Baraminic analysis of archaic and modern human genomes

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A recent paleogenomic study compared the whole genomes and several subgenomic regions of modern human and those of Neanderthal and Denisovan. This genomic comparison helps shed more light on the taxonomic relationships between modern and archaic humans than do prior morphological studies. The current paper seeks to interpret the results from this recent study and draw relevant implications for baraminology. Based on anthropological and genetic evidence, we should expect to find similarities between modern human and Neanderthal and Denisovan, and also differences between them and members of the ape holobaramin, such as chimpanzee. For example, there are several global genomic characteristics of the human, Neanderthal, and Denisovan genomes which underscore their similarity. Also, deletions of genomic regions present in archaic and missing from modern humans show that the human baranome underwent devolution, as opposed to evolution. Certain so-called 'accelerated' regions in the human genome are also present, and in some cases identical in the Neanderthal and Denisovan genomes, setting them apart from species in other baramins, such as apes. Overall, besides morphological and behavioural characteristics, genomic characteristics also bespeak the unity between members of the human holobaramin and differences between them and the ape holobaramin.

With the sequencing of the complete genomes of the archaic humans Neanderthal[1] and Denisovan,[2] small-scale genomic comparisons have been possible.[3] However, until now only one full-scale analysis and comparison of the whole genome sequence of modern and archaic humans has been performed.[4] In this study they scored, ranked, and compared the motifome (sequence motifs of lengths 6–10 bp), promoter regions, and introns of human, Neanderthal, and Denisovan. This has important scientific consequences in that, besides the characterization and comparison of fossil skeletal remains, a global analysis of the whole genome sequence can give us a deeper insight into the baraminic relationships between these three variants of humans and those of other species.

With the exception of the followers of the 'progressive' creationist school of Hugh Ross, there is little doubt that modern humans are related to two archaic variants of humans. Diverging from over 100 years of tradition, many modern studies now refer to them as subspecies of *Homo sapiens*, that is Neanderthal (*Homo sapiens neanderthalensis*) and Denisovan (*Homo sapiens denisova*).[5] Previous creationist studies have highlighted the flow of genetic material between modern humans and Denisovans, for example.[6] The Denisovan tooth is trapezoidal in shape, which is similar to *Homo erectus*.[7]

In this paper we will analyze the results coming from the Cserhati *et al.* study and derive conclusions which are important for the baraminic status of the human holobaramin. Baraminology involves an analysis of the relationship between different kinds of animals along biblical lines. A 'baramin' is made up of species corresponding to the kinds mentioned in Genesis 1. The 'holobaramin' corresponds to the full species membership of one of the kinds created during Creation Week. For example, dogs, wolves, jackals, and coyotes would belong to a single holobaramin[8]. A 'baranome' is a pluripotent, undifferentiated genome with an intrinsic ability for rapid adaptation and speciation.[9] Essentially, a pluripotent baranome can give rise to multiple species within a single holobaramin within the biblical timeframe.

According to baraminology, species within a kind should show some degree of continuity with one another, and discontinuity with species from other kinds. Thus, there should be a close relationship between human genomes. Conversely, human genomes should differ distinctly from the genomes of other kinds, such as apes.

General genomic characteristics of modern and archaic humans compared to those of chimpanzee

At a macroscopic level, the Neanderthal and Denisovan genomes are very similar to that of modern human. The genome size of all three human morphological variants is around 3 Gbp. All three have 23 pairs of chromosomes, as opposed to chimpanzee, which has 24 pairs. Previous creationist research has strongly argued that there is no site on human chromosome 2 which supposedly came about via the fusion of chimpanzee chromosomes 2a and 2b.[10,11] Table 1 lists general genomic characteristics of the genomes of modern human, Neanderthal, Denisovan, and chimpanzee

