Mitochondria and Metabolism

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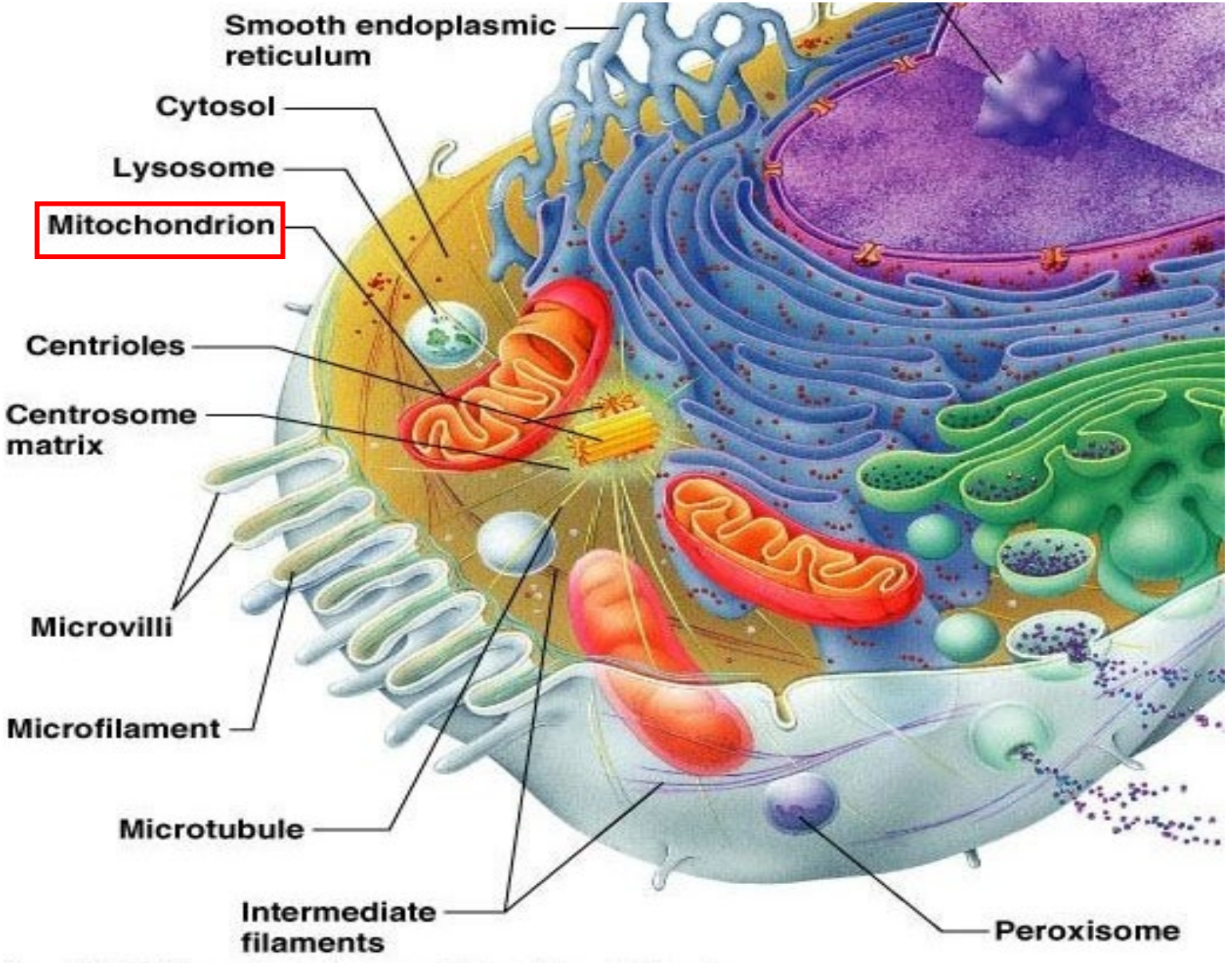
OLLI Fall 2023

Study Group : 426

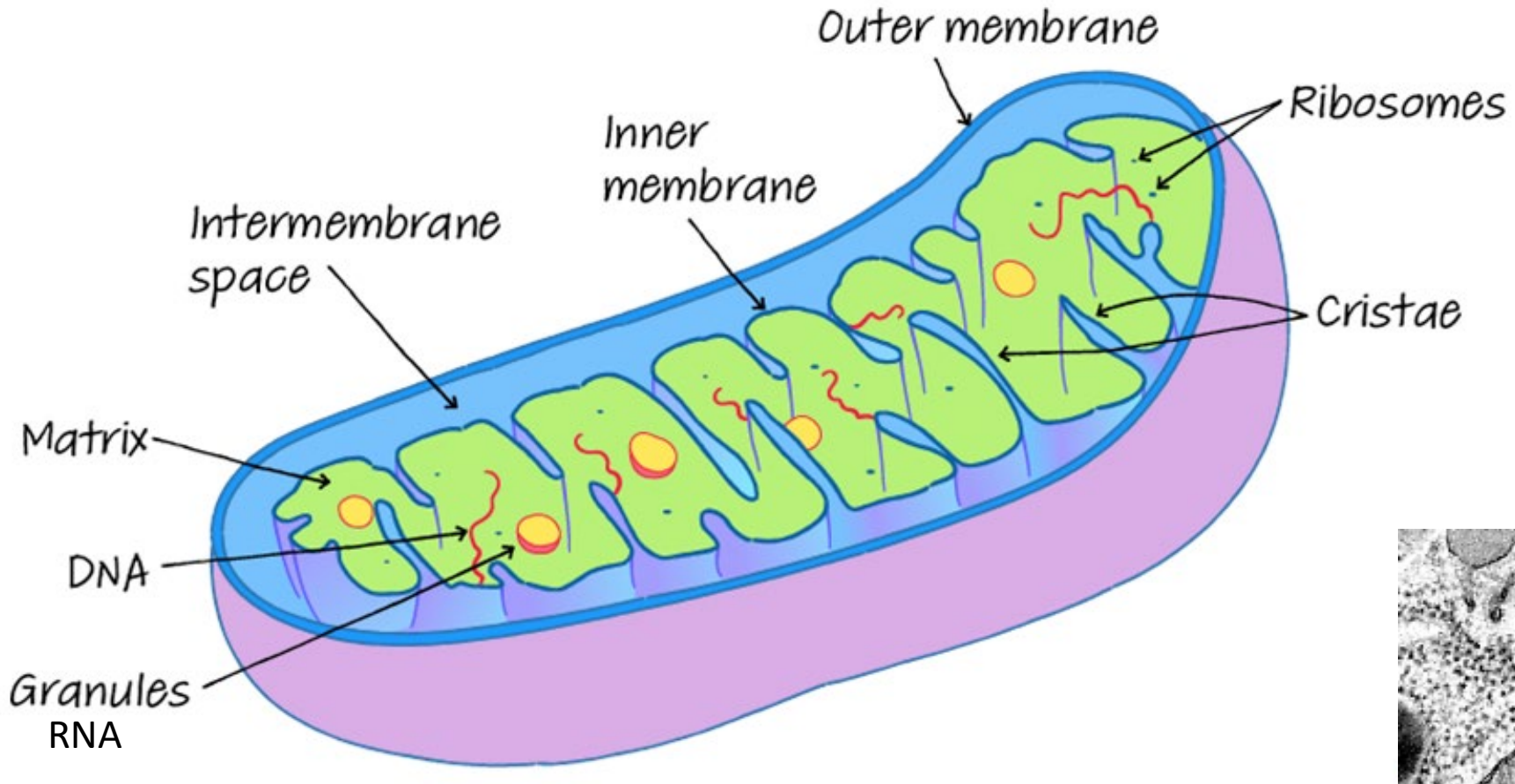
"Clandestine rulers of our world, masters of power, sex and suicide."

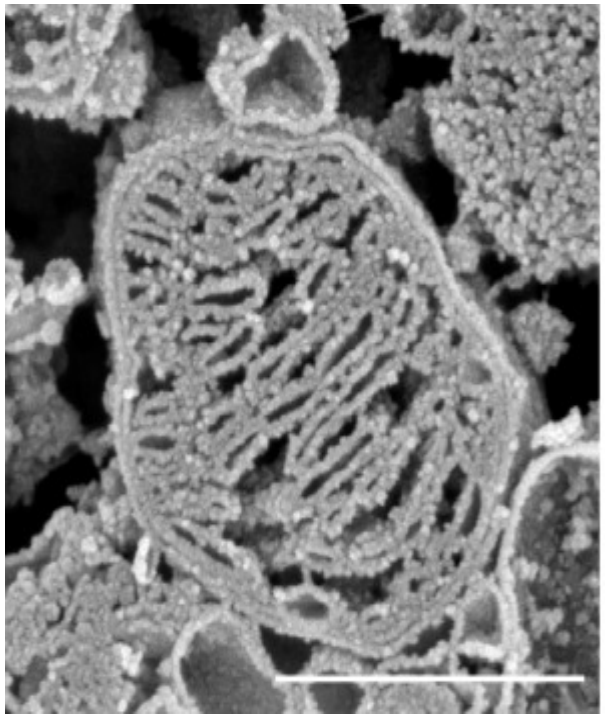
Nick Lane

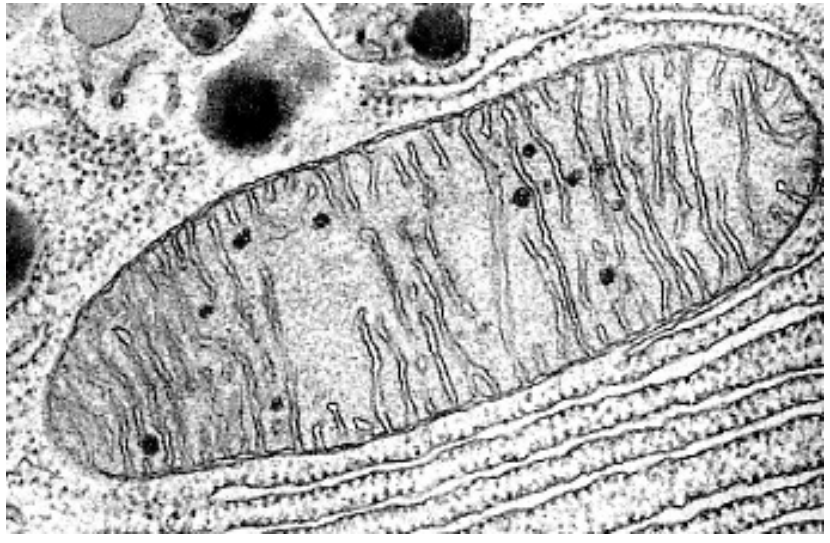
Powerhouses: Transform food molecules into ATP, the energy currency of the cell



