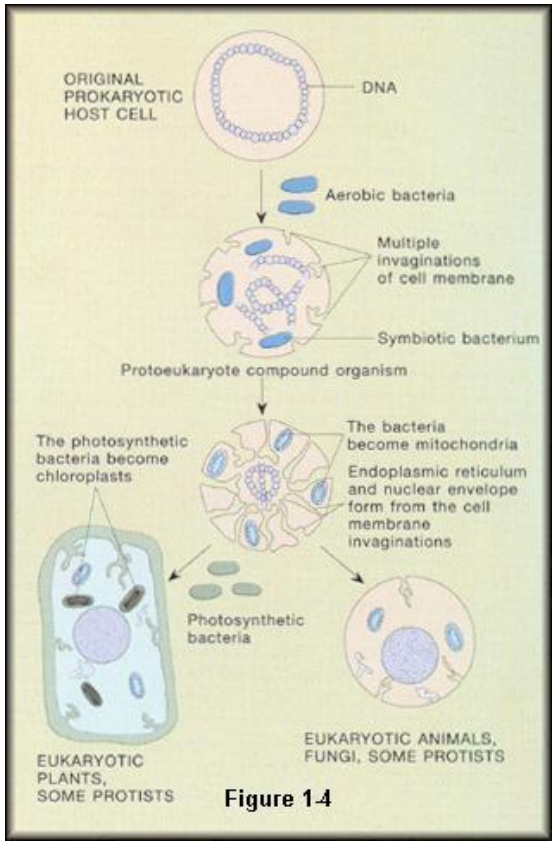
PÉCSI TUDOMÁNYEGYETEM
UNIVERSITY OF PÉCS

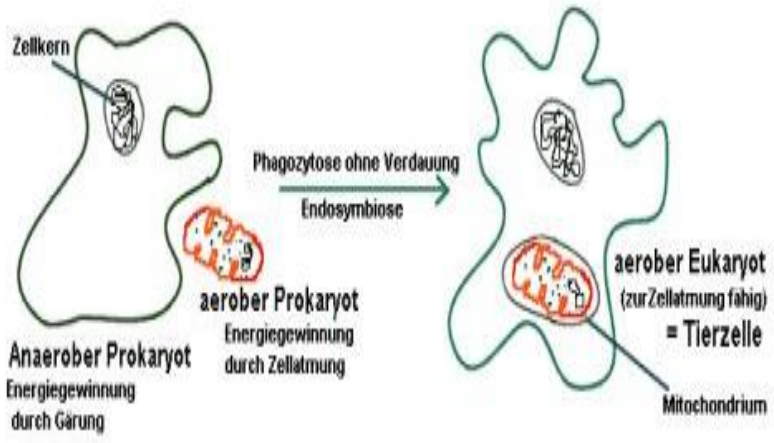
The Mitochondrion

Renáta Schipp

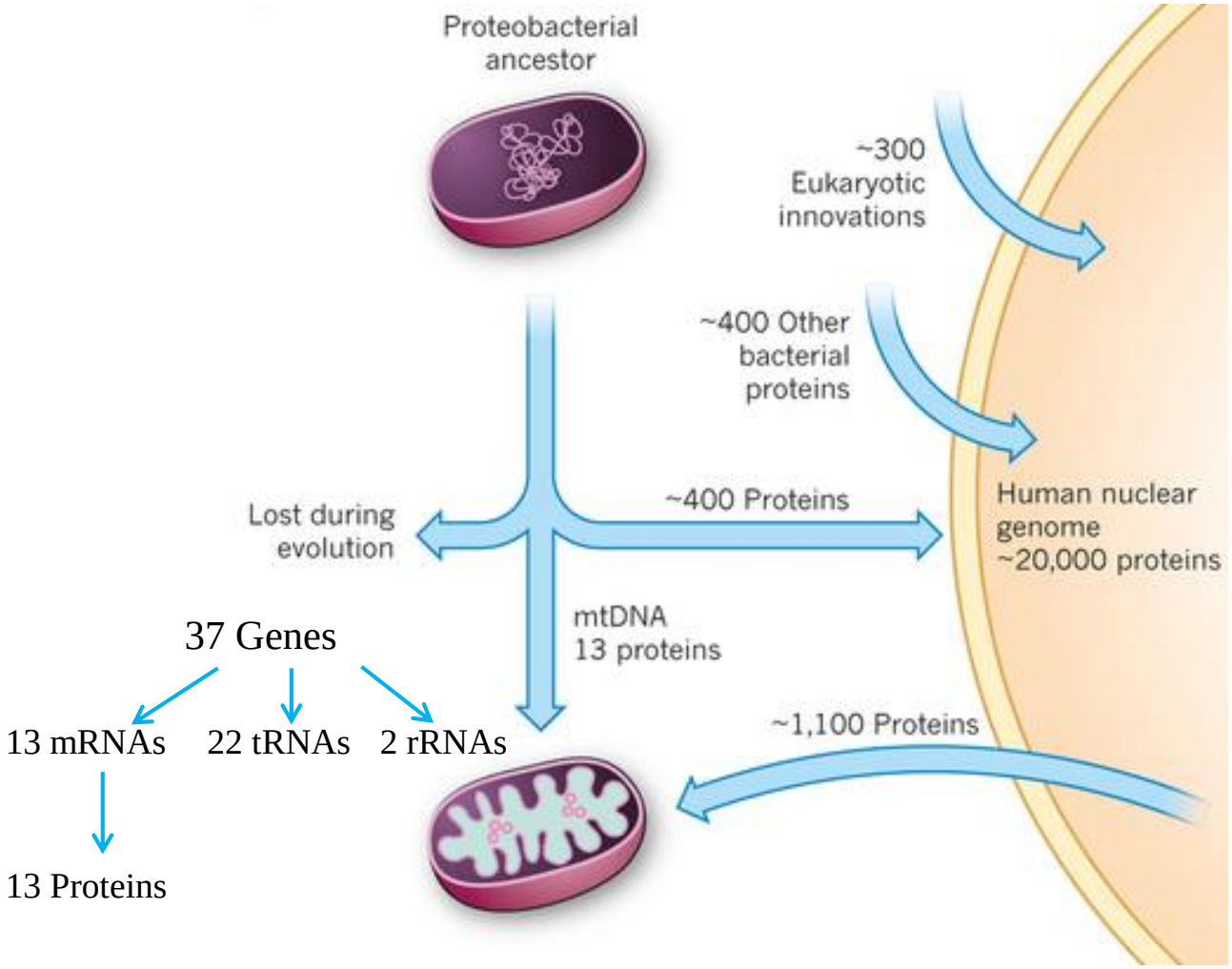
Origin

- Endosymbiothic theory
- the Mitochondria (and Chloroplastids) were originally **free-living cells**
- they lived in an endosymbiosis with a hostcell
- organellfree **anaerobe** Prokaryotes phagocyted **aerobe** Prokaryotes → Mitochondrion.

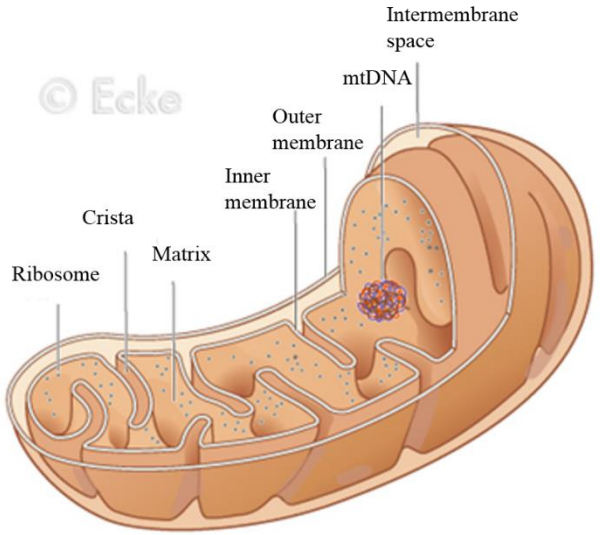




Origin


Proteobacterial ancestor
~300 Eukaryotic innovations
~400 Other bacterial proteins
~400 Proteins
Lost during evolution
Human nuclear genome ~20,000 proteins
mtDNA 13 proteins
37 Genes
13 mRNAs
22 tRNAs
2 rRNAs
13 Proteins
~1,100 Proteins

Structure



Outer membrane:

- enclose the whole mitochondrion
- no invaginations
- contains large number of integral proteins

➔ **Porin-highly permeable**

- Porins form channels➔ allow the exchange of different Molekuls and Ions

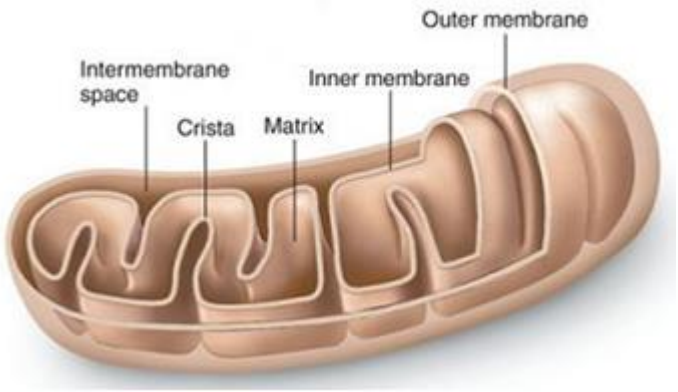
  small Molekuls pass freely

  bigger Proteins- signalsequenc

Intermembrane space:

- is the space between the outer membrane and the inner membrane
- composition is similar to that of the cytosol

Structure



Inner membrane:

- enclose the matrix
- is compartmentalized into numerous → Cristae
- rich in an unusual phospholipid → Cardiolipin→make the inner membrane impermeable
- contains more than 150 proteins → are classified into three functional groups

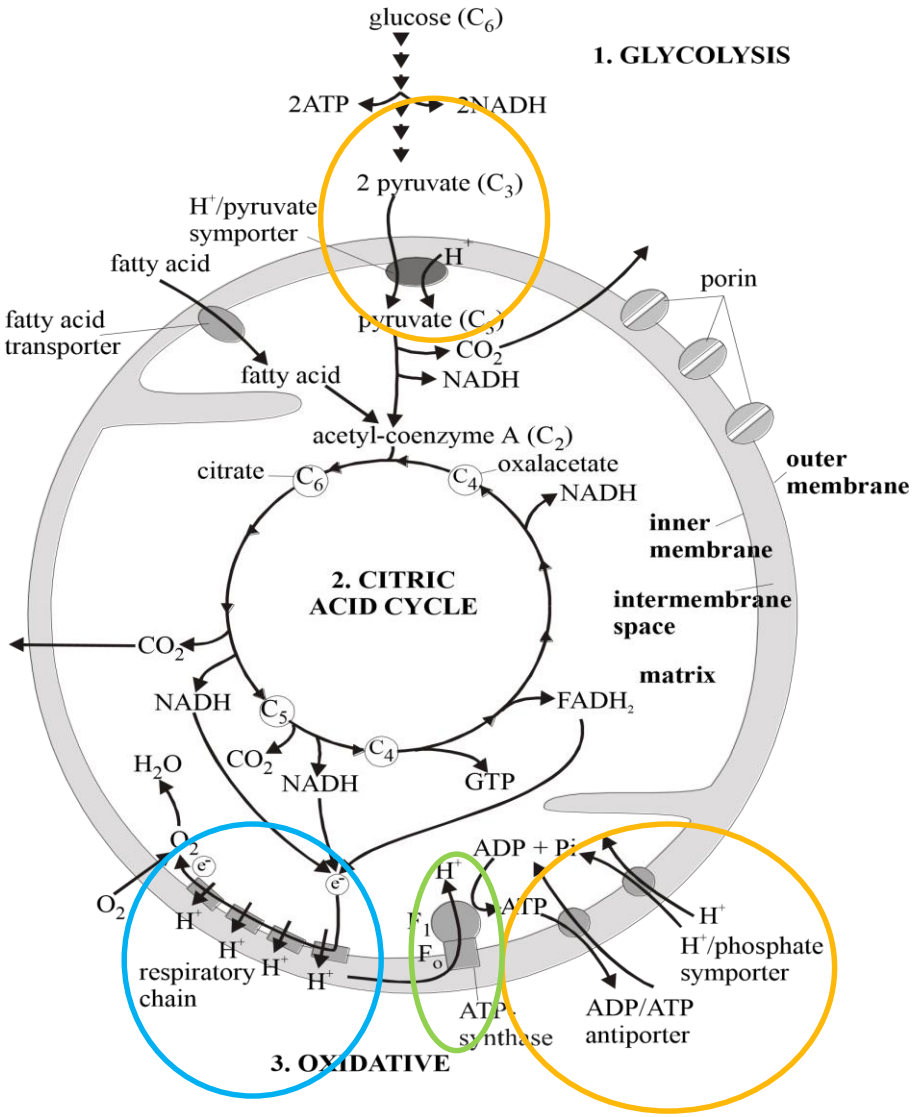
  Transportproteines: - H^+ /Pyruvate-Symporter

  - H^+ /Phosphate-Symporter

  - ADP/ATP-Antiporter

  Respiratory-chain Proteins: Electrontransport Proteins

  ATP-Synthase: Fo/F1 complex


glucose (C_6)
1. GLYCOLYSIS
2ATP
2NADH
2 pyruvate (C_3)
H^+/pyruvate symporter
fatty acid
fatty acid transporter
fatty acid
pyruvate (C_3)
CO_2
NADH
porin
acetyl-coenzyme A (C_2)
citrate
C_6
C_4
oxalacetate
NADH
outer membrane
inner membrane
intermembrane space
matrix
2. CITRIC ACID CYCLE
CO_2
NADH
C_5
$FADH_2$
CO_2
NADH
C_4
GTP
H_2O
O_2
O_2
e^-
e^-
H^+
H^+
H^+
H^+
respiratory chain
ADP + Pi
ATP
H^+
F_1
F_o
ATP-synthase
H^+
H^+/phosphate symporter
ADP/ATP antiporter
3. OXIDATIVE

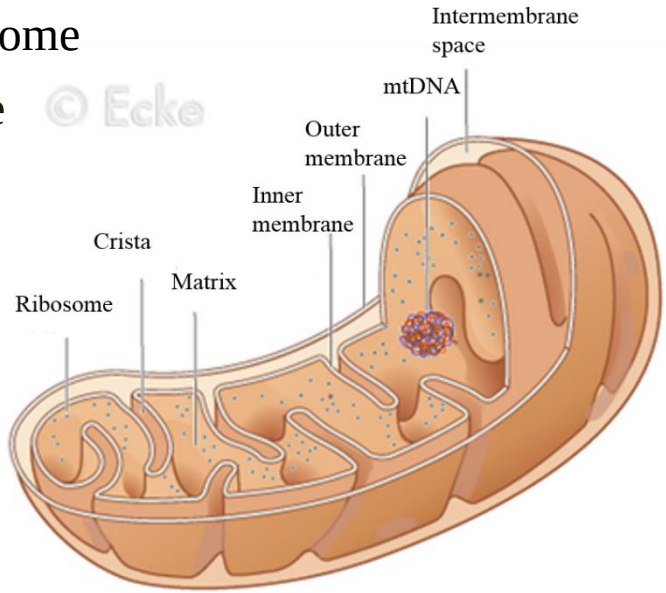
Structure

Cristae:

- inner membrane invaginations →expand the surface→enhancing the ATP synthesis

Matrix:

- is the space enclosed by the inner membrane
- contains - Proteins (Enzymes)
  - mitochondrial ribosomes and tRNAs
  - several copies of the mitochondrial genome
  - intermediates from the citric acid cycle



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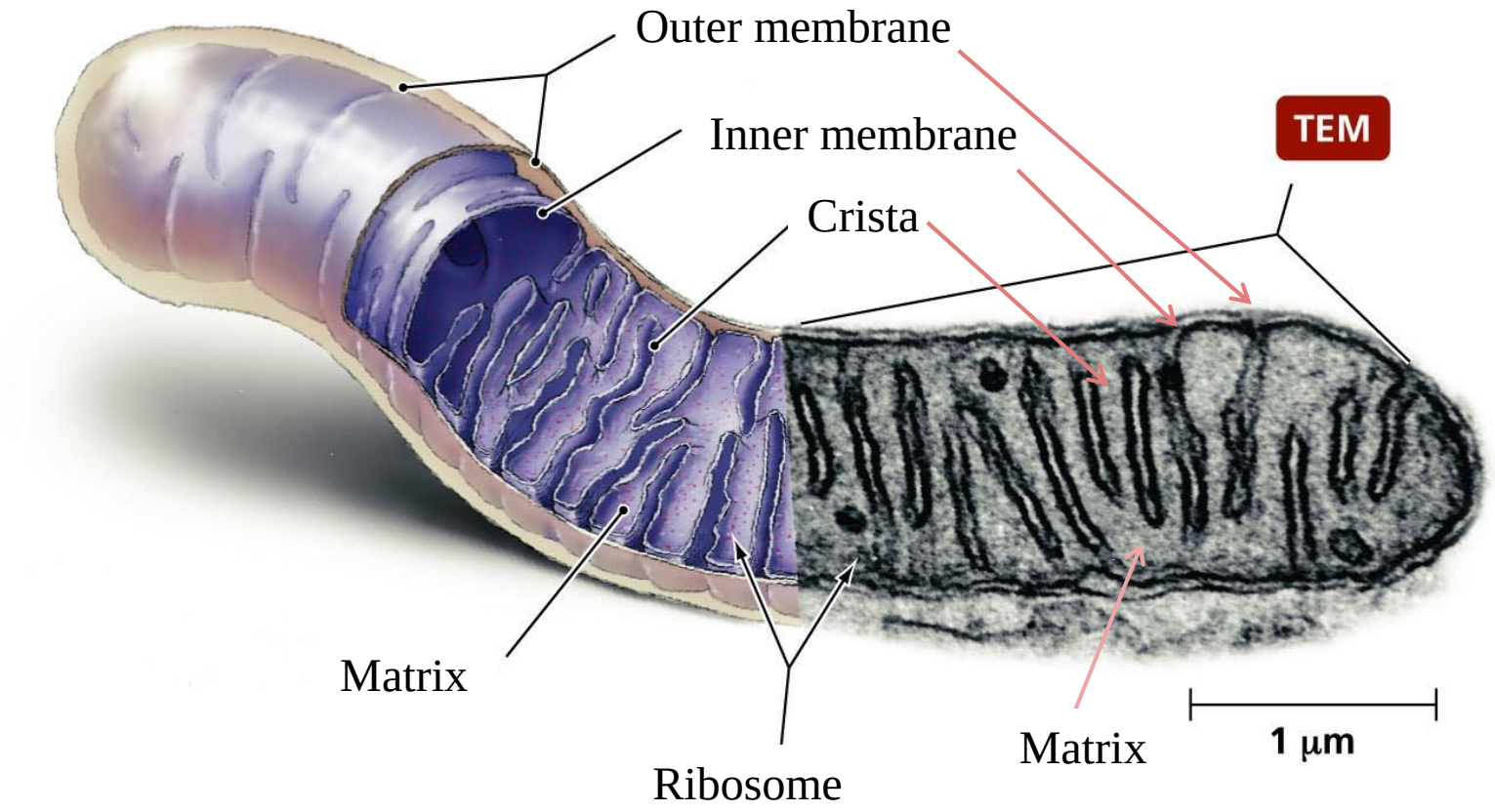
Structure



