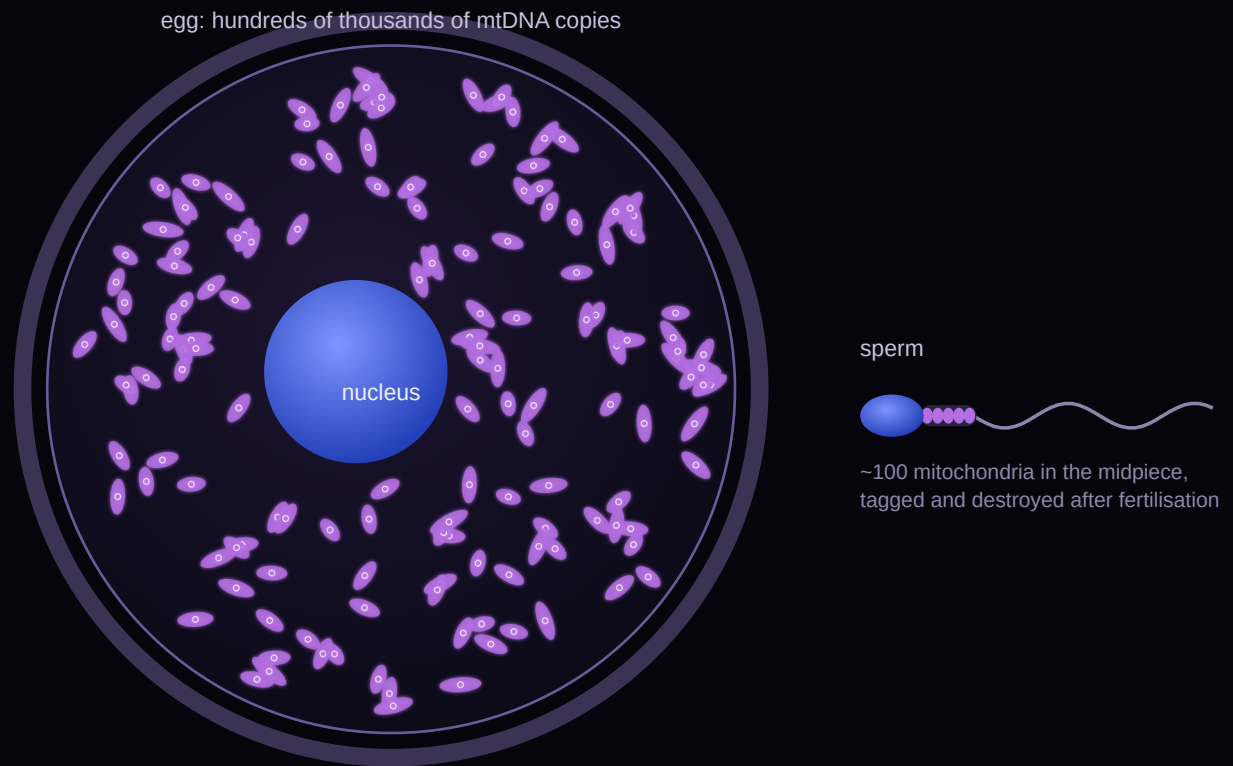




Why mitochondria come from your mother: the egg brings a vast population of mitochondria, the sperm only a handful, and those few are destroyed soon after fertilisation.

Extrachromosomal inheritance

Genes that live outside the nucleus, in mitochondria, chloroplasts, plasmids and symbionts, and the non-Mendelian patterns they produce.

— Mitochondria — Chloroplasts — Symbionts, plasmids, maternal effect — Nucleus

Contents

1. [What it is](#)
2. [How to recognise it](#)
3. [Organelle genomes and their origin](#)
4. [Plastid inheritance](#)
5. [Mitochondrial inheritance in fungi](#)
6. [Human mitochondrial genetics](#)
7. [Cytoplasmic male sterility](#)
8. [Infectious heredity](#)
9. [Plasmids and episomes](#)
10. [Look-alikes: maternal effect and imprinting](#)
11. [Quick revision](#)
12. [End-semester question bank](#)

1. What it is

Extra-chromosomal inheritance is the transmission of traits by genetic material that lies outside the nuclear chromosomes. It is also called **extranuclear**, **cytoplasmic** or **non-Mendelian inheritance**, and because in most organisms the cytoplasm of the zygote comes almost entirely from the egg, it frequently appears as **maternal** or **uniparental inheritance**.

The genes involved are called **plasmagenes**, and the whole set of them in a cell the **plasmon** (as opposed to the nuclear **genome**). They are carried by:

- **Mitochondria** : mitochondrial DNA (mtDNA), in almost all eukaryotes.
- **Chloroplasts** and other plastids: chloroplast DNA (cpDNA), in plants and algae.
- **Symbionts and infectious agents** : bacteria or viruses living in the cytoplasm (kappa in *Paramecium*, *Wolbachia* in insects).
- **Plasmids and episomes** : small self-replicating DNA circles (the F factor of *E. coli*, the 2 μ m plasmid of yeast).

The first clear examples came in **1909**, only nine years after Mendel's work was rediscovered, when **Carl Correns** (*Mirabilis jalapa*) and **Erwin Baur** (*Pelargonium*) described leaf-colour traits that did not follow Mendel's laws.

2. How to recognise it

A trait is suspected to be extranuclear when it shows several of these features:

1. **Reciprocal crosses give different results.** A ♀ × B ♂ differs from B ♀ × A ♂, and progeny resemble the mother. This is the single most useful test (sex-linked traits also differ in reciprocal crosses, but in a sex-specific way).
2. **No Mendelian ratios.** No 3:1, 1:2:1 or 1:1 segregation in F₂ or backcrosses.
3. **Not mappable.** The gene shows no linkage to any known nuclear gene or chromosome.
4. **Survives nuclear substitution.** The trait persists after repeated backcrossing to the male parent, which replaces the nuclear genome but keeps the original cytoplasm.
5. **Somatic segregation.** Cells with a mixture of organelle types sort them out during mitosis, giving variegation or mosaics.
6. **Transfer without nuclear change.** The trait can be moved by transplanting cytoplasm or organelles, or by infection.