Double-Membrane-bound organelles



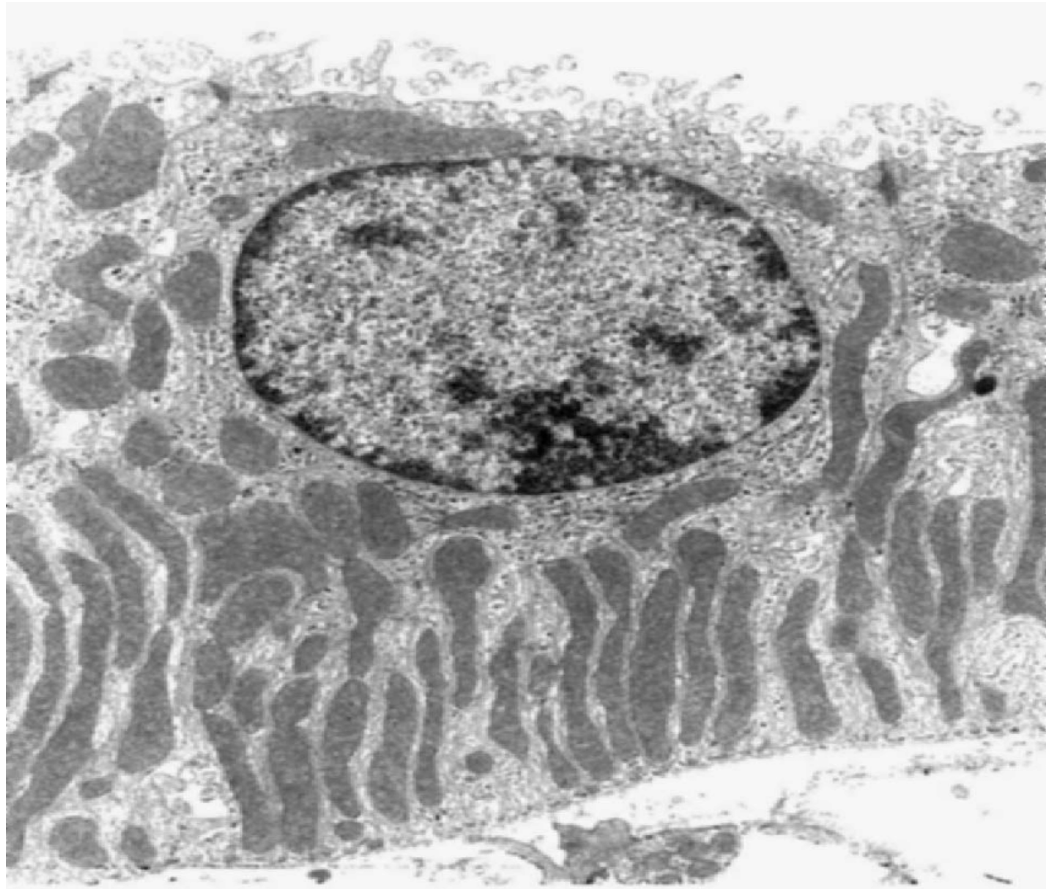


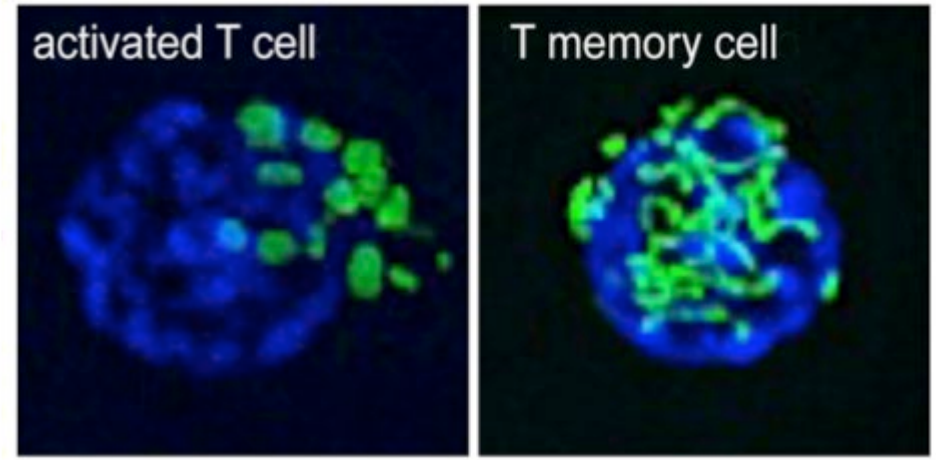


Enzymes for making ATP on the inner membrane

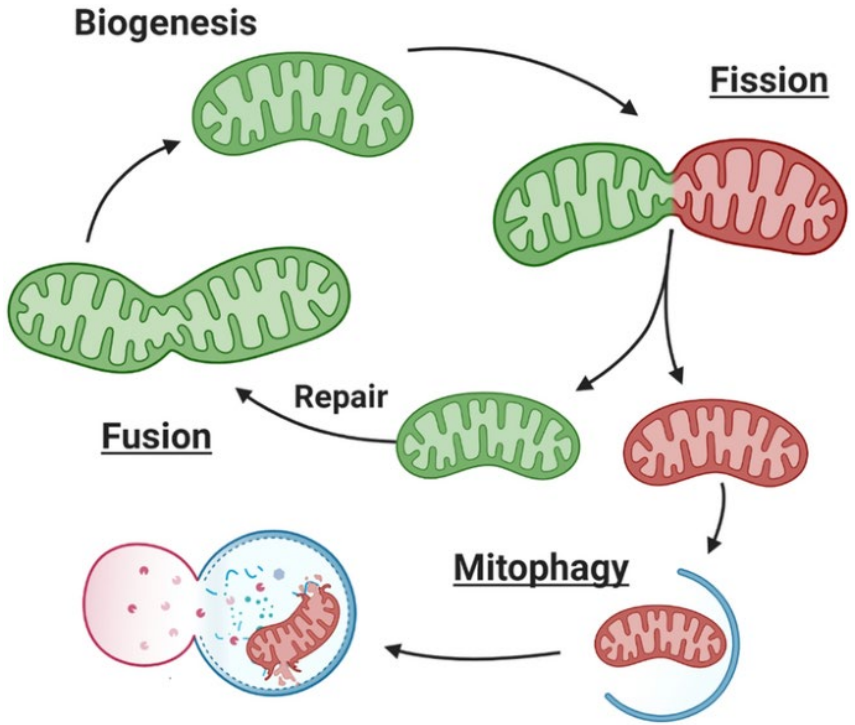
Dynamic

Change shape and numbers and locations according to how much and where energy is needed. Exercise increases # in muscle.



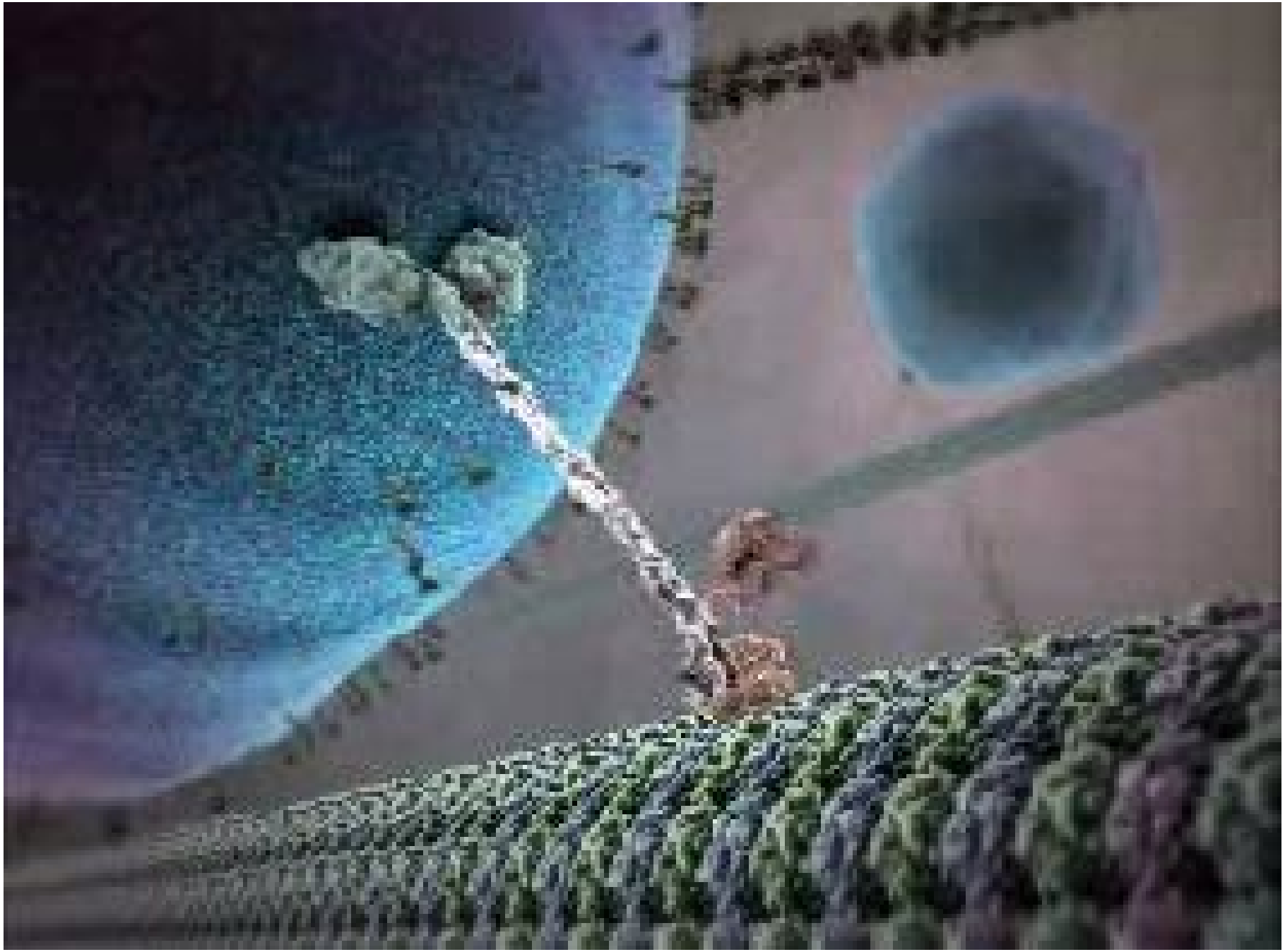


Green mitochondria changing shape during activation

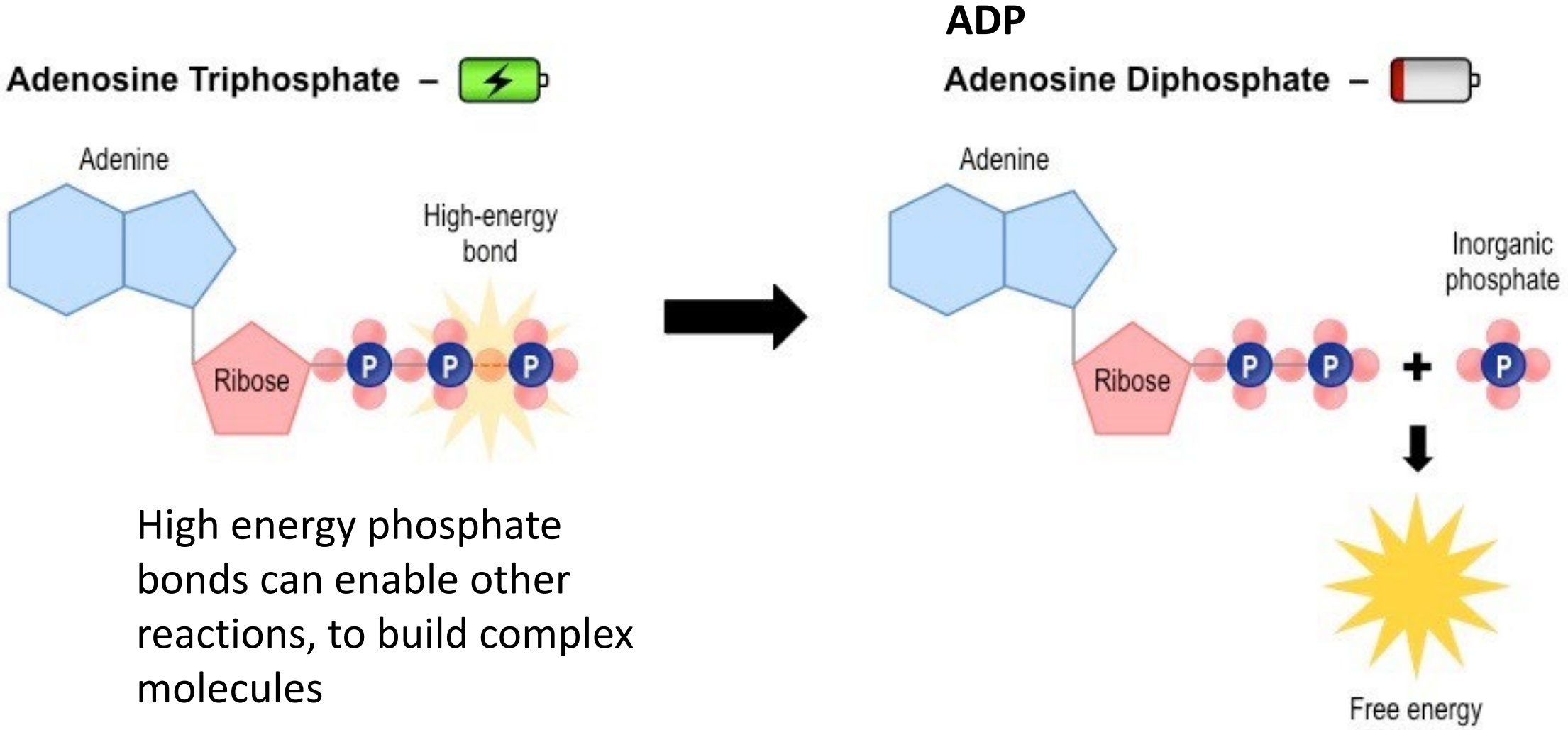


Mobile

Mitochondria and vesicles get pulled along microtubules by motor proteins (dynein and kinesin)



