



David L. Wilcox

## Article

# Genetic Insights for Human Origins in Africa and for Later Neanderthal Contact

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*It has become obvious that the scientific evidence for where and when the human race appeared is radically different from the traditional assumptions drawn from the narratives in Genesis. The evidence – skeletal, archeological, and genetic – clearly points to Africa, not to the Middle East. The genetic evidence for an ancient African root for humanity is particularly convincing, as is the evidence that human origins occurred to a small population, not to a single pair of humans. Further, some human beings who left Africa to settle the rest of the earth mated with the local Neanderthals. Neanderthal DNA has spread to all non-Africans. This article surveys and explains recent genetic data bearing on these topics.*

## Presuppositions: Setting the Stage—Integrating Scientific Data and the Scriptures

The earth and its fullness belong to the Lord—it is God’s creation. Therefore, expectations (predictions) about the earth that humans draw from the biblical narratives are verifiable or falsifiable by valid data from that creation. This includes theological statements that imply real world predictions. Creation’s data cannot be simply rejected, but require theological reconciliation. Traditional understandings of the scriptures predict (expect or state) patterns of data far different than those reported by modern investigation, producing a serious dilemma. And, in fact, the data supporting alternate views grows stronger year by year. It is true that all theories (scientific or theological) are human formulations, but the data they explain are not human creations; they are discoveries of God’s truth. Theology may reject the theories of science, but it cannot

reject the data of the creation and remain honest before its Creator. And that means giving the data a rational explanation rather than simply rejecting it.

My intent in this article is to survey the recent genetic discoveries related to the origin, nature, and early prehistory of the human species. These are indeed difficult issues, but difficult issues which must be faced and worked out by theologians and scientists in open discussion.<sup>1</sup>

## African Genealogies

Genealogies are constructed from genetic data by looking for slight differences in existing people, specifically changes in their DNA (mutations) caused at various times in the past. Since the most likely reason for two people to share one of these DNA differences is that the change happened in a common ancestor, computer algorithms can be designed to calculate the likely trees of descent. Likewise, the number of DNA differences which have accumulated between any two people can be used to estimate how long ago their common ancestor lived. Such comparisons can be carried out on mitochondrial

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DNA (female parent's line), the Y chromosome (male parent's line), and the autosome chromosomes (both parents' lines). These are the familiar tests done by commercial DNA genealogy sites such as "Family-TreeDNA" or "23andMe." By extending exactly the same techniques, one can construct "paleo-genealogy" lineages.

The traditional reading of Genesis would place the origin of the human race with two people living in the Middle East a few thousand years ago. This traditional reading generates a clear prediction for the genetic genealogy of the human race as a whole. It should be rather short (not too many accumulated changes), and the longest separate branches from the common root should be Middle Eastern. If other regions were settled from that center, they should all have equally shorter local genealogies. That is not what the data show. The basic message—an African origin for humanity—has remained the same since Cann, Stoneking, and Wilson's seminal paper in 1987.<sup>2</sup> In contrast, Wayne Frair's Separate Creation paradigm assumes (predicts) four genetically equidistant continental populations.<sup>3</sup>

Of course, since this is an area of very active research, the complexity and clarity of the data are constantly changing. And yes, there are some slight but significant differences between the specific point of origin within Africa indicated by Y chromosome genealogies, mtDNA, and autosomal DNA, not to speak of languages and archaeology.<sup>4</sup> However, every study which has been done over the last twenty-five years—and there have been hundreds—has confirmed the conclusions of that first paper. Here are a few results of the latest research.

First, the female line: a recalculation of the base of the human mtDNA genealogy ("mitochondrial Eve") places her date at around 185,000 years ago. This paper places her location in South Africa among the hunting and gathering Khoisan people. All the other people groups on Earth are on one main branch of the human genetic tree, and the Khoisan are on the other branch.<sup>5</sup> (Neanderthal mtDNA sequences form a similar tree with a 200,000-year root. The total mutational distance between the two trees is best explained as 500,000 years of separate descent.<sup>6</sup>) These ancient data are confirmed by other recent studies which have calculated a root of 99,000 to 148,000 years<sup>7</sup> based on when the New World was settled, or an estimate of 134,000 to 188,000 years

using ten ancient "modern human" samples (e.g., the "Iceman" and CroMagnon 1) for calibration.<sup>8</sup> That study also confirmed African origins—the "ancient moderns" are all non-African, part of the two unique non-African mtDNA haplogroups termed M and N (a haplogroup is a genetic sequence identified by a unique set of genetic markers). Using that data, the "out of Africa" branch of humanity originated between 62,000 and 95,000 years ago.<sup>9</sup> Another mtDNA study, focusing specifically on the Khoisan people, shows that the amount of genetic divergence (between the L0K and L0D haplogroups) found between their tribes required the tribes to have been isolated for most of the last 100,000 years.<sup>10</sup> The most recent analysis, looking at the Khoisan branch of the tree (the L0 haplotype), confirms mitochondrial Eve's date at 180,000 years ago, but places her in central Africa, showing that the Khoisan ancestors arrived in the south about 120,000 years ago.<sup>11</sup>

