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NEWS AND COMMENTARY

Ancient DNA closes on human uniqueness

The base nature of Neanderthals

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Evolutionary biology is by its nature comparative, but a key question in many studies is what should provide the comparative framework. In human evolutionary genetics, our closest living relative, the chimpanzees, have provided the closest comparison, but now there is a possibility that Neanderthals – closer to us, in evolutionary terms, by more than 4 million years – could provide a better framework.

The recent paper published in *Nature* (Green *et al*., 2006) by a group led by Svante Pääbo of the Max-Planck Institute for Evolutionary Anthropology, and a second related paper by Noonan *et al*. (2006) in *Science*, represent a major breakthrough in ancient DNA (aDNA) research. The sequences from nearly a million base pairs were extracted from a 38 000-year-old Neanderthal. This compares with the 400 odd bases of mitochondrial DNA (mtDNA) extracted in the first successful application of aDNA techniques to Neanderthals in 1997 (Krings *et al*., 1999). The technical details have been reviewed elsewhere (Lambert and Millar, 2006): there is little doubt they will come to be widely applied in archaeology and evolutionary biology more generally. The limit here will be the costs involved, which are likely, at this stage, to be prohibitive for most evolutionary and non-commercial laboratories.

Potentially, the approach and application could lead to a stage where sufficient Neanderthal genome is known to allow an identification of the genes not only to make a hominin different from an ape, but a member of *Homo sapiens* different from other species of hominin (Figure 1). We are still a long way from this, but these results do provide insights into three aspects of recent human evolution.

The first is the question of when the ancestors of modern humans and Neanderthals diverged and experienced separate evolutionary histories. The key results here are that humans and Neanderthals have an average divergence time (or time to their most recent common ancestor) for their nuclear genes that lies between 1015 and 465 kiloyears (kyr) (95% confidence levels for both papers); Noonan *et al*. provide an average of 706 kyr for this event, while Green *et al*., using a larger part of the genome, propose 516 kyr. These figures are similar to estimates mtDNA, both in these samples (461–825 kyr) and in those derived from earlier work (317–741 kyr) (Krings *et al*., 1997). The best estimate for the demographic split (i.e. the point beyond which no gene flow would have occurred) between the ancestors of modern humans and those of Neanderthals is 370 000 kyr. Depending on the comparison made, and the confidence levels used, this date may

