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THE CHIMPANZEE GENOME AND THE PROBLEM OF BIOLOGICAL SIMILARITY

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The Chimpanzee Genome and the Problem of Biological Similarity

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Abstract. Evidence for the great similarity between chimpanzees and humans was recently reinforced with the publication of a rough draft of the chimpanzee genome. The sequence is in >361,000 pieces with a median length of 15,700 nucleotides. The sequence differs from the human genome by 35 million nucleotide mismatches (1.23%) and 10 million alignment gaps (~3-4%). Rather than attempting to explain this similarity, I here propose principles that can guide creationist research in this area. I find that creationist genomics requires three important theories that still need to be developed before fruitful research can commence. The first need is a theory of biological similarity. The level of similarity observed between the human and chimpanzee genomes cannot be adequately explained simply by the will of the Creator, unless a theory can be developed to explain *why* the Creator would will such similarity. The most promising candidate for explaining biological similarity is a modified form of ReMine's message theory. The second greatest need for interpreting genomes is a theory of the genome, particularly its importance and biological function. The third need is a better understanding of baraminology and historical development of organisms.

In the spring of 1698, the English anatomist Edward Tyson obtained the remains of a young chimpanzee. The animal had been brought to England aboard a ship bound from Angola, but it contracted an infection *en route* and died soon after its arrival. Together with his friend and colleague William Cowper, an expert on muscle anatomy, Tyson dissected this chimpanzee and published his findings in the 1699 book *Orang-Outang, Sive Homo sylvestris, or, The Anatomy of a Pigmie*. Tyson's work was the first scientific description of the complete anatomy of a chimpanzee (Montagu 1943).

Tyson noticed the striking anatomical resemblance between the chimp and humans, and he interpreted this similarity in terms of the Chain of Being. According to Lovejoy (1936), the Chain of Being consists of two distinct ideas: the conviction that creation represents a linear progression from insensate matter to the divine and the "principle of plenitude." The principle of plenitude asserts that all possible things are realized in creation and therefore the Chain of Being has no gaps. In Tyson's words,

Thus in the *Ape* and *Monkey-kind*, *Aristotle's Cebus* [monkey] I look upon to be a degree above

his *Cynocephalus* [lemur]; and his *Pithecus* or *Ape* above his *Cebus*, and our *Pygmie* [chimpanzee] a higher degree above any of them, we yet know, and more resembling a *Man*: But at the same time I take him to be wholly a *Brute*, tho' in the formation of the Body, and in the *Sensitive* or *Brutal Soul*, it may be, more resembling a *Man*, than any other *Animal*; so that in this *Chain* of the *Creation*, as an intermediate Link between an *Ape* and a *Man*, I would place our *Pygmie* (Quoted in Montagu 1943, pp. 243-244).

So Tyson recognized the chimpanzee's intermediate morphological status between apes and man, but he interpreted this as evidence of the smooth, linear, and created Chain of Being.

Though the concept of transition or gradation may sound evolutionary to our modern ears, Tyson believed in a biological spectrum of form created by the Creator, rather than a temporal or evolutionary series. He commented,

This *Climax* or *Gradation* can't but be taken notice of, by any that are curious in observing the Wonders of *Creation*; and the more he observes it, the more venerable *Idea's* 'twill give him of the

Reference	Sample Type	Sample Size	Percent Nucleotide Mismatches
Britten 2002	Random sample	0.78 Mb	1.2-1.69%
Ebersberger et al. 2002	Random sample	1.9 Mb	1.24%
Liu et al. 2003	Chromosome 7	4.97 Mb	1.13%
Wildman et al. 2003	Gene exons	90 kb	0.87%
International Chimpanzee Chromosome 22 Consortium 2004	Finished chromosomal sequence	33.3 Mb	1.44%
Nielsen et al. 2005	Gene exons	18.5 Mb	0.6%
Chimpanzee Sequencing and Analysis Consortium 2005	Rough draft genome sequence	2700 Mb	1.23%

Table 1. Summary of Human/Chimpanzee Genome Similarity Estimates.

great *Creator* (quoted in Montague 1943, p. 243). To Tyson, then, “gradation” between species served not as an evidence of evolutionary relationship but as a testimony to the wonders of the “great Creator.”

Within two centuries, the anatomical similarity of apes and humans had been re-interpreted as evidence of common ancestry by Charles Darwin, T.H. Huxley, and their colleagues. Not surprisingly, the biochemical similarities that became increasingly apparent in the 1960s and 1970s were interpreted as further support for the evolutionary relationship between humans and apes. Indeed, Fitch (1970) argued that molecular sequences (of protein or DNA) are best explained as the result of common ancestry because the pattern of similarities observed in sequences matched the pattern expected according to evolution. Mammals were more similar to other mammals, then to birds, then to fish and invertebrates, as would be expected if mammals were related more closely to birds than fish or invertebrates.

What came as a surprise to primate researchers was the degree of similarity between the chimpanzees and humans. Studies of actual protein sequences from chimpanzees and humans, differences in alleles, and DNA heteroduplex melting points all pointed to greater than 98% identity (King and Wilson 1975). To account for this similarity, King and Wilson (1975) proposed that small mutations in genetic regulatory regions that produce significant differences in gene expression must be responsible for the anatomical and behavioral differences between humans and apes.

The high degree of genetic similarity between apes and humans has been repeatedly confirmed since King and Wilson’s (1975) summary. Chromosomal banding patterns revealed a high degree of correspondence between human and chimpanzee chromosomes (Miller 1977, Yunis et al. 1980, Yunis and Prakash 1982). Major chromosomal differences detected were a putative fusion of chimpanzee chromosomes 12 and 13 to form human chromosome 2, and pericentromeric inversions on human chromosomes 4, 5, 9, 12, 15, and 16 (Yunis and Prakash 1982). Subsequent small-scale sequencing efforts further confirmed the similarity. Hacia (2001) reviewed a number of studies that indicated single nucleotide differences were between 1.24% and 1.6%, and he predicted that the human and chimpanzee genomes would differ by ~35 million nucleotides.