This is confirmed by the autosomal data. A whole genome (autosome) study places the divergence of the Khoisan from the rest of the human race at 108,000 to 157,000 years ago.<sup>12</sup> These data support the consensus view that the Khoisan are the most anciently divergent human group, and have been significantly structured by long-term tribal separations since that ancient period. Another autosomal study confirms the centrality of the Khoisan in the origin of modern humans (*Homo sapiens*), showing their high internal genetic diversity, and their genetic separation from other African (and non-African) genomes.<sup>13</sup> Other studies show that autosomal SNPs (single nucleotide polymorphisms) are most diverse in the Khoisan, consistent with their divergence from the rest of our species around 100,000 years ago.<sup>14</sup> Another analysis of nuclear SNPs looked at Khoisan chromosomal components found in other South African tribes. The only non-Khoisan groups with a bit of Khoisan admixture were the Hadza and Sandawe, ancient Tanzanian click-speakers.<sup>15</sup>

There has been a fairly hot debate over the mutational rate used to calculate these ages, a debate with significant implications for when and where people left Africa.<sup>16</sup> The issue has been whether to use mutation rates as measured in current populations (which gives older dates) or to use the difference between the DNA of living people and ancient samples. This decision has implications for the emigrant population size and for their exit route—through the Sinai at 100,000 years ago or through Yemen around

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60,000 years ago.<sup>17</sup> Several different studies indicate that the later date is correct. One is the previously mentioned mtDNA study using ancient genomes.<sup>18</sup> Another used whole genomes to calculate an exit date of 38,000 to 64,000 years ago.<sup>19</sup> A third evaluated worldwide linkage disequilibrium (haplogroup size),<sup>20</sup> and a fourth looked at origin and expansion of the L3 African “parent haplotype” of the non-African M and N haplogroups.<sup>21</sup> Finally, the comprehensive and careful evaluation of Mellars et al. dates the origin of L3 (in Africa) to 70,200, N (in Arabia) to 65,000, and M (in south Asia) to 47,970 years ago.<sup>22</sup> The later dates and the southern route best fit the data.

The only consistent conclusion to the genetic data—and the fossil data—is that the modern human race appeared in Africa.<sup>23</sup> It is not just that the deepest roots of the human genealogy are in Africa. Every one of the thousands of human genomes from outside Africa which has been sequenced belongs to just two haplogroups—the M and N branches of the African L3 haplogroup—and those haplogroups were formed around 60,000 years ago. Every haplogroup branch formed during the 120,000 years before that date is found only in Africa. So if one is looking for an “Eden” at the “headwaters of the human race,” it will have to be in Africa. For example, if Adam was created directly from soil, macro-mutated from the prehuman, or was the first full human given a soul, the event must have occurred more than 200,000 years ago somewhere in Africa. If Adam was the leader or representative of a unique band of humans given the opportunity by God to lead the race into spiritual maturity, it could have occurred at a population bottleneck 150,000 years ago in Africa.

How well does the Y chromosome data match? Recent changes in the estimate have caused some confusion. In a series of jumps, the date for “Y Chromosome Adam” has gone from 59,000 years ago in 2000 to 209,000 years ago (or possibly 338,000 years ago) in 2013. Does this sound suspicious? It is perfectly reasonable. The date of the root is calculated from all of the available data. The changes were due to newly discovered, highly divergent Y sequences (in the A haplogroup) from a series of northwestern African men (the Mbo tribe). Their sequences pushed back the date, and confirmed the male origin in north central Africa.<sup>24</sup> Other recent papers also have calculated older Y chromosome convergence points—a Sardinian sample put it at 180,000 to 200,000 years.<sup>25</sup> A second paper dated it at 120,000 to 156,000 years

ago and further showed Y chromosome diversity among the Khoisan which was almost that deep.<sup>26</sup> So, the new data which moved the Y chromosome coalescence back to 200,000 years confirm African origins. Fifteen years ago, the oldest lineages outside Africa were almost as old as the oldest known African ones at 59,000 years ago. But the deeper branches since discovered are entirely African, the same pattern which the mtDNA and autosomes show. The first three-quarters of the Y chromosome branches are all African branches.

## Tracing Population History from Genetic Patterns

Keep in mind that “mitochondrial Eve and Y chromosome Adam” should not be identified with the two biblical individuals, nor do they prove the existence of Adam and Eve. They are simply constructs, deduced from the most distant common genetic sequences we can calculate. One would expect both sexes to have the same population history and have coalescence points at the same time and location. However, the true origin of our species could easily be earlier than these coalescence points, obscured by later history of population movements and changing population sizes. To a certain extent, this history can be derived from the amount of diversity retained in the genealogy at different points in the past (due to different rates of genetic drift).

