Basic notes to ORGANELLES and CELLULAR TRANSPORT

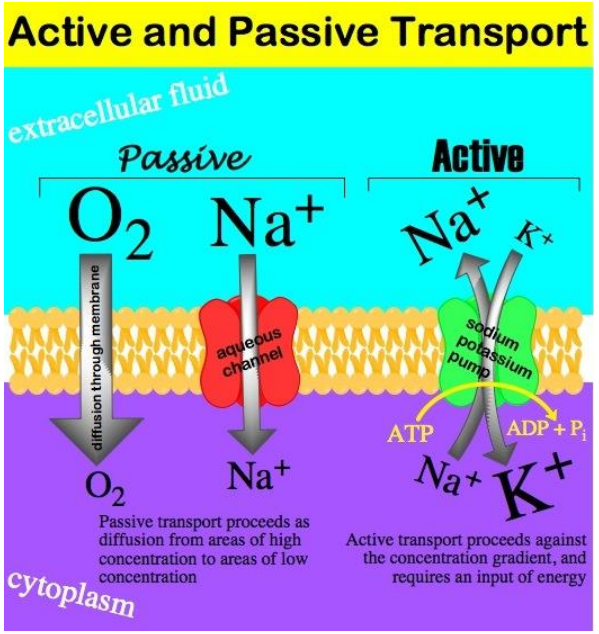
TRANSPORT

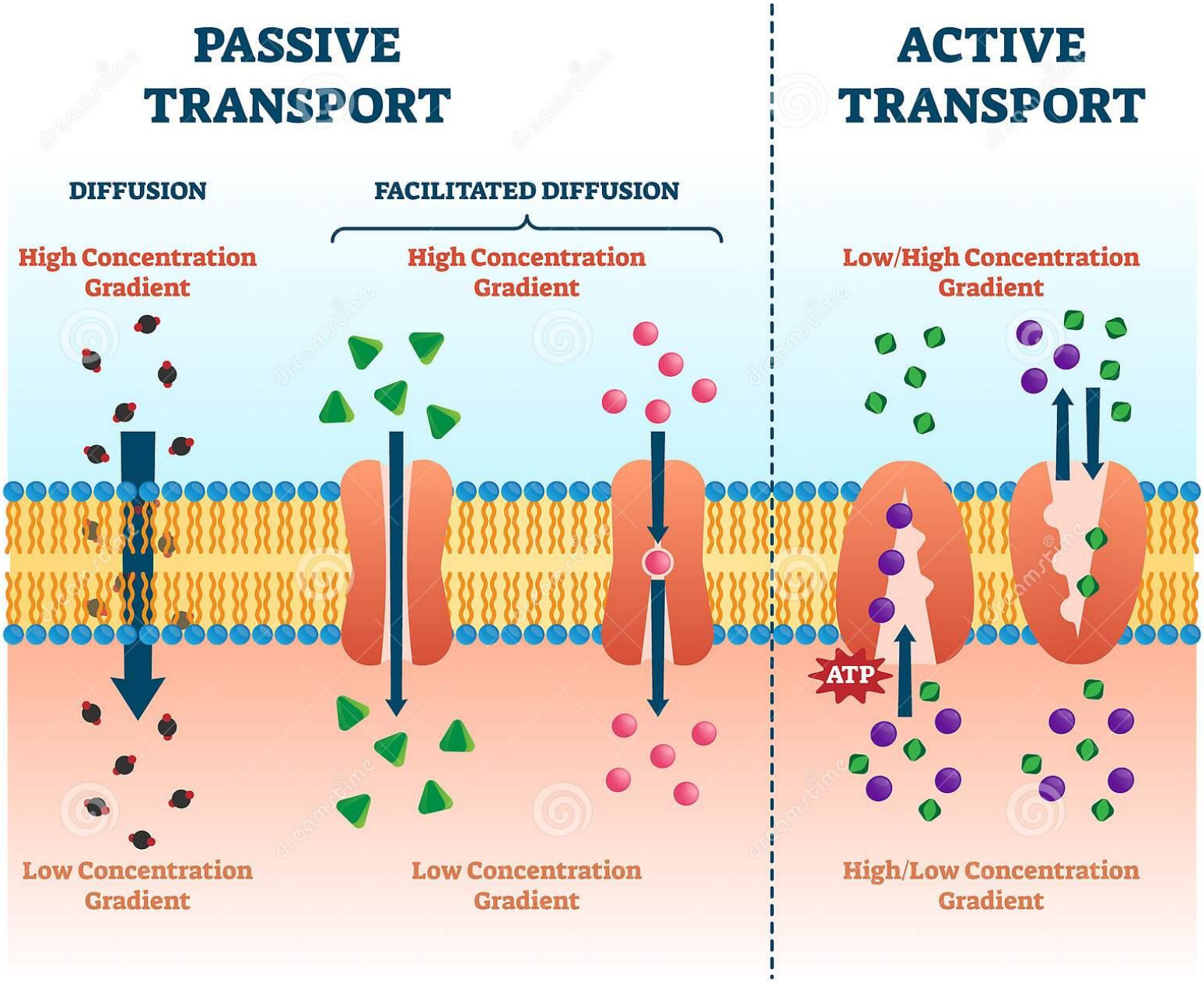
- Passive (diffusion) – in previous extra october lesson

  (compound had some gradient of concentration, movement is causd by simple physical forces inversly to gradient)

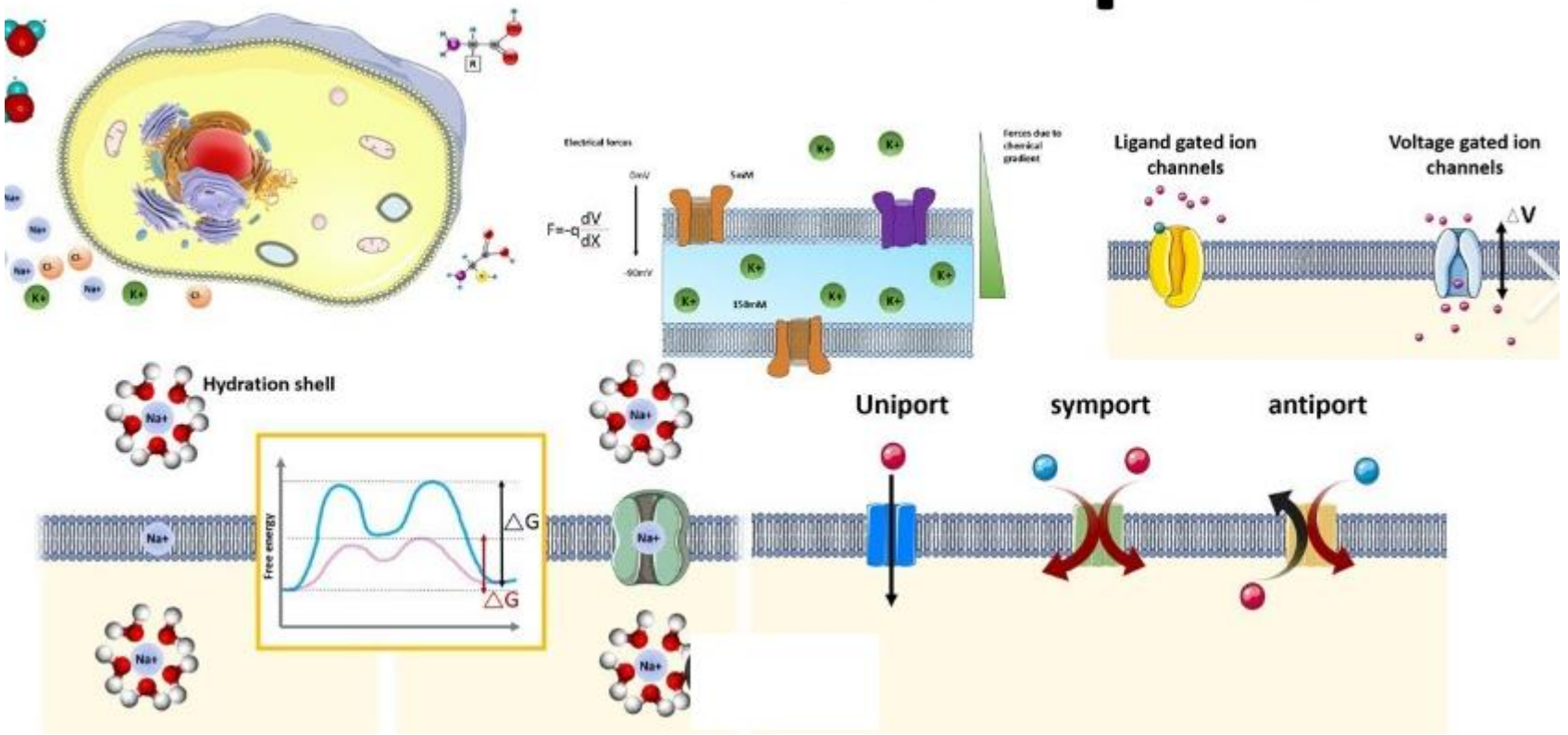
- Active - today

  (cell must use energy to transport)