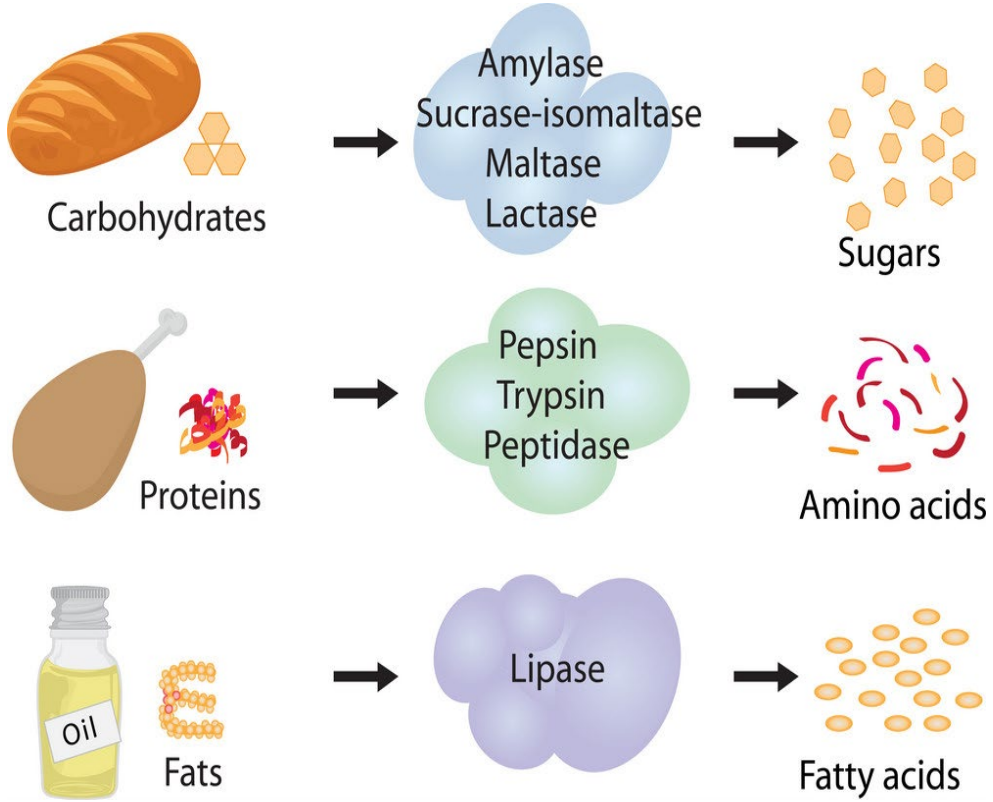
ATP: energy currency of the cell

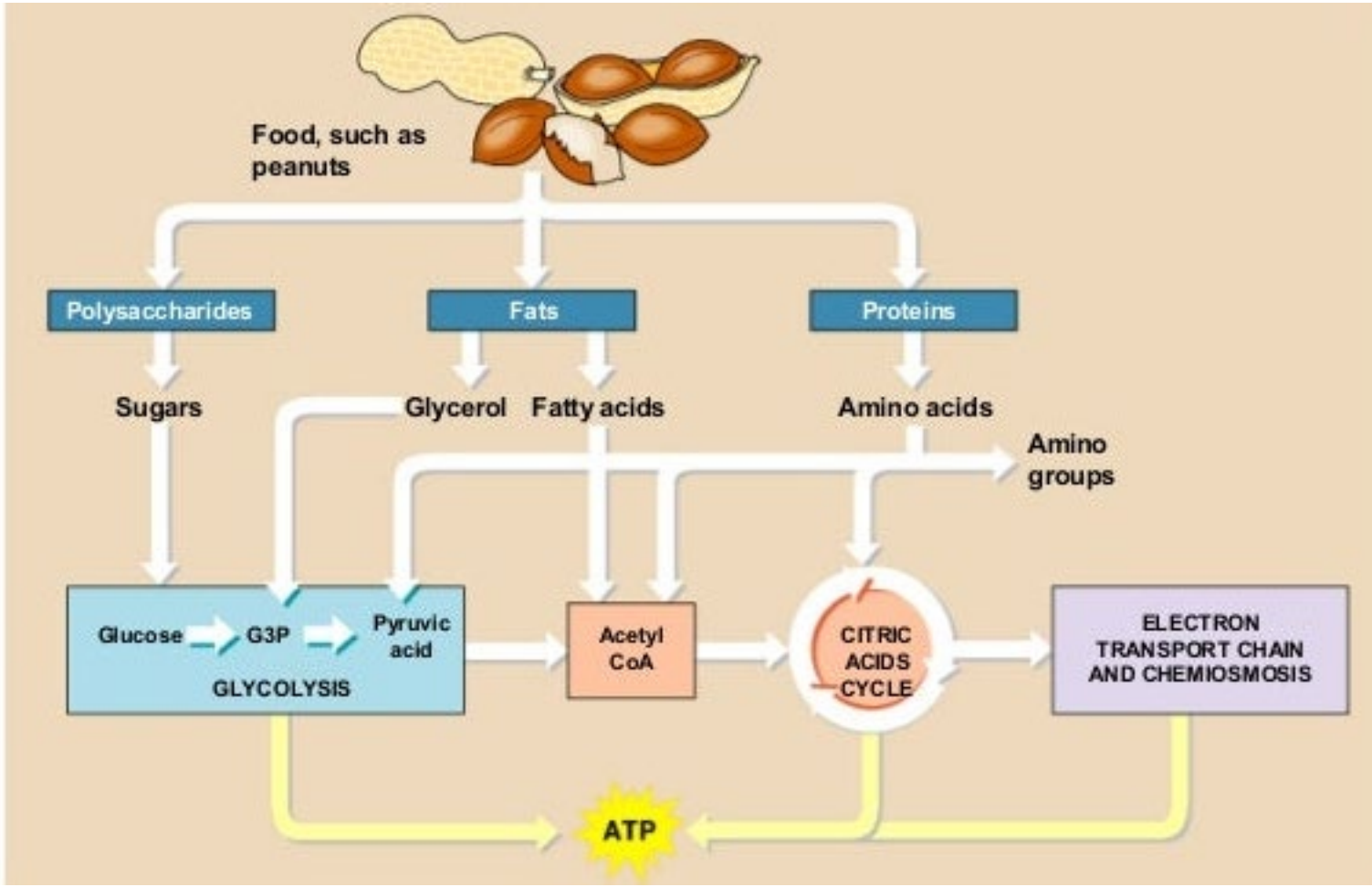


High energy phosphate bonds can enable other reactions, to build complex molecules

Energy

The energy we use to run our cells comes from the chemical bonds in food molecules. The bonds are broken in the cytosol by **glycolysis**, which yields small amounts of ATP, and by the **citric acid cycle**, in the mitochondria, which yields more ATP, and ETC.



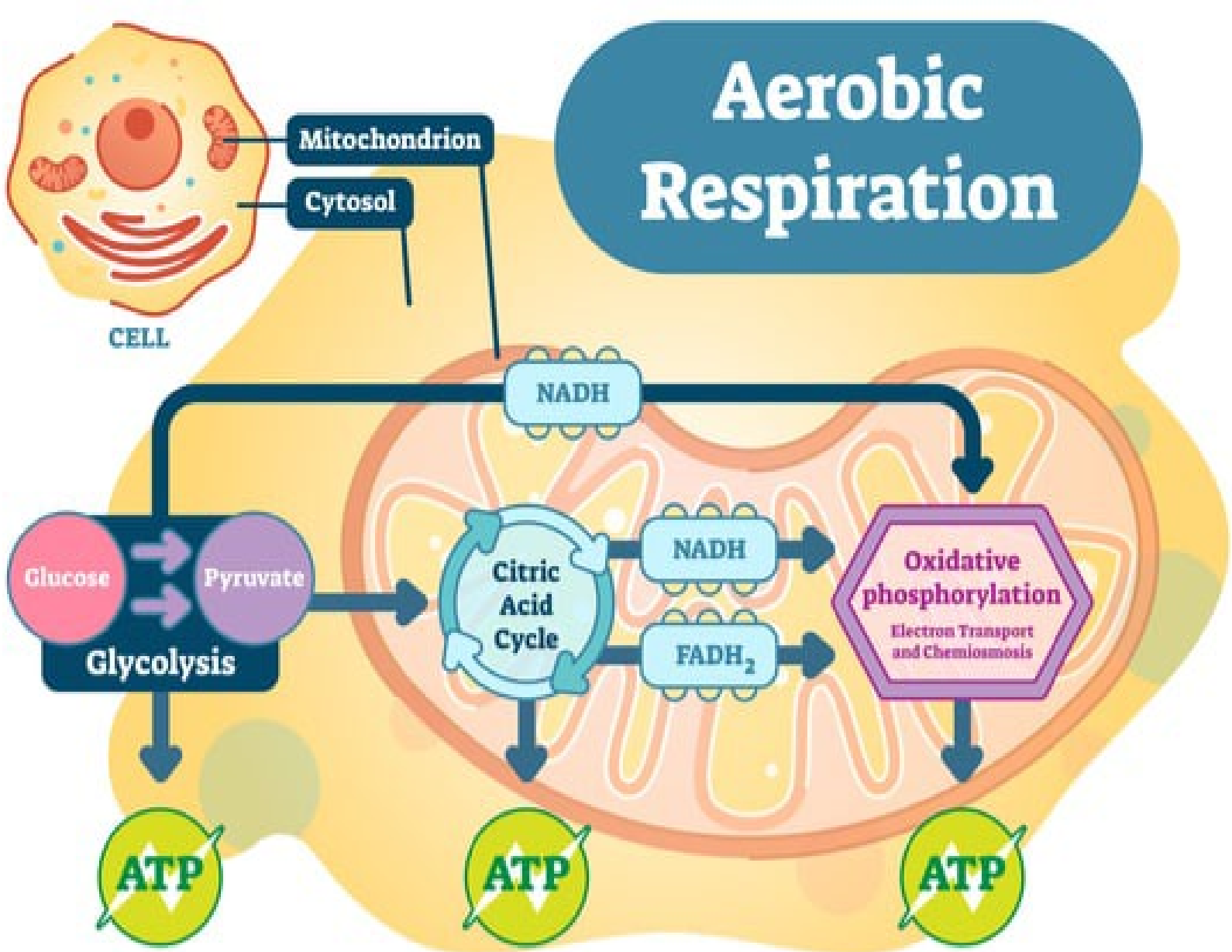


ATP production

3 step process:

1) Glycolysis
2) Citric acid cycle (Krebs cycle)
3) Electron-transport chain (oxidative phosphorylation)

Note high-energy molecules NADH and $FADH_2$



Combustion

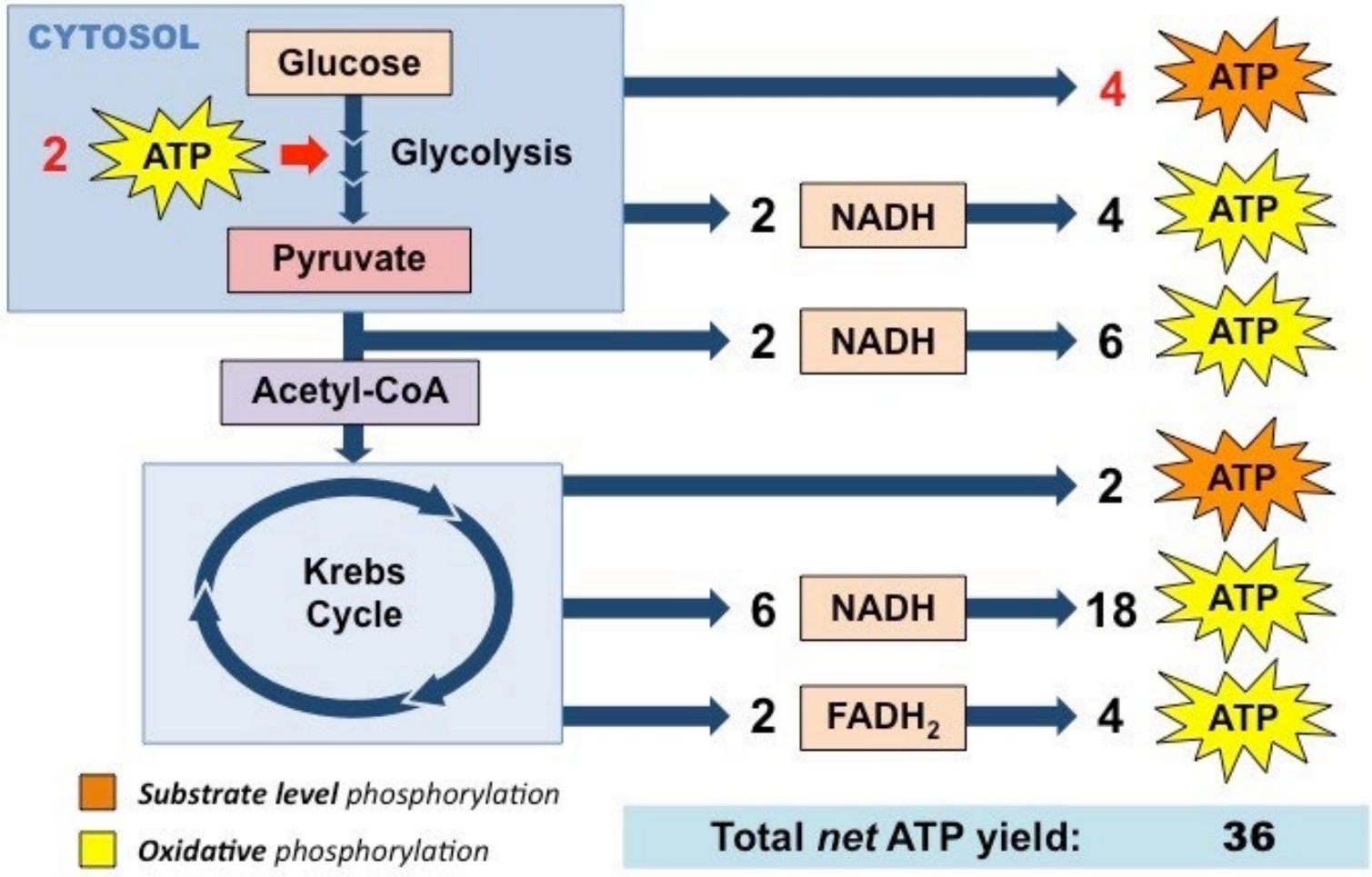
Combustion is a chemical reaction:

$$\text{Fuel} + O_2 \rightarrow CO_2 + H_2O$$

+ Energy!

