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# Mitochondrial DNA and human evolution: A review

*Henryk W. Witas, Przemysław Zawicki*

Department of Molecular Biology, Institute of Pediatrics,
Medical University of Łódź, Sporna 36/50, 91-736 Łódź, Poland;
E-mail: witas@alef.umed.lodz.pl

*ABSTRACT* It was not until a few decades ago that research into evolution and anthropology could be broadened by molecular biology techniques, especially those, making use of the most detailed record of the life's evolution – genetic material. A small fraction of a cell's DNA is present in mitochondria, organelle involved in energy production. Higher mutation rate, different mode of inheritance, and the large number of copies per cell are the main features of mtDNA. They allow us to study certain aspects of human evolution, namely: the origin of our species, kinship, possible interbreeding with other hominids, migrations and colonization of new regions of the world, from the maternal perspective.

*KEY WORDS* mtDNA, aDNA, anatomically modern humans, Neandertals, PCR

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## Introduction

Until a few decades ago, the only possible way of studying the evolution and migrations of mankind was realized mostly through the research on uncovered skeletal remains. However, the last two decades have brought for anthropologists several powerful tools, especially from the field of molecular biology. Although the history and evolution of certain biomolecules, e.g., proteins, could be analyzed and followed, it had not been precise enough until the early 80's. Then, researchers managed to achieve a deeper insight into DNA sequences. This enabled detailed analysis of relationships not only within a given population, but also *between* populations. Through the applied methodological tools, some molecular background information has been collected. This, in turn, led anthropologists to the formation of new theories of the history of our species.

DNA is the only biomolecule accumulating a record of life's evolution on Earth. It contains a variety of sequences, amongst them some carrying important information, e.g., functional genes which encode for the proteins that build our bodies or regulatory fragments, but

also a vast amount of non-coding and non-functional sequences, which are the remnants of switched-off genes, mutated genes and material inserted from other organisms, e.g., viruses and bacteria. The majority of our DNA is located within the cell nucleus. Minute amounts of genetic material, however, are present in a separate cellular organelle – the mitochondrion.

## Mitochondrial genome

Human mitochondrial DNA (mtDNA) (Fig. 1), made up of 16,569 base pairs, codes for 13 polypeptides (all engaged in oxidative phosphorylation), 2 rRNAs and 22 tRNAs – which enable translation of proteins inside the organelle. Many essential proteins, however, are encoded by nuclear genes and imported through the double mitochondrial membrane (e.g., DNA and RNA polymerases, RNA processing enzymes, ribosomal proteins) [CUMMINS 1998]. The distribution of Gs and Cs in both strands of the circular mtDNA is asymmetric, causing the formation of heavy and light strands (H- and L-strands respectively).

Although mitochondria have long been studied for their role in cell energetics, ageing, apoptosis and various pathological conditions, these semi-autonomous organelles have only recently been found to possess certain characteristics that make them very useful in tracking evolutionary events. The last three decades of research into mito-