With the onset of the genomic age, where large sets of DNA sequence information could be obtained quickly and affordably, new sequencing of chimpanzee DNA has confirmed earlier estimates of similarity (Table 1). Ebersberger et al. (2002) aligned 1.9 Mb (million nucleotides) of chimpanzee DNA to the human genome and found that it differed by 1.24% from the corresponding human sequences. Liu et al. (2003) compared 4.97 Mb of human DNA from chromosome 7 to chimpanzee orthologues and found 1.13% nucleotide mismatches. The finished euchromatic sequence of chimpanzee chromosome 22 revealed 1.44% nucleotide differences from human chromosome 21 (International Chimpanzee

Chromosome 22 Consortium 2004). Chimpanzee exons totaling 92 kb (Wildman et al. 2003) and 18.5 Mb (Nielsen et al. 2005) showed a mere 0.87% and 0.6% difference from human sequences, respectively.

THE CHIMPANZEE GENOME

In 2003, the National Human Genome Research Institute announced the completion of a rough draft of the chimpanzee genome sequence. As might be guessed from the name, a “rough draft” sequence differs from a finished sequence in the degree of effort expended on completing the sequencing. Any genome sequencing project begins with a phase of “shotgun” sequencing, wherein random pieces of DNA are isolated from the genome and sequenced. If the goal is to finish the genome, enough sequence is generated to cover the genome with eight-fold redundancy (8x coverage). The sequences are then fed into a computer program called an assembler that matches pieces of DNA taken from the same genomic region and reconstructs the unbroken sequence of each chromosome. The shotgun phase rarely generates enough sequence to cover the entire genome, requiring a directed sequencing phase called “finishing.” Finishing involves identification and sequencing of DNA pieces that cover regions missed in the shotgun phase. A rough draft sequence, by contrast, does not undergo finishing, and the shotgun coverage may be only three- or four-fold redundant (3-4x coverage). A rough draft sequence is therefore in many different pieces. Rough draft sequences are most advantageous when the genome sequence from a closely-related organism is available, which can serve as a reference in assembling the rough draft fragments. For more information on genome sequencing strategies, see Wood and Tomkins (2004).

An important point to remember about “finished” genome sequences is that they are not entirely finished in the colloquial sense. “Finished” refers to completion to a quality standard agreed upon by the research community. The human genome project recognized that repetitive regions that consist of arrays of tandemly duplicated sequence are difficult to sequence (Collins et al. 1998). They therefore recommended that any gaps that could not be sequenced should be noted and the gap size recorded. As a result of these standards, the finished human genome sequence lacks many different repetitive regions (known collectively

as heterochromatin), but it is still proper to refer to it as a finished sequence. As a rough draft sequence, the chimpanzee is not finished and contains many gaps of unknown size.

The chimpanzee genome was sequenced at a coverage of 3.6x for autosomes and 1.8x for the sex chromosomes (Chimpanzee Sequencing and Analysis Consortium 2005). Assembly of these shotgun sequences produced 361,782 contigs (contiguous fragments), with a median length of 15,700 nucleotides. The total coverage of the rough draft is 2.7 billion nucleotides, 94% of the chimpanzee genome. Even though the sequence is “only” a rough draft, the accuracy is quite high. The error rate was estimated to be $\leq 10^{-4}$. Comparison to finished sequences from the same chimpanzee, consisting of 1.3 million nucleotides, revealed a mismatch rate of 3×10^{-4} and 2×10^{-4} nucleotides omitted or inserted. Overall, an error rate of 1-3 nucleotides in 10,000 should be expected in the chimpanzee genome.

The rough draft sequence supports the initial findings of high similarity (Chimpanzee Sequencing and Analysis Consortium 2005). Due to the fragmentary nature of the sequence, researchers were only able to align about 2.4 Gb of high quality DNA sequence (about 80% of the human genome). They found that nucleotide mismatches over the whole alignment totaled ~35 million and averaged 1.23%.

To verify this similarity, I downloaded protein sequences of the predicted chimpanzee and human protein-coding genes from Ensembl (<http://www.ensembl.org>) and compared them. Using each human protein as a query sequence, I identified the most similar sequence in the chimpanzee dataset using the program SSEARCH (Pearson 1991). This kind of comparison will yield errors, since not all predicted proteins will be real genes, and therefore they may not have corresponding predicted genes from both species. Nevertheless, I found that 75% of the human predicted protein sequences matched a predicted chimpanzee sequence at >97.25% identity, and more than half were >99% identical (Figure 1). My analysis confirms the similarity reported by the Chimpanzee Sequencing and Analysis Consortium (2005).

In addition to mismatches, the chimpanzee and human genomes also differ in their lengths. When aligning any two sequences, it is occasionally necessary to insert or omit a nucleotide (or more) in

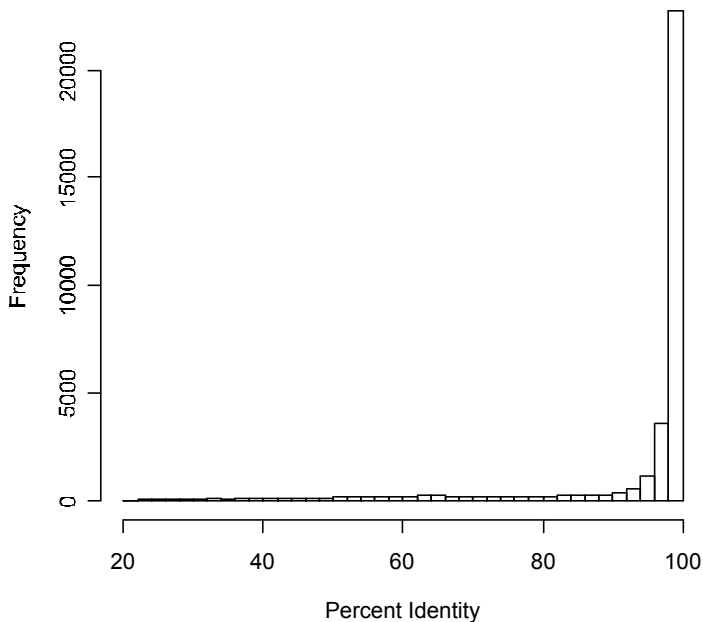


Figure 1. Similarity of Predicted Proteins of Human and Chimpanzee. Predicted protein sets from human (v. 35) and chimpanzee (v. 1) were downloaded from Ensembl (www.ensembl.org). Each human sequence was searched against the chimpanzee predicted proteome using the Smith-Waterman program SSEARCH. Top scores were recorded and their percent identities are shown here.

order to maintain the best alignment. Evolutionary biologists assume that such adjustments are necessary because nucleotides have been inserted or deleted over the course of evolution. Since I do not accept the common ancestry of humans and chimpanzees, I will refer to these adjustments as “gaps,” following the tradition of computational biology (e.g. Altschul et al. 1997; Pearson 1998). The chimpanzee/human genome alignment contains approximately ten million gaps, covering 67 million nucleotides. The vast majority of the gaps are very small (96% are less than 20 nucleotides), and a significant fraction of the larger gaps (>33%) are found in areas of satellite repeats.