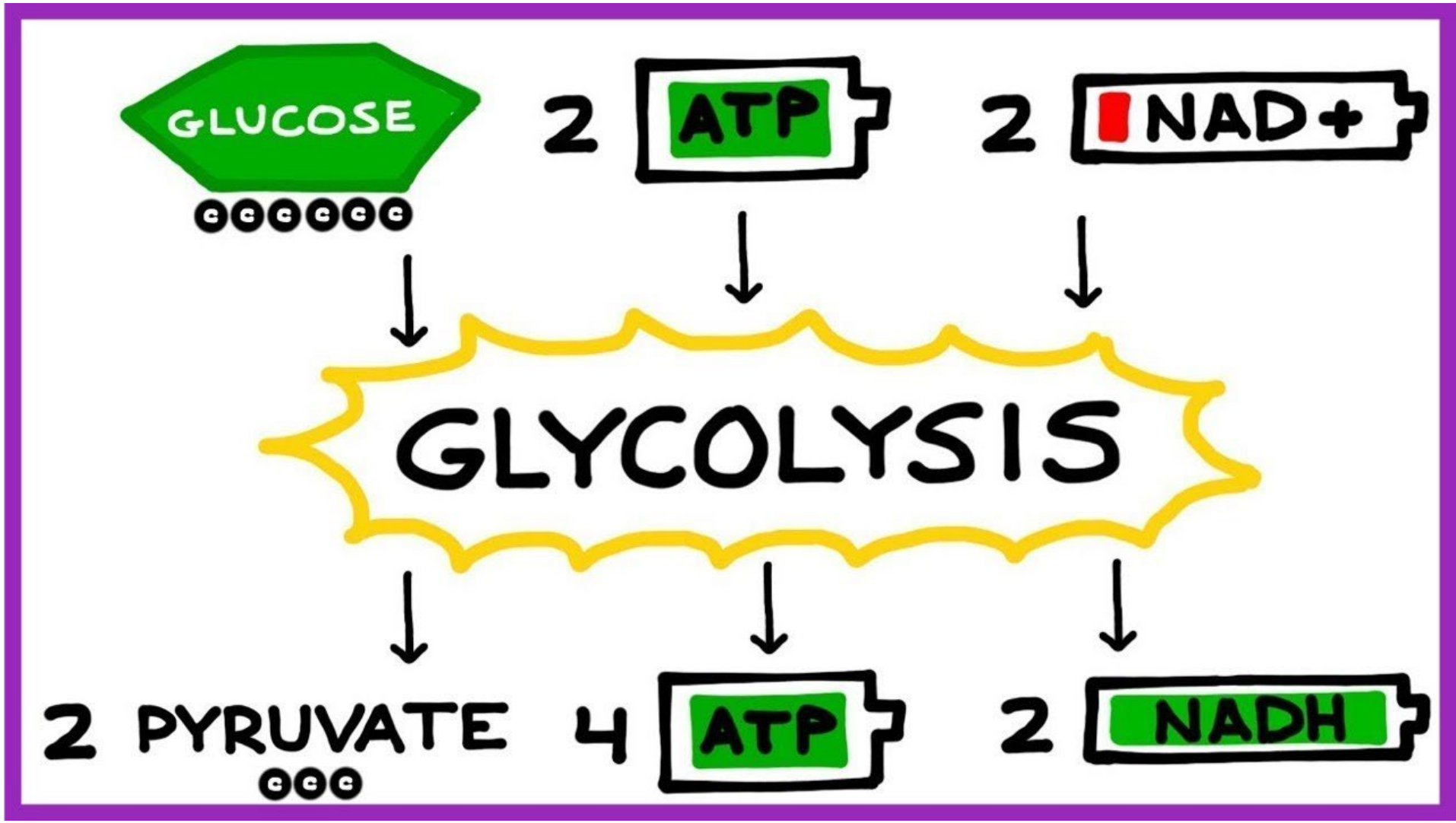
Energy Yields

Glycolysis doesn't need oxygen; used by anaerobic bacteria. Krebs cycle (citric acid cycle) and electron transport take place in mitochondria, need **oxygen**, and extract much more energy



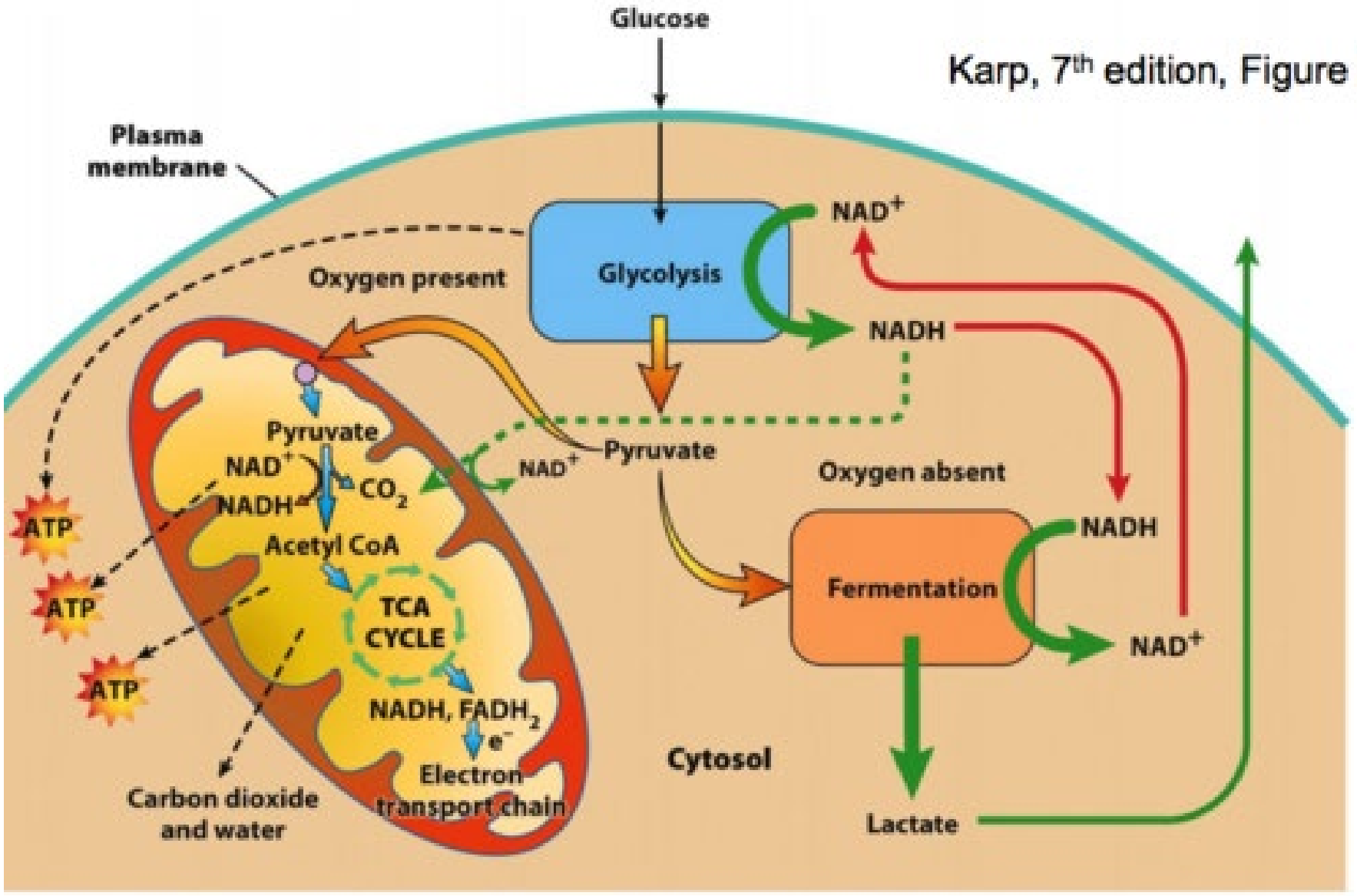
Glycolysis

Takes place in cytoplasm, without oxygen (anaerobic). Produces 2 **ATP/**glucose and 2 **NADH** to send to the electron transport chain and 2 molecules of **pyruvate**.



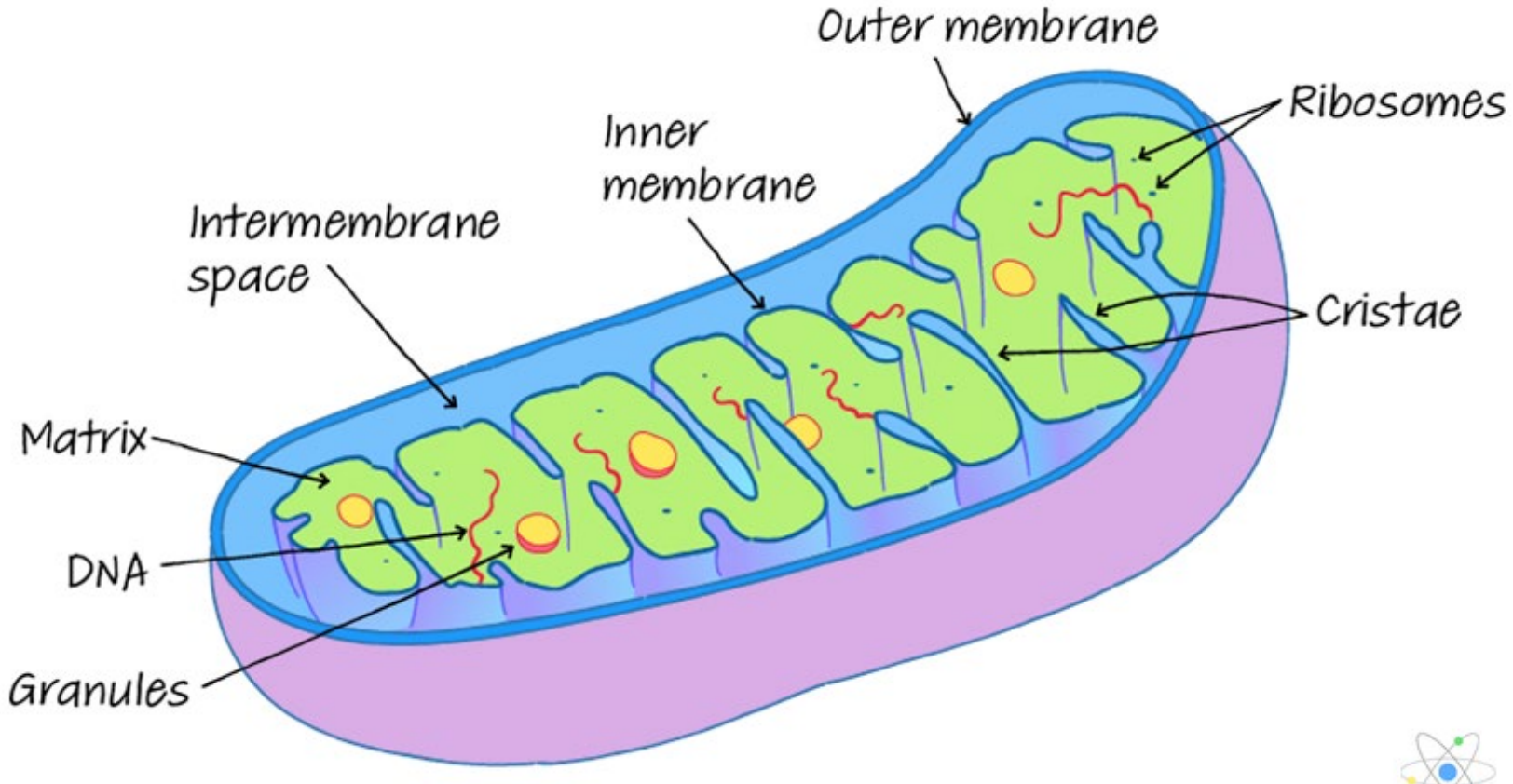
Aerobic vs anaerobic

If oxygen is scarce (heavy exercise), pyruvate becomes **lactic acid**, (fermentation). which enters blood (muscle fatigue). If oxygen is present, pyruvate enters the mitochondrion.



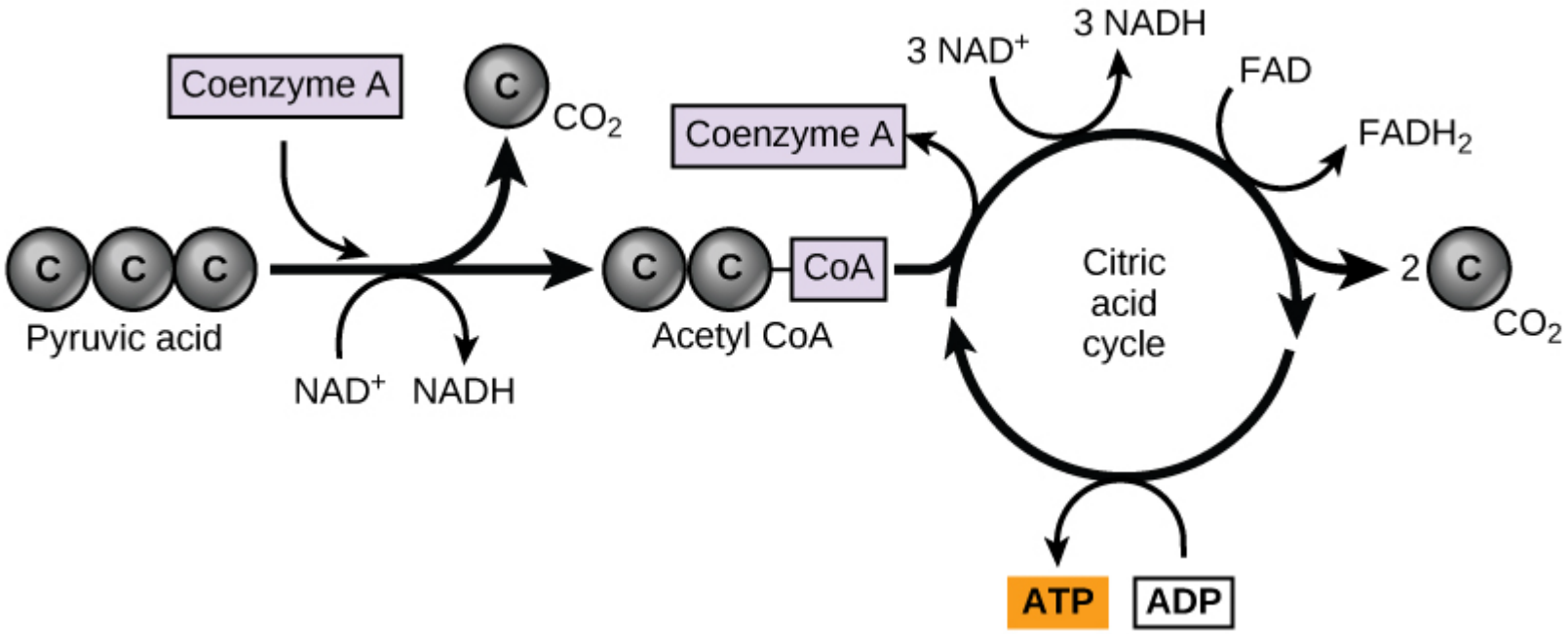
Matrix

If oxygen is present, pyruvate enters the **matrix** of the mitochondrion.