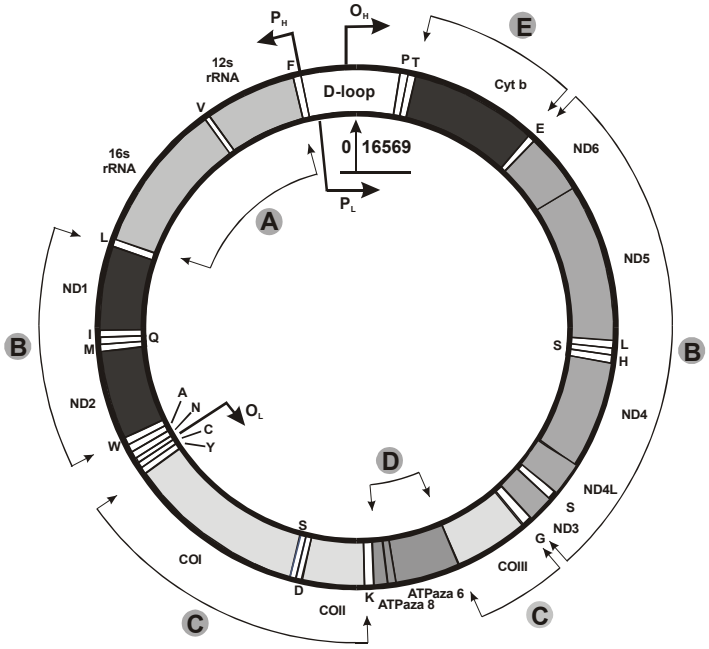


Fig. 1. Schematic representation of human mitochondrial DNA. A – ribosomal RNA genes, B – complex I genes (NADH dehydrogenase), C – complex IV genes (cytochrome C oxidase), E – complex III genes (ubiquinol-cytochrome C oxidoreductase). Other details in the text.

chondria have brought numerous data and hypotheses on the genetic affinities of different species and populations – among them, theories on kinship and migrations of our own species.

There are several reasons for which research into mtDNA might be of great importance in tracing recent human migrations and paths of species evolution. Unlike nuclear DNA, this circular molecule is present in our cells not only in one, but in a number of copies (there are usually 100 to 1000 mitochondria in each eukaryotic cell), which enables detection of much lower amount of the sequence of interest, especially that from fossil material. Due to the fact that only an egg contributes its mitochondria to the developing embryo with only rare exceptions, all human mtDNA is inherited maternally [GILES *et al*. 1980, CUMMINS 2000]. The molecule apparently lacks recombination [MERRIWETHER *et al*. 1991], which means that all differences between mtDNA sequences result only from fixed changes. The mutation rate in mitochondrial genomes was proven to be several times higher than that of nuclear sequences [BROWN *et al*. 1979, 1982; SACCONE 200] and may be the result of lack of repair mechanisms that slow down the nuclear genome mutation rate and/or the presence of free radicals formed during the phosphorylation process. Thus, it generates a high level of sequence variation between individuals [OLIVIO *et al*. 1983], accumulated in a relatively short period of time with respect to the common ancestral mtDNA molecule.

The constant rate of evolutionary change may serve as a molecular clock, enabling research into the age of particular lineages and the time of their divergence, as long as the clock is "calibrated", i.e., its rate is known. This is facilitated with help of paleontological and genetic data, which suggest that human and chimpanzee lineages diverged some 5 million years ago. As the mean genetic distance between sequences of both species is 0.17 substitutions per site, the mutation rate in mtDNA was estimated to be 1.7 times $10^{-8}$ substitutions per site per year [INGMAN *et al*. 2000]. This value might be slightly inaccurate in the light of recent findings that push back the time of divergence between hominids and apes – the discovery of *Sahelanthropus tchadensis* and *Orrorin tugenensis* which lived 6-7 million years ago and which could be ancestral to both groups [VIGNAUD *et al*. 2002, HARCOURT-SMITH and AIELLO 2004].

Not all parts of the mitochondrial genome, however, evolve at the same rate [PESOLE *et al*. 1999]. The most frequently changing part of the mtDNA is its non-coding, triple-stranded part (generated by synthesis of a short fragment of H-strand DNA) located in the control region of the molecule – the so-called D-loop (or displacement loop) [WALLACE *et al*. 1995]. This contains two hypervariable regions (HVR1 HVR2) [STONEKING 2000] and comprises approx. 7% of the mitochondrial genome. It is also the part that has been most extensively investigated [INGMAN *et al*. 2000] and has often given rise to debates as to the accuracy of the estimates. Unfortunately, owing to the high mutation rate of the D-loop sequence, several problems have been identified that influence the obtained information. Among them are the so-called back (again at the same site) and parallel (independent in

different lineages) mutations, as well as the presence of sites that are more susceptible to mutation (hot spots). Recently, the whole of the mitochondrial genome has been sequenced offering many more polymorphic sites for comparison. Almost no parallel and back mutations have been identified and the rates of evolution of different segments outside of the D-loop are thus rendered comparable.

Many other methods of studying mtDNA recently applied, such as restriction fragment length polymorphism (RFLP) analysis and direct sequencing, enable more precise calculations to be made. A number of techniques, developed in the last few decades have greatly contributed to the methodology used, with the most pronounced ones, such as polymerase chain reaction (PCR) based methods that allowed the copying of even minute amount of the sequence of interest.

