Ultraconserved sequences pose megaproblems for evolutionary theory

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According to Darwinian theory, in the past we had a common ancestor with baboons, further back with bananas and still further with bacteria. This dogma has spread like a 'meme', which is a contagious idea that propagates in a similar way as a virus by infecting brains, according to inventor of the word, Richard Dawkins.[1] In 2002, Roy Britten dispelled the first monkey meme that human and chimpanzee DNA sequences are 98.5% identical.[2] He showed that when indel-mutations were also taken into account, the difference suddenly became about 5%. The fact that chimpanzee genomes are about 10% larger than that of humans, a detail few people are aware of, raises the obvious question how a mere 5% difference, not to mention only 1%, could be mathematically even possible.

In 2005, the human and chimp genomes were compared. It became apparent that many protein coding genes found in humans are uniquely human and not found in chimpanzees.[3] What about most of the other DNA, which does not code for proteins, and differs between these organisms? Is there any significance to the differences, or are these biologically irrelevant?

MicroRNA

MicroRNA (miRNAs) genes, which do not code for proteins, are capturing headlines. MiRNAs are small single-stranded molecules consisting of *ca*. 22 nucleotides, and have been shown to regulate the expression of genes either by blocking translation or inducing the degradation of selected mRNA strands. Typically, each kind of miRNA regulates the expression of hundreds of different mRNA, an inconceivable challenge for natural selection. We will submit soon a series of papers which discuss the biogenesis, maturation and mode of action of miRNAs, with special emphasis on whether evolutionary mechanisms could produce such marvels. A large number of secular review articles cover current miRNA research findings.[4–6]

Using a new sequencing technique, Berezikov *et al.* examined miRNAs expressed in human and adult brains, finding 447 new versions which had not been known earlier. They reported[3] in December 2006 that about 8% of these new miRNA genes are uniquely human: *51* new sequences[7,8] were absent in the chimpanzee dataset. In addition, *25* miRNAs were found to be unique to the chimpanzee dataset, and none of these new miRNA are related to tRNAs, rRNAs or any other kinds of RNA expressed. Incidentally, there are hundreds of miRNA codes (miRNA does not appear in DNA) which appear in primate genomes but not in other taxa.[9]

This is highly significant, since each miRNA can regulate networks of dozens or hundreds of mRNAs.[10] This means that judicious mutations are needed at the location of potential targets to prevent false down-regulations and a multitude of additional trial-and-error attempts are needed to permit base-pairing with the correct mRNAs. Each of the 51 miRNA concentrations needs to be correctly regulated according to cell type. This multitude of changes must be selected for and fixed throughout the human lineage during at most 6 million years. This is a staggering endeavour, over and above all the other differences between apes and humans which evolutionary theory must explain. The details of this analysis are the subject of a paper in preparation.

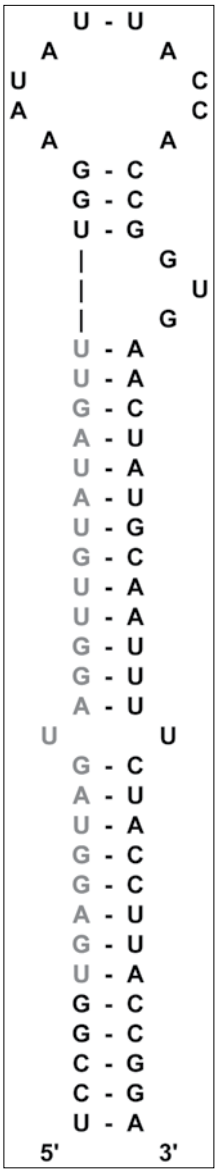

Figure 1. MiRNAs are *ca*. 22-nucleotide single strand RNA signals. A precise portion of a larger pre-miRNA strand, which contains a typical loop structure, is enzymatically extracted and used for gene regulatory purposes.

In another study[11] Chen and Rajewsky examined miRNA target sites for humans and reported[9,12] that few mutations seem to have occurred. They concluded that 85% of these target sites are likely to be functional.

Instead of a handful of differences between the human and chimpanzee genomes scientists must now confront the possibility that many among the tens of millions of differences actually have biological significance. Could random mutations plus natural selection have generated at least 51 new large precursor miRNAs from which miRNAs are spliced out, each now playing a role in controlling networks of genes, in about 6 million years? We do not believe so. This would require a vast number of mutations at precisely the right locations, even though the base pair mutation rates are only somewhere between 10^{-10} to 10^{-8} per nucleotide per generation.[13,14] Novel miRNAs can interfere with others of similar sequences.

And it is known that improper regulation of about 200 kinds of different miRNA examined lead to various forms of cancer.[15]

Producing new networks would demand a coordinated set of mutations leading to new miRNAs, and also the cognate mutations at precisely the correct locations of the mRNAs they are supposed to now regulate. The raw material consists of *random* mutations, and most of these would be incompatible with existing regulatory networks.

All these novelties would have had to occur one after the other and fixed throughout the whole human population. We consider this absurd.

We are preparing a paper to show this rigorously.

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