Approximately 175,000 gaps correspond to known transposable elements, which replicate and insert into the genome independently of the normal cellular DNA replication mechanism. The majority of these transposable elements are merely copies of other elements already present in both genomes. The copy number in one or the other genome has merely increased. In contrast, other elements were found to be significantly different. Two families of chimpanzee endogenous retroviruses (PtERV1 and PtERV2) were discovered to be entirely absent from the human

genome. Likewise, the number of Small Interspersed Nuclear Elements (SINEs) in the human genome was three times the number in the chimpanzee genome.

Overall, gaps account for approximately 32 million nucleotides of human-specific DNA and 35 million nucleotides of chimpanzee-specific DNA. If the entire chimpanzee genome had been sequenced, it would probably reveal 40-45 million nucleotides unique to each species. The difference in gaps may sound profound, but remember that the majority of nucleotides are contained in simple repeats, either of satellites or transposable elements. Further, even a length variation of 90 million nucleotides constitutes only 3% of the entire genome.

WHAT’S THE DIFFERENCE?

The high degree of similarity observed reinforces King and Wilson’s (1975) problem: How could such different organisms have such similar genomes? In addition to the obvious morphological and behavioral differences, chimpanzees differ in important physiological ways. For example, chimps rarely have heart attacks or go through menopause and are resistant to malaria caused by *Plasmodium falciparum* (Varki and Altheide 2005). Because of these differences, chimpanzees make poor models in human disease research. Since our genomes are so similar, what is the basis for the phenotypic differences? What differences in the genomes could correlate with phenotypic differences?

In detecting species-specific genomic differences between humans and chimps, it is necessary to identify differences that are polymorphic in one or both species, since polymorphisms cannot by definition be fixed, or species-specific, differences. For example, the frequency of single nucleotide polymorphisms (SNPs) in humans and chimpanzees suggests that the fixed differences between the two genomes may be as low as 1.06% (Chimpanzee Sequencing and Analysis Consortium 2005). The remaining differences in the published sequences are variants within one species or the other.

The first genomic differences recognized were the aforementioned inversions and chromosomal fusions (Yunis and Prakash 1982). Six human chromosomes differ from their chimpanzee counterparts by an inversion of gene order around the centromere. Within the inversions, the gene order is preserved, but

the human genes run in the opposite order from the chimpanzee genes. Human chromosome 2 corresponds to two separate chromosomes in chimpanzee. These findings have subsequently been confirmed in studies using fluorescence *in situ* hybridization (Müller and Wienberg 2001).

The evolutionary explanation for human chromosome 2 corresponding to two separate chromosomes in the great apes is that two chromosomes in a human ancestor fused at their ends (telomeres), with one of the centromeres becoming inactive. By examining the putative “fusion” point, researchers have discovered an inverted array of telomeric repeats (TTAGGG)_n (Ijdo et al. 1991) and other sequences found in subtelomeric chromosomal regions (Fan et al. 2002). Centromeric alpha satellite sequences have been detected on the long arm of chromosome 2, which seem to correspond to an inactive centromere (Alexandrov et al. 2001).

Also apparent in early cytogenetic studies were differences in human and chimpanzee heterochromatin. The word heterochromatin was introduced in the 1930s to describe chromosomal regions that remain condensed during interphase and do not unravel in telophase (Yunis and Yasmineh 1971), and we know now that these regions consist of large arrays of repetitive sequences. The location and extent of human heterochromatin differs from chimpanzee heterochromatin. Chromosomes 6, 8, 10, 11, 14, 19, 20, and X were found to contain extra regions of heterochromatin in their chimpanzee counterparts (Yunis et al. 1980). The chimpanzee Y chromosome is much smaller than the human Y chromosome due to less heterochromatin (Yunis and Prakash 1982). Other studies of repetitive DNA found a greater degree of sequence difference based on thermal stability (Deininger and Schmid 1976) and differences in chromosomal locations (Mitchell et al. 1977). More recent studies have revealed that even the sequence content of heterochromatin can be different. Toder et al. (1998) discovered a 32-nt AT-rich tandem repeat found in bonobos (*Pan paniscus*) but not humans.

Later research demonstrated that many heterochromatic differences are localized to pericentromeric and subtelomeric regions. Chromosomal centromeres form the attachment points for mitotic spindles during cell division, and telomeres cap the ends of linear chromosomes. Primate

centromeres and telomeres are formed from tandem arrays of repeated sequences. Centromeres consist of arrays of alpha satellite sequence, a 171 nucleotide sequence found in all human and chimpanzee centromeres (Vissel and Choo 1987; Waye and Willard 1987; Choo et al. 1991; Luke and Verma 1995). Identical telomeric repeats (TTAGGG)_n, produced by the enzyme telomerase, are found in both humans and chimpanzee chromosomes (Luke and Verma 1993). Sequences adjacent to the alpha satellite array of the functional centromeres are termed pericentromeric, and sequences adjacent to the (TTAGGG)_n telomeric repeats are subtelomeric. In all primates, subtelomeric and pericentromeric regions are repetitive and often differ from species to species.

Alpha satellite sequences in the centromeric region of human and chimpanzee chromosomes form higher order repeats that are collectively duplicated in centromeres. Monomers within these higher order repeats may differ by 30-50% but the higher order repeats differ by only 1-20% (Alexandrov et al. 2001). Alexandrov et al. (2001) divided the various monomers into five different subfamilies, according to the sequence similarity of the 171-nt monomers. Higher order alpha satellite repeats are constructed from monomers of one or more subfamilies.

Alpha satellites exhibit a remarkable similarity bias: Given any higher-order repeat, the most similar sequences will always be found in the same alpha satellite array on the same chromosome (differing by 1-5%). Alpha satellite sequences from the same subfamily but different chromosomes differ by 10-20% (Alexandrov et al. 2001). When compared to alpha satellite repeats from chimpanzee, human alpha satellites from the same subfamilies can be found on chromosomes 1, 11, 17, and X (Baldini et al. 1991, Laursen et al. 1992), but other chromosomes have alpha satellite arrays of different subfamilies at corresponding centromeres (Waye and Willard 1989; Archidiacono et al. 1995). Chimpanzee and human alpha satellites from the same subfamily are 91-97% identical, but alpha satellites from different subfamilies or exclusively monomeric subfamilies (4 & 5) range from 73% to 85% identical (Table 2).

