

# Gene Co-Inheritance and Gene Transfer

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The functional transfer of mitochondrial genes to the nucleus is an enigmatic feature of eukaryotic genome evolution (1). In angiosperms, functional gene transfer is characterized by periods of stasis punctuated with bursts of transfer activity, a large variance in the number of transfers among lineages, and a high frequency of recent and a dearth of ancient transfers (2, 3). Despite extensive documentation of mitonuclear gene transfer in angiosperms, there is no well-supported explanation for this “unfathomable” variation (3). To understand the variation in mitochondrial gene translocation (3) and the evolutionary forces affecting genomic transfer, we examined the association between number of functional mitonuclear gene transfer events and angiosperm reproductive mode.

When a gene moves from the mitochondria to the nucleus, its environment changes from a primarily nonrecombining, haploid, uniparentally inherited mitochondrial genome to a recombining, biparentally inherited nuclear genome. Thus, the evolutionary advantages of recombination may drive mitonuclear gene transfer, because recombination allows mitochondrial genes to escape degradation by Muller’s ratchet, the irreversible accumulation of deleterious mutations, or increases the rate of spread of advantageous mutations (4). If either of these selective forces drives mitonuclear gene transfer, more gene transfer should be observed in outcrossing taxa because they experience more effective recombination than selfing or clonal taxa.

Although selfing and clonal reproduction diminish recombination, they increase  $\theta_{MN}$ , the probability that mitonuclear gene pairs in the same individual are inherited together and thus are simultaneously identical by descent. High  $\theta_{MN}$  conserves mitonuclear gene combinations (5) across generations as well as nuclear gene combinations, increasing the effectiveness of selection on mitonuclear and nuclear-nuclear epistasis (6).

The opportunity for functional gene transfer

begins with the incorporation of a mitochondrial gene into a nuclear genome. The transferred gene must then acquire sequences conferring nuclear expression and sequences targeting the gene product to the mitochondrion (1). Lastly, the mitochondrial copy must be silenced or lost from the population while the nuclear copy is retained. Throughout this complex process, high  $\theta_{MN}$  preserves functional gene combinations, whereas reproduction with low  $\theta_{MN}$  breaks apart gene combinations, potentially uniting two nonfunctional complements.

If the process of gene transfer involves coadaptation of mitonuclear gene combinations, heritability of these combinations is necessary for a response to selection. Because adaptive function after transfer requires simultaneous genetic changes in both genomes, it is probable that co-inheritance is also essential to successful functional gene transfer (5). A positive association between co-inheritance and transfer numbers would provide support for this hypothesis.

Alternatively, mitonuclear transfer could be a neutral process, guided by random genetic drift, or an adaptive process, guided by genes with additive effects on fitness regardless of mating system. Neither of these hypotheses makes any prediction concerning the relationship between  $\theta_{MN}$  and the number of transfer events.

We tested these competing hypotheses by examining the relationship between independent mitochondrial gene losses [documented in (2)] and ancestral  $\theta_{MN}$  (ranked as high, intermediate, or low) across 170 angiosperm genera [see Sup-

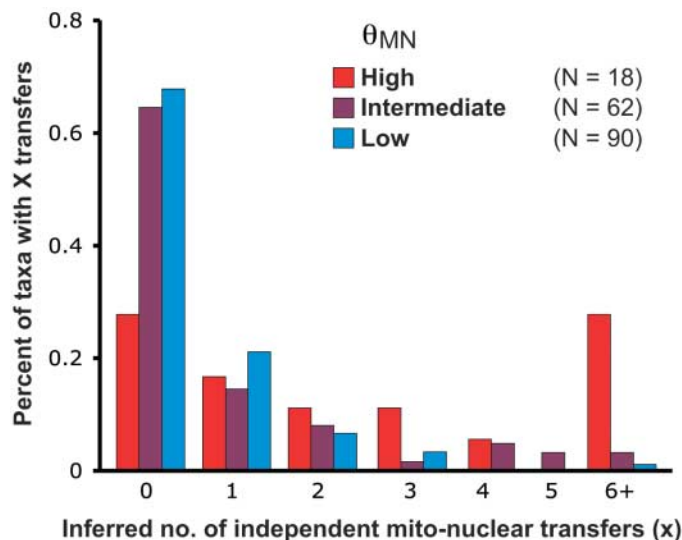


Fig. 1. Distribution of inferred number of gene transfers by  $\theta_{MN}$ .

porting Online Material (SOM) text for criteria, categorization, justification, and reference of each  $\theta_{MN}$ ]. Adams *et al.* (2) inferred loss of essential mitochondrial genes by Southern blots but did not confirm transfer between the mitochondria and nucleus. Sequenced plant mitochondrial genomes show that most inferred losses represent true losses and that functional copies of lost mitochondrial genes are usually found in the nucleus (1, 2), with exceptions removed from our analysis (detailed in SOM text). Similarly, our inference of ancestral reproductive mode is imperfect (SOM text), and thus greater resolution of the timing of gene transfer would facilitate better inference of ancestral  $\theta_{MN}$ , providing a stronger test of our hypothesis.

We found a strong, positive association between  $\theta_{MN}$  and the number of functional gene transfer events (Spearman’s  $\rho = 0.233$ , two-tailed  $P = 0.002$ , Fig. 1), consistent with the prediction that gene co-inheritance facilitates functional gene transfer and opposite to predictions that suggest these advantages are due to recombination (4). The range of variation in the number of transfer events and the value of  $\theta_{MN}$  within clades (fig. S1) rules out the possibility that this result is due to a phylogenetic coincidence. Furthermore, a positive association between  $\theta_{MN}$  and gene transfer is consistent with the observed phylogenetic distribution of many recent but few ancient transfers; if selfing and clonal reproduction represent a “dead end” (7), gene transfer in these high  $\theta_{MN}$  groups is followed by their extinction.

Evidence that chloroplast-to-nuclear gene transfers, movement of nuclear genes among chromosomes, or movement of genes between hosts and vertically transmitted endosymbionts are associated with higher  $\theta$  would further support our hypothesis. Overall, these findings and predictions demonstrate that the heritability of gene combinations provides a predictive framework for the evolution of genome architecture.

## References and Notes

1. K. L. Adams, J. D. Palmer, *Mol. Phylogenet. Evol.* **29**, 380 (2003).
2. K. L. Adams, Y. L. Qiu, M. Stoutemyer, J. D. Palmer, *Proc. Natl. Acad. Sci. U.S.A.* **99**, 9905 (2002).
3. J. D. Palmer *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **97**, 6960 (2000).
4. J. L. Blanchard, M. Lynch, *Trends Genet.* **16**, 315 (2000).
5. M. J. Wade, C. J. Goodnight, *Evolution* **60**, 643 (2006).
6. I. Eshel, M. W. Feldman, *Theor. Popul. Biol.* **1**, 88 (1970).
7. G. L. Stebbins, *Am. Nat.* **91**, 337 (1957).
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## Supporting Online Material

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SOM Text

Fig. S1

References

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