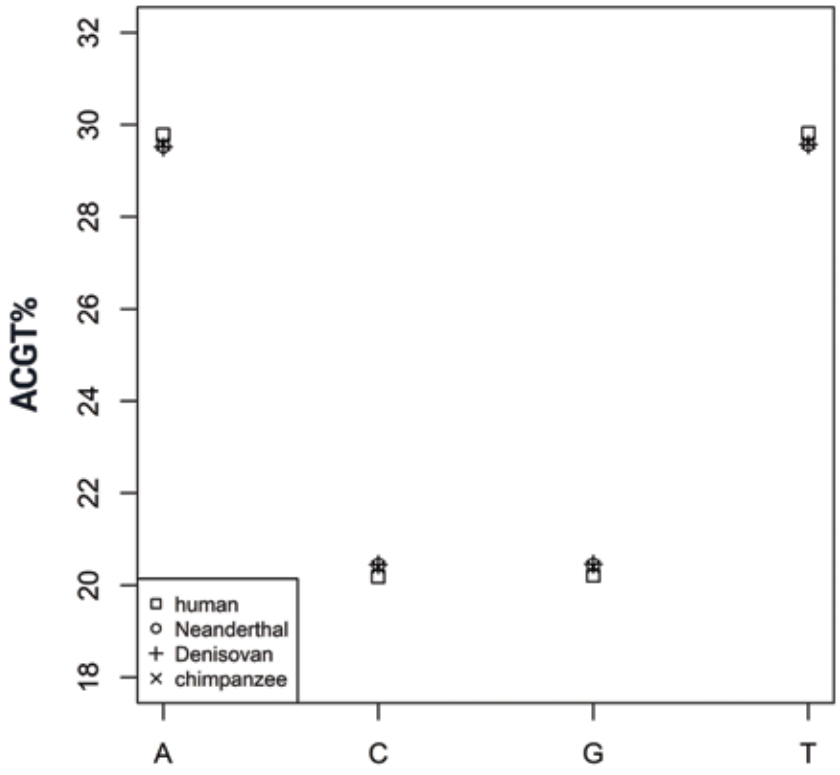

Figure 1. ACGT% in genomes of modern human, Neanderthal, Denisovan, and chimpanzee

for comparison. Figure 1 visualizes the ACGT% for all four genomes.

According to the Cserhati *et al.* study, 86.2% of the 1,000 highest-scoring hexamer whole-genome motifs are found in common among all three human morphological variants, whereas only 5.2% of their top 1,000 decamer whole-genome motifs are in common. This may be due to differential recombination or gene conversion with strong drift in Neanderthal and Denisovan in the intergenic regions.

On a subgenome level, things are more similar between modern human and Denisovan. For example, they have 96.5% of the 1,000 highest-scoring hexamer motifs in common in core promoters. Among decamers, 86.9% of their top 1,000 decamer motifs are in common in the core promoters (as opposed to the mere 5.2% common decamer motifs in the whole genome). This is significant, in that this implies that, to a very large part, the core regulatory machinery of the genes between modern human and Denisovan is the same.

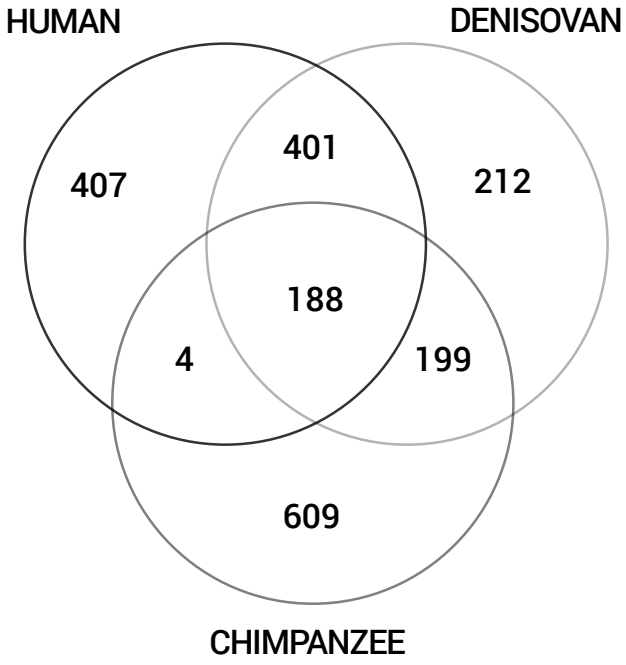

Figure 2. Number of common octamers from the top 1,000 octamers from the proximal promoter regions between modern human, Denisovan, and chimpanzee

