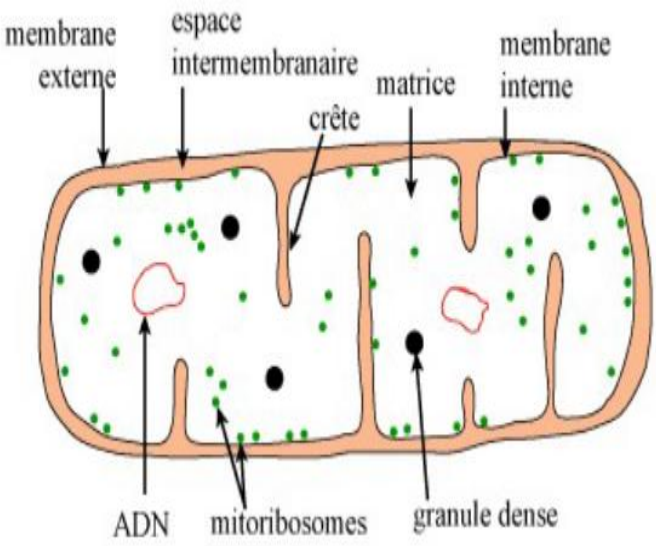
Lesson 11: Notions of extra-chromosomal genetics

Most of the eukaryotic genome is contained in the chromosomes of the nucleus (nuclear genome). However, in addition to nuclear DNA, some cellular organelles: mitochondria and chloroplasts also contain a genome that is "specific" to them.

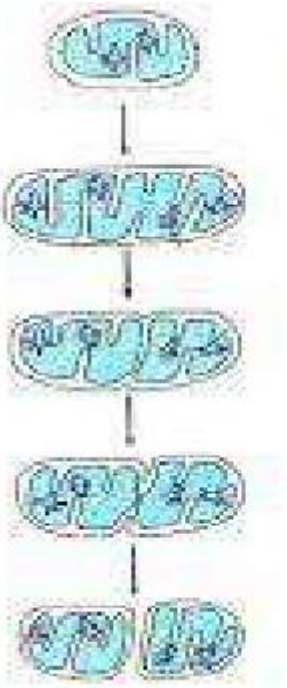
I. Mitochondrion

- Essential constituents of all aerobic animal and plant cells.
- Mitochondria are 0.5–1 μm in size and are bounded by two membranes
- Contain specific enzymes of the respiratory chain coupled with the synthesis of ATP by oxidative phosphorylation (energy production)
- Mitochondria are 0.5–1 μm in size and are bounded by two membranes



1. Biogenesis of mitochondria

Mitochondria grow and divide from parent mitochondria. These organelles undergo division by binary fission (scission).



2. Mitochondrial Genome

mtDNA can be circular or linear (linear mtDNA has been found in some ciliates, protozoa, algae, fungi).

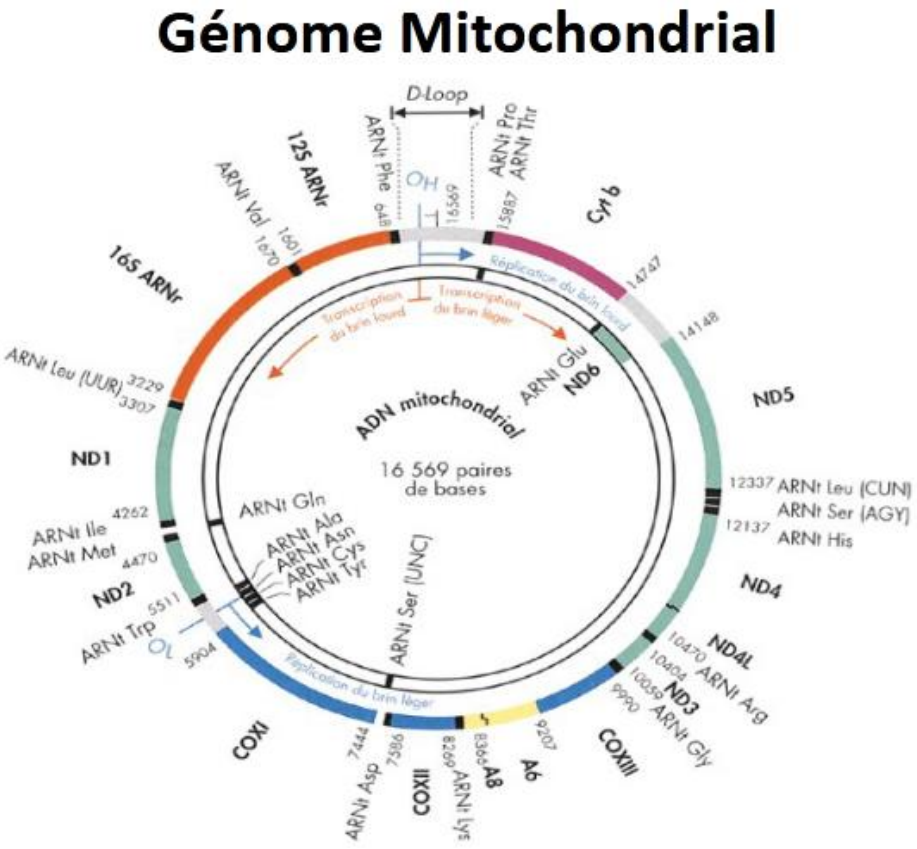
Mitochondrial DNA in human cells is a circular, double-stranded DNA molecule approximately 16,569,bp long . It consists of 37 genes; it encodes two mitochondrial ribosomal RNAs (12S and 16S), 22 tRNAs required for all amino acids, and messenger RNAs for 13 proteins. Most of the proteins in mitochondrial ribosomes originate externally and are encoded by nuclear genes.