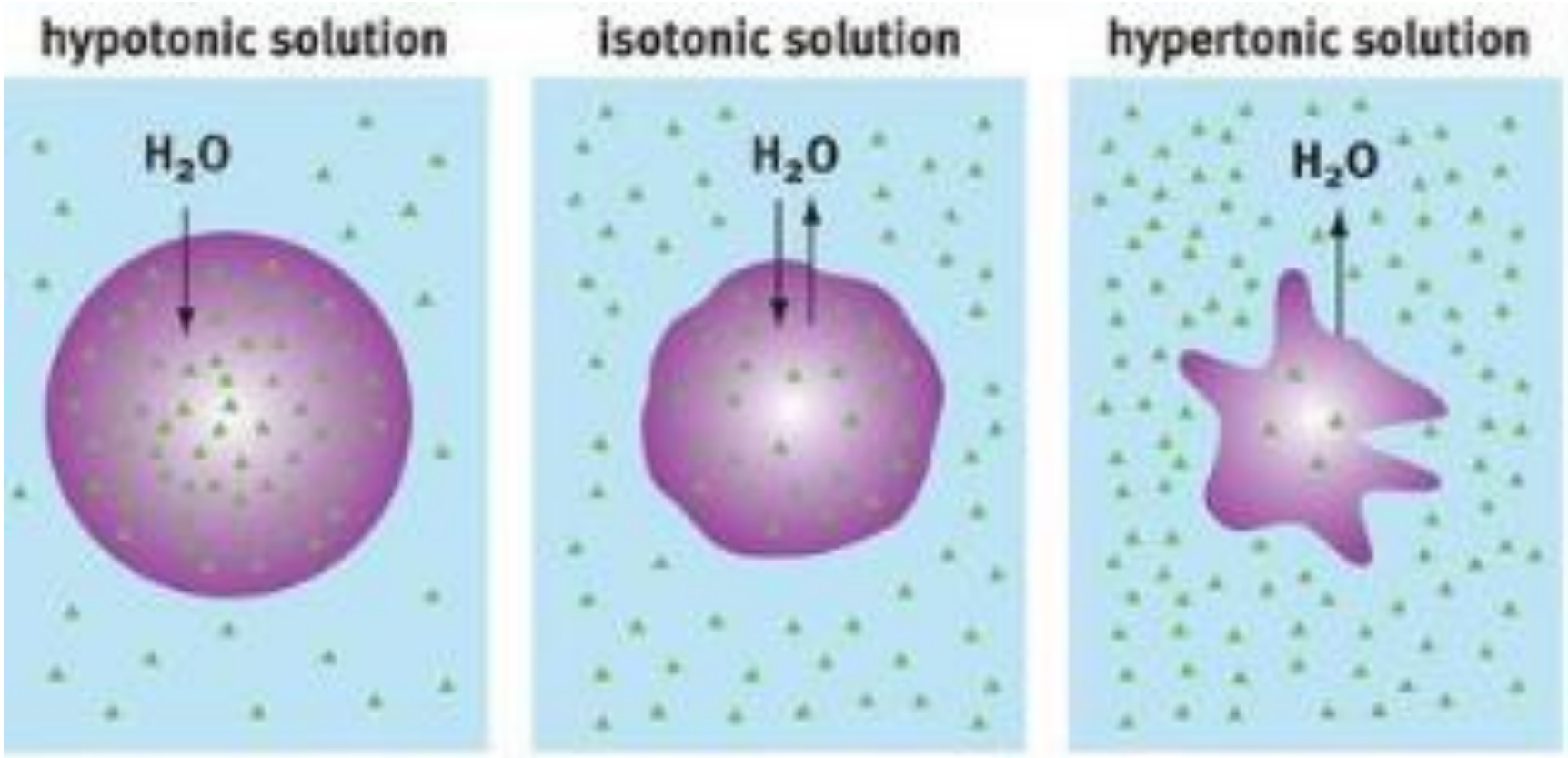




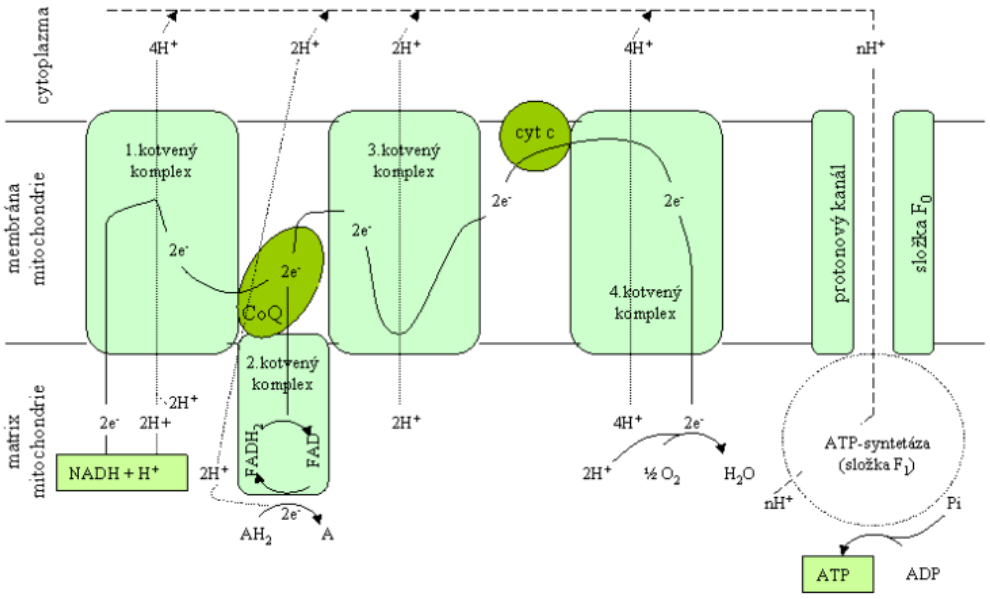
Membrane transport



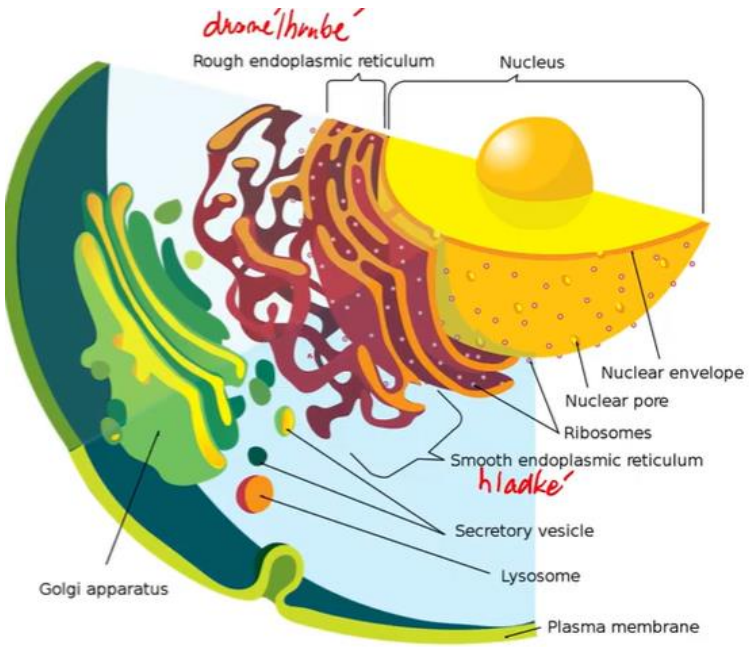
Specific osmotic water tansport:



ORGANELLES

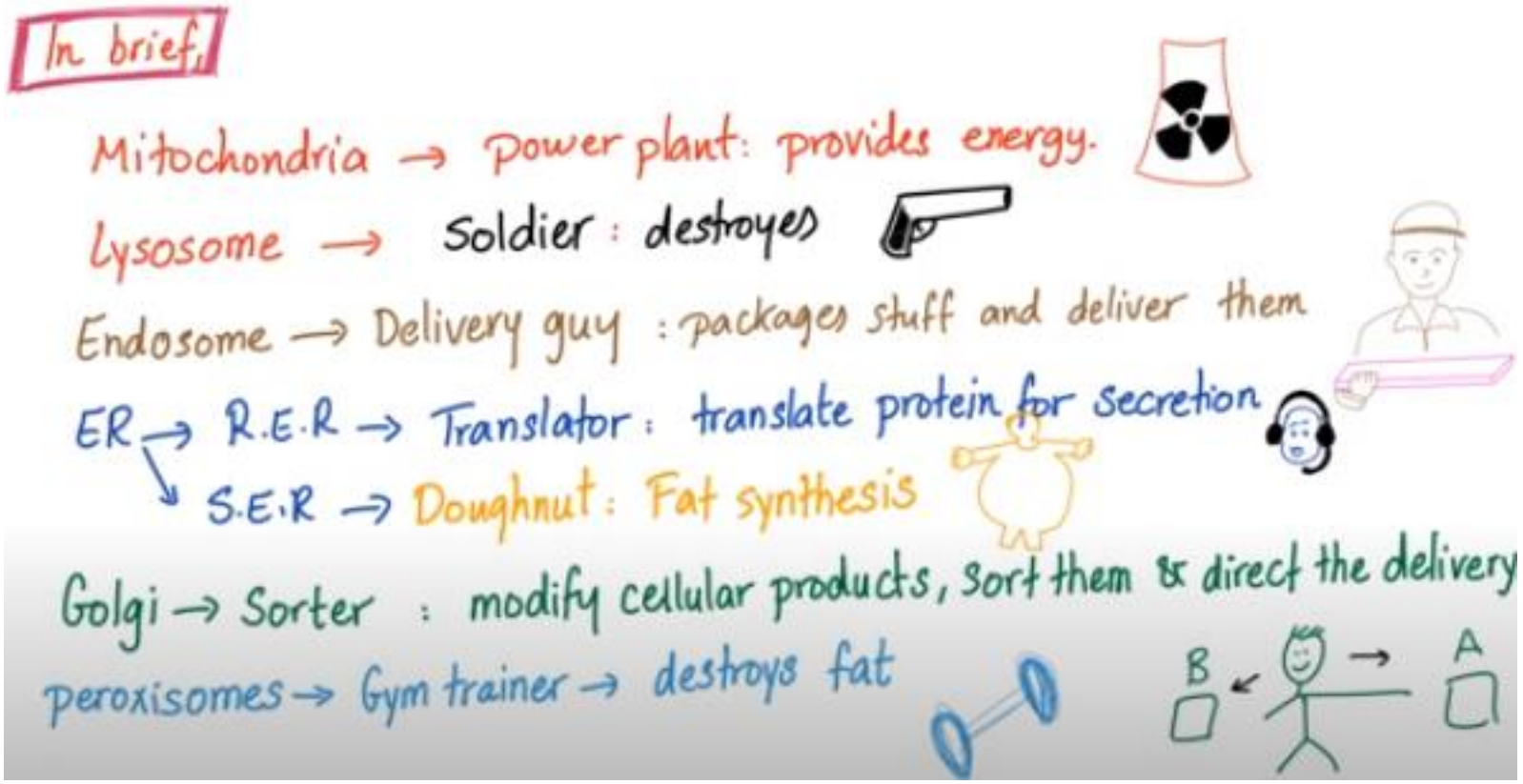


Obr 1. Dýchací řetězec



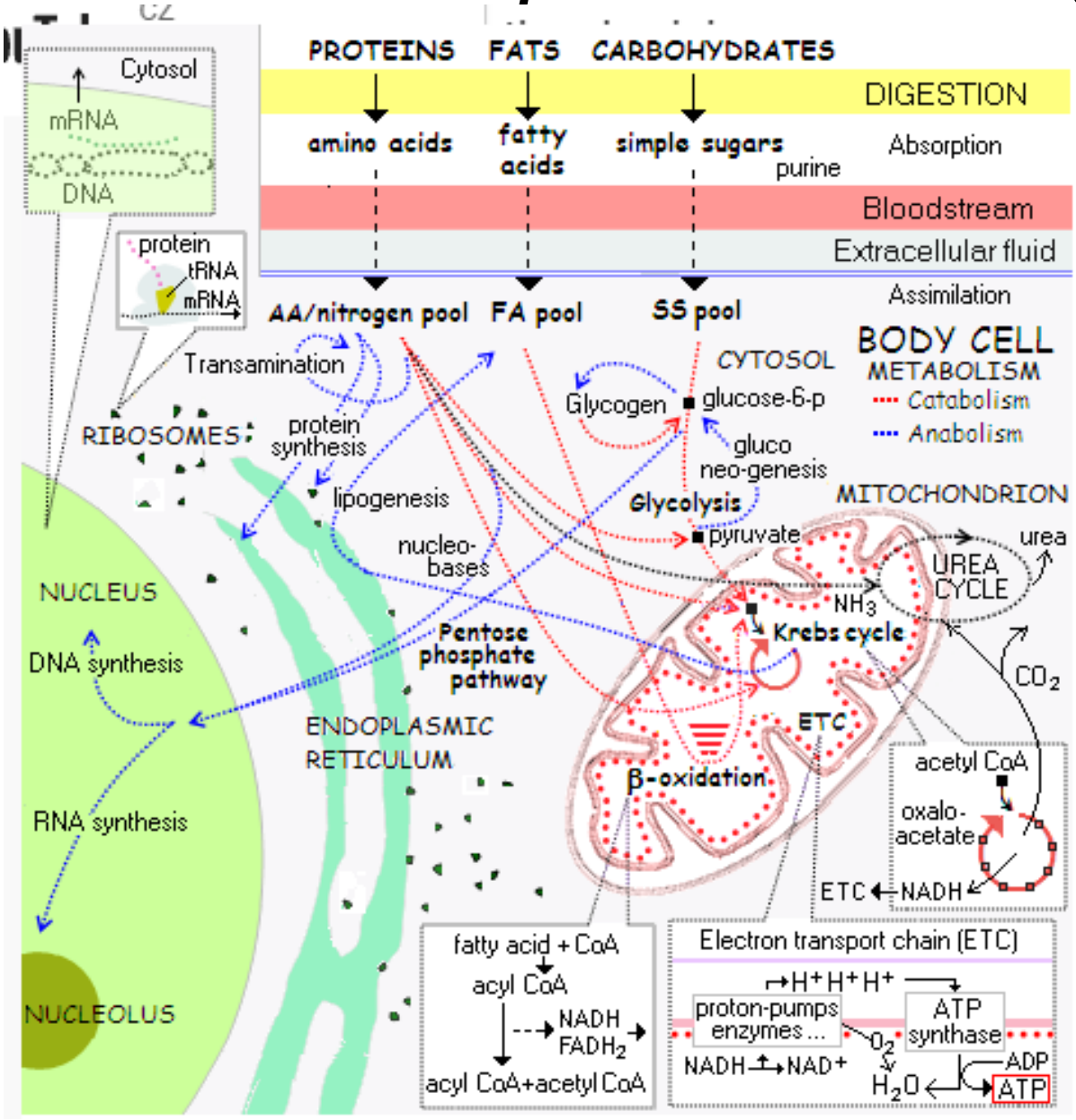
https://en.wikipedia.org/wiki/File:Endomembrane_system_diagram_en_(edit).svg

ANALOGY
orgnelles and city department

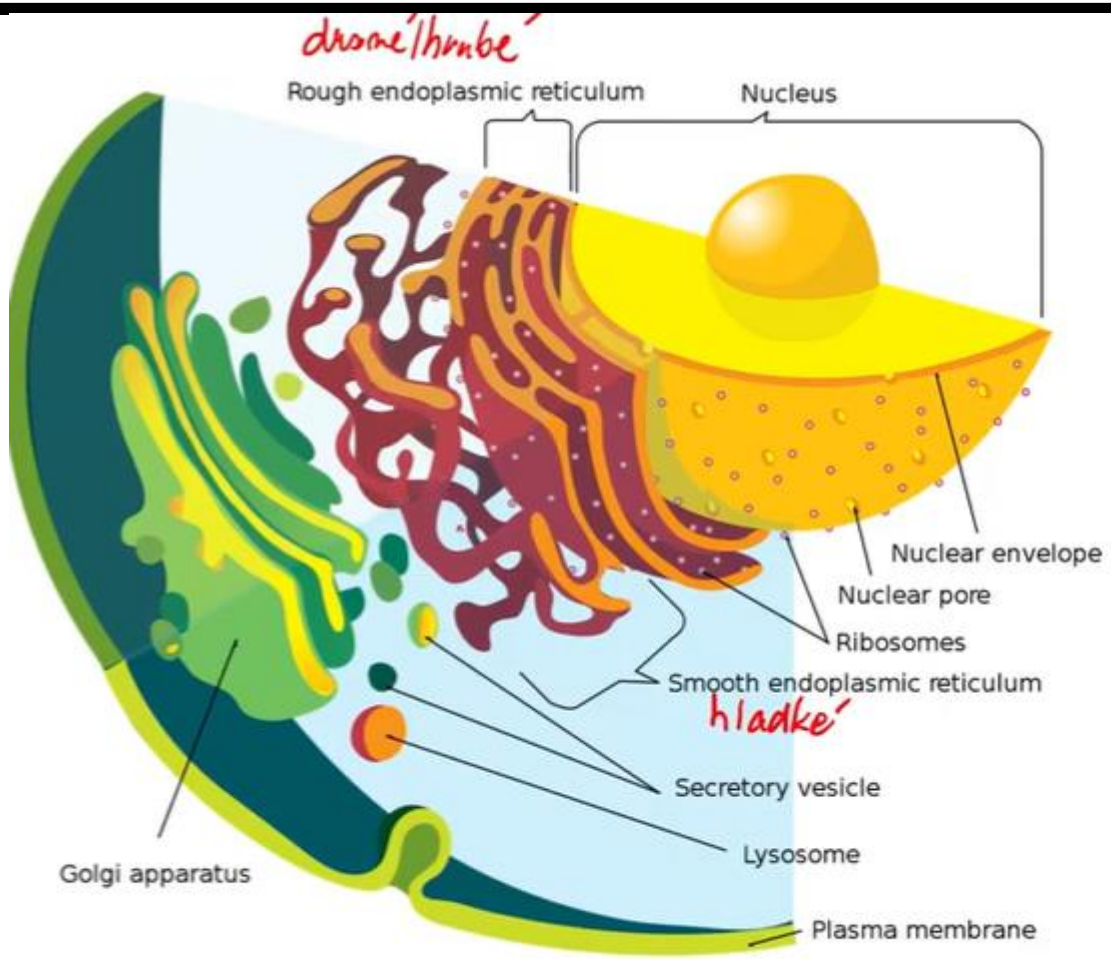


Cell nucleus – major of the city

Metabolic net -cooperation of organelles

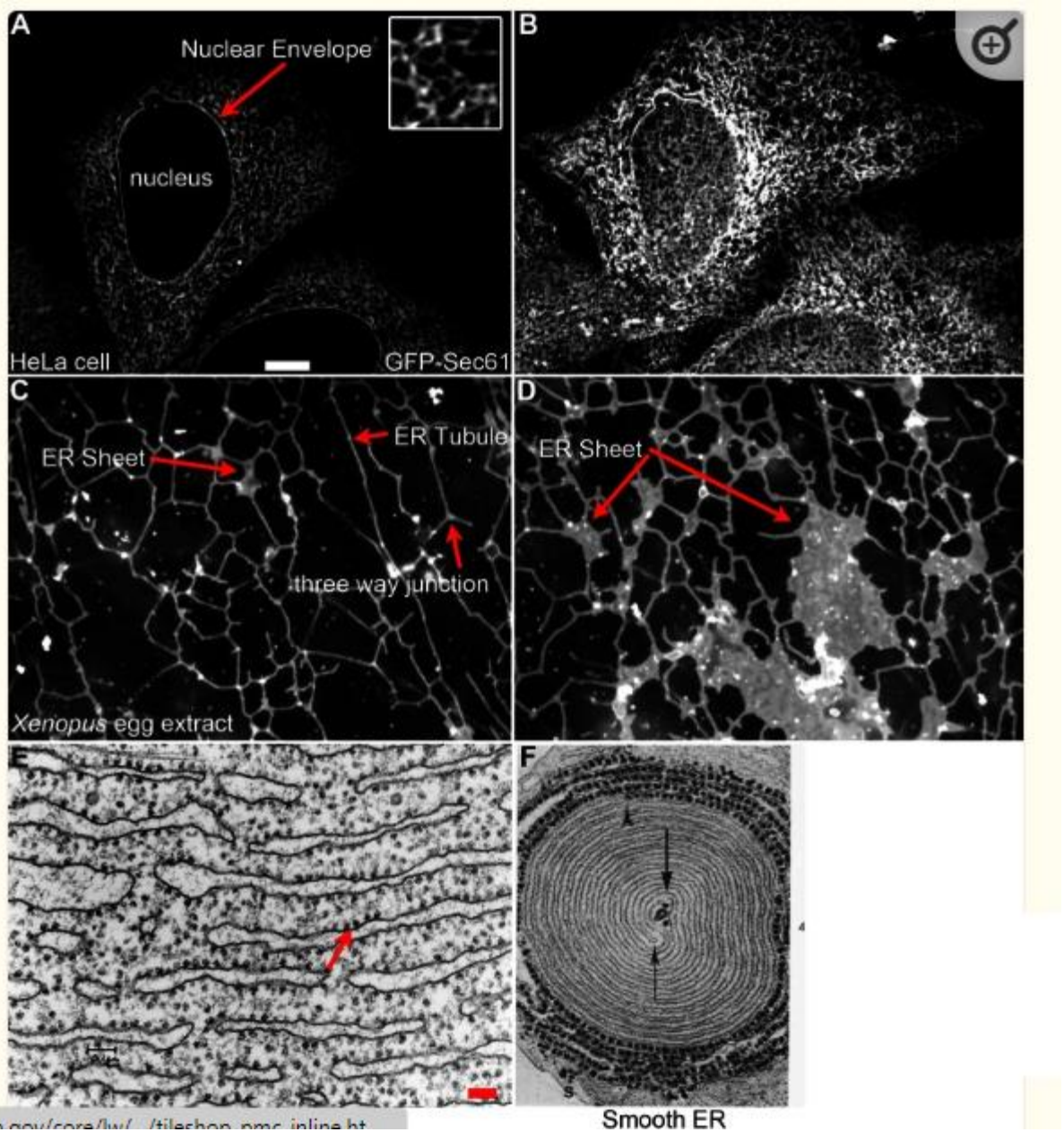


Endoplasmatic reticulum



https://en.wikipedia.org/wiki/File:Endomembrane_system_diagram_en_(edit).svg

- The ER is the largest organelle in the cell and is a major site of protein synthesis and transport, protein folding, lipid and steroid synthesis, carbohydrate metabolism and calcium storage [1–7]. The multi-functional nature of this organelle requires a myriad of proteins, unique physical structures and coordination with and response to changes in the intracellular environment. Work from a variety of systems has revealed that the ER is composed of multiple different structural domains.

