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## Tracing Our Lineage: Molecular Contributions to the Construction of the Human Phylogeny

#### Abstract

One of the most novel and important contributions to biological anthropology in the last two decades has been the implementation of the techniques of molecular genetics to address some of the field's fundamental debates. The ordering of the extant hominids into monophyletic clades has long been a source of contention, with human-chimpanzee, human-gorilla, and human-orangutan clades being proposed in various studies. An expanding genetic analysis culminating in over 20,000 sequence alignments of all extant hominids has shown that chimpanzees and humans form a monophyletic clade, the closest relative of which is the gorilla. Since the discovery of the first Neandertal specimens there has also been a sometimes vicious dichotomy between those that advocate interbreeding between modern humans and Neandertals (The Multiregional Continuity Model), and those who maintain that modern humans replaced all other hominids with absolutely no interbreeding (The Recent African Origin Model). Analysis of mitochondrial DNA accompanied by a draft sequence of the Neandertal nuclear genome has called into question the validity of both paradigms and promoted the emergence of a compromise in the form of The Partial Replacement Model. Finally, the debate on the division of the human species into geographic races has been raging for centuries. Genetic comparisons between populations demonstrate that the total amount of human variation is in fact very small and provides no basis for the concept of biologically distinct races. The contributions of molecular genetics to biological anthropology are inestimable and will only continue to increase as technological advances are made.

**Keywords** molecular genetics, human phylogeny

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#### **Tracing Our Lineage: Molecular Contributions to the Construction of the Human Phylogeny**

#### Randa Stringer

#### Introduction

One of the fundamental questions anthropology has long sought to answer is how the human species came to be what it is today. Though this debate has been going on for centuries, recent developments in molecular biology have provided a new and in many ways more definitive basis of evidence for analysis. This paper will examine the manner in which the expanding field of genetics has allowed us to enhance our understanding of how we came to be. Through determining our relationship with the extant non-human hominids, providing novel evidence regarding our interactions with Neandertals, and invalidating the concept of race, genetic analysis has been invaluable to biological anthropology and in defining who we truly are as a species.

#### Our Relationship to Extant Hominids

There has been a great deal of debate among biological anthropologists as to the exact nature of our relationship with the extant hominid species, which include gorillas. chimpanzees, bonobos. and orangutans (Grehan and Shwartz 2009). species While these are widelv acknowledged to be our closest extant relatives, disagreements arise when debating to which of these species we are most closely linked phylogenetically. Early conclusions were based primarily on morphological evidence (e.g., McHenry and Corruccini 1981; Shea 1983), but with the advent of genetic technology, comparisons at the molecular level become an increasingly powerful method through which to construct the phylogeny of the extant hominids and establish our place

among them. Three main relationships have been suggested in the literature: a humanorangutan clade (Grehan and Schwartz 2009), a human-gorilla clade, or a humanchimpanzee clade (Satta, Klein, and Takahata 2000). While each of these interpretations has had merits, it has been shown that the molecular evidence clearly demonstrates the existence of a humanchimpanzee clade (Ebersberger et al. 2007).

One of the most prominent studies in support of the human-orangutan relationship is that of Grehan and Schwartz (2009). They examined the extant hominids using humans (*H. sapiens*), gorillas (Gorilla), chimpanzees and bonobos (Pan), and orangutans (Pongo) as the ingroup taxa (those being analyzed in the study). A compilation of behavioural, structural, and physiological features was developed using traits that had been generated for previous studies of hominid relationships. Using these characters the authors concluded that the most parsimonious tree produced a monophyletic clade containing humans and orangutans, closely related to a sister group of chimpanzees and gorillas. Gibbons were the next closest relation, with various monkey species providing an outgroup. Grehan and Schwartz based their conclusions primarily on morphological data, arguing that this is in fact a better standard than molecular analysis because it is not based on unproven assumptions. However, as more and more molecular evidence is amassed, it has become clear that the methodology of this study is outdated and cannot refute the abundant genetic findings that counter this conclusion.

Thomas Huxley (1863) suggested in *Evidence as to Man's Place in Nature* that gorillas could be the closest extant relatives to humans. Since the advent of molecular analysis it has become increasingly apparent that there is little evidence supporting this notion. Early evaluation of mtDNA

sequence data by Kishino and Hasegawa (1989) demonstrated that orangutans are an outgroup of the extant great apes as compared to humans, chimpanzees, and gorillas. However, the study was unable to conclusively determine the cladistic ordering of the final three hominid species. Ferris et al. (1981) had already proposed a phylogeny based on mtDNA analysis in which chimpanzees and gorillas were the closest in ancestry, with humans taking a more distant relationship to this sister pair. Subsequent studies showed that depending on the choice of mtDNA genes used for evaluation, either a human-chimpanzee clade, a human-gorilla clade, or a chimpanzee-gorilla clade could be supported (Satta et al. 2000). This gave rise to the possibility of a trichotomy in which all three species were equally related.

