



University of HUDDERSFIELD

University of Huddersfield Repository

Richards, Martin B., Soares, Pedro and Torroni, Antonio

Palaeogenomics: Mitogenomes and Migrations in Europe's Past

Original Citation

Richards, Martin B., Soares, Pedro and Torroni, Antonio (2016) Palaeogenomics: Mitogenomes and Migrations in Europe's Past. *Current Biology*, 26 (6). R243-R246. ISSN 09609822

This version is available at <http://eprints.hud.ac.uk/id/eprint/30167/>

The University Repository is a digital collection of the research output of the University, available on Open Access. Copyright and Moral Rights for the items on this site are retained by the individual author and/or other copyright owners. Users may access full items free of charge; copies of full text items generally can be reproduced, displayed or performed and given to third parties in any format or medium for personal research or study, educational or not-for-profit purposes without prior permission or charge, provided:

- The authors, title and full bibliographic details is credited in any copy;
- A hyperlink and/or URL is included for the original metadata page; and
- The content is not changed in any way.

For more information, including our policy and submission procedure, please contact the Repository Team at: E.mailbox@hud.ac.uk.

<http://eprints.hud.ac.uk/>

Palaeogenomics: Ancient DNA unveils more surprises from Europe's past

The latest in a series of transformative studies of DNA from prehistoric Europeans focuses on the mitochondrial DNA, bringing fresh surprises and filling in important details of the early stages of a European ancestry stretching back more than 40,000 years.

Martin B. Richards¹, Pedro Soares² and Antonio Torroni³

¹Department of Biological Sciences, School of Applied Sciences, University of Huddersfield, Queensgate, Huddersfield, UK, E-mail: m.b.richards@hud.ac.uk;

²CBMA (Centre of Molecular and Environmental Biology), Department of Biology, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal;

³Dipartimento di Biologia e Biotechnologie "L. Spallanzani", Università di Pavia, Pavia, Italy

The last decade has seen a step-change in the recovery of DNA sequences from ancient human remains, with the study of the mitochondrial DNA (mtDNA) leading the way. The mtDNA traces the female line of descent, and the reconstruction in exquisite detail of the maternal genealogy makes it possible to test historical hypotheses using the phylogeographic approach, combining the tree with geographic information and a molecular clock. This led to the pioneering proposal in the 1980s that modern humans arose in Africa and dispersed recently around the rest of the world and, once the use of whole-mtDNA genome (mitogenome) analyses became routine, to a model suggesting a single exit from the Horn of Africa ~60 thousand years ago (ka). The model suggested that they dispersed first into Arabia or the Gulf, followed by rapid twin dispersals northwards into West Eurasia (Near East/Europe) and eastwards into East Eurasia/Australasia by 50 ka [1]. But all of this was based on inference from present-day lineages. The study by Posth et al. [2] is the latest in a breathtaking series that has brought an entirely new evidence base to our understanding of human history.

The new wave of ancient DNA studies focused first on a more recent European revolution, the

transition to agriculture, ~8 ka. Haak and colleagues [3] showed that early Neolithic populations from Central Europe differed significantly in their mtDNA profiles from modern populations in the same region. This was followed by studies that focused on the Mesolithic hunter-gather-fisher populations that preceded the spread of agriculture in Central and Northern Europe [4]. These pointed to significant differences between the foragers and the earliest farmers, with the former carrying higher frequencies of mitogenomes belonging to haplogroup U, especially U5 – already predicted to be the most ancient cluster of European mtDNAs on the basis of the coalescence ages of modern samples [5]. Subsequent work indicated not only a major dispersal into Central Europe with the Neolithic but pointed to a further, Late Neolithic dispersal from southern Russia, possibly associated with the spread of Indo-European languages [4].

This suggestion was dramatically confirmed as human palaeogenomics took off, with hundreds of complete nuclear genomes or genome-wide profiles now available [6]. Most modern European populations have a composite genome with what look like three major ancestral sources.

One traces to the Mesolithic foraging populations of Europe, and the second to the earliest farmers from the southeast. The third shares affinities with early Bronze Age Steppe pastoralists – favoured by many scholars as the source for the Indo-European languages. This scenario is also now receiving support from genomic-level analyses of the male-inherited Y chromosome, where reliable dating is finally becoming a reality [7].