Feature	Nuclear (Mendelian)	Extranuclear
Location of genes	Chromosomes in the nucleus	Mitochondria, plastids, symbionts, plasmids
Reciprocal crosses	Same result (autosomal genes)	Different; progeny resemble mother
Segregation	Regular in meiosis, fixed ratios	Irregular, no fixed ratios; somatic segregation
Mapping	Map to linkage groups	Cannot be mapped to chromosomes
Copy number per cell	Two (diploid)	Hundreds to thousands
Mixed states	Heterozygote (two alleles)	Heteroplasmy (any proportion)
Nuclear substitution	Trait changes	Trait persists

3. Organelle genomes and their origin

According to the **endosymbiont theory**, championed by **Lynn Margulis** (1967), mitochondria descend from an α -proteobacterium and chloroplasts from a cyanobacterium, each engulfed by an ancestral host cell. Over time most of the symbionts' genes moved into the nucleus (**endosymbiotic gene transfer**), leaving small organelle genomes behind.

Evidence for the theory:

- Organelles have their own circular DNA, not wrapped around histones, like bacteria.
- They divide by binary fission and cannot be made from scratch.
- Their ribosomes are 70S-type (55S in mammalian mitochondria), sensitive to antibiotics such as chloramphenicol and streptomycin.
- Protein synthesis starts with N-formylmethionine, as in bacteria.
- They are enclosed by a double membrane; the inner membrane resembles bacterial membranes (cardiolipin in mitochondria).
- rRNA sequences place mitochondria among the α -proteobacteria and plastids among the cyanobacteria.

Feature	Mitochondrial DNA	Chloroplast DNA
Size	Human 16.6 kb; yeast ≈80 kb; plants ≈200 kb to over 2 Mb	≈120–160 kb in most land plants
Genes	Human: 37 (13 proteins, 22 tRNAs, 2 rRNAs)	≈100–130 (photosynthesis, ribosomal proteins, tRNAs, rRNAs)
Form	Circular (linear in some protists and fungi)	Circular, with two large inverted repeats
Copies per cell	Hundreds to thousands; >100,000 in a human oocyte	Many copies per plastid, many plastids per cell
Genetic code	Variant code (in humans UGA = Trp, AUA = Met, AGA/AGG = stop)	Standard code
Example of shared control	Most respiratory-chain subunits are nuclear-encoded	Rubisco large subunit (<i>rbcL</i>) in cpDNA; small subunit (<i>rbcS</i>) in nucleus

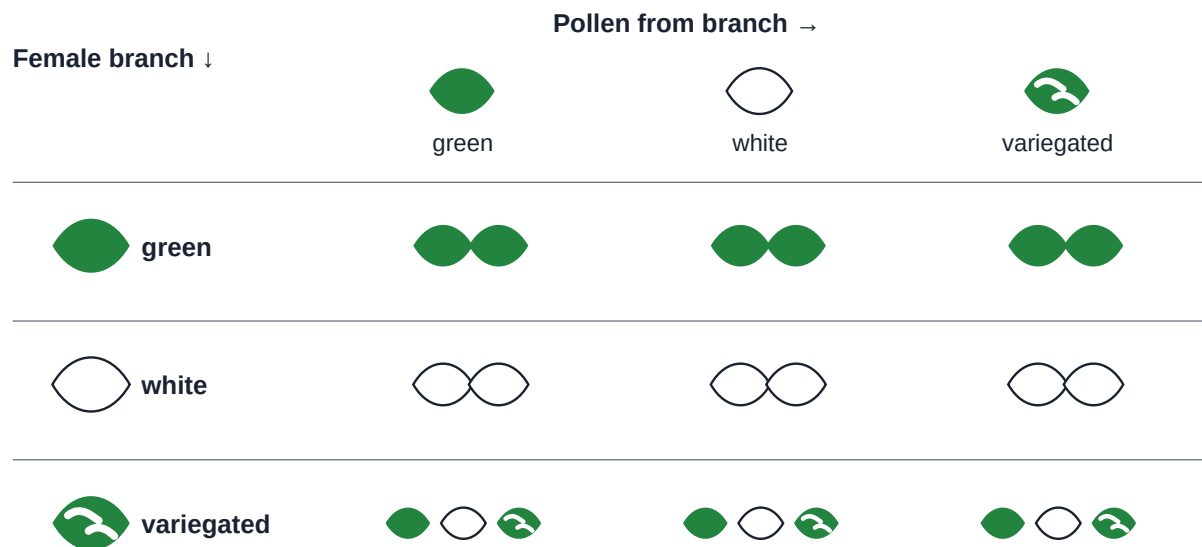
Why this matters for inheritance

Organelles are built jointly by two genomes. A mitochondrial disease or a plastid defect can therefore be caused by a mutation in organelle DNA (inherited maternally) or by a mutation in a nuclear gene for an organelle protein (inherited in a Mendelian way). Only the first is extra-chromosomal.

4. Plastid inheritance

Leaf variegation in *Mirabilis jalapa* (Correns, 1909)

The four o'clock plant often has branches of three kinds: fully green, white (lacking chlorophyll), and variegated. Correns pollinated flowers on each type of branch with pollen from each type and found that the seedlings always took after the **branch bearing the female flower**.



Each row is identical across columns: the pollen parent makes no difference.

Figure 1. Correns's reciprocal crosses in *Mirabilis*. Pollen contributes no plastids, so the egg's plastids decide the seedling's colour. White seedlings lack chlorophyll and die after the seed reserves run out. Variegated mothers pass on eggs with green plastids, white plastids or both, giving all three types in no fixed ratio.

