Is the human genome nearly identical to chimpanzee?—a reassessment of the literature

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A review of the available literature related to the common claim that few genetic differences exist between chimpanzees and humans was undertaken. While taking the published information at face value, we show that significant reported differences exist in regards to, not only genomic sequence, but gene regulation, regulatory genomic regions, microRNA code, and gene splicing. We conclude that multiple facets of differences in DNA sequences and genetic mechanisms as reported in the standard scientific literature, suggest that clear unbridgeable genetic differences exist between humans and chimpanzees.

Apopular claim is that the genomes of chimpanzees, or chimps (*Pan troglodytes*), and humans (*Homo sapiens*) are nearly identical, with some authors even suggesting that the two species should be placed in the same genus. As we will show, this paradigm is based primarily on cherry-picked highly homologous DNA and protein sequences. However, there is considerably more reported data in the literature that needs to be included when comparing the genomes of humans and chimpanzees.

The first 99% similarity claim, which Cohen calls 'The Myth of 1%', was first put forward in 1975 by Allen Wilson and Mary-Claire King using a technology called reassociation kinetics. Other reassociation studies reported average single-copy DNA similarities of about 98.5%. ²⁻⁴ In our companion paper (in this issue) we explain reassociation kinetics technology and its various caveats in more detail. It is sufficient to note here that in such studies a majority of the genomic DNA was excluded. Nevertheless, the supposed high similarities that were reported were actually a surprise to many scientists given the large differences in anatomy and behavioural traits between chimps and humans. The eventual explanation for this data was that small genetic differences between the two species result in very large physical differences. ⁶

The era of DNA sequencing—the legend grows

Today, DNA sequencing technologies have improved and have become considerably more proficient and automated. As a result, DNA similarity research between humans and chimps is able to utilize actual DNA basepair information on a larger scale. As noted by Marks, it is important to understand that since only four DNA bases exist in all genomes, any two random stretches of DNA of the same length will always be about 25% identical. In other words, the starting point in human–chimp DNA comparisons is not zero, but 25%.

A number of often-cited studies have reported various DNA sequence similarities of 94% or greater between human and chimp. For example, Britten reported a 95% similarity in 780,000 aligned bases in which he included insertions and deletions (indels; figure 1). When adjusted to include the query DNA sequence that was omitted from the alignments, Britten's data indicates an overall 87% similarity (see figure 2).8 While Britten's research was one of the first papers to include indels in the DNA alignment results, it was also one of the last.

As discussed in the companion paper to this review,⁵ we document, case by case, the majority of the major DNA sequence comparison publications that report percent similarities.⁵ The key papers that report DNA sequence similarities do so using multiple levels of biological sample and/or data preselection. In most cases, the authors only report the 'best of the best' data—a form of dogmadriven bioinformatic cherry picking. For example, only the protein-coding gene sequences of preselected highly similar DNA are often used—guaranteeing high levels of similarity.⁸

Perhaps the most widely cited paper that reported the initial 5x rough draft of the chimpanzee genome assembly is the most errantly cited. As discussed in our companion paper, the overall actual DNA similarity compared to the human genome at its concurrent state of completion in 2005 indicates a genome-wide similarity of about 70%. Furthermore, more recent research has not contradicted these statistics. In fact, preliminary data from research in progress at the Institute for Creation Research currently supports most of the overall DNA similarity statistics calculated from unpopularized data related to published evolutionary research.

In retrospect, it appears that the early reports of humanchimp DNA similarity, based on reassociation kinetics, has set a '98 to 99% Gold Standard' whereby the results of subsequent DNA sequence-based research conformed accordingly, even though the buried and obfuscated data related to these reports said otherwise. Such conformity to largely unspoken academic rules is typically required to achieve success in grantsmanship, publishing, tenure, and job security in general. ¹¹

Major structural differences between genomes

Many major structural differences between the human and chimp genomes have been detected and reported in a number of papers. ^{12–17} Indeed, many large stretches of DNA sequences show no consistent pattern in multiple alignments (DNA fragment comparisons) of the genomes for human, chimpanzee, and gorilla, leading to DNA-based genealogies that are different from the assumed Darwinian phylogenies (evolutionary trees) for >25% of the primate genomes being studied. ^{18–22} Unfortunately, these large evolutionary anomalies have become obfuscated within obscure evolutionary verbiage and data smoothing techniques. As a result, these important results never make it to the public sphere of knowledge.

