The Proceedings of the International Conference on Creationism

Volume 7 Article 27

2013

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Proceedings of the Seventh International Conference on Creationism.
Pittsburgh, PA: Creation Science Fellowship

THE CHASM BETWEEN THE HUMAN AND CHIMPANZEE GENOMES: A REVIEW OF THE EVOLUTIONARY LITERATURE

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KEYWORDS: Human genome, chimpanzee genome, human-chimp DNA similarity

ABSTRACT

Data has been extracted from secular literature that is contrary to the common claim that very few genetic differences exist between chimpanzees and humans. We found that significant reported differences exist in genomic similarity and gene regulation between chimpanzees and humans. The DNA sequence differences and genetic mechanisms reported in the literature support the conclusion that significant and unbridgeable genetic differences exist between humans and chimpanzees that defy evolutionary claims of a common ancestor.

INTRODUCTION

A common claim is that the chimpanzee (*Pan troglodytes*) and human (*Homo sapiens*) genomes are about 98 to 99% similar. The roots of this paradigm are based on DNA reassociation kinetics technology popular in the 1970's in the early days of the molecular biology revolution. Reassociation kinetics uses heat and/or chemistry to separate double-stranded DNA into single strands. When the DNA is allowed to reassociate in a controlled manner, it can be fractionated by various protocols. Three types of DNA can be recovered; high-copy (highly repetitive—gene poor), low-copy (moderately repetitive—low levels of genes), and single-copy (gene-rich).

Comparative studies collect the single-copy fraction of DNA from two species that are mixed together, then disassociated and allowed to reassociate so that human and chimp DNA can recombine. The level of complementary base matching between strands can be measured indirectly by a variety of methods. These early estimates of similarity used only the single-copy fractions of human and chimp genomes while the majority of DNA in the genome was omitted.

The first 99% similarity claim was made in 1975 by Allen Wilson and Mary-Claire King using reassociation kinetics of single-copy DNA (Cohen, 2007). Other similar studies came up with an average divergence in single-copy DNA that measured about 1.5%, producing the widely quoted 98.5% DNA sequence similarity (Hoyer, *et al*., 1972, Sibley and Ahlquist 1984; Sibley, *et al*.,

1990). Although the vast majority of the human and chimp genomes were actually excluded in these studies, the estimated high similarities in the relatively small portions represented by single copy fractions surprised researchers. The eventual consensus was that the dramatic differences between human and chimp anatomy and behavior were based on the assumption that small genetic differences produced enormous physical difference (Gibbons, 1998).

These initial reports fueled the early claims by popular evolutionists such as Richard Dawkins, who stated that chimps and humans "share more than 99 percent" of their genes" (Dawkins, 1986, p. 263). This statement was mooted with the publication of the initial drafts of the human and chimp genomes, announced in 2001 and 2005, respectively.

GENOMICS RESEARCH CHALLENGES THE MYTH

A major problem with this type of selective analysis is that nearly all of the entire genome is now believed to be functional, as stated in the recent ENCODE project consortium reports (2012). The non-coding regions have been shown to provide many critical control features and nucleotide templates (Dunham, *et al*., 2012; Wells, 2011; Bergman, 2001). Biochemical functions have been determined for at least 80% of the human genome and most of the rest is also predicted to be functional (Dunham, *et al*., 2012) to at least some degree. This research is significant for chimp-human comparisons because often only protein-coding sequences were compared under the widely accepted, but now debunked assumption that 95 percent of the genome is junk.

One of the first human-chimp DNA sequence papers that appeared at the beginning of the chimpanzee genome project used DNA segments from the chimp genome that were known to be similar to human (Britten, 2002). The total length of the DNA sequence for all five chimp segments was 846,016 bases. However, only 92% of this could be aligned to human DNA, thus the final statistics reported on only 779,132. The filtered data showed a DNA similarity of 95%. However, an accurate figure that includes the entire amount of DNA sequence being compared gives a final similarity of 87%. For a more thorough review of secular studies in this area, see Tomkins and Bergman (2012).

Most DNA sequence similarity studies between human and chimp use multiple levels of data pre-selection and the researchers only report the "best of the best" data. In many cases, this has involved only the protein coding gene sequences of pre-selected highly similar DNA present in both species – virtually guaranteeing high levels of similarity.