Function-Energy metabolism

ATP

ATP

ATP

ATP

ATP

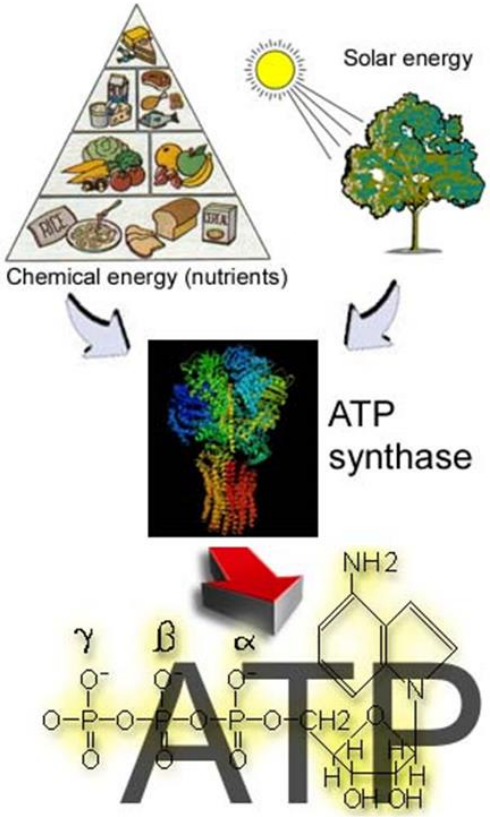
www.christinemarsh.com

Energy metabolism in mitochondria

- Breakdown of glucose (aerobic eukaryotes):

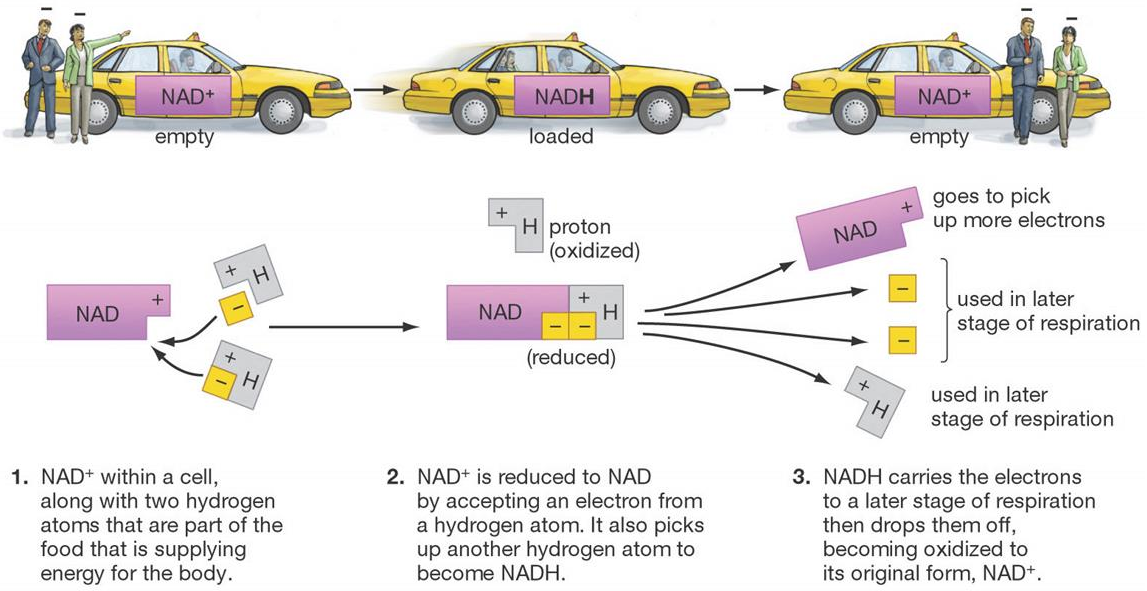
  1. glycolysis
  2. citric acid cycle (Szent-Györgyi-Krebs)
  3. oxidative phosphorylation

- $C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$



NAD(Nicotinamide adenine dinucleotide)

- Coenzyme
- transports electrons from one reaction to another
- NAD^+ → accepts electrons from other molecules and becomes reduced → NADH
- NADH → donate electrons and becomes oxidized to its original form → NAD^+



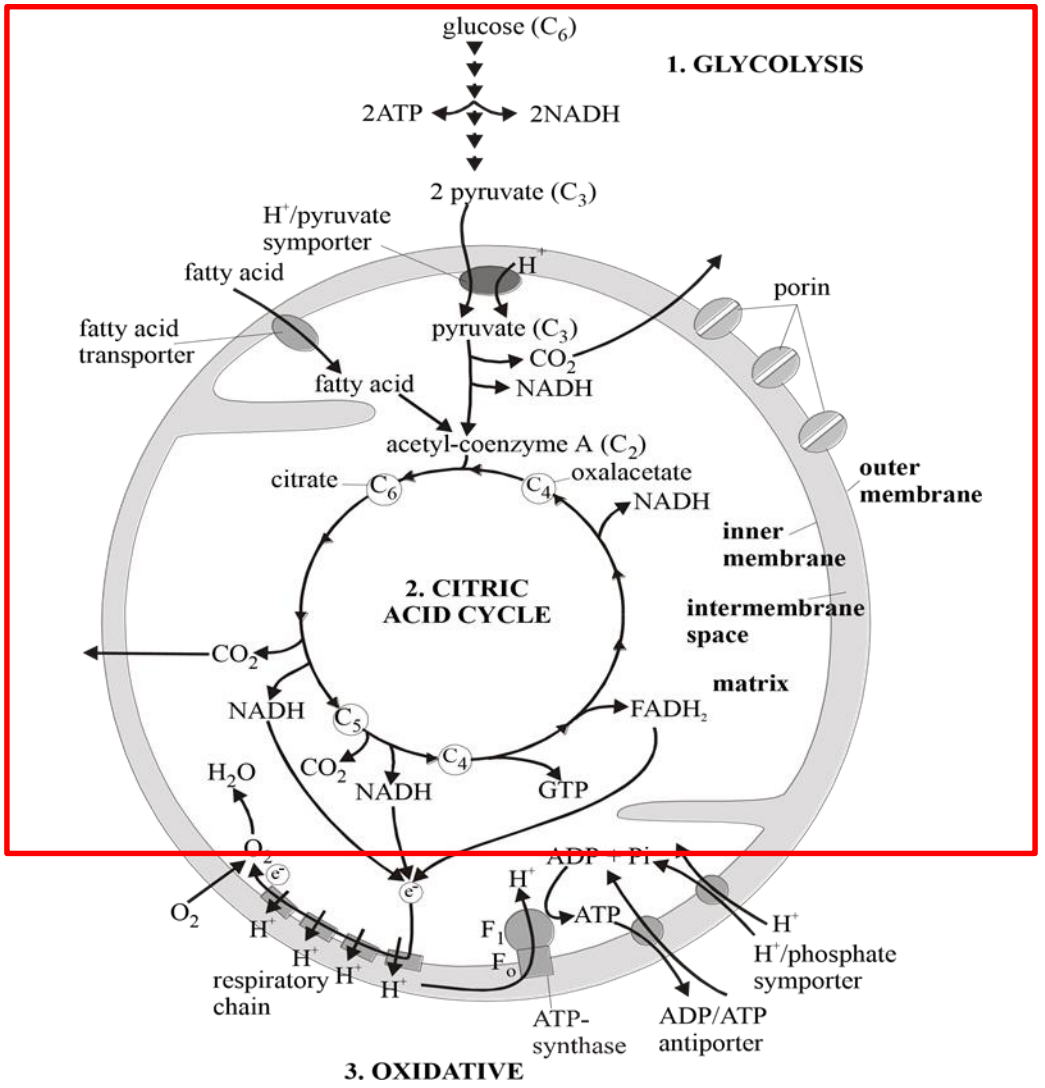
Energy metabolism in mitochondria – Glycolysis, citric acid cycle

- Glycolysis:
  - in the cytosol
  - glucose (C_6) converted into→ 2 pyruvate (C_3) molecules
  - 2 ATP and 2 NADH molecules are produced

- Citric acid cycle:
  - in the mitochondrial matrix
  - pyruvate → acetyl-coenzyme A (C_2)
  - acetyl-coenzyme A + oxalacetate (C_4) → citric acid (C_6) → cycle → oxalacetate
  - production of GTP, CO_2, reduced coenzymes (NADH, $FADH_2$)

