Other genomes: Extrachromosomal inheritance

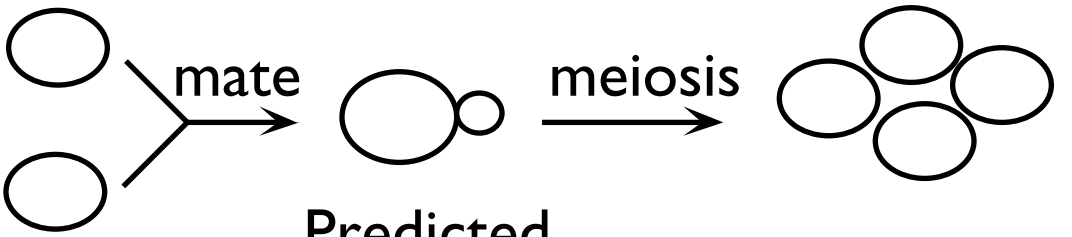
Discovery of **cytoplasmic inheritance**

Boris Ephrussi, ~1949: Genetics of respiration in yeast

- Respiration: oxidative breakdown of nutrients to release energy; coupled to ATP synthesis to allow cells to use the released energy
- Site of oxidative phosphorylation:
- "**Petite**" and "**grande**" yeast

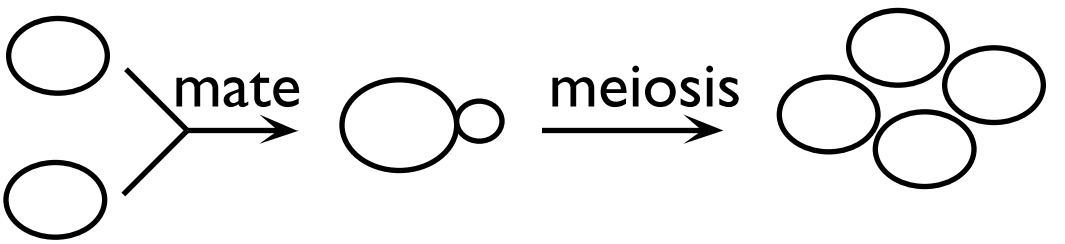
Two kinds of "petite" mutations:

- Normal **Mendelian** inheritance



Predicted genotype:

- **Non-Mendelian** inheritance



Ephrussi's explanation: cytoplasmic inheritance; predicted "rho factor" in mitochondria

