AT LAST—A PUTATIVE ADAM FOR PUTATIVE EVE?

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Don't be dazzled by the weekly updates emanating from the labs of Celera, on the North American side, and the Human Genome Project, on the European side. True, these continental giants will do combat. Their claims and counter-claims will rent fissures in the totems of received thought and shatter the most resolute faiths. But while their frenetic researches continue to detail the human genome, adding leaves to the book of human life, there are geneticists of a different stripe in pursuit of equally worthy quarry: the history of human beginnings.

Research approaches into human origins and evolution by population geneticists have themselves evolved significantly in the last fifty years. The most recent work of Peter Underhill[1] and his associates at Stanford University is a good example. Reported in the November 2000 issue of *Nature Genetics*, Underhill used mutations found on the Y chromosome as a 'molecular clock' to determine where and how long ago modern humans, Homo sapiens, appear to have broken away from our hominid ancestors. Their study does more than add greater strength to the claim that modern humans got their start on the African continent, it also traces our lineage back a figurative "Adam"——the father of us all——who lived in Africa around 59,000 years ago.

To appreciate the significance of this latest research carried out by Underhill and his group, and to show how far along the genetic sciences have come, perhaps it is easiest to return to the 'dark ages,' back to the 1940s and 1950s. Back then, investigators into human evolution believed that the split between the earliest modern humans and our chimpanzee relatives happened some 15 million years ago. Anthropologists and paleo-archeologists based their claims on measurements of fossil remains of skulls, teeth, and bones. At the time, the belief that modern humans had evolved from separate lines of hominid beginning over one million years ago, was also widely held. (Known as the 'multiregionalist' view of human evolution, it has been used by some to prop up racist claims of genetic superiority. This is unfortunate because the view itself is potentially scientifically valid.)

In the meantime, theoretical and technical developments in molecular biology made it possible for researchers to use entirely new approaches to establish genetic lineages among humans. Instead of relying on the traditional 'stones and bones' paradigm to address questions of human origins, molecular biologists could analyze the products of genes such as blood groups, antigens, proteins, and even the genes themselves.

Perhaps the first major study to reach a broad public audience was reported in 1967 by Vincent Sarich and Alan Wilson[2], two geneticists at UC Berkeley who examined blood proteins from baboons, chimpanzees, and humans. Their results suggested, in stark contrast to the accepted wisdom, that humans had broken away from their ape ancestors a mere 5-6 million years ago and not 15 million as had been believed. Naturally, their work caused a great deal of controversy and was rejected outright by most anthropologists and archeologists at the time. Eventually, however, Sarich and Wilson's findings were confirmed, not only by subsequent laboratory studies, but also by reanalysis of the physical evidence by the anthropologists themselves and new finds from archeological sites.

Years later, in 1987, Alan Wilson[3], still at UC Berkeley, again stunned the world with fresh laboratory evidence that all modern humans have descended from a woman who lived in Africa some 200,000 years ago. Immediately dubbed the "Eve Hypothesis," Wilson and his colleagues Rebecca Cann and Mark Stoneking were castigated by a majority of disbelieving researchers in the field of human evolution, while at the same time capturing the imagination of a fascinated public.

Wilson's research focused on the chromosome found in our cell's mitochondria. The mitochondria, called the powerhouse of the cell, is where all of the cell's chemical energy is produced. Each mitochondria has an O-shaped chromosome consisting of a comparatively small number of genes. What makes the mitochondria attractive as a research tool is the fact that the mitochondrial chromosomes do not undergo recombination as do the nuclear chromosomes during sexual reproduction. Instead, the mitochondria (along with the mitochondrial DNA, or mDNA) is passed on as is directly from the mother to the child. In other words, whereas each of us has a nuclear DNA set that consists of genes from both our parents (half from our mother and half from our father), we each have an identical set mitochondrial genes from our mother.

In theory, our mDNA would be identical to that of the putative "Eve"——our ancestral mother——were it not for the fact that DNA undergoes random mutations over time. Transcription errors will result in nitrogen base substitutions which, in turn, mean new base sequences. These transcription errors are believed to be neutral with respect to selectional forces, making them suitable for calibrating a kind of time machine.

On the assumption that the mutations in the mDNA occur at a regular rate, if you know how many mutations are in a given strand of mDNA, you are in a position to predict how much time it has taken for all of the mutations to have occurred. By making comparisons of the number of mutations accumulated among individuals from diverse human populations, and working backward to determine the order in which the mutations occurred, Wilson and his colleagues were able to arrive at both a time table for the emergence of humans and a genetic tree showing the relationships among them. The mDNA from the African-descended individuals showed the greatest diversity (i.e., number of mutations) making Africa the likely source of all mDNA. Using the mDNA mutations as a molecular clock, their results established that Eve lived in Africa about 200,000 years ago. According to one estimate, a mere 10,000 generations separates us from African Eve. These findings caused quite a furor because they went against the established view——no one had ever imagined that we were so young a species.