The many parts of the human and ape genomes that show no pattern of common ancestry comprise a phenomenon called 'Independent Lineage Sorting' or ILS. The issue of independent lineage sorting is not a new problem in the human–chimpanzee similarity controversy. Before the advent of the molecular biology revolution, usage of various anatomical trait measurements would, depending on the trait, produce different evolutionary trees.²³ The candid quote below from a fairly recent evolutionary paper states the issue very clearly.

"However, with both amount of data and number of studies increasing, the crux of the matter emerges. Regardless of the type of phylogenetically informative data chosen for analysis, the evolutionary history of humans is reconstructed differently with different sets of data."²⁴

Calculated trees that do not fit the expected Darwinian paradigm are called 'discordant'. The problem of discordant trees was not solved with the advent of molecular technologies that relied on proteins and DNA. In fact, the issue got worse. The biologist's answer to this dilemma was to simply turn the issue over to statistical mathematicians lacking a biological background who combined multiple data sets to produce the politically correct phylogenetic tree. Using select algorithms, combined with the existing methodological pattern of prescreening and preselecting for compliant data, the discordant trees were protected. There exists a sizeable number of papers in this field and a more thorough review of this topic is warranted in a future publication. Suffice it to say the key papers produce data that clearly shows extreme dissimilarity between not only human and chimpanzee, but all of the great apes.

If genome B is believed to have a common ancestor with genome A and B has in one area changed more than A it is judged to have *insertions*, and this is shown by dashes to show the additions, in this case tgcggc:

Genome A: atgccgt-----t
Genome B: atgccgttgcggct

If compared to A genome B lacks 6 base pairs, the following, called a *deletion*, would be produced:

Genome A: tggccctaaatccaat Genome B: tggccc----caat

Figure 1. Indels are of two types, insertions and deletions, based on evolutionary assumptions. In reality, all we have are differences between two sequences, and the concept of indels is an attempt to explain the differences by evolution.

If the actual data is as follows

Sequence 1: atgctgatattggc Sequence 2: atgggc

then the alignment (called the prescreaning process) would be:

Sequence 1: atgctgatattggc Sequence 2: atg-----ggc

Figure 2. BLAST (Basic Local Alignment Search Tool) performs pairwise comparisons between a biological sequence of interest (query) and a target sequence (subject), typically a database of many sequences. There are different variants of the BLAST algorithm depending on whether the sequence being tested is protein or nucleotide. For example, with default parameters for BLASTN (nucleotide version), only the alignment data for identities greater than 90% are typically returned. Furthermore, these alignments will omit many gaps in the query or subject sequence and this is why claims such as 98% similarity result when in fact huge differences exist. Indels are one problem which produces great differences in gene comparisons which are edited out by evolutionists to produce a higher similarity then in fact exists.

For example, Cheng et al. were one of the first groups that took to task the question of structural variation between human and chimp genomes. These researchers compared the numbers of repeated regions of the human and chimp genomes that showed evidence of shared and lineagespecific duplication.²⁵ The compared repeated blocks of sequence were preselected to be highly identical (>94%) and it was the level of duplication (repetition) for these blocks that was evaluated between genomes. However, for the autosomes (the non-sex chromosomes), only 66% of the total number of duplicated blocks were found in both human and chimp, 33% were duplicated in human and not in chimp, and a number of these characterized duplications contained genes. Of 177 gene sequences in these repeats, 88 were duplicated in human and not chimpanzee while 94 were duplicated in chimpanzee and not human. Since

gene copy number is a major regulator of gene expression, this was a significant finding because of it resulting in different genotypes, just as different genes result in different genotypes.

They also found that DNA sequences with a similarity higher than 97% were five times more likely to be incorrectly assembled in the chimpanzee genome. This results from using the human genome assembly as the framework or scaffold when they built the chimpanzee genome.²⁶

Orthologous proteins

It is estimated that more than 95% of the human genome consists of non-protein-coding DNA and many of the similarity studies that found a 1–2% nucleotide difference were based on protein-coding DNA of preselected homologs (similar sequences). Orthologous proteins are produced by genes in different species assumed to all have evolved from a single ancestral gene, such as the beta globin hemoglobin chain genes. Glazko et al. compared 44,000 amino acid residues of chimps and humans.²⁷ Of the 127 complete orthologous proteins examined, only 20% (25 proteins) showed identical amino acid sequences. In many of the others, the changes were small, with the greatest amount of changes in signal transduction genes. compared to enzyme, transporter, and other physiological house-keeping proteins. It is important to note that minor codon differences between two genes that produce similar proteins can, due to alternative splicing of the exons and introns and processing differences, end up producing proteins that have relatively large differences in their threedimensional shape and function. The differences that result depend on the protein's regulation and its specific amino acid differences. This factor must be considered when comparing phenotypes.

