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NEWS AND COMMENTARY

Sex chromosomes and mitochondrial DNA polymorphism in birds

The Hill–Robertson effects extend from nucleus to mitochondria

GAB Marais

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The evolutionary history of the human Y chromosome has been reconstructed (Skaletsky *et al*., 2003; Ross *et al*., 2005), and provides clear evidence of genetic degeneration. This uncomfortable conclusion for human males has even stimulated popular scientific accounts (Sykes, 2004). The Y chromosome's degeneration seems to be explained by its non-recombining nature. Absence of recombination in DNA has several consequences, including inefficient natural selection and low diversity—the so-called Hill–Robertson effects (see Charlesworth and Charlesworth, 2000 for review). These arise because an advantageous new mutation is unable to escape a poor haplotype (if that is where it first occurs), and because a disadvantageous new mutation can permanently blight the haplotype on which it arises.

Birds' sex chromosomes make a particularly interesting comparison with the XY system in humans and many other animals because, in birds, the females are heterogametic, rather than the males. In other words, the females have two distinct sex chromosomes called Z and W, whereas males are ZZ (and not XY). The avian Z and W are shared by all birds, indicating that they became established just before the bird radiation.

Following the complete sequencing of the chicken genome, recent analysis of its W chromosome has shown evidence of degeneration comparable to the human Y chromosome (Berlin and Ellegren, 2004, 2006). Bird mitochondrial genomes are also expected to suffer from Hill–Robertson effects. Berlin *et al*. (2007) point out that both the W and the mitochondrial genomes are non-recombining and are passed down from mother to daughter. Consequently, they are genetically (but not physically) linked. The Hill–Robertson effects affecting W would therefore be expected to extend to mitochondrial DNA (mtDNA) (see Figure 1).

Berlin *et al*. (2007) therefore conducted a meta-analysis of mtDNA polymorphism data from more than 50 bird species. They collected cytochrome *b* polymorphism data for 61 avian and 69 mammalian species from databases. What they found is that polymorphism level at synonymous sites (π_s) was three-fold lower in birds than in mammals even after controlling for body size—a well-known factor influencing genetic diversity—suggesting that mtDNA neutral polymorphism is reduced in birds compared to mammals. They also found that the ratio of non-synonymous polymorphism level and synonymous polymorphism level (π_a/π_s) was higher in birds than in mammals, which is consistent with natural selection being less efficient in removing slightly deleterious mutations in bird populations than in mammal populations. They found a similar ratio of non-synonymous divergence over synonymous divergence (K_a/K_s) for bird and mammal cytochrome *b*, which suggests that it is not affected too strongly by Hill–Robertson effects from the W chromosome on the long term. However, degeneration may well affect other mitochondrial genes under weaker functional constraints.

Although their data support the idea that, in birds, mtDNA polymorphism is low because of linkage with W chromosome, other interpretations are possible. Contrasting mitochondrial and nuclear polymorphism data, when this will be available, should help confirm their hypothesis. The linkage between W and mitochondria would be expected to work the other way round, so that Hill–Robertson effects on the mitochondrial genome should extend to the W chromosome, which could explain why the level of polymorphism on the W in chicken is so dramatically low (Berlin and Ellegren, 2004).

These results are also interesting with respect to a recent debate on the relationship between mtDNA polymorphism and population size (N_e) in animals. Bazin *et al*. (2006) have suggested that mitochondrial genetic diversity is not a good proxy for N_e, contrary to the assumption that has been widely held for decades. These authors gathered polymorphism data from very different groups of animals and found that intuitive estimates of N_e in these animals correlate with nuclear genetic diversity but not with mitochondrial genetic diversity. They concluded that there was no link between mtDNA polymorphism and N_e in animals.

