Aplicación del estudio evolutivo del proteoma mitocondrial a la identificación de genes implicados en enfermedades.

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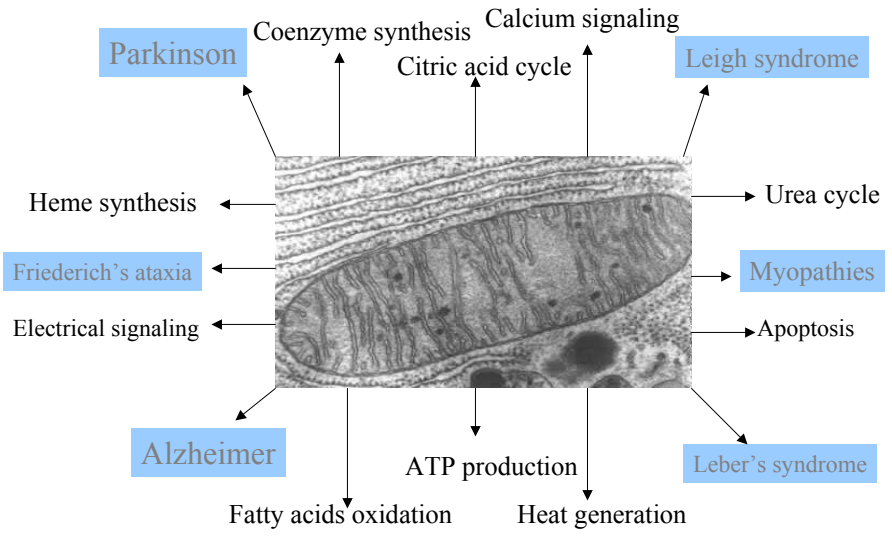
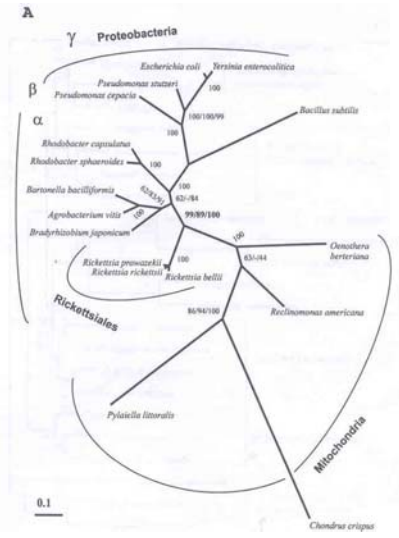
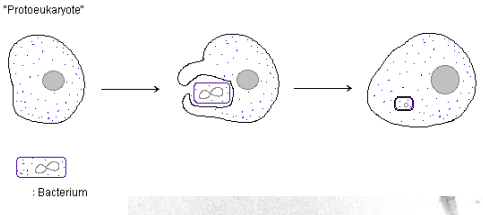
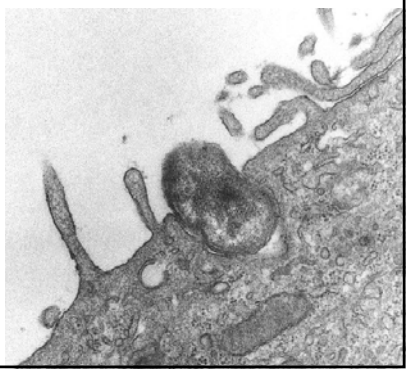
PRINCIPE FELIPE
CENTRO DE INVESTIGACION



