numbers dwindled gradually, or if the entire population was wiped out in a single post-Flood catastrophe. Rocks on the shores of Lake Victoria, Kenya have abundant fossils in soils that are 'sandwiched together' with ash-filled lava flows. This area would have been covered in deciduous trees in between these flows[26] and would have sustained great amounts of wildlife.

According to research published in the *Journal of the Geological Society* an entire population of *P. africanus* may have been killed instantly in a single volcanic explosion.[26] Much volcanic activity can be linked directly to the Flood itself (when the fountains of the great deep burst open, Genesis 7:11) and other such activity to post-Flood after shocks (Job 9:6).

The ability of volcanic rocks to give radiometric dates much older than their true age is well documented.[27] Thus a volcano may be both the cause of death for *Proconsul*, and also the source of the associated erroneous radiometric dates.

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Pseudogene function: more evidence

John Woodmorappe

According to standard evolutionary thinking, pseudogenes are simply disabled copies of genes. Arguments for shared evolutionary ancestry have been advanced based on the similarities in perceived disablements found in orthologous pseudogenes (counterpart pseudogenes in other primates).[1] However, a close examination shows that this presumed evidence is equivocal. Dissimilarities between the pseudogenes of presumably related organisms are at least as prominent as the similarities, and similarities in orthologous pseudogenes can arise independently of shared evolutionary ancestry.[2]

In addition, arguments for shared evolutionary ancestry assume that pseudogenes lack function, and so would not have been specially created with a series of shared similarities from organism to organism. This too is increasingly open to question. Pseudogenes of protein-coding genes are usually compared with their certainly-functional gene paralogs (gene copies within the same organism), and inferences are made about lack of function based on deviations in sequence that are perceived to prevent the eventual synthesis of a functional peptide. However, as elaborated elsewhere[3], the distinction between functional and nonfunctional gene copies is becoming harder and harder to draw. Pseudogenes can, at minimum, be expressed despite having such apparent lesions. Moreover, thanks to genomic recoding processes, at least some seeming disablements can be circumvented, leading to the eventual synthesis of a fully-functional peptide. In fact, more recent evidence shows that genomic recoding (in this case, the translational readthrough of premature stop codons) can, at least in yeast genes, no longer be reckoned a rare phenomenon:

'Our results demonstrate that the

presence of a stop codon in a large ORF [open reading frame] may not always correspond to a sequencing error, or a pseudogene, but can be a recoding signal in a functional gene. This emphasizes that genome annotation should take into account the fact that recoding signals could be more frequently used than previously expected.'[4]

In view of the fact that premature stop codons have traditionally been treated as one of the most obvious supposed 'gene killers', this takes on further significance.

Pseudogene function is not easily characterized

Pseudogene nonfunctionality tacitly assumes that any functional peptide synthesized should be the same or very similar to that encoded by the paralogous protein-coding gene. The actual or perceived inability of the pseudogene to direct synthesis of such a peptide is conventionally taken as proof of its 'junk' status. However, this long-held premise can no longer be sustained. It is now known that a snail's pseudogene can direct the synthesis of a useful shortened peptide. This truncated peptide can form a complex with the full-length peptide produced by the paralogous gene, thus functioning as a regulator of the abundance of this full-length protein.[5]

Nor is it correct to suppose that the pseudogene 'copy' of a protein-coding gene must necessarily be translated into *any* peptide in order to be functional. The snail's antiNOS (pseudo)gene functions as a regulator of the paralogous protein-coding nNOS gene by producing antisense RNA that forms a duplex with some of the gene's mRNA, thus regulating the latter's abundance.[6]

The recently discovered *Makorin1-p1* pseudogene,[7,8] the subject of this report, provides further evidence that the pseudogene copy of a protein-coding gene can not only function, but perform a function that is completely unrelated to protein-coding ability. Nor can RNA-only function be stereotyped. As described below, the RNA-only function of the murine *Makorin1-p1* pseudogene is completely different from the RNA-only function of the snail's antiNOS (pseudo)gene, a fact that further underlines the unpredictability of pseudogene function.

The serendipitous discovery of the functional *Makorin1-p1* pseudogene

A pseudogene can have one or more 'disabling lesions'. Examination of the murine *Makorin1-p1* pseudogene sequence indicates that it is riddled with insertions, deletions, and numerous nucleotide substitutions relative to the *Makorin1* gene.[9] The pseudogene also has an in-frame premature stop codon, and its entire 3' end is missing. If any pseudogene would, according to conventional thinking, be safely assumed to lack function, this particular one would certainly qualify.

Many discoveries in science occur by accident, and the discovery of function in the *Makorin1-p1* pseudogene certainly qualifies as one of them. The investigators, Hirotsune *et al*.,[7] were experimenting with the transfer of *Drosophila* genes into the mouse genome. They noticed that the expression of the mouse's *Makorin1* gene was altered, and eventually realized (and demonstrated by experiment) the fact that they had inadvertently disrupted the regulatory effects of the *Makorin1-p1* pseudogene upon the expression of the *Makorin1* gene.