Variegated leaves arise by **somatic segregation**: a cell containing both normal and defective plastids distributes them at random to its daughters at each division, until some cell lineages are left with only one kind and form pure green or pure white patches.

Biparental plastid inheritance in *Pelargonium* (Baur, 1909)

In *Pelargonium zonale* (geranium), plastids enter the zygote from **both** parents. Crosses between green and white plants therefore give some variegated offspring whichever way round the cross is made. Plastid inheritance is maternal in about two-thirds of flowering plants, biparental in some (*Pelargonium*, *Oenothera*), and mostly paternal in conifers.

Iojap in maize (Rhoades, 1943)

A recessive **nuclear** gene, *ij*, makes homozygous *ij/ij* plants striped with white. Once the plastids have been damaged, though, they are inherited maternally and independently of the nucleus: an *Ij/ij* or even *Ij/Ij* plant grown from a striped mother can still be striped. Iojap shows that a nuclear gene can cause a heritable change in the plastid, after which inheritance becomes cytoplasmic.

Streptomycin resistance in *Chlamydomonas* (Ruth Sager, 1954)

The alga *Chlamydomonas reinhardtii* has two mating types, mt^+ and mt^- , whose gametes look alike and contribute equal cytoplasm. Yet in a cross between a streptomycin-resistant and a sensitive strain, almost all progeny inherit the phenotype of the **mt^+** parent, while the

nuclear mating-type gene segregates 2:2 as expected. The mt^- chloroplast DNA is selectively destroyed in the zygote. Inheritance here is uniparental without being maternal, so "uniparental" is the more exact term.

5. Mitochondrial inheritance in fungi

Poky in *Neurospora crassa* (Mitchell and Mitchell, 1952)

Poky is a slow-growing mutant lacking cytochromes *a* and *b* (with excess cytochrome *c*). In *Neurospora* the protoperithecial ("female") parent contributes the cytoplasm, the conidial ("male") parent little more than a nucleus.

- $poky \text{ } \varnothing \times \text{ wild } \sigma \rightarrow \text{all progeny poky.}$
- $\text{wild } \varnothing \times poky \sigma \rightarrow \text{all progeny wild type.}$
- Nuclear markers in the same asci segregate 4:4 (1:1) as usual.

The defect was later traced to mtDNA: a deletion affecting the small subunit mitochondrial rRNA.

Petite mutants in yeast (Ephrussi, 1949)

On glucose medium, *Saccharomyces cerevisiae* occasionally produces **petite** colonies. They cannot respire and survive by fermentation alone. Crossing petites with normal (**grande**) strains revealed three kinds:

Type	Defect	Petite $\times$ grande diploid	Tetrads after meiosis
Segregational (nuclear, <i>pet</i>)	Nuclear gene for a mitochondrial protein	Grande	2 grande : 2 petite (Mendelian)
Neutral (ρ^0)	mtDNA lost completely	Grande	4 grande : 0 petite (mutant mtDNA simply absent)
Suppressive (ρ^-)	Large deletions; the remaining mtDNA is amplified	Mostly petite (varies by strain)	Petite diploids give all-petite tetrads

Suppressive petites "win" because their shortened mtDNA molecules, rich in replication origins, replicate faster and outcompete normal mtDNA in the zygote.

6. Human mitochondrial genetics

The genome

Human mtDNA is a 16,569 bp double-stranded circle (Anderson and colleagues, 1981, the "Cambridge Reference Sequence"). The two strands differ in base composition: the guanine-rich **heavy (H) strand** and the **light (L) strand**. It is extremely compact: no introns, almost no spacer DNA, some genes overlap (*ATP8/ATP6*, *ND4L/ND4*), and some stop codons are completed only by polyadenylation. The only sizeable non-coding stretch is the **D-loop** (control region, ≈ 1.1 kb), which holds the H-strand origin of replication and the promoters for both strands.