mtDNA is made up of two strands: the H (Heavy) strand, rich in G bases (guanine), and the L (Light) strand, rich in C bases (cytosine) .

The mammalian mitochondrial genome lacks introns; most sequences are unique, non-repetitive . In contrast, the yeast mitochondrial genome consists of exons and introns.

The only non-coding segment of mtDNA in all vertebrates is the "displacement loop" or "D-loop " or control region.

It contains an H-strand origin of replication (Oh) and regulatory sites for L- and H-strand transcription.



3. Mitochondrial DNA replication

mtDNA replication is independent of the cell cycle and nuclear DNA replication.

mtDNA replication is bidirectional but from two different origins of replication on the two strands: OH and OL

4. Mitochondrial DNA transcription

The RNA polymerase that transcribes mtDNA is encoded in nuclear DNA. Both strands are transcribed in full.

The D- loop contains a promoter for each strand, the long primary transcripts undergo maturation into mRNA, rRNA and tRNA .

5. Mitochondrial DNA translation

5.1 Initiating translation

a) Assembly of the mitochondrial ribosome:

- Mitochondrial ribosomes (55S in mammals) are formed of two subunits (39S and 28S) composed of mitochondrial proteins and rRNA.

b) Recognition of mRNA:

- Mitochondrial mRNA is recognized by a special initiator tRNA (tRNA -Met), which carries a formylated methionine (fMet) into the mitochondria, as in bacteria.

c) Formation of the initiation complex:

- The mRNA, mitochondrial ribosome, and initiator tRNA bind to form the initiation complex.

5.2 Elongation

a) Addition of amino acids:

- The mRNA codons are read by specific tRNAs which provide the corresponding amino acids.
- tRNAs often have a modified structure and a reduced number (22 tRNAs instead of 30-40 in the cytoplasm) .

b) Formation of peptide bonds:

- A peptide bond is formed between adjacent amino acids by the peptidyl transferase activity of the mitochondrial ribosome.

c) Movement of the ribosome:

- The ribosome moves along the mRNA to read the next codons, gradually adding amino acids to the polypeptide chain.

5.3 . Termination

a) Recognition of the stop codon:

- Translation terminates when a stop codon (UAA or UAG in human mitochondria) is encountered.

b) Release of the peptide chain:

- A mitochondrial release factor (mtRF) helps detach the peptide chain from the ribosome.

5.4 Protein maturation

- Proteins translated in mitochondria are often directly integrated into mitochondrial membranes or exported to specific regions of the mitochondria.
- Some undergo post-translational modifications, such as folding or addition of prosthetic groups.

Peculiarities of mitochondrial translation

1. **Modified genetic code** :
    - The mitochondrial genetic code differs slightly from the universal genetic code.
    - For example, UGA (stop in cytoplasm) codes for tryptophan in mitochondria.
2. **Specific machinery** :
    - Mitochondrial ribosomes are closer to bacterial ribosomes in terms of evolutionary origin, reflecting the endosymbiotic origin of mitochondria.
3. **Imported proteins** :
    - Although mitochondria translate some of their proteins, the majority of mitochondrial proteins are encoded by the nuclear genome and imported after cytoplasmic translation.

