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Using modern sequencing techniques to study ancient modern humans

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DNA that is left in the remains of long-dead plants, animals, or humans allows a direct look into the history of evolution. So far, studies of this kind on ancestral members of our own species have been hampered by scientists' inability to distinguish the ancient DNA from modern-day human DNA contamination. Now, research by Svante Pääbo from The Max-Planck Institute for Evolutionary Anthropology in Leipzig, published online on December 31st in *Current Biology* overcomes this hurdle and shows how it is possible to directly analyze DNA from a member of our own species who lived around 30,000 years ago.

DNA — the hereditary material contained in the nuclei and mitochondria of all body cells — is a hardy molecule and can persist, conditions permitting, for several tens of thousands of years. Such ancient DNA provides scientists with unique possibilities to directly glimpse into the genetic make-up of organisms that have long since vanished from the Earth. Using ancient DNA extracted from bones, the biology of extinct animals, such as mammoths, as well as of ancient humans, such as the Neanderthals, has been successfully studied in recent years.

The ancient DNA approach could not be easily applied to ancient members of our own species. This is because the ancient DNA fragments are multiplied with special molecular probes that target certain DNA sequences. These probes, however, cannot distinguish whether the DNA they recognize comes from the ancient human sample or was introduced much later, for instance by the archaeologists who handled the bones. Thus, conclusions about the genetic make-up of ancient humans of our own species were fraught with uncertainty.

Using the remains of humans that lived in Russia about 30,000 years ago, Pääbo and his colleagues now make use of the latest DNA sequencing (i.e., reading the sequence of bases that make up the DNA strands) techniques to overcome this problem. These techniques, known as "second-generation sequencing," enable the researchers to "read" directly from ancient DNA molecules, without having to use probes to multiply the DNA. Moreover, they can read from very short sequence fragments that are typical of DNA ancient remains because over time the DNA strands tend to break up. By contrast, DNA that is younger and only recently came in contact with the sample would consist of much longer fragments. This and other features, such as the chemical damage incurred by ancient as opposed to modern DNA, effectively enabled the researchers to distinguish between genuine ancient DNA molecules and modern contamination. "We can now do what I thought was impossible just a year ago - determine reliable DNA sequences from modern humans - but this is still possible only from very well-preserved specimens," says Pääbo.

The application of this technology to the remains of members of our own species that lived tens of thousands of years ago now opens a possibility to address questions about the evolution and prehistory of our own species that were not possible with previous methods, for instance whether the humans living in Europe 30,000 years ago are the direct ancestors of present-day Europeans or whether they were later replaced by immigrants that brought new technology such as farming with them.

More information: Paabo et al.: "A complete mtDNA genome of an early modern human from Kostenki, Russia." Publishing in Current Biology 20, January, 2010. www.current-biology.com

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