Evidence of convergent evolution in the nuclear and mitochondrial OXPHOS genes across Squamata deep lineages

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Introduction

The monophyletic origin of Iguania (Pleurodonta+Acrodonta) is rejected using mitochondrial markers, which instead strongly support a close sister relationship between Acrodonta (particularly the Agamidae family) and Serpentes (Figure 1). At the root of these contrasting topologies, there might be an ancient episode of convergent evolution between the two lineages in the OXPHOS pathway[1]. Four out of the five complexes that constitute the OXPHOS system are composed of both mitochondrial (mtOXPHOS) and nuclear (nucOXPHOS) subunits. Literature posits that these subunits must coevolve for proper OXPHOS functioning[2].

Dataset

- 56 species (25 families)
- 3 outgroups

896 BUSCO genes (Metazoa_odb10)

13 mtOXPHOS (NCBI, MITOS, MitoHifi+Spades)

75 nucOXPHOS (RefSeq, Miniprot)

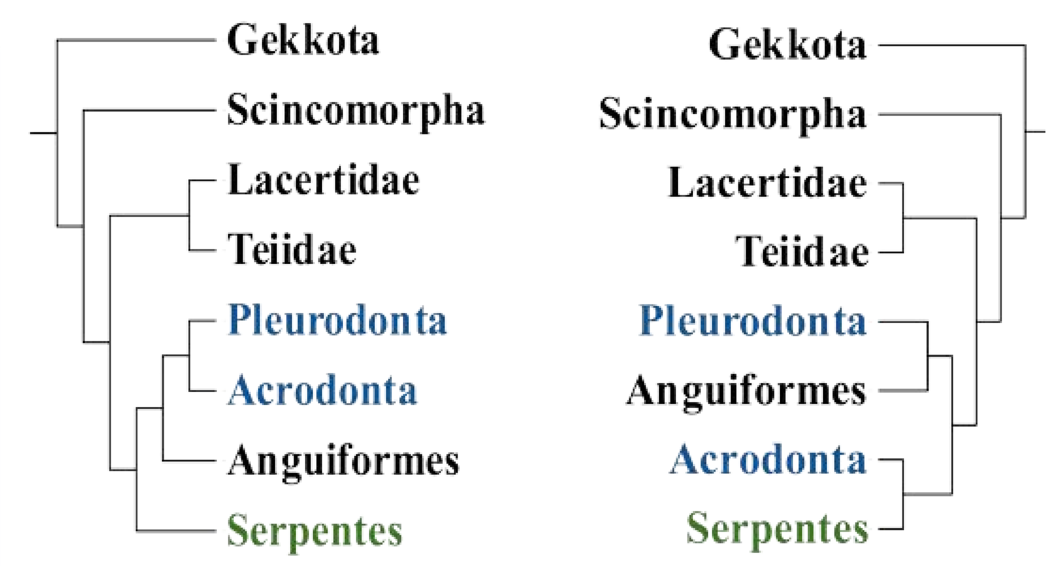

Figure 1. Nuclear (left) and mitochondrial (right) topologies

Can the Discordant Topology Extend to Nuclear OXPHOS?

The ML tree (IQ-TREE) based on nucOXPHOS and the likelihood mapping analysis (LMA) did not support the monophyly of Iguania, nor the agamid-snakes sister relationship (Fig. 2A). However, when restricting the analysis to the subset that tightly interacts with mitochondrial subunits (contact nucOXPHOS), the resulting topology mirrored the mitochondrial one (Fig. 2B). Furthermore, LMA strongly supported Agamidae+Serpentes when only the aforementioned subset was considered.