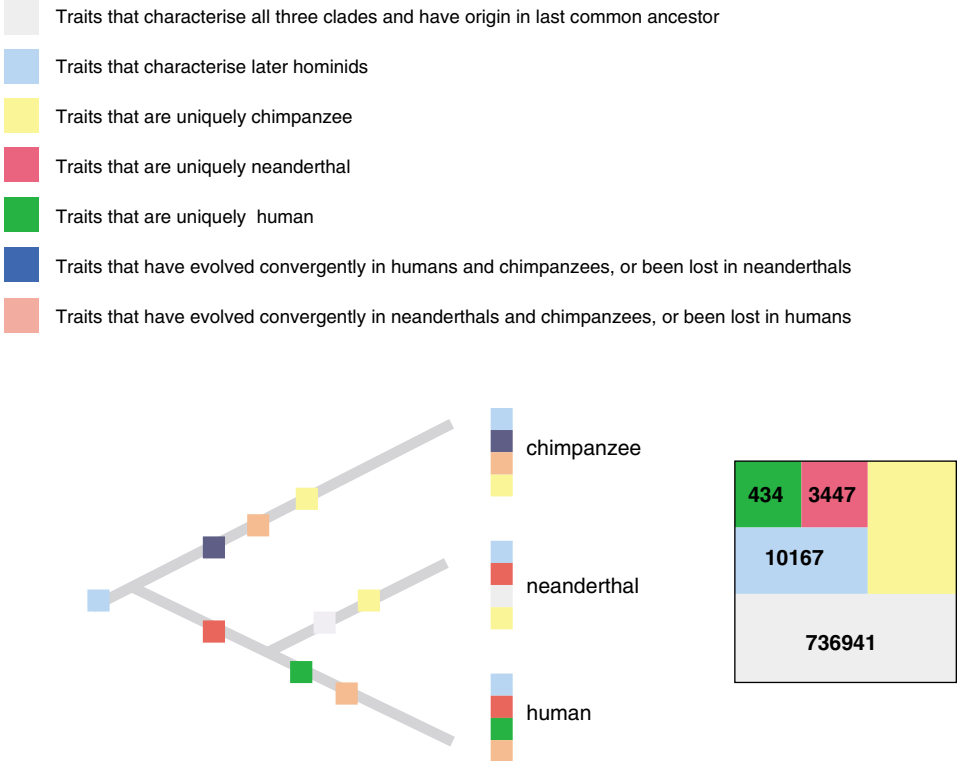

Figure 1 For a million base pairs it is possible to show which ones are shared across chimpanzees, humans, and Neanderthals (grey); which ones are derived for humans and Neanderthals but shared between them, and thus evolved in a common ancestor (light blue); and which ones are unique for either Neanderthals (red), chimpanzees (pale yellow) or humans (green). The distribution can be used phylogenetically to determine patterns of evolutionary genomics. The numbers indicate the distribution of alleles among the taxonomic groups. The number of unique Neanderthal alleles (3447) is elevated as an artefact of aDNA preservation, and the corrected value is around 430.

be as early as 670 kyr or as recent as 120 kyr.

How do these estimates compare with the fossil record? There is general consensus that modern humans and Neanderthals began a phase of independent evolution somewhere between a quarter (Foley and Lahr, 1997) and half a million years ago (Stringer and Hublin, 1999). The genetic results fall almost exactly between these two, but the range of uncertainty is such that they cannot really discriminate between them. However, they do suggest that it is possible to exclude a long-term independent evolution of Neanderthals over a period of more than half a million years, and that the most probable model will have a more recent rather than old split. However, although the archaeological record for this period is rich, there are relatively few well-dated hominin fossils, especially from Africa.

The second aspect is the effective population size of Neanderthals. Noonan *et al*. propose that the effective population size of Neanderthals was about 3000, possibly ranging up to 12 000. This confirms earlier estimates of effective population size and is close to that of the effective population size of ancestral modern humans (Harpending *et al*., 1998). These estimates contrast with those of apes, which are generally higher. If this is the case, then the tendency for hominins to have demographic processes that reduce their effective population size would appear to be ancient and not unique to modern humans. Green *et al*. propose that this may be a signature of a lineage experiencing major expansions and contractions – perhaps an example of where genetic structure reflects behavioural adaptation to a large extent.

The third aspect that both papers address is that of subsequent admixture between modern humans and Neanderthals, but here there are differences. Noonan *et al*. suggest that there is no evidence for admixture, and that according to various models, and as other studies have also suggested (Currat and Excoffier, 2004), it is extremely improbable, but cannot be entirely ruled out. On the other hand, Green *et al*. suggest that the presence of high numbers of derived (human) SNPs in the Neanderthal genome is incompatible with a simple population split model, and that there may have been gene flow between modern humans and Neanderthals. This gene flow could have been particularly from modern human males into the Neanderthal population, as the X chromosome shows a higher level of Neanderthal–modern human divergence than the other chromosomes.

While an intriguing possibility, as proposed recently on other lines of genetic evidence (Evans *et al*., 2006), there are difficulties in pursuing this. The high level of derived alleles in the Neanderthal genome – the data on which the inference about admixture is based – is high relative to the date of divergence assumed from the fossil record (400 kyr here), which in turn is tied into the evidence for a small effective population size at the base of the human–Neanderthal divergence. However, a younger divergence, as is perhaps supported by the Noonan *et al*. demographic split dates (370 kyr or less), would have the effect of making the high number of derived alleles less anomalous, and thus reducing the need to call on admixture.

Comparative hominin genomics still has a considerable way to go before we can understand the genetic basis of modern human uniqueness, but despite its enormous technical challenges, ancient DNA should provide a basis for this. And there are, of course, many other species of extinct hominin apart from Neanderthals.

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