Matrix: citric acid cycle

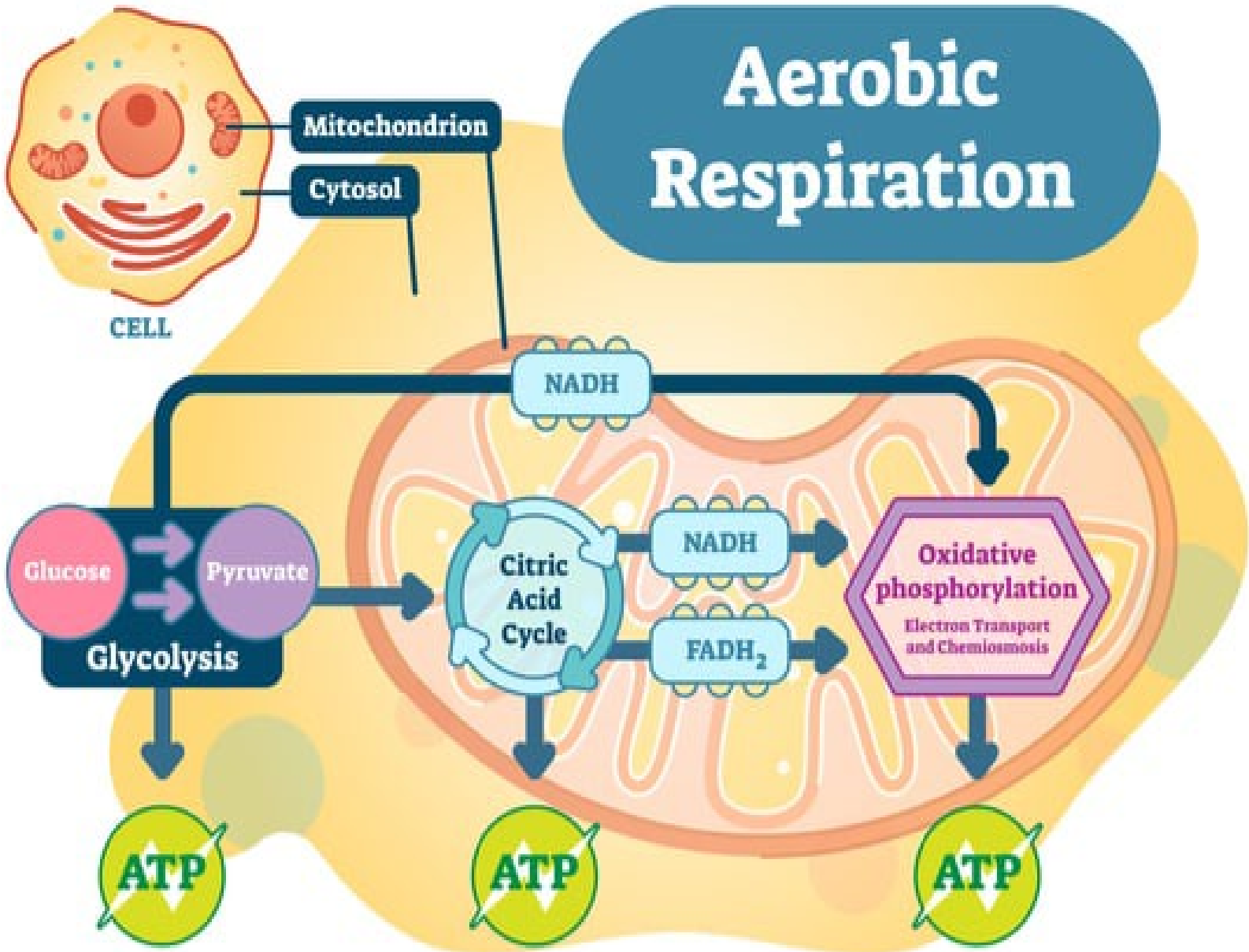
Pyruvate crosses the inner membrane into matrix. Enzymes there break down pyruvate to Acetyl Coenzyme A. CoA enters Citric Acid Cycle and generates **CO2, ATP and electron carriers NADH and $FADH_2$** (as well as molecules needed to build other cellular components)



Oxidative phosphorylation

Oxidative phosphorylation uses an **electron transport chain** to make more ATP and CO2

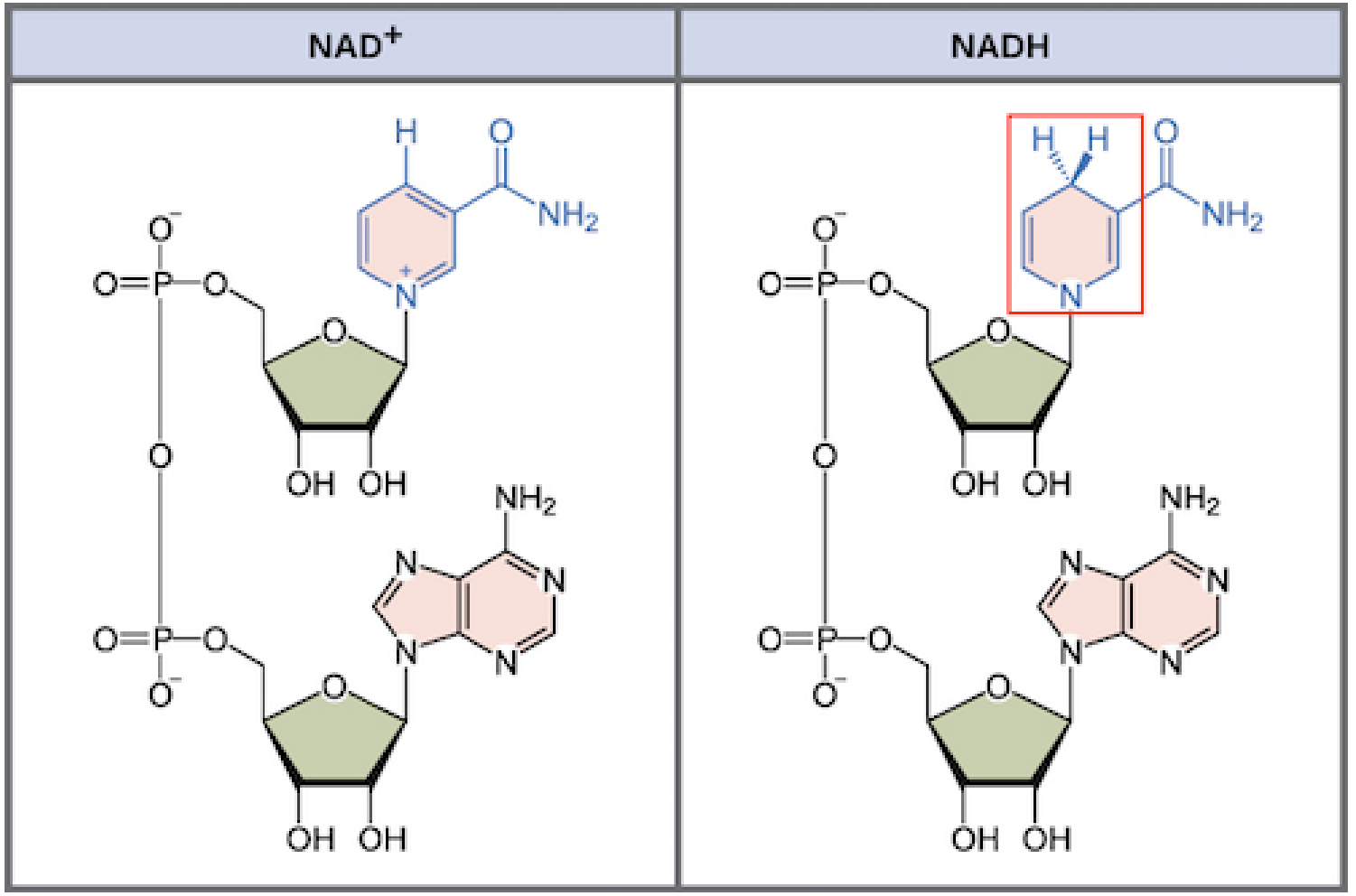
Note high-energy molecules NADH and $FADH_2$



NAD: electron carrier

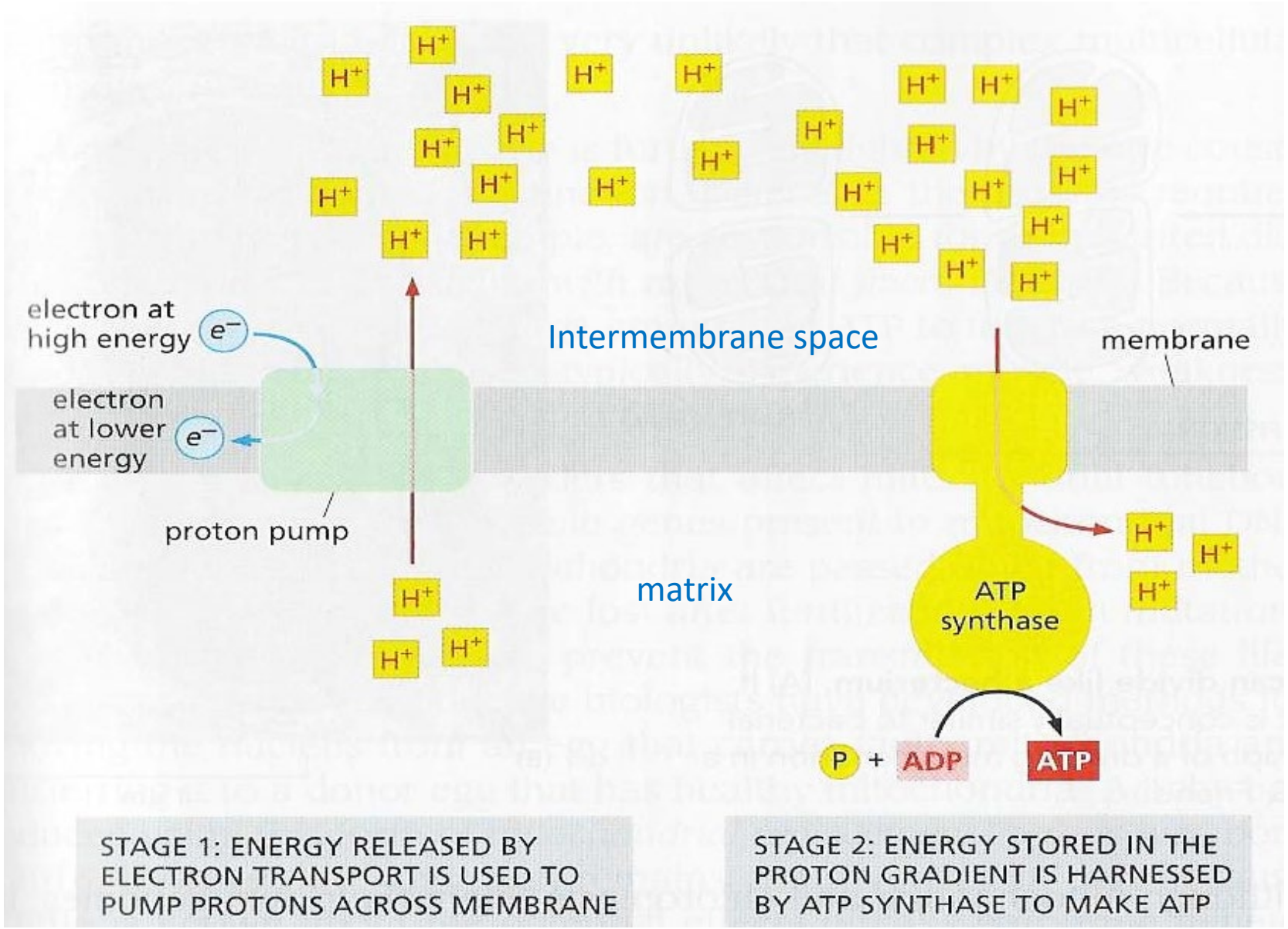
Electrons carried to electron-transport chain by NADH will use released energy to make a proton gradient. The "**proton motive force**" drives **ATP synthase** to make many ATP.

