

The toad's warts: Discordance creates bumpy expectations of mitochondrial-nuclear evolution between species

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Discordance between the mitochondrial and nuclear genomes is a prevalent phenomenon in nature, in which the underlying processes responsible are considered to be important in shaping genetic variation in natural populations. Among the evolutionary processes that best explain such genomic mismatches incomplete lineage sorting and introgression are commonly identified, however, many studies are unable to distinguish between these hypotheses, which has become a major challenge in the field. In this issue of *Molecular Ecology*, Firreno et al. (2020) present an elegant exploration of mitochondrial-nuclear discordance in Mesoamerican toads. Integrating genome-scale and spatial data to test between these hypotheses within an empirical model testing framework, they find strong support that incomplete lineage sorting explains the observed discordance. Their work, along with many previous articles in *Molecular Ecology*, highlights the commonality of mito-nuclear discordance among species despite the expectations of tightly concerted mitochondrial and nuclear genome evolution. It is increasingly clear that the nuclear genomes of many species are (at least for short periods of evolutionary time) functionally compatible with multiple, divergent mitochondrial haplotypes. As such, we suggest future research not only seeks to understand the processes causing spatial mito-nuclear discordance (e.g. incomplete lineage sorting, introgression), but also explores those that maintain discordance through time and space (e.g. relaxed selection on mito-nuclear interactions, heterozygosity, population demographics). We also discuss the vital role that taxonomy plays in interpreting patterns of mito-nuclear discordance when data-consistent yet differing taxonomies are used, such as treating allopatrically distributed taxa as multiple isolated populations versus multiple micro-endemic species.

KEYWORDS

amphibians, cytonuclear interactions, incomplete lineage sorting, introgression, phylogeography, population genetics, spatial discordance, systematics

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Mitochondrial and nuclear genomes may often reveal divergent geographic patterns in natural populations, with the processes underlying these mismatches considered to be important in shaping their genetic variation (Toews & Brelsford, 2012). With advancements in sequencing technologies, mito-nuclear discordance has been increasingly observed over the last two decades (Toews & Brelsford, 2012) across a range of vertebrate and invertebrate animals (e.g. Ivanov, Min Lee, & Mutanen, 2018; Zink & Barrowclough, 2008) as well as fungi (e.g. De Chiara et al., 2020). The observation of mito-nuclear discordance between species is somewhat unexpected given prevailing models of cytonuclear evolution and speciation that suggest divergent mitochondrial and nuclear genomes should not be maintained within species (Rand, Haney, & Fry, 2004). Nonetheless, the phylogeographical literature offers a plethora of empirical examples where multiple divergent mtDNA genomes persist within a single animal species, as demonstrated in this issue by Firreno et al. (2020).

A number of possible evolutionary explanations for mito-nuclear discordance have been posited, with mechanisms comprising selective causes, neutral demographic processes or both. The most frequent explanations of discordance (Dufresnes et al., 2020) include sex-biased dispersal (e.g. Dai, Wang, & Lei, 2013), introgression (e.g. Ivanov et al., 2018; Phuong, Bi, & Moritz, 2017) or incomplete lineage sorting (Firreno et al., 2020); however, many studies are unable to distinguish between them, which has become a major challenge in the field (Toews & Brelsford, 2012). In this issue, Firreno et al. (2020) identify between these mechanisms, highlighting a complex biogeographic history in a group of cryptic Mesoamerican toad species, which revealed both mito-nuclear and nuclear–nuclear patterns of genome discordance. The *Incilius coccifer* complex (containing three species: *I. coccifer*, *I. ibarra* and *I. porteri*, Figure 1) belong to the ‘true toad’ family (Amphibia: Anura: Bufonidae) that occur across a heterogeneous (highland versus lowland) landscape. The distribution of this species complex thus makes them a potentially exciting system to examine mito-nuclear discordances, since this phenomenon is suggested to occur more frequently in climatically unstable regions (Phuong et al., 2017), where repeated range shifts create opportunities for lineages to expand and admix (Dufresnes et al., 2020).

Using ddRADseq-derived nuclear DNA data (>1,000 ‘unlinked’ SNPs) and a mitochondrial DNA marker, the authors conduct an array of analyses including discovery operations (population and species delimitation), phylogenetic inference and divergence dating, nuclear DNA introgression tests, inference of joint-demographic

histories and species distribution modelling. While the authors pinpoint introgression in the nuclear genome of the Chortís Highland populations, which they infer as the likely result of climatic fluctuations driving cyclical range expansions, the authors suggest that this was not the key driver of the mito-nuclear discordance across the entire species complex. Instead based on clear geographical signal from the nuclear DNA, they concluded that incomplete lineage sorting of mitochondrial DNA haplotypes best explains the discordance.

Using extensive nuclear datasets, even from animals with relatively large genomes like amphibians (C value = 3–12 in most anurans), it is now feasible to test the possible causes of mito-nuclear discordance in historically unprecedented ways. This includes the opportunity for studying the factors that maintain mito-nuclear discordance between species in greater detail. Ease of sequencing whole mitochondrial genomes coupled with increasing numbers of reference nuclear genomes may provide the ability to differentiate neutral (e.g. relaxed selection on mito-nuclear interactions) from adaptive (e.g. diversifying selection) explanations for mito-nuclear discordance. Understanding how historic causes of discordance (e.g. incomplete lineage sorting, introgression), fitness consequences (e.g. Hill et al., 2018) and species-specific idiosyncrasy interface with ecological and spatial distribution represents a major, but exciting challenge for future studies of molecular ecology.

