

The study of molecular evidences for human evolution, gene flow, genetic isolation, interbreeding and their significance in the human physiology

Abstract

Human evolution, from its inception, has become an interesting topic for the scientific community as well as a very controversial and sensitive issue in different times, certain communities and ethnic groups. Evidences of evolution in the nineteenth century used to be mostly paleontological studies from fossil records and the comparative studies of the living organism. From the middle of the twentieth century, almost a hundred years after Darwin and Wallace's work, molecular biology has become an invaluable tool along with genetics and genomics for the study of evolution. Our understanding of the underlying molecular basis of human evolution provides us with the opportunity to closely examine the relationship between the DNA sequence element of anatomically modern humans, archaic humans and their closely related ape ancestors. Emerging evidence of specific DNA sequences within our genome and their expression in proteins aids our understanding of human health, survival advantages or to disease susceptibilities.

Keywords: human evolution, anatomical

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Abbreviations: SNP, single nucleotide polymorphism; YA, years ago; MYA, million years ago; HGP, human genome project; WHO, world health organization

Introduction

Evolutionary Biology is getting a different shape from the end of the twentieth century due to the advancements in genetics and molecular techniques. The advancements in molecular biology and DNA studies has brought tremendous excitement towards the study of human evolution and it is serving as an underlying basis for better understanding the advanced and modified features of the only surviving species in the Hominid family, the *Homo sapiens*. Evolution occurs by changes in the gene pool which could be affected by: mutation, genetic drift and migration, and speciation results from the geographic and reproductive isolation and anatomically modern humans are no exception from that. Still, we were in search for the interpretation of the almost same phenotypic expressions in the different geographical distribution of the humans. The human genome as well as some of the ape genomes (chimpanzees, bonobos and gorillas) have already been mapped, and are providing justification of the similarities and differences in the closed group using single nucleotide polymorphisms (SNP). Evidence has suggested that different illnesses, diseases, and other defects as well as other benefits have been linked to the differences of gene or in gene expression among humans. These changes also relate *Homo sapiens* to their ancient cousins in the Homo group, namely the *Homo neanderthalensis* and *Denisovans*. Through analysis it has been discovered that some modern humans share more genes with these archaic humans than others. Europeans tend to share more genes with the Neanderthals, and Polynesian and Eastern Asian populations tend to share higher percentages of genes with the *Denisovans*. Present day humans are still evolving in response to the selective pressures imposed by their environment like the exposure to pathogens and cultural exchanges. In this article we will revisit

the early phases for the study of human evolution using the fossil evidences and then take the journey to explore some of the ground breaking molecular and genetic discoveries which have opened a new horizon in the explanation of some physiological functions and phenotypic expressions in the light of human evolution.

Humans and the great apes

Evolution is all around us and working through billions of years in the living world, still the wondrous mind of the human keep on searching for the missing links and the secrets. After Darwin proposed the theory of Natural Selection for the origin of species,¹ paleontological evidences were the only resources available to the scientists in different fields to study the characteristics of a species and the variations over certain time. It was very surprising that *Carolus Linnaeus* after some careful observation placed apes and humans in the same family Hominidae² and also gave the scientific name of the humans, *Homo sapiens* in around the late eighteenth century.³ Starting from that time scientific community faced severe criticism from different corners of the society with theological perspectives. Even after all the criticism, Linnaeus didn't change the taxonomical hierarchy for humans, only modification he did was the introduction of Class Mammalia and Order Primates.⁴ Bipedalism and the larger brain have separated the Hominin family from the primates and great apes like gorillas and chimpanzees and upheld Linnaeus's taxonomical placement of *Homo sapiens*. After the Hominin group got diverged from Panina (chimpanzees) around 7mya,⁵ the prominent group from which modern day humans have evolved (1.9mya–70,000ya) were first called *Pithecanthropus erectus*;⁶ then being modified to *Homo erectus* (according to some referred as *Homo ergaster*).^{7,8} Along with the upright feature they have been found to be using fire and complex tools. From this group, the archaic humans have been evolved which includes *Homo heidelbergensis*, *Homo rhodesiensis* and the most recent one is the *Homo neanderthalensis*. Major distinctive feature