$FADH_2$ works the same way



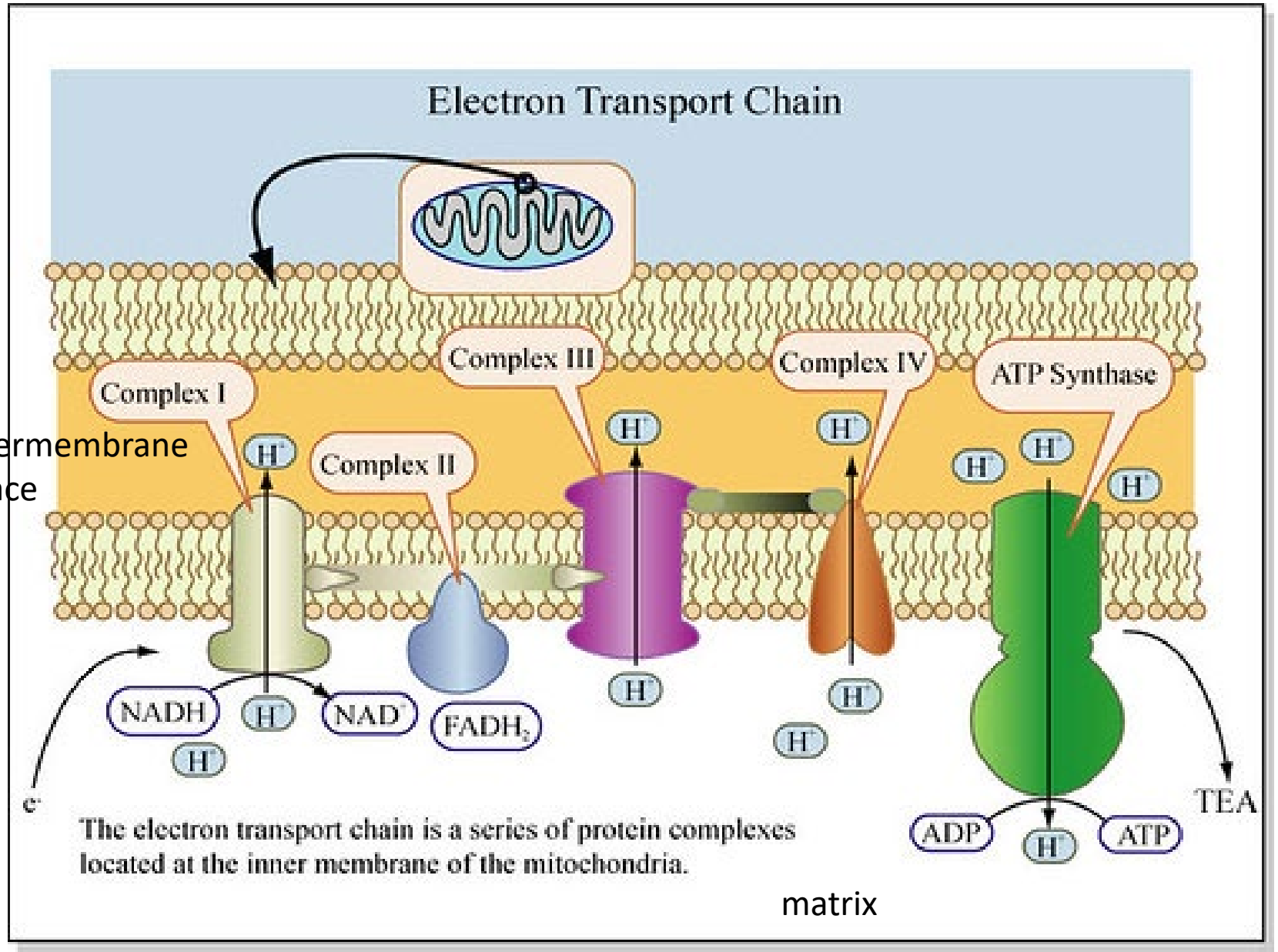
Proton gradient powers ATP production

NAD and $FADH_2$ donate electrons at high energy to proton pumps in the inner membrane. Protons concentrated in **intermembrane space**. Proton gradient powers **ATP synthase**.



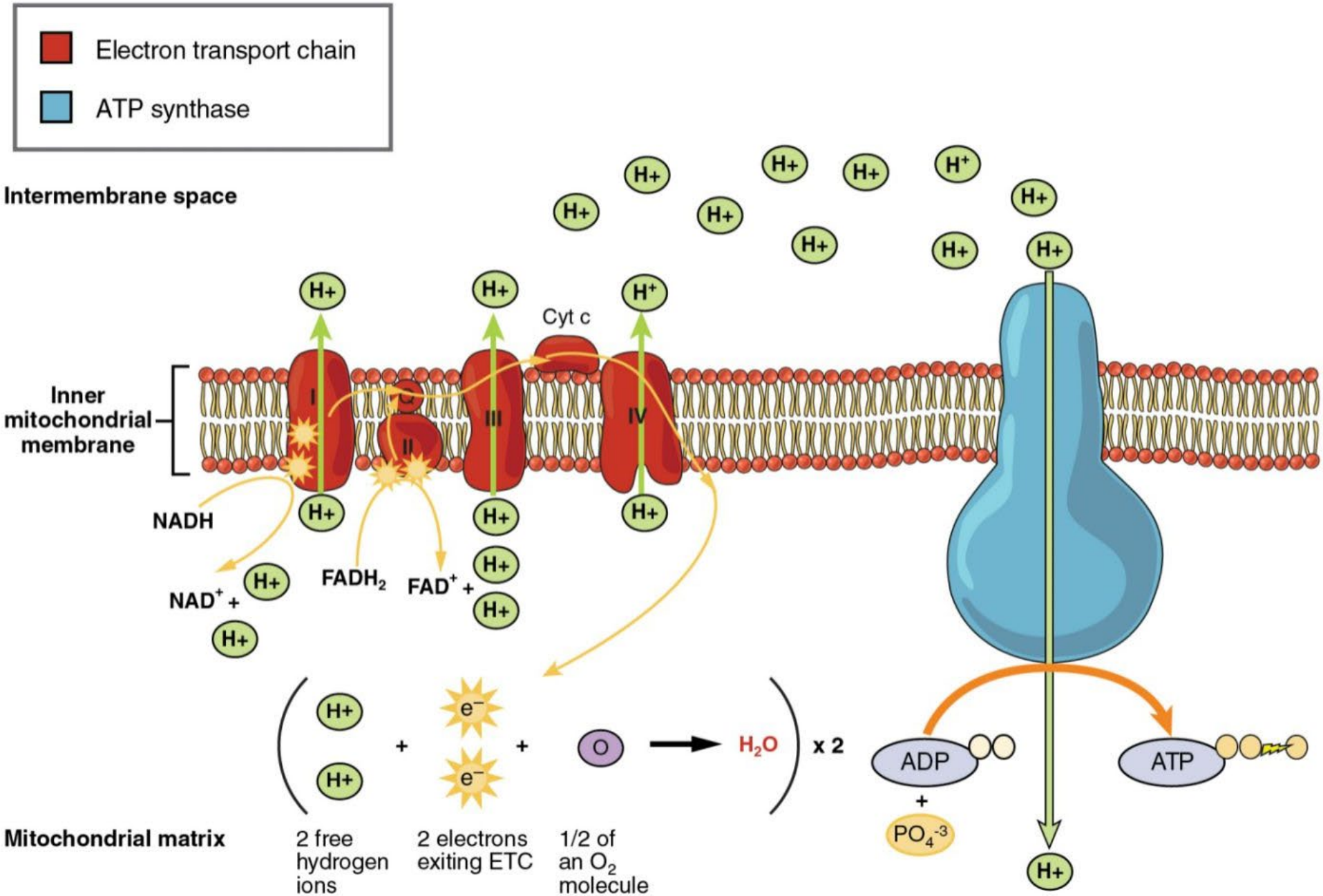
Electron Transport Chain

Series of proteins embedded in the cristae that carry electrons from NADH and $FADH_2$. This generates high proton (H^+) concentration in the intermembrane space and low proton concentration in the matrix. **Proton gradient** forces **ATP synthase** to produce ATP in the matrix.



Electron transport chain

NADH and FADH donate electrons to electron transport chain, which ultimately donates them to ***oxygen*** to make **water**. Cyanide blocks electron transport.



Combustion

Combustion is a chemical reaction:

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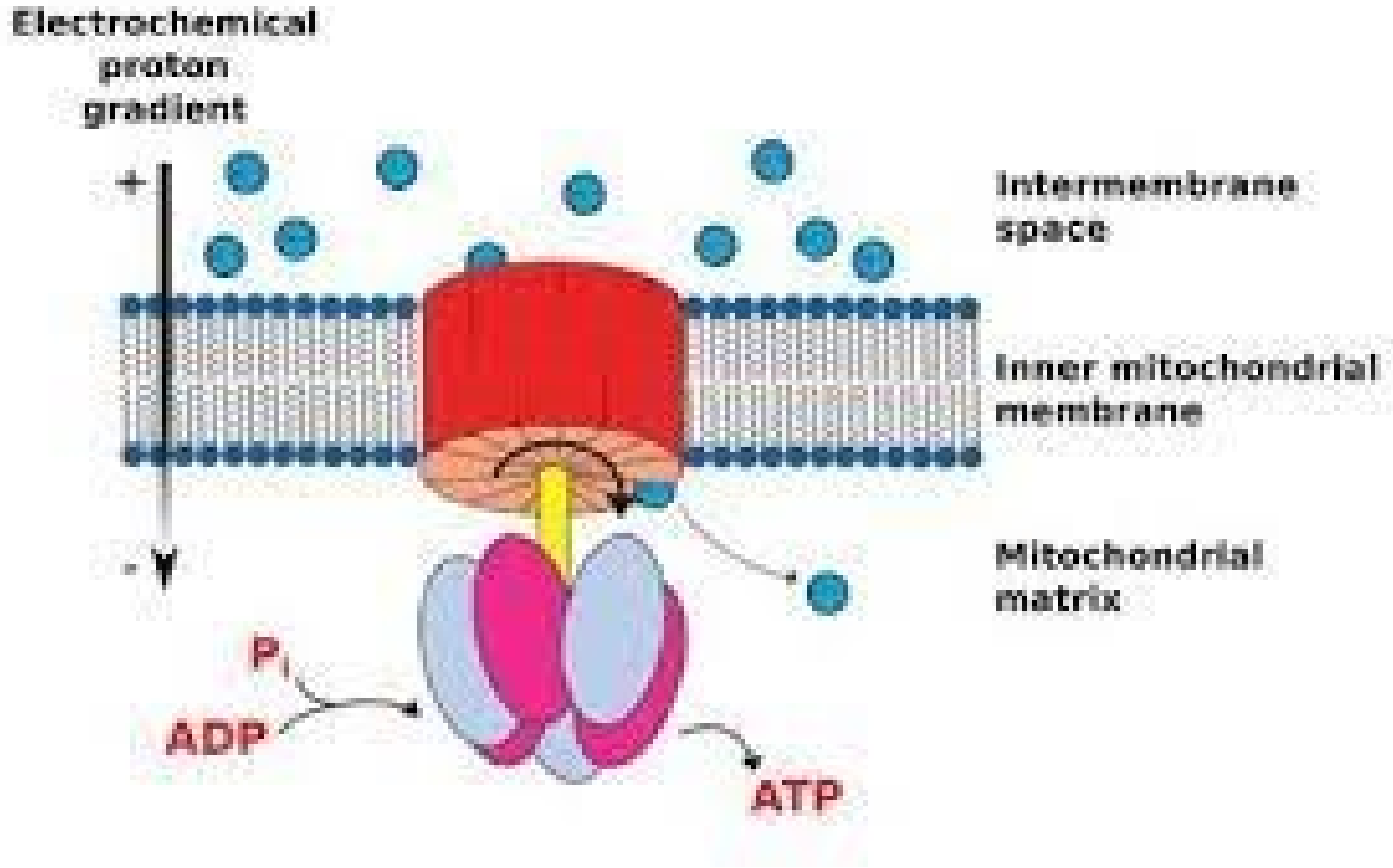
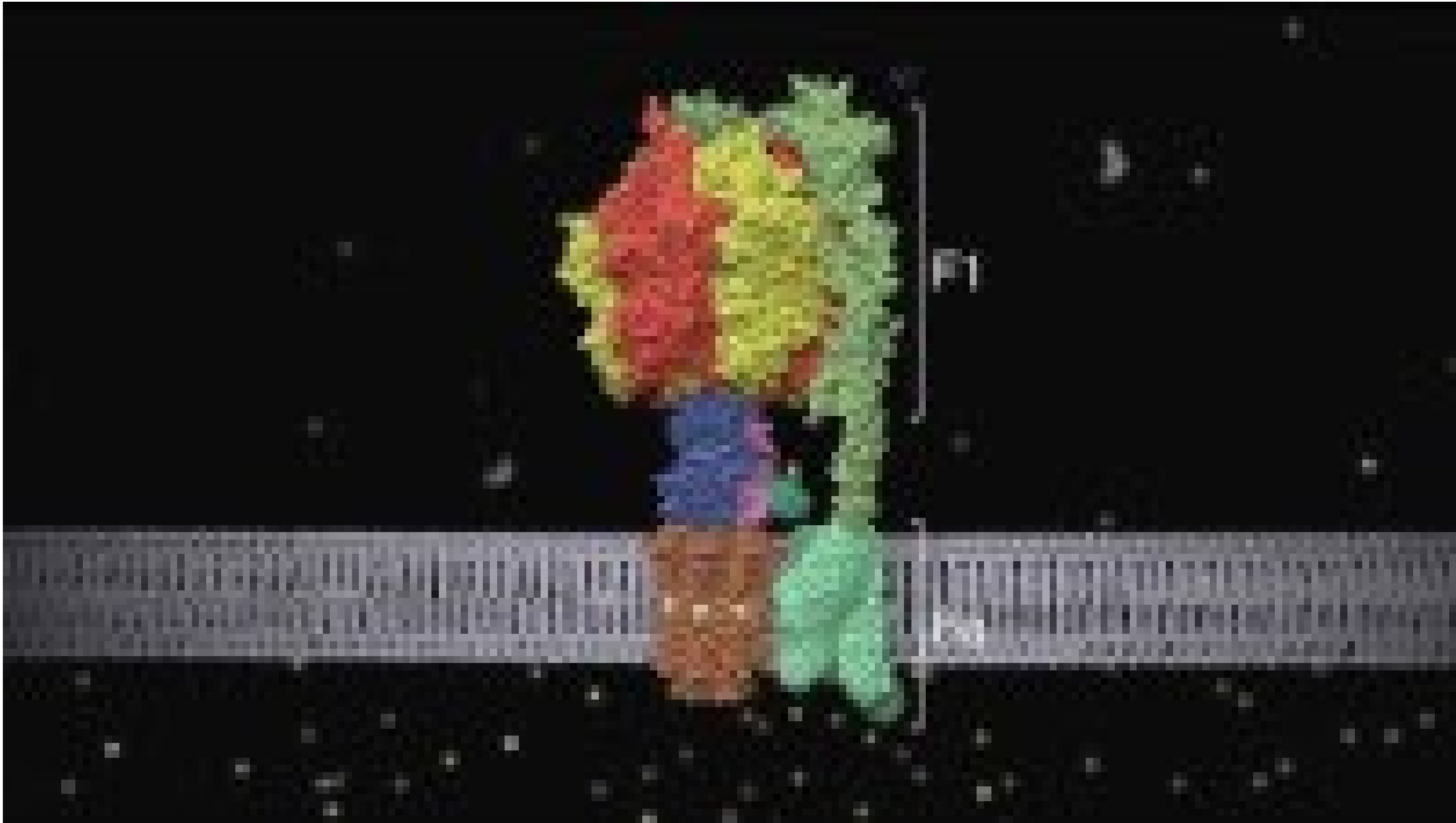
+ Energy!