One of the most widely cited efforts purporting to show high levels of human-chimp DNA similarity was the initial 5X rough draft of the chimpanzee genome assembly report in 2005 by the Chimpanzee Sequencing and Analysis Consortium. The researchers only reported the DNA similarity of the highly similar cherry-picked regions of the genomes and carefully avoided the

issue of overall genome similarity. Perhaps the best synopsis of the data came from geneticist Richard Buggs, who published a short news article in 2008 wherein he utilized the chimpanzee genome data to derive an accurate overall DNA similarity between humans and chimps:

> To compare the two genomes, the first thing we must do is to line up the parts of each genome that are similar. When we do this alignment, we discover that only 2400 million of the human genome's 3164.7 million 'letters' align with the chimpanzee genome – that is, 76% of the human genome.
>
> Looking closely at the chimpanzee-like 76% of the human genome, we find that to make an exact alignment, we often have to introduce artificial gaps in either the human or the chimp genome. These gaps give another 3% difference. So now we have a 73% similarity between the two genomes.
>
> In the neatly aligned sequences we now find another form of difference, where a single 'letter' is different between the human and chimp genomes. These provide another 1.23% difference between the two genomes. Thus, the percentage difference is now at around 72%.
>
> We also find places where two pieces of human genome align with only one piece of chimp genome, or two pieces of chimp genome align with one piece of human genome. This "copy number variation" causes another 2.7% difference between the two species. Therefore the total similarity of the genomes could be below 70%.
>
> This figure does not include differences in the organization of the two genomes. At present we cannot fully assess the difference in structure of the two genomes, because the human genome was used as a template (or "scaffold") when the chimpanzee draft genome was assembled.

GENOME STRUCTURAL DIFFERENCES

Several key reports have called the primate evolutionary paradigm dogma into question. Ebersberger, *et al*. (2007) used a large pool of human, chimp, orangutan, rhesus and gorilla genomic sequences in constructing phylogenies–multiple DNA alignments analyzed in an evolutionary tree format. As typical with these types of studies, the DNA sequence data was pre-selected for similarity, trimmed and filtered to achieve optimal alignments and maximum evolutionary outcome.

Despite extensive data filtering designed to produce the most favorable evolutionary alignment and trees, the results did not show a clear path of human common ancestry with any of the various apes. What emerged was a mosaic of unique human and primate DNA sequences. The

authors concluded that “For about 23% of our genome, we share no immediate genetic ancestry with our closest living relative, the chimpanzee” (Ebersberger, *et al*., 2007). They also state:

> …in two-thirds of the cases a genealogy results in which humans and chimpanzees are not each other’s closest genetic relatives. The corresponding genealogies are incongruent with the species tree. In accordance with the experimental evidences, this implies that there is no such thing as a unique evolutionary history of the human genome. *Rather, it resembles a patchwork of individual regions following their own genealogy…* (*emphasis* added)

and

> ~40% of the alignments provide no clear support for a single branching pattern.

The authors rationalized the lack of support for a consistent and clear evolutionary tree among humans and other primates by claiming the “inclusion of alignments with no clear phylogenetic signal”. This is a highly significant statement, given the fact that they used extremely high levels of data filtering and selection to favor an evolutionary outcome.

Structural differences resulting in DNA tree discrepancies between human, chimp, and other ape genomes have been reported in numerous papers (Tayler, *et al*., 2009; Cheng, 2005; Newman, 2005; Marques-Bonet, *et al*., 2009; Hobolth, 2007; Hughes, 2010). The results are always the same – stretches of DNA sequences show no consistent multiple alignment pattern (DNA fragment comparisons) leading to DNA-based genealogies that are different from the predicted Darwinian evolutionary trees (Chen, 2001; Yang, 2002; Wall, 2003; Patterson, 2006; Hobolth, 2007). These extreme evolutionary anomalies are typically obfuscated by obscure technical verbiage and data smoothing techniques. Consequently, these important results never become common public knowledge.

The many human and ape genome sections that show no pattern of common ancestry comprise a phenomenon called ‘Incomplete Lineage Sorting’ (ILS) and is a major problem for evolutionists in human-chimpanzee DNA similarity research. Before the advent of the molecular biology revolution, depending on the trait, various anatomical trait comparisons also produced very different evolutionary trees. Ebersberger, *et al*. (2002) say that as “both amount of data and number of studies increased” the problem emerges that “Regardless of the type of phylogenetically informative data chosen for analysis, the evolutionary history of humans is reconstructed differently with different sets of data.”

