Biogerontology (2009) 10:1–2
DOI 10.1007/s10522-008-9153-7

LETTER

Genes and the evolution of longevities

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Published online: 21 June 2008

In his article *The gene cluster hypothesis of aging and longevity* (Barja 2008), Professor Barja writes: "Aging rates seem able to change relatively rapidly during species evolution" (p. 61, 3rd sentence), and: "This could explain why longevity can vary relatively rapidly and easily during evolution in nature" (p. 65, end of first column). In neither case are any references provided, yet what he states is central to his argument. I do not think there is any strong evidence that longevity can change rapidly. One example in the literature is the claim that human longevity (100 years or more) is at least twice that of chimpanzees or gorillas (~50 years) (Cutler 1975). However, this is based on the longevity of a few zoo animals, whereas human longevity is based on many millions of cases documented by birth certificates. How long would, say, six people live in a zoo environment? I would guess 60–80 years, which is not so different from the great apes. Hominids diverged from the chimpanzee lineage 5 million years ago, which is around 250,000 generations. Barja also writes: "Closely related species can have very different lifespans" (p. 61, 2nd sentence). Again, no reference or examples are given.

The crucial question is whether you need gene clusters to explain changes in longevity. I certainly agree that to change longevity during evolution, there must be many changes in genes. In any population there will be genetic variability in the genes determining longevity, so natural selection can act on this variability either to increase or decrease lifespan. In the longer term, there will be new mutations that also have their effect. For the evolution of longevity there must be a degree of synchrony in the evolution of changes associated with aging. As Maynard Smith (1962) pointed out many years ago, it would be pointless to decrease/increase one age-associated trait, without affecting the others. They have to change together.

My second major comment is that ageing is not at all like development. Development is a strictly coordinated process leading to adulthood. Adults are maintained during their period of fecundity (25–30 years for human females). After that senescence gradually sets in. Aging is dependant on many genes, but I do not believe that it is a coordinated process like development. Also, as well as genes, stochastic events are important determinants of ageing. This is shown by the variable lifespans in a population of inbred mice, and also the fact that the longevities of human identical twins are often significantly different. As we all know, their development and adult phenotypes are identical.

My view is that ageing is the failure of the mechanisms that maintain a normal adult. I have reviewed many times the fact that at least 12 maintenance mechanisms can be identified. These

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depend on the activity of many genes. For instance, about 150 human genes are necessary for DNA repair (T. Lindahl, personal communication), and at least 1000 for the immune system (P. Hodgkin, personal communication). Detoxification also depends on a large family of genes. There is now convincing evidence that the efficiency of maintenance correlates well with longevity.

I see no reason why maintenance mechanisms should not become more or less efficient during evolution, without any gene clustering. One way efficiency could improve is by duplication of a gene important for maintenance, and then there could be divergence of the duplications. In this way two genes with related functions would replace just one. The efficiency of maintenance could be reduced simply by deletion of one or more genes. The resources saved could then be channeled into improved fecundity. Genome sequencing may reveal such changes in species with very different longevities, such as mouse and man.

A virtue of Barja's gene cluster hypothesis is that it can be tested. Identify genes coding for one or more of the features listed in his Table 2, and then look at their positions in the human genome. It should soon be possible to find out whether the clustering of genes he proposes actually exist.

References

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