As noted above, a small fraction of the human genome consists of sequences not found at the corresponding location in chimpanzee and vice versa for the chimpanzee genome. The majority

Chromosome	Chimpanzee		Human		Identity
	Subfamily	Accessions	Subfamily	Accessions	
2A	3	L08574	2	M81229	78%
5	5	X97002, X97003	5	AJ007752	79-84%
13	1	L01703- L01724	2	Z14068- Z14070	73-78%
14	1	L01725- L01732, M97592- M97599	2	M22273, M22274	75-81%
16	4	AF183379	4	AC002307	97%
17	3	- ²	3	- ²	91-92.3% ²
21	1	M26333- M26344	2	D29750	73-77%
22	1	L01733- L01752	2	M22288, M22289	73-85%
X	3	X66287, X66288	3	X02418	91%

Table 2. Similarity of alpha satellite arrays from corresponding centromeres of chimpanzee (*P. troglodytes*) and human (*H. sapiens*), as determined by BL2SEQ (Tatusova et al. 1999).¹

¹The sequences and subfamilies are taken from Tables 2 and 3 of Alexandrov et al. (2001), supplemented by Entrez searches of GenBank.

²The percent identity for these sequences was reported by Baldini et al. (1991) and Rudd et al. (2006).

of these larger segments correspond to a recently-identified class of repetitive element called segmental duplications or duplcons (Samonte and Eichler 2002). Segmental duplications are >90% identical to some other region of the genome (either on the same or different chromosomes), and they typically cover thousands of nucleotides. Samonte and Eichler (2002) estimate that ~5% of the human genome consists of segmental duplications. Segmental duplications are frequently found to vary significantly between humans and chimps. Cheng et al. (2005) surveyed the segmental duplications >20 kb and found that 26.5 of 79.8 Mb of duplcons were not shared between humans and chimpanzees. Newman et al. (2005) used genome survey sequences to identify 21.1 Mb of human duplcons not present in the chimpanzee genome. To put this in perspective, 25 Mb is approximately 0.83% of the human genome.

Segmental duplications are biased in their chromosomal location, with a 3-5x enrichment within

100kb adjacent to telomeres (subtelomeric region) and 1 Mb adjacent to centromeres (pericentromeric region) (Samonte and Eichler 2002; see also Cross et al. 1990; Rouyer et al. 1990; Samonte et al. 1997; Horvath et al. 2000; Park et al. 2000; Horvath et al. 2001; Riethman et al. 2004; Linardopoulou et al. 2005; Mewborn et al. 2005). In addition to being hotspots of segmental duplications, pericentromeric and subtelomeric regions are also hotspots for interspecific variation between humans and chimpanzees (Eichler et al. 1996; Zimonjic et al. 1997; Jackson et al. 1999; van Geel et al. 2002).

Given the variety of genomic differences discussed above, what is their significance for detecting species-specific differences? Cytogenetic differences, including chromosomal fusions and inversions, can be polymorphic within some species (e.g. Hauffe and Searle 1998). Indeed, in humans benign (asymptomatic), variant chromosomes include an inversion of chromosome 10 (Collinson et al. 1997)

and a large deletion on chromosome 2 (Sumpton and Barber 2001). Miller (1977) reported a spontaneous chromosomal inversion frequency of 10^{-4} in newborns. While the cytogenetic differences reported above are likely to be fixed, they could have occurred after creation. In fact, it is difficult to imagine a scenario other than chromosomal fusion to explain the inverted array of telomere and subtelomere repeats at the putative fusion site on chromosome 2 (Ijdo et al. 1991).

The significance of variation in heterochromatin is also difficult to judge. The earliest quantitative studies of human heterochromatin detected size polymorphisms in the heterochromatic regions of chromosomes 1, 9, 16, and Y (Yunis and Yasmineh 1971), which were all presumably asymptomatic. Alpha satellite size polymorphisms have been reported (Kiyama et al. 1986), as well as the curious occurrence of extrachromosomal, closed circular alpha satellite arrays (Riabowol et al. 1985; Ohki et al. 1995). Polymorphisms in alpha satellite arrays support the “concerted evolution” (Liao 1999) of alpha satellites, wherein the monomers or higher order repeats within an array are homogenized via unequal crossing over, maintaining a high degree of similarity within the array but allowing for divergence between different arrays. The lower degree of similarity observed between alpha satellites at the edge and the middle of the chromosome X array would also support unequal crossing over as the mechanism of concerted evolution (Schueler et al. 2001).

Although it might be tempting to point to differences in segmental duplications between humans and chimpanzees as the source of species specific phenotypes, these too must be carefully examined for polymorphisms. Particularly in subtelomeric and pericentromeric regions, large and frequent polymorphisms have been reported (Eichler et al. 1996; Ritchie et al. 1998; Samonte et al. 1998; Trask et al. 1998; Horvath et al. 2001; Riethman et al. 2005). While some of these polymorphisms are asymptomatic (Fantes et al. 2002), others are associated with genetic syndromes (Ji et al. 2000) or phenotypes such as male colorblindness (Neitz and Neitz 1995) or infertility (Vogt et al. 1996). Although real phenotypic consequences are likely to result from differences in human and chimpanzee segmental duplications (Nahon 2003; Cheng et al.

2005), it is significant that the regions of highest variation between the genomes are also sites of the highest polymorphism rates (e.g. Nusbaum et al. 2006). Newman et al. (2005) estimate that as much as 25-33% of segmental duplication differences are polymorphic in chimpanzee. Even with species-specific differences, the pericentromeric regions of humans and chimpanzees are still quite similar. Rudd et al. (2006) aligned 227 kb of human and chimpanzee pericentromeric sequence from chromosome 17 and found 98% sequence identity. Samonte and Eichler (2002) estimate that only ~5% of the human genome consists of segmental duplications.