## Geographic distribution of mtDNA variants

Owing to the relatively high rate of mutation events within the mtDNA molecule (the molecular clock ticks rapidly) many different variants of mtDNA are found in the human gene pool. They may vary in length, conformation, sequence of the control and coding regions or multiple restriction fragment length polymorphism (RFLP) [WALLACE *et al*. 1995]. Tracing migrations of *Homo sapiens* with the help of mtDNA is based on the observation that the occurrence of certain haplotypes is often associated with certain world regions and the assumption that this is a result of accumulation of various mutations in different maternal lineages that occurred as people migrated and inhabited new regions.

Two main theories exist about the origin and migrations of modern humans. These are expressed as the "Out of Africa model" [WILSON and CANN 1992, STRINGER and MCKIE 1996], and "Multiregional continuity model" [THORNE and WOLPOFF 1992 ]. The first one is more widely accepted due to strong genetic evidence. This theory arose on the basis of the degree of genetic variation patterns in modern human populations. In the late 1980s, CANN, STONEKING and WILSON [1987] demonstrated that human contemporary populations are surprisingly homogeneous, which was later confirmed by INGMAN *et al*. [2000]. It was in apparent contrast to our closest relatives, the chimpanzees [CAVALLI-SFORZA 2000]. CANN *et al*. [1987] has also showed that the highest variation of mtDNA sequences occurs in African populations.

### *Africa*

According to the African exodus theory, as confirmed by historical mtDNA sequence alterations, our most recent common ancestor (MCRA) arose in central Africa (Fig. 2). The time at which anatomically modern *Homo sapiens* diverged from other hominids was most probably between 100-200 ka. The first human lineages that dispersed were described as L1, L2 and L3, with the L1a subcluster being the oldest [WATSON *et al*. 2003]. The subsequent divergences gave rise to groups L1b, L1c and L2. All of them still dominate in sub-Saharan Africa, which is believed to be the aboriginal place of origin of all mitochondrial sequences, as it has the


Fig. 2. Geographical region of the origin of anatomically modern humans and presumable routes of migrations deduced from contemporary human mtDNA analysis.

highest diversity of mtDNA across the world [JORDE *et al*. 1998].

The next recorded divergence in the mtDNA (59-69 ka) led to the origin of L3, whose derivatives are now found in nearly all populations in Africa (and nowhere else), and in the clades that first migrated out of the continent.

### *Asia*

CAVALLI-SFORZA *et al*. [1996] suggested two possible ways of the colonization of Asia. Two major migrations from Africa are also marked in the mtDNA [MACA-MEYER *et al*. 2001]. The expansion of haplogroup M (30 – 60 ka), which can be traced from Ethiopia through the Arabian Peninsula to India and Eastern Asia, may represent the southern route, which leads from present-day Ethiopia through the Red Sea to Yemen and then through South Asia. It cannot be excluded, however, that the presence of M haplogroup derivatives along the route is due to back migration from Central Asia, since the M diversity is greater in India [KIVISILD *et al*. 1999] than in Ethiopia [QUINTARNA-MURCI *et al*. 1999].

The northern route, which led through The Middle East, was taken 40-50 ka by a colonizing group that split into three main clusters. One of them comprises haplogroups W, I and N1b now found in Europe, The Middle East and the Caucasus. I and N1b are also present in Egypt and on The Arabian Peninsula. The next group divided into haplogroup X, found

mainly in Europe, and A – common in Asia. The third group subdivided into four lineages. The first one gave rise to haplotype B, which is now found in East Asia, Japan and the southern Pacific Archipelagos. The second formed haplogroups J and T, whereas two others, H and V, belong to the third. Their derivatives are now found in Europe, North Africa and Central Asia. The fourth cluster – U – migrated into different parts of the Old World with the highest frequencies of its sub-haplogroups found in India (U2, U7), North Africa (U6, U3) and Europe (U5).

Lineages associated with sub-haplogroup U6 are the first that migrated back to North Africa, probably during the Upper Paleolithic [MACA-MEYER *et al.* 2003]. During the same period, lineage U5 was the first that migrated from the Middle East to Europe, where it had its major expansion.