Demuth *et al.* located 1,480 human genes that did *not* have any orthologs in the chimp genome.²⁸ These genes were not accounted for in the Glazko *et al.* study. Obviously it's not only the highly similar genes that are important to study, but the genes which are present and/or absent between species, as Hughes *et al.* discovered when comparing Y-chromosome sequences.²⁹ See the discussion of Y-chromosome genes in our companion paper.⁵

This research is especially significant because it is believed that non-protein-coding DNA sequences used for regulatory functions are far more likely to account for major physical and physiological differences between species. Much non-protein-coding DNA (formerly called junk DNA) consists of a wide variety of regulatory elements for both transcription and translation, many classes of regulatory RNAs, critical regulatory pseudogene code, and various nuclear matrix determining features.³⁰

Proteins are ultimately determined by not only their specific DNA transcripts but also processing. The mRNA

(messenger RNA) processing system involves the splicing of protein-coding segments in the transcribed RNA. Splicing is the process by which introns are removed and exons (the coding regions of the genes) are joined together to generate the mature mRNA that specify the proteins to be translated. Splicing differences for a single gene can generate many protein variants and this is controlled by very complex regulatory systems. In fact, research has documented that alternative splicing differs significantly between humans and chimps.³¹ The researchers found from 6 to 8% of the alternative splicing events which they evaluated showed protein differences: a variant they considered highly significant.³¹

Gene expression differences

According to Oldham *et al.*, a major genome paradigm is now recognized for which

"... the high extent of sequence homology between human and chimpanzee proteins supports the longstanding hypothesis that many phenotypic differences between the species reflect differences in the regulation of gene expression, in addition to differences in amino acid sequences." 32

In fact, as early as 1975 King and Wilson postulated that the major differences between humans and apes were due largely to factors controlling gene expression:

"We suggest that evolutionary changes in anatomy and way of life are more often based on changes in the mechanisms controlling the expression of genes than on sequence changes in proteins. We therefore propose that regulatory mutations account for the major biological differences between humans and chimpanzees." 33

Interspecies differences in genome-wide gene expression is a complicated issue. In humans and chimps we would expect small differences in regulation between highly conserved housekeeping genes that perform similar biochemical functions across not only primates, but mammals in general. Therefore, evolutionists have focused on the major features that make humans and apes different, such as brain function and major regulation differences between genes expressed in the brain. When this important factor is evaluated, many genetic differences between humans and chimps have been found.

One of the first studies of brain gene regulation, by Cáceres *et al.*, identified 169 genes that were differentially expressed in human, chimp, and macaque cerebral cortexes. Of these genes, fully 90% were upregulated at significantly higher levels in humans than in chimps. In contrast, the house-keeping genes in the liver showed similar levels of expression.³⁴ From their abstract, the authors concluded "The human brain displays a distinctive pattern of gene expression relative to non-human primates, with

higher expression levels for many genes belonging to a wide variety of functional classes."

A somewhat similar study Uddin *et al.*, confirmed these differences and added:

"... in the ancestry of both humans and chimpanzees, but to a greater extent in humans, are the up-regulated expression profiles of aerobic energy metabolism genes and neuronal function-related genes, suggesting that increased neuronal activity required increased supplies of energy."³⁵







Figure 3. Computers, digital cameras, and VCRs are all very different electronic devices, yet each contains many similar components. The essential difference lies in how the components relate to each other as a functional integrated unit.