Population logic provides multiple independent ways to estimate changes in past human effective population size ( $N_e$ ). As well as having higher levels of linkage disequilibrium, small populations lose diversity more rapidly (in insertion/deletion mutants, single nuclear polymorphisms, microsatellites, alleles, transposable elements, etc.). The smaller the population, the exponentially faster will be the loss. If a population is very small or decreasing, it will retain very little genetic diversity; if it is large or increasing, it will retain a lot. A level in a genealogy with many retained branch points indicates that it was increasing at that time; a level with few retained branch points indicates that it was declining. Why? A new mutation generates a potential branch point if both forms of the gene are retained. The larger the population, the better the chances for the preservation of both branches.  $N_e$  can therefore be independently calculated for mtDNA, Y chromosomes, X chromosomes, and sections of the

autosomes—sometimes with differing results. Note that Y chromosomes and mtDNA will show smaller  $N_e$  than autosomes because they are haploid (one copy per individual).

One important technique for extracting historical information from genes is linkage disequilibrium (LD). The logic is as follows: We receive matching (homologous) chromosomes from each parent. Homologous chromosomes exchange matching sections during meiosis (gamete formation), with “crossing over” occurring at random intervals along the chromosome. On the average, each human sperm or ova experiences thirty cross-over events—that is, one or two per chromosome, one crossover every 100 million bases or so. As the chromosomes continue to be recopied generation after generation, their sequences are being very gradually “homogenized” by such crossover events. Since this is a slow process, significant lengths of DNA sequences can remain unmixed for very long times. The average length of shared haplogroups (matching lengths of DNA found in many individuals) decreases with time, a fact which can be used to deduce a number of interesting historical measures.

One use of LD is to evaluate when a particularly favorable gene was first introduced by either mutation or interbreeding. If rapid selection for a “new” form (allele) of a gene has occurred (termed a selective sweep), the haplogroups flanking that gene will be unusually long. Due to their proximity to the selected gene, they will have “hitch-hiked” to high frequency in the population, being “selected” with the new gene too rapidly to have been “mixed in.”<sup>27</sup> How much “too long” they are is inversely proportional to the time since the beneficial allele was introduced. This sort of data shows that the sickle cell allele has been independently produced by mutation a half dozen times. (The sickle cell hemoglobin allele is positively selected and maintained in malarial areas.)

Another use of LD is to provide an effective evaluation of population mixture. When populations mix or exchange migrants, the cross-bred offspring have chromosomes from both populations. LD can measure how much admixture occurred, and how long ago it happened. As generations pass, the long “foreign” haplogroups are slowly homogenized. Their average length is inversely proportional to the time since the admixture event.<sup>28</sup> The percent-

age of the genome which is composed of such longer haplotypes (which show high LD) indicates how much admixture occurred. This sort of analysis, for instance, can show when interbreeding may have occurred between modern humans and Neanderthals.<sup>29</sup>

A third use of LD is to measure the length of time a population has lived in its present location. The average length of the haplogroups in the entire genome decreases with time, and is therefore inversely proportional to the long-term  $N_e$ . Multiple studies have confirmed that African populations have far shorter linkage groups than non-African populations, thus indicating a larger African  $N_e$  and a longer African history.<sup>30</sup> This supports the conclusion that Africa is the original source of the world’s other local populations.

## Implications of the Genetic Evidence for a Bottleneck

Obviously the question of the size of the human population at its origin is important to theology. The idea of a bottleneck can be attractive for certain integrative proposals. The evidence for such an event begins with significant differences in the patterns of genetic diversity in humans and apes. Chimpanzees and humans have about the same amount of diversity in their autosomal chromosomes. However, human mtDNA and Y chromosomes have only about one-tenth of the diversity expected from the equivalent chimp values and the autosomes.<sup>31</sup> For instance, the “mitochondrial Eve” of the pigmy chimpanzee is calculated to have lived 540,000 years ago, three-fold older than the human value.<sup>32</sup>

Blum and Jakobsson evaluate this discrepancy using calculations for the TMRCA (time to most recent common ancestor) for different parts of the human genome.<sup>33</sup> Autosomal and X-linked segments on average have TMRCA of, respectively, 1,500,000 and 1,000,000 years. Y chromosome and mtDNA TMRCA (“Adam” and “Eve”) are (as we have seen) around 200,000 years. They calculate that the depth of the autosomal TMRCA are consistent with an Out-of-Africa scenario—if the ancestral  $N_e$  was around 14,000. However, that  $N_e$  value is not consistent with the far more recent TMRCA of the mtDNA and the Y chromosomes. To explain this discrepancy, they propose a bottleneck in the Middle Pleistocene

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at around 150,000 years ago (long before the migration out of Africa). They calculate that this bottleneck could either be due to drastic population reduction or due to the survival of a single group from a larger ancestral structured population (“multiple archaic populations”). Either model could account for the eight-fold discrepancy, but they demonstrate that neither “recent admixture” (from Neanderthals) nor “long-standing admixture” (a long-term structured population) can explain the discrepancy.

