran et al. "Principles of Biochemistry, 5th ed." p. 680

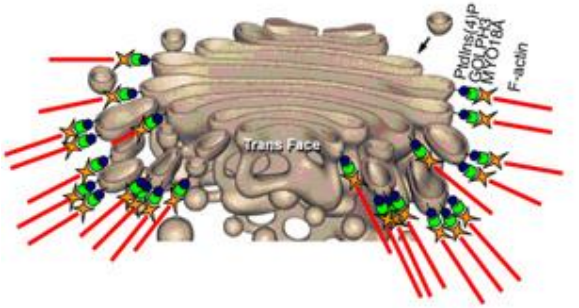
Ribosomy a antibiotika

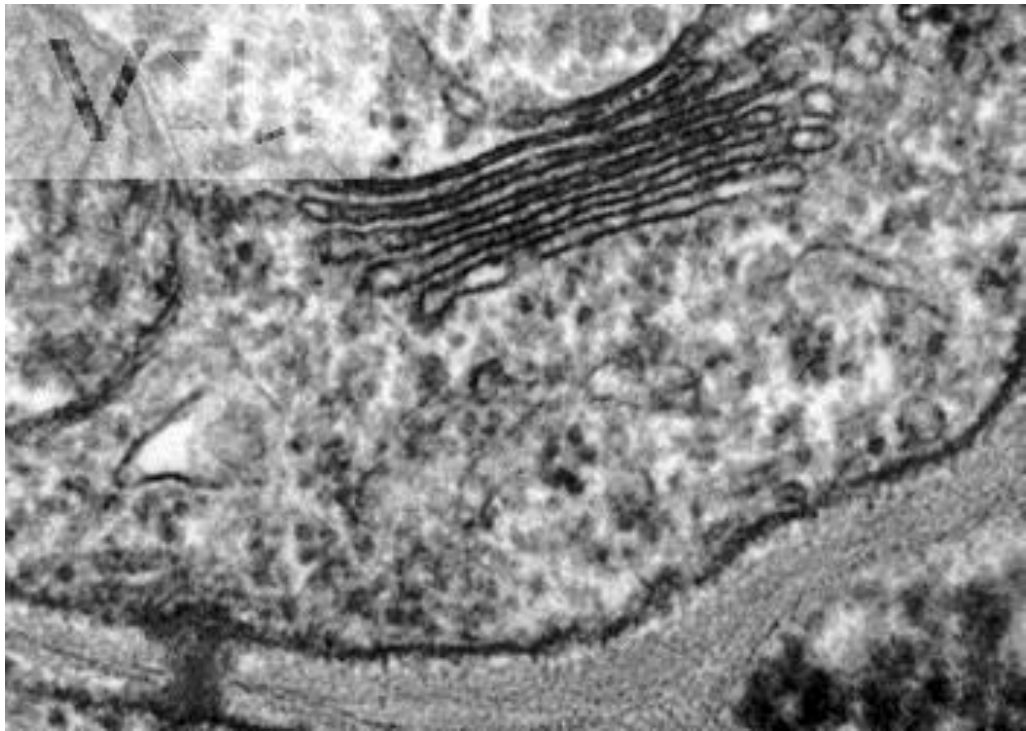


Golgiho aparát

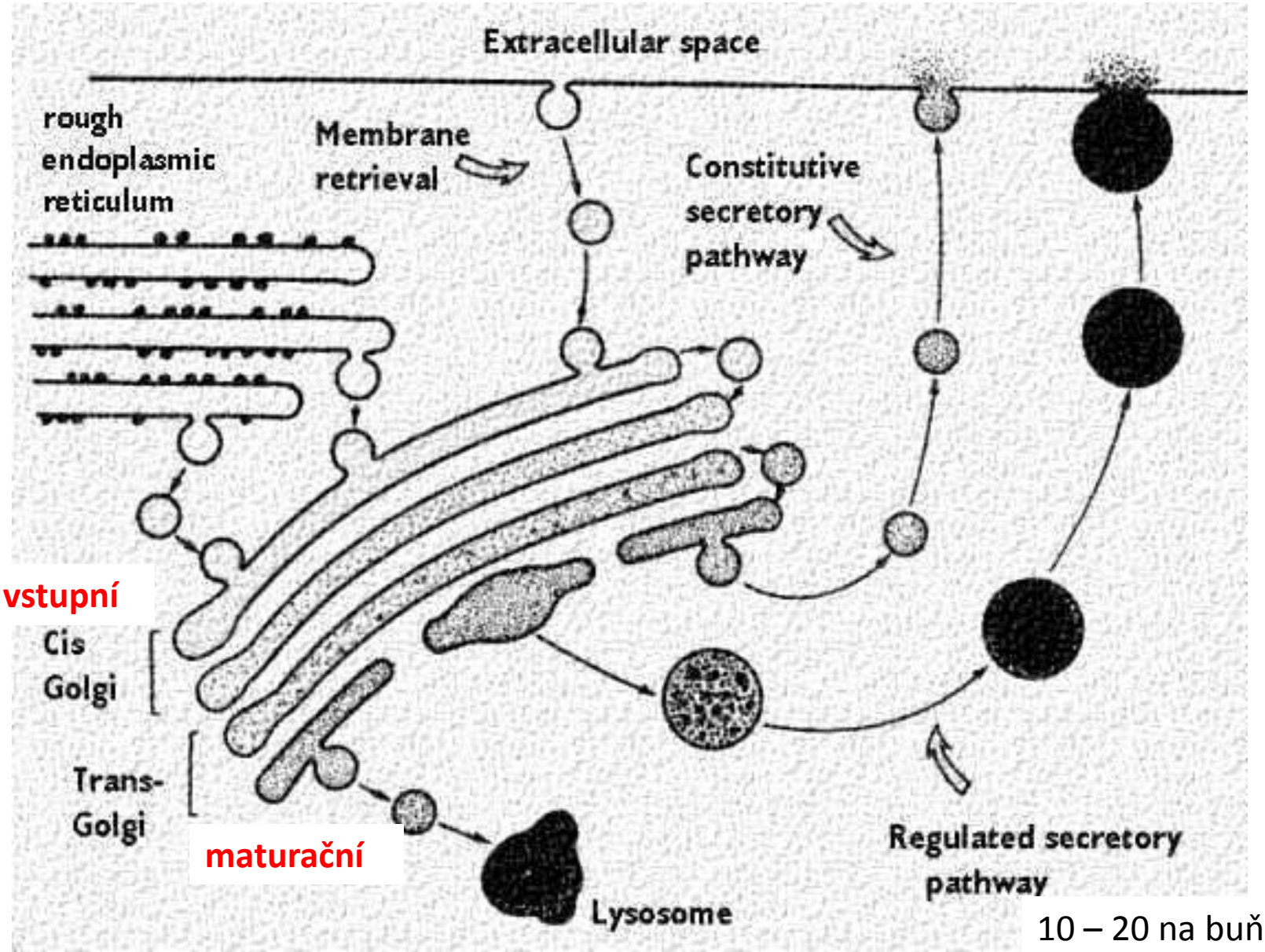
- **Struktura**
  - paralelně uspořádané cisterny (3-10)
  - malé váčky
  - větší vakuoly
- **Funkce**
  - finalizace produktů vyrobených buňkou
  - produkty
    - sekreční granula (na export)
    - primární lyzosomy
    - části buněčné membrány



