



Observations of an Owl (17)

Goodbye, Genes!

What did my sharp eyes discover last night when I silently slipped into my favourite library? A three page *Nature* news feature entitled “Of owls, larks and alarm clocks”. Wow, I thought, obviously, we owls were finally going to receive the attention we really deserve in your human life sciences (although I remained sceptical about the larks).

Of course, I immediately began reading – but my excitement rapidly turned to sharp disappointment as I commenced the second sentence. “Larks’ are people who naturally wake up early in the morning, and are the opposite of ‘owls’, who wake up and go to sleep late.”

What? You humans refer to your fellow beings with some quirky sleeping patterns as ‘owls’? My beak flipped open. And, angrily, it occurred to me that this was tantamount to owls calling our particularly clumsy feathered fellows, who almost manage to knot their wings and lose half of their feathers when simply trying to catch a mouse, ‘humans’. (Hmm... On the other hand, why not? I must tell the others chaps. It would be too good a revenge.)

Well, last night my hunger for vengeance was immediately gratified, as I began reading the next paper. A British team revealed that at least one hundred of your 20,000 human genes are apparently superfluous (*Am. J. Human Gen.* 84(2): 224-34). Hah! Screening the genomes of 1,151 individuals from all over the world they found 99 genes where, in several cases, both copies had been inactivated by point mutations (nonsense SNPs); of another 68 genes one copy had been inactivated in the same way with significant frequency. And not one of these mutations had any detectable effect on health. On average, the authors therefore concluded, an individual carries 14 homozygous and 18 heterozygous nonsense SNPs. (We know that even Craig Venter, one of your most famous genomics gurus, has 18 of those completely inactivated genes; as the authors had instantly checked in his published personal genome sequence.)

Hah, what do you say now? The number of genes that make you humans *human* is becoming smaller and smaller. Or is there anybody who is willing to bet against the prediction that in some thousand generations’ time, natural selection will have completely wiped those apparently dispensable genes out of your gene pool?

“So what,” you say? You don’t care? Okay, I admit it wasn’t really the best of efforts at a swift kick in the shins. Yes, yes, I also know that, in recent years, quite a number of studies have shown that losing genes is not half as worrying as many might first think. These days most experts have even come to agree that “use it or lose it” is actually a very strong principle in the evolution of genomes. It seems as if every gene is under constant pressure to prove it is essential to the organism to help face the current challenges of the environment. If not, the merciless molecular clock immediately starts kicking them out of function.

If you (those with teeth) chew this over for a while, this obvious drive towards the loss of useless genes might well become

quite plausible. Any gene, which has no effect on the reproductive success of a given species, can accumulate mutation after mutation without any disadvantageous effect concerning natural selection. This way, one fine day will see the gene completely inactivated in a couple of individuals. Since these, however, are still as reproductively successful as before, the inactivated version of the gene will slowly start to spread until the day it becomes fixed in the whole population. That means the active gene will have been completely replaced by its inactive version in all individuals – and a pseudogene is born. (And the pseudogene continues accumulating mutations until it is completely deleted or just disappears in the monotonous sea of random sequences so that nobody would even recognise it as a former gene).

Well, I guess that’s what has just started happening to those one hundred genes of yours inactivated by nonsense SNPs. According to the authors, the majority of them are involved in smell and nervous system functions. So prepare to say “goodbye” to them.

However, according to the authors, it will be a long “goodbye”. In one of their closing comments they state, “Our study suggests that overall, gene loss has not been a major evolutionary

force: our genome does not seem to be in a hurry to get rid of these ‘superfluous’ genes.” So, no reason to get excited. Particularly, since the authors also stated, “There is a theory that ‘less is more’ where genes are concerned and we already knew of a couple of examples of advantageous gene loss.”

These quotes, however, immediately reminded me of an earlier paper, which compared the genomes of the tuberculosis and the leprosy pathogens, *Mycobacterium tuberculosis* and *Mycobacterium leprae* and, overall, provided an astonishing example of how rapidly massive gene decay can proceed during adaptive evolution (*Nature* 409: 1007-11). To cut the story short, *Mycobacterium tuberculosis*’ 4.4 Mb genome contains about 4,000 genes and, amongst other things, codes for 1,800 soluble proteins; the 3.3 Mb genome of the leprosy bacillus, in contrast, harbours only 1,600 genes and codes for a mere 391 soluble proteins. At the same time, the authors found 1,116 inactivated pseudogenes in ‘leprae’, which had active counterparts in ‘tuberculosis’. Thus, since diverging from the last common mycobacterial ancestor, the leprosy bacillus may have lost more than 2,000 genes due to evolutionary adaptation to a new environment. Now *that* is a real case of “Goodbye”.

And what about us birds? Well, it’s a bit ... embarrassing, you know ... might as well tell you as you’ll figure it out anyway ... There was a paper last year in *Molecular Biology and Evolution* (vol. 25(12): 2681-8) entitled “Genome Size Reduction in the Chicken Has Involved Massive Loss of Ancestral Protein-Coding Genes” (It’s those wretched chickens again!)

By the way, did I forget to tell you that, personally, I am steadfastly convinced of that ‘less is more’ theory mentioned above?

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