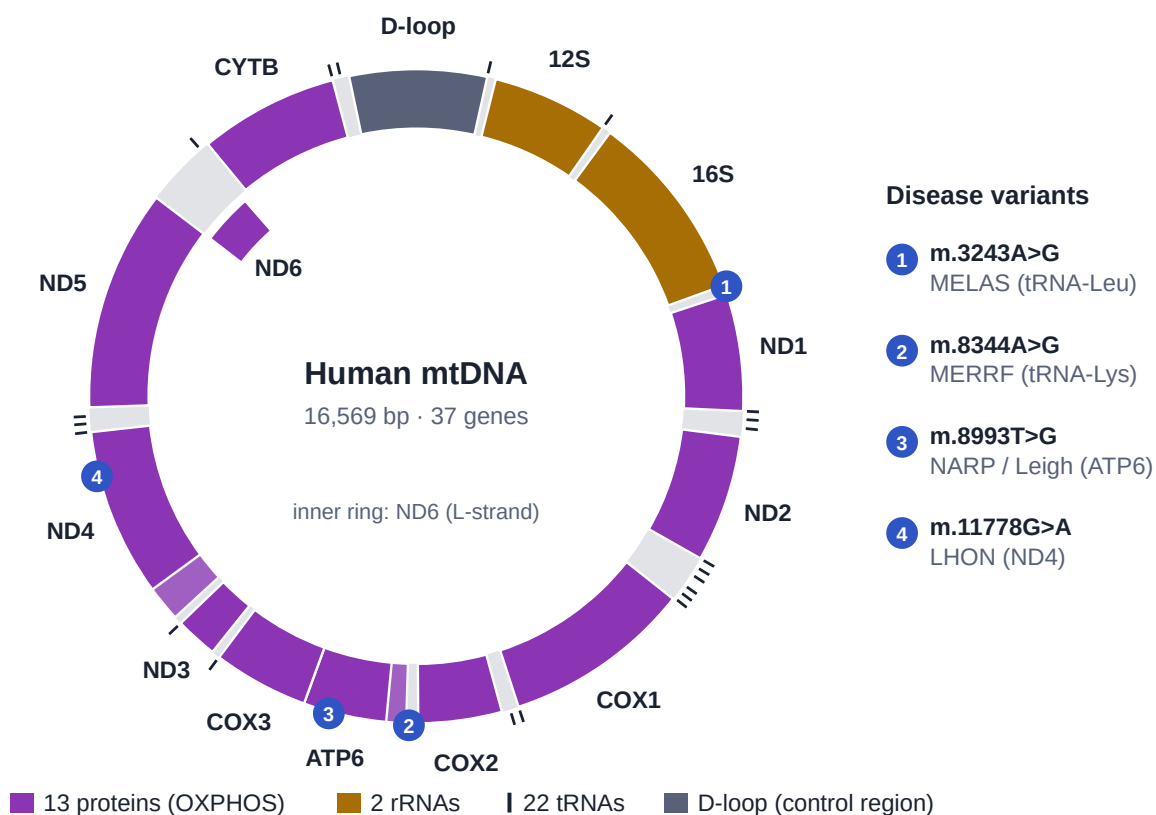


Figure 2. The human mitochondrial genome. Its 13 proteins are all subunits of the oxidative phosphorylation complexes (7 of complex I, 1 of complex III, 3 of complex IV, 2 of ATP synthase); complex II is entirely nuclear-encoded. The other $\approx 1,100$ mitochondrial proteins are made from nuclear genes and imported. Blue dots mark four well-known disease mutations.

mtDNA mutates about 10–20 times faster than nuclear DNA, because it sits close to the respiratory chain's reactive oxygen species, is not protected by histones, and has more limited repair.

Four principles of mitochondrial genetics

1. **Maternal inheritance.** Sperm mitochondria are marked with ubiquitin and destroyed in the early embryo. An affected mother can pass the mutation to all her children; an affected father passes it to none. (Rare cases of paternal leakage have been documented, the best-known reported by Schwartz and Vissing in 2002.)
2. **Heteroplasmy.** A cell can carry a mixture of normal and mutant mtDNA in any proportion. A cell with a single type is **homoplasmic**.
3. **Threshold effect.** Symptoms appear only when the mutant load exceeds a tissue-specific threshold, often 60–90%. Tissues most dependent on ATP, such as brain, heart, skeletal muscle, retina and kidney, cross it first.
4. **Replicative segregation and the bottleneck.** mtDNA copies are distributed randomly at cell division, so heteroplasmy levels drift. During egg formation only a small number of mtDNA genomes repopulate each oocyte, so a mildly affected mother can have children with very different mutant loads.

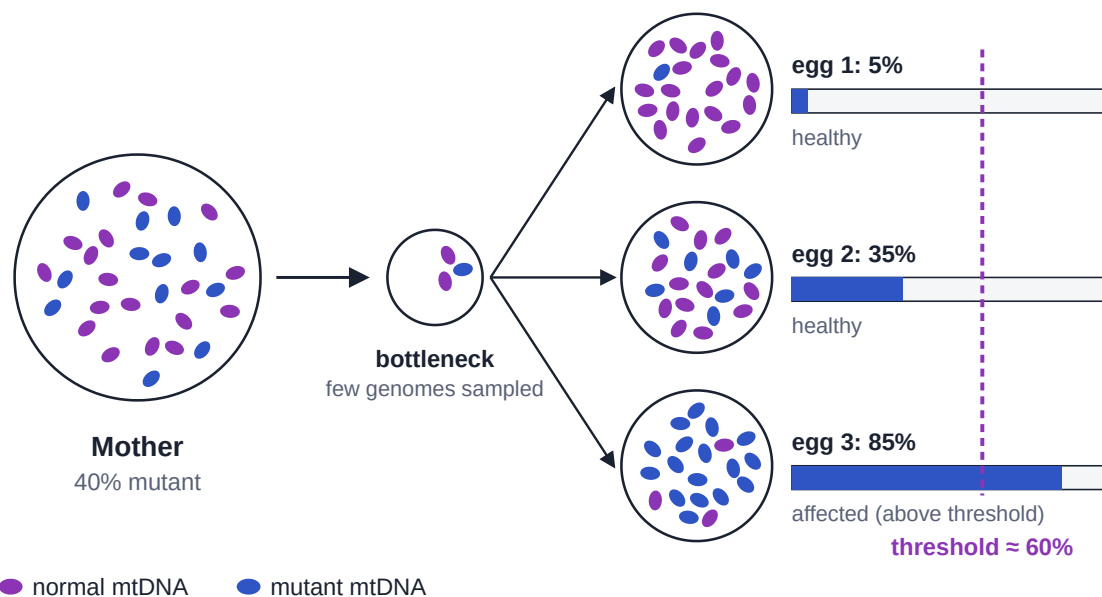


Figure 3. The mitochondrial bottleneck. Random sampling of a few genomes during oogenesis explains why severity varies so widely among the children of one mother, and why families can appear to "skip" affected individuals.

Reading a pedigree

Suspect mtDNA inheritance when affected mothers transmit to both sons and daughters, affected fathers never transmit, and severity varies widely within the family. Contrast X-linked inheritance, where affected fathers transmit to all daughters.