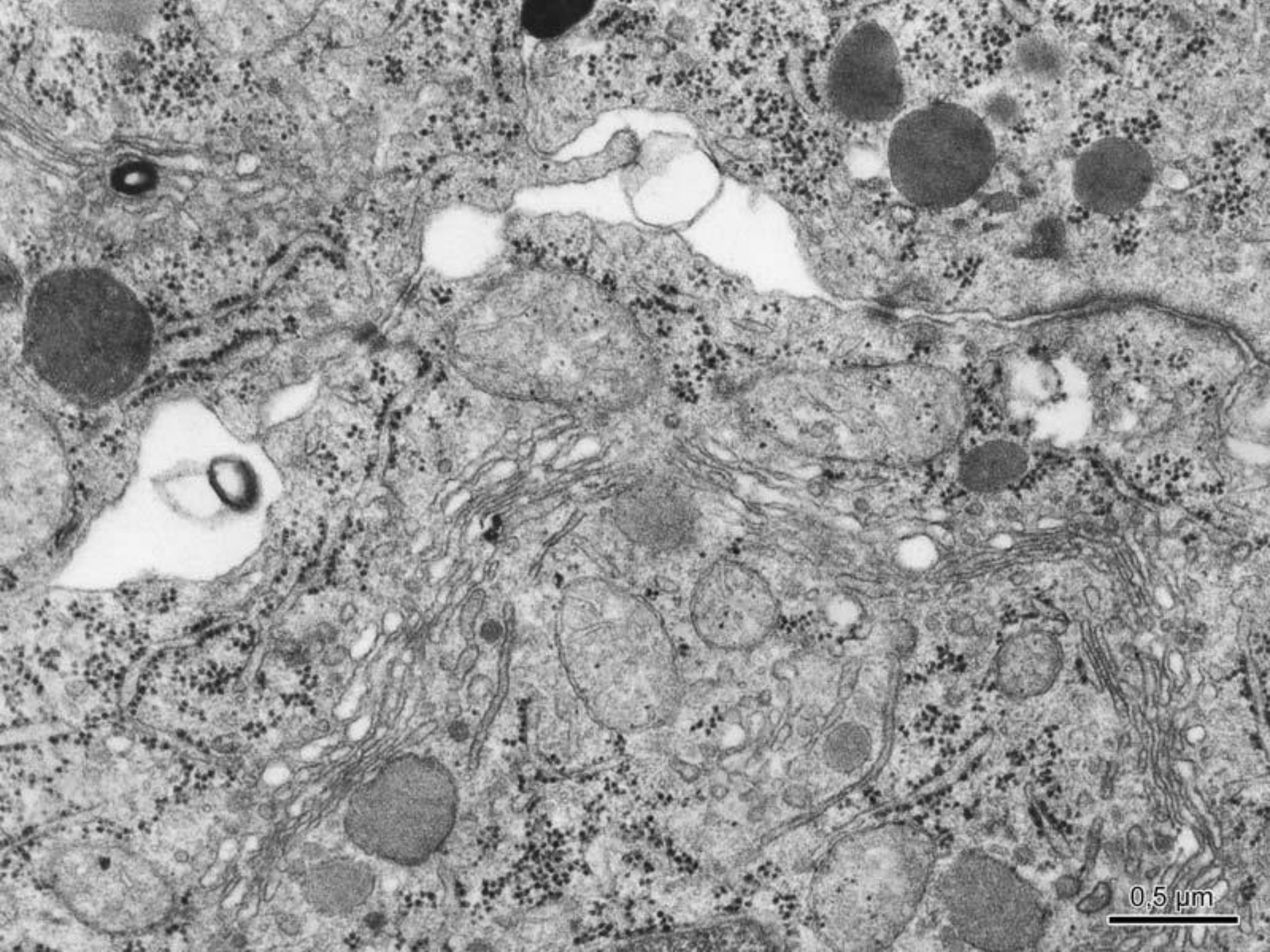


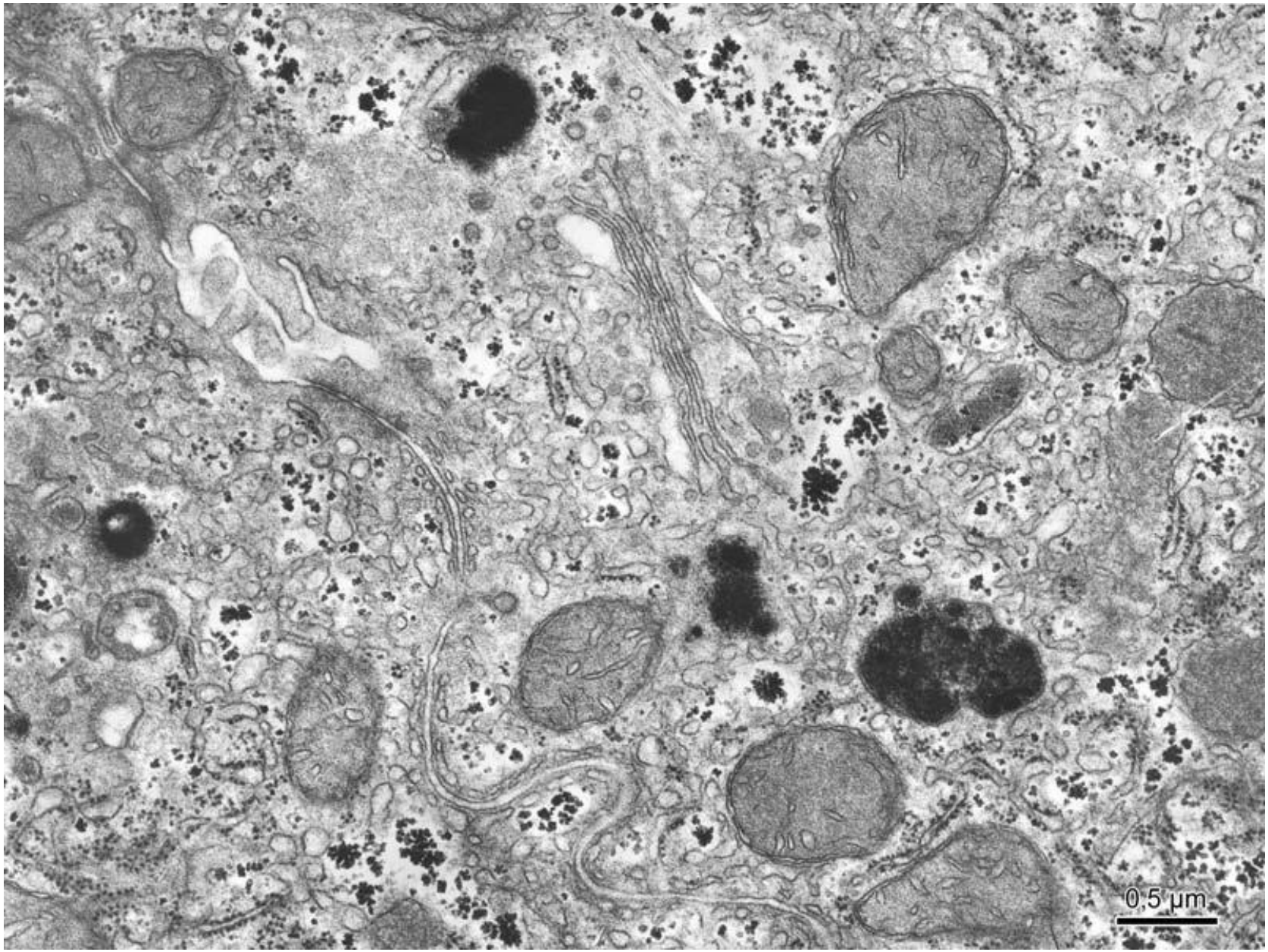


Golgiho aparát

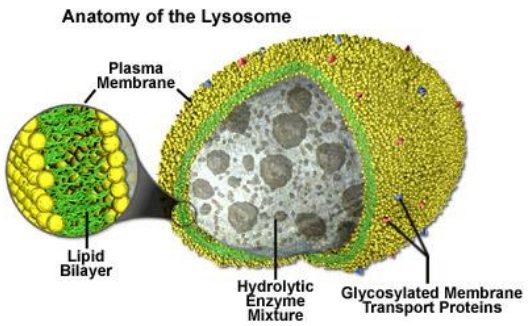


10 – 20 na buňku


0,5 µm


0,5 µm

Lyzosomy



Glycosidases

alpha-Galactosidase A/GLA	Endo-beta-N-acetylglucosaminidase H/Endo H
alpha-N-acetylgalactosaminidase/NAGA	Galactosylceramidase/GALC
alpha-N-acetylglucosaminidase/NAGLU	Glucosylceramidase/GBA
alpha-Galactosidase/a-Gal	Heparanase/HPSE
alpha-L-Fucosidase	Heparinase I
Tissue alpha-L-Fucosidase/FUCA1	Heparinase II
beta-Galactosidase-1/GLB1	Heparinase III