PREVIOUS CREATIONIST RESPONSES

Since the Bible clearly teaches the special creation of human beings (Gen. 1:26-27; 2:7, 21-22), what does the similarity of humans and chimpanzees mean for creationists? Creationists have responded to these studies in a variety of ways. A very popular argument is that similarity does not necessarily indicate common ancestry but could also imply common design (e.g. Batten 1996; Thompson and Harrub 2005; DeWitt 2005). While this is true, the mere fact of similarity is only a small part of the evolutionary argument. Far more important than the mere occurrence of similarity is the kind of similarity observed. Similarity is not random. Rather, it forms a detectable pattern with some groups of species more similar than others. As an example consider a 200,000 nucleotide region from human chromosome 1 (Figure 2). When compared to the chimpanzee, the two species differ by as little as 1-2%, but when compared to the mouse, the differences are much greater. Comparison to chicken reveals even greater differences. This is exactly the expected pattern of similarity that would result if humans and chimpanzees shared a recent common ancestor and mice and chickens were more distantly related. The question is not how similarity arose but why this particular pattern of similarity arose. To say that God could have created the pattern is merely *ad hoc*. The specific similarity we observe between humans and chimpanzees is not therefore evidence merely of their common ancestry but of their close relationship.

Evolutionary biologists also appeal to specific similarities that would be predicted by evolutionary descent. Max's (1986) argument for shared errors in the human and chimpanzee genomes would be an

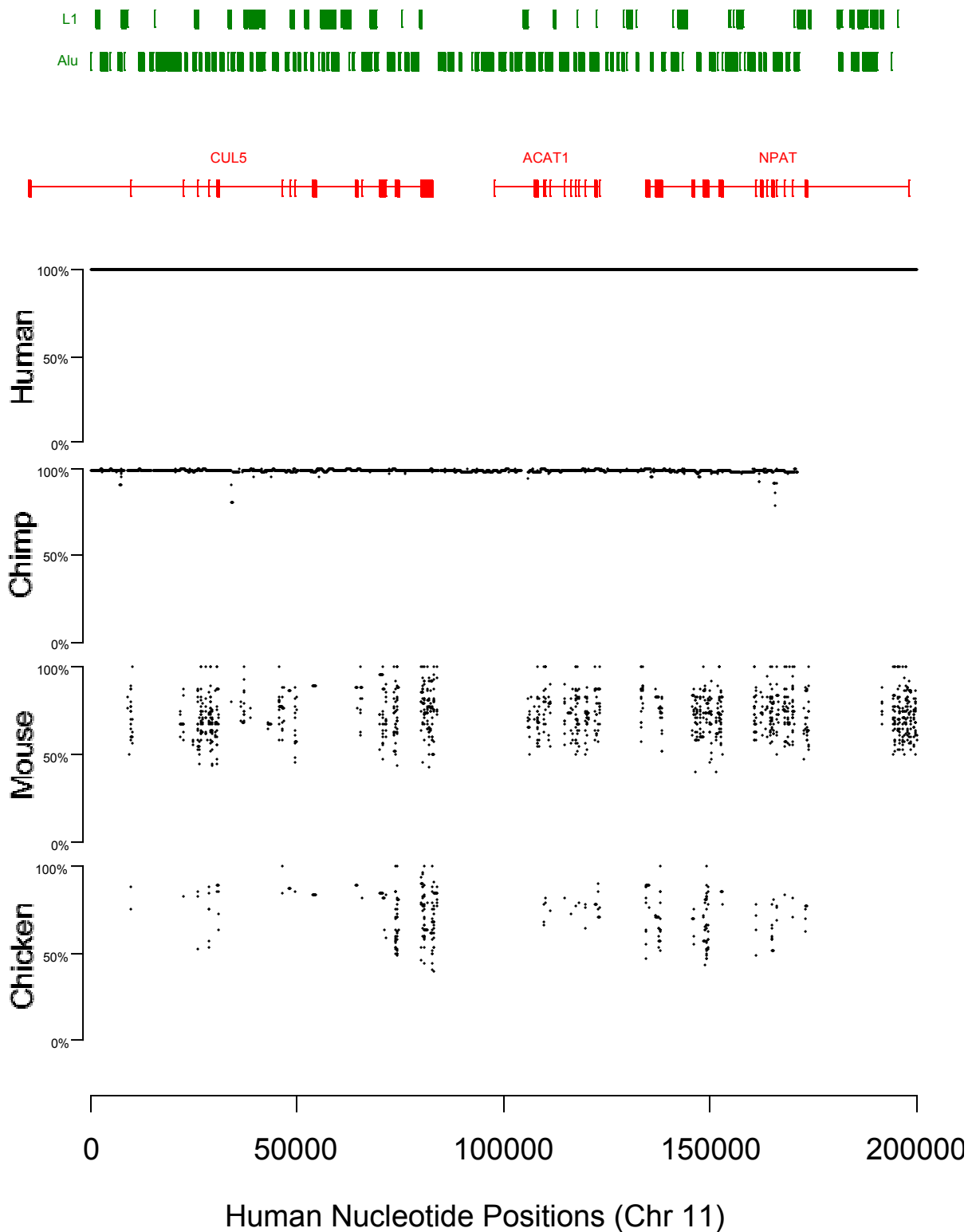


Figure 2. Similarity of a Region of the Human, Chimpanzee, Mouse, and Chicken Genomes. A region of the human genome (chromosome 11, nucleotides 107,400,000-107,600,000) was identified using the Ensembl browser (www.ensembl.org). The region contains three genes, cullen-5 (CUL5), acetyl-CoA acetyltransferase (ACAT1), and a nuclear protein (NPAT), the locations of which are shown in red. Locations of repetitive sequences were obtained from the UCSC human genome browser (genome.ucsc.edu). As a sample of repeat sequences, the locations of Alu and L1 elements are shown in green. Corresponding regions in the chimpanzee, mouse, and chicken genomes were identified using the Ensembl browser and aligned using PipMaker (Schwartz et al. 2000). PipMaker results were filtered to include nonrepetitive regions only. Graphed here are the percent identity of genomic alignments vs. the location of the aligned region in the human genome.

example of a specific similarity expected if evolution were true. This argument could be significantly amplified from recent findings of genomic studies. For example, Gilad et al. (2003) surveyed 50 olfactory receptor genes in humans and apes. They found that the open reading frame of 33 of the human genes were interrupted by nonsense codons or deletions, rendering them pseudogenes. Sixteen of these human pseudogenes were also pseudogenes in chimpanzee, and they all shared the exact same substitution or deletion as the human sequence. Eleven of the human pseudogenes were shared by chimpanzee, gorilla, and human and had the exact same substitution or deletion. While common design could be a reasonable first step to explain similarity of functional genes, it is difficult to explain why pseudogenes with the exact same substitutions or deletions would be shared between species that did not share a common ancestor.