Mitochondrial diseases

Disease	Typical mutation	Features
LHON (Leber hereditary optic neuropathy)	Point mutations in complex I genes, commonest m.11778G>A in <i>ND4</i> ; usually homoplasmic	Sudden, painless loss of central vision in young adults; incomplete penetrance, men affected about four times as often as women
MELAS	m.3243A>G in tRNA ^{Leu(UUR)}	Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes
MERRF	m.8344A>G in tRNA ^{Lys}	Myoclonic epilepsy with ragged-red fibres in muscle biopsy
NARP / maternally inherited Leigh syndrome	m.8993T>G in <i>ATP6</i>	Neuropathy, ataxia, retinitis pigmentosa at moderate load; Leigh syndrome (subacute necrotising encephalopathy) at very high load
Kearns–Sayre syndrome	Single large mtDNA deletion (often ≈5 kb), usually sporadic	Onset before 20: ophthalmoplegia, pigmentary retinopathy, heart block

Ragged-red fibres are muscle fibres in which abnormal mitochondria accumulate under the membrane, staining red with modified Gomori trichrome. Mitochondrial dysfunction also contributes to ageing, and somatic mtDNA deletions accumulate in old tissues.

Mitochondrial replacement therapy

To stop a woman passing on pathogenic mtDNA, her nuclear genetic material can be moved into a donor egg (or zygote) whose own nucleus has been removed, by **maternal spindle transfer** or **pronuclear transfer**. The child has nuclear DNA from both parents and mitochondria from the donor, the so-called "three-parent baby". The UK legalised the technique in 2015, and in 2025 the Newcastle team reported the births of eight children conceived by pronuclear transfer. The method prevents only mtDNA-encoded disease; it cannot help if the defect is in a nuclear gene for a mitochondrial protein.

mtDNA as a tool

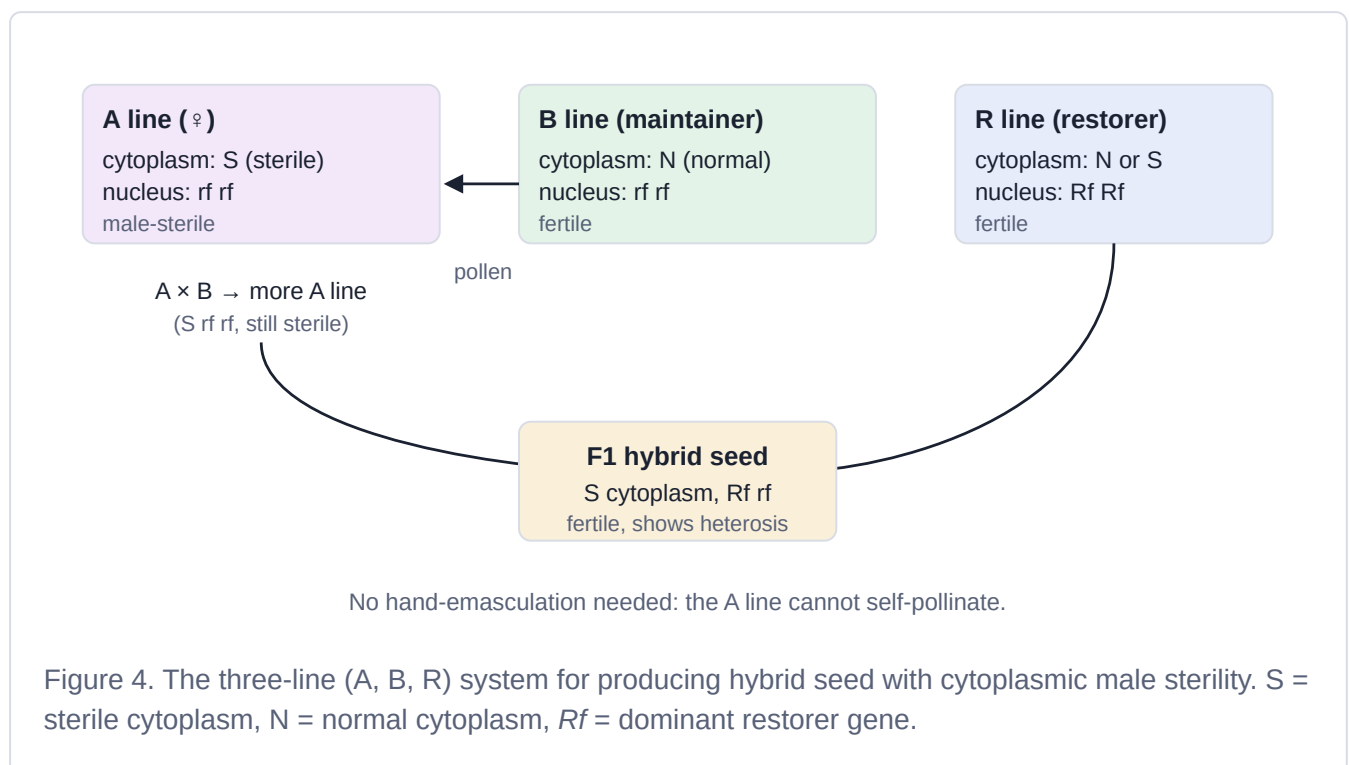
Maternal inheritance, lack of recombination and a fast mutation rate make mtDNA ideal for tracing lineages. Comparing mtDNA from populations worldwide traced all living humans' mtDNA to a common female ancestor in Africa, about 150,000–200,000 years ago ("mitochondrial Eve"; Cann, Stoneking and Wilson, 1987). Forensic scientists use mtDNA

from hair shafts, bones and degraded remains, which have many copies of mtDNA even when nuclear DNA is lost; the remains of the Russian royal family were identified this way.

7. Cytoplasmic male sterility (CMS)

In many crop plants a mitochondrial gene causes **pollen sterility** while the female organs remain normal. Because the trait is carried in mitochondria, it is inherited maternally. CMS arises from novel, rearranged mitochondrial open reading frames. It can be cancelled by dominant nuclear **restorer-of-fertility (Rf)** genes, a clear example of nuclear–cytoplasmic interaction.

Breeders exploit CMS to make hybrid seed without the labour of removing anthers by hand. The approach was first used in onion (Jones and Clarke, 1943) and is now standard in maize, rice, sorghum, sunflower and many vegetables.