beta-Glucuronidase/GUSB	Hexosaminidase A/HEXA
beta (1-3)-Galactosidase	Hyaluronan Lyase
beta (1-4)-Galactosidase	Hyaluronidase 1/HYAL1
Chitinase 3-like 1	Hyaluronidase 4/HYAL4
Chitinase 3-like 2	alpha-L-Iduronidase/IDUA
Chitinase 3-like 3/ECF-L	Klotho
Chitobiase/CTBS	Klotho beta
Chitotriosidase/CHIT1	Lactase-like Protein/LCTL
Chondroitin B Lyase/Chondroitinase B	MBD4
Chondroitinase ABC	NEU-1/Sialidase-1
Cytosolic beta-Glucosidase/GBA3	O-GlcNAcase/OGA
Endo-beta-N-acetylglucosaminidase F1/Endo F1	PNGase F
Endo-beta-N-acetylglucosaminidase F3/Endo F3	SPAM1

Lysosomal Proteases

AMSH/STAMBP	Cathepsin H
Cathepsin 3	Cathepsin K
Cathepsin 6	Cathepsin L
Cathepsin 7/Cathepsin 1	Cathepsin O
Cathepsin A/Lysosomal Carboxypeptidase A	Cathepsin S
Cathepsin B	Cathepsin V
Cathepsin C/DPPI	Cathepsin X/Z/P
Cathepsin D	Galactosylceramidase/GALC
Cathepsin F	Legumain/Asparaginyl Endopeptidase

Sulfatases

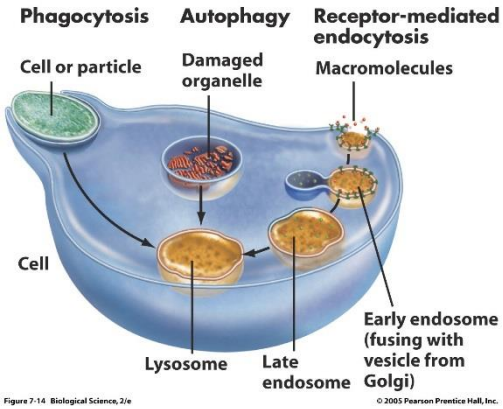
Arylsulfatase A/ARSA	Iduronate 2-Sulfatase/IDS
Arylsulfatase B/ARSB	Sulfamidase/SGSH
Arylsulfatase G/ARSG	Sulfatase-2/SULF2
Glucosamine (N-acetyl)-6-Sulfatase/GNS	

