THE WALL STREET JOURNAL.
WSJ.com

ENVIRONMENT & SCIENCE | MAY 6, 2010

Most People Carry Neanderthal Genes

Team Finds up to 4% of Human Genome Comes From Extinct Species, the First Evidence It Mated With Homo Sapiens

By ROBERT LEE HOTZ

The burly Ice Age hunters known as Neanderthals, a long-extinct species, survive today in the genes of almost everyone outside Africa, according to an international research team who offer the first molecular evidence that early humans mated and produced children in liaisons with Neanderthals.

In a significant advance, the researchers mapped most of the Neanderthal genome—the first time that the heredity of such an ancient human species has been reliably reconstructed. The researchers, able for the first time to compare the relatively complete genetic coding of modern and prehistoric human species, found the Neanderthal legacy accounts for up to 4% of the human genome among people in much of the world today.

By comparing the Neanderthal genetic information to the modern human genome, the scientists were able to home in on hints of subtle differences between the ancient and modern DNA affecting skin, stature, fertility and brain power that may have given Homo sapiens an edge over their predecessors.

"It is tantalizing to think that the Neanderthal is not totally extinct," said geneticist Svante Pääbo at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, who pioneered the $3.8 million research project. "A bit of them lives on in us today."

The discovery is the climax of a vociferous scholarly debate over the fate of the Neanderthals, a big-brained and barrel-chested group who roamed Europe, Russia and the Middle East between 400,000 years and 30,000 years ago, overlapping in many areas with the direct ancestors of modern humankind. Their remains were the first human-like fossils ever found. For more than 150 years, most scientists have considered the species one of evolution's failed experiments, one that died out—or was killed off—when it could not compete with more advanced Homo sapiens.

Previous fossil DNA studies, based on more fragmentary genetic samples, showed no evidence that Neanderthals left any traces in the modern human genome, as the complete set of an organism's genetic inheritance is called.

The new findings arise from a technological revolution in the study of ancient biology. Researchers used high-speed, genome-sequencing machines from 454 Life Sciences and Illumina Inc., along with powerful computational statistical tools, gene-splicing enzymes and microarray analysis techniques, to resurrect the information entombed in fossil DNA.

For their analysis, Dr. Pääbo and his colleagues extracted DNA mostly from the fossil remains of three Neanderthal women who lived and died in Croatia between 38,000 and 45,000 years ago. From thimblefuls of powdered bone, the researchers pieced together about three billion base pairs of DNA, covering about two-thirds of the Neanderthal genome. The researchers checked those samples against fragments of genetic code extracted from three other Neanderthal specimens.

"It is a tour de force to get a genome's worth," said genetic database expert Ewan Birney at the European Bioinformatics Institute in Cambridge, England.

In research published Thursday in Science, the researchers compared the Neanderthal DNA to the genomes drawn from five people from around the world: a San tribesman from South Africa; a Yoruba from West Africa; a Han Chinese; a West European; and a Pacific islander from Papua, New Guinea. They also checked it against the recently published genome of bio-entrepreneur Craig Venter. Traces of Neanderthal heredity turned up in all but the two African representatives.

"We do not find any evidence of Neanderthal gene flow into Africans," said population geneticist David Reich at Harvard University Medical School, who helped analyze the Neanderthal genome. "What we find is shared equally by Europeans, East Asians and Papua, New Guineans."

From that pattern, the researchers deduced that prehistoric humans encountered their Neanderthal mates in the

Middle East as small human bands first migrated out of their African homeland. There may have just been a few encounters. "A little interbreeding would have spread those genes far and wide," said British anthropologist Chris Stringer at London's Natural History Museum.

Based on these findings, several anthropologists questioned whether Neanderthals should continue to be considered a separate species. Typically, when different species mate, they don't produce fertile offspring. "I really think when you get up to 2%-to-5% genetic overlap, it is probably not wise to think of these as a separate species," said anthropologist Fred Smith at Illinois State University who studies Neanderthals.

In the long run, the researchers hope that they can use the Neanderthal genome as a yardstick against which they can measure evolutionary changes in more modern human genes that may have contributed to the success of Homo sapiens. By comparing and contrasting the modern human genome to both the Neanderthal and even more primitive chimpanzee genetic data, researchers hope to uncover uniquely human adaptations. Already, they have drawn up a list of 212 variations that appear to have been favored during modern human evolution, compared with the Neanderthals. Those include genes involved in energy metabolism, sperm motility, the development of the rib cage, collar bone and cranium, as well as genes that appear to be involved in cognition.

"This opens the way to studying genetic differences that make humans human," said ancient DNA specialist Alan Cooper at the University of Adelaide.

The new research is buttressed by an independent, unpublished survey of modern human diversity, involving DNA markers covering 100 population groups world-wide, which also offers evidence of ancient interbreeding between Homo sapiens and earlier archaic human species.

Evolutionary anthropologist Jeff Long at the University of New Mexico in Albuquerque presented the work at a science conference last month. "We felt you had to introduce some archaic admixture to explain the diversity of modern populations," Dr. Long said.

Despite its recent advances, the field of molecular anthropology is treacherous terrain. Bones are easily sullied as they decompose. Microbes so thoroughly infiltrated the Neanderthal bones that almost 99% of the DNA the researchers found actually belonged to bacteria and had to be painstakingly excluded. They also can be easily contaminated by modern human DNA when they are excavated and handled in the laboratory.

"By touching the bone, you leave more DNA on its surface than actually is in the bone itself," said geneticist Johannes Krause at the Max Planck Institute, who worked on the Neanderthal specimens. "That is one of the biggest risks we have."

Indeed, Dr. Pääbo and his colleagues were publicly embarrassed when an earlier analysis of Neanderthal DNA turned out to be thoroughly contaminated by modern human genes from lab workers. To avoid such errors in the new study, they tagged each Neanderthal DNA strand with a unique molecular bar-code, to distinguish it biochemically from any extraneous genetic material.

"Their laboratory work is impeccable," said molecular anthropologist Todd Disotell at New York University, who studied the findings but was not involved in the project. "I am very confident their data is bon fide."

Write to Robert Lee Hotz at sciencejournal@wsj.com