Khaitovich *et al.* examined gene expression differences in brain, heart, liver, kidney, and testis between human and chimp. In agreement with the aforementioned expression studies, brain expression differences were again found to be highly significant.³⁶ These researchers also picked up significant differences in expression levels for kidney, liver, and testis. Most notably, sexchromosome gene expression differences associated with Y-chromosome genes were exceptionally marked in the testis.³⁷ These results were later supported by a 2010 report that showed dramatic differences between the structure of the Y-chromosomes of humans and chimps, particularly for testis-expressed genes.¹⁶

In regard to the study of differences in regulatory sequences, Duke University scientists carried out a study of the promoter regions of certain genes in the human, chimp, and macaque genomes. These are the DNA sections that precede the gene and help regulate its expression levels. They identified 575 human gene promoters that were very different from those in chimps.³⁸ Most of the differences were involved in promoters that control nerve cell development, but some were involved in other functions, such as carbohydrate metabolism. As mentioned earlier. increased metabolism coincides with enhanced levels of brain activity. Like the actual protein-coding regions of genes (exons), promoter regions often involve a small number of nucleotides on a genome-wide basis, but small DNA differences in these regions can have an enormous effect.

As stated by Oldham et al.:

"... comparisons of gene expression between human and non-human primate brains have identified hundreds of differentially expressed genes, yet translating these lists into key functional distinctions between species has proved difficult."³⁹

An important conclusion of Oldham's research is that comparisons of genes from different animals requires the study of the set of products of a large number of genes in order to understand both the magnitude and the qualitative differences. Complicating matters in these types of analyses is the fact that a majority of genes in the genome produce multiple transcript variants.⁴⁰

However, some genes that are highly conserved across life, particularly those that share similarities in metabolic systems, can produce elements of homology in their transcriptomes. For example, all life uses ATP, ADP and many other common biochemical structures. Consequently, the manufacture and regulation of these biomolecules is expected to share much similarity, and ATP synthase is close to identical in many biological systems. The focus should, therefore, be on the sets of transcripts that show key interspecies differences in their regulation and structure.

A unique way to look at gene expression is to identify overlapping subsets of genes among module of genes that are expressed. Genes are often expressed in modules or gene sets and the overlapping subset of genes common to interrelated modules are termed network connections. One study found that 17.4% of gene network connections were specific to humans and not chimpanzees. ⁴¹ Furthermore, humans have 689 known expressed genes not possessed by chimps, and no doubt more will be discovered as research progresses.

Use of commercial gene chip technology, called microarrays, to measure expression levels of thousands of different genes in humans and chimps has found little difference in gene expression in blood and liver cells between the two species, but enormous differences in brain gene expression. The researchers found the difference to be so large that if humans and chimps once shared a common ancestor, the rate of change must have been 5.5 times faster in humans than in chimps.⁴²

By using 2-dimensional gel electrophoresis to separate human and chimp brain proteins on the basis of their size and charge, two kinds of data were gathered: qualitative, measuring the differences in protein types, and quantitative, measuring the differences in protein amounts. ⁴³ Using this technique, they found major differences between humans and chimps. A 7% qualitative difference was calculated,

but a quantitative difference over four times higher (31%) was determined, reflecting the vastly different patterns of gene expression occurring in the neuronal cells of humans versus chimps. Even though many genes are remarkably similar in the two organisms, many genes are expressed very differently in each species. ⁴⁴ Interestingly, as the gene chip technology improved, Geschwind *et al.* found distinct comparative differences in liver gene expression in addition to many differences in brain gene expression. ⁴¹

Another level of the genome often ignored when evaluating similarity is the nature of interactomes, how certain expressed gene sets interact with other expressed gene sets. A simplified example would be the functions of computers, digital cameras, and VCRs (figure 3). Although all these electronic devices are very different, each contains many similar components, including transistors, resistors, capacitors, transformers, circuit boards, and wires. The essential difference lies not in the components used, but rather in how the components relate to each other as an integrated whole. Likewise, humans and chimps share similar sets of genes but they are used and interact in different ways to form completely different creatures. Changing one connection between the system's components (genes) requires many other concurrent calculated changes to occur for the system to function.

Gene regulation, including the timing and the level of gene expression, involves both genetic and epigenetic regulation. One important genetic regulation system is the micro RNA (miRNA) system. In general, miRNAs are about 22 base-pairs long and help regulate many genes. In one study comparing humans and chimps, 447 new miRNA's were identified in humans. Furthermore, the miRNA aided in identifying 51 unique genes that were found in humans, but not in chimps, 371 that were in both, and 25 in chimps only. While this study has many limitations as detailed in part 2, it indicates miRNA differences in chimps and humans are significant.

