Genetic Variation and Human Evolution.

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The article is no longer available online. It is archived at the American Society of Human Genetics www.ashg.org.

The article provides background information about the use of mitochondrial DNA and Y-chromosome DNA studies to determine a possible path for human evolution. Students could carry out their own research after reading this article.

Genetic Variation and Human Evolution

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The past two decades have witnessed an explosion of human genetic data. Innumerable DNA sequences and genotypes have been generated, and they have led to significant biomedical advances. In addition, these data have greatly increased our understanding of patterns of genetic diversity among individuals and populations. The purpose of this brief review is to show how our knowledge of genetic variation can contribute to an understanding of our similarities and differences, our origins, and our evolutionary history.

Patterns of genetic diversity inform us about population history because each major demographic event leaves an imprint on a population's collective genomic diversity. A reduction in population size reduces genetic diversity, and an increase in population size eventually increases diversity. The exchange of migrants between populations inevitably results in greater genetic similarity, while isolation preserves genetic uniqueness. These demographic signatures are passed from generation to generation, such that the genomes of modern individuals reflect their demographic history. Thus, it is reasonable to say that our history is written in our DNA. As we accumulate more and more data on DNA variation,

and as we develop better tools to analyze these data, our history will become increasingly clear.

How diverse are we?

Perhaps the most widely cited statistic about human genetic diversity is that any two humans differ, on average, at about 1 in 1,000 DNA base pairs (0.1%). Human genetic diversity is substantially lower than that of many other species, including our nearest evolutionary relative, the chimpanzee. Genetic diversity is a function of a population's "age" (i.e., the amount of time during which mutations accumulate to generate diversity) and its size. Our genetic homogeneity implies that anatomically modern humans arose relatively recently (perhaps 200,000 years ago) and that our population size was quite small at one time (perhaps 10,000 breeding individuals).

To put the 0.1% genetic diversity estimate into perspective, it is useful to remember that humans have approximately 3 billion base pairs in a **haploid** cell. Thus, any pair of humans differs by approximately 3 million base pairs. These differences contain much useful information about the evolutionary history of our species. In addition, the small proportion of differences that occur within genes can lead to critical inferences about the effects of **natural selection**.

How is genetic diversity distributed within and between populations?

Human populations can be defined along geographic, political, linguistic, religious, or ethnic boundaries. Using a common definition that groups populations into major continents (Africa, Asia, Europe, and North and South America), many studies have shown that approximately 90% of genetic variation can be found within these populations, and only about 10% of genetic variation separates the populations. Thus, the great majority of genetic differences can be found between individuals from any one of the major continents, and, on average, only a small proportion of additional differences will be found between individuals from two different continents. Furthermore, because human history is a history of population movement, and because humans are extraordinarily adept at sharing their DNA, the genetic boundaries between populations are typically indistinct. For any given DNA sequence or gene, two individuals from different populations are sometimes more similar to one another than are two individuals from the same population.

The fact that humans are relatively homogeneous at the DNA level, combined with the fact that between-population variation is modest, has significant social implications. Importantly, these patterns imply that the DNA differences between individuals, and between populations, are relatively scant and do not provide a biological basis for any form of discrimination.

What can patterns of genetic diversity tell us about our evolutionary history?

Studies of our evolutionary history have benefited enormously from analyses of **mitochondrial DNA** (mtDNA) and the non-recombining portion of the human **Y chromosome**. Because these regions are not shuffled by **recombination**, they are transmitted intact from one generation to the next, revealing the paternal and maternal lineages of a population. Populations share mtDNA or Y chromosome lineages as a result of common origins or **gene flow**. Comparisons of Y and mtDNA variation in a number of populations have indicated greater levels of mtDNA lineage sharing among populations, suggesting that females may have experienced more mobility during much of our history than have males. This hypothesis needs further testing to determine how general the pattern may be.

One must also exercise caution in interpreting analyses of Y chromosome and mtDNA variation. Because each system is essentially one highly variable **"locus,"** statistical estimates of parameters (e.g., the age of the most recent common ancestor of a group of individuals) are highly inexact. More reliable estimates of such parameters can be obtained by analyzing multiple, independent **autosomal** loci (**single nucleotide polymorphisms** or **short tandem repeat polymorphisms**, for example). In addition, genetic data must be combined with archaeological, linguistic, and historical data to achieve an accurate interpretation of human evolutionary history.

The African origin of modern humans

Perhaps the most basic question about human history concerns the origin of anatomically modern humans. For some time, discussion of this question has been framed by two competing hypotheses. The first, usually termed the Multiregional Hypothesis, states that modern humans evolved from more archaic forms, such as Neandertals, in several different parts of the Old World (e.g., Africa, Asia, and Europe). The genetic similarities seen in contemporary populations are the result of gene flow between these populations, as well as natural selection for similar adaptive traits. In contrast, the Out of Africa hypothesis states that modern humans originated first in Africa and then migrated to Europe and Asia, less than 100,000 years ago, to replace existing archaic human populations.

Most genetic evidence supports the Out of Africa hypothesis, or a close variant of it. Nearly all genetic studies indicate greater diversity in African populations (Figure 1), which is consistent with an African origin of modern humans. (Because diversity is a function of both time and population size, however, this pattern could merely be the result of a larger historical population size in Africa.) The fact that most genetic variation in non-African populations is a subset of the variation found in African populations lends further support to the African origin hypothesis and is difficult to reconcile with the Multiregional

Hypothesis. Non-African populations also tend to be more similar to one another than they are to African populations, a finding that lends additional support to the hypothesis that a subset of the African population left the continent to colonize the rest of the world. Genetic evidence also indicates that the early human population was quite small for some time (approximately 10,000 or so breeding individuals). That is inconsistent with the Multiregional Hypothesis, because continuous gene flow among human populations scattered broadly over the Old World would require a much larger population.