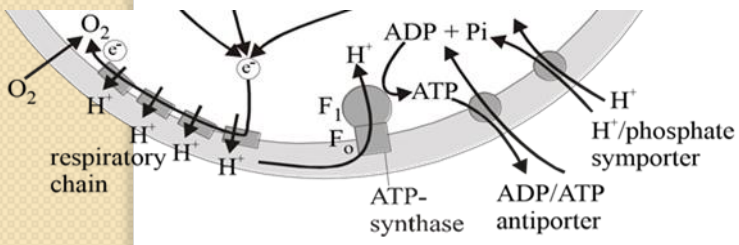
formation of:
2 ATP
2 NADH

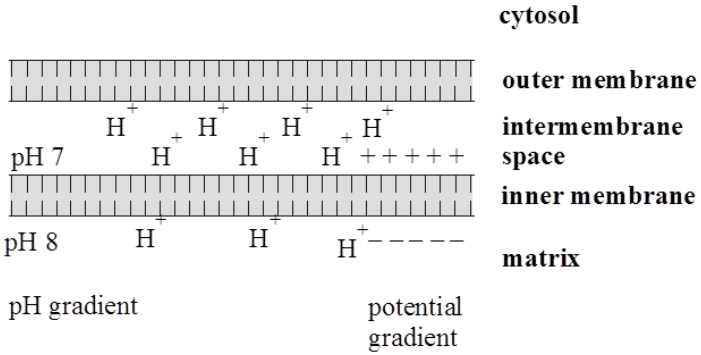
formation of:
2 CO_2
3 NADH
1 $FADH_2$
1 GTP

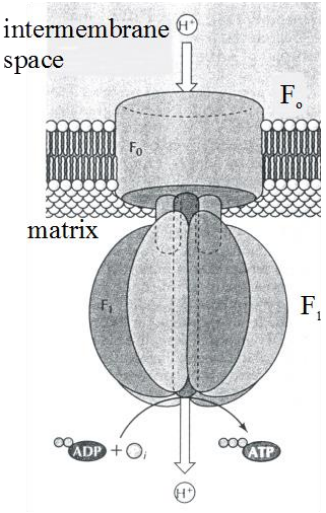


Energy metabolism in mitochondria – Oxidative phosphorylation

- Oxidative phosphorylation:
  - in the inner membrane
  - electrons: reduced coenzymes → respiratory chain (electron transport system) → O_2 → H_2O
  - generation of electrochemical proton gradient (chemiosmosis mechanism)
  - ATP synthase: ATP-production (ADP + P_i → ATP)
  - The final electron acceptor is molecular oxygen → is reduced to water (harmful intermediates are generated =ROS)





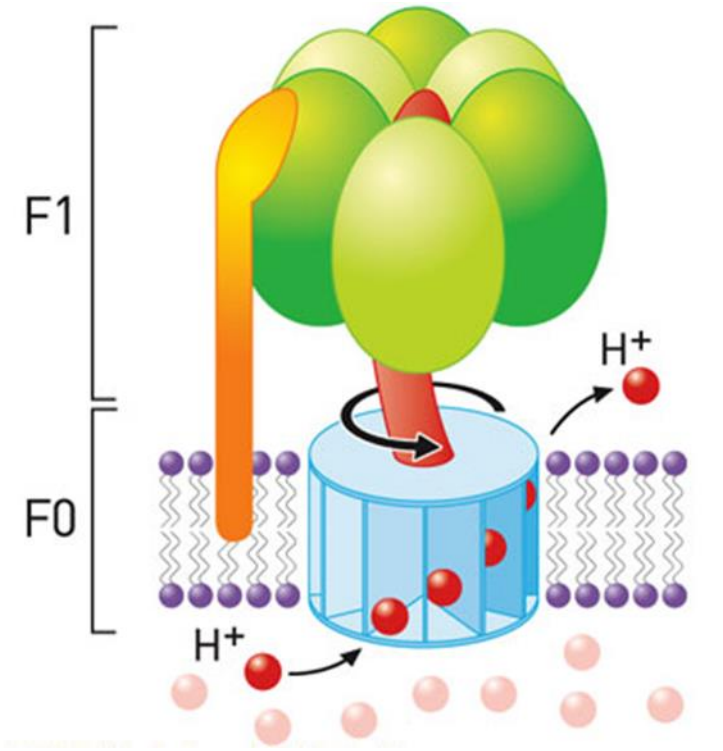


matrix

F1

intermembrane space

F0



primawarta.blogspot.com

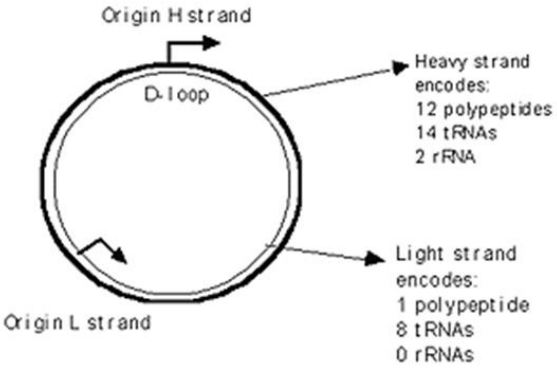
1 Proton- 30°
1ATP- 4 Protons-120°
360°- 3ATP

Fully oxidation of 1 glucose molecule

- Glycolysis:
  - Production of 4 ATP but 2 are consumed → 2 ATP
- Citric acid cycle:
  - 2 ATP (indirectly)
- Oxidative phosphorylation:
  - 30 or 32 ATP

→ 34 or 36 ATP molecules

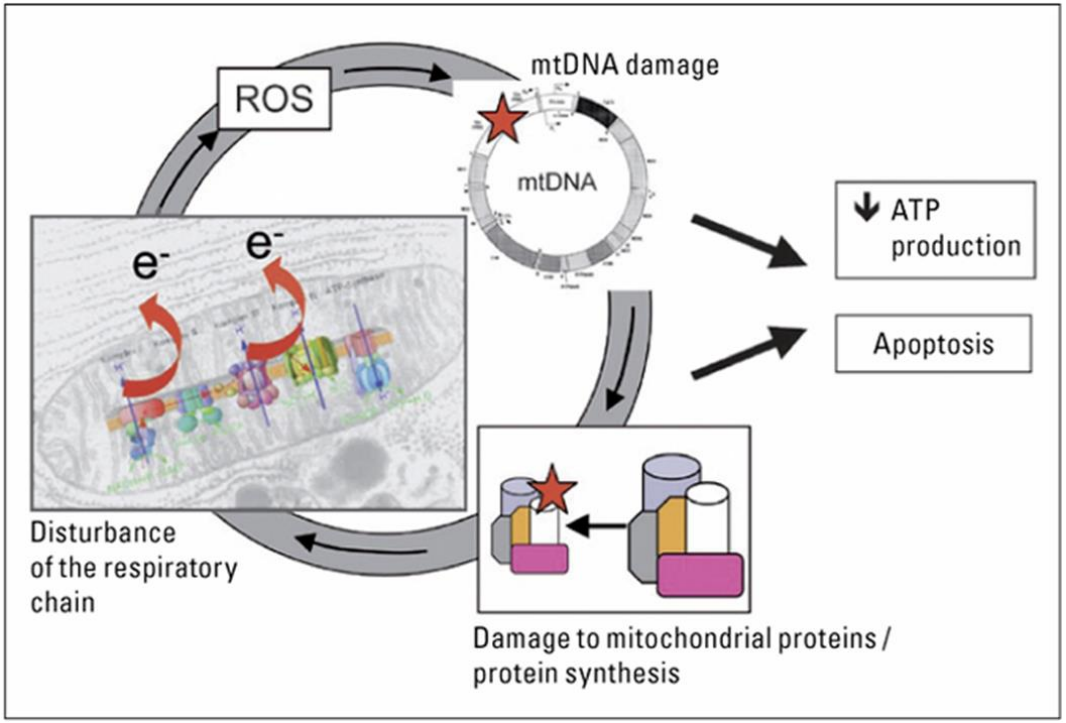
The human mitochondrial genetic apparatus



- Mitochondrial DNA:
  - small
  - circular
  - double-stranded → heavy (H) and light (L) chain
  - 2-10 copies/mitochondrion
  - in the mitochondrial matrix
  - mostly coding regions → rRNAs, tRNAs, mRNAs
  - symmetrical transcription
  - no RNA import or export
  - no protein export
  - protein import
  - high mutation rate

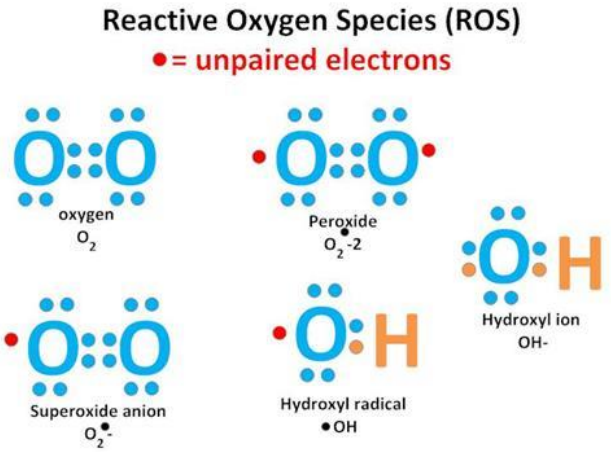
Mutation of mtDNA

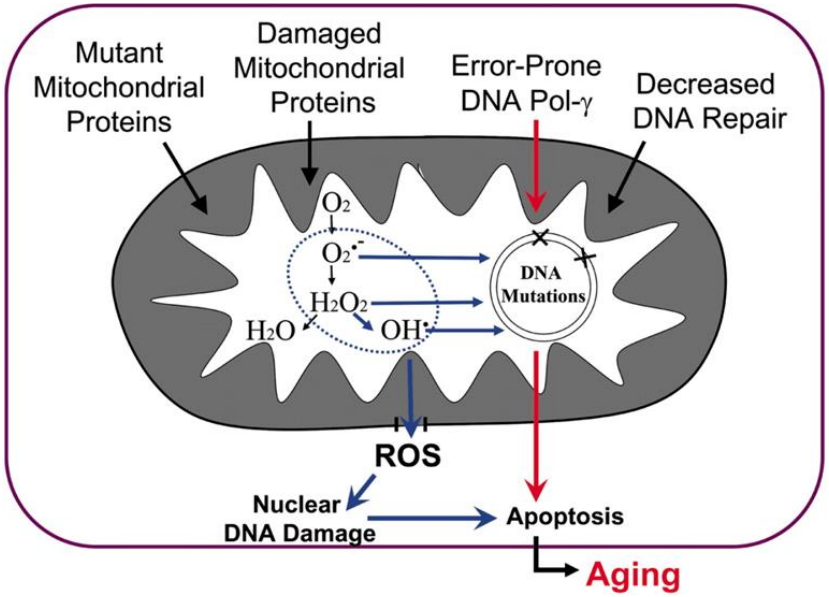
- Free radicals
- No histon proteins
- Proofreading and repair are weak



