Endosymbiotic gene transfer:
mechanisms and forces involved.

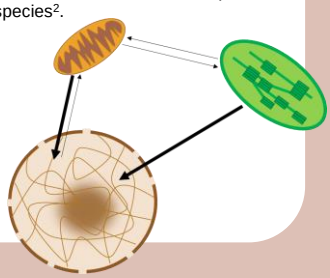
Alejandro Allo Anido, Bachelor's Degree in Genetics, Universitat Autònoma de Barcelona, Barcelona, Spain 2018

Introduction

Endosymbiotic gene transfer (EGT) refers to the flux of genes between the nucleus, mitochondria and chloroplasts[1].

EGT has followed different rates along evolution, and, therefore, the present organellar genetic content varies between species[2].

Animals are the most static group, where total transfer is no longer taking place[3]. However, fragments of mtDNA continue to insert into the nuclear genome, giving rise to theoretically inactive sequences known as nuclear insertions of mitochondrial origin (NUMTs)[4].



Objectives

1. Exposing the hypothesis stated for the transfer or maintenance of mitochondrial genes.
2. Explaining the mechanism proposed for EGT.
3. Presenting some examples of transferred genes.
4. Asses if NUMT-contained pseudogenes are being expressed.

Methodology

The bibliography used in this work was obtained from PubMed database, searching for reviews with the terms "mitochondria" OR "mitochondrial" AND "gene transfer" OR "endosymbiotic transfer" in their Title/Abstract.

Additionally, several online databases and tools were used as a source of information and to align sequences: GTEx portal, Ensembl, USCS Genome Browser, Clustal Omega, Blast and ExPASy Translate Tool.

State of the art and results

Forces involved in EGT

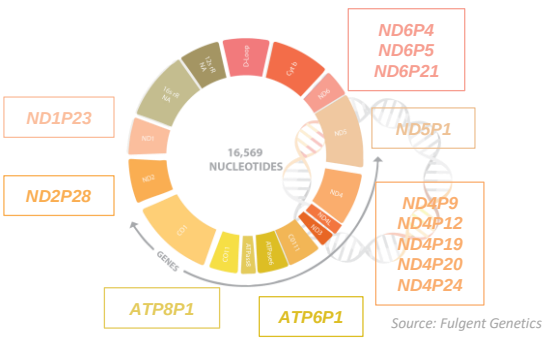
Favoring EGT:

- Reactive oxygen species (ROS)[3].
- Muller's ratchet[3,5].
- Fixation of beneficious mutations at nucleus[5].
- Mitochondrial streamlining[3,5].

Preventing EGT:

- Hydrophobicity[1,3].
- Differences in genetic code[3].
- Toxicity at cytosol[3].
- Colocation of gene and gene product for redox regulation of gene expression (CoRR)[1,3].

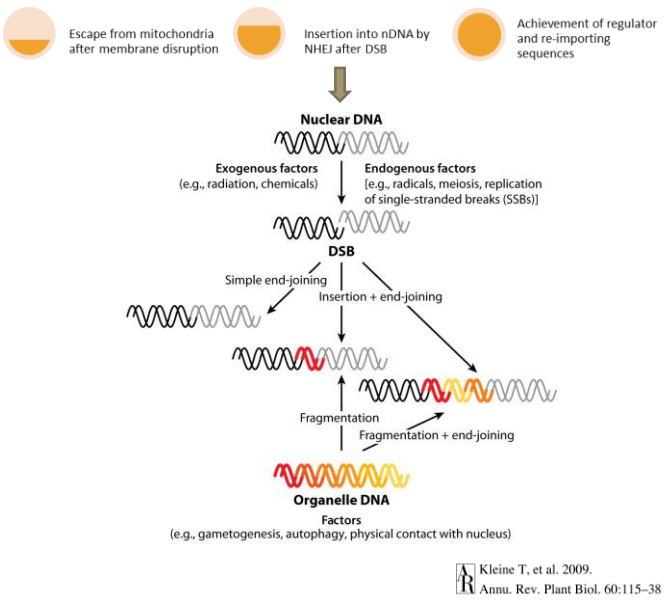
Expression of NUMT-contained pseudogenes



Source: Fulgent Genetics

CODE FOR ORIGINAL PROTEIN	CONTAINED WITHIN OTHER GENE	NEW CYTOPLASMIC FUNCTION
NUMT-contained genes could have reverted the amino acidic changes inherent in the genetic code's differences. *Most of the NUMTs have an identity higher than 90% with mtDNA.* *But none of the genes revert back to the mitochondrial protein.*	Transcripts of other genes may have been assigned to these pseudogenes because the latter are contained in the coding region of the former. *However, all of them are located in intergenic, intronic or reverse complementary sequences.*	NUMT-contained genes may be genuinely expressed because they code for a functional product with a new role. *ND2P28 GREBP (94% id./100% qc)* *ATP8P1 DC48 (90% id./37% qc)*

Mechanism of EGT



Kleine T, et al. 2009. Annu. Rev. Plant Biol. 60:115–38

Conclusions

Different forces have acted to promote EGT or keep some mitochondrial genes from being transferred to the nucleus. Not all of them have constrained the same set of genes or had a prominent role along eukaryotic evolution. Additionally, most of these forces are not applicable to plant organelles, whose genes seem to be transferred in a mainly neutral manner.

Once released from the organelle because of membrane disruption, mtDNA can be inserted into the nuclear genome by NHEJ after DSB. If regulatory and targeting sequences are acquired, the transferred genes can be expressed, its product re-imported, and the mitochondrial gene replaced—although alternative outcomes are possible.

The current opinion about NUMT-contained pseudogenes may be wrong, as some of them are being expressed and give rise to products that may have taken a cytoplasmic role.

1. Kleine T, Maier UG, Leister D. DNA Transfer from Organelles to the Nucleus: The Idiosyncratic Genetics of Endosymbiosis. Annu Rev Plant Biol. 2009;60(1):115–38.
2. Timmis JN, Ayliff MA, Huang CY, Martin W. Endosymbiotic gene transfer: Organelle genomes forge eukaryotic chromosomes. Nat Rev Genet. 2004;5(2):123–35.
3. Adams KL, Palmer JD. Evolution of mitochondrial gene content: Gene loss and transfer to the nucleus. Mol Phylogenet Evol. 2003;29(3):380–95.
4. Ramos A, Barbena E, Mateiu L, del Mar González M, Mairal Q, Lima M, et al. Nuclear insertions of mitochondrial origin: Database updating and usefulness in cancer studies. Mitochondrion. 2011;11(6):946–53.
5. Blanchard JL, Lynch M. Organellar genes why do they end up in the nucleus? Trends Genet. 2000;16(7):315–20.