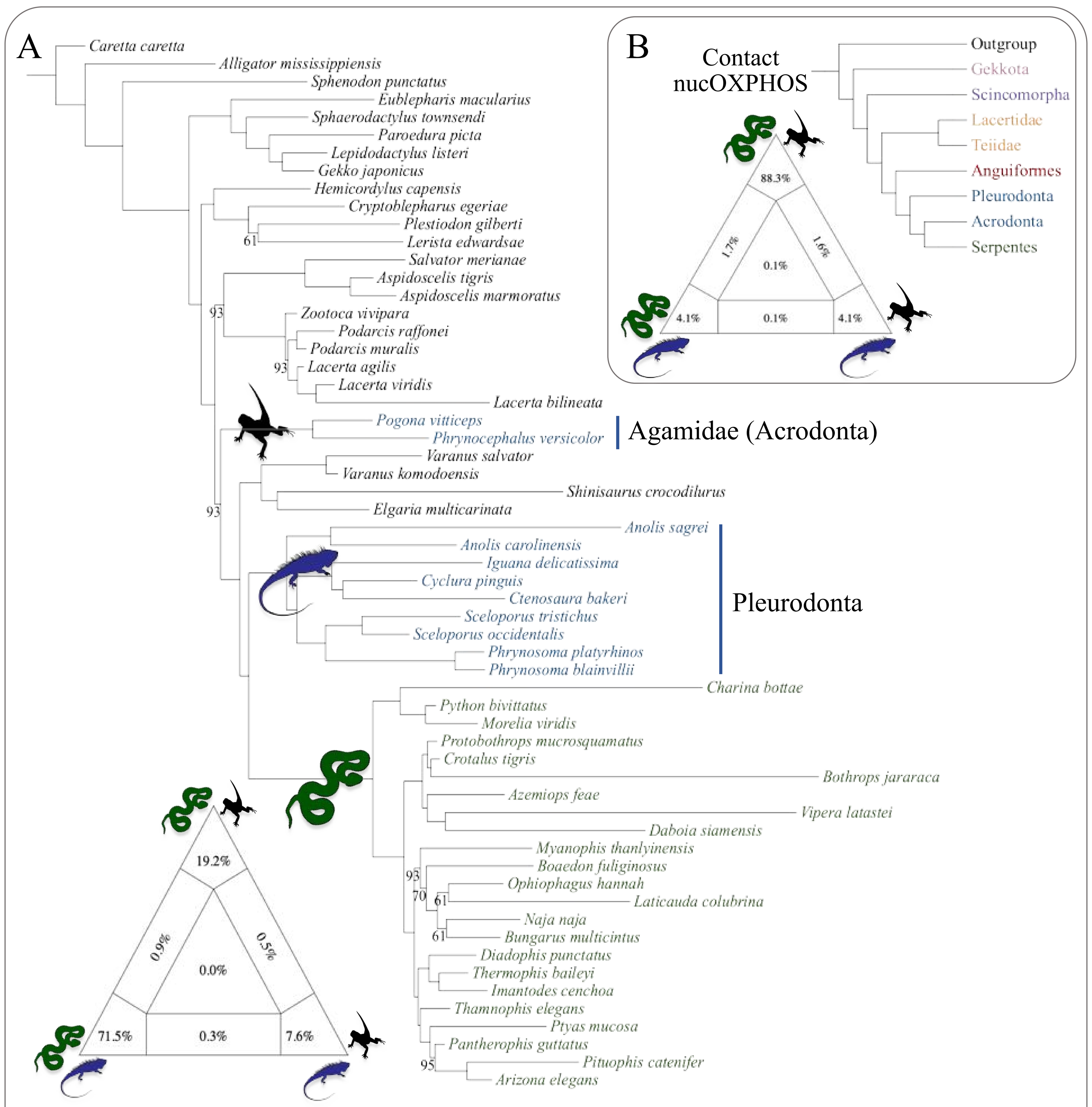

Figure 2. (A) ML tree based on nucOXPHOS, (B) ML tree topology from contact nucOXPHOS

How Do mt- and nucOXPHOS Coevolve in Squamata?

Evolutionary Rate Correlation (ERC) between mtOXPHOS and nucOXPHOS reported a Spearman's ρ of 0.65 (Fig. 3A). To test the robustness of this result, we normalized OXPHOS genes using 1000 random subsets of BUSCO genes and performed ERC. The distributions of Spearman's ρ are presented in Figure 3B. Similarly to snakes, agamid lizards exhibited evolutionary rates of BUSCO genes lower than those of mtOXPHOS and nucOXPHOS genes (Fig. 3C).

