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## Review

## Trend of different molecular markers in the last decades for studying human migrations

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## ABSTRACT

Anatomically modern humans are known to have widely migrated throughout history. Different scientific evidences suggest that the entire human population descended from just several thousand African migrants. About 85,000 years ago, the first wave of human migration was out of Africa, that followed the coasts through the Middle East, into Southern Asia via Sri Lanka, and in due course around Indonesia and into Australia. Another wave of migration between 40,000 and 12,000 years ago brought humans northward into Europe. However, the frozen north limited human expansion in Europe, and created a land bridge, "Bering land bridge", connecting Asia with North America about 25,000 years ago. Although fossil data give the most direct information about our past, it has certain anomalies. So, molecular archeologists are now using different molecular markers to trace the "most recent common ancestor" and also the migration pattern of modern humans. In this study, we have studied the trend of molecular markers and also the methodologies implemented in the last decades (2003–2014). From our observation, we can say that D-loop region of mtDNA and Y chromosome based markers are predominant. Nevertheless, mtDNA, especially the D-loop region, has some unique features, which makes it a more effective marker for tracing prehistoric footprints of modern human populations. Although, natural selection should also be taken into account in studying mtDNA based human migration. As per technology is concerned, Sanger sequencing is the major technique that is being used in almost all studies. But, the emergence of different cost-effective-and-easy-to-handle NGS platforms has increased its popularity over Sanger sequencing in studying human migration.

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## 1. Introduction

Modern humans are well acquainted to have widely migrated throughout history. Around 90,000 years ago early humans first ventured out of Africa (Sullivan, 2010) and nowadays, modern *Homo sapiens* inhabit almost every corner of the world. Different scientific evidences suggest that the entire human population descended from just several thousand African migrants. About 85,000 years ago, the first wave of human migration out of Africa followed the coasts through the Middle East, into Southern Asia via Sri Lanka, and sooner or later around Indonesia and into Australia. Another wave of migration between 40,000 and 12,000 years ago brought humans northward into

Europe. Although, the frozen north limited human expansion in Europe, it created a land bridge connecting Asia with North America. The ancestors of the Native Americans took this route, called the "Bering land bridge", about 25,000 years ago (Grabianowski, 2007; Sullivan, 2010) (Fig. 1). But there is a lack of any direct historical/archeological evidence.

Regarding the origins of modern humans, there are two distinct views. According to the first hypothesis, it is an outcome of multiregional evolution. Globally, the present-day modern humans are the descendants of in situ evolution after an initial dispersal of *Homo erectus* from Africa during the Lower Pleistocene. However, as per alternative view, i.e. the most prevailing Out-of-Africa hypothesis, present-day biologically superior modern humans are descended from a recent common ancestor who lived in East Africa ~150,000 years ago, the population of which replaced all regional populations (Finlayson, 2005).

## 2. Evolution of modern human

It is almost impossible to say exactly when the *H. sapiens* arrived on earth after a rigorous process of evolution. From different fossil evidences (Wood and Collard, 1999; Gabunia et al., 2000; Asfaw et al., 2002; Vekua et al., 2002; Zhu et al., 2004; McBrearty and Jablonski, 1971

**Abbreviations:** AFLP, amplified fragment length polymorphism; D-loop, displacement loop; *H. pylori*, *Helicobacter pylori*; HLA, human leukocyte antigen; KIR, killer-cell immunoglobulin-like receptor; kyr, thousand years ago; MLST, Multi Locus Sequence Typing; mtDNA, mitochondrial DNA; mtD-Loop, Mitochondrial Displacement Loop; NGS, Next Gen Sequencing; RAPD, random amplified polymorphic DNA; RFLP, restriction fragment length polymorphism; SNP, single nucleotide polymorphism; STR, Short Tandem Repeats.

