

Atypical mitochondrial inheritance patterns in eukaryotes

Sophie Breton and Donald T. Stewart

Abstract: Mitochondrial DNA (mtDNA) is predominantly maternally inherited in eukaryotes. Diverse molecular mechanisms underlying the phenomenon of strict maternal inheritance (SMI) of mtDNA have been described, but the evolutionary forces responsible for its predominance in eukaryotes remain to be elucidated. Exceptions to SMI have been reported in diverse eukaryotic taxa, leading to the prediction that several distinct molecular mechanisms controlling mtDNA transmission are present among the eukaryotes. We propose that these mechanisms will be better understood by studying the deviations from the predominating pattern of SMI. This minireview summarizes studies on eukaryote species with unusual or rare mitochondrial inheritance patterns, i.e., other than the predominant SMI pattern, such as maternal inheritance of stable heteroplasmy, paternal leakage of mtDNA, biparental and strictly paternal inheritance, and doubly uniparental inheritance of mtDNA. The potential genes and mechanisms involved in controlling mitochondrial inheritance in these organisms are discussed. The linkage between mitochondrial inheritance and sex determination is also discussed, given that the atypical systems of mtDNA inheritance examined in this minireview are frequently found in organisms with uncommon sexual systems such as gynodioecy, monoecy, or andromonoecy. The potential of deviations from SMI for facilitating a better understanding of a number of fundamental questions in biology, such as the evolution of mtDNA inheritance, the coevolution of nuclear and mitochondrial genomes, and, perhaps, the role of mitochondria in sex determination, is considerable.

Key words: mitochondrial DNA, mitochondrial inheritance, sex determination, paternal leakage, heteroplasmy.

Résumé : L'ADN mitochondrial (l'ADNmt) est principalement hérité de la mère chez les eucaryotes. Divers mécanismes moléculaires sous-jacents au phénomène ont été décrits, mais les forces évolutives responsables de sa prédominance chez les eucaryotes restent encore à être élucidées. Des exceptions à la transmission strictement maternelle de l'ADNmt (« strict maternal inheritance » ou SMI) ont été signalées chez divers taxons eucaryotes, laissant penser que plusieurs nouveaux mécanismes moléculaires de transmission de l'ADNmt existent chez les eucaryotes. Nous proposons que ces mécanismes seront mieux compris en étudiant les exceptions au type prédominant de transmission mitochondriale SMI. Cette mini-revue résume les études sur les espèces eucaryotes avec des systèmes de transmission mitochondriale inhabituels ou rares, c'est-à-dire autres que la SMI, tels que la transmission maternelle stable d'une hétéroplasmie, la transmission occasionnelle de l'ADNmt paternel (« paternal leakage »), la transmission biparentale ou encore strictement paternelle de l'ADNmt et la transmission doublement uniparentale de l'ADNmt. Les gènes et les mécanismes impliqués dans le contrôle de la transmission mitochondriale chez ces organismes « déviants » sont discutés. Le lien étroit entre la transmission mitochondriale et la détermination du sexe est également abordé, puisque les systèmes atypiques d'héritabilité de l'ADNmt examinés dans cette étude sont surtout présents chez des organismes avec des systèmes sexuels rares comme la gynodioécie, la monoécie et l'andromonoécie. L'étude de ces exceptions permettra incontestablement une meilleure compréhension d'un certain nombre de questions fondamentales en biologie, comme l'évolution des mécanismes de transmission de l'ADNmt, la coévolution des génomes nucléaires et mitochondriaux et, peut-être, le rôle des mitochondries dans la détermination du sexe. [Traduit par la Rédaction]

Mots-clés : ADN mitochondrial, transmission mitochondriale, détermination du sexe, transmission paternelle occasionnelle, hétéroplasmie.