Mitochondria originated from the endosymbiosis of an alpha-proteobacterium

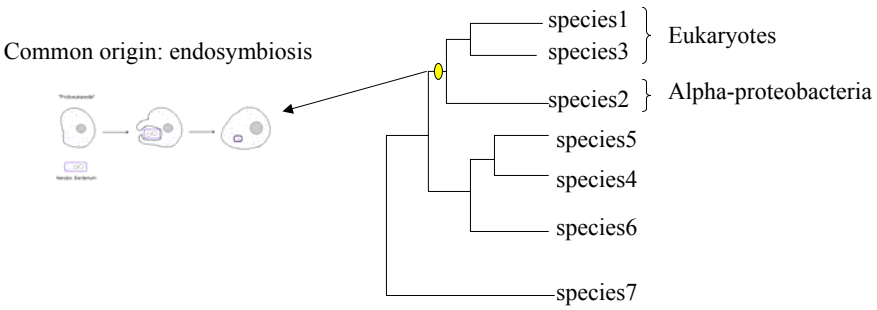


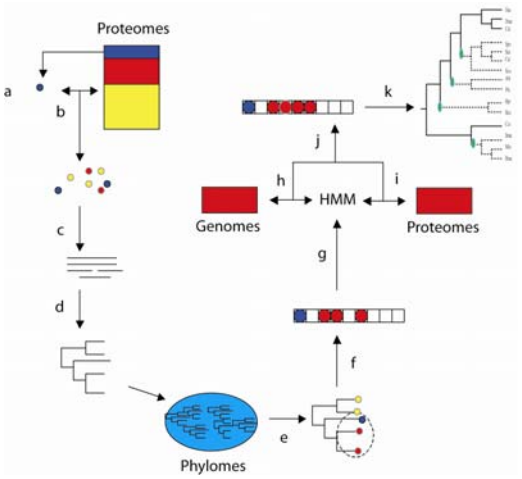




Our approach:

Identify eukaryotic proteins with a likely alpha-proteobacterial origin based on its phylogeny.



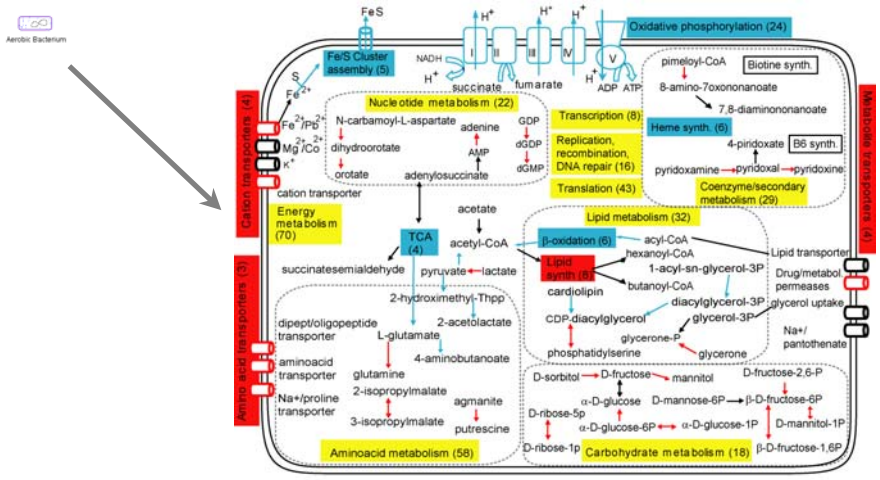


RESULTS:

species	size	Selected	%	Groups
Rickettsia provazekii	835	196	23,5	173
Rickettsia conorii	1374	235	17,1	192
Caulobacter crescentus	3718	668	17,9	480
Brucella melitensis	3188	578	18,1	403
Rhizobium loti	7260	969	13,3	516
Rhizobium meliloti	6150	821	13,3	446

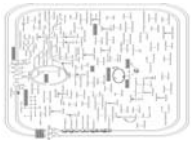
Non-redundant orthologous groups: 630

Reconstruction of an ancestral metabolism

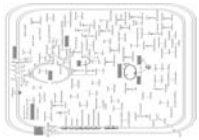


Gabaldón T. and Huynen M. *Science* (2003)