There is supporting physical evidence. The middle of the previous glacial maximum, a time of maximum dryness in Africa, was 150,000 years ago. Modern humans are thought to have been forced into refugia along the eastern coast and lake regions in Africa, tied to coastal resources for the long-chained polyunsaturated fatty acids required for constructing our large brains.<sup>34</sup> Modern humans would be particularly vulnerable because of our unique, very rapid, brain growth in early infancy.<sup>35</sup>

Such a refuge-based bottleneck would have increased local density, cross-cultural contact, and environmental challenges—all of which are elements thought to speed up cultural development.<sup>36</sup> Although cultural changes do not necessarily produce human genetic signatures, they can alter the environment of our commensals and parasites, and thus, the selection pressures which can be reflected in their genomes. One intriguing bit of data is that lice apparently started to live in our clothes sometime between 170,000 and 80,000 years ago. At least, that is when clothing (body) lice became a separate genetic lineage,<sup>37</sup> indicating that the wearing of clothing had become common and continuous, a behavior with both adaptive and symbolic significance.

Climate change may also explain a good deal of the subsequent movement of populations. During glacial maxima and minima (we are now in a glacial minimum), North Africa is extreme desert (the Sahara). But during many of the intermediate periods, patterns of rainfall shift, and for tens of thousands of years, the Sahara becomes habitable savannah and/or grassland.<sup>38</sup> So, after glacial maxima or minima, human populations spread northward across the Sahara. The Saharan climate worsened dramatically around 73,000 years ago when the eruption of the Indonesian super volcano at Toba accelerated the cooling of the earth. This would have forced the Saharan population to abruptly flee southward,

invading the territories of local tribes. To some extent, northern males (with their Y chromosomes) would replace local males (and their Y chromosomes), but the local autosomes and mtDNAs would have been spared due to interbreeding, producing a somewhat divergent estimate of the location of the oldest sequences.

So, how and when was the earth settled? Both mtDNA and Y chromosome data show that the emigrants left Africa about 65,000 years ago, crossing the southern end of the Red Sea into Yemen. The first wave moved eastward along the coast of the Indian Ocean settling East and South Asia, and arrived in Australia around 50,000 years ago. The population which remained in refuges along the Arabian coast and the area of the Persian Gulf produced a second wave, which left the Middle East around 45,000 years ago—moving eastward through Asia and north-westward across Europe. The migrations have been traced via the progressive divisions of M and N mtDNA haplogroups (females) and the F, C, and D haplogroups of the Y chromosomes (males), as illustrated on numerous websites such as the National Geographic Project.<sup>39</sup> The timing (pre- and post-Toba) is debated due to disagreements over mutation rate and archeological evidences, as previously discussed.<sup>40</sup> I think the later date best fits the data.

## How Many “First Humans” Were There?

Another critical question for theological issues is the population size of the first true human population. Different models for how to (or how not to) integrate the story of Eden with the scientific data depend on that value. Genetic data indeed limit the possibilities. There is a general consensus that our over-all (African) ancestral  $N_e$  was about 10,000. Recent published estimates have been based variously on nucleotide diversity, LD, SNPs located near ALUs, whole genomes, allelic diversity, admixture calculations, and the comparative diversities of mtDNA, Y chromosomes, X chromosomes, and autosomes. Estimated  $N_e$  values in nine studies over the last five years range from 4,000 to 15,000.<sup>41</sup>

Huff has compared this value to other living and extinct species. His estimate of  $N_e$  for the human lineage was 9,300, but only for the last 1.2 million years.

Before that (which would be prior to *Homo heidelbergensis*), the value was 18,500 and 26,000, comparable to the ancestral  $N_e$ s of gorillas (25,000) and common chimpanzees (21,000), and greater than that of the pigmy chimpanzees (12,300).<sup>42</sup> Despite our present worldwide distribution, at some point the human lineage must have been significantly reduced, comparable to the pigmy chimp. That species has always had a very limited range south of the Zambezi River, utilizing swampy rainforest—a habitat which practically disappears during glacial maxima, producing its own “bottleneck effect.” Low human values only make sense if our lineage was also a very “localized” phenomenon. Again, a very low  $N_e$  can either be due to a long stretch of time with a small population or to a relatively brief bottleneck episode.

What did Blum and Jakobsson’s proposal give us?<sup>43</sup> A bottleneck at 150,000 years does not mean that *Homo sapiens* was formed at that time—it simply reduces the amount of past genetic diversity retained. If an “Eden” event happened at that time, it might have involved a fairly small (tribal) population, but they had ancestors who certainly looked like modern humans. An “integrative” scenario involving changes in the functional nature of humanity could fit at that point in time, and it does mean that we are all descended from that single stock. The data are problematic for the idea of locating Eden at the “headwaters” of the human race at an earlier date, at the time when the modern physical form appears. Although the TMRCA of the mtDNA and Y chromosomes are around the same date as the earliest fossils with modern morphology, the much higher levels of retained diversity in the autosomal chromosomes are only compatible with an earlier bottleneck, not with two people.