It has been established that the whole-genome similarity between modern humans and chimpanzees is not more than 85%.[12] Thus, despite the fact that, on a macroscopic level, the genomes of both modern and archaic humans and chimpanzee have approximately the same ACGT%, the significant difference in their genome sequence still implies that there is discontinuity between the human holobaramin and chimpanzee. Deyneko *et al.*[13] studied the sequence similarity of promoter regions between modern human and chimpanzee and found that, although 6,050 of the 9,329 promoters they studied were more than 65% similar, the similarity around 35% of the studied promoters (3,279) was less than 90%. Furthermore, they performed in-depth promoter comparison only on chromosome 21. This implies that many chimpanzee promoters could be very differently regulated than the promoters of their homolog genes in human. Heissig *et al.*[14] also think that there are differences in proximal promoter activity between humans and chimpanzees. As many as 10% of all genes in the brain are differentially expressed between humans and chimpanzees.[15] This is significant as it affects cognition, which is a very important differentiating factor between humans and non-humans. Another study showed that fully 80% of proteins are different between humans and chimpanzees.[16] Demuth *et al*. also showed that humans have 689 genes not present

Table 1. General characteristics of the genomes of modern and archaic humans and chimpanzee

Species	No. chromosomes	Size of genome (Gbp)	No. proteins predicted by Augustus	ACGT%
Homo sapiens	23	3.21	33,321	29.78%/20.19%/20.21%/29.82%
Neanderthal	23	2.85	33,049	29.53%/20.45%/20.45%/29.57%
Denisovan	23	3.00	32,733	29.52%/20.45%/20.46%/29.57%
Chimpanzee	24	3.23	46,094	29.59%/20.39%/20.4%/29.62%

Table 2. Alignment similarities between the proximal promoters of modern human, Denisovan, and chimpanzee

First species	Second species	Average similarity	Average length	Average matching bases
Human	Chimpanzee	97.27%	462.5 bp	449.9 bp
Denisovan	Chimpanzee	95.61%	477.0 bp	456.1 bp
Human	Denisovan	99.79%	459.2 bp	458.2 bp

in chimpanzee, and that chimpanzees have 86 genes that are lacking in human, and that their DNA differs by 6%, as opposed to the oft-cited figure of only 1.5%.[17]

In our own comparison, we obtained the proximal promoter sets (1 Kbp sequences) for chimpanzee from the UCSC Genome Browser, the promoters for modern human from the Eukaryotic Promoter Database, and the Denisovan promoters from the website of Cserhati *et al.* for supplemental data and performed mutual sequence comparisons (alignments) among all three. Promoters for Neanderthal are not yet available. The results can be seen in table 2. We observe that the average alignment length (that is, the average length of the most homologous region of the promoter between the two species, the promoters of which are being compared) is about the same for all three species comparisons. However, the average alignment *similarity* between modern human and Denisovan was almost identical at 99.79%, whereas the average similarity between chimpanzee and the two human morphological variants was lower at 95.61% and 97.27% for the Denisovan-chimpanzee and the modern human-chimpanzee comparisons, respectively. Figure 2 shows a Venn diagram depicting the number of common octamers coming from the top 1,000 octamers from the proximal promoter regions between modern human, Denisovan, and chimpanzee. Modern human and Denisovan have a higher ratio of overlapping common top-scoring octamers at 41.7%. This ratio is lower between chimpanzee and modern human at 10.6% and between chimpanzee and Denisovan at 24%.

Table 3. Location of 49 Human Accelerated Regions (HARs) in the human genome, number of matching motifs from Neanderthal and Denisovan, and number of HARs matching between human and Neanderthal and Denisovan (after Cserhati *et al.* 2018). An additional two in the coding region and one in the RNA were not studied further.

