Mitochondrial DNA, August 2009; 20(4): 65–68

informa
healthcare

Mito-communications

SIMON Y.W. HO & ROBERT LANFEAR*

Centre for Macroevolution and Macroecology, Research School of Biology, Australian National University, Canberra, Australia

(Received 1 June 2009; In final form 4 June 2009)

Downloaded By: [Australian National University] At: 00:19 27 July 2009

Mitochondrial phylogeography of house mice

Various lines of inquiry can be used to establish the direction and timing of past human movements, including archaeology and analysis of ancient and modern human DNA. However, human presence does not necessarily leave enduring or detectable physical, documentary, or genetic traces. Instead, it is possible to trace human movements using one of a number of proxies, such as domestic or commensal animals. For example, prehistoric human migrations in Oceania have been investigated using genetic studies of breadfruit (Zerega et al. 2004), bottle gourds (Clarke et al. 2006), and pigs (Larson et al. 2007).

In a pair of papers published in the *Proceedings of the Royal Society B*, Jeremy Searle and colleagues present phylogeographic analyses of house mice (*Mus musculus* ssp.; Searle et al. 2009a, 2009b). In the first paper, Searle et al. (2009a) obtain samples of *M. m. domesticus* from across the British Isles, finding a distinctive lineage with a geographic distribution including Orkney, Shetland, Isle of Man, the Outer Hebrides, and Ireland. The distribution of this 'Orkney' clade, which is also found to be predominant in coastal Norway, coincides with that of the former presence of Norwegian Vikings. The results of the study raise the possibility of using analyses of house mice to investigate Viking activities across the northern Atlantic, such as their exploration of Greenland, Iceland, and Newfoundland.

In their second paper, Searle et al. (2009b) study an extensive sample of house mice from New Zealand. Not surprisingly, the dominant subspecies is the western European *M. m. domesticus*, but the authors find representatives of other subspecies (*M. m. musculus* from central Europe and *M. m. castaneus* from southern Asia). Analyses of both nuclear and mitochondrial DNA reveal that hybridization has taken place among the subspecies.

References

Clarke AC, Burtenshaw MK, McLenachan PA, Erickson DL, Penny D. 2006. Reconstructing the origins and dispersal of the Polynesian bottle gourd (*Lagenaria siceraria*). Mol Biol Evol 23: 893–900.

Larson G, Cucchi T, Fujita M, Matisoo-Smith E, Robins J, Anderson A, Rolett B, Spriggs M, Dolman G, Kim T-H, Thuy NTD, Randi E, Doherty M, Due RA, Bollt R, Djubiantono T, Griffin B, Intoh M, Keane E, Kirch P, Li K-T, Morwood M, Pedriña LM, Piper PJ, Rabett RJ, Shooter P, Van den Bergh G, West E, Wickler S, Yuan J, Cooper A, Dobney K. 2007. Phylogeny and ancient DNA of *Sus* provides insights into Neolithic expansion in Island Southeast Asia and Oceania. Proc Natl Acad Sci USA 104:4834–4839.

Searle JB, Jones CS, Gündüz I, Scascitelli M, Jones EP, Herman JS, Rambau RV, Noble LR, Berry RJ, Giménez MD, Jóhannesdóttir F. 2009a. Of mice and (Viking?) men: Phylogeography of British and Irish house mice. Proc R Soc Lond B: Biol Sci 276: 201–207.

Searle JB, Jamieson PM, Gündüz I, Stevens MI, Jones EP, Gemmill CEC, King CM. 2009b. The diverse origins of New Zealand house mice. Proc R Soc Lond B: Biol Sci 276: 209–217.

Zerega NJC, Ragone D, Motley TJ. 2004. Complex origins of breadfruit (*Artocarpus altilis* Moraceae): Implications for human migrations in Oceania. Am J Bot 91:760–766.

Correspondence: R. Lanfear, Centre for Macroevolution and Macroecology, Research School of Biology, Australian National University, Building 116 Daley Road, Canberra, Australian Capital Territory 0200, Australia. Fax: + 61 2 6125 5573. E-mail: rob.lanfear@anu.edu.au

ISSN 1940-1736 print/ISSN 1940-1744 online © 2009 Informa UK Ltd.
DOI: 10.1080/19401730903093703

Downloaded By: [Australian National University] At: 00:19 27 July 2009

Two migration routes for the first Americans

The spatial and temporal patterns of human colonization of the New World have received considerable research attention in recent years, from archaeologists, linguists, and geneticists. While it has been established that Native Americans descended from Asian colonists arriving at least 14,000 years ago, the exact timing and path(s) of their migration have been contentious issues (e.g. Fagundes et al. 2008; Gilbert et al. 2008; Goebel et al. 2008; Ho and Endicott 2008).

