HUMAN EVOLUTION

Oldest *Homo sapiens* Genome Pinpoints Neandertal Input

SITGES, SPAIN—In 2008, Siberian ivory carver Nikolay Peristov was searching for ancient mammoth tusks eroding from the banks of the Irtysh River in western Siberia, when he found fossilized bones instead. Back in his workshop in Omsk, he showed the bones to local paleontologist Aleksey Bondarev, who recognized a human thighbone. Bondarev in turn showed it to an anthropologist friend, and it was passed on up the chain to some of the world's top experts in human evolution. They dated it to 45,000 years ago, making it one of the oldest known modern humans in northern Asia and Europe.

Now, the bone has opened a window on the genetics of our species at a crucial moment: soon after their arrival in northern Eurasia. At a meeting* here last week, paleogeneticist Svante Pääbo of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, announced that his team has sequenced the thighbone's entire nuclear genome to high accuracy—an astonishing 42x coverage. "This is by far the oldest sequenced genome of a modern human," he said.

The as-yet unpublished bone and genome are yielding new insight into when moderns interbred with our extinct cousins, the Neandertals. "Genetically we now have a modern human that just barely postdates the Neandertal introgression into modern humans," explains Bence Viola of the Max Planck, who was not at the meeting but has studied the bone, found near the village of Ust-Ishim.

Geneticists have sequenced the complete genomes of even older Neandertals as well as those of a third kind of Stone Age human from Denisova Cave in Siberia. But the DNA of ancient members of our own species has been elusive, partly because it is hard to rule out contamination from people who handled the bones. Now, high-resolution sequencing techniques can distinguish ancient genomes from current ones, researchers say. The next oldest genome of a *Homo sapiens*, announced last fall, comes from a boy who died 24,000 years ago near the Siberian village of Mal'ta (*Science*, 25 October 2013, p. 409).

Nearly twice as old as the Mal'ta bones, the Ust-Ishim femur shows that almost as soon as modern humans arrived in northern Eurasia, they made themselves at home in harsh climates, Viola says. "Ust-Ishim is at about the latitude of Stockholm or Juneau, Alaska," he notes. "It was not that much warmer at the time, so they must have been quite well adapted to northern environments."

In his talk, however, Pääbo zeroed in on one issue: interbreeding between Neandertals and modern humans. Scrutiny of the genomes of living people and ancient Neandertals has shown that 1% to 3% of the DNA of Europeans and Asians comes from Neandertals. But how extensive the original mixing was, and where and when it happened, have been the subject of debate.

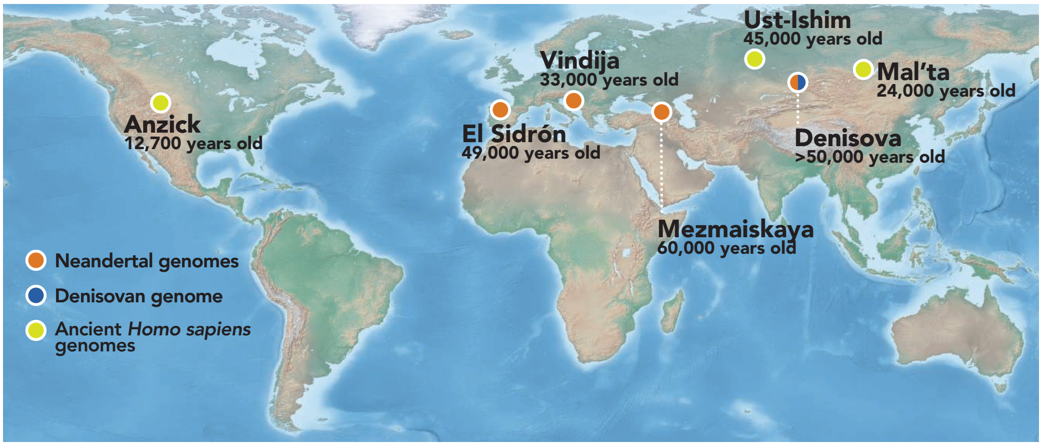
Modern humans moved from Africa into the Middle East as early as 120,000 years ago, according to fossils of archaic modern humans at Skhul and Qafzeh caves in Israel. But they apparently skirted the colder climes of Europe and northern Asia until much later, about 40,000 to 45,000 years ago. Neandertals, meanwhile, arose somewhere in Europe or Asia; they occupied the same caves as modern humans in the Middle East and Denisova, although at different times, and both groups overlapped in Europe from about 30,000 to 45,000 years ago.

Because all living people in Europe and Asia carry roughly the same amount of Neandertal DNA, Pääbo's team thought that the interbreeding probably took place in the Middle East, as moderns first made their way out of Africa. Middle Eastern Neandertal sites are close to Skhul and Qafzeh, so some researchers suspected that those populations were the ones that mingled. But the team's analysis favors a more recent rendezvous. The femur belonged to an *H. sapiens* man who had slightly more Neandertal DNA, distributed in different parts of his genome, than do living Europeans and Asians. His Neandertal DNA is also concentrated into longer chunks than in living people, Pääbo reported. That indicates that the sequences were recently introduced: With each passing generation, any new segment of DNA gets broken up into shorter chunks as chromosomes from each parent cross over and exchange DNA. Both features of the Neandertal DNA in the femur suggest that the Ust-Ishim man lived soon after the interbreeding, which Pääbo estimated at 50,000 to 60,000 years ago.

Researchers still think the Middle East is a likely place for the encounters. Other fossils in Israel, such as a 49,000-year-old Neandertal at Tabun Cave, might belong to people who were alive at the time of the unions or just after, says archaeologist Ofer Bar-Yosef of Harvard University, who was not a member of the team.

Pääbo's team is now analyzing the Siberian man's genome to see just what genes he inherited from Neandertals. They have already found one: the Neandertal form of a gene that shapes the curvature of the spine. Evolutionary geneticist Sarah Tishkoff of the University of Pennsylvania says she's eager to learn what else the genome reveals. "It's like having a time machine, to go back 45,000 years to see how the genomes of modern humans differed both from our own and also from Neandertals and Denisovans."

–ANN GIBBONS



Stone Age genomics. Researchers have complete genomes from three types of humans who coexisted during the last Ice Age: Neandertals (orange); Denisovans (blue); and *Homo sapiens* (yellow).

CREDIT: BENCE VIOLA

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Ann Gibbons

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