There is an additional reason why the ancestral human population cannot be reduced to just two people—previous ancestors or not. The problem is that two people can have a total of only four alleles (alternate forms) at any specific locus. If our species were ever just two people, all the alleles presently found at each locus in the entire species would have to be produced by mutations from those four ancestral alleles. But there are far too many divergent alleles in humans to be produced by that process, particularly in the histocompatibility loci central to immunity (in which high diversity is maintained by selection). Also, the existing arrays of very different

human alleles are frequently homologs to matching sets of alleles found in other primate species, implying that the alleles originated before the lineages became separate species.<sup>44</sup>

It has been argued that this immune diversity could have been generated independently in apes and humans, but this is problematic. The usual argument is that since the introns (noncoding sections) of the HLA-DRB loci are more alike within the species, whereas the exons (coding sections) are more alike between species, the exons must also have separately diverged within each species.<sup>45</sup> However, specific HLA alleles are under strong specific selection, and changes in the introns are mostly neutral. Thus, most mutations and cross-overs will be tolerated in introns. Over millions of years, crossing over will allow introns to become homogenized within lineages. But at the same time, strong stabilizing selection is able to retain an adaptive array of different exon sequences.

Supporting this analysis, the initial report on the chimpanzee genome evaluated the coding (exon) and noncoding (intron) differences between the human and chimp genomes for 13,355 out of 21,000 protein-coding loci.<sup>46</sup> Retained substitutions in the introns were 5.5 times more frequent than retained substitution in the exons. Further, synonymous exon substitutions were 33% more frequently retained, and substitutions in intron splicing junctions were three times *less* frequently retained. This distribution precisely follows the impact of these various changes on working protein production, and demonstrates the ability of purifying selection to retain functional protein-coding sequences (including those found in immune alleles) over millions of years, while allowing significant change to accumulate in introns.

Further, the last few years have given us data which indicate that the population which left Africa to settle the world interbred to a small extent with the Neanderthals and another archaic lineage, the Denisovans.<sup>47</sup> We non-Africans apparently picked up some “archaic” alleles involved with immunity (due to selection for non-African immune alleles). Parham’s team reported that 50% of the HLA-A alleles found in Europeans, up to 80% in Asians, and up to 95% in Papua New Guineans have an archaic origin.<sup>48</sup> If so, selection in the HLA antigen series is not simply based on diversity, but on specific

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diversity—on specific functional alleles, the sort of selective pressure which could indeed carry an array of specific alleles through a lineage split.

But, if some human beings did mate with Neanderthals, it clearly raises questions about what it means to be human, as well as further confusing the issue of “finding Adam.” This is the topic of the next section of this paper.

### So, Did Grandma Marry a Neanderthal?

First, were Neanderthals really fully “human” or not? If they were, interbreeding raises no problems except pushing our common ancestors back to half a million years. The Neanderthals were a lot like us. Their bodies were as upright as ours, although far more powerful. Their brains were as large as ours, although their skulls were long and low rather than globular like ours. Their faces were visually different—they lacked pointed chins, had tall faces with pushed out cheeks, and foreheads which sloped back from heavy brow-ridges. But surely humanity is not to be measured by facial appearance. How can we measure the shape of their souls?

Looking for cultural differences is equivocal. Neanderthals made much the same sorts of stone tools as did the first physically modern humans. Possibly they buried their dead, and they may have started using a bit of symbolism (shell beads) around the time modern humans arrived in Europe. But there is little data, and a lot of passionate disagreement about the meaning of shell bead finds.<sup>49</sup> For instance, the few “evidences” for Neanderthal symbolism date from around 40,000 years ago, and only one site has Neanderthal remains.<sup>50</sup> Also, improved radiocarbon dating places the first modern people in Europe by that era, so those artifacts could possibly be “modern” or due to modern acculturation.<sup>51</sup> Further, European Neanderthals may have been decimated around 40,000 years ago by a major volcanic event in Italy. If so, there may have only been a depleted remnant to oppose the entrance of modern humans into Europe.<sup>52</sup> Invoking the culture of tool or bead making does not solve the puzzle—it only increases the heat of the debate.