Related to the ILS phenomena, Cheng, *et al*. (2005) were one of the first groups that researched the 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 lineage specific duplication. Repeated sequence blocks compared were pre-selected to be highly identical (>94%) and the level of duplication (repetition) for these blocks was evaluated

between genomes. For the autosomes (the non-sex chromosomes), only 66% of the total number of duplicated blocks were found in both humans 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. They also found that DNA sequences with a similarity higher than 97% were five times more likely to be "incorrectly" assembled in the chimp genome as a result of using the human genome assembly as the framework when building the chimpanzee genome.

GENE REGULATION DIFFERENCES

The Darwinian interpretation of the accumulating human-chimp molecular data is reflected in Oldham, *et al*., (2006), that 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.

We would expect small regulation differences between humans and chimps in housekeeping genes that perform similar biochemical functions in not only primates, but in mammals in general. Evolutionists have therefore focused on the major features that make humans and apes different, such as regulation differences between genes expressed in the brain.

One study of brain gene regulation identified 169 genes that were differentially expressed in human, chimp and macaque cerebral cortexes, and 90% were up-regulated at significantly higher levels in humans compared to chimps. In contrast, the liver house-keeping genes showed more similar levels of expression (Cáceres, 2003). 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 similar study by Uddin, *et al*. (2004) confirmed these differences, stating that "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" (see also Fu, *et al*., 2011).

Khaitovich, *et al*. (2005) examined gene expression differences in brain, heart, liver, kidney, and testis between human and chimp. They found significant differences in expression levels for kidney, liver and testis but brain expression and Y-chromosome genes differences were highly significant. These results were later supported by a study that showed dramatic differences

between the humans and chimp Y-chromosomes structure, particularly for testis-expressed genes (Hughes, *et al*., 2010).

A study of the promoter regulatory sequences of certain human, chimp and macaque genes identified 575 human gene promoters that were very different from those in chimps (Haygood, *et al*., 2007). Most of the promoter chimp-human differences control nerve cell development, but some were involved in metabolism. Increased metabolism coincides with enhanced levels of brain activity. Like protein coding regions of genes (exons), promoter regions often involve a relatively small number of nucleotides but small DNA differences in these regions can have an enormous effect. As "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" (Oldham, *et al*., 2006).

Gene comparisons between different animals requires the study of a large number of gene products to understand both the magnitude and qualitative differences. Complicating matters in these types of analyses is the fact that a majority of genes in the genome produce multiple transcript variants (Barash, 2010).

GENOME SIZE

An example of how misleading the 94-98% numbers are the fact that estimations of nuclear DNA content by mass in picograms results in a chimp genome about 6–10% larger than the human genome. This process involves extracting nuclei from cells in an isotonic buffer to prevent rupture and then passing it through a cell cytometer sensor calibrated by a known standard in serial fashion to measure DNA amount by fluorescence. One study reported that the chimp genome contains 3.8 billion base pairs compared to close 3.2 billion for humans (Pellicciari, 1982). A variety of estimates for up to a 10% increase in genome size for chimp compared to human exist (www.genomesize.com).

In confirmation of these cytometry reports, the most recent golden-path assembly data released by the joint scientific project between the European Bioinformatics Institute and the Wellcome Trust Sanger Institute 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 fold-redundant coverage. Using this comparison alone, only 92% similarity exists before sequence identity can even be ascertained. Next, the level of redundant sequence data must be determined. If 1000 copies of a highly similar repeat exist in one species and only 10 copies in another, one cannot claim a 99% sequence similarity exists (Wildman, *et al*., 2003).

THE Y-CHROMOSOME CHASM

The most dogma-damaging secular research in recent years is the Y-chromosome comparison between humans and chimps (Hughes, *et al*., 2010). This study compared human and chimp male specific regions (MSY)—a large portion of the Y-chromosome that contains most of the key genes. To accomplish this, a fair amount of re-sequencing was required because the chimp sequence in this area was fragmented and incomplete. The end result was 25,800,000 bases of highly accurate chimp Y-chromosome sequence distributed among eight contiguous segments, the longest of which was 10,100,000 bases. When compared to the human Y-chromosome "about half of the chimpanzee ampliconic sequence has no homologous, alignable counterpart in the human MSY, and vice versa" (Hughes, *et al*., 2010).

The ampliconic sequence contains ornate repeat units called palindromes that read the same forwards as backwards. Dispersed within these palindromes are gene families expressed primarily in the male testes. Over half of this sequence type failed to align between human and chimp in the Y-chromosome, and humans had over twice as many MSY total genes (60 in humans vs. 25 in chimp). There were also three complete gene families in humans not present in chimps. The authors note related to this large difference in gene content that, "Despite the elaborate structure of the chimpanzee MSY, its gene repertoire is considerably smaller and simpler than that of the human MSY" and "the chimpanzee MSY contains only two-thirds as many distinct genes or gene families as the human MSY, and only half as many protein-coding transcription units" (Hughes, *et al*., 2010).