A warning from 1970

By the late 1960s most US hybrid maize was made using Texas (T) male-sterile cytoplasm. T-cytoplasm carries the mitochondrial gene *T-urf13*, whose protein made the plants vulnerable to a toxin from race T of the fungus *Bipolaris maydis* (*Helminthosporium maydis*). The Southern corn leaf blight epidemic of 1970 destroyed about 15% of the US crop. Every hybrid shared the same cytoplasm, so different nuclear backgrounds gave no protection. The episode remains the textbook case for the dangers of genetic uniformity.

8. Infectious heredity

Some cytoplasmic traits are caused by symbiotic or parasitic organisms that are passed from mother to offspring through the egg cytoplasm.

Kappa particles in *Paramecium* (Sonneborn, 1943)

"Killer" strains of *Paramecium aurelia* release a toxin (paramecin) that kills "sensitive" strains. Killers carry cytoplasmic particles called **kappa**, now known to be bacteria (*Caedibacter taeniospiralis*) whose toxic protein is made in refractile "R bodies". Kappa survives only in cells with at least one dominant nuclear allele **K**: kappa needs K, and killing needs both.

- **Short conjugation** (only nuclei exchanged): $KK + \text{kappa} \times kk \text{ sensitive} \rightarrow \text{both exconjugants } Kk$. The one with killer cytoplasm stays a killer; the other stays sensitive.
- **Long conjugation** (cytoplasm exchanged too): both exconjugants receive kappa and become killers.
- **Autogamy** of a Kk killer gives KK and kk cells in equal numbers. The kk cells lose kappa over successive divisions and become sensitive.

Other examples

Trait	Organism	Agent	Effect
CO₂ sensitivity	<i>Drosophila</i>	Sigma virus (a rhabdovirus), L'Héritier	Flies become paralysed and die after exposure to CO ₂ ; passed mainly through the egg
Sex ratio	<i>Drosophila willistoni</i> and relatives	<i>Spiroplasma</i> bacteria	Male embryos die; broods are nearly all female
Cytoplasmic incompatibility	Many insects	<i>Wolbachia</i> bacteria	Infected males' sperm fail with uninfected eggs; used to control dengue-carrying mosquitoes
Milk factor	Mice	Mouse mammary tumour virus (Bittner, 1936)	Mammary cancer passed to pups through milk, so it follows the foster mother, not the genetic mother

9. Plasmids and episomes

Plasmids are small, usually circular, self-replicating DNA molecules separate from the main chromosome. They carry non-essential but often valuable genes: antibiotic resistance (**R plasmids**), toxin production, sugar metabolism, or conjugation (**F factor**). An **episome** (Jacob and Wollman, 1958) is a plasmid that can either replicate on its own in the cytoplasm or integrate into the host chromosome. The F factor is the classic example: free in F^+ cells, integrated in Hfr cells. The yeast **2 μ m plasmid** is a eukaryotic example, and plasmids are the workhorses of recombinant DNA technology.

10. Look-alikes: maternal effect and imprinting

Some nuclear genes also make offspring resemble their mother. These are not extra-chromosomal, and telling them apart is a favourite exam question.

Maternal effect: shell coiling in *Limnaea peregra*

The pond snail's shell coils either to the right (**dextral**, allele D , dominant) or to the left (**sinistral**, d). Boycott and Diver described the pattern, and Sturtevant explained it in 1923. The direction of coiling is fixed by the orientation of the spindle in the **first cleavage divisions**, which is controlled by gene products the mother deposited in the egg. So the **phenotype of an individual depends on its mother's genotype**, not its own.



Figure 5. Maternal effect in *Limnaea*. The expected Mendelian 3:1 ratio does appear, but one generation late and among families rather than individuals. That delay is what separates a maternal effect from cytoplasmic inheritance, where the maternal pattern continues in every generation.

Other maternal-effect genes include *bicoid* in *Drosophila*, whose mRNA is placed at the anterior pole of the egg and sets up the head-to-tail axis, and the eye-pigment case in the moth *Ephesia*, where kynurenine supplied by an *A*-bearing mother temporarily colours the larvae of *aa* offspring.

Genomic imprinting

For a few nuclear genes, only the copy from one parent is active, because of DNA methylation marks laid down in the egg or sperm. A deletion at chromosome 15q11-q13 causes **Prader-Willi syndrome** when inherited from the father and **Angelman syndrome** when inherited from the mother.

Feature	Cytoplasmic inheritance	Maternal effect	Sex linkage
Genes located in	Organelles, symbionts	Nucleus (autosomal)	Nucleus (sex chromosomes)
Offspring phenotype set by	Mother's cytoplasm	Mother's nuclear genotype	Offspring's own genotype

Feature	Cytoplasmic inheritance	Maternal effect	Sex linkage
Reciprocal crosses	Differ; follow mother	Differ in F ₁	Differ, with sons and daughters differing
Mendelian ratios	Never	Yes, delayed one generation	Yes, sex-specific
Persistence	Every generation through the female line	Only one generation	Follows X or Z chromosome
Example	<i>Mirabilis</i> , <i>poky</i> , LHON	<i>Limnaea</i> coiling, <i>bicoid</i>	Haemophilia, white eye in <i>Drosophila</i>

11. Quick revision

Remember	Fact
First examples	Correns (<i>Mirabilis</i> , maternal) and Baur (<i>Pelargonium</i> , biparental), 1909
Key test	Reciprocal crosses differ, and the progeny follow the mother
Human mtDNA	16,569 bp; 37 genes: 13 polypeptides, 22 tRNAs, 2 rRNAs; D-loop
Terms	Plasmon, plasmagene, heteroplasmy, homoplasmy, threshold, bottleneck
Uniparental, not maternal	<i>Chlamydomonas</i> : chloroplast genes from mt ⁺ parent
Yeast petites	Segregational (2:2), neutral (4:0 grande), suppressive (mostly petite)
<i>Neurospora</i>	<i>poky</i> : follows the protoperithecial parent
Nuclear gene → plastid defect	lojap in maize
Infectious heredity	Kappa (needs K), sigma virus, <i>Spiroplasma</i> , <i>Wolbachia</i> , milk factor
Maternal effect	<i>Limnaea</i> ; Mendelian ratio delayed by one generation