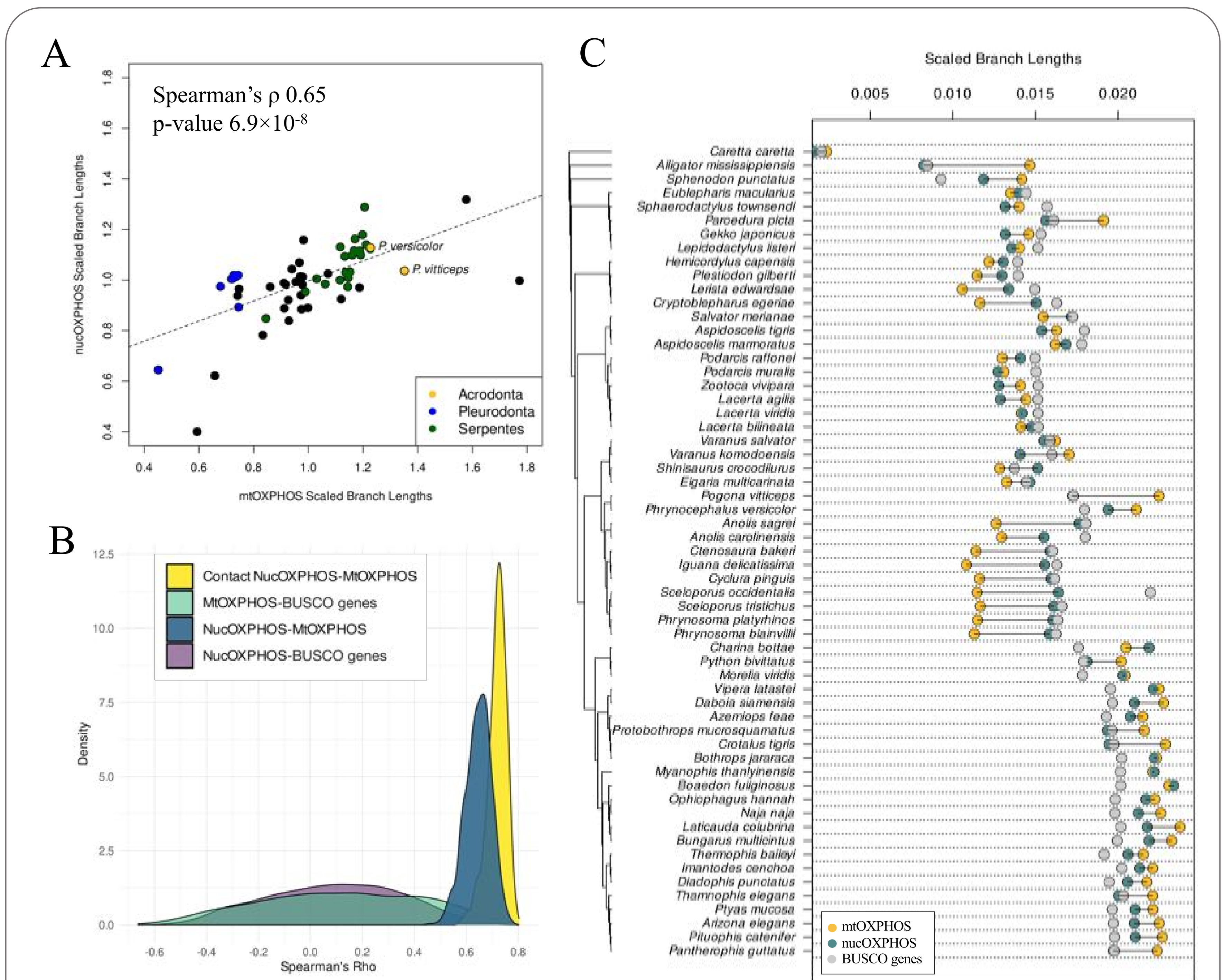

Figure 3. ERC between gene datasets

Are There Signals of Convergent Evolution Between Agamidae and Serpentes?

Each substitution that led to the same amino acid on two independent branches was defined as convergent. For each OXPHOS gene, we estimated the number of convergent and divergent substitutions in all pairs of branches along the Squamata topology. We related the number of convergent substitutions to the number of divergent substitutions using orthogonal regressions and calculated the residuals for each point. **11 out of 13** mtOXPHOS genes had residuals for the Agamidae-Serpentes pair in the top positive 2.5% of all residuals (Fig. 4A), and **26 out of 75** nucOXPHOS genes followed the same pattern. Of these 26, 17 were contact subunits (Fig. 4B).