### *Europe*

The present major European lineages are U5, H, I, J, K, T, V, W and X [RICHARDS *et al*. 1998]. In contrast to data obtained from analysis of nuclear loci, blood groups and protein markers, the mitochondrial DNA sequence differences suggest only one major colonization and dispersal of human groups in Europe. This conclusion is based on the observation that, with one exception, the territory of Sami [SAJANTILA *et al*. 1995], the mitochondrial gene pool is very similar throughout the continent [PULT *et al*. 1994] and shows almost no structure, even in regions inhabited by isolated populations such as the Basques [BERTRANPETIT *et al*. 1995]. It has therefore been concluded that the present population structure reflects the first Paleolithic expansion [COMAS *et al*. 1997] and subsequent founder effects, with only minor changes brought by the Neolithic spread of agriculture [RICHARDS *et al*. 1996] as evidenced by archeological records. This was further confirmed by estimation of the time of emergence of the European haplogroups as 50 ka for the U5 and 11-14 ka for H, V, I, W, T, K. The latter groups are likely to have diverged from U5 when human populations started to disperse from the glacial refugia after the last Ice Age.

Haplogroup J, dating back to 8.5 ka, and which encompasses about 16% of all European mtDNA, is most likely the only one brought to Europe by Neolithic farmers. Its subclades J1b and J1a are clearly distributed along two possible arrival routes: one leading through the valleys of central Europe and the other along the coasts of the Mediterranean Sea and the Atlantic Ocean [SYKES 1999].

### *The New World*

Although some early studies on mitochondrial DNA suggested more than one wave of migration into the Americas [TORRONI *et al*. 1992, HORAI *et al*. 1993], more recent studies indicate only one – an early entry of a single, ancestral lineage of Asian origin [BONATTO and SALZANO 1997, SILVA *et al*. 2002]. The four most common American haplogroups – A, B, C and D, though relatively old (the estimated time of divergence is 29-42 ka), are very similar in their nucleotide diversity, which suggests their common origin [SILVA *et al*. 2002]. Mitochondrial DNA data supports the hypothesis of colonization of Americas through Beringia, where the

first inhabitants entered the New World. Some of them migrated into the continent through the ice-free corridor of Alberta, while the others found themselves isolated from the first group after the passage became impassable. Research shows that the diversity of mtDNA among the Amerind, Na-Dene and Eskimo populations is very similar, and that they may be descendents of this population, while Native Americans appear to relate to the Chukchi. Both groups are most likely to have originated from the population that migrated out of Beringia [BONATTO and SALZANO 1997].

## Ancient mtDNA studies

Because of the large number of mitochondrial DNA copies present in cells, this material is relatively more accessible from fossil remains, and thus easier to study than nuclear DNA. These traits are of great advantage to evolutional archeology, since studies are now no longer bound to the analysis of sequences of present-day variants. Several studies have been carried out on ancient DNA (aDNA) isolated from fossil specimens, which enabled direct insight into the mitochondrial diversity and identification of haplotypes which did not survive to the present day.

Analysis of HVR1 and HVR2 of mtDNA from Neandertal specimens, conducted during the past decade, revealed that the human-Neandertal split occurred ca 500 ka ago [KRINGS *et al*. 1997] and that their mitochondiral DNA sequences are outside the range of human mtDNAs diversity, thereby indicating that Neandertals had not contributed to the present mitochondrial gene pool [KRINGS *et al*. 1997, 1999, OVCHINNIKOV *et al*. 2000]. It is conceivable, however, that early humans shared some mitochondrial sequences with Neandertals but, due to genetic drift, those haplotypes simply have not survived to the present day. To investigate this, mtDNAs from well-preserved specimens of four Neandertals (out of 24 analyzed) and five early modern humans (out of 40 analyzed) have recently been sequenced [SERRE *et al*. 2004]. Although applied methods are very sophisticated and accurate, it is nonetheless currently difficult to distinguish contaminating, ubiquitous co-isolated modern human DNA molecules from those replicated during the lifetime of an analyzed specimen. However, it is possible to identify the presence or absence of characteristic Neandertal mtDNA regions in ancient and modern remains. The results showed no Neandertal sequences (even when amplified with specific PCR primers) present within molecules isolated from early human samples, thus excluding the probability of any admixture having had occurred.