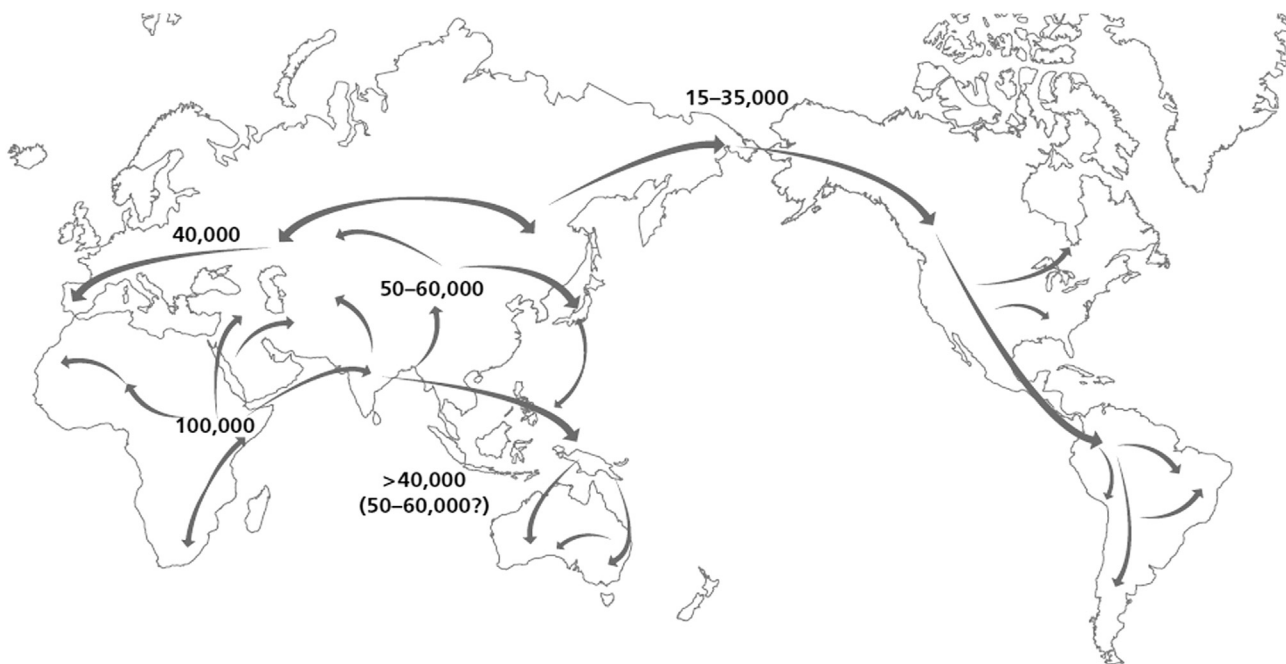
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**Fig. 1.** The migration of modern *Homo sapiens* (figure taken from Cavalli-Sforza, L.L., Feldman, M.W., *Nat Genet.* 2003). The scheme outlined above begins with a radiation from East Africa to the rest of Africa about 100 kya and is followed by an expansion from the same area to Asia, probably by two routes, southern and northern between 60 and 40 kya. Oceania, Europe and America were settled from Asia in that order.

2005) scientists have differentiated *H. sapiens* from earlier species in the genus *Homo*, such as *H. erectus* (Java man) or *Homo neanderthalensis* (Neanderthals).

Paleoanthropologists have several theories based on the best evidence available. Like, in a study by Ponce de León and Zollikofer using computerized fossil reconstruction and geometric morphometrics, they showed that distinctive differences in cranial and mandibular shape between Neanderthals and modern humans were deep rooted and they arose early during development, possibly prenatally, and were maintained throughout postnatal ontogeny (Marcia and Christoph, 2001).

As per various genetic and fossil data, *H. sapiens* coexisted with earlier hominids such as Neanderthals. With their greater intelligence and organization, *H. sapiens* out-competed other pre-human species for resources (Jordan, 2013). So, the biologically superior modern humans might be the cause of the downfall of all other worldwide *Homo* populations (Finlayson, 2005; Grabianowski, 2007). Based on a formal statistical analysis of human haplotype trees for mitochondrial DNA, Y-chromosomal DNA, two X-linked regions and six autosomal regions, we can say that Africa has played in influencing the modern human gene pool through at least two major expansions after the original range extension of *H. erectus* out of Africa (Templeton, 2002).

### 3. Migration & evolution

There are four basic mechanisms by which biological evolution takes place viz. mutation, migration, genetic drift, and natural selection. These factors are capable of altering the frequencies in a gene pool and as a consequence, they all are capable of driving successor with modification. Migration, also known as gene flow, is the movement of genes between subpopulations of a species. In nature, a species is often divided into multiple local subpopulations. When individuals from different subpopulations move easily from one subpopulation to another for a variety of reasons like food, space, weather & climate, war & politics, economics, etc., genes flow freely among those subpopulations, and they remain genetically similar. However, when individuals from the different subpopulations have difficulty in moving between other subpopulations, gene flow is constrained. This may cause them genetically

somewhat different (Klappenbach, 2009). Here comes the natural selection. A human population living in a given area faces certain pressures, which depend on the size of the population, the resources available and the community's ability to exploit those resources. Now, if a sub-population group migrates to some place where they became dominant over the local aboriginal group, then the population of this inferior group may collapse for falling under the negative selection pressure. Thus the new superior group survives in due course of the process of evolution.

### 4. Advent of different molecular markers

The most direct information about our past comes from the fossil records. Establishing the evolution of archaic humans in Africa, skeletal remains have been playing a significant role, and they also have provided important information about the appearance of modern *H. sapiens*. However, the fossil record is sometimes blotchy, and many critical gaps remain (Jorde et al., 1998). As a consequence, molecular archeologists are now using different molecular markers to trace the "most recent common ancestor" and also the migration pattern of modern humans.

In less than half a century, the concept of molecular markers has totally revolutionized our view of nature, and in this process, they have also evolved themselves. However, all of the molecular methods developed so far are based on conceptually three different classes of markers; protein variants (allozymes), DNA sequence polymorphism and DNA repeat variation. The latest techniques guarantee to afford a cheap and high-throughput method for genotyping the existing markers (Schlötterer, 2004).

There is a recurrent abate and flow in marker system popularity. The upcoming 'cutting edge' marker system is always remained on the horizon of the technological state-of-art. Schlötterer (2004) gave an apposite review on *The Evolution of Molecular Markers*, which includes a timeline of the relative importance of the different marker system (Fig. 2). Though, this figure is outdated, the trends have been followed in the last decades. Nowadays, there is an augmenting appreciation of the importance of various kinds of DNA variations (mitochondrial as well as nuclear) for reconstructing the human evolution and also for

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