But genome-wide data has some limitations at present. The volume is overwhelming and, although new statistical methods for handling this goldmine are coming thick and fast, few yet make full use of the high information value present in haplotypes. This means that most current approaches, whilst gaining power by using multiple independent recombining loci across the genome, lack the ability to detect the detailed nesting relationships provided by the non-recombining mtDNA and Y chromosome. Hence, as well as the development of such approaches for whole genomes [8], we are also likely to see a resurgent interest in mitogenomes. There is another reason for this: published nuclear genomes come along with their (usually high-quality) mitogenomes, but these are often side-lined in the analyses in favour of their autosomal counterpart. Moreover, sometimes (because of the higher copy number) only the mtDNA survives in some of the most interesting samples.

All of these points motivate the exciting new study by Posth et al. [2]. Their work includes 35 new pre-Neolithic mitogenomes from Europe, almost tripling the existing database of 20, opening up a significant new window onto genetic variation across Europe between 7 and 40 ka.

Their most striking result is the detection of a novel branch of haplogroup M, named M0 in Figure 1, in three Early Upper Palaeolithic individuals from north-western Europe. Haplogroups M and N are twin non-African

mtDNA founders thought to have arisen outside Africa from the African L3 haplogroup after ~60 ka [1]. Most of the Palaeolithic European lineages, like the Mesolithic lineages already discussed, belong to haplogroup U, a subcluster of R which is, in turn, the major subcluster of haplogroup N.

However, there are some long-standing puzzles in the M and N distributions. Firstly, most age estimates for N (and R) are earlier than those for M, even though parsimony urges that they arose and dispersed together [1]. Secondly, whilst N and R are globally distributed outside sub-Saharan Africa, M is almost absent from West Eurasia [5]. This suggested that M might have arisen a little later than N and R, and to have missed out on the early settlement of West Eurasia, spreading only to the east.

By incorporating the ancient DNA sequences into their analysis, Posth et al. [2] re-date M and N to similar ages, ~50 ka. This, alongside their discovery of M0 in Europe, leads them to suggest a parallel history of the twin haplogroups – spreading into both West and East Eurasia at a similar time, after ~55 ka. This chimes with another anomaly in the haplogroup M distribution. Most M branches are found in the Indian Subcontinent and Southeast Asia, with further widespread branches in East Asia, the Pacific and the Americas. However, a single branch, M1, is uniquely distributed around the Mediterranean and North and Eastern Africa [9]. M1 derives directly (or almost directly) from the root of M, thus its antiquity in Western Eurasia might match the date of M0 in Europe (27–35 ka).

Strikingly, both M0 and M1 are deep-rooting lineages and each is the only representative of M in its geographical context – a marked contrast to India, where dozens of branches radiate from the M root, with a diminution of the diversity moving further east [1]. This suggests a subsequent discrete dispersal of the ancestor of M0 from Western Asia, in parallel with that of M1 (Figure

1), and a later but possibly concomitant Upper Palaeolithic spread of the first (together with haplogroup U5) into Europe and of the second (together with haplogroup U6) into North Africa (Figure 1).

The aligning of the M and N ages seen by Posth et al. [2] should perhaps be regarded with some caution, though. The estimates were made with much fewer, perhaps less representative data than those using only modern samples, and uneven distributions of both ancient and modern samples may skew the estimates in ways that are not well understood [1]. Nevertheless, in broad terms, their results provide strong support for the model of a single rapid expansion out of Africa after ~60 ka.

The second big discovery results from finally being able to start charting changes in the European population over time. There are a number of major lineages seen in the Upper Palaeolithic and Mesolithic of Europeans: haplogroups U5a and U5b, U8 and U2, as well as undifferentiated lineages belonging to U and its ancestor haplogroup R (U* and R*). Whereas the presence of U*, U5 and U8 in the oldest Europeans was expected from the phylogeography of contemporary Europeans [5, 10-12], the relict status of U2 in modern Europeans has made inferences more difficult; and the presence of R* in early Italy is especially intriguing, since the ancestry of its descendant haplogroup R0 (including the enigmatic haplogroup H, which comprises almost half of modern Europeans) is as yet undetermined.