While the trichotomy proposal seemed to fit the data at the time, further information on the nature of genetic evolution provided the reason as to why any of the three clades could be supported depending on the genes examined: gene trees are not necessarily the same as species trees (Nichols 2001). Although phylogenies are generally drawn with distinct branching points, these apparent speciation events may not reflect the divergence of ancestral genes (Nichols 2001). Certain loci may diverge at different times, resulting in conflicting interpretations when attempting to construct species trees using genetic data (Nichols Since these discrepancies are 2001). generally small, analysis of a greater number of sequence alignments provides a sample size large enough to overwhelm these differences and produce a more accurate species tree through molecular analysis (Satta et al. 2000).

A recent study by Ebersberger et al. (2007) used this technique to demonstrate that humans and chimpanzees show the closest evolutionary relationship and constitute a monophyletic clade, therefore

sharing a distinct common ancestor. This study made use of the advances in genome sequencing that have provided a full sequence of the human genome, a draft sequence of the chimpanzee and rhesus genomes, and extensive preliminary shotgun sequencing of the orangutan and gorilla genomes. By examining 23,210 sequence alignments from these primates (using the rhesus monkey as an outgroup), they determined the percentage of alignments that would support each of the possible phylogenetic trees that could be created from various ancestral arrangements of these Of these alignments 13,869, a species. 59.75% majority, suggested a human-chimp cladistic arrangement, with gorillas being the next closest relative. Of the ingroup, orangutans were the most distantly related to humans, with the rhesus monkey maintaining its outgroup status. This extensive examination of such a large sample of sequence alignments has come as close as is currently possible to determining the monophyly of the chimp-human clade.

Although publication of the full genome sequences of the gorilla and orangutan may in the future yield unforeseen results that could change our interpretation of the hominid phylogeny, at this point it seems that our closest extant relative is in fact the chimpanzee. Molecular genetics has been invaluable in the construction of this phylogeny. It is imperative that we understand our relationship with the extant hominids in order to better reconstruct our own evolutionary history.

#### Our Relationship to Neandertals

Since the discovery of the first Neandertal specimens, anthropologists have been debating two forms of the same question: whether Neandertals are a member of our species, and whether, during our period of coexistence, Neandertals and humans interbred. The answers to these questions have implications not only in reconstructing the path of evolution that led to modern humans, but also in understanding our current genetic make-up. If Neandertals and humans did interbreed, it is possible that components of our genome were in fact acquired from Neandertals through this mechanism.

Two main models have addressed the question of our relationship with Neandertals. The Multiregional Continuity Model suggests that Homo erectus migrated out of Africa one to two million years ago and since then there has been concurrent evolution of modern humans across the Old World through constant gene flow (Fohran et al. 2008). Inherent in this model is the idea that humans and Neandertals were members of the same species and would have interbred. The Recent African Origin Model suggests that modern Homo sapiens evolved once in Africa, migrating out to the rest of the Old World 100 to 200,000 years ago and replaced all existing hominins with no interbreeding (Fohran et al. 2008).

While the original debate between these models relied on morphological evidence, advancements in genomics have provided a new and effective manner by which to analyze the possibilities. Both mitochondrial and nuclear DNA have been successfully extracted from several Neandertal specimens, allowing comparison of sequence variations (Green et al. 2008, 2010). The Multiregional Continuity Model would predict that there would be great similarities between the Neandertal and human genomes, potentially to the point where they would be indistinguishable (Fohran et al. 2008). If The Recent African Origin Model were correct, the human genome would be expected to contain no sequences that could only be explained through interbreeding with Neandertals (Fohran et al. 2008).

Preliminary genetic analysis came from the sequencing by Krings et al. (1997) of hypervariable region 1 (HVR1) in the Neandertal mitochondrial genome. The comparison of this mtDNA sequence to that of modern humans revealed 27 genetic mutations (24 transitions, two transversions, and one insertion), all corresponding in nature and location to what would be expected in typical mtDNA evolution. The average number of mutations generally observed in this region within modern humans is only eight (Tattersall 1998). This means that the number of mutations between humans and Neandertals is approximately three times that seen among humans. This level of variation is supportive of The Recent African Origins Model. Other sequencing projects focussing on this same region have found similar results. confirming the original study (Weaver and Roseman 2005).