Anatomy may be less ambiguous. There are significant differences in cerebral development driven by

significant genetic differences. Modern craniums are high and domed, positioned above the face. Neanderthals’ craniums were low and long, positioned behind the face. These differences are due to alterations in sphenoid bone and cribriform plate which change the cranial base angle and enlarge the middle cranial fossa (temporal lobe).<sup>53</sup> And temporal lobe changes are significant. The human temporal lobe is 25% larger than expected from scaling up a chimpanzee brain. It has far denser neuropil (white matter—meaning increased synaptic complexity) and specialized new areas related to recursive language, high-level integration (the default system, involved with long-term planning), and possibly responses to spiritual experiences.<sup>54</sup>

Modern human brains also have larger olfactory bulbs, which, it has been suggested, indicate more neural commitment to the “higher olfactory functions” of memory and emotion, located in enlarged limbic systems.<sup>55</sup> Complementing that, the neural commitment of the Neanderthals to the control of their heavy musculature and to enlarged visual systems (shown by larger orbits and parietal lobe spreading), may have cost them usable cerebral cortex. It is estimated that they had only three-quarters of the amount of cerebral cortex available to modern humans for social intelligence, a central aspect of human adaptation. Thus, it is suggested, modern humans were able to manage larger social groups and needed more complex language.<sup>56</sup> Stringer estimates the Neanderthal encephalization quotient at 4.3 to 4.8 versus an early modern value of 5.3 to 5.4.<sup>57</sup>

There were significant differences in developmental timing. Comparisons in tooth enamel growth rings indicate significantly slower general and neural development in modern humans.<sup>58</sup> Brain growth and neuronal maturation were two-thirds faster in Neanderthals than in even the earliest modern humans. Chimpanzees reach 75% of their adult brain size by nine months; Neanderthals, by fifteen months; but modern humans, by thirty months.<sup>59</sup> This gives modern humans an extended period of neural plasticity, allowing the “nurture” of individual experience to shape the hard-wiring of neural circuits. This developmental difference is also reflected by a unique modern trajectory of cranial growth. The globular shape of the modern cranium is produced during an unusual growth phase during the first year of life. This globularization event is absent in

chimpanzees—and in the Neanderthals.<sup>60</sup> Such cranial changes reflect functional changes to the brain and to the mind, thus indicating real differences in important human characteristics.

What of genetic differences? The altered patterns of brain growth are tied to altered gene activation. In living humans, compared to the chimpanzee, there are specific differences in the expression of genes in particular cerebral areas. There is a significant slowing in the expression of genes for synaptic functions in the human cerebral cortex, but not in the cerebellum. Human neocortical myelination is also developmentally protracted. Chimpanzees' myelination density is completed at approximately the time of sexual maturity (age seven). In modern humans, myelination continues throughout childhood, and neural maturation extends beyond late adolescence.<sup>61</sup> The extensive cortical rewiring during adolescence interconnects specialized cortical areas into higher networks of complexity.<sup>62</sup> Coupling delayed synaptic maturation with increased brain volume allows the modern prefrontal regions to be rapidly reformatted with reciprocal connections to posterior cortical centers during development.<sup>63</sup> These processes transform the human brain, and they are key to understanding the flexible nature of human intelligence, language, and culture. Human social complexity literally reshapes neural connectivity of the growing brain.<sup>64</sup> All of this suggests that the differences between modern humans and Neanderthals were more than superficial.

## Genetic Differences

In light of such developmental differences, should we view these two archaic populations as human in the same sense that we are? If they are truly different, we can expect some significant genetic differences. Important clues concerning our genetic uniqueness have come from recent advances in the processing of ancient DNA which have produced complete high quality genome sequences for archaic humans—both the Neanderthals and the Denisovans.<sup>65</sup> (The Denisovans were a group of archaic humans in Asia with genomes close to the Neanderthals and evidence for significant interbreeding.) Comparative genomics indicates that both archaic populations diverged around 500,000 years ago from the African lineage leading to modern humans. The Denisovians were

apparently a more widespread, genetically diverse population, whereas the Neanderthals were inbred and genetically reduced.<sup>66</sup>

Since the quality of sequencing of these archaic genomes is as good as those of living humans, very precise gene-on-gene comparisons can be made across the entire genome. This has already allowed the identification of thousands of genetic differences unique to *Homo sapiens*.<sup>67</sup> Most of the 113,000 SNPs and INDELs are probably meaningless, but 250 of these alter amino acids sites, 72 affect splice junctions, and thirty-five affect known regulatory sites.

So how much of that is functionally significant? Of the twenty-three most conserved loci with significant amino acid changes, eight affect genes active in nervous system function or development. SLITRK1 and KATNA1 control axonal and dendritic growth, ARHGAP32 and HTR2B are involved in synaptic transmission, and ADSL and CNTNAP2 are implicated in autism. CNTNAP2 is a target of FOX-P2—the mutants interfere with speech development. NOVA1 is a neuron specific RNA binding protein, and LUZP1 is a leucine zipper protein (transcription factor) active in neural tube development. The last two loci are subject to alternative splicing. They also located four unique modern human loci affecting the skin and six loci which affect the eye.<sup>68</sup>

Another altered modern gene with neural activity, MEF2A, delays synaptic development, thus allowing extended synaptic plasticity.<sup>69</sup> The expression of this locus peaks before one year in chimps; in modern humans, it peaks at around five years. Linkage data indicates that the selective sweep for the modern allele occurred after our lineage split from the two archaic lineages. This modern slow-down fits with the slower maturation of the modern brain.