Remember	Fact
CMS	Mitochondrial; restored by nuclear <i>Rf</i> ; T-cytoplasm and 1970 blight

12. End-semester question bank

Long answer (10–15 marks)

1. What is extra-chromosomal inheritance? Describe its characteristic features and explain how it can be distinguished from chromosomal inheritance, with suitable examples.
2. Describe plastid inheritance with reference to *Mirabilis jalapa*, *Pelargonium*, iojap in maize and *Chlamydomonas*.
3. Give an account of mitochondrial inheritance in *Neurospora* and yeast. Explain the different types of petite mutants and how they behave in crosses.
4. Describe the organisation of the human mitochondrial genome. Explain heteroplasmy, the threshold effect and the mitochondrial bottleneck, and discuss mitochondrial diseases in humans.
5. Distinguish between maternal inheritance and maternal effect, with a detailed account of shell coiling in *Limnaea*.
6. What is cytoplasmic male sterility? Explain its genetic basis, the role of restorer genes and its use in hybrid seed production.
7. Write an essay on infectious heredity, with special reference to kappa particles in *Paramecium*.
8. Discuss the endosymbiont theory and the evidence that mitochondria and chloroplasts have their own genetic systems.

Short notes (5 marks)

1. Plasmon and plasmagones
2. Leaf variegation in *Mirabilis*
3. *Poky* mutant of *Neurospora*
4. Petite mutants in yeast
5. Heteroplasmy
6. Leber hereditary optic neuropathy
7. Mitochondrial replacement therapy

8. Kappa particles
9. Episomes
10. Sigma virus and CO₂ sensitivity in *Drosophila*

Differentiate between

1. Chromosomal and extra-chromosomal inheritance
2. Maternal inheritance and maternal effect
3. Neutral and suppressive petites
4. Heteroplasmy and homoplasmy
5. Short and long conjugation in *Paramecium*
6. mtDNA and cpDNA

Draw and label

1. The human mitochondrial genome
2. Reciprocal crosses in *Mirabilis jalapa*
3. Crosses showing shell coiling in *Limnaea* up to F₃
4. The three-line system of hybrid seed production

Problems

1. A dextral *Limnaea* snail, when selfed, produces only sinistral offspring. What are its genotype and its mother's genotype?
2. A *Chlamydomonas* strain that is streptomycin-resistant and mt⁻ is crossed with a sensitive mt⁺ strain. Predict the phenotypes of the progeny and the ratio of mating types.
3. A woman with 30% heteroplasmy for m.3243A>G has three children. Explain why their mutant loads might be 5%, 40% and 90%.

▼ Answers to problems and very short questions

Problems. (1) Its offspring are sinistral, so it must be *dd*; it is dextral because its mother carried *D* (*Dd* or *DD*; since it received *d* from her, she was *Dd*). (2) All progeny are streptomycin-sensitive (chloroplast genes come from mt⁺); mating types segregate 1 mt⁺ : 1 mt⁻. (3) The mitochondrial bottleneck during oogenesis samples only a few mtDNA genomes into each egg, so loads drift randomly in both directions.

1. Who described plastid inheritance in *Mirabilis*? **Carl Correns, 1909**
2. Size of human mtDNA? **16,569 bp**

3. Number of polypeptides encoded by human mtDNA? **13**
 4. Non-coding control region of mtDNA? **D-loop**
 5. Bacterium responsible for the killer trait in *Paramecium*? ***Caedibacter (kappa)***
 6. Nuclear gene needed to maintain kappa? **K (dominant)**
 7. Petite type whose mtDNA is completely lost? **Neutral (ρ^0)**
 8. Gene responsible for T-cytoplasm male sterility in maize? ***T-urf13***
 9. Agent of CO₂ sensitivity in *Drosophila*? **Sigma virus**
 10. The codon UGA in human mitochondria codes for? **Tryptophan**
 11. Who proposed the endosymbiont theory in its modern form? **Lynn Margulis**
 12. Organism in which Sager showed uniparental chloroplast inheritance? ***Chlamydomonas reinhardtii***
-

13. Case-based MCQs

Ten hard questions that test application rather than recall. Choose an answer before opening the explanation.

Q1. A three-generation family shows a progressive muscle disorder. Every child of affected women is affected to some degree, ranging from mild exercise intolerance to severe encephalopathy. None of the children of two affected men are affected. The pattern and its variability are best explained by:

- A. X-linked dominant inheritance with variable expressivity
- B. Mitochondrial inheritance with heteroplasmy and a threshold effect
- C. Autosomal dominant inheritance with genomic imprinting
- D. Autosomal recessive inheritance with consanguinity

▼ **Show answer**

Answer: B. Transmission only through females to children of both sexes is the signature of mtDNA inheritance. X-linked dominant inheritance is ruled out because affected fathers would pass it to all daughters. The wide range of severity reflects different proportions of mutant mtDNA (heteroplasmy) produced by the bottleneck, and different tissues crossing their thresholds.