Besides the large gene content differences between human and chimp MSY regions, the overall structural differences were enormous. The authors state that

> … the MSY sequences retained in both lineages have been extraordinarily subject to rearrangement: whole chromosome dot-plot comparison of chimpanzee and human MSYs shows marked differences in gross structure…Contrary to the decelerating decay theory, the chimpanzee and human MSYs differ markedly in sequence structure …

and

> Chimpanzee ampliconic regions are particularly massive (44% larger than in human) and architecturally ornate, with 19 palindromes (compared to eight in human) and elaborate mirroring of nucleotide sequences between the short and long arms of the chromosome, a feature not found in the human MSY…Of the 19 chimpanzee palindromes, only 7 are also found in the human MSY; the other 12 are chimpanzee-specific. Unlike the human MSY, nearly all of the chimpanzee MSY palindromes exist in multiple copies.

The large differences in both structural arrangements of unique DNA features and gene content described in the Y-chromosome study is very damaging to human-chimp DNA similarity mythos

and primate evolution. The authors note that given:

> 6 million years of separation, the difference in MSY gene content in chimpanzee and human is more comparable to the difference in autosomal gene content in chicken and human, at 310 million years of separation. (Hughes, *et al*., 2010)

The Darwinian dogma cannot account for these drastic differences between human and chimp Y-chromosomes. A large study of genetic variation in the human genome showed that the Y-chromosome was very stable and had five times less genetic variation than the autosomes (non-sex chromosomes) which in evolutionary dogma, indicates that it evolves very slowly (International SNP Map Working Group, 2001). The lack of variation in the Y-chromosome is because it has no similar homolog in the genome and undergoes very little recombination with the X-chromosome during meiosis. This low level of recombination and sequence diversity on the Y-chromosome produces a serious problem for the primate evolution model because, if common ancestor theory is true, the human and chimp Y-chromosomes should be very similar to each other.

SOME DNA SIMILARITY MAY BE DUE TO CONTAMINATION

Another problem is that some cases of high DNA sequence similarity between human and chimps may be due to contamination with human DNA. Not only is the chimpanzee genome assembly still largely based on the human genomic framework, but it is also known that the wide-spread contamination of non-human databases with human DNA is a serious problem and can be as high as 10% (Longo, *et al*., 2010). Human contamination results from the process of processing DNA fragments in a sequencing lab due to airborne human cells from coughing, sneezing and even physical contact with contaminated fingers. Apart from replication in a clean lab, contamination of human DNA in primate databases is very difficult to prevent and ascertain. The problem is compounded by the use of the human framework for chimp sequence assembly and annotation.

In addition to the possibility of lab contamination, human DNA sequence is added to the chimp genome intentionally during the process of annotation. The EMBL-EBI and the Wellcome Trust Sanger Institute bioinformatics working group openly admitted this fact on their web site (www.sanger.ac.uk):

> Owing to the small number of proteins (many of which aligned in the same location) an additional layer of gene structures was added by projection of human genes. The high-quality annotation of the human genome and the high degree of similarity between the human and chimpanzee genomes enables us to identify genes in chimpanzee by transfer of human genes to

the corresponding location in chimp.

> The protein-coding transcripts of the human gene structures are projected through the WGA [whole genome assembly] onto the chromosomes in the chimp genome. Small insertions/deletions that disrupt the reading-frame of the resultant transcripts are corrected for by inserting 'frame-shift' introns into the structure.

CONCLUSIONS

It is clear that a chasm exists between the human and chimpanzee genomes. The common claim that they are nearly identical is very questionable, based on an analysis of the methodology and data outlined in reported secular research. Reported high DNA sequence similarity estimates are based primarily on pre-selected and pre-screened biological samples and/or data. In addition, data that are too dissimilar to be conveniently aligned are typically omitted, masked and/or not reported. Furthermore, gap data from final alignments is also often discarded, further inflating final similarity estimates. This highly selective process driven by Darwinian assumptions produces the commonly touted 98% similarity figure for human-chimp DNA comparisons. Based on human chimp genome data, a more realistic analysis of the data provided in published secular reports indicates that the similarity may be as low as 70% genome-wide.

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