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News

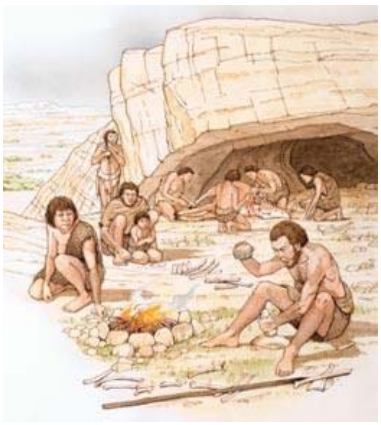
Neanderthal census reveals diversity

Sequencing method uses mitochondrial DNA to build up a picture of the species.

Lucas Laursen

Scientists have estimated that fewer than 3,500 breeding Neanderthal females lived in Europe at any one time between about 38,000 and 70,000 years ago — using a faster and potentially much cheaper method than sequencing whole genomes.

Science celebrities such as Craig Venter may have had their personal genomes sequenced, but Neanderthal remains are too fragmentary and contaminated to make sequencing their entire genomes cost-effective, according to Adrian W. Briggs, a graduate student in Svante Pääbo's evolutionary genetics lab at the Max-Planck Institute for Evolutionary Anthropology in Leipzig, Germany. Briggs and his colleagues in Spain, Croatia, Russia and elsewhere in Germany have instead pinpointed short stretches of the Neanderthal genome to study the genetic diversity of five Neanderthals from those countries.



Low variation in Neanderthal DNA suggests they lived in small, isolated communites.

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The sequencing technique, called primer extension capture, compares target sequences chosen from a reference genome — in this case a previously sequenced mitochondrial Neanderthal genome[1] — to DNA that has been extracted and amplified from a new sample, such as another Neanderthal's leg bone.

The study, which is published in *Science*[2], also puts the new method through its paces by tackling questions about Neanderthal diversity.

Close-knit species

Researchers use genetic diversity as a clock to measure how long groups of individuals have lived apart from each other. When the team compared the genetic diversity of the mitochondrial DNA (mtDNA) from six Neanderthal individuals, they found much lower diversity than they would expect compared with six similarly far-flung modern Europeans.

The difference implies that between 38,000 and 70,000 years ago, Neanderthals lived in smaller, more isolated pockets. The team estimates that around 270 to 3,500 breeding females would have lived at any one time as part of a total population that would have included their families and non-breeding Neanderthals. The team's estimate of the number of breeding females is in a similar range to a previous estimate that was based on a single Neanderthal genome[3].

But anthropologist Anna Degioanni at the University of the Mediterranean in Marseilles, France, notes that the region of mtDNA the Briggs group studied does not vary as much as other regions, such as the one her group used to identify different subgroups of Neanderthals earlier this year[4]. That may mean that the new study underestimates the genetic diversity of Neanderthals, she believes.

Both Degioanni and Briggs expect that future studies of nuclear DNA, which is more complex and contains more potential variations, will help settle the diversity question more definitively.

Palaeogenomics for the masses

Briggs, Pääbo and their colleagues are part of The Neandertal Genome Project, an international consortium that is working to sequence the entire Neanderthal genome. Together with a parallel project run by Edward Rubin at the Lawrence Berkeley National Laboratory in Berkeley, California, the teams have sequenced large sections of Neanderthal genomes over the past few years using 'shotgun' sequencing — in which DNA is broken down into small fragments, sequenced and reassembled by looking for overlaps. They have estimated when Neanderthals and humans diverged and have examined physical traits that might have been coded in Neanderthal genes, such as hair colour and the capacity for speech[5,6,7].

Shotgun sequencing remains the best way to obtain a full genome sequence. But using the method to sequence ancient samples can be difficult because they are often contaminated with foreign DNA. Briggs says: "You have to sift through an awful lot of junk before you get the sequence of interest. A typical bone we would use would have something like 99% bacterial DNA." DNA from modern humans can also contaminate samples.

Using mtDNA, copies of which are more plentiful in each cell than nuclear DNA, researchers can generate a consensus sequence based on how the different fragments of sequenced mtDNA overlap, which helps to eliminate the errors inherent in degraded, contaminated samples.

Biologist Tom Gilbert of the University of Copenhagen in Denmark agrees. "[Primer extension capture] pretty much guarantees that every nucleotide is sequenced many times, thus enabling an accurate consensus sequence to be obtained," he says. Given that Briggs and colleagues were able to use this method to study Neanderthals, Gilbert says it may prompt some researchers to return to previously studied samples in other Palaeolithic species, such as woolly mammoths.

High-profile sequencing projects require significant funds to pay for expensive full-genome sequencing. But this cheaper method of primer extension capture, together with other probe-based approaches that are under development, are "a key step to opening up palaeogenomics to the masses", Gilbert says.

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