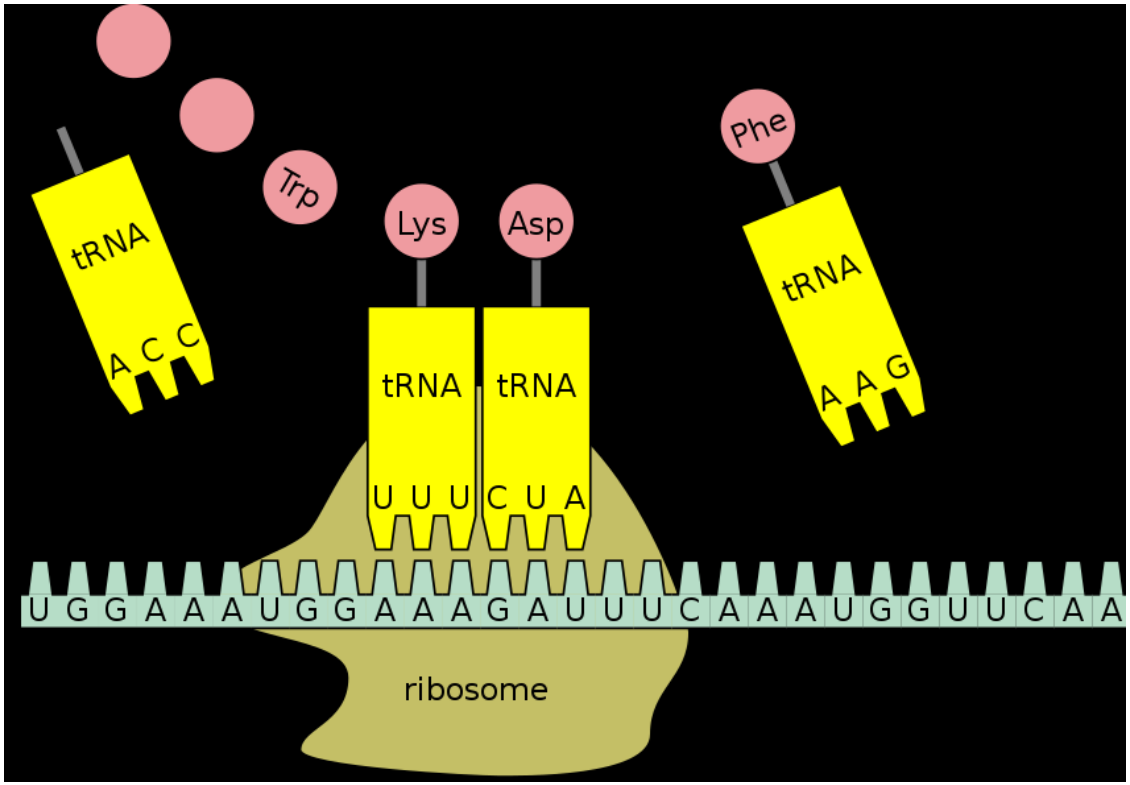

A
Nuclear Envelope
nucleus
HeLa cell
GFP-Sec61
B
C
ER Sheet
ER Tubule
three way junction
Xenopus egg extract
D
ER Sheet
E
F
Smooth ER

- **Rough Endoplasmic Reticulum** is that there are ribosomes all along the membrane that pass along Messenger RNA through the membrane into the channel. These ribosomes appear on the surface to give this a very rough and bumpy look, giving it the name Rough Endoplasmic Reticulum. In an average liver cell, there are about 13 million ribosomes on the endoplasmic reticulum. The rough Endoplasmic Reticulum works with the ribosomes in its membrane to take polypeptides and amino acids away from the cytosol and continues protein production.

- Smooth Endoplasmic Reticulum is a tube-like organelle that forms a network of tubes throughout the cytoplasm. The inside of the smooth ER is called the lumen, and it is surrounded by a phospholipid membrane. It is quite dispersed, unlike the Rough ER which is bunched up more-so near to the nucleus and Golgi Apparatus. The reason for the Smooth Endoplasmic Reticulum having its name is that it is not studded with ribosomes, giving it a smooth appearance.

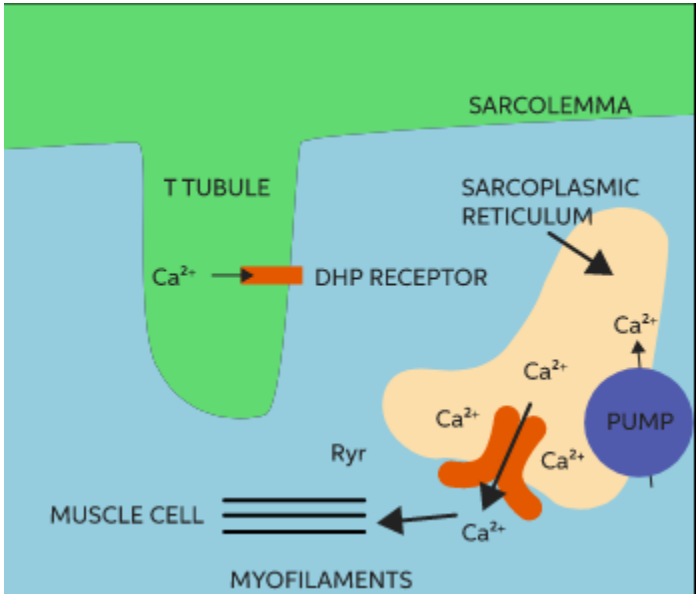
(Ribosom)

- Transletion of mRNA to tRNA to PROTEIN

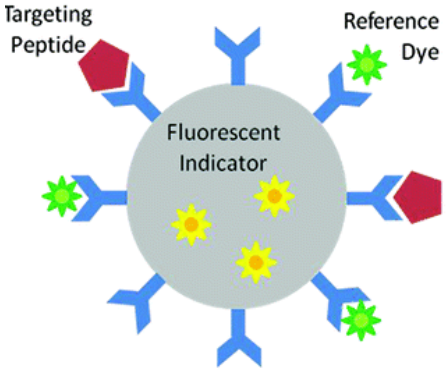


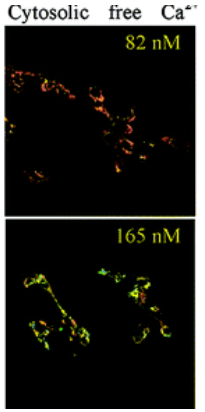
Endoplasmatic reticulum in muscle

= SARCOplasmatic reticulum

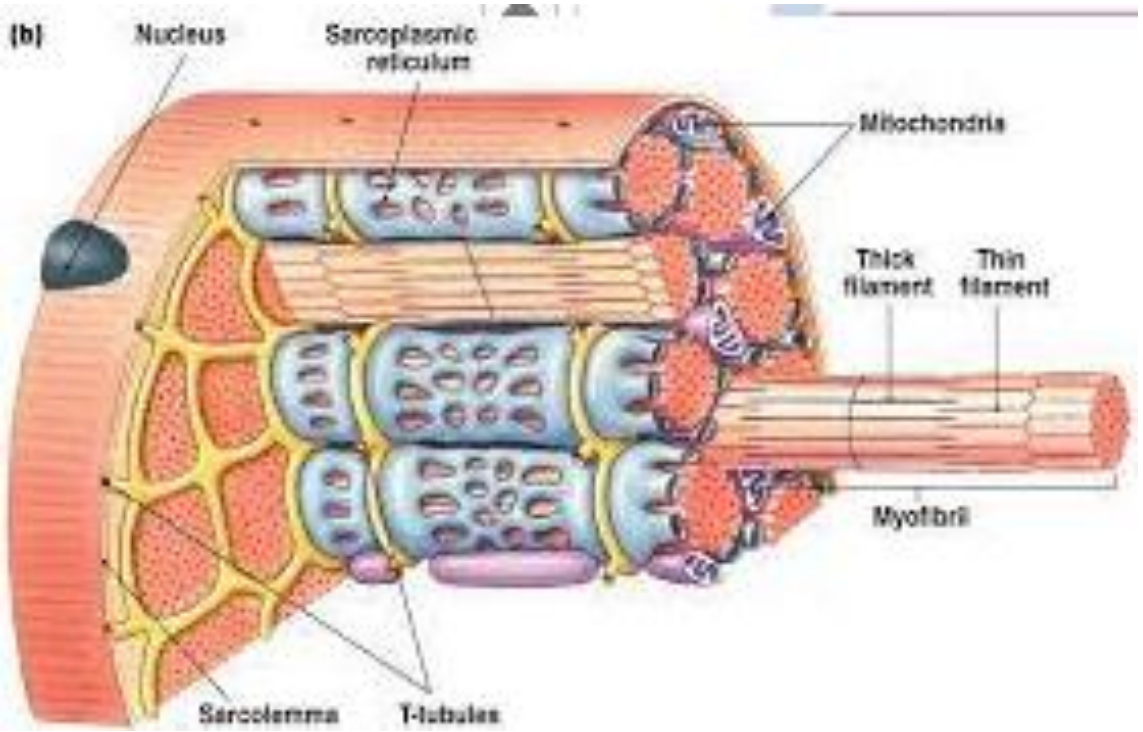


- Technical notes: How make visibilit of Ca 2+ release http://pubs.acs.org/doi/pdf/10.1021/ac202521e

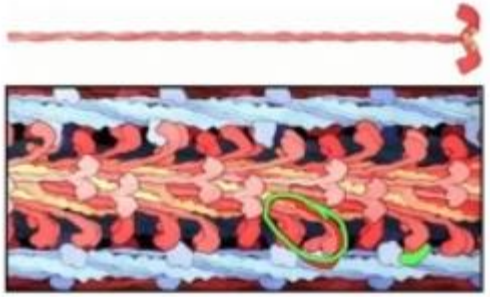


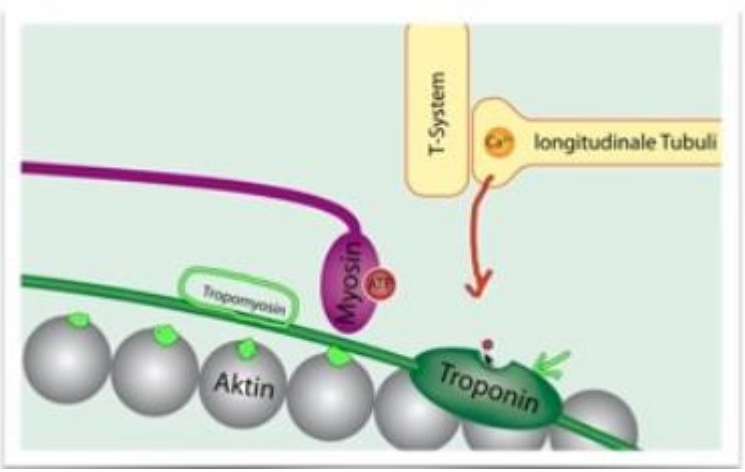


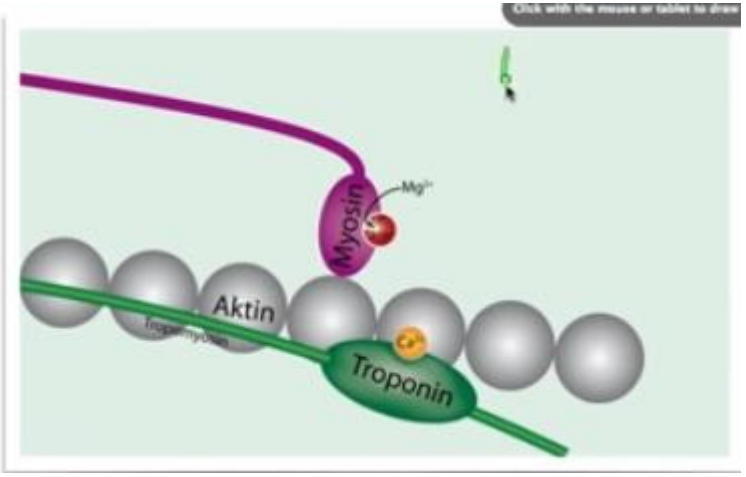
Endoplasmatic reticulum - Real morphology in cell:



What makes Ca2+ exlux from SARCOplasmatic reticulum







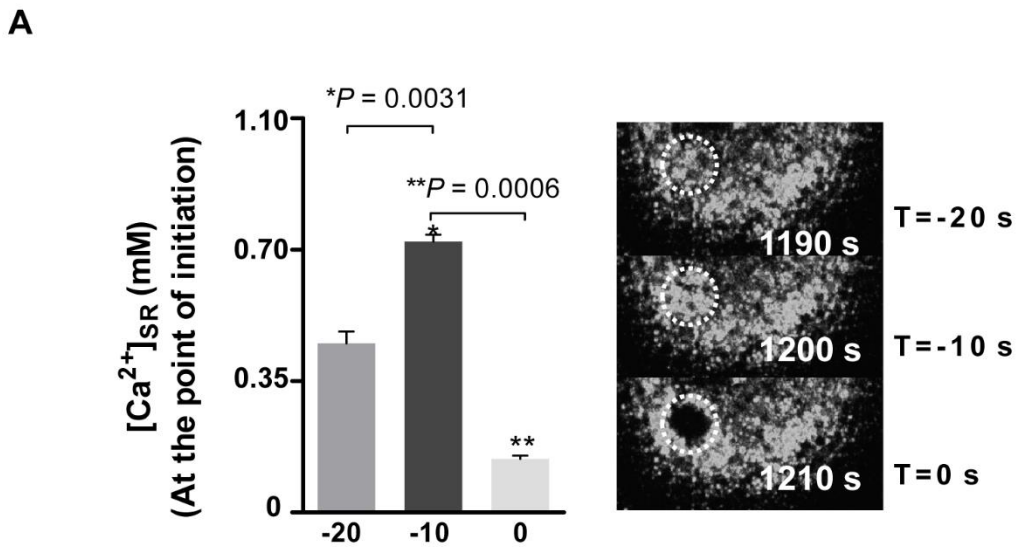
1: Ca^{2+} Release from Terminal Cisternae binding site exposure
2: Myosin head binds to Actin binding Sites (ATP hydrolized)
3: Release of ADP and Pi causes Power Stroke
4: ATP causes Myosin head to be released
5: ATP is hydrolyzed, re-energizes the myosin head
6: Ca^{2+} are pumped back into the Terminal Cysternae

(Sarcoplasmatic retikulum)

Endotelové buňky

Waves of Calcium Depletion in the Sarcoplasmic Reticulum of Vascular Smooth Muscle Cells: An Inside View of Spatiotemporal Ca^{2+} Regulation

- Mitra Esfandiarei ,



MITOCHONDRIA

Eeach piece of breakfast is reconstitute to glucose or similar compounds and they are remaking to ENERGY in mitochondria.

MITOCHONDRIA

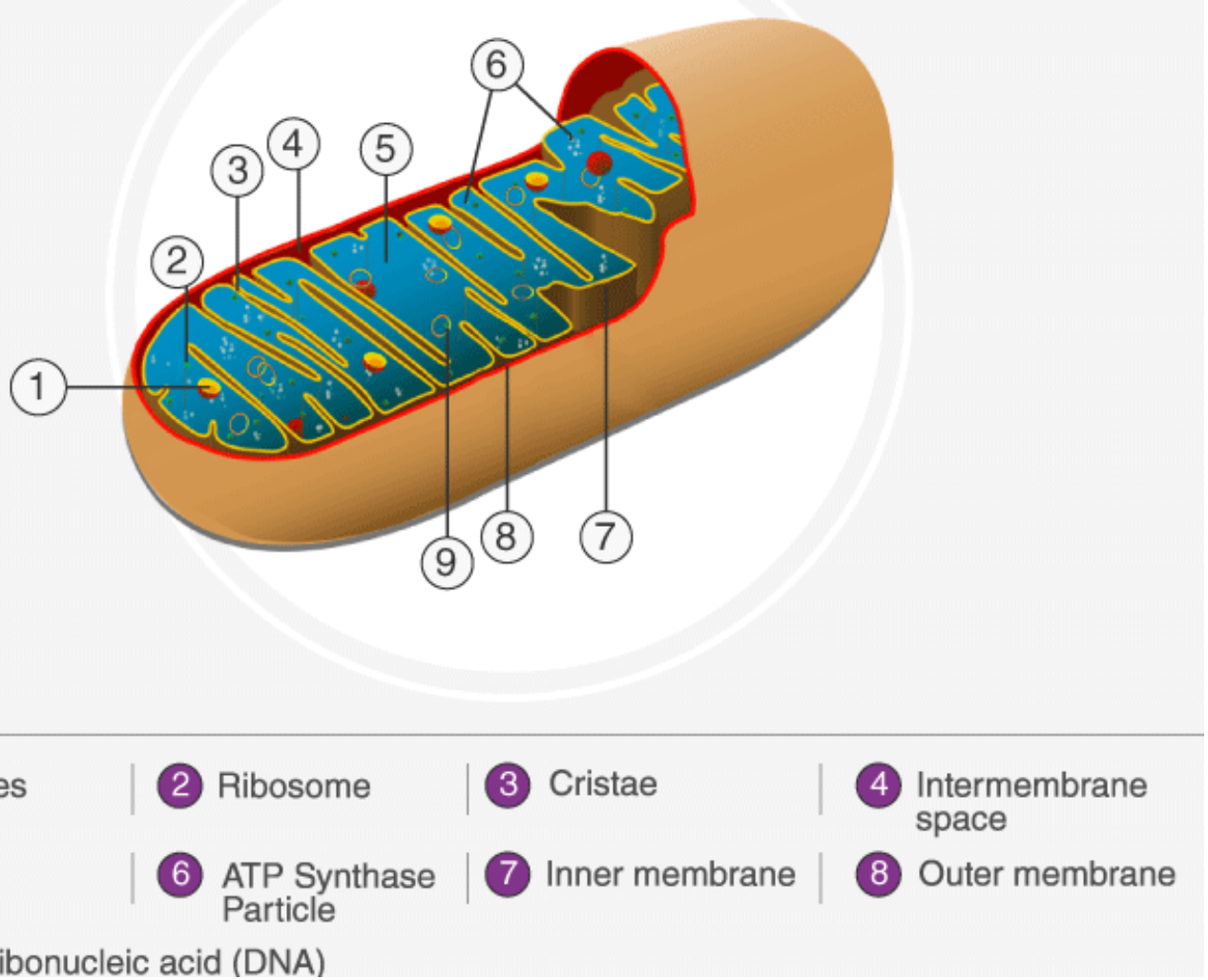
Mitochodnria is very original organelle

- Original RIBOSOMES inside –own proteosynthesi independent to ER
- Original DNA – own genetic DNA
- ATP synthasis – original energy production in cell

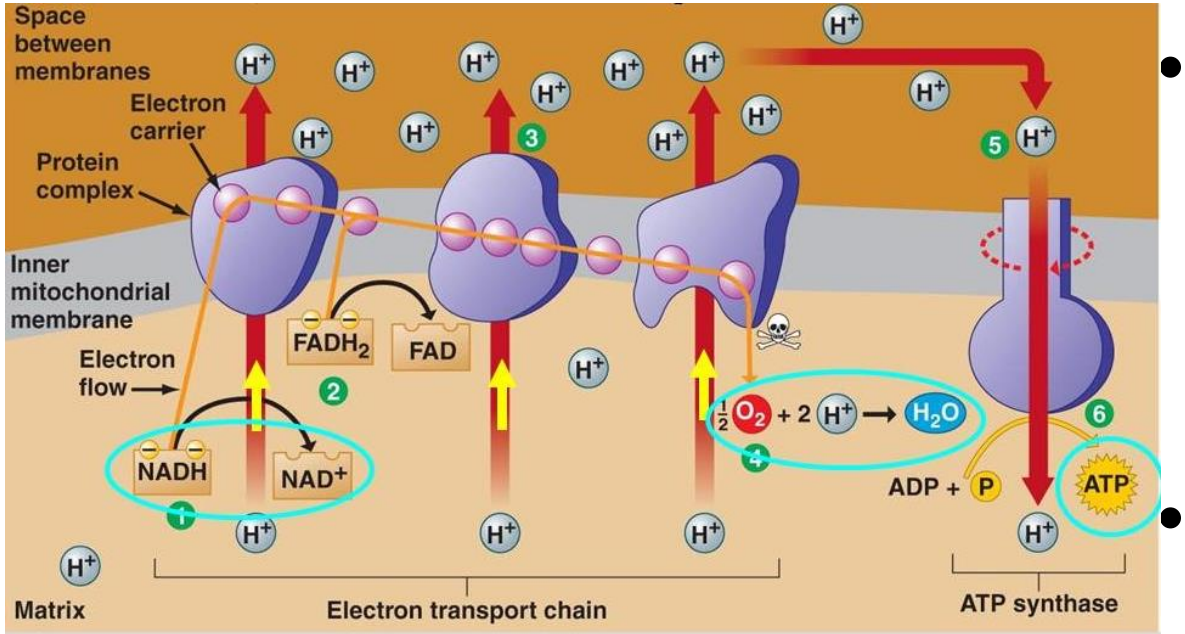
(=endosymbiotic theory …hypothesis of bacteria transfer in evolution)

Heteroplasmy is the presence of more than one type of organellar genome (mitochondrial DNA or plastid DNA) within a cell or individual. It is an important factor in considering the severity of mitochondrial diseases.

See LHON disease at the end of the presentation.