But the various branches of haplogroup U are not equally represented over time. Various lineages ancestral to modern U subclusters, including U*, U5* and members of U8 and U2, are seen in the Upper Palaeolithic, and U2 and U8 remain prominent until well after the LGM, 19–15 ka. However, after 15 ka, there is a major expansion of U5b, predicted from both modern data and short ancient mtDNA sequences to have spread from the southwest European glacial refuge at

this time [4, 12-14]. U5a, which more likely spread from the east [4, 12], appears in Central Europe only after ~11 ka. After 15 ka, U8 and U2 mitogenomes become much less frequent. Perhaps these lineages are the remnants of “cryptic refugia” in Central Europe, but they are usually classified as Magdalenian, with a source in southwest Europe. Another possibility, then, is that this pattern supports two waves of Late Glacial re-colonisation of central Europe, perhaps corresponding to Gamble’s “pioneer phase” and “residential phase” [15].

A great deal has come together recently in piecing together the ancestry of European populations, but many outstanding issues remain. The new data challenge the view that European foraging populations were genetically uniform before the spread of farming, but they leave intact a prevailing assumption that all pre-Neolithic European populations differed genetically from the farmers who subsequently dispersed from south to north, in turn implying a major impact from early farming Near Eastern populations [16, 17]. But there are some marked differences between Neolithic Anatolians sampled to date and Early Neolithic Central Europeans [18] and there is still an important gap in the Mesolithic ancient DNA record for Mediterranean (as well as Atlantic) Europe. Studies of modern mitogenomes in fact suggest a more complex picture, with Late Glacial/Mesolithic dispersals from the Near East into Europe prior to fresh waves of migration with the onset of farming [19, 20]. Moreover, the first two mtDNA lineages from Mesolithic Greece belong to haplogroup K1, often assumed to have dispersed from Anatolia with the Neolithic [16].

What is especially exciting, though, is that all such suggestions based on modern distributions can now be tested with ancient DNA, and mitogenomes will surely play their part alongside genome-wide data in resolving these issues.