Introduction

The mitochondrial DNA (mtDNA) codes for some of the genes necessary to produce the proteins required in the oxidative phosphorylation (OXPHOS) reaction that produces ATP. In contrast to the nuclear DNA, it is pri-

marily only the female parent that transmits mitochondria (and hence mtDNA) to offspring in eukaryotes (Birky 2001). This uniparental mode of inheritance is partly responsible for offspring homoplasmy, i.e., the state when all mitochondrial genomes in an individual are genetically

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identical (Birky 2001; Mishra and Chan 2014; Stewart and Larsson 2014). In humans, disruption of mitochondrial homoplasmy may result in mitochondrial dysfunction or disease including diabetes and cancer (Wallace and Chalkia 2013). Strict maternal inheritance (SMI) of mtDNA and a series of mtDNA bottleneck mechanisms during oogenesis and after fertilization are proximate mechanisms that help to ensure mitochondrial homoplasmy (Ballard and Whitlock 2004; Hoekstra 2011; Lane 2011; Jokinen and Battersby 2013; Mishra and Chan 2014). The bottleneck mechanisms have been most thoroughly studied in mammals and include the following: (i) a physical bottleneck during oogenesis that greatly reduces mitochondrial genome copy number and exposes deleterious mutations to purifying selection before the re-initialization of mtDNA replication during oocyte maturation; (ii) a genetic bottleneck during oogenesis that occurs as a result of selective replication of a subset of mtDNA molecules; and (iii) another genetic bottleneck during early embryogenesis that occurs as a result of reduction in mtDNA copies per cell owing to dilution as cells rapidly divide, followed by amplification of a subpopulation of mtDNA molecules (see Jokinen and Battersby (2013) and Mishra and Chan (2014) for reviews). The current state of knowledge of the molecular mechanisms underlying the elimination of paternal mtDNA or mitochondrial structures for ensuring the maternal transmission of mtDNA has also been addressed in recent reviews (Bendich 2013; Sato and Sato 2013; Song et al. 2014; Greiner et al. 2015). For example, studies in mammals suggest that elimination of paternal mtDNA is dependent on a mechanism involving the ubiquitin-proteasome system (Sutovsky et al. 1999). In *Caenorhabditis elegans*, autophagy of non-ubiquitinated sperm mitochondria during early embryogenesis, including their engulfment by autophagosomes and degradation by lysosomes, prevents paternal mtDNA transmission (Al Rawi et al. 2011; Sato and Sato 2011). Autophagy is also implicated in the degradation of ubiquitinated sperm mitochondria in mammals (Al Rawi et al. 2011). Taken together, these data suggest that autophagy is a conserved process that is required for the maternal inheritance of mtDNA in animals (Al Rawi et al. 2011; Sato and Sato 2011). However, a panoply of different mechanisms ensuring SMI have been reported in the literature, even in closely related taxa. Furthermore, in most cases where there is no maternal inheritance, mitochondria are nonetheless inherited uniparentally, suggesting that a general explanation might exist for the repeated evolution of diverse mechanisms to achieve uniparental inheritance (UPI) of mitochondria. It has been proposed that UPI has been selected as a mechanism to avoid the spread of selfish cytoplasmic elements and limit mitonuclear conflicts (Ballard and Whitlock 2004; Hoekstra 2011; Lane 2011; Bendich 2013; Sato and Sato 2013; Song et al. 2014; Greiner et al. 2015). Another recent and perhaps not mutually exclusive explanation for the evolution of UPI and other mechanisms ensuring mitochondrial homoplasmy is sim-

ply selection against heteroplasmy (Christie et al. 2015). This hypothesis fits with recent empirical evidence showing that the maintenance of two different, but individually fully functional, mtDNAs within a cell can cause mitochondrial dysfunction (Sharpley et al. 2012).

Building on the aforementioned ideas, a unifying model for organellar inheritance has recently been proposed by Greiner et al. (2015). Key components of this model are as follows: (i) UPI of mitochondria arises to avoid the spread of selfish organellar genomes (maladaptive and (or) incompatible with the host nucleus); (ii) UPI is unstable because mitochondria are susceptible to Muller's ratchet (UPI and low recombination rates cause the accumulation of deleterious mutations in the mtDNA — but see Bendich (2013)); (iii) Muller's ratchet drives a relaxation of UPI via occasional paternal (or maternal) leakage or regular biparental transmission; and (iv) the evolution of selfish mtDNAs is again possible during biparental inheritance episodes and therefore, UPI is restored (and repeatedly lost) over evolutionary timeframes (Greiner et al. 2015). According to these authors, if UPI is evolutionarily unstable, three major patterns in mitochondrial inheritance should be observable — the repeated and independent evolution of biparental transmission, frequent paternal leakage (in the predominant SMI situation), and a switch to UPI by various mechanisms even between closely related species — and this is indeed what is reported in the literature (Greiner et al. 2015).