Problems with interpreting DNA alphabet similarity

If published research statements concerning highly selective cherry-picked data are taken at face value, to conclude that human and chimpanzee DNA are 94% (or greater) similarity is still seriously misleading. The problem is that we tend to think of DNA sequence as a human-written language, in standard linear format similar to the English 26 letter alphabet. Such reasoning evaluates differences as if one would line up parallel written texts. Two books written by humans that are 98% similar are essentially the same book. Evolutionists often use this analogy, but it is completely inappropriate. The DNA four-letter alphabet code that designates twenty different amino acids by codons (triplet bases of specific sequences) considers only the small fraction of the genome that actually codes for protein.

The rest of the genome involves many other DNA code types that includes for regulatory function, nuclear matrix attachment features, nuclear arrangement and packaging, and a whole diversity of two- and three-dimensional structures. The extreme diversity of informational code in the genome also occurs, not only in multiple abstract layers of extreme informational complexity, but also in both two- and three-dimensional formats (topology-based information) that are interactive with linear-based sequence information. Many linear-based genomic codes (genomic features) also contain multiple levels of meaning and are far beyond the complexity of the human alphabet or any man-made, high-level, object-oriented computer code. 46

Did the chimp genome project settle the issue?

The sequencing consortium publications produced a shotgun draft (five-fold redundant) coverage of the chimp genome. ⁴⁷ This study actually obfuscated the DNA similarity issue by obtaining levels of 98–99% similarity due to cherry-picked data and excluding indels. Not more than 70% of the chimp DNA could be aligned to the human genome assembly (see companion paper in this issue⁵), even after making generous allowances for gaps and masking low-complexity sequences in the alignments.

The authors also hold to the common but false assumption that repetitive DNA ('junk' DNA) is irrelevant. By using techniques similar to those used in making comparisons between humans and chimps, human DNA also turns out to be, roughly, estimated to be about 35% identical to daffodil DNA, but it does not follow that we are physically 35% daffodil. ⁴⁸ Chimp and human share greater DNA similarities than either chimp or human compared to a daffodil, but putting a precise measure on the similarity is not a trivial task, and the published numbers are clearly misleading due to their beguiling appearance of simplicity, the unstated assumptions required to produce them, and the illusion of precision that they convey.

What about genome size

An example of how misleading the 94–98% numbers can be is the fact that the chimp genome has been consistently reported to be about 6–10% larger than the human genome by estimating nuclear DNA content (mass in picograms). This is a process whereby nuclei are extracted from cells in an isotonic buffer to prevent rupture and then passed through a cell cytometer sensor in serial fashion that measures the amount of DNA based on fluorescence. A known standard is used to calibrate the machine. One study reports that the chimp genome contains 3.8 billion base pairs compared to close to 3.2 billion for humans.⁴⁹ The website 'www.genomesize.com' includes a variety of estimates for up to a 10% increase in genome size for chimp compared to human.

In confirmation of these cytometry reports, the most recent 'golden-path assembly' data released by the ENSEMBL group (joint scientific project between the European Bioinformatics Institute and the Wellcome Trust Sanger Institute; www.ensembl.org) places chimpanzee at 8% larger than human. The golden path assembly estimate is the contiguous amount of assembled chimpanzee genome sequence that now represents greater than a 6.5 fold-redundant coverage. Therefore, using this comparison alone, only 92% similarity exists before sequence identity is even ascertained. Next, the level of redundant sequence data must be determined. If 1,000 copies of a highly similar repeat exist in one species and only 10 copies exist in another, one cannot claim a 99% similarity in the sequence. ⁵⁰

Paradox or logical prediction

The paradox for the evolutionist is how to understand the clearly observed major genetic differences in humans and chimps in spite of their various regions of genetic similarity. Many gross morphological and physiological similarities exist between humans and chimps, including their internal body organs. As creationists or intelligent design researchers, we would obviously expect these phenotypic similarities to be reflected in genetics. Yet, bone for bone, muscle for muscle, organ for organ, the bodies of humans and apes often differ in very subtle to very dramatic ways, depending on the feature being compared.

A recent book by BBC science writer Jeremy Taylor highlighted a variety of these critical differences.⁵¹ In addition, the genetic differences are clearly ignored, minimized, and obfuscated by the popular press and, unfortunately, by trained biologists as well.^{52–57} The companion paper describes in detail how key data is often omitted from human–chimp DNA alignments.⁵ It also shows how most data used for human–chimp similarity research is pre-screened and cherry-picked to support the most favourable evolutionary outcome.

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