Further mtDNA sequencing bv Green et al. (2008) focussed on the COX2 subunit 2 gene. which encodes of cytochrome c oxidase, a protein involved in mitochondrial electron transport. This gene has been shown to be subject to particularly quick evolution in primate lineages, which makes it especially useful for analysis. Since our divergence with Neandertals, the COX2 gene was found to have developed four amino acid substitutions. The ancestral amino acid was found at only one site out of four in only one modern human out of 2704 examined. This individual's deviation from the norm was interpreted as an isolated reversion to the ancestral state. This information again supported The Recent African Origin Model, as it appears that the amino acid substitutions evolved after our divergence with Neandertals, but no interbreeding took place to re-introduce the ancestral alleles into the modern human population.

The first nuclear DNA analysis conducted by Krause et al. (2007) focussed particularly on the FOXP2 gene, which is currently the only gene known to be specifically involved in speech and language development. While FOXP2 is extremely conserved among mammals, there have been two amino acid substitutions at positions 911 and 917 since our divergence from chimpanzees. Sequencing of this gene from Neandertal specimens revealed that they too carried the derived amino acid at each of these positions. For proponents of The Multiregional Continuity Model, the presence of the derived alleles in Neandertals is a clear indication of admixture (Herrera et al. 2009). However, the original interpretation of the data by Krause et al. (2007) indicated that the commonality of alleles between humans and Neandertals was simply due to the evolution occurring prior to the divergence of the two species. This alternate suggestion is weakly supportive of The Recent African Origin Model.

While the preliminary data generated by the above studies provided a basis for genetics-based discourse on the Neandertalhuman relationship, more informative data was provided recently by the draft sequence of the Neandertal genome. Green et al. (2010) sequenced 4 billion base pairs of Neandertal nuclear DNA from three individuals. In total over 5.3 Gb of DNA sequence was obtained from only 400 mg of bone powder. Because Neandertals and modern humans coexisted primarily in western Eurasia, the study compared sequences in Europeans to both Neandertals and modern humans of African origin. It was found that in some cases the European sequences actually showed more similarity to that of the Neandertal genome than they did to the African members of their own species. Through this analysis Green et al. estimated that approximately 1-4% of the

human genome may have been contributed to us by Neandertals.

These results do not seem to fully support either proposed model of human origins. The Recent African Origin Model rejects the idea of any interbreeding between Neandertals and modern humans, and the discovery of sequences in our genome obtained from Neandertals clearly indicates some degree of genetic admixture. On the other hand, a contribution to our genome of only 4% indicates a very limited amount of interbreeding. which is not entirely consistent with The Multiregional Continuity Model (Green et al. 2010).

The growing acknowledgement that neither of these two models perfectly fits the available data has led to the development of the Partial Replacement, or Assimilation, Model (Relethford 2008). This model states that anatomically modern humans originated in Africa and dispersed across the Old World 100 - 200 thousand years ago, and dispersion that during this some interbreeding occurred between modern humans and the populations they encountered (Relethford 2008). This in many ways is a compromise between the dichotomy of The Multiregional Continuity and The Recent African Origin Models. It incorporates the small level of admixture seen in the draft genome (Green et al. 2010) as well as potentially explaining the ambiguous derived state of the Neandertal FOXP2 gene (Krause et al. 2007). While accepting the premise of some interbreeding, it nevertheless rejects the concept that constant gene flow has prevented speciation for the last one to two million years, as originally suggested by The Multiregional Continuity Model (Fohran et al. 2008). The growing acceptance of this model is a clear indication that the evidence generated through genetic analysis has been and will continue to be a key factor in the assessment of our relationship to Neandertals.

#### *Our Relationship to Each Other*

Throughout history there has been a tendency to divide humans into specific categories based on external physical characteristics. In the famous 1757 Systemae Naturae, Carolus Linnaeus actually broke humanity into four distinct subspecies: Ното sapiens europeaus ("white", or Caucasians), Homo sapiens asiaticus ("pale-yellow", or Asians), Homo or sapiens americanus ("red", First Nations), and Homo sapiens africanus ("black", or African) (Linnaeus, 1757). While these divisions to the point of subspecies are no longer accepted, the concept of 'race' has continued to be debated not only in anthropology but in society at large. Genetic analysis has provided a new set of evidence that shows how truly minimal the differences between us really are (Long et al. 2009). Though the idea may not have fully permeated general society yet, it has become clear that, biologically speaking, there is no such thing as 'race'.