Q2. In *Neurospora crassa*, a slow-growing strain is used as the protoperithecial parent with a wild-type conidial parent: all progeny are slow-growing. The reciprocal cross gives all wild-type progeny. A nuclear marker in the same asci segregates 4:4. The most valid conclusion is:

- A. The slow-growth gene is tightly linked to the centromere
- B. The trait is controlled by a maternal-effect nuclear gene
- C. The trait is determined by a cytoplasmic (mitochondrial) factor contributed by the protoperithecial parent
- D. The trait is sex-linked

▼ Show answer

Answer: C. This is the *poky* pattern. The protoperithecial parent supplies nearly all the cytoplasm. The normal 4:4 segregation of the nuclear marker proves meiosis was regular, so the absence of any segregation for slow growth means the trait is not in the nucleus. A maternal-effect gene would still segregate in the next generation.

Q3. A yeast petite is crossed with a grande strain. The diploids are all grande. After sporulation every tetrad contains four grande spores. The petite was most likely:

- A. Segregational (nuclear pet mutation)
- B. Neutral (ρ^0), lacking mtDNA
- C. Suppressible (ρ^-)
- D. A respiration-competent revertant

▼ Show answer

Answer: B. A segregational petite would give 2:2 tetrads. A suppressible petite would make many diploids petite. In a neutral petite the mutant mtDNA is absent, so the grande parent's mtDNA fills the zygote and all spores are grande: the petite trait simply disappears.

Q4. A sinistrally coiled *Limnaea* snail is self-fertilised and all its offspring are dextral. Which is the snail's genotype?

- A. dd
- B. DD
- C. Dd
- D. It cannot be determined without its offspring's genotypes

▼ **Show answer**

Answer: C. Coiling depends on the mother's genotype. The offspring are dextral, so this snail carries at least one *D*. It is itself sinistral, so its own mother was *dd*, meaning it must have received a *d* from her. The only genotype consistent with both is *Dd*.

Q5. Pollen from a flower on a variegated branch of *Mirabilis jalapa* is used to fertilise a flower on an all-green branch. The seedlings will be:

- A. All green
- B. Green, white and variegated in no fixed ratio
- C. Green and white in a 3:1 ratio
- D. All variegated

▼ **Show answer**

Answer: A. In *Mirabilis* plastids come only through the egg. The female flower is on a green branch, so every seedling receives only green plastids, whatever the pollen carried.

Q6. A streptomycin-resistant mt^+ *Chlamydomonas* strain is crossed with a sensitive mt^- strain. Nearly all progeny are resistant, and mating type segregates 1:1. The reciprocal cross gives nearly all sensitive progeny. The best explanation is:

- A. Streptomycin resistance is a maternal-effect nuclear trait
- B. The resistance gene is in chloroplast DNA, and the mt^- chloroplast genome is degraded in the zygote
- C. The resistance gene is linked to the mating-type locus
- D. Resistance is caused by an infectious symbiont

▼ Show answer

Answer: B. Sager's experiments showed that chloroplast genes are transmitted by the mt^+ parent even though both gametes contribute equal cytoplasm. If the gene were linked to mating type, resistance would segregate 1:1 with it; it does not. This is uniparental, not strictly maternal, inheritance.

Q7. A *Paramecium* killer of genotype *KK* (with kappa) undergoes short conjugation with a sensitive *kk* cell. The exconjugant from the killer cell then undergoes autogamy. What fraction of the resulting clones will eventually be killers?

- A. All
- B. One-half
- C. One-quarter
- D. None

▼ Show answer

Answer: B. Short conjugation exchanges only nuclei, so both exconjugants become *Kk*, and the killer's exconjugant keeps its kappa. Autogamy makes a *Kk* cell homozygous: half become *KK* and half *kk*. Kappa cannot be maintained without *K*, so the *kk* clones lose it and become sensitive, leaving one-half as killers.

Q8. A woman with 20% m.3243A>G in her blood is healthy. Her son has severe MELAS, and a muscle biopsy shows 85% mutant mtDNA. The best explanation for the difference is:

- A. A new mutation arose in the son
- B. Paternal transmission of the mutation
- C. Random drift in the mtDNA bottleneck during oogenesis, together with tissue-specific segregation
- D. Genomic imprinting of the mitochondrial genome

▼ **Show answer**

Answer: C. Only a small sample of mtDNA genomes repopulates each egg, so a child's starting load can differ greatly from the mother's. Loads then differ again between tissues, and blood often shows lower levels of m.3243A>G than muscle. mtDNA is not imprinted, and paternal transmission is extremely rare.

Q9. During the 1970 Southern corn leaf blight epidemic, hybrids from many different breeding programmes, with very different nuclear backgrounds, were all susceptible. The most direct reason is that:

- A. They all carried the same recessive nuclear susceptibility allele
- B. They were all produced using Texas male-sterile cytoplasm, whose mitochondrial *T-urf13* product is the toxin target
- C. The fungus infected only plants lacking restorer genes
- D. The fungus was transmitted through the seed cytoplasm

▼ **Show answer**

Answer: B. Susceptibility was inherited through the mitochondria of the T-cytoplasm female line, which almost every hybrid shared. Nuclear diversity could not protect them. Restorer genes restore pollen fertility but do not remove the URF13 protein's sensitivity to the toxin.

Q10. A couple opts for pronuclear transfer to prevent a mitochondrial disease in their child. In which case would the procedure **not** prevent the disease?

- A. The mother carries m.8993T>G in *ATP6* at high heteroplasmy
- B. The mother carries m.3243A>G
- C. The disease is Leigh syndrome caused by biallelic mutations in the nuclear gene *SURF1*
- D. The mother has homoplasmic m.11778G>A (LHON)

▼ **Show answer**

Answer: C. Pronuclear transfer replaces the mother's mitochondria with a donor's but keeps both parents' nuclear DNA. It can only prevent diseases caused by mtDNA variants. *SURF1* is a nuclear gene for a complex IV assembly factor, so its mutations are inherited in the normal autosomal recessive way and are unaffected by swapping mitochondria.

For further reading: Griffiths et al., *Introduction to Genetic Analysis*; Snustad and Simmons, *Principles of Genetics*; Russell, *iGenetics*; Strickberger, *Genetics*.