between Pithecanthropus and Archaic Humans is the expansion of the cranium thereby the size or mass of the brain. The first known fossil of anatomically modern human known as “The Red Lady of Paviland” was discovered by William Buckland in Paviland Cave, United Kingdom in 1823.⁹ The interesting fact was Buckland was a theologian but also a paleontologist and geologist. After that, subsequently all the fossils discovered of *H. sapiens* were from different parts of Europe like France,¹⁰ Czech Republic (1894), etc. So for a long time paleontologists held a strong belief that the origin of *H. sapiens* occurred at different parts of Europe and Asia. This concept was challenged when the skull of a young *Australopithecus africanus* named “Taung Child” was discovered in Taung, South Africa by Raymond Dart¹¹ and immediately identified as the missing link between the apes and the human. This discovery clearly supported the prediction of Darwin¹² that Africa is the place for the origin of species *H. sapiens*. So the “Taung child” challenged the prevalent idea about the origin of modern day humans in Eurasia. Dart’s findings were dismissed for quite some time and then eventually accepted by the scientific community later in the twentieth century. Successively in late 1950s a number of other fossil bones were discovered in a cave from the northeast of Johannesburg, Africa which emphasized the fact that the cradle of human origin is Africa.

The fossil of oldest hominin (believed to be more than 3million years old) was found later in 1974 by paleoanthropologist Johanson from Afar Triangle, Ethiopia. This was the well-known fossil of *Australopithecus afarensis* female who was named “Lucy”,¹³ showed a small brain case but had a pelvic structure for bipedal support. The discovery of Taung Child and Lucy helped to create the new phylogenetic tree for the family Hominidae and it was clear that the selective pressure was mainly the bipedalism while the increase in the size of the brain evolved much later.^{14,15} The paleoanthropological

findings were later supported by carbon, argon, potassium or other radiometric dating.¹⁶ Anthropologists inferred that the increase in vast savannah acted as a selective pressure and has influenced the *Homo* group to come out of the trees, walk on two legs and start hunting using the tools to gather food which required higher brain function with conscious mind.¹⁷ Later, the human has migrated from Africa to almost all possible niches (Figure 1).¹⁸ Until the late twentieth century most of the focus was on the evolution of Anatomically Modern Human as most of the paleoanthropologists, anatomists thought that the Archaic Humans became extinct before modern humans and there was no mixing between the *Homo sapiens* and other members in the Hominidae family.²¹ During the late nineteenth century fossils of *Homo neanderthalensis* were found from Germany, Belgium and other parts of Europe. First of them was discovered right after “The Lady of Paviland”¹⁹ from the Liege province of Belgium, but wasn’t recognized until 1936 and the age of the fossil is now thought to be 30,000-70,000 ya.²² Among the three prominent species included as Archaic Humans (*Homo heidelbergensis*, *Homo rhodesiensis* and *Homo neanderthalensis*), Neanderthalensis or more commonly known as Neanderthal man are the most recent one according to the fossil studies. The name Neanderthal was given to the fossil discovered in 1856 from Neanderthal valley of Germany by Johann Karl Fuhlrott.²¹ Although a lot of information about the evolution and the divergences of different members in the *Homo* group were coming out from the paleoanthropological studies, still some information were missing due to limitations about the availabilities of bones and fossils. Therefore the timings for the reign of different species of *Homo* were little foggy from the mid nineteenth century to mid twentieth century. Right around this time, in 1960s the DNA structure was established and opened up new possibilities for explaining different phenomenon using molecular biology and techniques.