Perego et al. (2009) tackle this question by concentrating on two rare mitochondrial haplogroups, D4h3 and X2a, found among Native Americans. By analysing a set of 69 complete mitochondrial genomes and considering their geographical distribution, the authors find that members of the two haplogroups took different routes into the continent. While haplogroup D4h3 took a coastal path, as with the four common pan-American haplogroups (A2, B2, C1, and D1), haplogroup X2a appears to have taken an interior route through the putative ice-free corridor between the Laurentide and Cordilleran ice sheets. Perego et al. (2009) place the timing of migration to the Americas around 16,000 years before present.

The findings of Perego et al. (2009) challenge the 'single wave' hypothesis of American colonization that has been posited on genetic grounds (e.g. Merriwether et al. 1995; Fagundes et al. 2008). This has significant implications for the interpretation of linguistic and archaeological evidence.

References

Fagundes NJ, Kanitz R, Eckert R, Valls AC, Bogo MR, Salzano FM, Smith DG, Silva WA, Zago MA, Ribeiro-dos-Santos AK, Santos SEB, Petzl-Erler ML, Bonatto SL. 2008. Mitochondrial population genomics supports a single pre-Clovis origin with a coastal route for the peopling of the Americas. Am J Hum Genet 82:583–592.

Gilbert MTP, Jenkins DL, Götherström A, Naveran N, Sanchez JJ, Hofreiter M, Thomsen PF, Binladen J, Higham TFG, Yohe IIRM, Parr R, Cummings LS, Willerslev E. 2008. DNA from pre-Clovis human coprolites in Oregon, North America. Science 320:786–789.

Goebel T, Waters MR, O'Rourke DH. 2008. The late Pleistocene dispersal of modern humans in the Americas. Science 319: 1497–1502.

Ho SYW, Endicott P. 2008. The crucial role of calibration in molecular date estimates for the peopling of the Americas. Am J Hum Genet 83:142–146.

Merriwether DA, Rothhammer F, Ferrell RE. 1995. Distribution of the four-founding lineage haplotypes in Native Americans suggests a single wave of migration for the New World. Am J Phys Anthropol 98:411–430.

Perego UA, Achilli A, Angerhofer N, Accetturo M, Pala M, Olivieri A, Kashani BH, Ritchie KH, Scozzari R, Kong Q-P, Myres NM, Salas A, Semino O, Bandelt H-J, Woodward SR, Torroni A. 2009. Distinctive Paleo-Indian migration routes from Beringia marked by two rare mtDNA haplogroups. Curr Biol 19:1–8.

The influence of altitude on mitochondrial evolution in mammals

Living at high altitude introduces a number of problems for mammalian mitochondria. First, the reduced availability of oxygen decreases the efficiency of oxidative phosphorylation. Second, the thinner atmosphere provides less protection from ultraviolet radiation. Third, the lower temperatures elicit an increase in oxidative metabolism. All three of these factors serve to elevate the production of reactive oxygen species, which can be detrimental to proteins and nucleic acids. This suggests that mammals living at high altitude might experience selective pressure on their mitochondrial DNA to mitigate the effects of oxygen radicals. Some studies have detected an influence of climate in the evolution of human mitochondrial genomes (e.g. Mishmar et al. 2003), although subsequent studies have not supported this hypothesis (e.g. Elson et al. 2004).

In a paper published recently in *Heredity*, Gering et al. (2009) examined the DNA sequences of the cytochrome *b* gene in deer mice, species of which inhabit a range of different environments. The authors tested a number of competing models of nucleotide change among branches in the phylogenetic trees, but found no evidence of positive selection in cytochrome *b* in haplogroups or species of deer mice living at high altitudes.

Investigating a similar question, Hassanin et al. (2009) analysed the complete mitogenomes of 20 species of the tribe Caprini (including goats, sheep, and ibex), along with those of four outgroup taxa. After conducting detailed investigations of nucleotide composition, sequence variability, and patterns of non-synonymous substitutions among lineages, Hassanin et al. (2009) identify an acceleration in the evolutionary rate of the ATPase complex of Caprini. Upon considering several lines of evidence, the authors conclude that this rate increase is associated with an elevated production of reactive oxygen species, rather than an increase in metabolic rate at high altitude.

The influence of altitude on mammalian mitochondrial evolution remains a somewhat open question. Studies performed at a larger taxonomic scale, coupled with detailed investigations of the impacts

of specific non-synonymous substitutions on protein structure and function, will undoubtedly provide further insight into this interesting issue.