Though it is still possible that at some point Neandertals contributed their mitochondrial and/or nuclear sequences to the human gene pool, no evidence has yet been found and is not likely to be found, for two reasons:

– comparison of nuclear DNA is limited, or even not possible, due to extensive damage of the molecules in fossil specimens,

– exclusion of a minute contribution of Neandertal DNA to genomes of modern human contemporaries would require a greater amount of early modern human remains to be analyzed, which at present is unavailable.

Molecular genetics suggests that anatomically modern humans and Neandertals were distinct, or, at least, that the theoretically possible interbreeding of these two forms did not change the human genetic pool substantially. Moreover, studies indicate that Neandertals, similar to human populations, may have expanded after a bottleneck. This conclusion is drawn from the comparison of the DNA of all specimens thus far studied, which shows that their sequence diversity is lower than in populations of the great apes but similar to that of contemporary humans [KRINGS *et al*. 2000].

Sequencing of mitochondrial DNA from human remains found in Australia dating back to several thousands years BP, especially from a specimen named LM3 (after the location where excavated - Lake Mungo), revealed yet more surprising evidence. MtDNA of LM3 is currently the oldest aDNA sequenced, since the skeleton was dated during first analysis as 60 ka. If this is indeed so, its age is beyond the range of present human mitochondrial diversity, thus indicating its existence before the MRCA for all living human mitochondrial DNAs [ADCOCK *et al*. 2001]. This would suggest that the lineage to which the individual belonged predates the first "African" split recorded in contemporary mitochondrial sequences and, in fact, calls into question the genetic evidence and timing of the well-established "Out of Africa" theory. The finding would indicate that people had already inhabited Australia long before the first exodus from the African continent was recorded in contemporary mtDNA.

However, the age of the finding has been questioned. Reliable dating of the Mungo burials, the source of the world's oldest human mitochondrial DNA, has proved to be difficult, as different techniques have revealed various dates, raging from 30 to 60 ka (e.g., BOWLER *et al.* [1972], THORNE *et al*. [1999]). Finally, the age of studied burials at Lake Mungo has been established as 40 ka by optical dating of the lunette sediments, using the optically stimulated luminescence (OSL) signal from quartz [BOWLER *et al.* 2003]. The data obtained also suggest that humans came to Lake Mungo 46-50 ka ago, almost at the same time, or soon after, the initial occupation of north Australia [ROBERTS *et al.* 1990].

## Regions/sequences providing additional data on the history of modern humans

Although mtDNA is a potent tool in our understanding of human evolution, a number of other regions within nuclear genome have been examined so far. Efforts have been made to analyze sex chromosomes. One of the recently analyzed regions at Xp11.23 is located within one of the long introns of the *CLCN5* gene, encoding voltage-gated chloride ion channel, and was selected for its low recombination rate. It is flanked by a highly variable minisatellite – DXS255. Analyzed together, both sequences offer the possibility of obtaining the more informative combined haplotypes [ALONSO and ARMOUR 2003]. Calculated origins of the abovementioned sequence diversity, as well as of the other located on the sex chromosomes (e.g., INGMAN *et al* [2000]), including the much more extensively investigated chromosome Y (e.g., HAM-