| Evolution of Modern Day Humans | | | | | | | |
|--------------------------------|----------------------------------|---------------------|---------------------|-------------------|-----------------------|-----------------------|----------------------------|
| Ardipithecus | | Australopithecus | | Paranthropus | | Homo | |
| 7 mya – 6 mya | <i>Sahelanthropus tchadensis</i> | 4.2 mya – 3.9 mya | <i>A. anamensis</i> | 2.7 mya – 2.3 mya | <i>P. aethiopicus</i> | 2.4 mya - 1.4 mya | <i>H. habilis</i> |
| 6.2 mya – 5.8 mya | <i>Orrorin tugenensis</i> | 3.85 mya – 2.95 mya | <i>A. afarensis</i> | 2.3 mya – 1.2 mya | <i>P. Boisei</i> | 1.9 mya - 1.8 mya | <i>H. rudolfensis</i> |
| 5.8 mya – 5.2 mya | <i>A. kadabba</i> | 2.5 mya | <i>A. garhi</i> | 1.8 mya – 1.2 mya | <i>P. robustus</i> | 1.89 mya - 143 kya | <i>H. erectus</i> |
| 4.4 mya | <i>H. ramidus</i> | 3.3 mya – 2.1 mya | <i>A. africanus</i> | | | 700 kya - 200 kya | <i>H. heidelbergensis</i> |
| | | | | | | 400 kya – 40 kya | <i>H. neanderthalensis</i> |
| | | | | | | 95 kya – 17 kya | <i>H. floresiensis</i> |
| | | | | | | 200 kya - present day | <i>H. sapiens</i> |

Figure 1 Timeline showing the gradual transition from the primates towards becoming humans. Ardipithecus is the first group separated from primates and to stand and walk upright; then gradual transition occurred with the anatomical changes from primates with: strong knee and hip support, longer leg bones and curved spine. Also the advancement occurred in the larger brain size and cognitive function. Paranthropus means “near homo”, so they are the closest in the time line for evolution to modern day humans. *Homo erectus* is also referred as *Homo ergaster*¹⁹ *H. neanderthalensis* and *H. heidelbergensis* are referred as Archaic Human. *Homo antecessor*, a disputable species is also thought to be a link between *H. Neanderthal* and *H. Sapiens*.²⁰

The table is created using the information available from Smithsonian Institute of Human Origin.

(<http://humanorigins.si.edu/evidence/human-family-tree>)

Human evolution and molecular studies

From around the late 70s evolutionary studies of *Homo sapiens* started taking a new shape as molecular studies constantly shedding new lights of understanding the normal functions as well as the abnormalities or differences to better explain the cause of diseases or variations among the ethnic groups. One of the features towards the evolution of anatomically modern humans was the inventions and the proper use of highly sophisticated contrivance. It is very interesting to observe that the recent progression in the knowledge of genetics, genomics and proteomics reestablishes the fact that early feature of the proper designing and use of advanced tools not only gave distinct advantages to the modern humans in their survival, but was also a reflection of their higher cognitive power.

Using the molecular biology to study the diversity in unity was proposed by Christian Evolutionary Biologist Dobzhansky.²³ DNA is comprised of four bases across all the living species within prokaryotes and eukaryotes as well as all the extinct species. But one small mutation at the molecular level in copying and translating the sequence can cause dramatic changes to a species over the generations, leading to speciation on a large scale. It has been found that even though apparently it seems like a gap in the time scale when the fossil studies were done, molecular studies could establish a trail of unseen footprint.

To establish the common ancestry between the apes and the humans instead of only relying on morphology and fossils genetic relationships might be a better option. Though structure of DNA has been established in 60s, still in the 70s the technological advancement didn't progress that much. The concept of molecular clock was first proposed by Allan Wilson.²⁴ The morphological differences are due to the expression of the proteins - Wilson started his major work based on this hypothesis and used blood proteins, antigens and antibodies. This study supported the much debated concept that the ancestor of humans are apes and the chimpanzees and humans are genetically almost 99% alike; the differences are mostly due to the gene expression or epigenetic factor.

A Few years after Human Genome Project (HGP)²⁵ have been completed in 2003, the genome of chimpanzee,²⁶ orang-utan,²⁷ gorillas²⁸ and bonobos²⁹ have been sequenced.

From these genome studies it has been found that humans differ only in 1.2% genes with both chimpanzees and bonobos and differ in 1.6% with gorillas making chimpanzees and bonobos our closest ape ancestors. Also it has been found that there is same difference in the gene (1.6%) between the gorillas and the chimpanzees and bonobos.

In late 80s another historical advancement occurred in the field of human evolution when mitochondrial DNA was used to trace the origin of human race. Mitochondrial DNA comprises of only 0.001% of our DNA, but it is simpler for the analysis and it is passed only through the matrilineal line without recombination.