The predominance of maternal (vs. paternal) inheritance of mitochondria in sexually reproducing eukaryotes could be explained by a higher mutational load in the paternal gamete due to higher oxidative damage, thus favouring the evolution of paternal gamete-controlled organelle exclusion mechanisms (Greiner et al. 2015). However, despite the growing number of studies describing the diverse molecular mechanisms underlying the maternal inheritance of mitochondria, the potential causes of the near-universal stability of the SMI system are still far from being fully understood (Bendich 2013; Sato and Sato 2013; Song et al. 2014; Greiner et al. 2015). Furthermore, exceptions to SMI have been reported in diverse eukaryotic taxa, leading to the prediction that several distinct molecular mechanisms controlling mtDNA transmission are present among the eukaryotes. We propose that these mechanisms will be better understood by studying the deviations from the predominating pattern of SMI. The primary aim of this minireview is to summarize studies on eukaryote species with unusual or rare mitochondrial inheritance patterns, i.e., patterns other than the standard SMI system, including maternal inheritance of stable heteroplasmy for normal and mutant mtDNAs, as well as biparental, strictly paternal, and doubly uniparental inheritance (DUI) of mtDNA. We also discuss the potential genes and mechanisms involved in controlling mitochondrial inheritance in these organ-

isms. For example, “sex”-determining genes have been shown to influence mtDNA inheritance in some eukaryote species (e.g., Xu 2005; Shakya and Idnurm 2014). It is noteworthy that most atypical systems of mtDNA inheritance discussed in this minireview are found in organisms with uncommon sexual systems, such as monoecy, gynodioecy, and androdioecy. A brief discussion is also included on how these patterns of atypical inheritance might impact our ability to broadly use mitochondrial markers (e.g., barcode markers) in ecology, evolution, and conservation. Cases of disruption of maternal mitochondrial inheritance following interspecies hybridization, which might interfere with mitonuclear interactions and alter the proper function of the mechanisms that eliminate paternal mitochondria, will not be discussed in detail.

Maternal inheritance of stable/constitutive heteroplasmy

Heteroplasmy, a situation in which there are two or more mtDNA genomes present within the cells of an individual, has been considered as an evolutionarily ephemeral phenomenon, with homoplasmy being resolved within a few generations (e.g., Cree et al. 2008; White et al. 2008). However, some organisms deviate from this “mitochondrial tenet”. As we will discuss in the following sections, a degree of heteroplasmy can be reached by recurrent paternal leakage or biparental transmission, but there are also a few exceptions where heteroplasmy persists via the maternal germline and is stably transmitted maternally for several generations. For example, one impressive example of a stable, maternally inherited state of heteroplasmy has been reported in terrestrial isopod crustaceans (Doublet et al. 2008). This system is characterized by a complex, effectively heteroplasmic state consisting of three nearly identical ~14 kb monomers, two of which form an ~28 kb dimer and the other remaining as a monomer (Doublet et al. 2008). According to the authors, balancing selection has maintained this atypical mitochondrial system for over 30 million years because it maintains two mutational forms of a single tRNA locus that are the source of two mitochondrial tRNA molecules, tRNA^{Ala} and tRNA^{Val} (Doublet et al. 2008, 2012).

With the advent of next-generation sequencing technologies and the potential for very high coverage, the study of heteroplasmy no longer constitutes an insurmountable challenge. For example, while previous technologies such as DHPLC or pyrosequencing allowed the detection of heteroplasmy of single nucleotide polymorphisms at levels of >1.5%–10% within an organism or a tissue, amplicon resequencing on Illumina GA/Solexa or 454 GS FLX platforms, for example, have become methods of choice for ultra-deep resequencing (Payne et al. 2013). Resolution in the 0.1%–1% variant frequency range has been described (e.g., Giuliani et al. 2014) and using this method, it has been demonstrated that low levels of mtDNA heteroplasmy down to 0.1%–1% can be maternally