Region	Number of HARs	No. of matching Neanderthal motifs/HAR regions	No. of matching Denisovan motifs/HAR regions
Intergenic regions	26	184/26	175/25
Introns	20	not studied	160/18

Conserved deleted regions in human

McLean *et al.*[18] studied 584 so-called hCONDEL (human conserved deletions) regions in chimpanzee and human. These appear in intergenic regions of the chimpanzee genome (median size of 2,804 bp) but are missing from the human genome. It would be interesting to see whether these regions correspond to any regions in the Neanderthal or Denisovan genomes. If they do, this would mean that these genomic regions have been deleted from modern human genomes. This would support the idea of the devolution of the human baranome through time, as opposed to the evolutionary assumption of genomic build-up.

For example, Hinds *et al.*[19] found 215 deletions within 600 Mbp of the human genome ranging from 70 bp to 10 Kbp, 41 of which had an allele frequency of at least 10%. These may represent a source of common genetic variation, and which also may cause phenotypic differences in complex traits. Similarly, McCarroll *et al.*[20] found 541 deletion variants ranging from 1 to 745 Kbp—278 of which were found in multiple, unrelated individuals. Deletions were found in the exons of ten genes in the homozygous state, two of which were related to olfaction. Similarly, Hughes *et al.*[21] found that several combinations of 20 olfactory receptors (OR) were differentially lost in modern humans, Neanderthals, and Denisovans.

According to the Cserhati *et al.* study, of the 583 hCONDEL regions, 287 (49.2%) of them had a significant hit at least 50bp long in at least one of the archaic human genomes, with at least 90% sequence identity. This means that

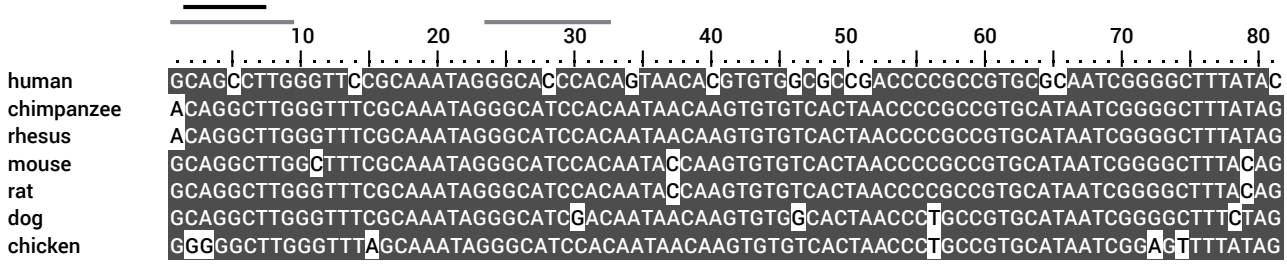

Figure 3. The 81-bp segment from the enhancer element between the CENTG2 and GBX2 genes on human chromosome 2, showing 13 human-specific substitutions, compared with the corresponding region in chimpanzee, rhesus, mouse, rat, dog, and chicken

about half of these deletions happened after the split between modern and archaic humans.

Human accelerated sequences

Prabhakar *et al.*[22] studied a 546-bp enhancer element between the CENTG2 and GBX2 genes on human chromosome 2 inside what they called the human-accelerated conserved non-coding sequence 1 (HACNS1). This is responsible for differential limb development in mammals, and is expressed in the anterior limb bud, pharyngeal arches, ear, and eye in the developing embryo. Compared to chimpanzee, mouse, rat, dog, and chicken, this enhancer element has 16 human-specific substitutions. Furthermore, a shorter, 81-bp segment contains 13 of these 16 substitutions (figure 3).

Evolutionists argue that, for some unknown reason, this part of the human genome underwent accelerated mutation, which led to differential human morphology. However, if this is true, then it remains a mystery as to how and why this small, isolated segment of the genome remained relatively conserved while the surrounding region changed through evolutionary time. This implies that this enhancer element, with its special human-specific functionality, was differentially created in the human genome.[23] It should also be noted that position 1 in this 81-bp stretch of DNA is the same in chimpanzee and the rhesus macaque, which could arguably belong to a monkey holobaramin. The same is true for positions 37 and 79 for mouse and rat.