Creationists have addressed these more specific arguments in a variety of ways. Batten (1996) makes three arguments: (1) similarity is necessary to reveal a single Creator, since dissimilarity implies multiple creators (also in ReMine 1993, p. 23), (2) biochemical similarity is functionally necessary in order for humans (and other organisms) to obtain food (also in Wise 1992), (3) the anatomical similarity of humans and chimpanzees should imply a molecular similarity as well (also in Wise 1992; Rana 2001; Wieland 2002). The first two arguments are good reasons to create some degree of biological or biochemical similarity but they do not explain degrees of similarity. If there were no nonhuman primates, humans would still be recognizably mammalian and therefore revealed as part of the design of a single Creator, but humans would also stand out as special mammals not closely similar to any other particular group of mammals. The necessity for a common biochemistry for nutrient cycles does not explain why chimpanzees exist. They neither form a major source of dietary nutrients for most humans nor share a significant fraction of the diet of most humans. Further, common biochemistry would not explain shared pseudogenes. The third argument merely shifts the problem to the anatomical level. The question remains as to why God created an animal that is so similar to humans.

More recently, creationists have begun to argue that the similarity between chimpanzees and humans is less – sometimes much less – than claimed

by evolutionary biologists (DeWitt 2003, 2005; Criswell 2005; Thompson and Harrub 2005). These arguments are inspired in part by a study by Britten (2002) that concluded that the overall similarity of human and chimpanzee genomes is ~95%. Britten arrived at this greater dissimilarity by including in his calculations not only nucleotide mismatches but also alignment gaps. Creationists also tend to emphasize other important differences between the human and chimpanzee genomes, including the differing chromosome numbers (DeWitt 2003, 2005) and the differences in gene expression in the humans and chimpanzees (Rana 2001).

Differences are certainly important, and there are many differences between the human and chimpanzee genomes, as detailed above. However, emphasizing these differences does not resolve the problem of similarity. Even if the chimpanzee genome were more than 5% or 10% different from the human genome, the differences are still vastly outnumbered by the similarities (at least 9 to 1). The major pattern that requires explanation is the surprising degree of genomic similarity, as King and Wilson (1975) noted thirty years ago. Listing differences between the genomes does not alter the overall pattern. If anything, the differences are more striking because of the overwhelming similarity.

A specific critique of human/chimpanzee similarity was made by Criswell (2005). Criswell analyzed an unspecified sample of chimpanzee sequences and predicted that the similarity to the human genome could be less than 90%. Since I have not seen his analysis, I can only comment that such a finding would contradict the majority of research on the subject (e.g. King and Wilson 1975; Hacia 2001; Britten 2002; International Chimpanzee Chromosome 22 Consortium 2004; Nielsen et al. 2005) and especially the reported similarity of the completed draft sequence (Chimpanzee Sequencing and Analysis Consortium 2005) (see also Table 1). All such studies indicate that the nucleotide mismatches are ~1.2-1.4% and the gaps constitute ~3-4%, making a total difference ~5%. Even heterochromatic regions, such as the pericentromeric region of chromosome 17 (Rudd et al. 2006) or the alpha satellite repeats on chromosomes 16, 17, and X (Table 2), are greater than 90% identical. Other heterochromatic regions can dip to less than 80% identical (Table 2), but these will have to be quantified

before an overall level of similarity can be calculated. The weight of the evidence still favors a >90% identity between the human and chimpanzee genomes.

Based on a 10% dissimilarity between the human and chimpanzee genomes, Criswell argued that humans and chimpanzees could not have evolved from a common ancestor. Criswell reasoned that if evolution were true, a 10% difference would mean that 300 million *mutations* had been fixed in the human and chimpanzee genomes, or roughly 150 million mutations in each species. Assuming that the human/chimpanzee last common ancestor lived 5 million years ago (Ma), he calculated that an average of 600 “beneficial mutations” must have been fixed in each generation. He concluded that Haldane’s dilemma prohibits such a large number of mutations fixed by selection.

Even conceding his assertion of <90% identity between human and chimpanzee genomes, his argument suffers from some errors. First, he assumed the 10% difference would result from 300 million *mutations*. Since he included alignment gaps in his 10% difference figure, only the number of gaps should be counted rather than the total nucleotides. An insertion or deletion of 1000 nucleotides is only one mutational event, even though the total difference is 1000 nucleotides. The published figures for nucleotide mismatches and gaps are ~35 million and ~10 million respectively (Chimpanzee Sequencing and Analysis Consortium 2005). Second, Criswell claimed that all the differences were fixed, but as I have shown above, many of the differences represent intraspecific variation and cannot therefore be counted as true species differences. The Chimpanzee Sequencing and Analysis Consortium (2005) estimated a polymorphism frequency among the nucleotide mismatches of 14-22%, implying an actual fixed difference as low as 1.06%. Similarly, Newman et al. (2005) estimate that 25-33% of segmental duplications are polymorphic in chimpanzee. Third, by invoking Haldane’s dilemma, Criswell assumed that all differences were fixed by selection (i.e. “beneficial mutations”). Since even segmental duplications can occur without a corresponding phenotype, many – if not most – of the differences between humans and chimpanzees are neutral differences. Neutral mutations can be fixed by genetic drift, a completely random process that can occur very rapidly in small populations. The

neutrality of most differences in the human and chimpanzee genomes is confirmed by various attempts by evolutionary biologists to identify specific evidence of selection in human and chimpanzee genes (e.g. Clark et al. 2003; Nielsen et al. 2005; Chimpanzee Sequencing and Analysis Consortium 2005).

AN ALTERNATIVE CREATIONIST RESPONSE

Having found most popular arguments about the human/chimpanzee genome similarity insufficient, I find myself in the unenviable position of devising my own explanation. Since I have none, I will attempt instead to develop some principles that could guide research into this problem. These principles all spring from the importance of context. The similarity of the human and chimpanzee genomes should not be considered in isolation from other, more general issues in creationism. For example, a good theory of biological similarity should help us to understand why any animal is similar to humans. Likewise, a good conception of the role of the genome will aid our understanding of how and why genomes can be similar or different. Finally, a better understanding of baraminology will enrich and be enriched by studies of genomic similarity. Ignoring these more general issues will only lead to frustration and failure when dealing with specific problems of biological similarity.