References

Elson JL, Turnbull DM, Howell N. 2004. Comparative genomics and the evolution of human mitochondrial DNA: Assessing the effects of selection. Am J Hum Genet 74:229–238.

Gering EJ, Opazo JC, Storz JF. 2009. Molecular evolution of cytochrome *b* in high- and low-altitude deer mice (genus *Peromyscus*). Heredity 102:226–235.

Hassanin A, Ropiquet A, Couloux A, Cruaud C. 2009. Evolution of the mitochondrial genome in mammals living at high altitude: New insights from a study of the tribe Caprini (Bovidae Antilopinae). J Mol Evol 68:293–310.

Mishmar D, Ruiz-Pesini E, Golik P, Macaulay V, Clark AG, Hosseini S, Brandon M, Easley K, Chen E, Brown MD, Sukernik RI, Olckers A, Wallace DC. 2003. Natural selection shaped regional mtDNA variation in humans. Proc Natl Acad Sci USA 100:171–176.

Extreme organization

Most animal mitochondrial genomes are about the same size and contain more or less the same set of genes. These features usually serve to make animal mitogenomes highly amenable to traditional sequencing methods, where it helps to have some idea of what you're looking for before you start. Shao et al. (2009) tried a number of times to sequence the mitogenomes of blood-sucking lice, but with no success. It was not until the human body-louse genome project was completed that the reason for the problems became clear—rather than being arranged in a single large chromosome, the mitochondrial DNA of the human body-louse *Pediculus humanus* is arranged into 18 circular mini-chromosomes. Each of these 3–4 kb chromosomes contains between one and three genes as well as a lot of non-coding DNA. Although this arrangement is not completely unknown, *P. humanus* is the first reported animal in which the typical mitochondrial chromosome appears to have been entirely replaced by the fragmented mini-chromosomes. Quite why this fragmented genome organization has evolved in the blood-sucking louse lineage is not clear, although it is intriguing to consider the possibility that this novel arrangement might confer some functional advantage to the lice, associated with their blood-sucking lifestyle.

While most animal mitochondrial genomes are around 15–19 kb in length, and have 30–40 genes, plant mitochondrial genomes show no such restraint (Figure 1). In a recent study, Goremykin et al. (2009) report the largest mitogenome sequenced to date—that of the grape *Vitis vinifera*. At 773 kb it is not the largest known mitochondrial genome (an honour currently held by the mitogenome of the melon *Cucumis melo* at 2400 kb), but complete sequencing and careful gene annotation allowed the authors to re-examine some provocative hypotheses about rampant horizontal gene transfer in plants (e.g. Bergthorsson et al. 2003). Goremykin et al. (2009) disagree with the hypothesis that horizontal gene transfer has been prevalent among plant mitogenomes. They attribute the large degree of incongruence found among gene trees from different mitochondrial genes to be symptomatic of problems with phylogenetic methodology, a lack of phylogenetic signal, and the difficulties associated with the use of paralogs for phylogenetic inference. They support this view by showing that there is also a great deal of incongruence among chloroplast gene trees despite there being little doubt that horizontal gene transfer has not occurred between chloroplast genomes.

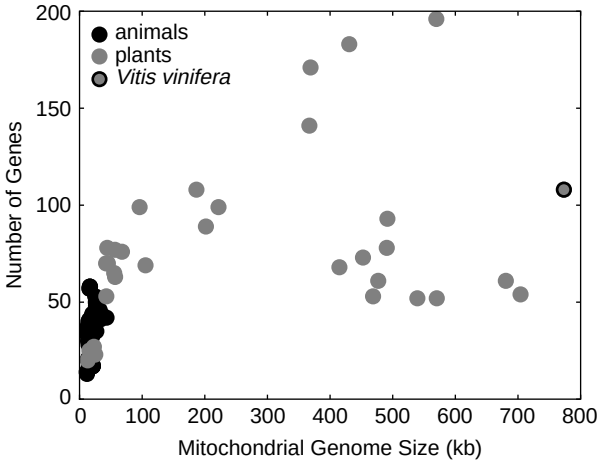

Figure 1. Fully sequenced plant and animal mitogenomes available in GenBank. At 773 kb, *V. vinifera* is the largest sequenced genome to date.

In the course of their analyses, Goremykin et al. (2009) may also have stumbled across a novel DNA transfer route. They identified a region of the chloroplast genome of the wild carrot *Daucus carota*, which appears to contain two short sequences of mitochondrial origin. If this result is confirmed (crucially, it relies on the correct assembly of the *D. carota* chloroplast genome), then this would represent the first report of the transfer of DNA from the mitochondrial to the chloroplast genomes.