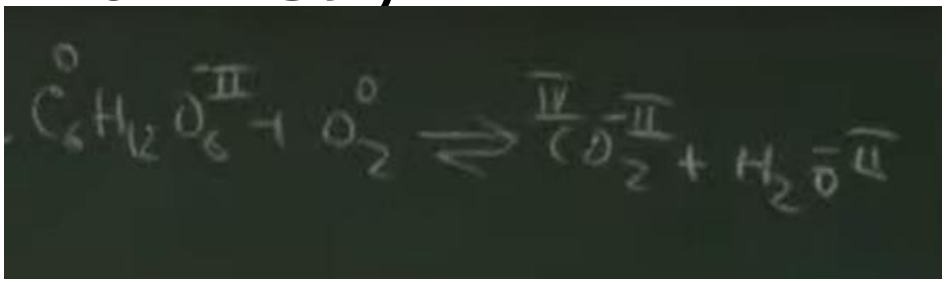

1 Granules
2 Ribosome
3 Cristae
4 Intermembrane space
5 Matrix
6 ATP Synthase Particle
7 Inner membrane
8 Outer membrane
9 Deoxyribonucleic acid (DNA)

Energy production (ATP synthesis using gradient of H+ ion)

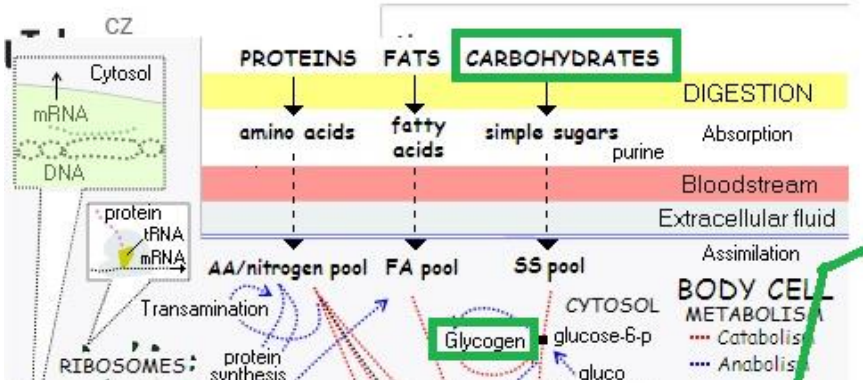


- High concentration H+
- Low concentration H+

- Summary in chmistry:



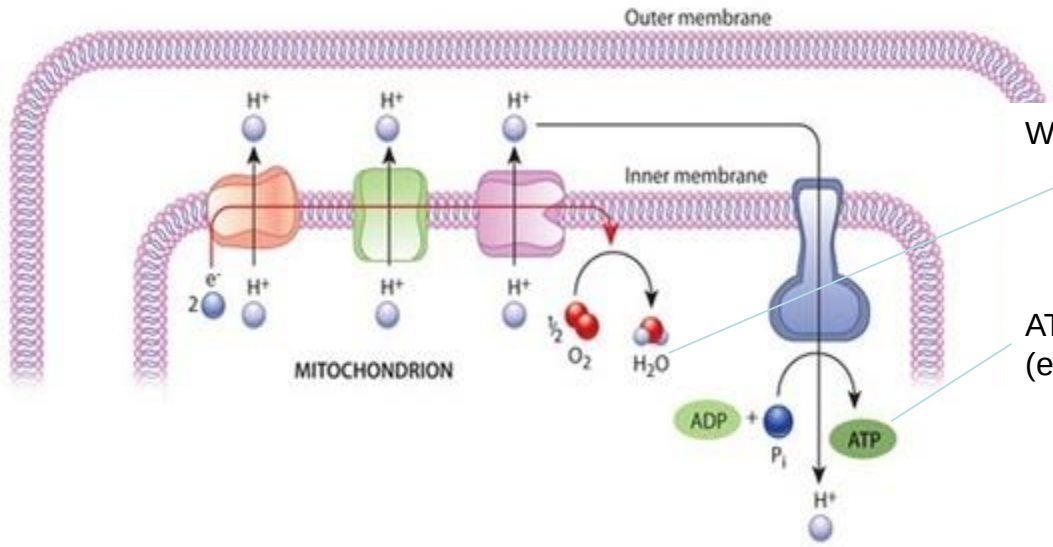
- Real biology of sugar Exchange to energy:



GLUCOSE

OXYGEN

GO INTO THE REACTION

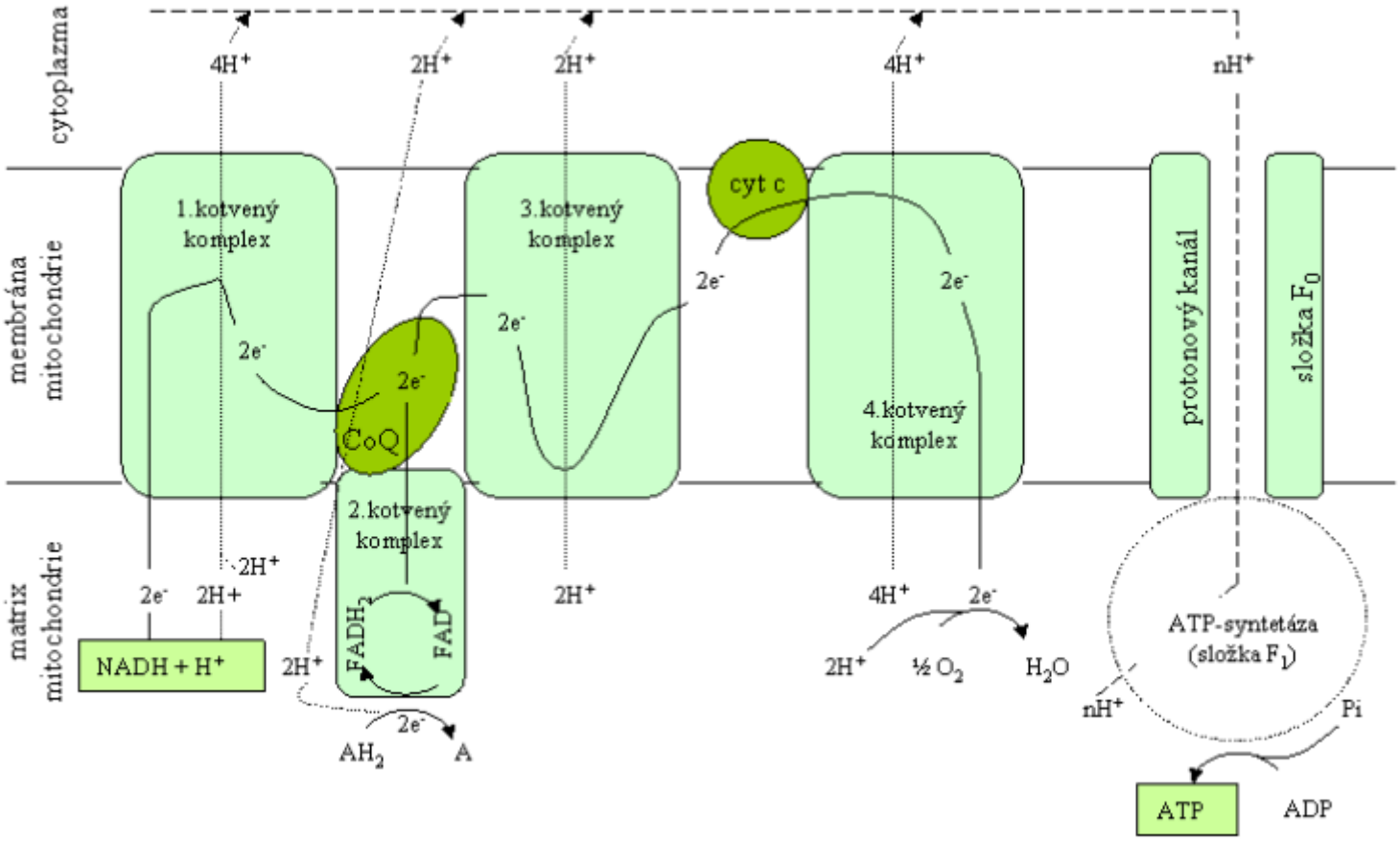


WATER

ATP (energy)

GO OUT From the reaction

In another scheme



Obr 1. Dýchací řetězec

…advanced details

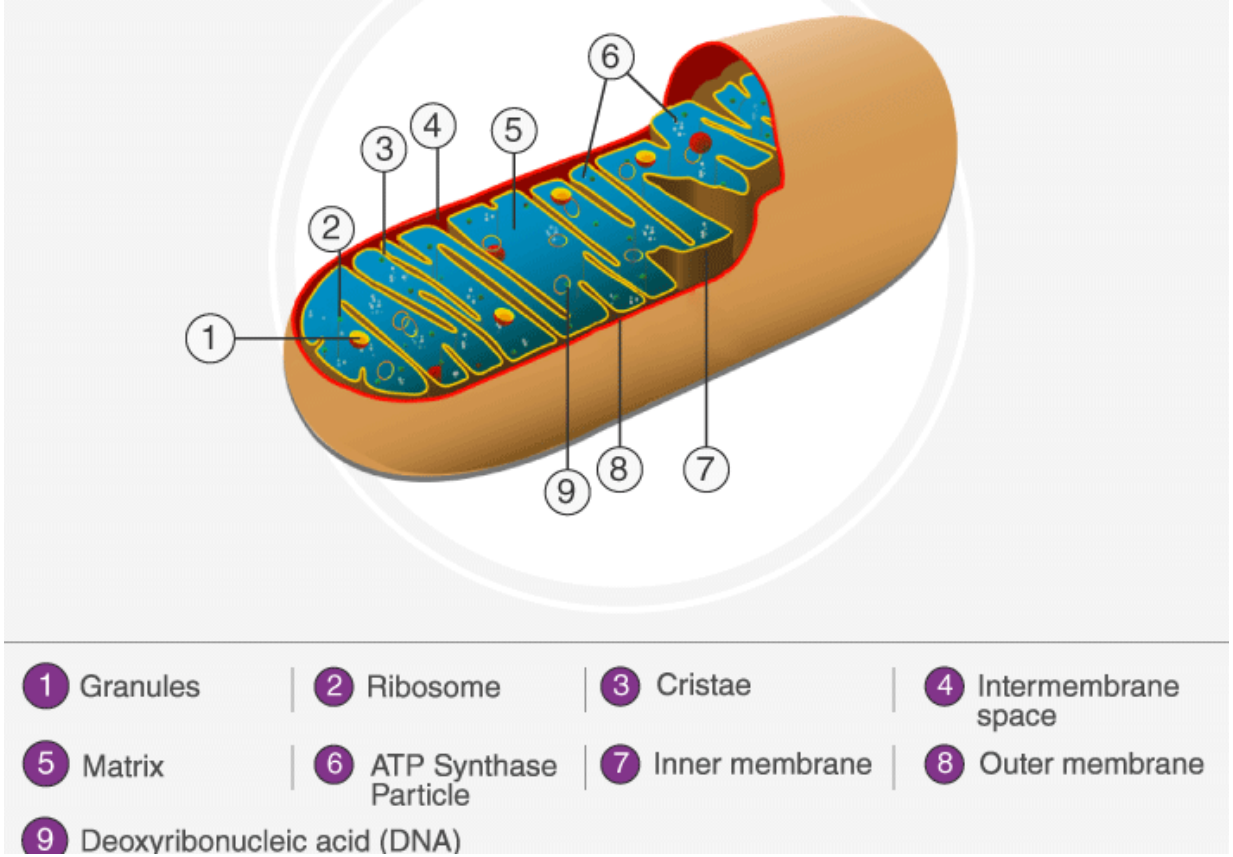
Electron transport– biophysical problem of electron step-by-step jumping to higher electropositive potential

$$A_{ox} + B_{red} \longrightarrow A_{red} + B_{ox}$$

$$NADH + H^+ + Q \longrightarrow NAD^+ + QH_2$$
$$QH_2 + cyt(Fe^{3+}) \longrightarrow Q + cyt(Fe^{2+})$$
$$cyt(Fe^{2+}) + 2H^+ + 1/2O_2 \longrightarrow cyt(Fe^{3+}) + H_2O$$