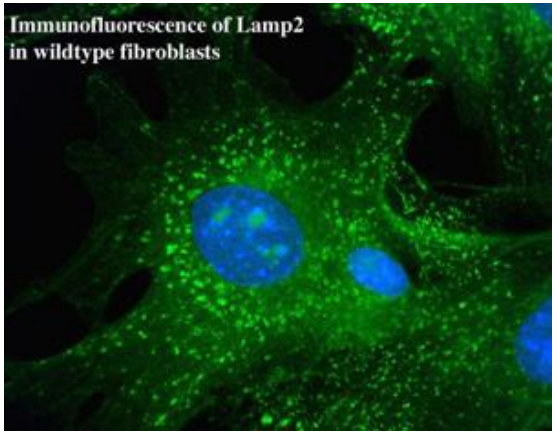
Other Lysosomal Proteins

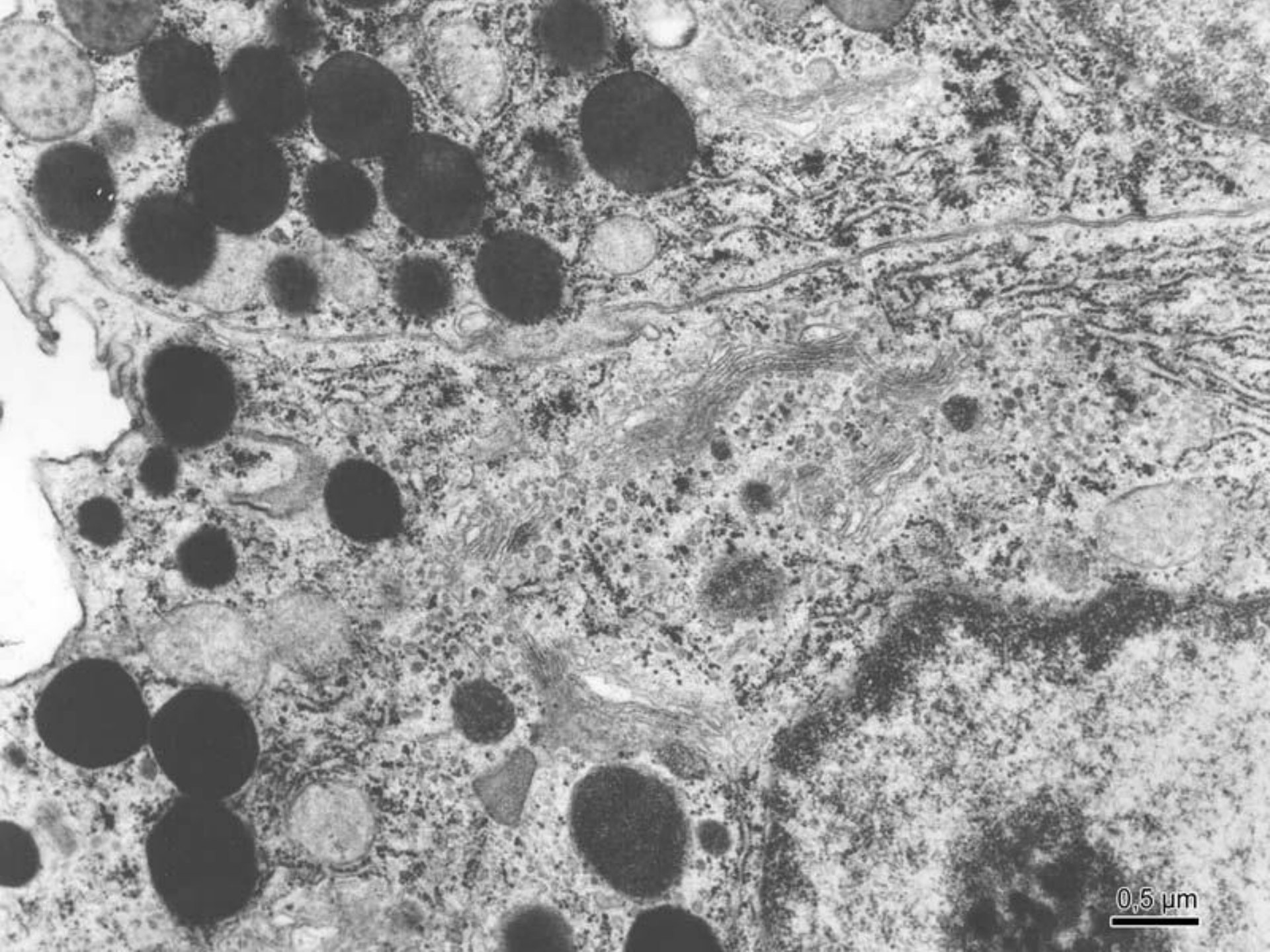
BAD-LAMP/LAMP5	DC-LAMP
CD63	Hyaluronidase 1/HYAL1
CD-M6PR	LAMP1/CD107a
Clathrin Heavy Chain 1/CHC17	LAMP2/CD107b
Clathrin Heavy Chain 2/CHC22	Rab27a