MER *et al*. [1998], THOMSON *et al.* [2000]), are more or less compatible with each other over a wide range and support the out-of Africa replacement scenario based on mtDNA analysis. However, when compared with other nuclear sequences (e.g., HARDING *et al*. [1997], LI *et al*. [1999]) the discrepancies are much more evident. In 2002, Templeton published the results of a synthetic calculation [TEMPLETON 2002] which combined not only the haplotype trees based on mtDNA and Y chromosomal studies but also two new X chromosome locations and six autosomal regions. On testing all ten sequences, of which two are mono and eight bisexually inherited regions/genes, Templeton concluded that after the first major expansion of humans out of Africa, well described by fossil data documenting *Homo erectus* spreading 1.5-2.0 Ma, two further expansions took place. The first occurred between 840 000-420 000 years ago, and the second coinciding with that calculated by CANN *et al*. [1987] (150-80 ka ago), and confirmed by a number of other data (e.g., ZHIVOTOVSKY *et al.* [2003]). Apart from that expansion, which took hundreds of years, the main discrepancy between models arises from Templeton's suggestion that humans emigrating from Africa continued interbreeding but did not replace *Homo erectus* and its successor populations inhabiting Eurasia. The newly proposed model is similar to the "Assimilation" [SMITH *et al*. 1989], "Multiregional continuity' [THORNE and WOLPOFF 1992], and "Mostly out of Africa" [RELETHFORD 2001] hypotheses. The synthesis of the data presented by Templeton results from the examination of many DNA regions, yet different inheritance types and temporal information (recombinant regions mutate faster than non-recombinant ones) may produce conflicting results and, thus, incorrect conclusions. Moreover, the number of samples studied seems not to be high enough to make such global statements [CANN 2002]. Templeton's model, in assuming continuous interbreeding, does not explain the fact that none of the studied early modern and contemporary humans contained Neandertal mtDNA sequences [SERRE *et al*. 2004].

Human origin is constantly the subject of intense discussion and change as our knowledge increases with fresh ideas. The existence of a number of models of modern human evolution demonstrates ironically rather the inadequacies of current knowledge. It should, nonetheless, be emphasized that the role of African populations they played in modern humans history is undisputed and common to all models thus far presented.

## Final remarks

In general, mtDNA data seem to contradict the archeological, linguistic and genetic evidence on the colonization of the Old World, with a few exceptions [KNIGHT *et al.* 2003]. This is most probably a result of different population histories being reflected in mtDNA lineages and nuclear gene frequencies or language changes. Taking into account different inheritance patterns of both forms of DNA material, the lack of clustering of mtDNA haplotypes, with clear structure of autosomal and sex genes throughout the continent, might be explained by differences in mobility between men and women. It is not clear,

however, which of the sexes moved more frequently. SEIELSTAD *et al*. [1998] suggest that the tendency of the Y chromosome sequences to be more geographically structured than the mitochondrial haplogroups may have resulted from patrilocality (the tendency of families to reside in the husband's abode), or from polygyny, which would have led to higher female than male mobility. In contrast, SIMONI *et al*. [2000] suggest that such distribution of nuclear and mitochondrial markers might have resulted from higher male than female migration rate in the period of Mesolithic recolonisation, when Northern Europe became inhabitable again after the Ice Age. This problem is further complicated by simulations of the population structure of large mammals. This suggests that female migration, more than male, may affect the structure of nuclear genes. Such situations occur when offspring migrate together with their mothers during gravidity or lactation [TIEDEMANN *et al*. 2000].

Concerning the divergence times of mitochondrial lineages, it should be recognized that they are not the same as the times of arrival of populations into the new lands. People that carried new variants may have settled some time after the diversity was created. It should also be mentioned that the selection process may also have played a role in creating characteristic regional variations of human mtDNA which, until recently, was exclusively attributed to genetic drift. The variability pattern of particular mtDNA sequences, e.g., the *ATP6* gene from different temperature zones (arctic, temperate and tropics), confirm the involvement of selection factors, e.g., climate, in shaping regional mtDNA variants [MISHMARA *et al.* 2003].

The history of *Homo sapiens* is far from being completely understood, and recent findings on Flores Island [BROWN *et al.* 2004] starkly demonstrates just how little we still know about evolution. This discovery of a tiny 14-18 ka skeleton may yet alter current theories if it is confirmed as a hitherto unknown representative species of the genus *Homo*. The finding of the so-called *Homo floresiensis*, the form which is purported to have coexisted with modern humans, may serve as yet another source of DNA for study in addition to that of the Neandertals. Careful dating of human remains, introducing of the new molecular methodologies as well as analysis of higher numbers of genetically identified samples should surely brighten the darkness still enshrouding our history.