Mitochondrial DNA analysis suggests that modern day humans have originated from the common ancestor, known as "Mitochondrial Eve", 200,000-100,000years ago in Africa. This study by Allan Wilson and Rebecca Cann reestablished the fact that the origin of modern day humans occurred in Africa,³⁰ then they migrated to the different parts of the world. This study linked all studied subjects to one common ancestor (mother) (Figure 2 & Figure 3).

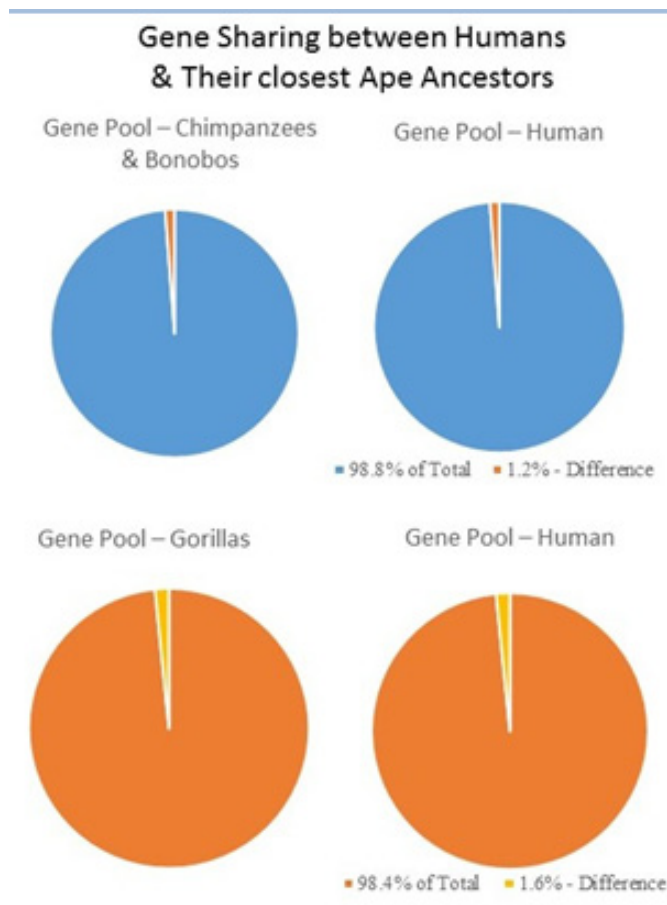


Figure 2 Similarities and differences in the gene pool:

Comparison among Humans and the Great Apes.

Humans, Chimpanzees and Bonobos Share 98.8% of the total genes, difference is in only 1.2% (top); Humans and Gorilla share 98.4% of the total gene; while the difference with Gorillas and Humans are 1.6% (bottom) making the gorillas distant cousins than the chimpanzees.

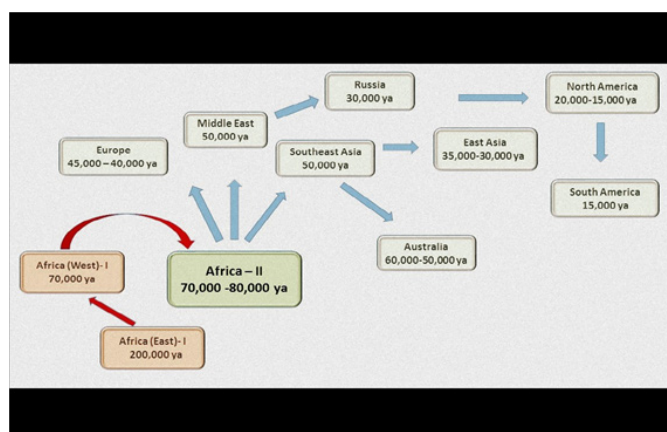


Figure3 Route of migration using the fossil record for modern human (Not scaled). This route is later supported by molecular evidences using Mitochondrial DNA,³⁰ Mitochondrial DNA analysis suggests that modern day humans have originated from the common ancestor in 200,000-100,000years back in Africa.