The regulatory effect is probably caused by the enhancement of the stability of the mRNA transcribed by the *Makorin1* gene.

> *'Makorin1-p1* must function as an RNA, as it cannot code for a protein. Protection from mRNA decay of Makorin1 by *Makorin1-p1* was easily reproduced by expression constructs in several cell lines and in transgenic mice, suggesting that this type of regulation may be a general phenomenon.'[10]

Clearly, the pseudogene acts as a 'switch' that governs gene expression. There are two possible mechanisms proposed to account for this regulatory effect. Both of these mechanisms involve the pseudogene acting as a 'sponge' that absorbs a repressor substance that would otherwise flood the gene and prevent

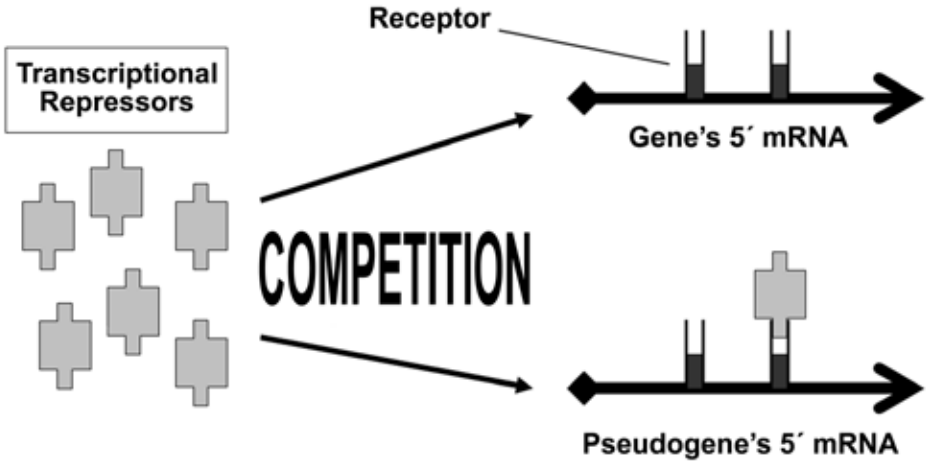

Figure 1. *One proposed mechanism by which the Makorin1 gene's expression is regulated by the* Makorin1-p1 *pseudogene. Both the gene and pseudogene contain receptor sites (or a similar recognition factor) for transcriptional repressors (RNA-binding peptides). The pseudogene competes for the freely available repressor molecules that would otherwise flood the gene's receptors and severely inhibit its expression. This frees the gene to synthesize a peptide.*

its expression (Figure 1). Unlike the case in the earlier-discussed antiNOS (pseudo)gene,[6] the respective RNA species of gene and pseudogene do not interact directly, and no antisense RNA is produced by the *Makorin1-p1* pseudogene.[9]

According to the first proposed mechanism, the repressor substance, probably an RNA-binding destabilizing protein, acts not directly on the *Makorin1* gene but upon the mRNA that is transcribed by the gene. The repressor substance acts by attaching itself to a receptor (actually, a recognition site) on the mRNA molecule, provoking the rapid degradation of the affected mRNA. Bereft of its mRNA transcript, the gene is effectively shut off, as it cannot direct the synthesis of a peptide. However, the *Makorin1-p1* pseudogene is also producing mRNA containing the recognition site, and this competes with the gene for the repressor substance (Figure 1). Relieved of the excessive burden of repressor substance attaching to it, the *Makorin1* gene's mRNA transcript is now stable long enough to be translated into a functional peptide of varying abundance.

Lee proposes a slightly different mechanism of pseudogene-gene interaction.[11] As with the first proposed mechanism, recognition is made of the fact that the pseudogene enables the gene to express itself by 'mopping up' excess transcription-binding substance. However, instead of binding to receptors on the mRNA of gene and pseudogene in a competitive manner (Figure 1), the transcription-binding substance attaches itself to receptors on the DNA sequence of gene and pseudogene. This can readily be visualized by examining Figure 1 and substituting 'Gene's 5′ DNA sequence' for 'Gene's 5′ mRNA', and substituting 'Pseudogene's 5′ DNA sequence' for 'Pseudogene's 5′ mRNA'.

Broad applicability of this discovery

By all accounts, the *Makorin1-p1* pseudogene appears to be very crippled. It is commonly supposed that a pseudogene lacks function, relative to its counterpart gene paralog, because it lacks an entire large segment of sequence. The *Makorin1-p1* pseudogene demonstrates that this is not the case. Only the first 700 nucleotides of the mRNA transcript of this pseudogene correspond approximately to the mRNA transcript of the paralogous *Makorin1* gene. Yet the fragmentary pseudogene DNA segment that is transcribed into this RNA sequence is more than sufficient for the *Makorin1-p1* pseudogene to perform its function. This pointedly warns against assuming that even a highly fragmented pseudogene inevitably lacks function.