Although genetic data offer broad support to the hypothesis that modern humans first evolved in Africa, it is more difficult to establish that archaic populations from other parts of the world made no genetic contribution to today's population (i.e., that there was no mixing between anatomically modern humans from Africa and archaic populations from Europe or Asia). Ancient nuclear sequences are sometimes observed in non-African populations (e.g., beta-globin sequences in modern Asian populations that derive from a common ancestor who lived 800,000 years ago). These sequences may have descended from archaic humans living in Asia long before the emergence of modern humans. However, it is also possible that such sequences did originate in Africa and were carried to Asia or Europe by modern humans themselves. This picture should become clearer as more and more autosomal sequences are analyzed and compared in multiple human populations.

Origins and affinities of specific human populations

In addition to addressing broad questions about the origins of our species, genetic data have been used extensively to study the origins and affinities of specific population groups. For example, analyses of genetic variation in Ashkenazi Jewish populations show that these populations are most similar to one another and to other populations from the Mideast and are distinct from non-Jewish European populations (although they have received some genetic contributions from these populations). Intriguingly, approximately two-thirds of Jewish males with the last name Cohen, the name associated with the Jewish priesthood, have essentially the same Y chromosome. This finding is consistent with the strict tradition of father-son inheritance of both this surname and the priesthood.

Analyses of Y chromosome, mtDNA, and autosomal DNA support the relatively recent derivation of Native American populations from populations that lived in Northeast Asia. These data also indicate that there may have been substantial **bottlenecks** as the founding populations entered the Americas some 20,000 years ago.

Another, even more recent, event is the human settlement of the Polynesian South Pacific islands, estimated to have taken place just 3,000 years ago. Most evidence supports a Southeast Asian origin of Polynesian populations, with mixture between these individuals and Melanesian populations as they spread through the South Pacific. An analysis of mtDNA, Y chromosome, and autosomal variation in South Indian caste populations indicated less differentiation among castes for mtDNA than for Y chromosome DNA. This

reflects greater levels of female (mtDNA) gene flow among castes than male (Y chromosome) gene flow, which in turn is consistent with ethnographic and historical evidence that females can occasionally join the caste of their husband, while males seldom change caste affiliation. Incidentally, comparisons of genetic variation in populations from India with Roma ("Gypsy") populations support an Indian derivation of many of these populations, which is consistent with the Roma's own accounts of their origins.

Summary

This brief review has outlined the ways in which studies of genetic variation can inform us about our origins and history. Humans are relatively homogenous genetically, reflecting a recent, common origin. Anatomically modern humans probably originated in Africa, undergoing population bottlenecks as some left to colonize the rest of the world. Because these events are fairly recent, and because of extensive gene flow within major human populations, most genetic variation can be found within major human populations.

Genetic data also provide useful information about the origins and histories of individual human populations. As our capacity to collect and analyze data on human genetic variation increases, our understanding of human evolutionary history will continue to grow.

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Glossary

Autosomal. Referring to chromosomes that are not sex chromosomes. In Homo sapiens, the autosomes are pairs 1 -22.

Bottleneck. A short-term reduction in the size of a population, followed by expansion in size. A bottleneck can reduce the amount of genetic variation in a population.

Gene flow. The exchange of genes between populations of the same species. One result of gene flow is that different populations can become genetically more similar to one another.

Haploid cell. A cell that has a single set of chromosomes. In Homo sapiens, haploid cells – sperm and ova – have 23 chromosomes. Haploid cells unite during fertilization, resulting in the formation of a diploid cell. In Homo sapiens, diploid cells have 46 chromosomes – 23 pairs.

Locus. The position that a gene occupies on a chromosome. Variation at a given locus often is the subject of investigation. Because most of the Y chromosomes and the mtDNA are transmitted intact, along with any mutations they have accumulated, each constitutes a single, highly variable locus.

Mitochondrial DNA (mtDNA). DNA that is contained in cellular structures called mitochondria. This DNA is not part of the DNA that is found in the nucleus. mtDNA is passed from one generation to the next only by females, and mtDNA does not undergo recombination (q.v.). These facts make detection of mutations easier in mtDNA than in nuclear DNA, aiding the tracing of maternal lineages through time.

Natural selection. A central mechanism of evolution. Natural selection results in increased survival of individuals who posses traits that provide adaptive advantages. Selection for the same traits in different populations can produce genetic similarities between those populations.

Recombination. The exchange of genetic materials between chromosomes during the formation of sperm and ova. One result of recombination is that offspring have combinations of genes that their parents do not. This shuffling of gene combinations tends to complicate the tracing of autosomal lineages through time.

Short tandem repeat polymorphisms. Variable segments of DNA that are 3, 4, or 5 bases long, repeated over and over.

Single nucleotide polymorphism (SNP, pronounced, "snip"). A variation in one base pair at a particular location in the genome. SNPs are useful in comparing genetic variations between individuals and in populations.

Y chromosome. In Homo sapiens, one of the sex chromosomes. Human females have two X chromosomes (XX); human males have one X and one Y (XY). Most of the Y chromosome does not undergo recombination (q.v.), a fact that aides in the detection of paternal lineages.

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