transmitted and maintained within families in humans (Payne et al. 2013; Giuliani et al. 2014). These low-level heteroplasmies have been suggested to constitute a potential source of rare variants that could play a role in determining healthy aging and longevity (Giuliani et al. 2014). Although the exact mechanisms of inheritance, as well as the origin of these heteroplasmic events, are not completely understood (Payne et al. 2013; Giuliani et al. 2014), these studies suggest that mtDNA heteroplasmy observed in nature (e.g., White et al. 2008) could partly be due to low-level inherited mtDNA variants. This reservoir of mitochondrial genetic variability could be beneficial by increasing the capacity of cells and organisms to cope with environmental and physiological stressors (Giuliani et al. 2014).

Paternal leakage and biparental inheritance

Given that maternal inheritance of mtDNA is the norm in eukaryotic reproductive systems, transmission of the male parent’s mitochondria to offspring has been viewed as anomalous and referred to as paternal leakage (e.g., Budowle et al. 2003). Many cases of paternal leakage of mtDNA have been demonstrated in interspecific crosses of a number of diverse species (e.g., Lansman et al. 1983; Gyllenstein et al. 1991; Shitara et al. 1998; McCauley 2013; Morgan et al. 2013). Consistent with the hypothesis that paternal leakage in interspecific crosses may result from a breakdown in mitonuclear mechanisms that normally maintain SMI is the observation of examples of paternally derived mitochondrial genomes in crosses between individuals from different subspecies or from divergent (often allopatric) populations (e.g., Magoulas and Zouros 1993; Meusel and Moritz 1993; Kvist et al. 2003; Ujvari et al. 2007).

The distinction between paternal leakage and biparental inheritance may be a fine line depending upon one’s definition of biparental inheritance. For example, Magoulas and Zouros (1993) refer to the low frequency of mitochondrial heteroplasmy of two divergent mtDNA haplotypes in anchovy as a form of “incidental” biparental inheritance. Some authors have made reference to the presence of biparental inheritance of mtDNA in a number of taxa. While incidental paternal leakage clearly constitutes a form of biparental transmission of mtDNA, for the purpose of this paper, we define “true” biparental transmission as the systematic transfer of mitochondrial genomes from both parents (or from two distinct mating types) to zygotes as part of normal reproductive processes within a species followed by the persistence of both parental mitochondrial types throughout development. To our knowledge, no organisms strictly follow this more narrowly defined mode of biparental inheritance of mtDNA. In contrast, Wilson and Xu (2012) defined biparental inheritance as the transmission of “mitochondria from both mating contributors, creating offspring with either or both parental mitochondrial DNA sequences.” Using their definition, biparental

inheritance of mtDNA is observed in the inkcap mushroom, *Coprinopsis cinerea*, in which progeny cells inherit either, but not both parental types. This results from the differential migration of parental nuclei, but not mitochondria, to the cells of the mating partner to create heterokaryotic hyphae at the ends of the fused mycelium. The mitochondrial inheritance pattern is thus defined as biparental at the level of the whole colony of dikaryotic cells (Wilson and Xu 2012). Wilson and Xu (2012) review a number of other variations on mitochondrial inheritance in fungi. The most notable deviation from strictly UPI of mtDNA that does involve an element of biparental inheritance is referred to as sample location-dependent mtDNA inheritance, which is found in a number of filamentous basidiomycetes, as well as filamentous ascomycetes and ascomycete yeasts (see Wilson and Xu (2012) and Xu and Wang (2015) for reviews of taxa exhibiting this mode of mtDNA transmission). Under this system, when progeny bud off the fused zygote, cells budding off either end of the zygote will contain only mitochondria from the parental cell that contributed cytoplasm to that side of the zygote. However, if buds are produced from the central axis of the zygote, these progeny will contain (i) a mix of parental mitochondria and (ii) mitochondria with recombinant genomes (Wilson and Xu 2012). However, Xu and Wang (2015) note that although most ascomycete zygotes are heteroplasmic for both parental types, the mtDNA haplotypes segregate rapidly in subsequent generations.