As elaborated elsewhere,[3] there is an entire previously unsuspected 'hidden world' of RNA-only functions in the genome. The RNA-only function of the *Makorin1-p1* pseudogene opens another window to this long-hidden world:

> 'Our findings demonstrate a specific regulatory role of an expressed pseudogene, and point to the functional significance of non-coding RNAs.'[12]

The functional *Makorin1-p1* pseudogene is described as the first known instance of a biological function for any pseudogene.[13] Actually, this is not correct. The two earlier-described snail pseudogenes, antiNOS-1 and antiNOS-2, are also examples of functional pseudogenes.[5,6] Speaking more broadly, 'functional pseudogenes' is a matter of semantics. Whenever a gene sequence is reckoned to lack function, it is labeled a pseudogene. A reversal of this reckoning causes the re-labeling of this sequence as a gene. As noted earlier, there is an entire set of indisputably functional genes that contain pseudogenic features that are circumvented by recoding processes.[3] These recoded genes technically qualify as functional pseudogenes. After all, they would not function properly, if at all, was it not for the recoding processes acting upon their pseudogenic features.

It is perhaps ironic that even if the functional *Makorin1-p1* pseudogene is taken to be a unique occurrence, it nevertheless retains a broad significance that cannot be minimized:

> ' "Pseudogenes" are produced from functional genes during evolution, and are thought to be simply molecular fossils. The unexpected discovery of a biological function for one pseudogene challenges that popular belief.'[14]

It certainly does. Of course, one does not have to accept the evolutionary spin about functional pseudogenes having been 'recruited for function' by evolutionary processes. Instead, we can consider functional pseudogenes as a type of unconventionally behaving gene that, like all genes, were designed to function in their present manner since being specially created.

Conclusions

The functional *Makorin1-p1* pseudogene provides another example of a pseudogene that functions by regulating the expression of its gene paralog. The 'lesions' that ostensibly prevent the synthesis of a peptide are completely irrelevant to the fact of its function.

Of course, the foregoing discussion hardly exhausts the scope of potential pseudogene function. Pseudogenes, along with a variety of other so-called junk DNA, may have a whole set of functions related to intracellular immunobiology.[15] Note that this presents a large avenue of further research that is completely independent from that of pseudogenes as regulators of gene expression.

The variety of known or suspected pseudogene functions discovered to date suggests that pseudogenes as a whole have a wide range of previously unsuspected functions. It is hoped that the evolutionistic 'pseudogenes are dead gene copies' mindset that has dominated molecular biology for so long will be decisively abandoned. Now more than ever, the examination of pseudogenes for function should be henceforth conducted in a systematic and large-scale manner.

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Do genetic differences disprove that Neandertals and modern humans interbred?

Michael Oard

New research results from the comparison of mitochondrial DNAs (mtDNA) have shown substantial differences between Neandertals and modern humans, including the Cro-Magnons of Ice Age Europe.[1–3] (Mitochondrial DNA, which is not the same as that carried on the chromosomes (nuclear DNA), is generally inherited directly from the mother). The differences have been taken as evidence that Neandertals were a different 'species' from humans.

However, even some evolutionary scientists express caution over the new mtDNA results. Mark Stoneking, a supporter of the mitochondrial Eve hypothesis (which actually favours the idea of Neandertal non-humanity[4]), is concerned about possible DNA contamination, which can occur easily.[3] Furthermore, the number of Neandertal and Cro-Magnon specimens was quite small, and certain modern people groups were over-represented. Therefore, the results may not apply to larger populations.

Alan Cooper, an evolutionary molecular biologist at Oxford, believes there is a slim possibility that Neandertals are ancestors of modern humans and may have contributed mtDNA to modern human populations which was lost during human population bottlenecks at the end of the Ice Age.[5]

This is quite possible according to creationist biologist David DeWitt, an associate professor at Liberty University, Virginia, who has discovered that many of the mtDNA differences occur at mutational 'hotspots' unlike the differences between modern humans and chimps.[6,7] These are sectors where substantial mutational change (without much, if any, effect on the whole organism) can occur in short periods of time. Last year, Gutierrez *et al*. showed that the 'Neanderthal-Human and Human-Human pairwise distance distributions overlap more than previous studies suggest.'[8] They also said, 'The separate phylogenetic position of Neanderthals is not supported when these (other) factors are considered [i.e. the high substitution rate variation at these hot spots].'[8] This is similar to recently discovered rapid mtDNA changes in mice from the Chicago area.[9,10] Thus, these mtDNA findings do not disagree with the conclusion, from the evidence of fossil hybrids and artefacts, that Neandertals were fully human (descendants of Adam and Eve) and interbred with anatomically modern *Homo sapiens*.[11]

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