To explain this finding, they invoke Gillespie's (2000) 'genetic draft' theory. Gillespie's predictions differ from the classical results of the neutral theory of molecular evolution (see Kimura, 1979) in which the level of neutral polymorphism depends on the mutation rate and N_e. Under the neutral theory, in small populations, genetic drift is strong and it reduces neutral polymorphism. As N_e increases, genetic drift gets weaker and neutral polymorphism increases. Gillespie claimed that this may be correct for small to moderate N_e, but for large N_e, the relationship with neutral polymorphism should flatten because of genetic draft. In large populations, natural selection is more efficient and there is much more opportunity for fixation of advantageous mutations that will sweep through the population and reduce the neutral polymorphism at linked sites. Recurrent selective sweeps will reduce genetic diversity in these large populations. Empirical data tend to fit with these expectations: in mammals where N_e are thought to be small, there seems to be a positive correlation between N_e and the level of polymorphism (Mulligan *et al*., 2006; Berlin *et al*., 2007; Nabholz *et al*., 2007); for other groups such as invertebrates with much larger N_e, no relationship is observed (Bazin *et al*., 2006).

But then comes the question of why there should be these recurrent selective sweeps. Recurrent episodes of selection could be due to parasites that are maternally transmitted such as Wolbachia found in arthropods and nematods (Hurst and Jiggins, 2005). This kind of maternally transmitted parasites may not be present in all animals; so there must be other factors. A change in breeding system could be such a factor. Paland and Lynch (2006) have recently reported that in Daphnia, transition from sexuality to asexuality leads to accelerated evolution in mitochondrial genome, which suggests that the lack of sex and recombination in the nuclear genome has secondary effects on the mitochondrial genome. Berlin *et al*.'s results suggest that W chromosome could also be a contributing factor to obscuring the correlation between mtDNA polymorphism and N_e. Birds do have a larger population size than mammals and mtDNA polymorphism is lower in birds than in mammals. This supports the general conclusions of Hurst and Jiggins

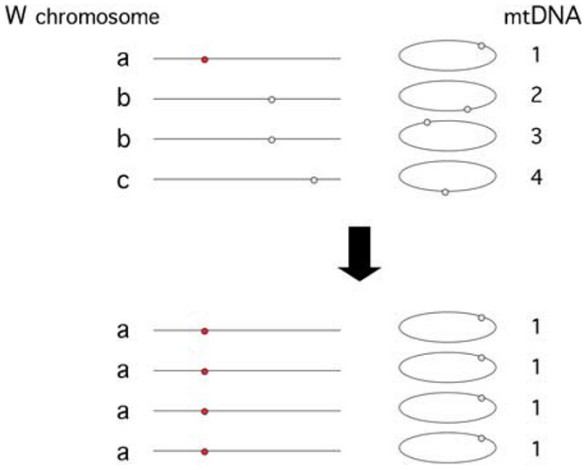

Figure 1 Selective sweep on W chromosome and mitochondrial DNA. This sketch explains how Hill–Robertson effects can affect both W chromosome and mitochondrial genome. It illustrates a special case of Hill–Robertson effects: a selective sweep. An advantageous mutation has just appeared on a W chromosome. There are different W chromosomes in the population: a (with an advantageous mutation), b and c (with neutral mutations). There are also different mitochondrial genomes (mtDNA) in the population carrying different neutral mutations: 1, 2, 3 and 4. $mtDNA_1$ was associated with W_a when mutation a appeared. Because the W chromosome and mitochondrial genome are maternally inherited, all the descendants of the first W_a individual will have $mtDNA_1$. After the end of the selective event, W_a has been fixed in the population as well as $mtDNA_1$ because of genetic hitchhiking. All the polymorphism on both W chromosome and mtDNA has been swept out. Mutation 1 in mtDNA could also be slightly deleterious. In this case, fixation of advantageous mutation a in W chromosome would have driven fixation of deleterious allele 1 in mtDNA. An advantageous mutation on mtDNA can also produce a selective sweep on the W chromosome. Red dot = advantageous mutation; blue dot = neutral mutation.

(2005) and Bazin *et al*. (2006) that inferring N_e from mitochondrial data may be a risky business.

Dr GAB Marais is at the Université de Lyon, Laboratoire de Biométrie et Biologie Evolutive, 16 rue Raphaël Dubois, Villeurbanne, France.

e-mail: marais@biomserv.univ-lyon1.fr

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