Biological Similarity. The problem of biological similarity may be the most important issue in creation biology. Prior to Darwin, biological similarity was interpreted as evidence of the unity of design, as in Owen’s archetypes. It is in this context that perhaps the most satisfying explanation of extremely high human/chimpanzee similarity is found: Tyson’s. Tyson’s conception of the continuous Chain of Being necessitated a uniform morphological gradient from animal to human, and thereby necessitated the creation and persistence of extremely anthropomorphic animals. Since Tyson’s time, however, the linear arrangement of organismal form has been rejected, largely in favor of a unique nested hierarchy, as advocated most famously by Linnaeus and Cuvier. Although the Chain of Being might explain why some organisms should be so much more similar to humans than others, it does not explain the particular pattern of similarity that actually exists. For example, baraminology research is revealing a discontinuous arrangement of organismal form (e.g. Wood 2005). Also, there does appear to be a non-

linear, quasi-hierarchical pattern to similarities among living things (e.g. Kunin et al. 2005). As appealing as it is superficially, Tyson's explanation is unsatisfactory.

When Darwin began developing his theory of common descent, the unique, nested hierarchy of organismal form was a key piece in Darwin's argument. In his Essay of 1844, Darwin wrote,

I must here premise that, according to the view ordinarily received, the myriads of organisms, which have during past and present times peopled this world, have been created by so many distinct acts of creation. It is impossible to reason concerning the will of the Creator, and therefore, according to this view, we can see no cause why or why not the individual organism should have been created on any fixed scheme. That all organisms of this world have been produced on a scheme is certain from their general affinities; and if this scheme can be shown to be the same with that which would result from allied organic beings descending from common stocks, it becomes highly improbable that they have been separately created by individual acts of the will of a Creator (Barrett and Freeman 1987, p. 101).

Though Darwin's argument is logically flawed, this quote exemplifies his argument very well. The first flaw is the theological assumption that the Creator's will is unknowable. Since God reveals His will to us through the various forms of revelation, it is possible to know and understand His will (although knowledge of His will is not unlimited and does not mean we will necessarily discover the answers to all of our questions). The second flaw is the conclusion: If the scheme can be shown to be the same as resulting from common descent, it does not necessarily diminish the probability that God created it that way (since we don't know why God created similarities). Instead, Darwin should have concluded that it becomes probable that common descent produced the scheme, assuming that no other explanation can be found - either natural or as determined from divine will.

As mentioned already, the common creationist response to this argument is to appeal to a designer as the source of the similarity. Although this is undoubtedly true, it is trivial. The point Darwin makes is not that similarity alone indicates common ancestry but that the particular pattern or scheme of similarities across all organisms is the same pattern we would

expect from common descent. As Darwin noted in the quote above, appealing to the will of the Creator does not explain the particular pattern of similarity that we observe, except in an *ad hoc* fashion. Creation biology needs an explanation of the pattern of similarities, not merely an *ad hoc* appeal to a common designer.

If most of the creationist responses are inadequate, what prospects for an adequate answer exist? ReMine's message theory (1993) is the only recent attempt to explain the pattern of organismal similarity. According to ReMine, organisms were designed to convey a clear message that life was designed by a single designer. ReMine argued that the pattern of similarities serves the message (in part) by revealing a single designer. Completely unique organisms might be mistaken for the products of multiple designers. ReMine claimed that the unique, nested hierarchy is singularly suited to conveying this message because of its noise resistance properties. Most humans cannot observe all organisms and therefore cannot see the entire pattern of similarity. The absence of parts of the message (organisms) due to our limited view can be understood as "noise." As a result of noise, a pattern needs to be clear even if only a few organisms are known. Since a nested hierarchy is apparent even with only a handful of organisms, it is noise resistant.

A complete discussion of ReMine's argument is beyond the scope of this paper, but there are problems with his proposal. A significant difficulty is the evidence against the unique nested hierarchy revealed by comparative genomics (e.g. Brown and Doolittle 1997; Nelson et al. 1999; Doolittle 1999, 2000; Kunin et al. 2005). This evidence has been interpreted as rampant lateral gene transfer. Similarly, Wise (1998) argued theologically that the God of the Bible creates non-nested, non-unique hierarchies. Thus, both evolutionists and creationists are abandoning the unique, nested hierarchy, and in the case of evolution, researchers are modifying their depiction of the dominant evolutionary mechanism (lateral gene transfer vs. mutation and vertical inheritance). In addition, ReMine's argument for the unique, nested hierarchy also suffers from the nonspecificity that other creationist arguments do. ReMine's argument does not explain why there should be one hierarchy of organismal similarities over another. More specifically, ReMine's proposal does not explain animals that are very similar to humans.

Despite these shortcomings, it is possible that ReMine's message theory could be modified to explain biological similarity. Although ReMine (1993, p. 368) claimed that his message theory would be invalidated if the unique, nested hierarchy of organisms was falsified, other interpretations of the biotic message could be consistent with non-nested or non-hierarchical patterns. For example, a network pattern of similarity can also serve as a message because a network pattern has the attributes of language. In written language, a very limited number of letters can be rearranged to form a great number of words, which in turn can be rearranged (following rules of grammar and syntax) to express a virtually unlimited number of ideas. If organisms and their genomes are conveying a message (or messages) from the Creator, we should expect a high degree of repetition, both within and between genomes, because of the nature of language. It is therefore intriguing that the human and chimpanzee genomes contain a high fraction of repetitive DNA and that some of the more significant differences between the genomes are in their repetitive DNA (segmental duplication and transposable element) content. If correct, this line of reasoning would imply that a proper understanding of the similarity of humans and primates would depend on detecting rules of "syntax" and "grammar" in the biotic message and applying them.

Furthermore, a network pattern of similarity resulting from transposition could serve a non-naturalistic function since a network pattern is not expected from tree-like inheritance. ReMine (1993, pp. 342-343) argued that evolution "does not predict a nested hierarchy," but that is only true if evolution is understood in the broadest possible way to include many different (and potentially contradictory) theories. Specific theories of evolution (like Darwin's) do predict nested hierarchies. Other theories (e.g. Woese 1998) could be constructed to accommodate widespread transposition, but these arguments are not arguments for common *descent*. As a result, a network pattern of similarity resist simple explanation by naturalistic theories (although complicated theories of transposition might explain it), thus reinforcing its origin by design. The potential for a network pattern to resist noise is a more complicated issue and will be dealt with in a forthcoming paper.