Proto-mitochondrion

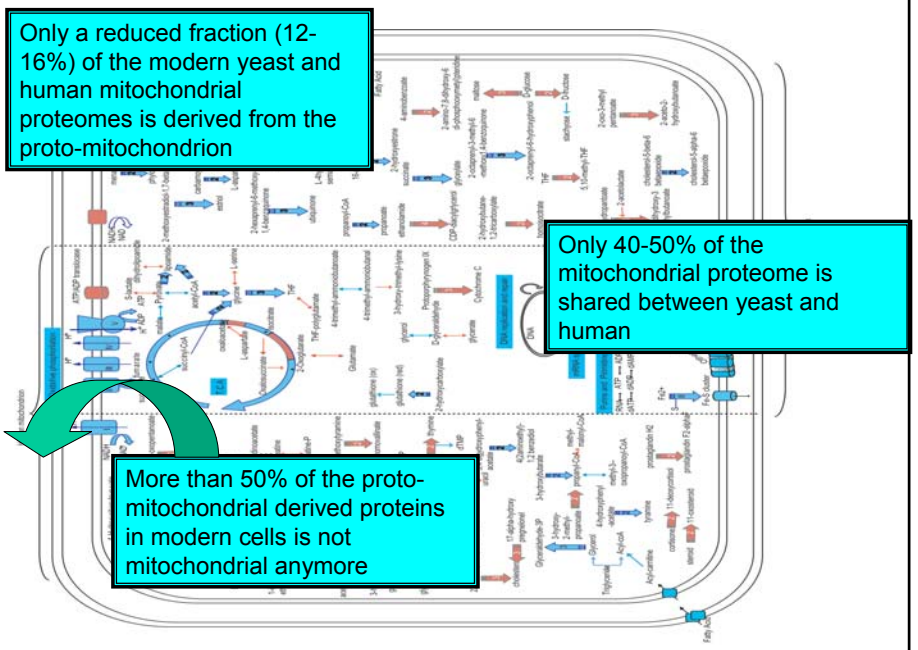


Yeast mitochondria

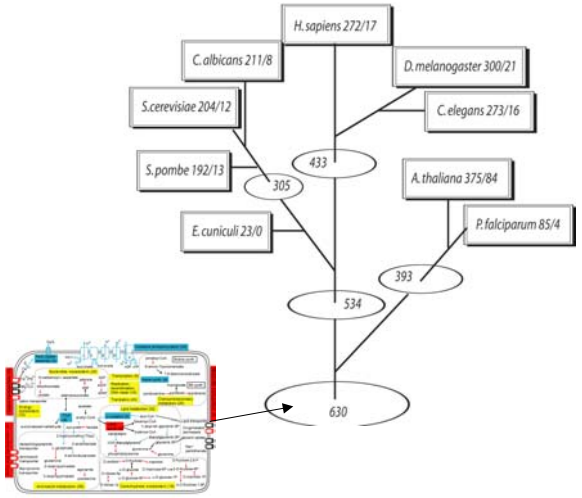


Human mitochondria

Proteomics



Eukaryotes underwent extensive lineage-specific gene loss of the proto-mitochondrial derived set (2,98 losses/family)

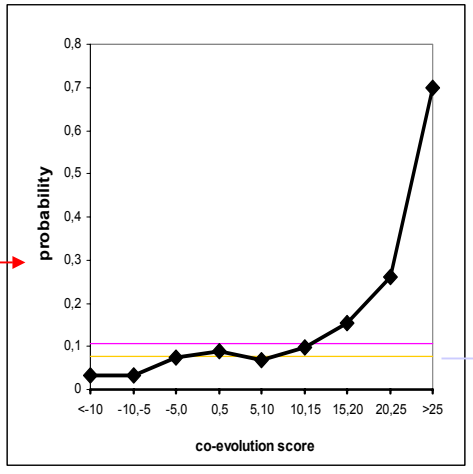


Use of co-ordinated evolution to predict function of proteins.

Do proto-mitochondrial derived proteins involved in the same processes evolve co-ordinately?