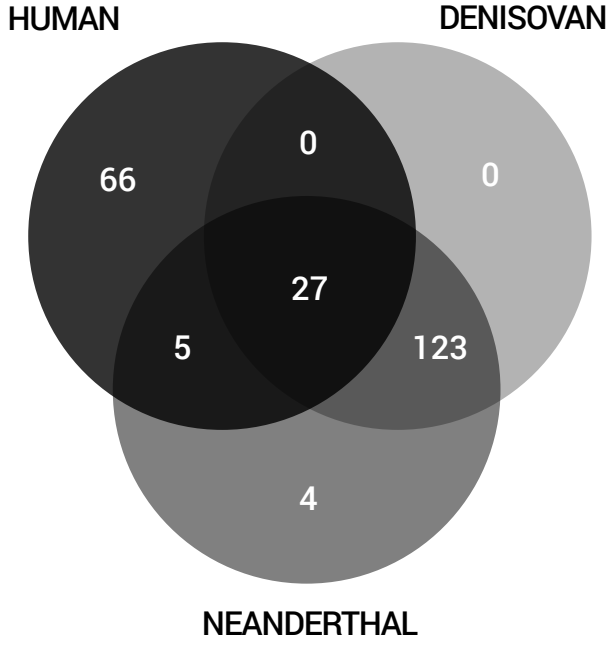

Figure 4. Intergenic motifs in Human Accelerated Regions (HARs) shared among modern human, Neanderthal, and Denisovan

This 81-bp segment is identical in Denisovan and modern humans, which implies that they belong to the same holobaramin. Furthermore, according to the Cserhati *et al.* study, a genome motif, CAGCCT, which was found within this 81-bp segment (black bar in figure 3), was found to be among the highest-scoring motifs in modern human, whereas the high-scoring motifs GCAGCCTTG and GGCACCCAC (grey bars in figure 3) were discovered in Denisovan, implying that this enhancer has biological function in both variants of human.

Besides HACNS1, Pollard *et al.*[24] identified 49 Human Accelerated Regions (HARs) with substantial functional differences between human and other mammals. Forty-six of these are located in non-coding regions of the genome, but also have significant BLAST hits with the genomes of Neanderthal and Denisovan. Table 3 lists the number of these elements in different subregions of the genome of modern human. Also listed are the number of significant motifs from Neanderthal and Denisovan which match these human HARs and the number of HARs which have a match in different subgenomic regions of the Neanderthal and Denisovan genomes. The Cserhati *et al.* study identified 225 statistically significant whole genome motifs in modern human, Neanderthal, and Denisovan which were found in 26 intergenic HAR regions identified by Pollard *et al.* Modern human shares approximately the same proportion of intergenic motifs with Neanderthal (14.2%), as with Denisovan (12.2%), whereas Neanderthal and Denisovan share 94.3% of these motifs among themselves (see figure 4).

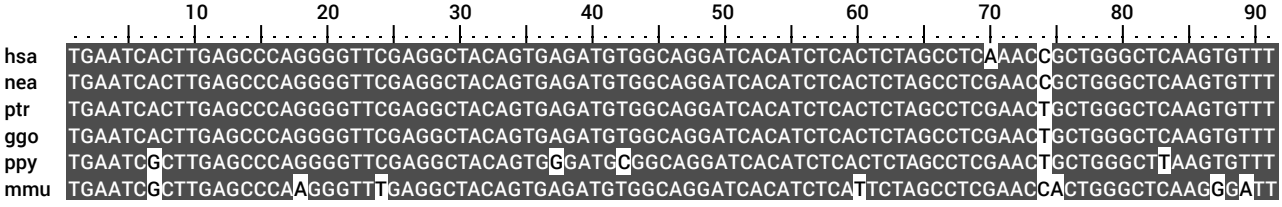

Figure 5. Significant MicroRNA species motifs in 91 bp miR-1304 sequence: hsa = *Homo sapiens*; nea = Neanderthal; ptr = *Pan troglodytes*; ggo = *Gorilla gorilla*; ppy = *Pongo pygmaeus*; mmu = *Mus musculus*.