What is a Genome? This might seem like a trivial

and self-evident question, but its simplicity hides a deep challenge (Wood 2001). The Bible teaches that God created adult organisms and presumably even complete ecosystems by covering the land with plants. Thus, the Bible favors a holistic perspective of organisms. Modern molecular biology has favored the opposite perspective: that life is the complicated interaction of molecules and that DNA is the "code of life." If the molecular viewpoint is correct, then the differences between organisms that really matter are indeed the differences in the DNA. If a holistic perspective is correct, then perhaps differences in the DNA are not paramount to understanding organismal differences.

Complicating this reasoning is the fact that differences in DNA do indeed cause differences at the organismal level. There is a definite relationship between phenotype and genotype, even though the relationship is not as simple as Mendel might have imagined it. We could understand the genome as a repository of some of the information necessary for the physical composition of the organism (Wood 2001). In that case, far more important than the genome may be its cellular context, which interprets and applies the information stored in the genome. Since some of the cellular context is coded by the genome, we have something of a chicken/egg problem, which can only be resolved by a creation event.

The similarity of the human and chimpanzee genomes offers evidence that the genome could primarily be a repository. If the fixed nucleotide mismatches between the chimpanzee and human genomes are 1.06%, then the original nucleotide identity could be as high as 99%. At that high level of similarity, perhaps it is not impossible to believe that God created humans and chimpanzees with *identical* genomes. The known differences between human and chimpanzee biochemistry (see Varki 2000; Varki and Atheide 2005) may well rule this out, but it is an intriguing possibility. Even at 99% identity, however, the biological and behavioral differences between chimpanzees and humans indicate that the source of these differences is not likely to be found entirely in the genome sequences. Theologically, the high similarity of humans and chimpanzees reinforces our spiritual – not physical (Ecc. 3:18-21) – distinctiveness from the animals. It is the image of God that makes us human not some intrinsically valuable genetic element.

Baraminology. I have previously argued (e.g. Wood 2002a) that sequence information is not useful for distinguishing baramins. I based my claim on the holistic perspective implied by the creation account and Adam's naming of the animals. Similarity of DNA sequences overwhelm differences that are readily apparent at the morphological level, causing organisms that appear to be discontinuous to appear superficially continuous (Wood 2002a). Robinson and Cavanaugh's (1998a) use of mitochondrial DNA and protein sequences also produced poor results, with known discontinuity between humans and apes undetectable with such molecular data.

The similarity between the human and chimpanzee genomes reinforces these earlier findings, but especially when we consider the molecular diversity of other baramins. For example, Robinson and Cavanaugh (1998b) concluded that all extant felids belong to the same baramin and presumably descended from a single pair of cats on the Ark, but Slattery and O'Brien (1998) found distances >5% among felid Zfy genes and >3% among felid Zfx genes. Certainly if felid sequences can vary by that amount, what is to preclude the conclusion that the much lower differences observed between human and chimpanzees genomes indicates their cobaraminic status?

Using a genomic argument, I previously proposed that *Mycoplasma genitalium* and *Mycoplasma pneumoniae* share a common ancestor, because both bacteria shared almost all of their genes, and the genes unique to *M. pneumoniae* could be explained by a chromosomal deletion in *M. genitalium*. As with the genetic diversity of cats, what is to preclude application of this same argument to chimpanzees and humans with the conclusion that we share a common ancestor with an animal?

To put this question another way, how can we maintain that felids or mycoplasmas share a common ancestor with their genomic differences, and deny that the smaller differences between humans and chimpanzees could not also arise from a common ancestor? The only way to do this is to favor other data in baraminology, and to deny the primacy of the genome in determining true phylogenetic or baraminic relationships. The alternative would be to scrap baraminology and revert to a position very close to species fixity.

What can molecular sequence analysis do for

baraminology, if not identify baramins? I have argued elsewhere (Wood 2002b, 2003) that genomic differences within baramins can aid in understanding the process of intrabaraminic diversification. When the genomes of cobaraminic species are compared, chromosomal transpositions and rearrangements are frequently evident, as are differences in transposable elements. I proposed a process called genomic modularity wherein rearrangements of the genome induce phenotypic differences that lead to rapid speciation (Wood 2003).

Even though chimpanzees and humans belong to different baramins, the chimpanzee genome reinforces the foundational assumption of genomic modularity: that the arrangement of genes influences their expression. When comparing the chimpanzee and human genomes, we find a near identity of gene sequences but important differences in transpositional features (including differences in chromosome number, chromosomal inversions, and transposable element content). As noted above, this implies that the important biological differences are not so much in the genes themselves but in how the genes are expressed, which may be related to the substantive differences between the genetic context that arise from transposable or repetitive elements. Thus, if morphological differences exist between two species of a baramin, it is reasonable to assume that at least part of the basis of those differences lies in the transpositional differences between the two genomes.

Since the chimpanzee comes from a different baramin than humans, the chimpanzee genome also calls for further investigation of genomic modularity. Because many differences between the human and chimpanzee genomes may have been created rather than arising during post-creation history, we are left with the challenge of distinguishing created differences from differences that arose during the history of the two baramins. This problem is further compounded when dealing with the more variant genomes found within animal and plant baramins: How can we recognize genomic differences that were created and those that developed since creation? The development of good creationist theories of similarity and/or intrabaraminic change would be a good start. A theory of similarity could specify which features of organisms are part of the overall message of the scheme of organismal similarity (and were therefore part of the original

creation), and a theory of intrabaraminic change could reveal which features can vary in known ways.

THE FUTURE OF CREATIONIST GENOMICS

The genome revolution, exciting though it is, is not an obvious victory for creationism. Although more data allows for better testing of ideas, the data that we have present significant challenges to creationist theory, particularly in the realm of biological similarity. I am confident that a solution to most of the problems in this article will be forthcoming. How quickly these issues are resolved, however, will depend entirely on our research priorities and how we choose to pursue those priorities. If we wish to be good stewards of our very limited resources, we should avoid projects that are unlikely to be productive (e.g. overemphasizing potentially insignificant differences or trivializing the striking similarities) and focus instead on one of the most pressing problems in biology, biological similarity.

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