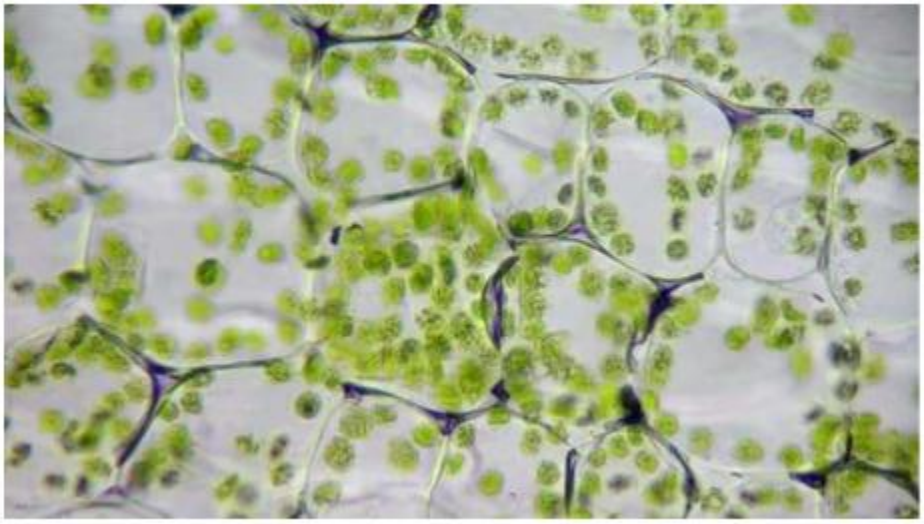
Code génétique des mitochondries

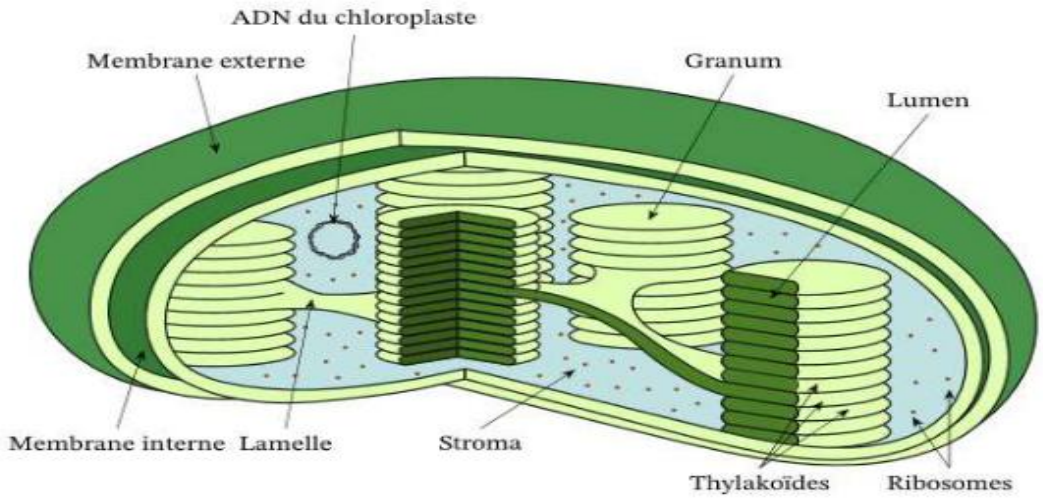
UUU Phe	UCU Ser	UAU Tyr	UGU Cys
UUC Phe	UCC Ser	UAC Tyr	UGC Cys
UUA Leu	UCA Ser	UAA Stop	UGA ¦*Trp*¦
UUG Leu	UCG Ser	UAG Stop	UGG Trp
CUU Leu	CCU Pro	CAU His	CGU Arg
CUC Leu	CCC Pro	CAC His	CGC Arg
CUA Leu	CCA Pro	CAA Gln	CGA Arg
CUG Leu	CCG Pro	CAG Gln	CGG Arg
AUU Ile	ACU Thr	AAU Asn	AGU Ser
AUC Ile	ACC Thr	AAC Asn	AGC Ser
AUA Met	ACA Thr	AAA Lys	AGA ¦*Stop*¦
AUG Met	ACG Thr	AAG Lys	AGG ¦*Stop*¦
GUU Val	GCU Ala	GAU Asp	GGU Gly
GUC Val	GCC Ala	GAC Asp	GGC Gly
GUA Val	GCA Ala	GAA Glu	GGA Gly
GUG Val	GCG Ala	GAG Glu	GGG Gly

Code génétique universel

UUU Phe	UCU Ser	UAU Tyr	UGU Cys
UUC Phe	UCC Ser	UAC Tyr	UGC Cys
UUA Leu	UCA Ser	UAA Stop	UGA Stop
UUG Leu	UCG Ser	UAG Stop	UGG Trp
CUU Leu	CCU Pro	CAU His	CGU Arg
CUC Leu	CCC Pro	CAC His	CGC Arg
CUA Leu	CCA Pro	CAA Gln	CGA Arg
CUG Leu	CCG Pro	CAG Gln	CGG Arg
AUU Ile	ACU Thr	AAU Asn	AGU Ser
AUC Ile	ACC Thr	AAC Asn	AGC Ser
AUA Ile	ACA Thr	AAA Lys	AGA Arg
AUG Met	ACG Thr	AAG Lys	AGG Arg
GUU Val	GCU Ala	GAU Asp	GGU Gly
GUC Val	GCC Ala	GAC Asp	GGC Gly
GUA Val	GCA Ala	GAA Glu	GGA Gly
GUG Val	GCG Ala	GAG Glu	GGG Gly

II The Chloroplast





● cpDNA is circular, double-stranded, replicated in a semi- conservative fashion, but lacks the DNA-associated proteins characteristic of eukaryotic DNA.