ATP synthase

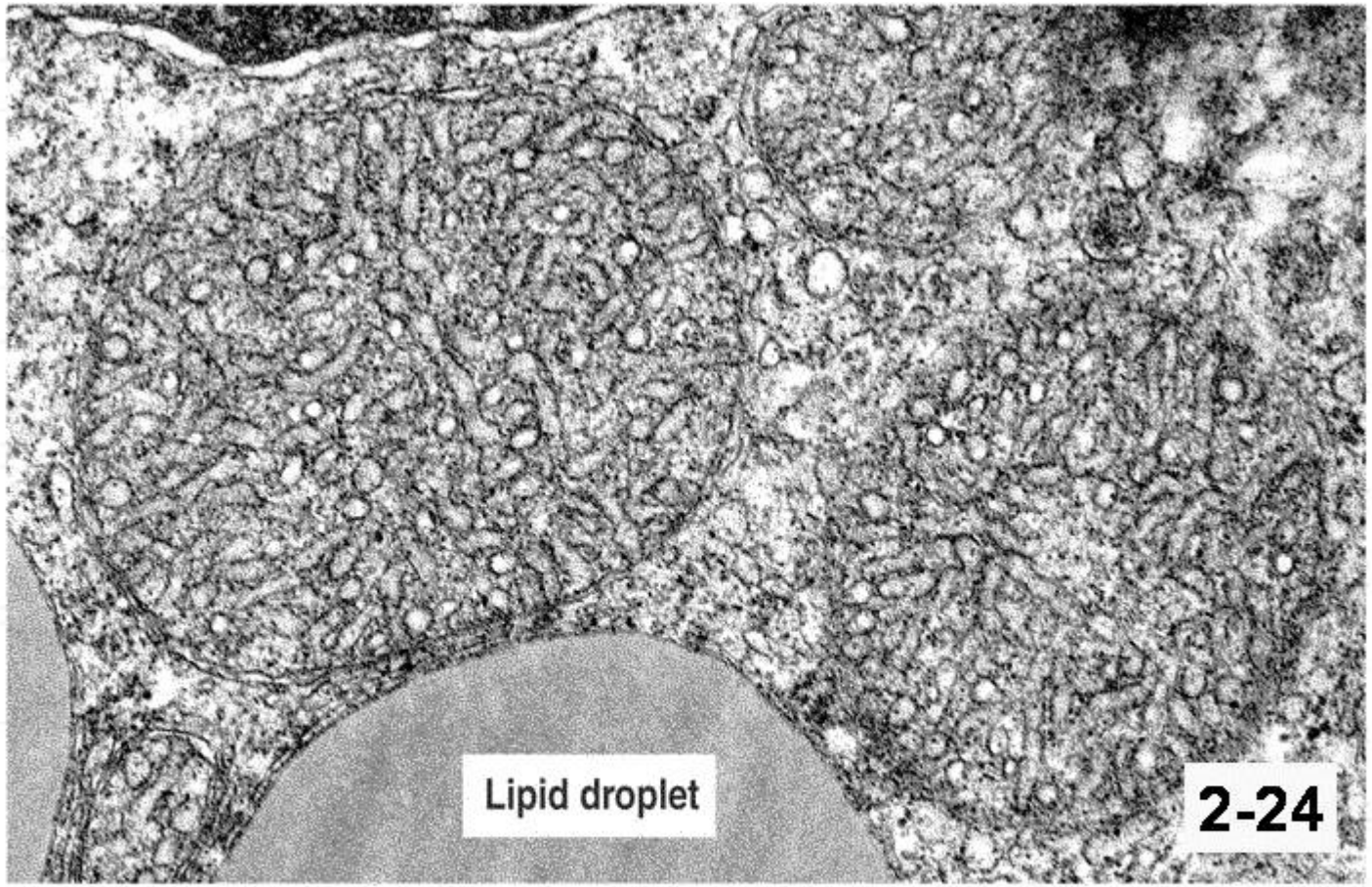
Proton gradient powers the ATP synthase. Water and **34** ATP/glucose, released back into cytosol !





Sex: production of steroid hormones

Cells that secrete steroid hormones (estrogen, testosterone etc.) have mitochondria with tubular (instead of shelf-like) cristae, which contain needed enzymes. Also rich in smooth ER and lipid droplets (cholesterol)

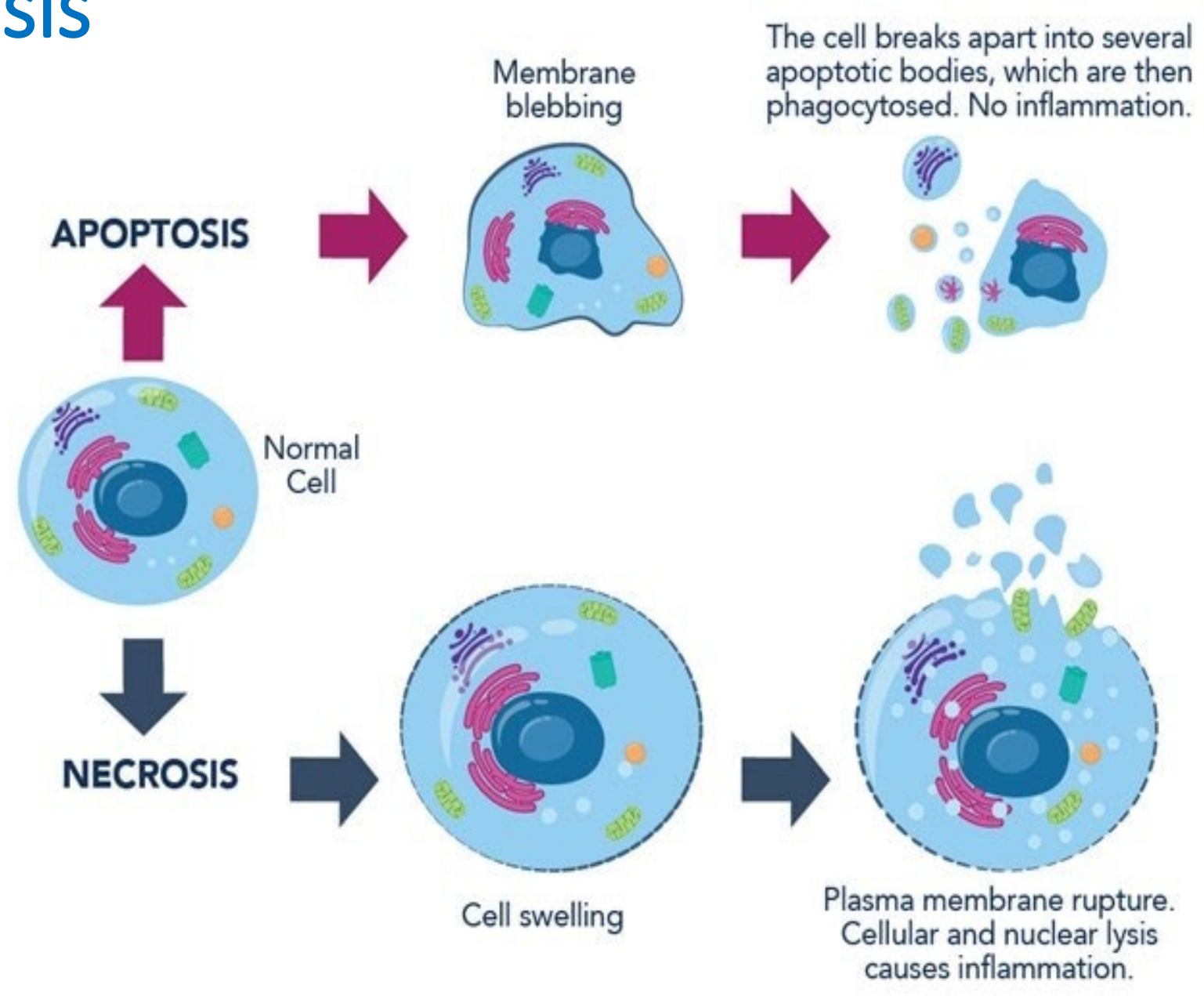


Mitochondria with **tubular cristae** are typical of steroid-producing cells –adrenal cortex (shown above), corpus luteum (ovary), Leydig cells (testis).

Suicide: apoptosis

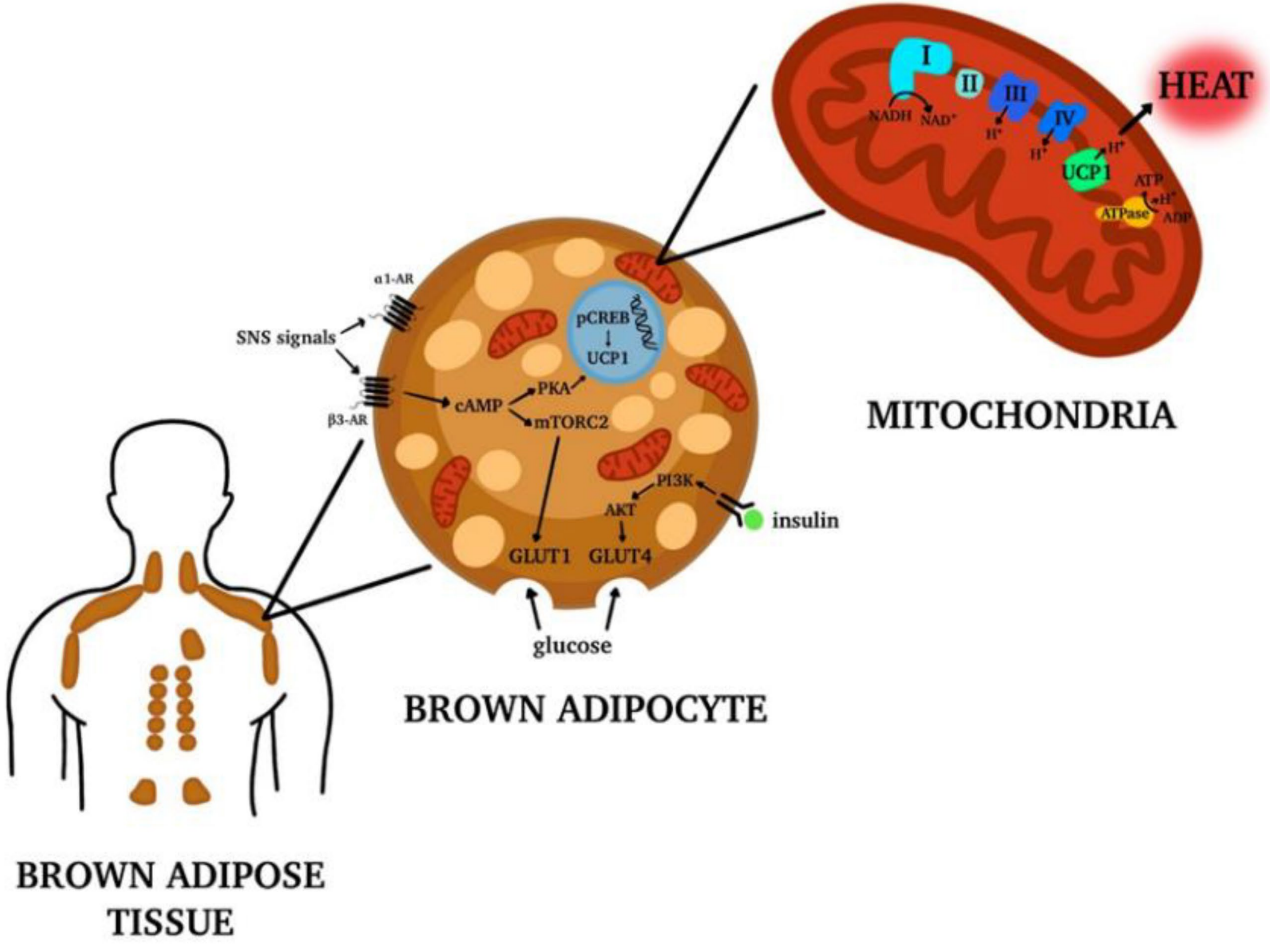
Signals for **programed cell death** originate in mitochondria during embryonic development, ageing, cell damage and neurodegenerative diseases.
Different from necrosis; no inflammation.

Molecules released by mitochondria trigger the cascade.



Thermogenesis

Brown fat produces more heat than white fat because ATP synthase is *uncoupled*; protons flow through membrane produce heat, not ATP. Present in newborns and hibernating animals. (What if we could convert our white fat to brown fat?)



Mitochondria:

"Clandestine rulers of our world, masters of power, sex and suicide."