Reactive oxygen species (ROS)

- During reduction of oxygen → harmful, instable intermediates are produced (superoxide or peroxide anions)
- These are called reactive oxygen species (ROS):
  - are very harmful to cells
  - oxidize proteins, destroy the membrane and cause mutations in DNA
  - cause diseases and is proposed as one cause of aging

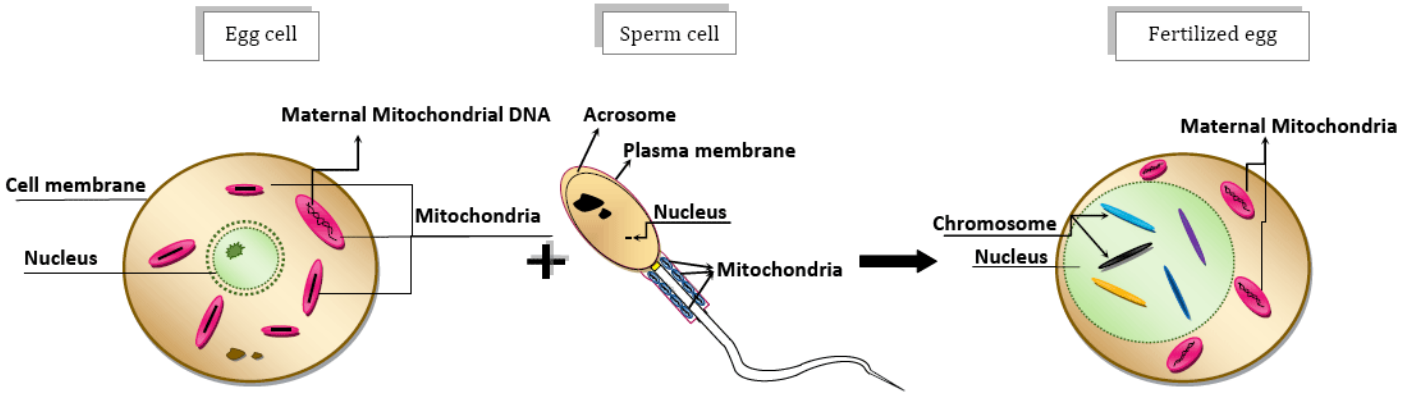




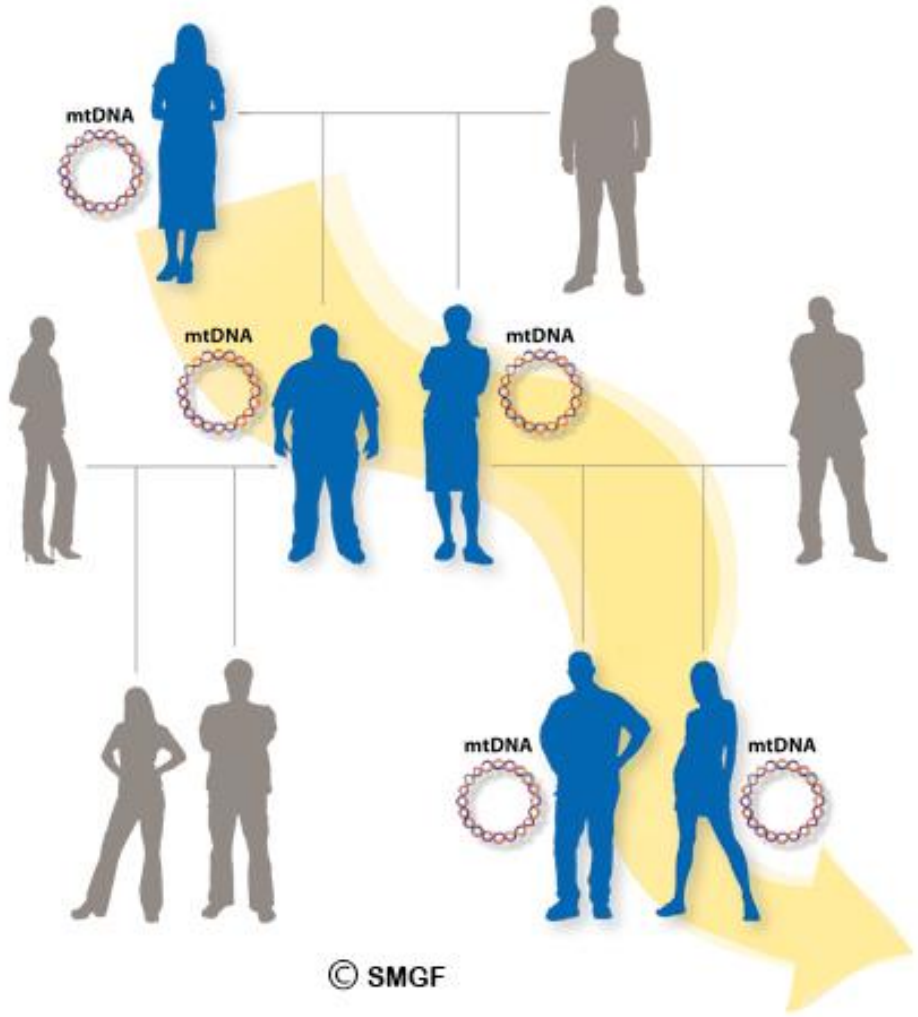
Inheritance

Maternal: mitochondria are inherited only from mothers

non- mendelian inheritance

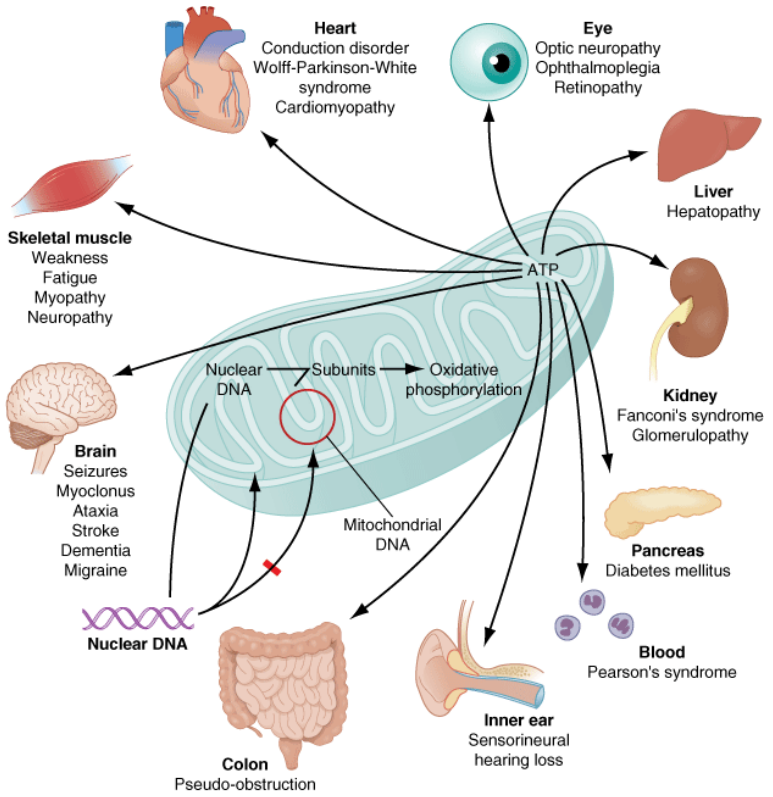


Inheritance



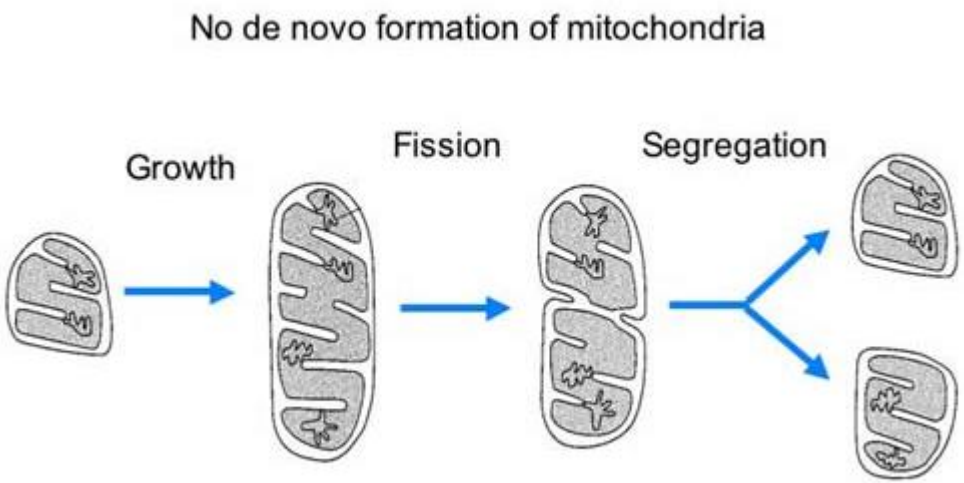
Mitochondrial diseases

- mutations in the mitochondrial DNA → decrease in ATP production
- those tissues/organs are affected, which require lots of energy
- Leber's hereditary optic neuropathy
- Parkinson disease
- Alzheimer disease
- diabetes mellitus
- physiological aging

