



Admixture with other hominin species may have provided genetic variation that enabled humans to successfully adapt to new environments, according to the findings of a new study. Huerta-Sánchez *et al.* show that adaptation of Tibetans to the hypoxic high-altitude Tibetan plateau might be linked to introgression of DNA from archaic Denisovan-like humans.

At >4,000 m above sea level, the Tibetan plateau is an inhospitable environment owing to low oxygen pressure, limited resources and cold climate. Tibetans have lower infant mortality and higher fertility rates in this environment than populations from lower altitudes. *EPAS1* (endothelial PAS domain-containing protein 1) is a hypoxia pathway gene that is associated with differences in haemoglobin concentration at high altitudes and that has previously been identified as having the most extreme signal of selection in Tibetans.

The researchers sequenced a region of ~129 kb surrounding the *EPAS1* gene in 40 Tibetan and 40 Han Chinese individuals to a depth of >200X. They show that a particular haplotype motif, which consists of five single-nucleotide polymorphisms (SNPs), occurs at a high frequency in Tibetans but is absent from the Han Chinese samples. To search for potential donor populations, the investigators reviewed data from the 1000 Genomes Project and another data set that includes whole-genome sequences of both extant populations and an archaic Denisovan individual. Notably, the five-SNP motif was absent in all of the populations in the 1000 Genome Project apart from two Han Chinese individuals in the data set. The team calculated the fixation index (F_{ST}), which is a measure of genetic variability between populations and ranges from zero (interbreeding freely) to one (no sharing of genetic diversity). The F_{ST} value was highly elevated in the Han Chinese and Tibetan genomes in this region compared with genome-wide values, which is suggestive of local selection. Furthermore, sequence divergence between the common Tibetan haplotype and the Denisovan individual in this region was lower ($P = 0.0028$) than expected from genome-wide comparisons between humans and Denisovans. This finding was also confirmed by statistical measures used to detect archaic introgression (D and S^*).

The authors conclude that the haplotype associated with adaptation to high altitudes in Tibetans is probably a product of introgression from Denisovans or Denisovan-related populations. Adaptation to local environments might therefore have been facilitated by genetic introgression from archaic humans that had already adapted to living in those particular environments.

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WEB SITES

Rasmus Nielsen's web site: <http://cteg.berkeley.edu/~nielsen/>

BGI's web site: <http://www.genomics.cn>