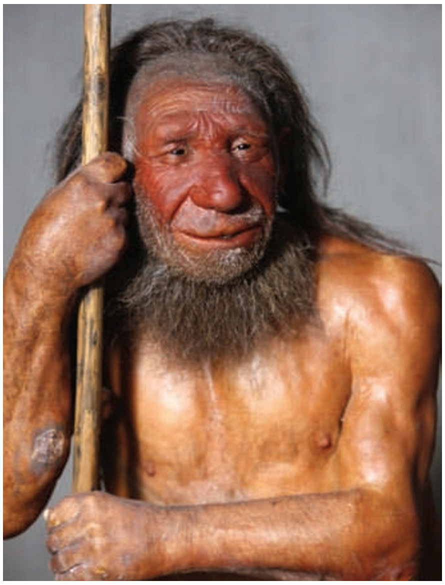
Ancient DNA set to rewrite human history

Discovery that some humans are part-Neanderthal reveals the promise of comparing genomes old and new.

The worlds of ancient and modern DNA exploration have collided in spectacular fashion in the past few months. Last week saw the publication of a long-awaited draft genome of the Neanderthal, an archaic hominin from about 40,000 years ago[1]. Just three months earlier, researchers in Denmark reported the genome of a 4,000-year-old Saqqaq Palaeo-Eskimo[2] that was plucked from the Greenland permafrost and sequenced in China using the latest technology.

As researchers compare these ancient genomes with the ever-expanding number from today's humans, they expect to gain insights into human evolution and migration — with more discoveries to come as they decipher DNA from other branches of the human evolutionary tree. "For the first time, ancient and modern genetic research is going hand in hand," says Eske Willerslev, whose team at the University of Copenhagen led the Palaeo-Eskimo sequencing project. "It is really a fantastic time."

Already, analysis of the Neanderthal genome has helped to resolve a debate about whether there was interbreeding between Neanderthals and *Homo sapiens*: genome comparisons suggest that the two groups mated an estimated 45,000–80,000 years ago in the eastern Mediterranean area. The sequencing study, from a consortium led by Svante Pääbo of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, found that the genomes of non-African *H. sapiens* today contain around 1–4% of sequence inherited from Neanderthals.



PHOTOLIBRARY

Neanderthals once bred with *Homo sapiens*.

The breakthroughs have been driven by the plummeting cost of sequencing, together with new strategies for reducing or detecting contamination by near-identical modern human DNA. These days, labs such as Pääbo's and Willerslev's might piece together a complete genome from the degraded scraps of DNA present in ancient bone, hair or teeth in as little as a month. Researchers from geneticists to fossil specialists can't wait for more.

Some hope to use ancient–modern genome comparisons to chart splits in human populations and how they might have correlated with climatic changes. "I call this molecular stratigraphy," says Jeffrey Long, a genetic anthropologist at the University of New Mexico in Albuquerque. "I then want to use this relative chronology of genetic events to compare to the palaeoclimate of Earth's biomes."

For Willerslev, ancient genomes offer the opportunity to trace prehistoric migration routes. By comparing the ancient Saqqaq genome with those of modern human populations, Willerslev and his team linked it to the present-day Chukchi people of Siberia, revealing that ancestors of this group trekked from eastern Siberia to Greenland about 5,500 years ago. "The genomes will allow us to test theories about peoples and migrations debated for a century," says Willerslev. "In the next five years, we will see a whole spectrum of discoveries." For example,

China and Taiwan strengthen academic ties

After a year of debate that on several occasions descended into fisticuffs, Taiwanese legislators this week opted for pragmatism over nationalism and put the finishing touches to amendments that will allow about 2,000 mainland Chinese students to enter Taiwan's graduate and undergraduate university programmes every year. The change, to be finalized this month, will open the door to a large and much-needed pool of young minds for Taiwan's universities as early as this autumn.

Taiwan has strong research universities but a shortage of students. Many mainlanders already head to Taiwan for postdoctoral studies, and some go as short-term graduate or undergraduate exchange students. But, thus far, Taiwanese law has barred them from graduate or undergraduate degree programmes.

Taiwan's Chinese Nationalist Party government proposed relaxing these rules more than a year ago, as part of a warming relationship that has seen increased business and transportation links with mainland China. But, fearing that both the universities and the workforce could be overrun by mainlanders, opposition party members resisted, with some resorting to grappling a speaker to the floor of the legislature last month in an attempt to block the motion. On 10 May, violence broke out again before a subcommittee finalized the amendments.