E^0 … standardní oxidačně – redukční **potenciál**

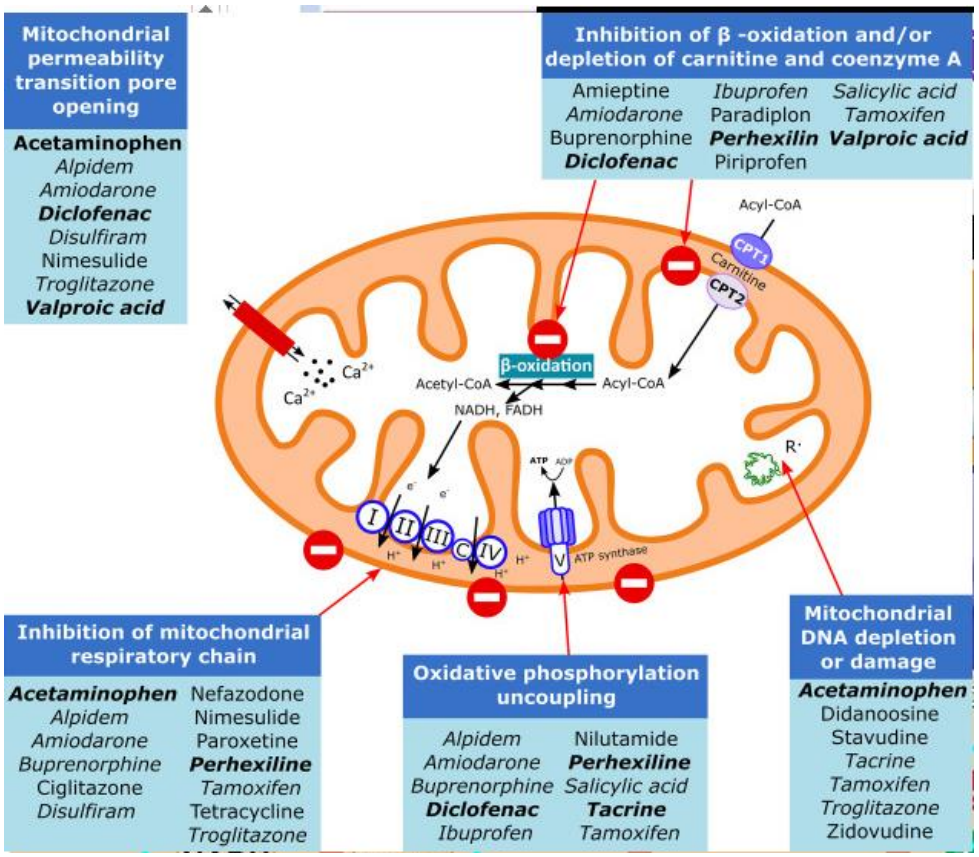
Redoxní systém	**$E^{0'}$ [V]**
$NAD^+/NADH + H^+$	- 0,32
pyruvát/laktát	- 0,19
oxalacetát/malát	- 0,17
$FAD/FADH_2$	- 0,12
$2H^+/H_2$ (pH = 0)	0
fumarát/sukcinát	+ 0,03
ubichinon oxidovaný/redukovaný	+ 0,10
cytochrom c (Fe^{3+}/Fe^{2+})	+ 0,23
cytochrom a_3 (Fe^{3+}/Fe^{2+}, Cu^{2+}/Cu^+)	+ 0,39
$1/2\ O_2/H_2O$	+ 0,81



- Outer memb. – well permable for diffusion
- Inner memb. – ver limited diffusion, transporter are needed

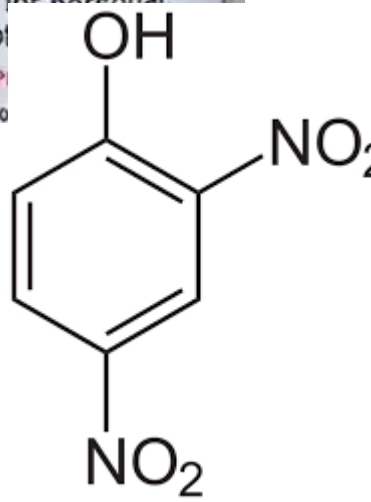
Toxicology of mitochondria

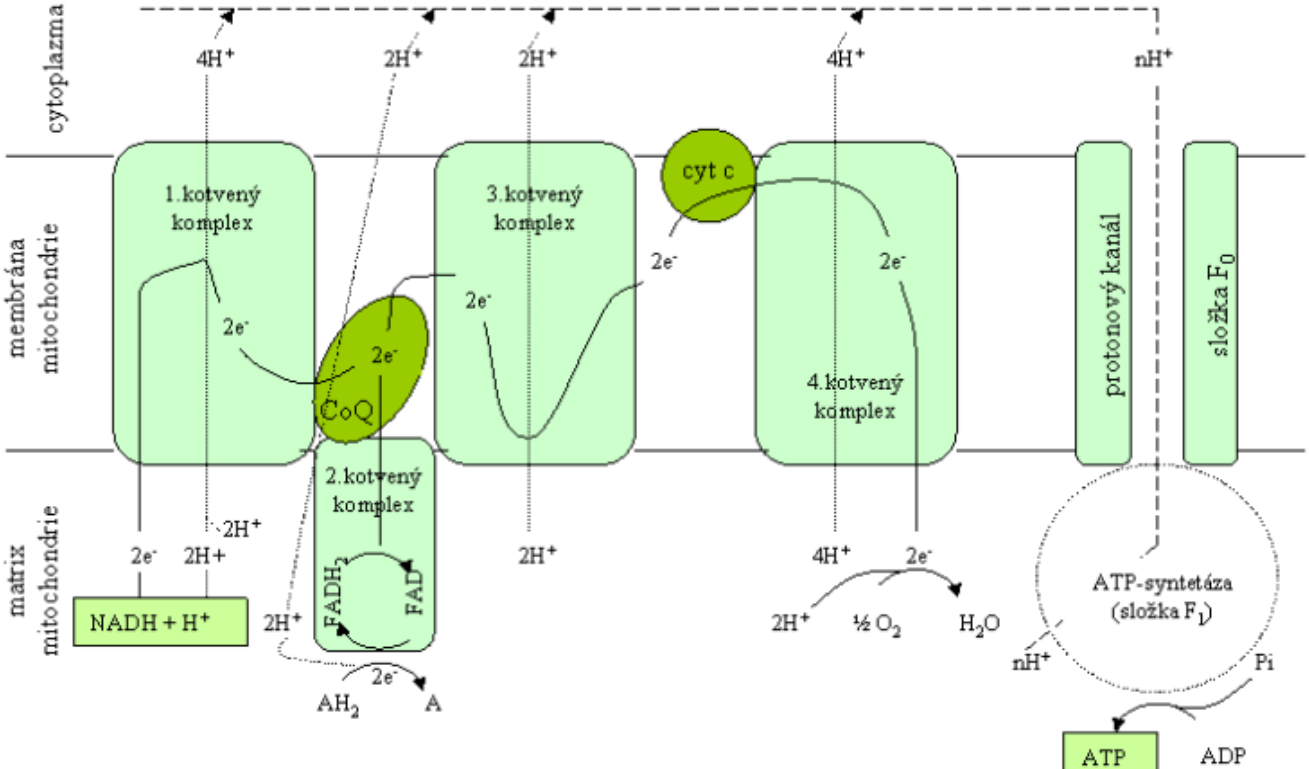
If mitochondria is „internal symbiotic bacteria“,
then many drugs and toxin can affect disruption of some specific biochemical step inside mitochondria:



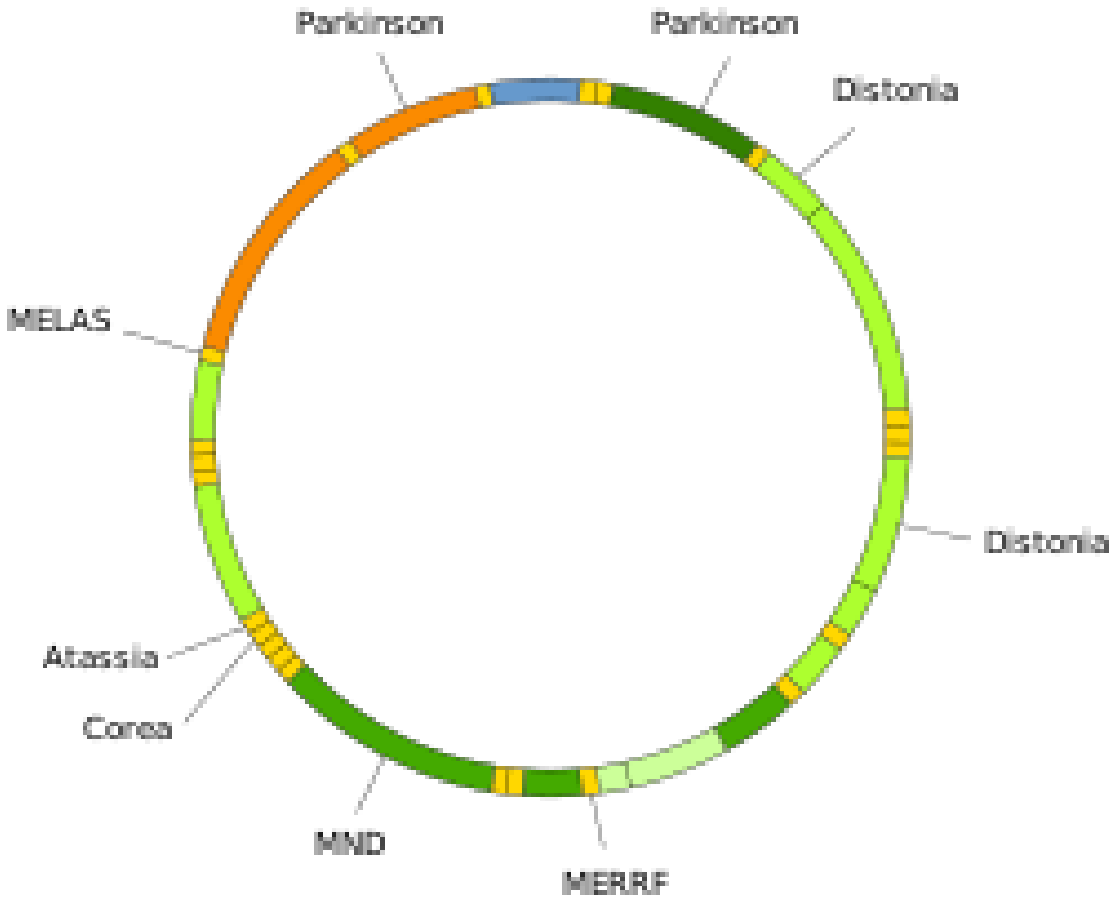
- Odpřahující proteiny (UCP)