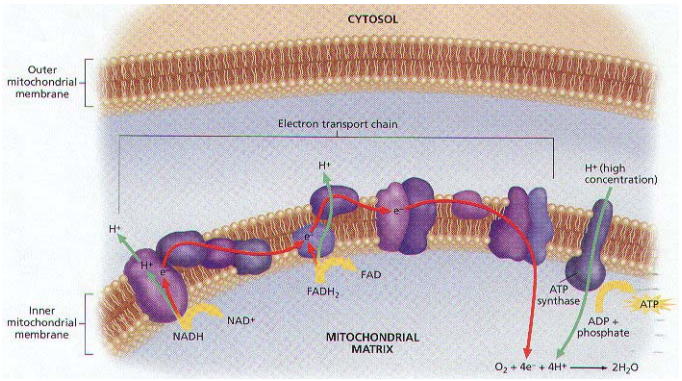
Proteins that have a similar evolution tend to function in the same biological process

Fraction of proteins Functioning in the same biochemical pathway



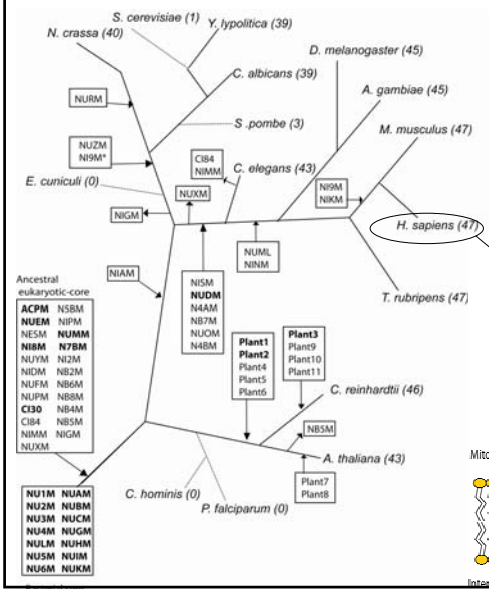
Average

Gabaldón & Huynen. *Bioinformatics* 2005



-Complex I deficiency
-Hereditary
-Severe (patients < 5 years old)
-No mutation found in C.I genes.
-???

Focusing on CI evolution: more candidates predicted.

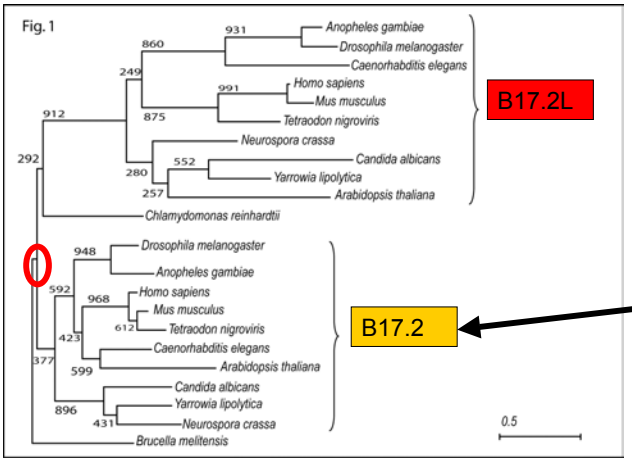


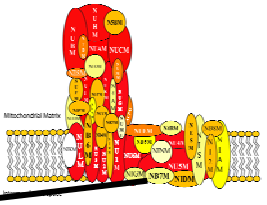
-Use more eukaryotic species,

-Include subunits not derived from bacteria

-Investigate also lineage-specific gains and duplications

Gabaldón et al. J. Mol. Biol. (2005)





Just in !!

October 2005 issue of the Journal of Clinical Investigation

Research article Related Commentary, page 2689

A molecular chaperone for mitochondrial complex I assembly is mutated in a progressive encephalopathy

Isla Ogilvie,[1] Nancy G. Kennaway,[2] and Eric A. Shoubridge[1,3]

[1]Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada. [2]Department of Molecular and Medical Genetics, Oregon Health & Science University, Portland, Oregon, USA. [3]Department of Human Genetics, McGill University, Montreal, Quebec, Canada.

of complex I structural subunits from normal human heart mitochondria. These results demonstrate that B17.2L is a bona fide molecular chaperone that is essential for the assembly of complex I and for the normal function of the nervous system.

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