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# Comment on “Population Size Does Not Influence Mitochondrial Genetic Diversity in Animals”

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Bazin *et al.* (Reports, 28 April, 2006, p. 570) found no relationship between mitochondrial DNA (mtDNA) diversity and population size when comparing across large groups of animals. We show empirically that species with smaller populations, as represented by eutherian mammals, exhibit a positive correlation between mtDNA and allozyme variation, suggesting that mtDNA diversity may correlate with population size in these animals.

Bazin *et al.* (1) did not find a positive relationship between mitochondrial DNA (mtDNA) diversity and population size as predicted from population genetics theory for animal groups with larger versus smaller populations, e.g., invertebrates versus vertebrates. In contrast, this relationship holds for nuclear DNA and allozyme markers. The authors propose that the expected relationship is not found for mtDNA because recurrent selective sweeps have reduced mtDNA diversity and thereby homogenized mitochondrial variation across animal groups.

In an accompanying article, Eyre-Walker (2) noted that humans are an exception to this mtDNA pattern because of their smaller population size. Specifically, he cites the many studies of human mtDNA, autosomes, and Y chromosomes that have converged on a final estimate of ~10,000 individuals (males and females) [summarized in (3)]. Various studies of the X chromosome have also led to a similar estimate of ~10,000 (4, 5), further corroborating the utility of mtDNA for population size estimation in humans. In species with smaller populations, selective sweeps are less likely to occur because fewer beneficial mutations arise and selection is less efficient. Therefore, in species like humans, selective sweeps become less of a concern when estimating population size from mtDNA.

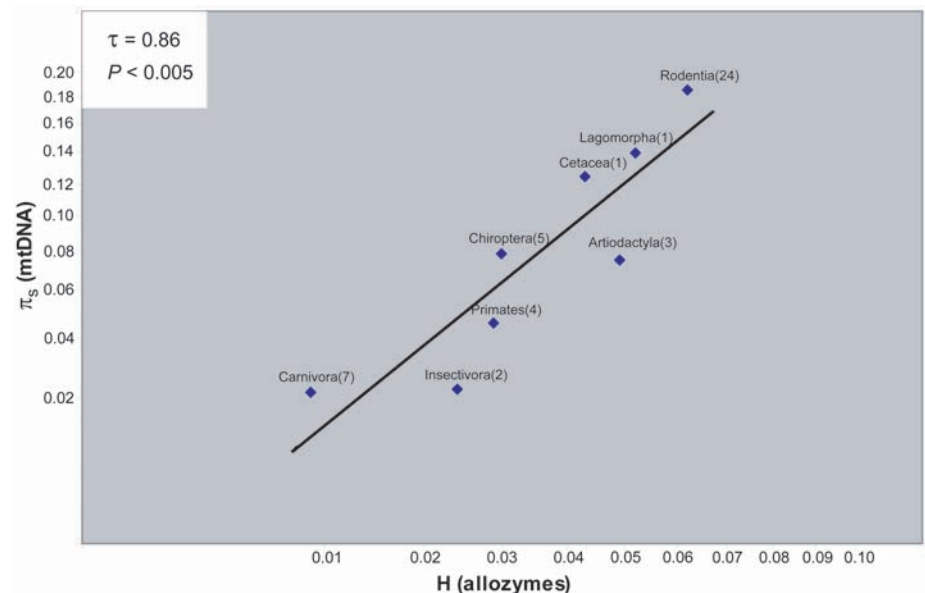
As an initial test of this hypothesis, we extended Bazin *et al.*'s analysis with a focus on the 47 species of eutherian (placental) mammals in their mtDNA data set for which allozyme heterozygosities (H) were also available (6). We focused on eutherian mammals because of their expected smaller population sizes as well as their greater representation in both databases and closer phylogenetic ties

to humans. We edited the alignments for misplaced gaps, calculated both synonymous and total mtDNA diversities for coding sequences ( $\pi_S$  and  $\pi_T$ ), and then plotted mean  $\pi_S$  and  $\pi_T$  against average H for each order (Fig. 1). A significant positive correlation was found between both  $\pi_S$  and  $\pi_T$  versus H (Kendall test,  $\tau = 0.86$  and  $0.84$ ,  $P < 0.005$  for each comparison). Thus, we find a positive correlation between mtDNA diversity and allozyme heterozygosity, suggesting that the former correlates with population size as does the latter (1). Interestingly, the order with the greatest mtDNA and allozyme variability (Rodentia) is the one

with the larger expected populations, whereas that with the least variation (Carnivora) is predicted to have smaller populations because they are higher-order predators.

This significant correlation for eutherian orders is consistent with the hypothesis that mtDNA diversity and population size are positively related in animal groups with known or expected smaller populations. However, other factors may also be involved. For example, correlated mutation rates between mtDNA and allozymes and/or variable population subdivision and migration among the eutherian orders may also underlie the observed relationship. Nevertheless, this correlation constitutes an important next step in the study of mtDNA diversity and population size, and its significance warrants further testing with other groups and more detailed analyses.

In animal groups with large populations, e.g., invertebrates, selective sweeps can frequently reduce mtDNA diversity such that the species' standing variation primarily reflects the time since its last “genetic draft” (1). However, many animal groups of broad interest to both the scientific community and the general public are those with known or expected smaller populations, for example, humans, endangered species, and “charismatic” animals. It is in such groups that we predict mtDNA will remain a valuable genetic marker for the study of population history and demography.



**Fig. 1.** Arcsine square root plot of mean  $\pi_S$  versus H for eight orders of eutherian mammals (numbers of species are given in parentheses). A nearly identical relationship exists for mean  $\pi_T$  versus H ( $\tau = 0.84$ ,  $P < 0.005$ ). Furthermore, our results are robust in that  $P$  remains  $< 0.005$  when three pairs of orders with nearly identical  $\pi$  or H diversities, i.e., Artiodactyla/Chiroptera, Carnivora/Insectivora, and Chiroptera/Primates are counted as ties in the Kendall tests. Individual  $\pi_S$  and  $\pi_T$  estimates for each species were based on the Nei-Gojobori method with a Jukes-Cantor correction and on the Kimura two-parameter distance with a gamma distribution ( $\alpha = 0.5$ ), respectively (7). Otherwise, our methods followed those of Bazin *et al.* (1).

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