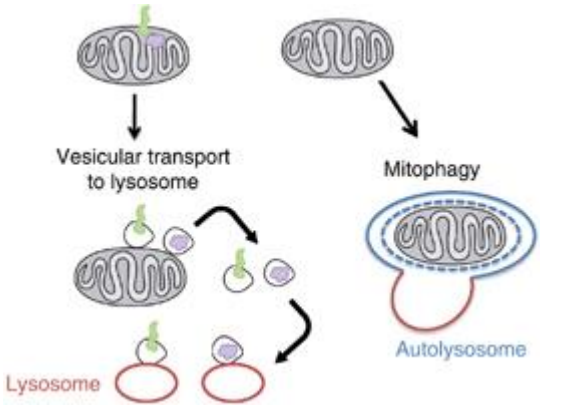


Formation and degradation

- no de novo formation
- are generated trough growth and binary fission
- lysosomal degradation



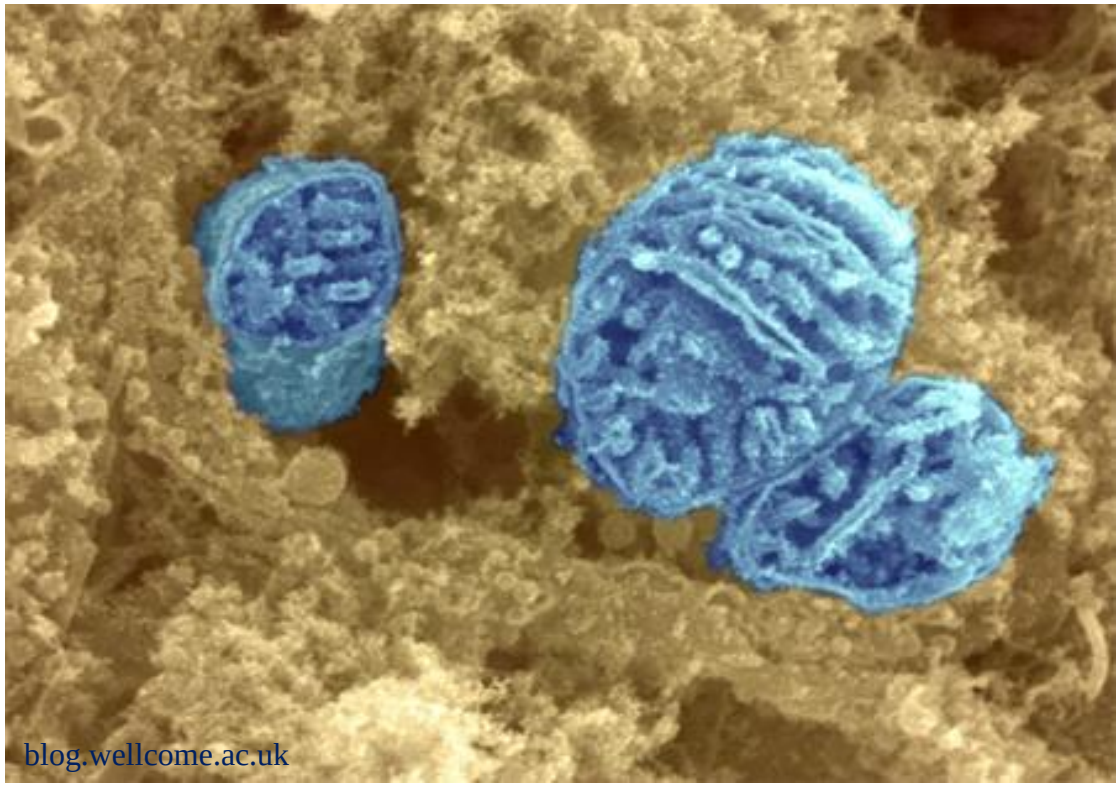
Fission



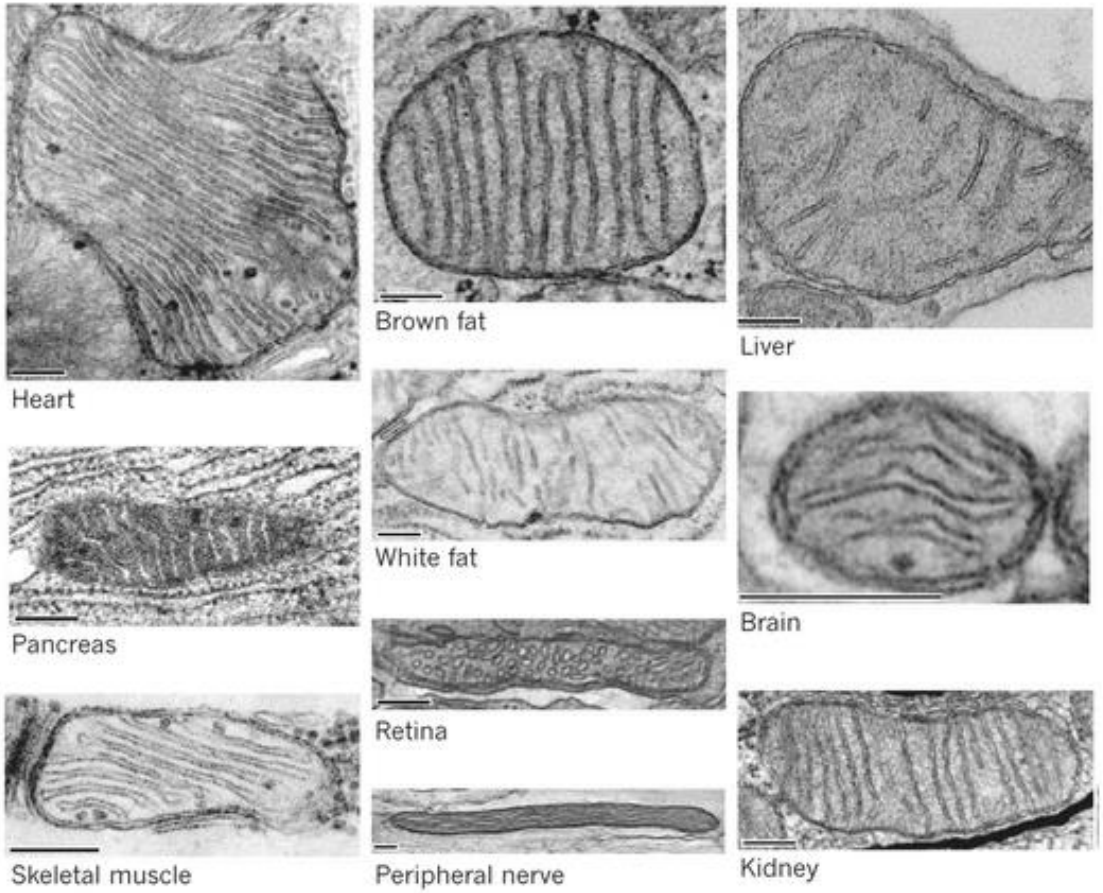
www.nature.com

Degradation

Thank you for your attention!



Structure



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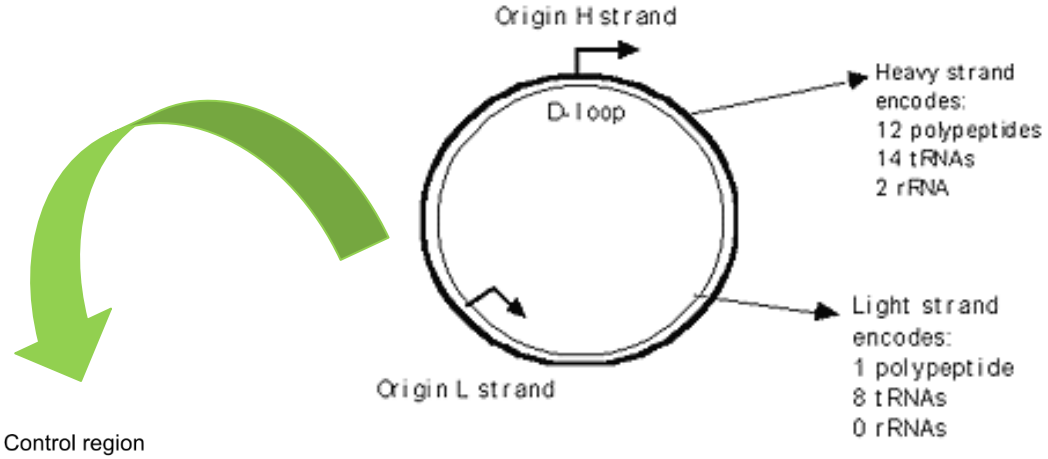
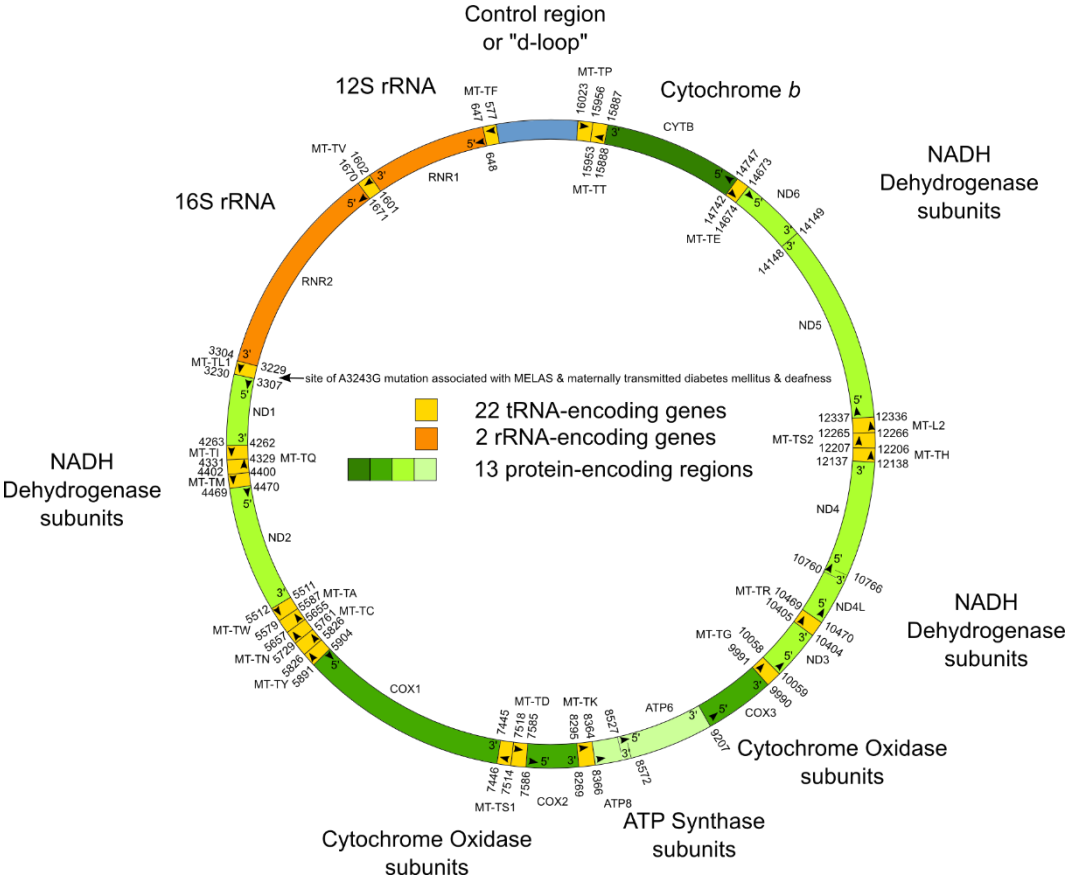
(auf Seite 114)