Enzymy degradující všechny biologické polymery

Google



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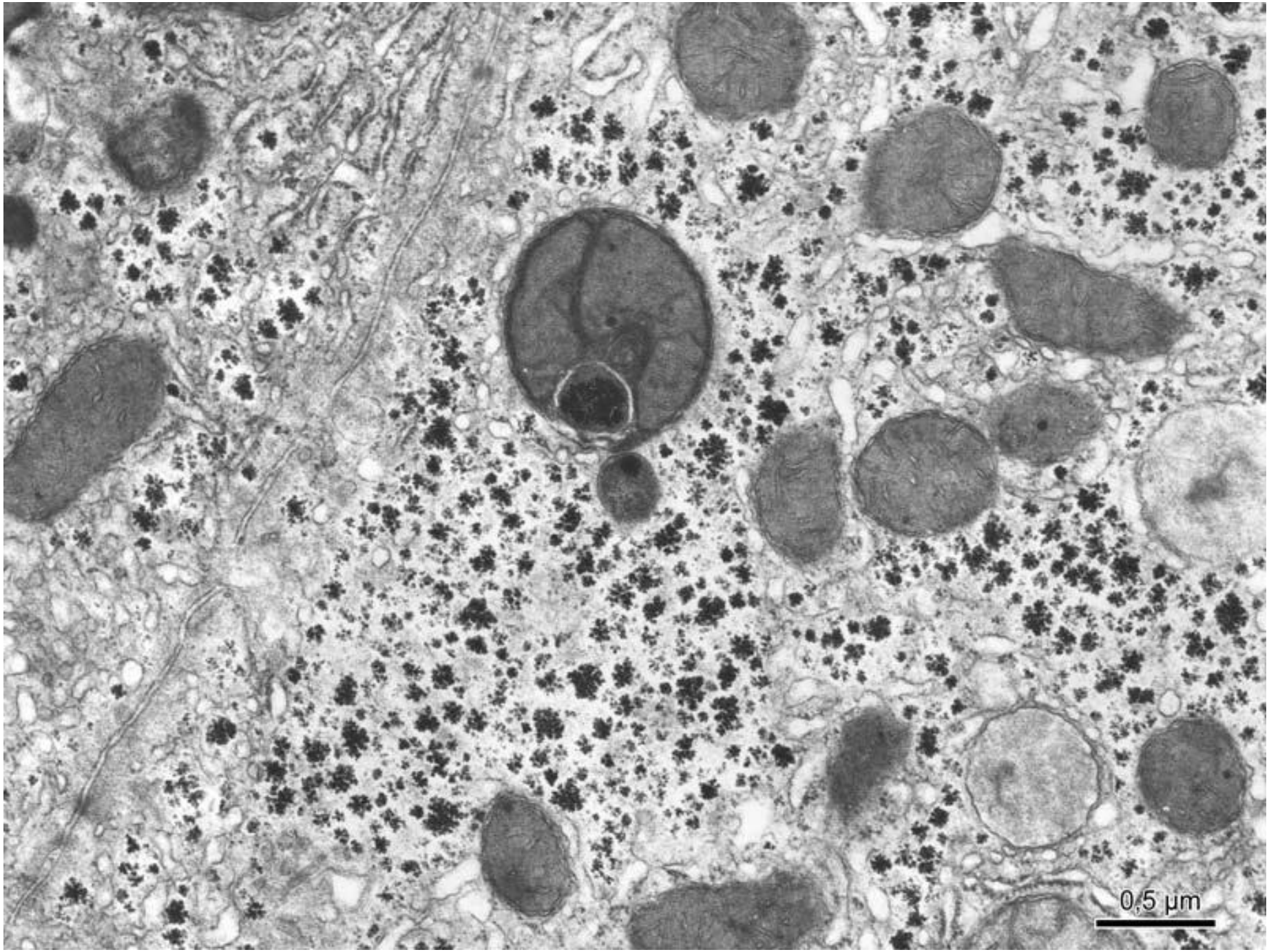
0,5 µm


L

Děkuji za pozornost

ATLAS EM

Snímky 1-15; 23; 32; 35-36; 42; 43; 45; 46

Pro další studium:

Např. http://www.ncbi.nlm.nih.gov/books