In the 19<sup>th</sup> century the scientific of encompassed all concept race phenotypically diverse groups that were separated ancestrally by their geographic origins (Templeton 1999). Implied in this definition was the idea that there would be major differences in allele frequencies these populations that could between account for the distinct physical characteristics observed (Smedley and Smedley 2005). This paradigm effectively established divisions between groups of people that were not necessarily accurate. A psychological study conducted by Williams and Eberhardt (2008) found that when race is portrayed as a biologically supported concept, it allows people to view a racial outgroup as unrelated to themselves. This was not necessarily due to preconceived prejudice; rather, the idea that another race was biologically distinct produced a feeling of distance that made empathy more difficult and less desired. Therefore the stance of the scientific community on the concept of race is extremely important in mediating the way society views race.

The advent of genetic technology provided a new method by which to evaluate the race concept. Templeton (1999) noted that a main issue with race is that it is an ambiguous term; even when used as a synonym to subspecies, there is still no clear definition of what actually constitutes a subspecies. The main determining factor in constructing a subspecies is the genetic difference between populations, but at what level do these differences justify a division in race? Templeton suggests setting a quantitative threshold of genetic differentiation through which a decision can be made. While potentially providing a good basis for interpretation, this does still not account for phenotypically intermediate populations or for individuals with ancestry from multiple geographic regions (Long and Kittles 2003). However, as the genetic data accumulates, it seems that the answer to the question of race may be so unequivocal that quantifications recommended the by Templeton become unnecessary.

Long et al. (2009) analyzed two data sets in order to determine the range of genetic diversity within various populations. The first set compared 63 loci from 32 individuals from eight populations, while the second analyzed 580 loci of short tandem repeats (short nucleotide sequences repeated adjacent to each other) from 928 individuals from 46 populations. They concluded that the standard classifications of the races, often similar to those originally proposed by Linnaeus, do not accurately describe the true pattern of diversity within humanity. Europeans appeared to belong to more than one race, while Sub-Saharan Africans could not be fit into any race at all. While a great deal of genetic variation was found between populations, it became apparent that the

genetic data did not fit into the standard classifications of race.

In order for races to exist biologically, it is implied that from a certain point they must each have a largely separate evolutionary history (Hunley et al. 2009). Hunley et al. (2009) studied models of potential effects on human populations throughout our recent evolution. Bv comparing the pattern of human variation seen in genetic analyses to various simulated population movements, they determined a most likely scenario involving a repeated pattern of population fissions, bottlenecks, and migrations that led to each of the major colonizations of new geographic regions. These movement patterns, coupled with the between-group genetic variation observed in the study, indicated that populations are nested rather than distinct, with no clear divisions by which to categorize them into races.

While studies of human variation within and between populations effectively undermine the concept of race, additional evidence comes from the comparison of humans to the extant great ape species. Kaessmann et al. (2001) compared the chimpanzee and human genomes and observed that the inter-individual variation within chimpanzees is more than three times that found between humans. Through further comparisons with noncoding sequence from gorillas and orangutans, it was demonstrated that chimpanzees and humans are not outliers at either end of the spectrum of genetic variation (Kaessmann et al. 2001). Instead, the human species contains a much lower level of genetic variation than any of the extant great ape species (Kaessmann et al. 2001). Because the variation in our species is so small as compared to our closest relatives, it seems superfluous to suggest a genetic basis upon which to further subdivide humanity.

While molecular studies have often focussed on defining divisions, these genetic advances have instead helped to unify our species. From a biological perspective, the concept of race is obsolete. Scientific interpretation has unfortunately promoted the division and degradation of races in the and hopefully as these past, new interpretations come to light, they can bring society a novel perspective by which to understand what it means to be human

#### Conclusions

Through an examination of these three anthropological controversies it is apparent just how important genetic analysis has become when answering the questions of our origins and evolution. Comparative sequence alignments using preliminary sequencing genome from the extant hominids has conclusively demonstrated that chimpanzees humans and form а monophyletic clade. revealing our relationships with the extant hominids. The our relationship question of with Neandertals is one that has been plaguing anthropologists for over a century, as it encompasses so many larger issues regarding our place in the hominid evolutionary tree. The publication of the draft sequence of the Neandertal genome provides a more unbiased basis for the interpretation of the Neandertals and has revised our thinking on the origins and evolution of modern Homo sapiens. While the issue of race is embedded in all societies, genetic analyses are providing an evergrowing body of evidence which demonstrates that biological races do not exist and may encourage societies to embrace the notion that we truly are all members of the same species. The impacts genetic technology has had already are staggering, and this constantly expanding field promises to provide even more revelations in the future

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