Downloaded By: [Australian National University] At: 00:19 27 July 2009

References

Bergthorsson U, Adams KL, Thomason B, Palmer JD. 2003. Widespread horizontal transfer of mitochondrial genes in flowering plants. Nature 424:197–201.

Goremykin VV, Salamini F, Velasco R, Viola R. 2009. Mitochondrial DNA of *Vitis vinifera* and the issue of rampant horizontal gene transfer. Mol Biol Evol 26:99–110.

Shao RE, Kirkness EF, Barker SC. 2009. The single mitochondrial chromosome typical of animals has evolved into 18 minichromosomes in the human body louse *Pediculus humanus*. Genome Res 19:904–912.

The effective population size of mitochondrial DNA

One of the more fundamental results of population genetics is that levels of neutral diversity should scale with population size. Mitochondrial DNA (mtDNA) is often assumed to be a neutral marker, and consequently it has often been used to infer population-level processes. The recent discovery that the relationship between diversity and population size does not hold between major animal groups or life histories, therefore, was something of a surprise (Bazin et al. 2006). For instance, insects do not have higher mtDNA diversity than mammals, and marine molluscs do not have higher mtDNA diversity than terrestrial molluscs, despite huge differences in census population sizes. The absence of the relationship in animal mtDNA was attributed to positive selection. Since mtDNA forms a single locus, a mitochondrial genome containing a beneficial mutation will occasionally be swept to fixation in the population, thereby drastically reducing mtDNA diversity (a process known as genetic draft). If genetic draft events are more common in larger populations (for instance, because selection is more efficient in larger populations, or because larger populations tend to produce beneficial mutations more often), then it is possible that this process could render the effective population size of mtDNA relatively constant among different animal groups. This result is potentially problematic for anyone using mtDNA to measure or compare effective population sizes, or to infer demographic histories.

In contrast to the between-groups approach taken by Bazin et al. (2006), three further studies have shown that the effective population size of mtDNA does appear to vary within mammals (Mulligan et al. 2006; Popadin et al. 2007; Nabholz et al. 2008). In a significant extension to this approach, Piganeau and Eyre-Walker (2009) show that the effective population size of mtDNA varies significantly within a broad range of animal taxa. To do this they use two methods. First, they show that allozyme heterozygosity and synonymous mtDNA diversity are correlated within a range of vertebrate groups. Second, they show that the level of purifying selection on non-synonymous mutations correlates with levels of synonymous mtDNA variation in diversity within a large range of vertebrate and invertebrate groups—as would be expected if there is significant variation in the effective population size of mtDNA.

These observations represent a glimmer of hope for those relying on mtDNA for population genetic studies. However, it is notable that despite significant variation in mtDNA diversity within animal groups, the differences in diversity between species are still much lower than would be predicted by simple population genetic theory. Piganeau and Eyre-Walker (2009) suggest that, in addition to a number of hypotheses such as genetic draft, a negative correlation between the mutation rate per generation and census population size (in mammals at least) might be keeping levels of mtDNA diversity relatively constant. This is because although species with high per-generation mutation rates (such as chimps) will tend to generate more diversity per generation, these species also tend to have small census population sizes, and so diversity is quickly lost through drift. It is plausible that the negative correlation between these variables serves to keep levels of diversity much more constant that we would otherwise expect.

Piganeau and Eyre-Walker (2009) also show that in cases where the per-generation mutation rate can be estimated, it is possible to derive rough corrected estimates of the effective population size of mtDNA. The resulting effective population size estimates (such as 5000–10,000 for humans and chimps) are remarkably sensible, and appear to broadly agree with those estimated by other (non-mtDNA) means.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

Bazin E, Glemin S, Galtier N. 2006. Population size does not influence mitochondrial genetic diversity in animals. Science 312:570–572.

Mulligan CJ, Kitchen A, Miyamoto MM. 2006. Comment on 'Population size does not influence mitochondrial genetic diversity in animals'. Science 314:1390a.

Nabholz B, Mauffrey JF, Bazin E, Galtier N, Glemin S. 2008. Determination of mitochondrial genetic diversity in mammals. Genetics 178:351–361.

Piganeau G, Eyre-Walker A. 2009. Evidence for variation in the effective population size of animal mitochondrial DNA. PLoS ONE 4:e4396.

Popadin K, Polishchuk LV, Mamirova L, Knorre D, Gunbin K. 2007. Accumulation of slightly deleterious mutations in mitochondrial protein-coding genes of large versus small mammals. Proc Natl Acad Sci USA 104:13390–13395.

Downloaded By: [Australian National University] At: 00:19 27 July 2009