But these are just coding sites. An unchanged control protein may still have significant altered function through altered regulation sites and target loci. Evidence of noncoding regulatory genetic changes can be harder to detect, but is probably far more widespread and important. An interesting example is FOX-P2, the well-known and highly evolved “speech gene.” It regulates mRNA production and slows synaptic maturation in genes involved with axonal and synaptic development.<sup>70</sup> Chimp and mouse alleles are identical, but the human allele has two altered sites. Mice genetically engineered

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to express the human KE mutation show abnormal striatal activity in the basal ganglia when faced with learning a new task.<sup>71</sup> Since Neanderthals made the modern allele, does this mean that they could speak? There are not enough data to say. However, the FOX-P2 *locus* is not exactly the same. The eighth intron (introns are noncoding) of the FOX-P2 locus in modern humans has an altered recognition site for POU3F2, a protein which decreases the level of FOX-P2 production, and shows signs of a selective sweep (positive selection).<sup>72</sup> The Neanderthal control sequence is unchanged, the same as in the chimp (and the Zebra fish). So, there is an altered control site—and an altered target CNTNAP2 mentioned above is one of the targets of FOX-P2. But even if there are detectable differences in the modern and archaic genomes, were they really significant? The best test is interbreeding.

### Evidence of Interbreeding

And they did. A series of analyses, and further improvements in the quality of the data, have made it irrational to deny that. Two massive studies reported in early 2014 evaluated 1,000 modern genomes from Asia, Europe, and Africa for the presence of Neanderthal sequences.<sup>73</sup> Using completely different techniques, they came up with exactly the same results. All modern humans outside Africa have a few (2% on the average) “Neanderthal” haplogroups—whether Celtic European, Han Chinese, Native Australian, or Native American—but African populations do not. Both studies showed that approximately 20% of the Neanderthal genome can be retrieved from modern human genomes. And both studies showed the same genomic distribution of areas of significant positive and negative selection. But were these archaic northern hominines the same species as modern humans?

Comparison with several Neanderthal genomes indicates that the sequences of these “borrowed” Neanderthal genes best match the genomes of Neanderthals from the Caucasus, suggesting that local population is their source.<sup>74</sup> Supporting this, the complete genome sequencing of a modern human remains in Siberia dated at 46,000 years ago contains Neanderthal sequences, with a low level of linkage disequilibrium (not much cross-over mixing) which confirms a rather recent interbreeding period.<sup>75</sup>

However, the Tianyuan specimen from 40,000 years ago has no more Neanderthal DNA than modern genomes, showing the speed with which it was eliminated.<sup>76</sup> In addition to this broad Neanderthal contribution, many modern Melanesian populations have enough Denisovan haplotypes to make up an additional 5% of their genome.<sup>77</sup>

For perspective, keep in mind that 92% to 98% of the genes of all living non-African populations are of African origin, and the modern African genome diverged from the Neanderthal genome half a million years ago. That is 250,000 to 300,000 years before the earliest skeletal evidence of modern skeletal morphology (Omo Kibish)<sup>78</sup>—and for that matter, long before the specific Neanderthal characteristics developed in northern populations from *Homo heidelbergensis*.<sup>79</sup> Still, although long separated, the presence of archaic gene sequences in non-Africans is hard to explain without a significant amount of interbreeding.

Where and when did this admixture (interbreeding) occur? The necessary background is the pattern of human migration out of Africa. Recall the consensus view of the National Geographic Project.<sup>80</sup> A small group of East African emigrants arrived in southern Yemen about 60,000 years ago. Their descendants settled the rest of the earth. The first wave out of Yemen followed the coast of the Indian Ocean, arriving in Australia around 50,000 years ago. The second wave headed northward out of the Middle East about 45,000 years ago, spreading east and west into Europe and Asia (and on to the Americas). The evidence indicates that they met the Neanderthals in the Middle East, and the Denisovans further to the west.<sup>81</sup>

There has been a series of papers proposing alternate scenarios of interbreeding.<sup>82</sup> For instance, Currat and Excoffier proposed that a continuous but very unfruitful process of interbreeding occurred along the migration routes as they reached archaic hominine ranges.<sup>83</sup> Interbreeding would have to be low indeed—perhaps one fertile mating per generation worldwide over 6,000 years. Higher levels of successful interbreeding would have produced a “surfing” effect along the migration route (a serial founder effect). The moving emigrant wave would have accumulated archaic genes, becoming predominantly archaic. The large recent studies support this conclusion.<sup>84</sup>

The Denisovan admixture is a separate issue. Again, there is more than one model—possibly a single event along the coast, or a second smaller event inland.<sup>85</sup> Mainland populations are reported to have some specific archaic immune (HLA) alleles, whereas Melanesian populations have a larger and more diverse set of Denisovian genes.