Jannotti-Passos et al. (2001) examined several generations of offspring for evidence of maternal and paternal mitochondrial genomes in the parasitic trematode *Schistosoma mansoni* and concluded that there was evidence for biparental inheritance in this highly inbred line of parasites. However, Bieberich and Minchella (2001) subsequently determined that the apparent paternally transmitted genomes were due to rapid evolution of the number of a tandemly repeated 62-bp repeat in the mitochondrial genome and that this process of molecular evolution results in the appearance of partial paternal inheritance of mitochondrial genomes in a system that actually exhibits maternal inheritance.

Silliker et al. (2002) studied mitochondrial transmission patterns in the slime mold *Didymium iridis* and found evidence for rare biparental inheritance. The pattern of transmission was found to be normally uniparental, and included a complex pattern of dominance of one mitochondrial type over another. Silliker et al. (2002) concluded that the rare cases of heteroplasmy could be due to forced mating between taxa that do not normally interact with one another in nature; were this to happen in the wild, they speculate that local mating types would collapse into binary donor and recipient strains as predicted by the binary mating system model of Hurst and Hamilton (1992).

Guo and Hu (1995) confirmed a form of biparental inheritance of mitochondria in the geranium *Pelargonium*, a pattern first proposed by Kuroiwa et al. (1993), although the authors noted that further embryological studies were required to determine if the sperm transmitted mitochondria persisted beyond embryogeny. In interspecific crosses of *Pelargonium zonale* and *Pelargonium inquinans*, Weihe et al. (2009) demonstrated a substantial contribution of the paternal mitochondria to the progeny, which they defined as “genuine” biparental mtDNA inheritance. However, because this was an interspecific cross, it may have exhibited some degree of breakdown in cytonuclear controls that limit persistence of paternally derived mitochondria. Guo et al. (2005) also presented evidence for biparental inheritance in Chinese Pine, *Pinus tabulaeformis*, although they conclude that the paternal contribution is small and that the proportion of maternally derived mitochondria increased greatly during development. Similar patterns have been described for other conifers (reviewed in Guo et al. 2005). This system is, therefore, more akin to paternal leakage than true biparental inheritance.

Yan et al. (2007) conducted experimental manipulations on the fungus *Cryptococcus neoformis* to evaluate patterns of mtDNA inheritance in controlled crosses of parents with different mating types (e.g., MAT α and MAT α). Although mitochondria are predominantly inherited from one parent, these authors noted that among these mating types, some degree of biparental inheritance was detected in unmanipulated crosses (Yan et al. 2007). To test the hypothesis that a process such as methylation or ubiquitination normally ensures UPI of mtDNA, they experimented with altered temperature and UV light regimes, as well as introducing methylation and ubiquitination inhibitors. The environmental stressors of higher temperature and increased UV light levels, but not either of the other manipulations, led to an increase in the proportion of biparental transmission of mtDNA and mitochondrial heteroplasmy. Although the predominant mode of mtDNA transmission in this group of fungi is uniparental, the authors speculate that biparental inheritance, coupled with mitochondrial recombination, could be a potentially adaptive strategy under challenging environmental situations.

Strict paternal inheritance

Strict paternal inheritance of mtDNA has been documented in a number of taxa, primarily plants and marine alga including sequoia (Neale et al. 1989), bananas (Fauré et al. 1994), cucumber (Havey et al. 2004), melon (Zhao et al. 2014), and the green alga *Chlamydomonas* (Aoyama et al. 2006; Nakamura 2010). Although some gross patterns of segregation of mitochondria have been observed in some species detailed, mechanisms controlling paternal transmission of mitochondria in these taxa are largely unknown.

Doubly uniparental inheritance

In contrast to algae and plants, mtDNA is typically strictly maternally inherited (SMI) in animals. To our knowledge, only one taxon, i.e., the Bivalvia, has a different inheritance system known as doubly uniparental inheritance (DUI) (reviewed in Breton et al. 2007; Passamonti and Ghiselli 2009; Zouros 2013). Indeed, in some bivalve molluscs, two highly divergent mitochondrial lineages exist and are transmitted in a sex-specific manner. The female genome (F mtDNA) is inherited from the mother by both sons and daughters, which is what is found in a typical SMI case. However, the male genome (M mtDNA) is inherited from the father only by sons (males do not transmit the F mtDNA to their progeny). This represents a “mother-to-daughter” and “father-to-son” mitochondrial inheritance system, with M versus F DNA divergence >40% in some orders of bivalves (Breton et al. 2007; Passamonti and Ghiselli 2009; Zouros 2013).

