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Human Evolution

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To better understand human evolutionary history, we employ two different approaches. The first approach is the retrieval of DNA from archaeological and paleontological remains where our group has developed technical approaches as well as criteria to produce authenticated results (for a review, see Pääbo et al., 2004). Using these techniques, we have recovery of DNA sequences from the Neanderthal type specimen (Krings et al., 1997) and other Neandertal individuals (Serre et al., 2004) and have demonstrated that they are unlikely to have contributed to any great extent to the gene pool of present-day humans. Together with the finding that humans differ from the great apes in having little genetic variation (Kaessmann et al., 2001), this suggests that modern humans originated from small African populations that colonized the rest of the World without much mixing with resident archaic humans.

The second approach our group uses to study human evolution relies the comparative analysis of genomes and gene expression in humans and the great apes. The goal is to understand how functional aspects of the human genome evolve (for a review, see Enard and Pääbo, 2004). We are particularly interested in the evolution of gene expression in the brain and genetic changes that may underlie aspects of human cognition and the human ability for articulate speech.

We have shown that whereas the genomes of humans and chimpanzees differ by a mere 1.2% (Ebersberger et al., 2002), about of 10% of genes differ significantly in expression between the two species (Enard et al., 2002a; Khaitovich et al., 2004a). We have suggested most of these gene expression differences are likely to be of little or no functional consequence and so Kimura's neutral theory of evolution can be applied to the evolution of gene expression (Khaitovich et al., 2004b). This is important because it makes it possible to identify genes that have changed their expression due to positive selection (Khaitovich et al., 2004c). Indeed, we have recently shown that both expression changes and amino acid changes have been more frequent on the human evolutionary linage than on the chimpanzee lineage among genes expressed in the brain than among gene expressed in four other tissues (Khaitovich et al., 2004d). We are currently focusing on the identification of specific genes that have been changed during recent human evolution and may have influenced traits that distinguish humans from apes.

One such candidate genes is *FOXP2*, a gene that when mutated causes severe language and speech problems in humans. We have shown that this gene has experienced two amino acid changes on the human lineage and that the pattern of polymorphisms around these amino acid changes indicates that they were the targets of strong positive selection during human evolution (Enard et al., 2002b). When we dated this selective sweep by a coalescent-based approach, we showed that it is likely to have reached fixation among humans during the last 250,000 years, *i.e.* substantially later than the divergence between anatomically modern humans and

Neandertals which occurred in the order of half a million years ago (Krings et al., 1997). This suggests that articulate language was a trait that distinguished modern humans and Neanderthals. In order to understand the physiological effects of the changes that were positively selected in *FOXP2* we currently attempt to establish an animal model in which aspects of the effects of the human-specific changes can be studied.

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