Many scientists see the plan as an opportunity to keep the island internationally competitive. "The talent and the hard-working attitude in general of the mainland students will be a boost to research," says Ben Chao, dean of the Earth sciences college at Taiwan's National Central University in Jhongli City. Kuo-Fong Ma, a seismologist at the university, says that it will also benefit science on the mainland. Taiwan has a strong record in earthquake early warning systems, for example, and educating mainland students could help to establish more research collaborations and transfer knowledge that could benefit the whole of China.

An explosion in the number of universities in Taiwan — from 40 to 175 during the past 20 years — along with a declining birth rate means that there are plenty of places available for mainlanders: about 55,000 by 2015, according to census figures. And there will be no shortage of applicants, says Cong Cao at the Levin Institute in New York, who studies China's science and technology manpower issues. He points out that students will not suffer the language problems or culture shock that study abroad could bring. "Moreover, professors at Taiwan's universities are more serious about advising students," Cao argues.

But the amendments still bar

the work could reveal whether the first Native Americans included migrants from Europe who crossed the ice-age Atlantic Ocean.

Pääbo and his team had nearly completed the Neanderthal genome by early 2009, about four years after the sequencing effort began. But, to carry out their analysis, the researchers raced to sequence five genomes of people from diverse modern populations in Europe, Asia and Africa. By comparing these to the Neanderthal genome, they found 78 protein-altering sequence changes that seem to have arisen since the divergence from Neanderthals several hundred thousand years ago, plus a handful of other genomic regions that show signs of positive selection in modern humans. These are linked to sperm motility, wound healing, skin function, genetic transcription control and cognitive development. The team also found that only the modern African genomes lacked segments of Neanderthal ancestry, indicating that interbreeding between the two groups probably occurred after humans migrated out of Africa.

"For the first time, ancient and modern genetic research is going hand in hand."

That revelation is likely to revive the debate about whether or not the two groups are separate species, says anthropologist Fred Smith of Illinois State University in Normal, who has studied Neanderthals in Europe. Smith thinks that they are a subspecies of *H. sapiens*. Now that the genomes can be compared, it will be possible to investigate the genetic roots of some shared features. For instance, he points to the development of the occipital bun, a bulge at the back of the skull that is found in Neanderthals and in some modern humans. "We need to look and clarify certain characteristics in Neanderthal morphology with genetics," he says.

Most researchers in the field anticipate that the next ancient human genome will be completed by Pääbo's group, from a tiny finger bone found in a cave in the Altai Mountains in southern Siberia. In March, the group reported the mitochondrial DNA sequence from this individual[3], an unknown hominin that, so far, does not genetically match either Neanderthals or *H. sapiens* and may represent a new species. The team dated the bone to about 40,000 years ago, but others say that the sediments around the bone may be as old as 100,000 years. There is speculation that the bone could be the remains of an older species of *Homo*, perhaps even of a remnant population of *Homo heidelbergensis*, known in Europe from 300,000 to 500,000 years ago, or of *Homo erectus*, found as early as 1.8 million years ago from Africa to Indonesia. A full sequence may help to resolve this.

Obtaining the genome of a human ancestor this old was previously unimaginable. "I honestly believe this new era will change our view of human evolution," Willerslev says. ■

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2. Rasmussen, M. *et al. Nature* **463,** 757–762 (2010).
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J.-M. HU/INST. ECOL. AND EVOL. BIOL., NATL TAIWAN UNIV.

Taiwan's universities are set to take in Chinese students.

the major national universities from accepting Chinese undergraduates — a big caveat — and withhold Taiwanese government scholarships from mainlanders. This is a potential deal breaker, says Xiao-fan Wang, a cancer biologist at Duke University in Durham, North Carolina, and the first mainland-born scientist to be president of the Society of Chinese Bioscientists in America, a formerly Taiwanese-dominated academic networking group (see *Nature* 459, 1044; 2009). Wang says that when Hong Kong opened up to mainland students, scholarships were a big draw. "I am not sure there will be a flood of students who want to go to Taiwan," he says. Yi Rao, dean of the life-sciences school at Peking University in Beijing, adds that many mainland students prefer to do graduate work at US universities.

Andrew Wang, vice-president of Taiwan's premier scientific institute, Academia Sinica, says that mainlanders may be wary of returning from Taiwan with a freshly minted diploma bearing the phrase 'National Taiwan University' — a rubric that challenges Beijing's assertion that Taiwan is part of China, and not an independent nation. There is also concern that if places at top universities are held for mainland graduate students, Taiwanese people might feel slighted. "These issues have to be worked out before we move ahead," says Andrew Wang. ■

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