To date, DUI has been found in four orders and nine families out of ~105 bivalve families (i.e., Mytiloidea (Mytilidae); Nuculanoida (Nuculanidae); Unionoidea (Unionidae, Margaritiferidae, and Hyriidae); and Veneroidea (Veneridae, Solenidae, Semelidae, and Donacidae) (Doucet-Beaupré et al. 2010; Boyle and Etter 2013). In DUI species, the embryo is always heteroplasmic, but this status is generally only maintained in males, where M mitochondria aggregate and localize into a single blastomere from which the gonad is formed, indicating a non-random segregation (i.e., M mtDNA localizes in the sperm and F mtDNA in somatic tissues). Conversely, in female embryos M mitochondria disperse randomly and M mtDNA eventually completely disappears, restoring the homoplasmic condition (Cao et al. 2004; Milani et al. 2012). In other words, post-fertilization depletion of paternal mtDNA usually occurs in DUI females, a mechanism that is typical of mammals, whereas DUI males remain heteroplasmic for two highly divergent mtDNAs in a tissue-specific manner (but see Zouros (2013) for a review of the exceptions).

In addition to their atypical system of mtDNA transmission, DUI bivalves also have novel, sex-specific mitochondrial protein-coding genes; F-orf in the F mtDNA and M-orf in the M mtDNA, both of which are relatively conserved across species within a family (Breton et al. 2009, 2011; Milani et al. 2013; Stewart et al. 2013). Their functions are still unknown, although the presence of gene products in the nucleus indicates that they are not involved in ATP production, like other typical mtDNA-encoded proteins (Breton et al. 2011, 2014; Milani et al. 2014). An initial hypothesis proposed that these genes may play a role in sex determination because of the observation that gonochorism (i.e., separate male and female sexes) in freshwater bivalves is absolutely correlated with the presence of DUI and these novel sex-specific proteins whereas closely related hermaphroditic species lack the M mtDNA (i.e., possess SMI) and have macromu-

tations in the F-orf in their F mtDNAs (Breton et al. 2011). If true, this would make DUI the first animal sex determination system involving mtDNA-encoded proteins, and explain its long-term persistence in bivalves (as heteromorphic sex chromosomes are absent in this taxa). However, the link between DUI and sex determination still remain to be elucidated. Based on crossing experiments, it has been suggested that the coupling of maleness and M mtDNA is associative rather than causative (reviewed in Zouros 2013) such that a germ line can produce sperm in the absence of the M genome. However, these conclusions were largely based on interspecific crosses and (or) chemically induced triploid zygotes, manipulations that could breakdown or alter natural mitochondrial transmission and sex determination patterns. The cause of deviation from the “SMI rule” in bivalves thus remains an open question.

Atypical mitochondrial inheritance and uncommon sexual systems

A strong association between mitochondria and sex determination has been observed in several eukaryotic taxa (e.g., Xu 2005; Chase 2007; Shakya and Idnurm 2014; Perlman et al. 2015). For example, mitochondrial inheritance can be directly controlled by sex-determining genes, as in the fungus *Phycomyces blakesleeanus* (Shakya and Idnurm 2014). Alternatively, mtDNA itself can be a key element in sex determination, as described below for several plant species with nuclear-cytoplasmic sex determining system (Bailey and Delph 2007; Chase 2007), or mtDNA can effect extreme sex ratio distortion, as recently demonstrated in the booklouse (specifically a strain referred to as *Liposcelis* nr. *bostrychophila* by Perlman et al. (2015)).