An important, but often underappreciated point discussed by Firreno et al. (2020), is the role that taxonomy may play in causing mito-nuclear discordance. In a phylogenetic sense, the evolutionary entities we decide represent ‘species’ can operationally introduce mito-nuclear discordance (sensu Ivanov et al., 2018). For example, visualizing three allopatric taxa (A, B and C; Figure 2) sequenced for mitochondrial and nuclear DNA. Sequence data are further generated from a close relative (taxon D) and a more distantly related outgroup (taxon E). First, treating A, B and C as distinct evolutionary entities, evidence of mito-nuclear discordance is identified (top tree; Figure 2). However, most taxonomists only recognize A, B and C as a single species (taxon X). As such, if we are interested in interspecific patterns, the branches in the top tree would need to be collapsed, effectively making the mitochondrial and nuclear phylogenies congruent in terms of monophyly (bottom tree; Figure 2). Thus, in terms of interspecific patterns, the existence of mito-nuclear discordance is entirely dependent on how we apply alpha taxonomy.

Mito-nuclear coevolution across the animal tree of life is clearly dynamic. Studies like Firreno et al. (2020) provide strong empirical

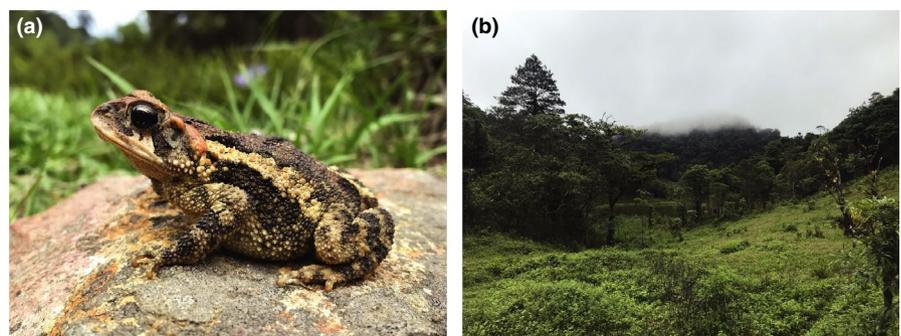


FIGURE 1 a, The highland toad species, *Incilius porteri* from the Chortís Highlands of Honduras—one of the three species from the *Incilius coccifer* complex. b, Highland sampling habitat (Images provided by T. Firreno)

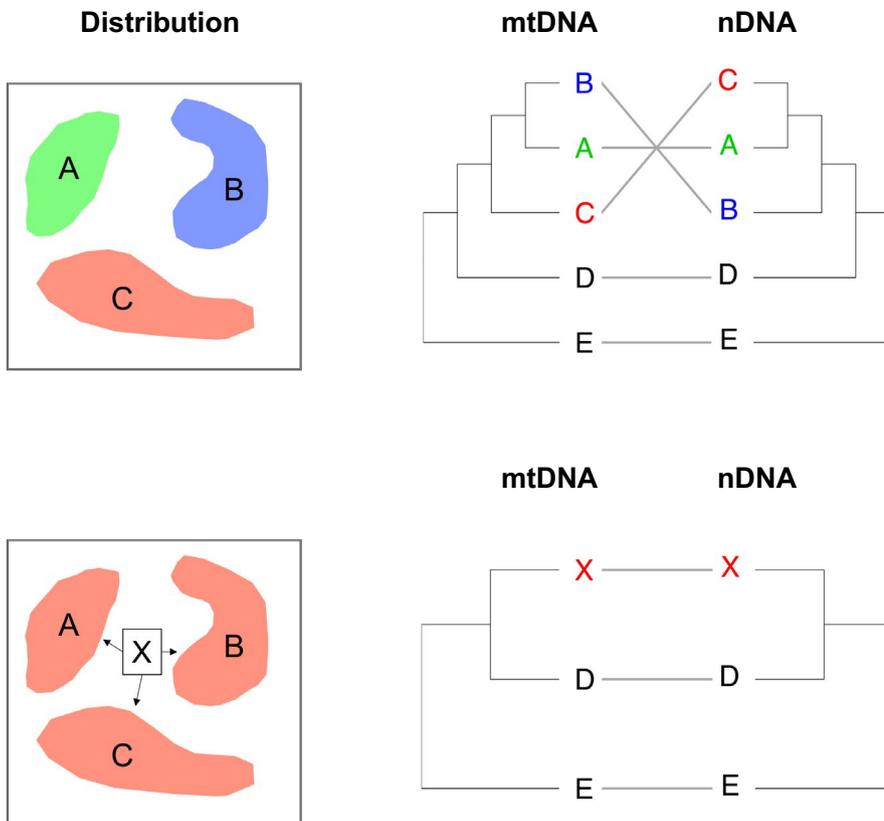


FIGURE 2 Illustrative example of three allopatrically distributed focal taxa (A, B and C), with phylogenetic comparisons to a close relative (taxon D) and a distant outgroup (taxon E). In the top tree, we recognize these three focal taxa as ‘independent’ micro-endemic species and note the occurrence of mitochondrial-nuclear discordance. In the bottom tree, we treat the focal taxa as multiple isolated populations of a single species (taxon X) and there is no evidence of discordance among species

evidence that patterns of mito-nuclear coevolution vary through space and among species. They also suggest that species-specific idiosyncrasies are more important to consider than generalized expectations of cytonuclear coevolution.

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