(uncoupling proteins; UCP)



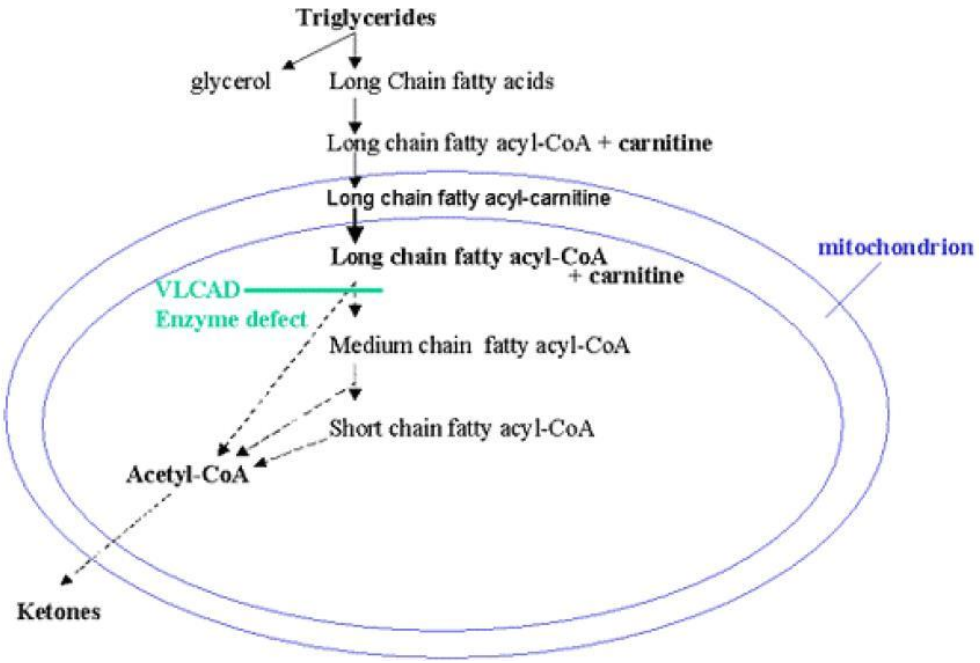


Mitochondrial disease



MITOCHONDRIA DISEASE

- VLCAD

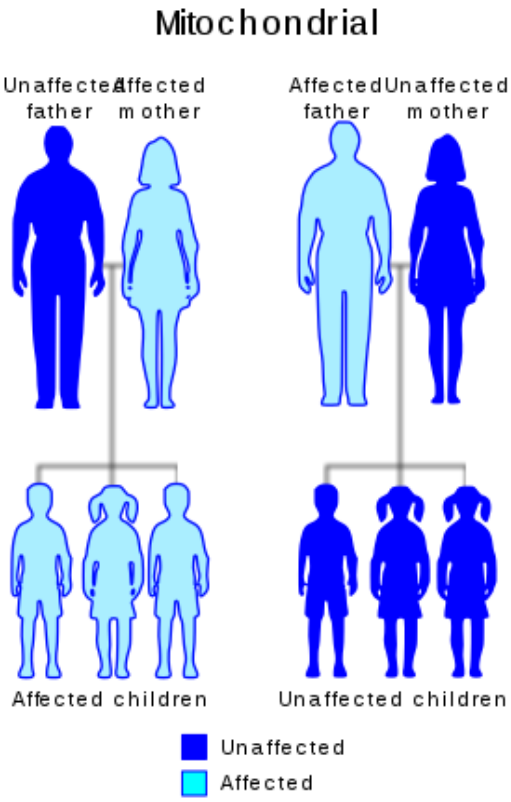


- MELAS (Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes) syndrome is a rare disorder that begins in childhood, usually between two and fifteen years of age, and mostly affects the nervous system and muscles. The most common early symptoms are seizures, recurrent headaches, loss of appetite and recurrent vomiting. Stroke-like episodes with temporary muscle weakness on one side of the body (hemiparesis) may also occur and this can lead to altered consciousness, vision and hearing loss, loss of motor skills and intellectual disability. MELAS is caused by mutations in mitochondrial DNA

Diagnostic tool: MELAS is diagnosed based on clinical findings and molecular genetic testing. Clinical testing may include measurement of lactate and pyruvate concentrations and CSF protein which are elevated in MELAS syndrome. Brain imaging techniques such as magnetic resonance imaging (MRI) may be used to look for stroke-like lesions and magnetic resonance spectroscopy (MRS) may be used to look for a lactate peak in the brain

- LHON

is a **mitochondrially inherited** (transmitted from mother to offspring)
Pathology is based on degeneration of retinal ganglion cells (RGCs) and their axons that
leads to an acute or subacute loss of central vision; it predominantly affects young adult males
LHON is transmitted only through the mother, as it is primarily
due to mutations in the mitochondrial (not nuclear) genome, and only the egg contributes mitochondria to the embryo.



Mitochondria is affected also after infection and patogen invasion

Many bacteria and viruses hijack cellular metabolism for their own benefit. *Mycobacterium* is the best-known bacterium that influences host metabolism by enhancing aerobic glycolysis. Epithelial cells and immune cells infected with *Mycobacterium* exhibit a reduction in the tricarboxylic acid (TCA) cycle and a corresponding increase in the glycolytic flux. Elevated aerobic glycolysis is also observed in *Mycobacterium*-infected lung granulomas in animal models of infection and in patients with active tuberculosis. *Legionella* also promotes glycolytic flux similar to *Mycobacterium*, thus enhancing aerobic glycolysis.

ADVANCED READING:
https://www.sciencedirect.com/science/article/pii/S096289242030018O

Mitochondrial Functions in Infection and Immunity
Author links open overlay panel

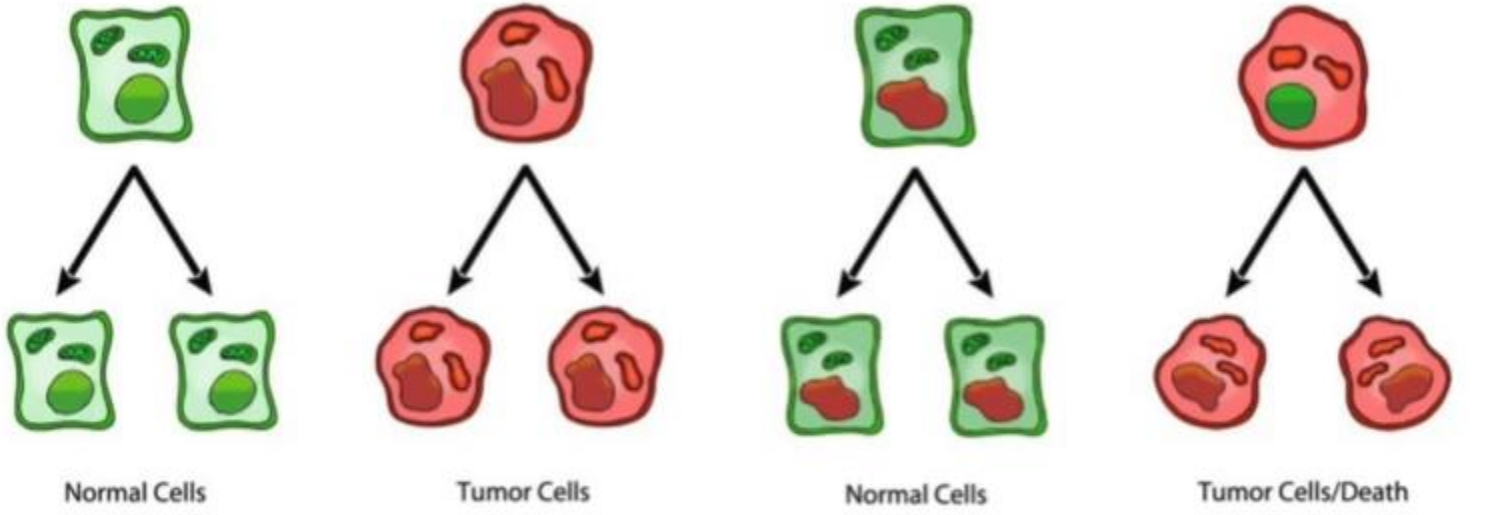
- Type of medication
  for MITOCHONDRIAL diseases:

1) NON-Causal therapy (vitamines, glucose regulation, hormones …)

2) CAUSAL therapy(„change of mitochondria“

- (legal in United Kingdom.)

Mitochondria is key for cancer?



Cancer as a mitochondrial metabolic disease, Thomas N. Seyfried, Front Cell Dev Biol. 2015; 3: 43. Published online 2015 Jul 7. doi: 10.3389/fcell.2015.00043

Till today under intensive investigation of details?

Lysosomes

- Lysosomes are membrane-bound, dense granular structures containing hydrolytic **enzymes** responsible mainly for intracellular and extracellular digestion.
- It is an important cell organelle responsible for the inter and extracellular breakdown of substances. They are more commonly found in animal cells while only in some lower Lysosomes occur freely in the cytoplasm.
- In the lysosoms is pH decreased to cca 5

(H+ gradient is created by ATPase) (ATPase is enzymes that catalyze the decomposition of adenosine triphosphate (ATP) into adenosine diphosphate (ADP) and a free phosphate ion and produce ENERGY; compare to ATP synthse in mitochondria)

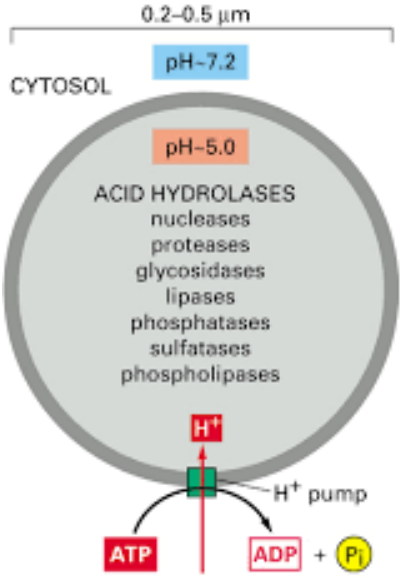


Figure 13–31. Molecular Biology of the Cell, 4th Edition.