Motif content similarity within the miR-1304 microRNA element

MicroRNA species have been known to regulate as much as 30% of all genes in human, and also take part in complex cellular networks.[25] The miR-1304 element has been shown to be involved in dental and craniofacial differences[26] and regulates two genes, ENAM and AMTN, which take part in odontogenesis.[27] Five Neanderthal motifs from the Cserhati *et al.* study (with the consensus sequence of CCTGCCTCG) were found to overlap the seed region (a conserved core region of the miR-1304 sequence which binds with the mRNA of the gene that it is regulating) of miR-1304, GCCTCGA (here the underlined part of the consensus motif sequence and the seed region indicate where they overlap). It should also be mentioned that the target site for the miR-1304 element in the 3' UTR of both the ENAM and AMTN genes is exactly the same.

Neanderthals were known to have different craniofacial characteristics compared to modern humans, and the differential expression of genes involved in tooth formation might cause phenotypic differences between Neanderthals and modern humans, even though they belong to the same holobaramin. For example, modern humans have thicker enamel than Neanderthals do, possibly due to the miR-1304 element.[26,28]

Ten significant motifs from the Cserhati *et al.* study from modern humans and two from Neanderthal were found in the 22-bp seed motif of miR-1304 (CACATCTCACTGTAGCCTC[A/G]AA). The 91 bp miR-1304 sequence (figure 5) contains only 1 bp difference between modern human and Neanderthal, whereas a difference exists at two different positions between modern human and two ape species, chimpanzee and gorilla, and a difference at six positions between modern human and orangutan.

Conclusions

The genomes of modern humans, Neanderthals, and Denisovans are very similar to each other. Besides this general similarity (genome size, number of proteins, ACGT%, chromosome number), they also have a similar high-scoring motif content. Since some genomic regions (hCONDELs) are present in the genomes of archaic humans but missing in modern human, this shows that the human baranome is devolving, not evolving. Also, on a finer level of genetic elements, such as among human accelerated regions and microRNAs, we see that archaic human sequences are nearly identical to modern humans. This suggests that modern and archaic humans are members of the human holobaramin. Thus, besides morphology[29] and behavioural characteristics,[30] Neanderthals are similar to modern humans genomically, something which has been demonstrated in previous studies, but has now been demonstrated on a sub-genome level as well.

While chimpanzees may have a similar ACGT% to humans, their *overall* genome similarity is different. Furthermore, on a gene regulatory level, chimpanzee promoters are dissimilar, implying that divergent genetic regulation is the reason behind the phenotypic differences between humans and chimpanzees. The genomes of archaic and modern humans are much more similar to one another, and different from all other species. This implies common ancestry for the three. Modern and archaic humans form one single species, *Homo sapiens*. Truly, according to Acts 17:26: "And he made from one man every nation of mankind to live on all the face of the earth" (ESV).

Materials and Methods

The Neanderthal and Denisovan whole-genome sequence and Denisovan core promoter set was downloaded from golgi.unmc.edu/HumanMotifomeData. A set of 1,577 proximal promoters for chimpanzee was downloaded from the UCSC Genome Browser at hgdownload.soe.ucsc.edu/goldenPath/panTro5/bigZips/upstream1000.fa.gz. Human, Denisovan and chimpanzee proximal promoters (human proximal promoters were downloaded from the Eukaryotic Promoter Database, EPD)[31] were aligned with the BLAST algorithm[32] using the *-n* parameter setting to search in MEGABLAST mode, which is useful in aligning longer sequences that differ only slightly from one another. The number of protein sequences for modern human, Neanderthal, Denisovan, and chimpanzee were predicted by using version 2.5.5 of the Augustus gene prediction

algorithm,[33] using human as a comparison species. Figure 1 was created in R, version 3.4.3. Figure 2 was created using the Venn diagram software at bioinformatics.psb.ugent.be/cgi-bin/liste/Venn/calculate_venn.htpl. Figures 3 and 5 were created using version 7.2.6.1 of BioEdit.[34] Figure 4 was taken from the Cserhati *et al.* paper with the author's permission.

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