➢ Our results strongly supported the hypothesis of **convergence** on OXPHOS genes between snakes and agamid lizards.

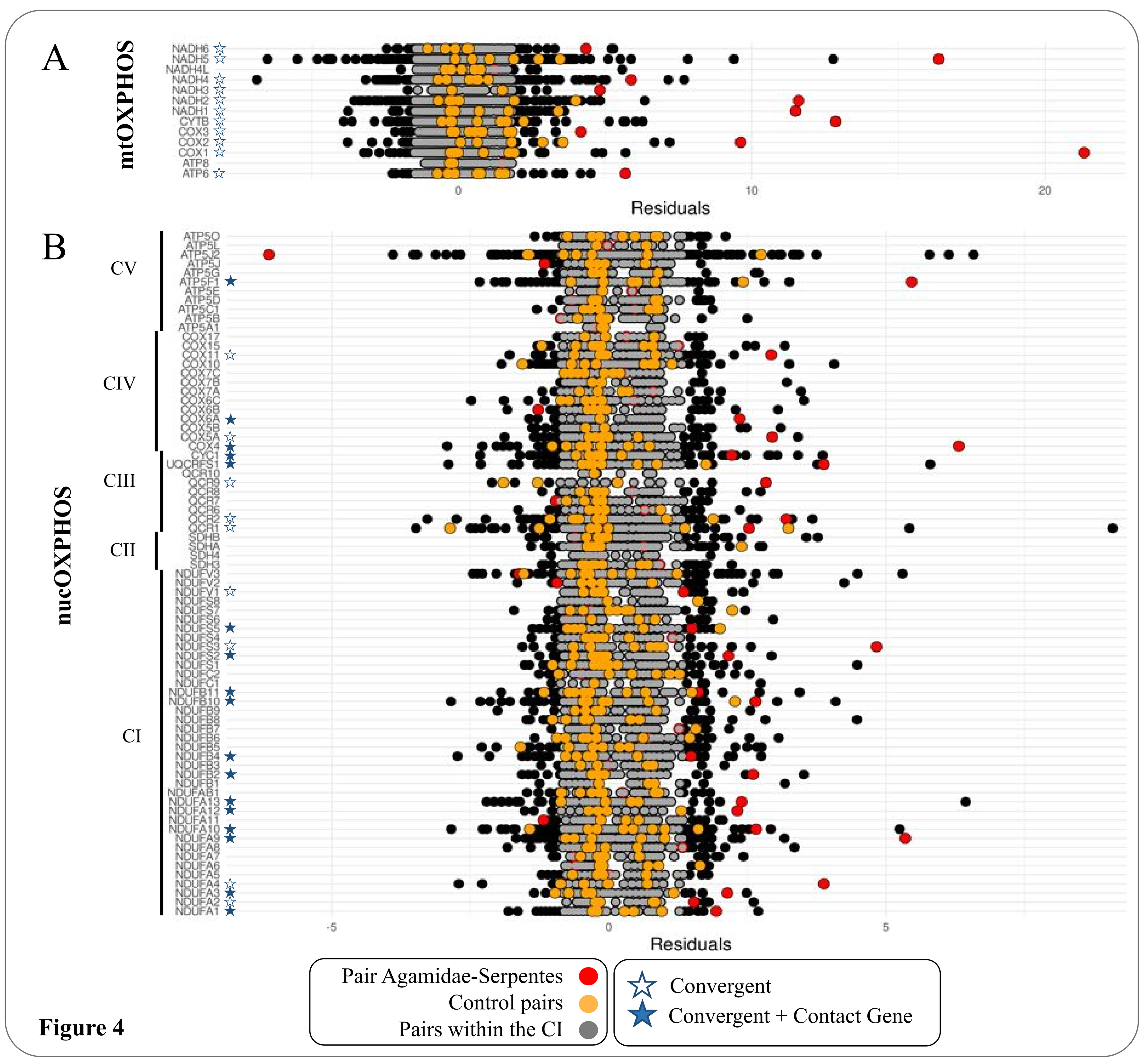

Figure 4

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Donazione Canziani

References

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(2) Hill (2020), *Trends Genet,* 36:403–414. doi:10.1016/j.tig.2020.03.002