Just a year later, in 1988, the results of another study, massive and ambitious, were presented by Cavalli-Sforza[4] and his colleagues at universities in the United States and Italy. Using gene frequency data for 120 alleles from many thousands of individuals grouped into 42 populations from around the world, their findings supported and extended Wilson's work. (Their study, really a lifetime project, has since been published in a fascinating volume titled *The History and Geography of Human Genes* in 1996 by Princeton University Press.) They estimated that the earliest migration of modern humans out of Africa took place around 100,000 years ago. The genius of their 1988 paper, however, was in the form of a data table which lined up, side by side, the results of their wide-ranging work showing the genetic relations among all major human populations with a family tree showing the lineages of the seventeen major language families or phyla. The language data was taken from the work of historical linguist Merritt Ruhlen[5] of Stanford University who based his findings for 'genetic' relationships among language phyla on cross comparisons of core vocabulary. The two family trees appeared to be mirror images of one another, so striking was their correspondence.

This matching of human populations to languages caused a sensation. Within a short period of time, the data table had been reprinted in journals and magazines around the world. All at once, it appeared, in one audacious stroke, that the deep speculation made by the evolutionist Charles Darwin[6] had been realized. In the first edition of his *Origin of Species*, Darwin wrote:

> *If we possessed a perfect pedigree of mankind, a genealogical arrangement of the*

races of man would afford the best classification of the various languages now spoken throughout the world... (pp. 562-563)

Even if there were many who questioned the validity of Cavalli-Sforza's inspired drawing together of two entirely independent bodies of data or the approach to historical linguistics adopted by Ruhlen (Ruhlen's techniques in tracing back language lineages have been dismissed by some linguists), one could not help but be impressed by the high degree of correspondence between human populations and languages. There is, after all, something intuitively appealing in the idea——a feeling not lost on Darwin himself.

Since 1988, even as techniques have become more sophisticated, studies in population genetics have continued by-and-large to support the major claims laid out by Alan Wilson. A research team in Japan led by Satoshi Horai[7] reported in 1995 on a study that analyzed the *complete* mitochondrial DNA sequences of three humans (an African, a European, and a Japanese), three kinds of African apes and one orangutan. Their results show the last common human ancestor to have lived in Africa around 143,000 years ago, while the split between African and non-African lineage was estimated to be 117,000 years ago. Certainly the most innovative application of the recent mDNA work is that of a European-American team led by Matthias Krings[8] at the University of Munich. In a scenario worthy of a technothriller, they extracted mDNA from a Neanderthal humerus bone and compared the Neanderthal mDNA sequences with that of more than two thousand humans and fifty-nine chimpanzees. In a major blow to the multiregionalists, Krings and his co-workers found that the Neanderthal mDNA fell well outside the variation of human mDNA indicating that Neanderthals did not contribute to the human gene pool and are therefore not our ancestors.

Which brings us more or less up-to-date. For anyone who has followed the developing picture of our human origins over the years, it may come as no great surprise that the latest piece of research on the Y chromosome confirms, yet once again, the view that modern humans came out of Africa in the not too distant past. So even if our African Eve never did meet our African Adam, separated as they are statistically by tens of thousands of years, we can still picture them in imagined space, sharing the day's gossip over the warmth of an early evening fire, the horizon stretching out before them into time immemorial over the virtual African plain.

But there is more. The deeper significance of these findings in population genetics is this: they are quite clear in showing how young a species we are and, therefore, how shallow are the differences between us. For example, skin color is an adaptation to climate: darker skin in areas such as Africa for protection from the sun; lighter skin in regions such as Europe to absorb the sunlight to produce vitamin D. Skin color has evolved independently many times in human populations around the globe. These studies show that the division of humanity into "races," as popularly known, has absolutely no basis in biological fact. We are all descendants of a common entity. It is certain that, in time, these findings and others from population geneticists will overthrow prejudices that run deep and long in the human psyche and present us with solid leads into who we are and where we come from.

NOTES

(1) Underhill, P. et. al. (2000). Y chromosome sequence variation and the history of human populations. *Nature Genetics*, 26:358-361.

(2) Sarich, V. & Wilson, A. (1967). *Science*, 158:1200-1203.

(3) Cann, R. et. al. (1987). Mitochondial DNA and human evolution. *Nature*, 325: 31-36.

(4) Cavalli-Sforza, L. et. al. (1988). Reconstruction of human evolution: Bringing together genetic, archeological, and linguistic data. In: *Proceedings Of The National Academy Of Sciences USA*, 85:6002-6006.

(5) Ruhlen, Merritt (1994). *The Origin of Language: Tracing the Evolution of the Mother Tongue*. John Wiley & Sons, Inc.

(6) Darwin, C. (1859). *Origin of Species*. Modern Library.

(7) Horai, S. et. al. (1995). Recent African origin of modern humans revealed by complete sequences of hominoid mitochondrial DNAs. *Proceedings Of The National Academy Of Sciences USA*, 92:532-536.

(8) Krings M. et. al. (1997) Neandertal DNA sequences and the origin of modern humans. *Cell*, 90:19-30.