

New tools identify key evolutionary advantages from ancient hominid interbreeding

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Neanderthals. Denisovans. *Homo sapiens*. Around 50,000 years ago, these hominids not only interbred, but in some cases, modern humans may have also received a special evolutionary advantage from doing so. As more and more data from archaic genomes are becoming available, scientists have become keenly interested in pinpointing these regions to better understand the potential benefits that may have been bestowed to us.

One of the most striking recent examples is the EPAS1 gene, which confers a selective advantage in Tibetans by making them less prone to hypoxia at high altitudes. We now know that the Denisovans introduced it into the human gene pool.

Inspired by this example, in a new study published in the advanced online edition of *Molecular Biology and Evolution*, computational biologists Fernando Racimo, Davide Marnetto and Emilia Huerta-Sánchez have developed statistical tools and simulations to successfully identify the signatures of these interbred genomic regions. "Many studies had focused on the patterns of archaic introgression at the genome-wide level, and we realized that we knew very little about what to expect for a local region of the genome," said Huerta-Sánchez, who led the study. "We wanted to know whether the patterns of genetic variation observed at the EPAS1 gene could be used to identify other introgressed regions that were also beneficial for <u>modern humans</u>"



"We looked for long <u>genomic regions</u> of certain present-day human populations that looked extremely similar to the Neanderthal or Denisovan genomes, and also very different from the genomes of other present-day populations," said Racimo, the first author of the study.

Furthermore, they adapted their tools to examine the 1000 Genomes dataset and identified and expanded on the number of promising candidate genes within these regions. These mostly include genes involved in fat metabolism, pigmentation and the immune system. The authors speculate that these unique changes may have allowed archaic humans to survive in Eurasia during the Pleistocene, and may have been passed on to present-day human populations during their expansion out of Africa.

Finally, their approach is versatile enough to begin to trace back other signatures from species to provide new insights into their biology and evolutionary history and better understand how populations of organisms respond to these interbreeding events.

"We are aiming to democratize the study of adaptive introgression, so that it becomes easy to do this at a fine scale in non-human organisms as well," said Racimo.

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