Genome

Characteristic	Nuclear Genome	Mitochondrial Genome
Size	~ $3.3x10^9$bp	16,569bp
Form of DNA	linear, doublestranded	circular, doublestranded H-strand, L-strand
Number of DNA- molecules per cell	23 (haploid) 46 (diploid)	tausende Kopien pro Zelle 2-10 Kopien pro Mitochondrium
Percentage of coding DNA	~ 3% vorwiegend nichtkodierend	~ 93% vorwiegend kodierend
Number of Genes encoded	~20.000-30.000	37 13mRNAs, 22tRNAs, 2rRNAs
Associated proteins	Histone and non-Histone-Proteins	no Histones (Nucleoid)
Mutations-rate	< 20 %	no Histones weak Proofreading free radicals (ROS)

Genome

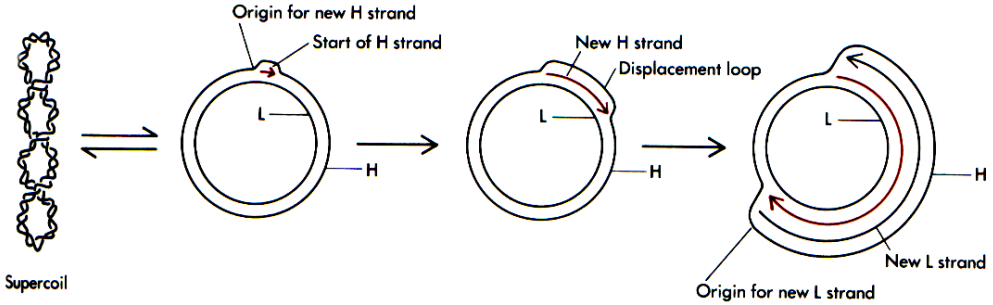




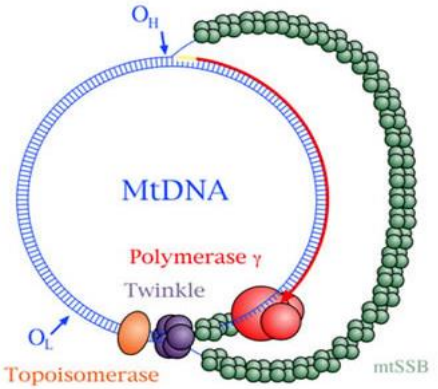
en.wikipedia.org

mtDNA Synthesis

Characteristic	Nunlear Genome	Mitochondrial Genome
DNA Replication	symmetric	asymmetric
Replication enzymes	in nuclear genom encoded DNA-Polymerase α,δ,ε	in nuclear genom encoded DNA-Polymerase γ
Proofreading	normal	weak



L→H, H→L



Initiation Factors:
RNA Polymerase
mtTFA
mtTFB1
mtTFB2

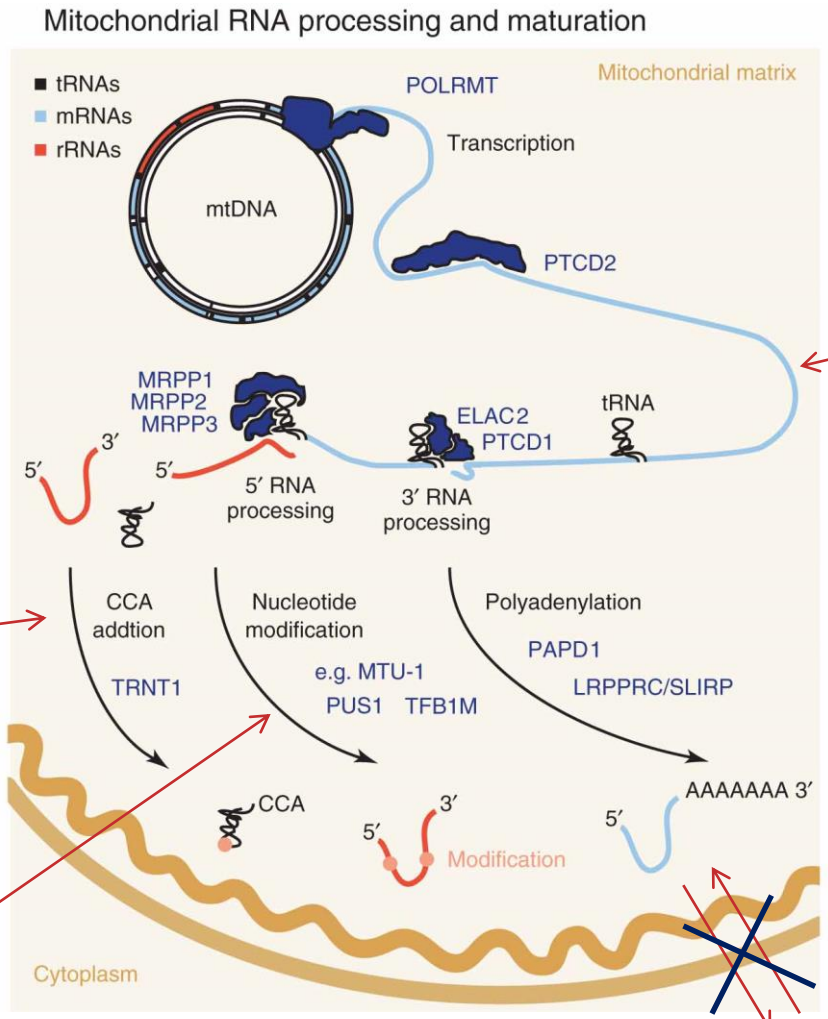
Additional Activities:
Priming
RNaseH1/5'-3' Exonuclease
Ligase III

bricker.tcnj.edu

Transcription

Characteristic	Nuclear Genome	Mitochondrial Genome
Transcription	asymmetric	symmetric
RNA Polymerase	in nuclear genom encoded	in nuclear genom encoded
Introns	highly repeated	no
Splicing	✓	–
5’ Cap	✓	–
Poly A tail	✓	✓

Posttranscriptional Modificatios of mtRNAs



„polycistronic" RNA Transcript

Nucleotid-Addition
CCA to 3' tRNA

Polyadenylation
3' mRNA

Base-Modification
Ex. rRNAs, tRNAs

No RNA Export, Import

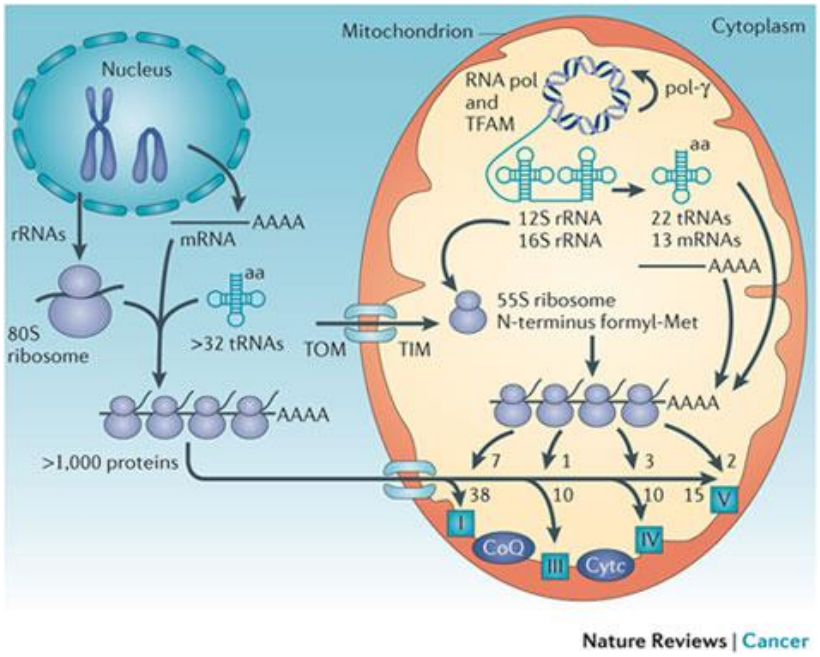
Modification with Endonucleases
Ex. rRNAs, tRNAs, monocystronic mRNA