## Effects of Interbreeding

So, did the interbreeding contribute anything useful? Some “Neanderthal” alleles do seem to have been subject to positive selection, to be “enriched” in modern genomes. Adaptive archaic alleles for immune system loci have been reported by Parham’s team. Perhaps 50% of the HLA-A alleles found in Europeans, up to 80% in Asians, and up to 95% in Papua New Guineans have an archaic origin, as well as other immune system loci such as STAT2 and OAS.<sup>86</sup> A selective sweep driven by strong immune benefits could have caused a significant amount of background selection/genetic hitchhiking. The recent large genome studies suggest that Neanderthal alleles are related to a variety of auto-immune diseases such as Crohn’s disease and Lupus.<sup>87</sup> They also report a significant tie to smoking behavior, diabetes, size of the optic disk, and levels of interleukin. The only other “enriched” loci they report are a few alleles for keratin alleles (the protein in our nails and hair). Another recent study also reports Neanderthal alleles for fat-processing genes in the brain.<sup>88</sup>

On the other hand, the large studies show widespread genomic areas with far lower levels of Neanderthal sequences than would be expected—areas in which the Neanderthal sequences were cleaned out by purifying selection. These areas of “enriched” modern sequences were quite significant: they involve a wide variety of loci active in nucleic acid processing and cell signaling—the base levels of genomic integration. This was especially true for the X chromosome. They conclude that modern and archaic humans were extremely infertile.<sup>89</sup>

It is not biologically unreasonable to propose some interbreeding between modern and archaic human populations—even if they are not the same species. As sister species go, half a million years is not much of a separation. In comparison, common and pygmy chimps, separated for two million years,

will cross-breed successfully.<sup>90</sup> Many living species do interbreed to varying extents in the wild, and can even absorb significant genetic changes. For example, coyotes found in New York are larger than those in Missouri due to a significant number of timber wolf genes absorbed in Canada on their ancestors’ eastward migration.<sup>91</sup> We too might have picked up a few useful genes, without meaning that we belong to the same species. In fact, the high level of purifying selection suggests that we did not.

The core to a species’ biological identity is a “differentiated” genetic blueprint, a “genetic program” which constrains the expression of genes.<sup>92</sup> When a new allele is added (by breeding or mutation), its first selective hurdle is the test of genetic compatibility. If it does not work well, its owner/organism does not produce many offspring, and it disappears. For two species to truly fuse, their genomes must differentiate a compromise genetic program. The red wolf of the American south, a coyote/gray wolf fusion species, is an example.<sup>93</sup> But this did not happen to the African emigrant populations that mated with the Neanderthals. Almost all significant Neanderthal loci were apparently filtered/selected out by the modern “program.” A few alleles were neutral, or perhaps increased the efficiency of the immune system for the north latitudes. But the genetics and the “human nature” of the emigrants remained essentially unchanged, a package for “being human” which was put together in Africa hundreds of thousands of years after our ancestors went their separate ways from the ancestors of the Neanderthals (and the Denisovans).<sup>94</sup>

In summary, the recent data on the presence of Neanderthal genes in all non-African populations do have implications for our humanity. I concede that the exact human status of the Neanderthals remains debatable. However, I am not a theologian, and I do not want to speculate on their status before God. Biologically speaking, however, they were apparently a functionally different species, probably showing a more limited rationality and social intelligence.<sup>95</sup> Whatever their human status, however, a very limited amount of Neanderthal interbreeding with modern humans did occur. All non-Africans are evidently part Neanderthal, but there is little evidence that this altered our species in any significant way. And if the interbreeding did not alter our humanity, it should not alter our understanding of what it

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means to be human. I simply would point out that the Sovereign God knew what he was doing when he allowed it to occur.

In conclusion, recent data from genetics continue to confirm that *Homo sapiens*, modern humans, people with our cerebral morphology and our pattern of development, first appeared in Africa. And, that the probable date of that appearance was at least 200,000 years ago, and possibly significantly earlier. And, that the first members of our species were likely few in number, but nothing like the biblical two, Adam and Eve. And, that the rest of the world was settled by African emigration around 60,000 years ago, first to Asia. And, that a few of the people who migrated out of Africa mated with Neanderthals, spreading some advantageous genes, although the two populations were on the edge of genetic incompatibility. None of this was expected thirty years ago by either theology or anthropology.

Should we conclude that the scriptures are in error, or should we concede that we might have misunderstood them? In this article, I am not trying to harmonize the scientific data with a particular theological perspective. There is a large literature proposing alternative scenarios for Adam, but I am not advocating one.<sup>96</sup> My intent has simply been to lay out the above data as groundwork for a further honest, comprehensive discussion. Unexpected, but accurate, data come from the hand of God, whatever the motives of those who discover them. Of course, such data do not come with attached meaning. We have to figure it out. But we should have confidence that God already knows how it all rightly fits together. Our challenge is to solve the puzzle he has set us, without losing fellowship with each other. We must follow the Lion wherever he goes—and give him glory for the works of his hands. ☞

### Notes

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