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## Streszczenie

Rozwój technik biologii molekularnej w ostatnich dziesięcioleciach znacznie przyczynił się do rozwoju badań w antropologii, w tym dotyczących ewolucji człowieka. Badania DNA, który zawiera informacje nie tylko o organizmach żyjących współcześnie, ale również o tym jak ewoluowały, jest nieocenioną pomocą w rekonstruowaniu wydarzeń ewolucyjnych, pokrewieństwa gatunków oraz osobników. Mitochondrialny DNA (mtDNA), który jest niewielką frakcją materiału genetycznego, ze względu na: sposób dziedziczenia (w linii matczynej), szybkie tempo zmian i obecność w komórce w dużej liczbie kopii, nadaje się do badań zarówno nad ewolucją i migracjami *Homo sapiens*, jak i badaniem różnorodności w populacjach wymarłych.

Analizując strukturę pierwszorzędową mtDNA neandertalczyka potwierdzono znaczne odstępstwa od stopnia zróżnicowania występującego wśród ludzi, zarówno tych obecnie żyjących, jak i im współczesnych, które każą wątpić w możliwość krzyżowanie się neandertalczyków z ludźmi anatomicznie współczesnymi. Badania mtDNA wydają się potwierdzać teorię, według której współcześni ludzie wyewoluowali w Afryce miedzy 100 a 200 tysięcy lat temu, a następnie wyemigrowali przez Bliski Wschód (59-69 tys. lat temu) i rozprzestrzenili się, kolonizując Azję, Europę, Australię i Amerykę. Teoria „Pożegnania z Afryką" może jednak być poddana w wątpliwość w obliczu znaleziska szczątków anatomicznie nowoczesnego człowieka z Mungo w Australii, którego szczątki datowano początkowo na 60 tys. lat. Znaczna różnica pomiędzy wyizolowanym z nich i współczesnym mtDNA mogłaby

sugerować wygasłą linię anatomicznie nowoczesnych ludzi, którzy mogli opuścić Afrykę znacznie wcześniej niż sugerują to badania dzisiejszych sekwencji. Jednak ponowne datowanie usytuowało te same szczątki 40 tys. lat temu. W przeciwieństwie do badań markerów białkowych oraz sekwencji jądrowego DNA, badania mtDNA sugerują, że największy wpływ na strukturę populacji europejskiej odegrała ekspansja człowieka podczas epoki paleolitycznej, z niewielkimi tylko zmianami wprowadzonymi przez migracje związane z neolitycznym rozwojem rolnictwa.

Odtwarzanie historii *Homo sapiens* jest oparte nie tylko na klasycznych metodach stosowanych w archeologii i antropologii, ale także na wynikach badania zmienności DNA. Do niedawna analizowano wyłącznie mtDNA, obecnie obiektem zainteresowania stało się wiele regionów genomu jądrowego, w tym nie tylko w obrębie chromosomów warunkujących płeć, ale także autosomów. Ostatnio podjęto próbę opisania głównych wydarzeń z historii człowieka nowoczesnego w oparciu o jednoczesne badanie i porównanie zmian w sekwencji 10 różnych regionów DNA, i to nie tylko z mtDNA, chromosomu X, czy chromosomu Y, ale także z autosomów. Uzyskane wyniki wskazują, w przeciwieństwie do założeń modelu „mitochondrialnej Ewy" na wcześniejsze, ciągłe migracje ludzi z Afryki i ich kojarzenie się z potomkami przybyłego do Euroazji 1,7 mln temu *H. erectus*, a nie jego wypieranie. Według niektórych autorów, formułowanie uogólnień na podstawie małej liczebności badanej próby, a także włączanie do analizy fragmentów o różnej szybkości mutacji każe wstrzymać się z ostatecznymi wnioskami. Ponadto, obserwowany brak charakterystycznej dla neandertalczyków sekwencji w genomach mitochondrialnych człowieka anatomicznie nowoczesnego pozostaje w niezgodzie z oczekiwanym efektem ciągłych migracji i krzyżowania, a nie zastępowania na nowych terenach. Należy podkreślić, że analiza DNA nie może stanowić jedynego źródła informacji o migracjach, ze względu na jego dziedziczenie w linii matczynej; także czasu wyodrębnienia się nowej linii rodowodowej nie należy utożsamiać z czasem zasiedlania nowego obszaru przez populację, jako że zmiana w materiale genetycznym mogła znacznie ten czas poprzedzać.