References

1. Mellars, P., Gori, K.C., Carr, M., Soares, P.A., and Richards, M.B. (2013). Genetic and archaeological perspectives on the initial modern human colonization of southern Asia. *Proc. Natl. Acad. Sci. U. S. A.* *110*, 10699–10704.
2. Posth, C., Renaud, G., Mittnik, A., Drucker, D.G., Rougier, H., Cupillard, C., Valentin, F., Thevenet, C., Furtwängler, A., Wißing, C., et al. (2016). Pleistocene mitochondrial genomes suggest a single major dispersal of non-Africans and a Late Glacial population turnover in Europe. *Curr. Biol. in press*.
3. Haak, W., Forster, P., Bramanti, B., Matsumura, S., Brandt, G., Tanzer, M., Villems, R., Renfrew, C., Gronenborn, D., Alt, K.W., et al. (2005). Ancient DNA from the first European farmers in 7500-year-old Neolithic sites. *Science* *310*, 1016–1018.
4. Brandt, G., Szecsenyi-Nagy, A., Roth, C., Alt, K.W., and Haak, W. (2014). Human paleogenetics of Europe - the known knowns and the known unknowns. *J. Hum. Evol.* *79*, 73–92.
5. Richards, M., Macaulay, V., Hickey, E., Vega, E., Sykes, B., Guida, V., Rengo, C., Sellitto, D., Cruciani, F., Kivisild, T., et al. (2000). Tracing European founder lineages in the Near Eastern mtDNA pool. *Am. J. Hum. Genet.* *67*, 1251–1276.
6. Haak, W., Lazaridis, I., Patterson, N., Rohland, N., Mallick, S., Llamas, B., Brandt, G., Nordenfelt, S., Harney, E., Stewardson, K., et al. (2015). Massive migration from the steppe is a source for Indo-European languages in Europe. *Nature* *522*, 207–211.
7. Batini, C., Hallast, P., Zadik, D., Delsler, P.M., Benazzo, A., Ghirotto, S., Arroyo-Pardo, E., Cavalleri, G.L., de Knijff, P., Dupuy, B.M., et al. (2015). Large-scale recent expansion of European patrilineages shown by population resequencing. *Nat Commun* *6*, 7152.
8. Leslie, S., Winney, B., Hellenthal, G., Davison, D., Boumertit, A., Day, T., Hutnik, K., Royrvik, E.C., Cunliffe, B., Lawson, D.J., et al. (2015). The fine-scale genetic structure of the British population. *Nature* *519*, 309–314.
9. Olivieri, A., Achilli, A., Pala, M., Battaglia, V., Fornarino, S., Al-Zahery, N., Scozzari, R., Cruciani, F., Behar, D.M., Dugoujon, J.-M., et al. (2006). The mtDNA legacy of the Levantine Early Upper Palaeolithic in Africa. *Science* *314*, 1767–1770.
10. Soares, P., Achilli, A., Semino, O., Davies, W., Macaulay, V., Bandelt, H.-J., Torroni, A., and Richards, M.B. (2010). The archaeogenetics of Europe. *Curr. Biol.* *20*, R174–R183.
11. Costa, M.D., Pereira, J.B., Pala, M., Fernandes, V., Olivieri, A., Achilli, A., Perego, U.A., Rychkov, S., Naumova, O., Hatina, J., et al. (2013). A substantial prehistoric European ancestry amongst Ashkenazi maternal lineages. *Nature Communications* *4*, 2543.
12. Malyarchuk, B., Derenko, M., Grzybowski, T., Perkova, M., Rogalla, U., Vanecek, T., and Tsybovsky, I. (2010). The peopling of Europe from the mitochondrial haplogroup U5 perspective. *PLoS One* *21*, e10285.
13. Achilli, A., Rengo, C., Battaglia, V., Pala, M., Olivieri, A., Fomarina, S., Magri, C., Scozzari, R., Babudri, N., Santachiara-Benerecetti, A.S., et al. (2005). Saami and Berbers—An unexpected mitochondrial DNA link. *Am. J. Hum. Genet.* *76*, 883–886.
14. Tambets, K., Rootsi, S., Kivisild, T., Help, H., Serk, P., Loogväli, E.L., Tolk, H.V., Reidla, M., Metspalu, E., Pliss, L., et al. (2004). The western and eastern roots of the Saami - the story of genetic "outliers" told by mitochondrial DNA and Y chromosomes. *Am. J. Hum. Genet.* *74*, 661–682.
15. Gamble, C., Davies, W., Pettitt, P., Hazelwood, L., and Richards, M. (2005). The archaeological and genetic foundations of the European population during the Late Glacial: implications for 'agricultural thinking'. *Camb Archaeol J* *15*, 193–223
16. Hofmanová, Z., Kreutzer, S., Hellenthal, G., Sell, C., Diekmann, Y., Díez-del-Molino, D., van Dorp, L., López, S., Kousathanas, A., Link, V., et al. (2016). Early farmers from across Europe directly descended from Neolithic Aegeans. *bioRxiv online*.
17. Omrak, A., Gunther, T., Valdiosera, C., Svensson, E.M., Malmstrom, H., Kiesewetter, H., Aylward, W., Stora, J., Jakobsson, M., and Gotherstrom, A. (2016). Genomic evidence establishes Anatolia as the source of the European Neolithic gene pool. *Curr. Biol.* <http://dx.doi.org/10.1016/j.cub.2015.12.019>.
18. Mathieson, I., Lazaridis, I., Rohland, N., Mallick, S., Patterson, N., Roodenberg, S.A., Harney, E., Stewardson, K., Fernandes, D., Novak, M., et al. (2015). Genome-wide patterns of selection in 230 ancient Eurasians. *Nature* *528*, 499–503.
19. Olivieri, A., Pala, P., Gandini, F., Hooshiar Kashani, B., Perego, U.A., Woodward, S.R., Grugni, V., Battaglia, B., Semino, O., Achilli, A., et al. (2013). Mitogenomes from two uncommon haplogroups mark Late

Glacial/postglacial expansions from the Near East and Neolithic dispersals within Europe. PLoS ONE 8, e70492.

20. Pala, M., Olivieri, A., Achilli, A., Accetturo, M., Metspalu, E., Reidla, M., Tamm, E., Karmin, M., Reisberg, T., Hooshiar Kashani, B., et al.

(2012). Mitochondrial DNA signals of Late Glacial re-colonization of Europe from Near Eastern refugia. Am. J. Hum. Genet. 90, 915-924.

Figure 1. The out-of-Africa exit and subsequent events from an mtDNA perspective.

The illustrated scenario summarises the currently available modern and ancient mitogenome evidence, linking the novel detection of M0 in Europe (2) with earlier findings. It shows a dispersal out of Africa carrying the African mtDNA haplogroup L3, followed by the emergence of the major out-of-Africa haplogroups M and N (and N’s descendants, R and U) in the vicinity of a putative ‘Gulf oasis’. From there, further dispersals are shown: eastwards into South Asia and north-westwards into the Fertile Crescent, Europe and North Africa.

