Neandertal Genome Study Reveals That We Have a Little Caveman in Us

The sequence shows that Neandertals and modern humans interbred, and that their DNA persists in us

Kate Wong May 6, 2010

Credit: Frank Vinken

Researchers sequencing Neandertal DNA have concluded that between 1 and 4 percent of the DNA of people today who live outside Africa came from Neandertals, the result of interbreeding between Neandertals and early modern humans.

A team of scientists led by Svante Pääbo of the Max Planck Institute for Evolutionary Anthropology in Leipzig pieced together the first draft of the sequence—which represents about 60 percent of the entire genome—using DNA obtained from three Neandertal bones that come from Vindija cave in Croatia and are more than 38,000 years old. The researchers detail their analysis of the sequence in the May 7 *Science*.

The evidence that Neandertals contributed DNA to modern humans came as a shock to the investigators. "First I thought it was some kind of statistical fluke," Pääbo remarked during a press teleconference on May 5. "We as a consortium came into this with a very, very strong bias against gene flow," added team member David Reich of Harvard University. But when the researchers conducted additional analyses, the results all pointed to the same conclusion.

Rethinking the Gene Pool

The finding contrasts sharply with Pääbo's previous work. In 1997 he and his colleagues sequenced the first Neandertal mitochondrial DNA . Mitochondria are the cell's energy-generating organelles, and they have their own DNA, which is distinct from the much longer DNA sequence that resides in the cell's nucleus. Their analysis revealed that Neandertals had not made any contributions to modern mitochondrial DNA. Yet because mitochondrial DNA represents only a tiny fraction of an individual's genetic makeup, the possibility remained that Neandertal nuclear DNA might tell a different story. Still, additional genetic analyses have typically led researchers to conclude that *Homo sapiens* arose in Africa and replaced the archaic humans it encountered as it spread out from its birthplace without mingling with them.

But mingle they apparently did, according to the new study. When Pääbo's team looked at patterns of nuclear genome variation in present-day humans, it identified 12 genome regions where non-Africans exhibited variants that were not seen in Africans and that were thus candidates for being derived from the Neandertals, who lived not in Africa but Eurasia. Comparing those regions with the same regions in the newly assembled Neandertal sequence, the researchers found 10 matches, meaning 10 of these 12 variants in non-Africans came from Neandertals. (Where the other two segments came from remains unknown.)

Intriguingly, the researchers failed to detect a special affinity to Europeans—a link that might have been expected given that Neandertals seem to have persisted in Europe longer than anywhere else before disappearing around 28,000 years ago. Rather, the Neandertal sequence was equally close to sequences from present-day people from France, Papua New Guinea and China, even though no Neandertal specimens have turned up in the latter two parts of the world. By way of explanation, the investigators suggest that the interbreeding occurred in the Middle East between 45,000 and 80,000 years ago, before moderns fanned out to other parts of the Old World and split into different groups.

Bolstering Multiregional Theory?

Intermixing does not surprise paleoanthropologists who have long argued on the basis of fossils that archaic humans, such as the Neandertals in Eurasia and *Homo erectus* in East Asia, mated with early moderns and can be counted among our ancestors—the so-called multiregional evolution theory of modern human origins. The detection of Neandertal DNA in present-day people thus comes as welcome news to these scientists. “It is important evidence for multiregional evolution,” comments Milford H. Wolpoff of the University of Michigan, the leading proponent of the theory.

The new finding shows that “gene flow across taxonomic boundaries happens,” observes geneticist Michael F. Hammer of the University of

Arizona. Hammer is among the minority of geneticists who have espoused the idea of gene flow between archaic and modern populations. His own studies of the DNA of people living today have uncovered, for example, a stretch of DNA that seems to have come from encounters between moderns and *H. erectus*.

Some experts suspect that the estimate for the amount of Neandertal DNA people carry today could rise with further studies—if a Neandertal from the Middle East were sequenced, for instance. In addition, says paleoanthropologist John Hawks of the University of Wisconsin, the current study might be obscuring a contribution of Neandertal genes to the African gene pool, because the team specifically looked to explain genetic diversity in non-Africans compared with Africans. He and his colleagues are currently working on a way to assess that possibility.

Many researchers concur that the results disprove the strict Out of Africa replacement model of modern human origins. In a prepared statement Out of Africa theorist Christopher B. Stringer of the Natural History Museum in London said "although I have never ruled out the possibility of interbreeding, I have considered this to have been small and insignificant in the bigger picture of our evolution— for example, the results of isolated interbreeding events could easily have been lost in the intervening millennia. Now, the Neanderthal genome strongly suggests those genes were not lost, and that many of us outside of Africa have some Neanderthal inheritance." But Stringer maintains that the origin of our species is mostly an Out of Africa story.

Population geneticist Laurent Excoffier of the University of Bern in Switzerland agrees that Out of Africa is still the most plausible model of modern human origins, noting that the alleged admixture did not continue as moderns moved into Europe. “In all scenarios of speciation, there is a time during which two diverging species remain interfertile,” he explains.

Other Forebears as Well?

Pääbo, for his part, says that now that his team has shown that early modern humans interbred with one archaic group, he thinks other archaic humans might have passed along genes to us through interbreeding. Whether such contributions might have been beneficial remains unknown, however, although the Neandertal DNA in non-Africans does not seem to encode anything particularly important from a functional standpoint.

In addition to illuminating how Neandertals and moderns interacted, the Neandertal genome is helping researchers to figure out which parts of the modern human genome separate us from all other creatures. “Many traits that distinguish humans from chimps are believed to have evolved more recently than the human–Neanderthal split,” observes biostatistician Katherine S. Pollard of the Gladstone Institutes at the University of California, San Francisco. “A Neanderthal genome is a very important step towards determining the genetic basis for these characteristics that define the modern human species.”

Thus far, Pääbo’s group has identified a number of modern human genome regions containing sequence variation that is not seen in Neandertals and that may have helped modern humans adapt. Some of these regions play a role in cognitive development, sperm movement and the physiology of the skin.

But exactly how these slight changes to the modern human sequence affected the functioning of these genome regions remains to be determined. “A complete understanding of this is really a stepwise process,” team member Richard E. Green of the University of California, Santa Cruz, remarked at the press teleconference. “What we have done here is take a really important step forward. We can say exactly what changes happened recently with very high resolution.” Says Pääbo: “This is just the beginning of the exploration of human uniqueness that is now possible.”