● It has a greater number of genes than mtDNA

● Contains many non-coding sequences (introns).

● Genetic recombinations between multiple copies of DNA within chloroplasts have been described in some organisms.

● Many gene products encoded by chloroplast DNA participate in the translational process of the organelle. In addition, chloroplast DNA encodes many tRNAs , many ribosomal proteins specific to chloroplast ribosomes.

● Chloroplast ribosomes have a sedimentation coefficient slightly lower than 70S. Although some chloroplast ribosomal proteins are encoded by chloroplast DNA and others by nuclear DNA, most, if not all, of them are distinct from their counterparts on cytoplasmic ribosomes.

● Chloroplast genes, specific to photosynthesis, have been identified. These include, for example, genes that encode proteins that are part of the thylakoid membrane . Mutations in these genes can inactivate photosynthesis.

●A typical distribution of genes between the nucleus and the chloroplast is illustrated by one of the major enzymes of photosynthesis, ribulose-1,5-bisphosphate carboxylase (Rubisco). The small subunit of this enzyme is encoded by a nuclear gene, whereas the large one is encoded by cpDNA .

1. Chloroplast genome

In most organisms, the chloroplast genome contains two inverted repeat regions (IR) . Repeat).

Chloroplast IR sequences carry the genes for rRNAs.

The chloroplast genome contains 120 to 130 genes. The genome encodes ribosomal proteins (3 to 5) and also tRNAs (about 30). Chloroplast genes are often organized in "Clusters" = groups of genes and are cotranscribed into polycistronic pre-RNAs which are then matured into smaller RNAs.

Chloroplast DNA contains coding genes :

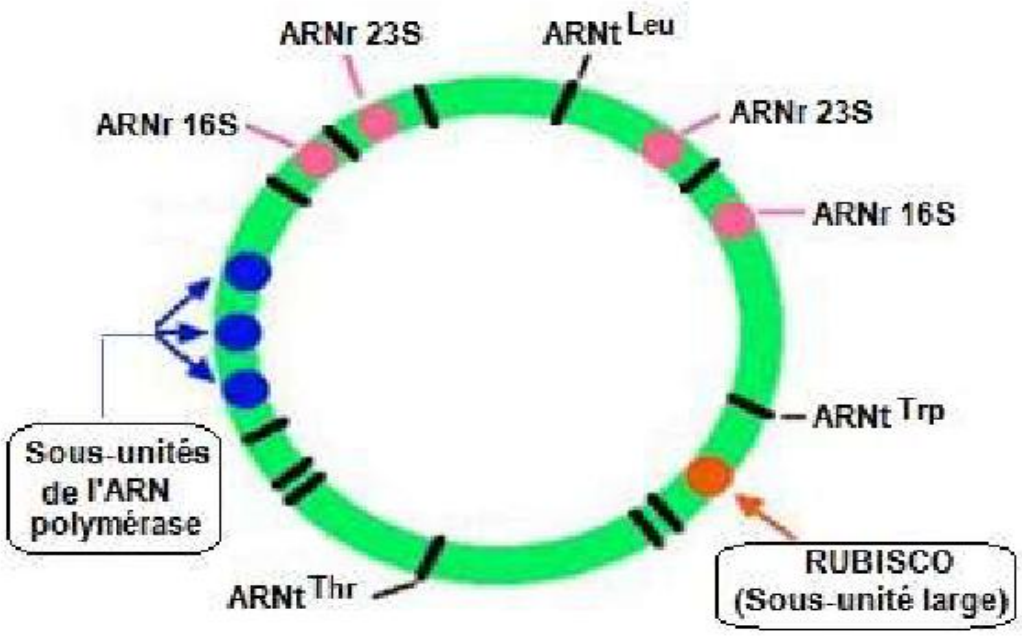
• Ribosomal RNA

plastid translation

• genes for the chloroplastic ribosome

• genes encoding subunits of RNA polymerase

• A gene for the large subunit of RUBISCO (key enzyme enabling CO2 fixation in plant biomass).



2. Comparison between Mitochondrial and Chloroplastic Genomes

Features	Chloroplast	Mitochondrion
Structure	Circular DNA, larger (120-160 kb)	Circular DNA, smaller (~16 kb)
Main role	Photosynthesis	Cellular respiration
Number of genes	100-200	~37
Legacy	Single-parent (often maternal)	Single-parent (strictly maternal)