Seven major lineages based on the haplotypes of mitochondrial DNA studies have been established,³¹ and thereby popularly known as the seven daughters of Eve.³² Differences in DNA among humans and other groups could be traced by studying haplotype and SNP. Haplotype refers to the set of genes inherited from a single parent (haploid). By examining haplotypes, patterns of genetic variation and inheritance of more than one copy of the same chromosome due to genetic linkages can be identified. The study of the haplotype thereby gives the advantage of tracing any particular disease or disorder that have been inherited from a particular parent. When a haplotype is found to be associated with a certain disease, by examining the stretches of DNA near the SNP cluster could also be helpful in identifying the gene or genes responsible for causing that particular disease.

After the debate about the origin of humans from the ape ancestors another major question has surfaced, that how is it possible that with only this little difference, humans have dominated almost every ecological environment, whereas the other apes are struggling to survive. Higher level brain function was a major evolutionary advancement distinguishing *Homo sapiens* from their ancestors.^{33,34} Though the deduction from the phenotypically larger size of the cranium points out to the fact that increase in the cranium is associated with increased brain size and intellectual capabilities, molecular studies recently have connected this morphological observation using with some other uniqueness of modern day humans the gene duplication and improved adaptation. The genes of special mention are SRGAP2 (significant in neurodevelopmental process),³⁵ FOXP2 (significant in language and cognitive development),³⁶ MYH16 (associated with the modification in the musculature of the jaw),³⁷ etc. In the history of mammalian evolution, the gene SRGAP2 have been highly conserved except for in humans where duplication occurred three times which affected the neuronal structure and the higher motor learning capabilities.³⁸ This phenomenon distinctly separated the modern day humans from the apes as the gene is still conserved there and also matches with the time of the divergence of *Homo* from the *Australopithecus* group.³⁵

As been mentioned earlier, human evolution from its inception has become an interesting topic for the scientific community as well as a very controversial topic. For more than two centuries, the evolutionary biologists, paleoanthropologists, zoologists, and anatomists studying and following the human evolution held the belief that there was no overlap and there was no interbreeding between the members of *Homo* group and that the modern day humans are a pure race. But some evolutionary geneticists had an inkling that there might be some chances of coexistence of *Homo sapiens* and *Homo neanderthalensis* as the Neanderthals show so many similarities with humans: like a large cranial capacity, strong body structure, proper use of tools, etc. But the truth is, the *Neanderthals* are extinct and the DNA collected from the fossil was not sufficient enough to analyze. Finally with a new approach and new techniques the Neanderthal genome has been sequenced³⁹ and revealed the fact that there was interbreeding between modern day humans and archaic *neanderthals* and except for the region of sub-Saharan Africa, average of 2-3% genes are related to Neanderthals. Another archaic group, *Denisovans*, have found to contribute about 5% of the genomes to the people living in Papua New Guinea and Australia.⁴⁰ The gene sharing has captured attention as it has been found that while some genes inherited from Neanderthals give some advantages for the survival of humans outside of Africa in colder places, some genes have found to be a disadvantage, being associated with higher risk of diabetes and increased rate of male infertility.⁴¹

Conclusion

Historically, it has been observed that natural selection has given preference to the reproductive success for the propagation of species instead of higher mortality rate for a particular species. Survival seems to be effected after migration to a different environment when some traits become non-suitable in that new environment. Still we have to admit that the process of natural selection has favored human species towards their survival and expansion. As the unveiling of genomic expressions progresses with the advancement of molecular technologies, the way we execute health care is also changing drastically. Understanding how gene sharing affects our bodies allows us to better aid patients and personalize health care as every person is an unique individual. Therefore, the research done in this field can now be directed towards application on patients with unique DNA make-ups. Comparative Human Genome has become an essential tool for the understanding of the genetic isolation, genetic drift and the gene expression for modern day humans. World Health Organization (WHO) also has taken initiatives to better connect the evolutionary biology with the medicine and its possible application in public health. With new discoveries on genes, their nature and behavior, understanding of the human body and physiology has already been advanced and expected to move towards this direction much faster than the twentieth century.

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Conflict of interest

Author declares that there is no conflict of interest.

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