Could this linkage between sex determination and mitochondria be involved, in some way, in the existence of the above-described exceptions to SMI? Put another way, are deviations from SMI associated with uncommon sexual systems, i.e., with sexual strategies other than the predominant states of hermaphroditism in plants or gonochorism (i.e., separate males and females) in animals (Weeks 2012)? As far as we are aware, strict paternal inheritance is almost uniquely found in taxa that do not use one of these two most widespread forms of reproduction. Reproductive strategies vary among these taxa including the following: monoecy (e.g., sequoia, which have both male (pollen-producing) and female (seed-bearing) cones on different branches on the same tree) (Coder 2008); andromonoecy (e.g., melon, which may have both perfect (bisexual) and male flowers on the same plant); monoecy or gynoecey (e.g., cucumber, which may possess both bisexual and female flowers on the same plant) (Foucart et al. 2012); monoecy with separate male and female flowers on the same plant but also with some, usually non-reproductive, hermaphroditic flowers (e.g., banana) (Fauré et al. 1994); and isogamy with two distinct mating types (i.e., the unicellular green alga

Chlamydomonas, which is also known to alternate between asexual and sexual life cycles but for which leakage of mtDNA, biparental inheritance, and recombinant mitochondrial haplotypes have regularly been detected (Xu 2005)).

Strict paternal transmission of mtDNA is particularly intriguing in plants given that their anisogamous form of reproduction, i.e., large eggs with many mitochondria and small sperm with few mitochondria, might be the most common mechanism for reducing the likelihood that cytoplasmic genomes from the male are passed on to the embryo. This likely implies strong selection for paternal inheritance, by whatever mechanism that happened to work in these particular lineages. What remains to be established is whether the genes that control the sex of these organisms also control mitochondrial inheritance (or may have done so in the past), and (or) if the mitochondrial genome itself is (or has been) involved in sex determination.

Interestingly, the only known sex determination system in which the mtDNA is directly involved is found in hermaphroditic angiosperm plants exhibiting cytoplasmic male sterility (CMS) (Chase and Gabay-Laughnan 2004; Bailey and Delph 2007; Chase 2007). Specifically, this nuclear-cytoplasmic sex determining system involves CMS mutations, which may be unique mutations, rearrangements, or recombinations in the plant mitochondrial genome, that greatly reduce or eliminate the development of fertile pollen in hermaphroditic individuals (e.g., Carlsson and Glimelius 2012; Tuteja et al. 2013). Thus, in plant populations polymorphic for normal and CMS-specifying mtDNA, the breeding system will be gynodioecious: there will be some hermaphroditic individuals with perfect flowers and some with male-sterile (functionally female) flowers (McCauley and Olson 2008; McCauley and Bailey 2009). In such populations, CMS can lead to selection for a diverse array of nuclear responses. Male fertility may be restored via “restorer genes” (McCauley and Olson 2008; McCauley and Bailey 2009; Carlsson and Glimelius 2012), which can, over time, eliminate the female flower type (thus causing the population to revert to the ancestral hermaphroditic breeding system). Alternatively, the remaining hermaphrodites may be “masculinized” (thus yielding a gynodioecy to dioecy breeding system transition). In theory, CMS could also select for a reversal of maternal inheritance; because mitochondria in pollen are less likely to carry a CMS gene than mitochondria in ovules, nuclear genes could be selected to promote paternally derived mitochondria over maternally derived ones (Burt and Trivers 2006; McCauley and Olson 2008; McCauley and Bailey 2009). Such a scenario could explain the origin of strict paternal inheritance in the angiosperm plants described above.

Conclusion and perspectives

This minireview illustrates the great diversity of mitochondrial inheritance patterns seen in eukaryotes. With the employment of highly sensitive techniques and analytical methods, it is conceivable that deviations from SMI will be reported in many other organisms. A thorough appreciation of the exceptions to SMI will clearly have implications for how mitochondrial markers are used in reconstructing phylogenies for taxonomic and other practical applications (e.g., the use of mtDNA in molecular ecology and conservation biology) (see Galtier et al. 2009; Krishnamurthy and Francis 2012). To uncover and fully appreciate the implications of mitochondrial novelties as encountered in bivalves and plants, we must expand taxonomic sampling in a comprehensive manner. In addition to providing more rigorous phylogenies, more extensive studies of species with atypical sexual systems will significantly contribute to a better understanding of fundamental evolutionary processes, such as the selective forces that maintain SMI in most eukaryotes, and of the role of intergenomic conflict in sex determination and other fundamental cellular processes.

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