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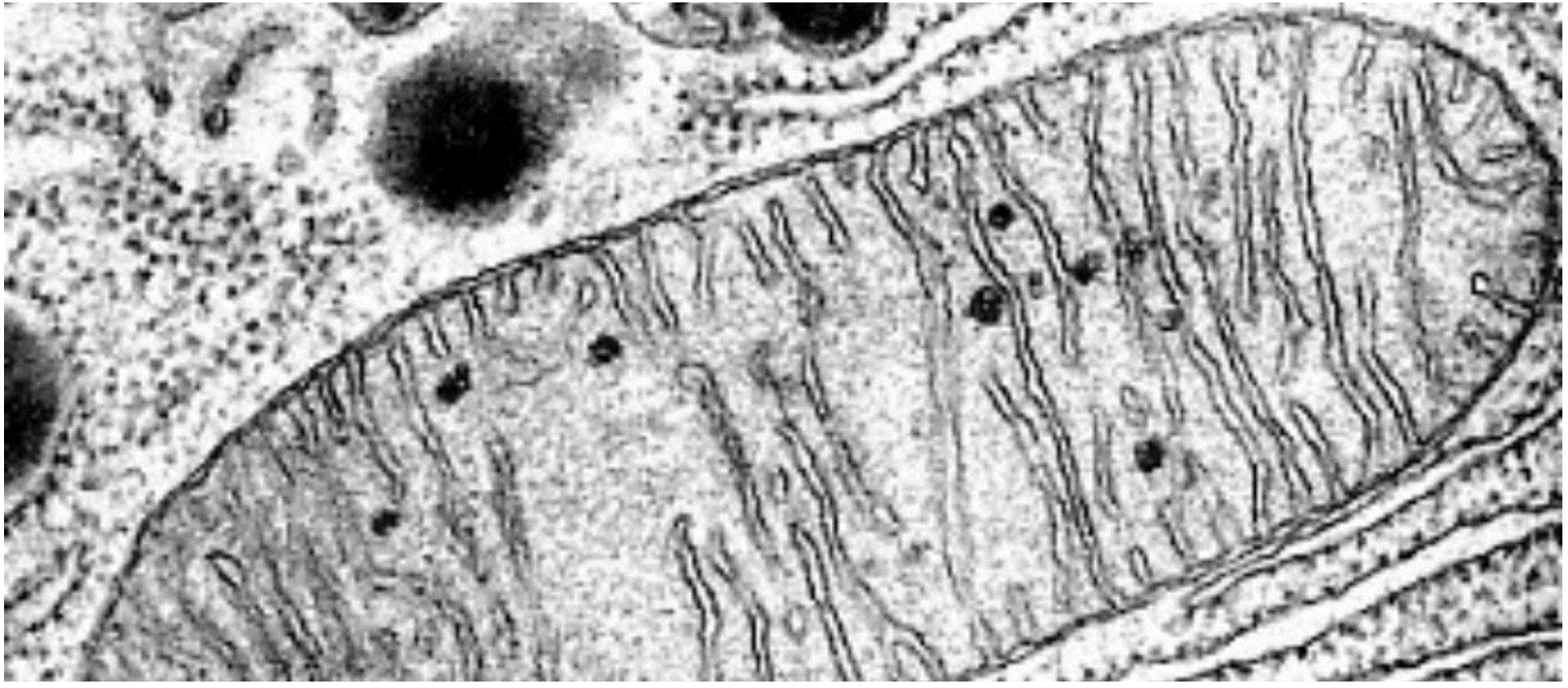
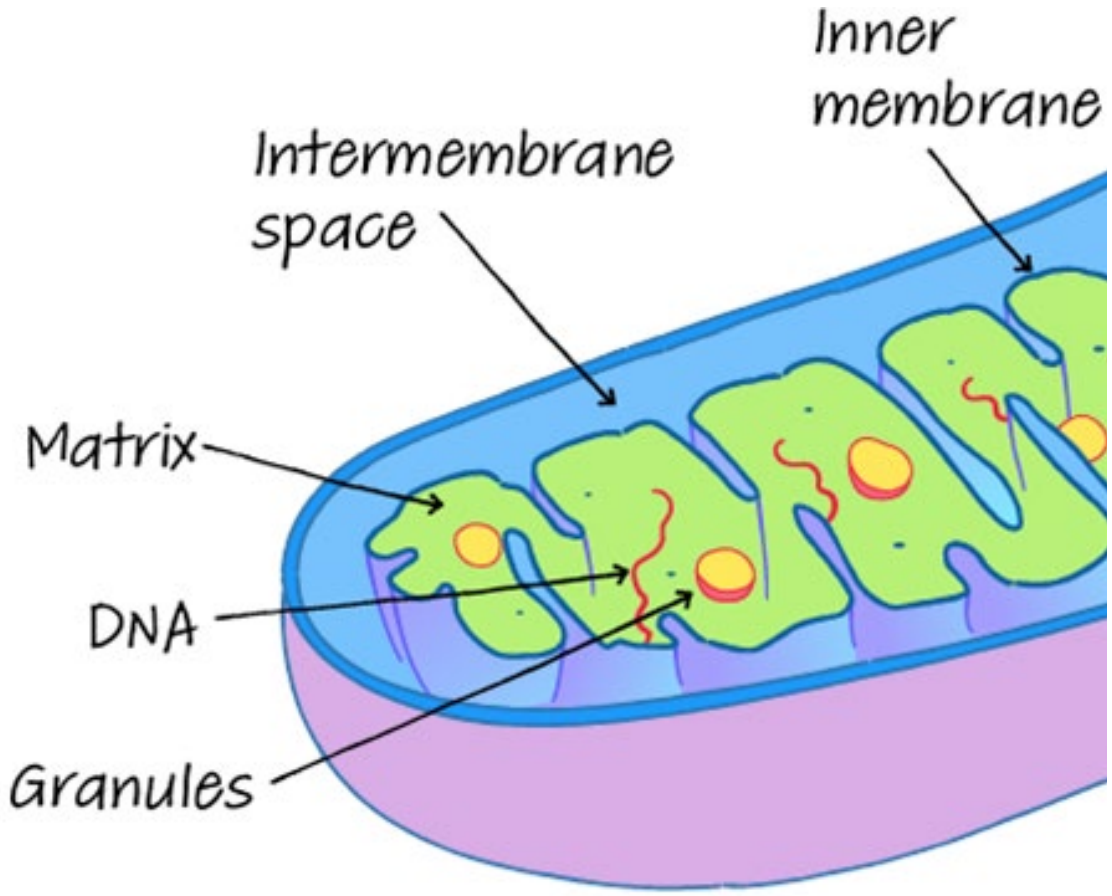


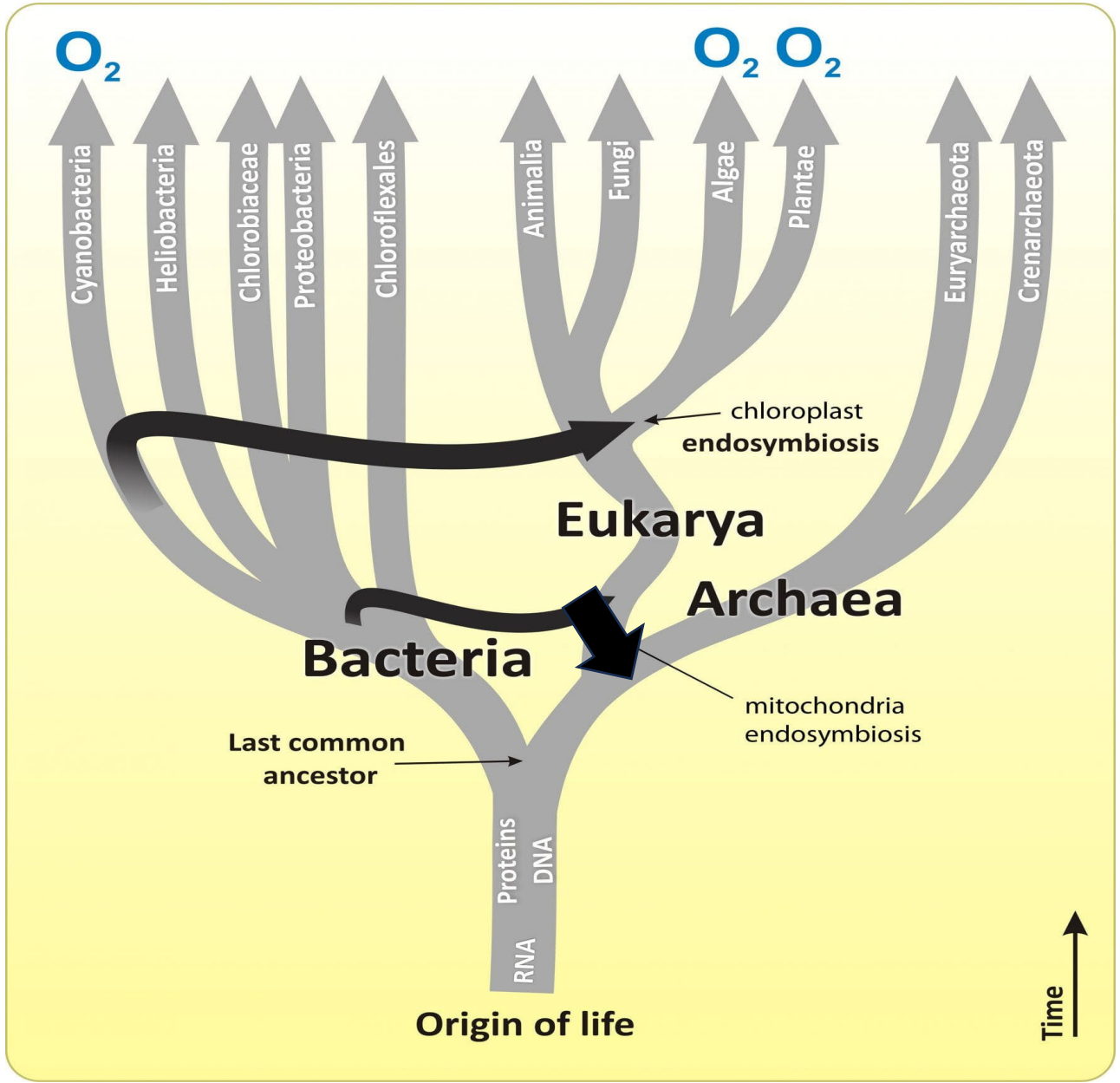
Origins

Mitochondria contain their own DNA which is bacteria-like. Thought to originate as bacteria incorporated into other one-cell organisms. Divide like bacteria and have bacteria-like ribosomes. Can be used to trace maternal lineage since all are inherited from the mother (as are mitochondrial diseases).

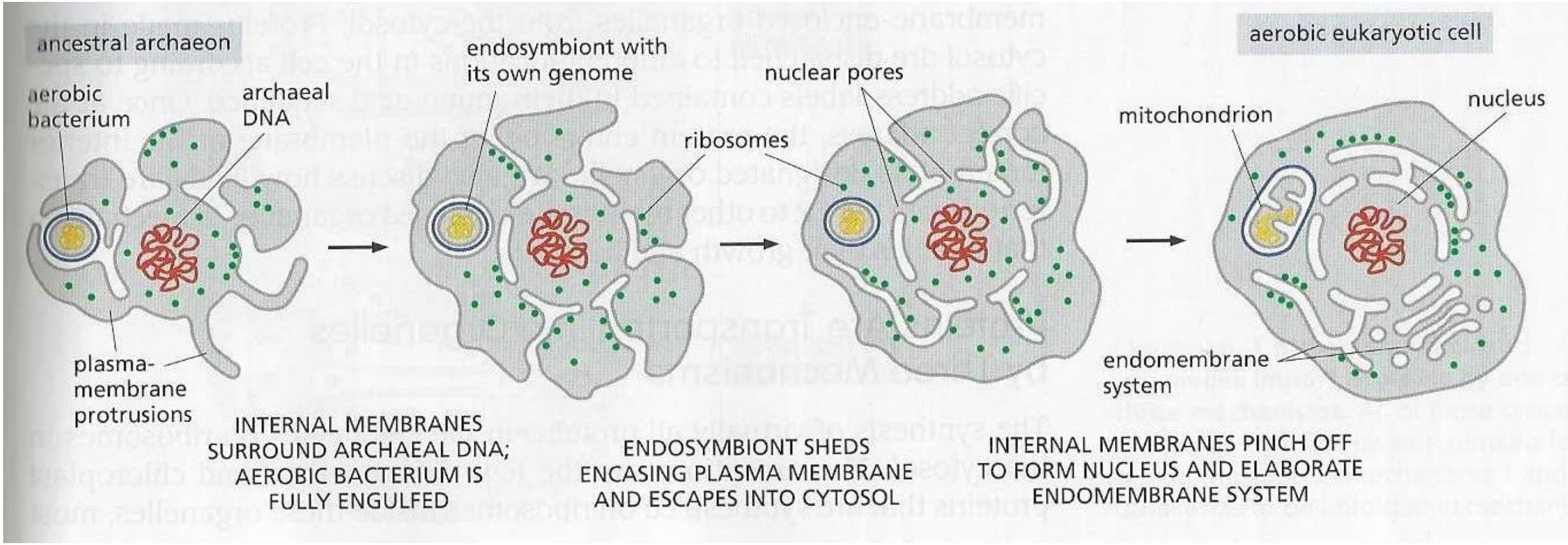


Evolution of eucaryotic cells

First living cells (procaryotes) used food molecules in the environment and used glycolysis to generate ATP (fermentation). This led to high lactic acid concentrations inside the cell.
Cells that evolved **proton pumps** to eject acid would survive better.
As oxygen levels on the planet rose, aerobic bacteria developed, using oxygen to digest food in the citric acid cycle.
Mitochondria stem from engulfed aerobic bacteria.



Evolution of Membranes



Correcting mitochondrial defects