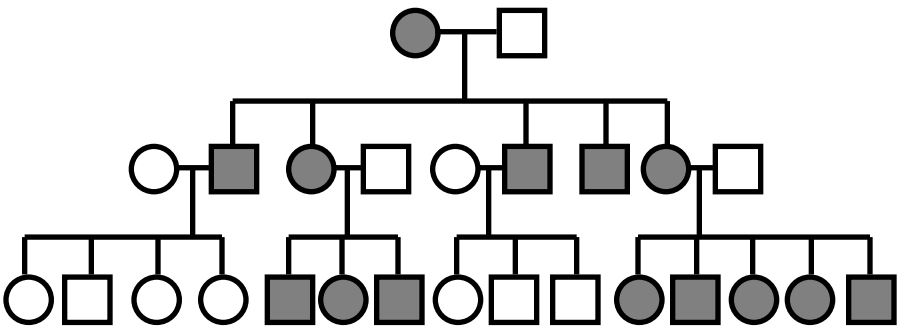
The mitochondrial genome

- Yeast

- Human
  - 37 genes

  - Expression coordinated with nuclear genes

Maternal inheritance of mtDNA



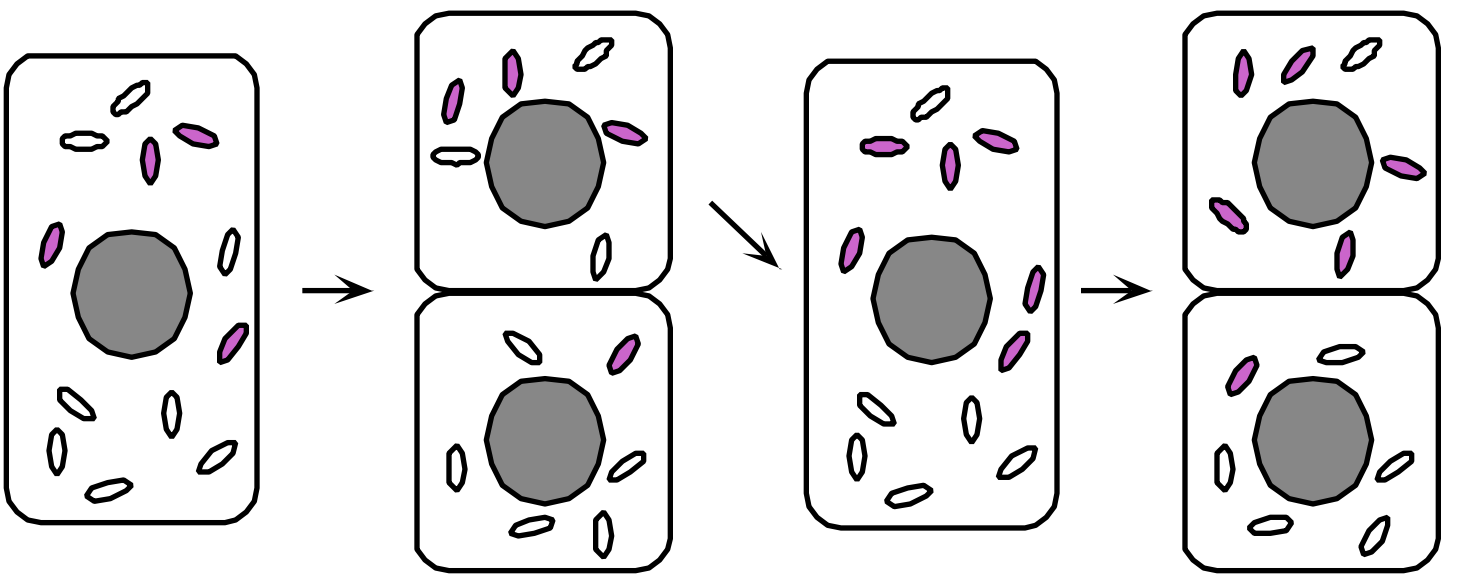
Explanation: Mitochondrial contribution of sperm vs. egg

Mitochondrial DNA disorders in humans

- inherited
- spontaneous mutations in egg or early embryo
- somatic mutations during the life of the individual

But with >>100's of mtDNAs per cell, how could sporadic (recessive) changes give a disease phenotype?

- Cumulative changes –
- Impaired central function (e.g., protein synthesis)
- Random segregation of mitochondria: **homoplasmy** from **heteroplasmy**

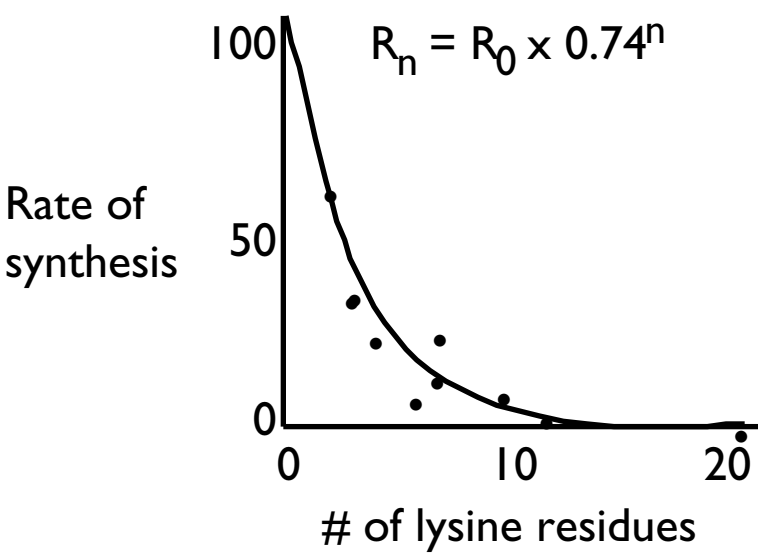


MERRF (Myoclonic epilepsy and ragged red fibers):

Defect:

non-functional lysine tRNA ($tRNA^{Lys}$)

Different proteins affected to different extents:



Interaction with the environment

- Nonsyndromic deafness
- Mutation: A1555G — in 12S rRNA gene
- Variable age-of-onset, severity
- Common thread? Correlation between manifestation of disorder and treatment with aminoglycosides

Why the high mutation rate?

- little or no DNA repair, poor error-correction
- proximity of oxidative phosphorylation centers – free radicals!
- A connection with aging?

Practical applications

- Forensics
- Tracing population migrations