Translation

Characteristic	Nuclear Genome	Mitochondrial Genome
Proteins	All in cytoplasm translated	1% in Mitochondrion 99% at free Ribosomes in cytoplasm
Genetic Code	Universal	unique codes

99 %

All other Proteins
(Functional)

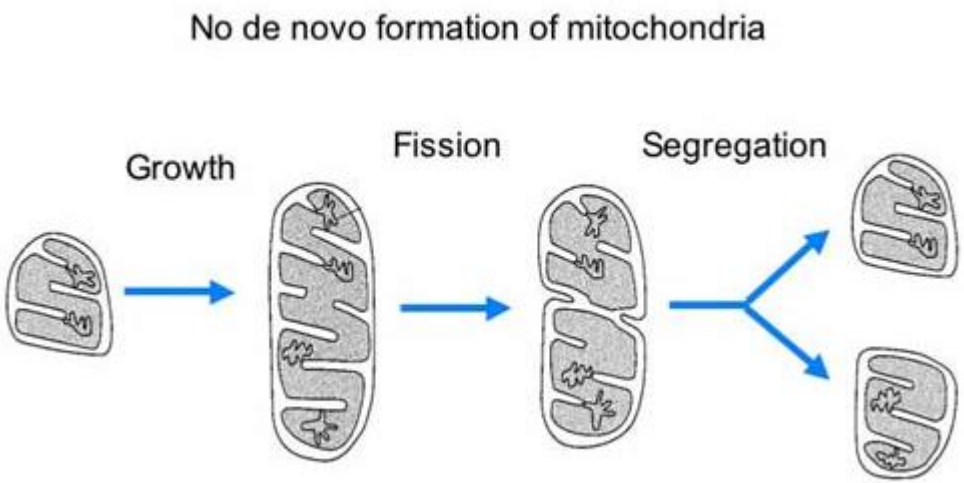


1%

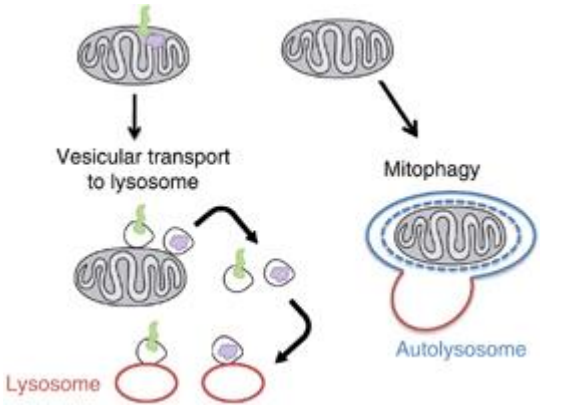
Subunites of respiratory chain proteins

Formation and degradation

- no de novo formation
- are generated trough growth and binary fission
- lysosomal degradation



Fission



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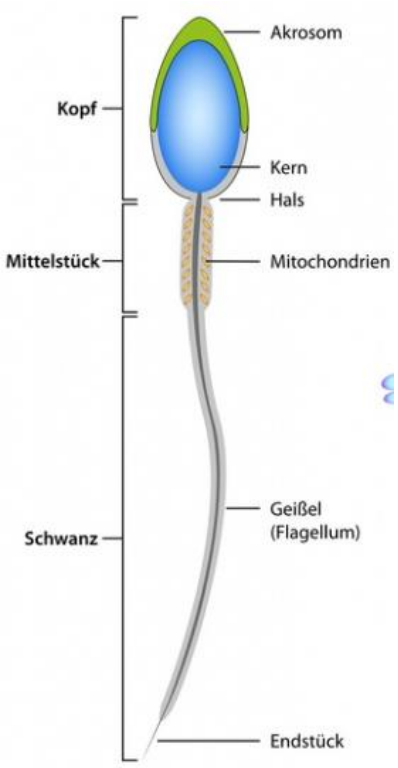
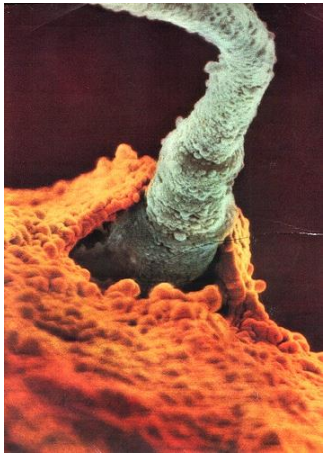
Degradation

Inheritance

Maternal: mitochondria are inherited only from mothers

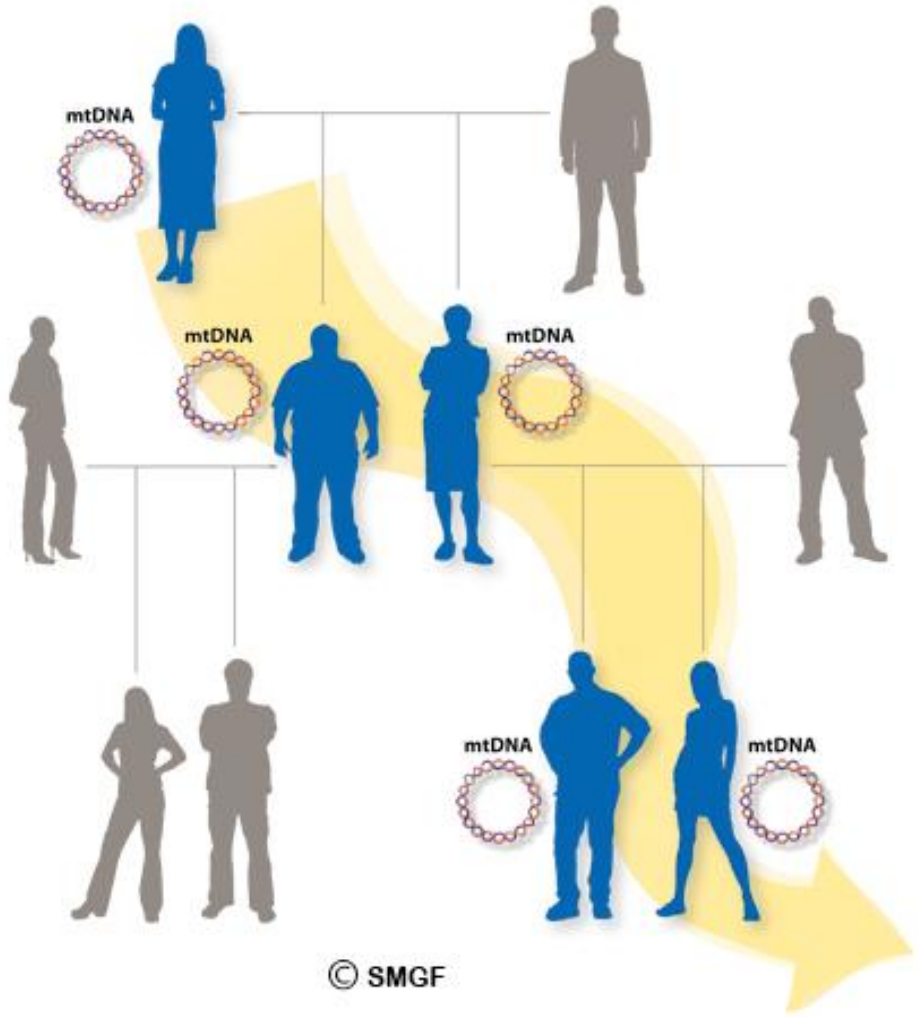


www.symptomat.de



www.hgate.net

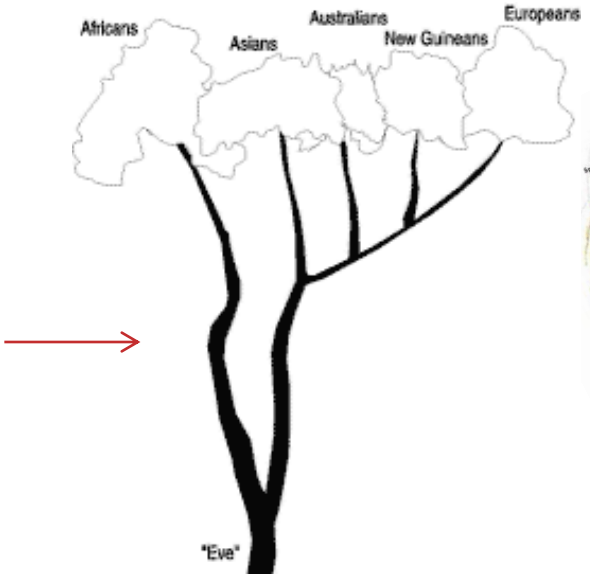
Inheritance



Eva Hypothesis

she is the woman from whom all living humans today descend on their mother's side

lesveritesscientifiques.com



Family tree of recent human evolution as proposed by Cann, et al. (1987).

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