ETHICS

Aboriginal genome analysis comes to grips with ethics

Sequencing effort provides a model for future studies of museum samples.

BY EWEN CALLAWAY

En route from Sydney to Perth, Australia, in the early 1920s, British ethnologist Alfred Cort Haddon acquired a tuft of human hair from a young Aboriginal man. He added it to his sizeable collection of hair from people living around the world.

Ninety years later, those locks have yielded the first complete genome sequence of an Aboriginal Australian, and provided clues about the timing of human migrations from Africa to Asia[1] (see 'Early human explorers charted a bold course'). The work has also underscored the bioethical dilemmas involved in plumbing the genomes of indigenous populations — especially when the DNA comes from an archived specimen such as Haddon's. "To be sequencing DNA from the hair of a deceased indigenous person is uncharted ethical territory," says Emma Kowal, a cultural anthropologist at the University of Melbourne.

The genome project, led by Eske Willerslev at the University of Copenhagen, received approval for the work from a group that represents Aboriginals in the region in which the man probably lived. But some scientists are jittery about how others in the Aboriginal community might receive the project, and worry that it could set back efforts to engage Aboriginals in genetic research. "In a sense, every Aboriginal Australian has had something about themselves revealed to the world without their consent," says Hank Greely, who directs the Center for Law and the Biosciences at Stanford University in California.

"Sequencing DNA from the hair of a deceased indigenous person is uncharted ethical territory."

Aboriginal Australians endured centuries of repression by European colonists, but their wariness of genetic research owes much to the Human Genome Diversity Project (HGDP). This 1990s international collaboration aimed to catalogue the genetic diversity of populations worldwide, but sparked concerns that indigenous peoples were being subjected to neocolonial 'bioprospecting'. "Probably the strongest opposition we ran into anywhere in the world" was in Australia, says Greely, who was an ethical adviser to the project. Plans to include Aboriginal Australian DNA were eventually scrapped, and the furore's impact continues to reverberate, says Kowal. "The damage that the HGDP has done for the prospect of doing genetic research with Aboriginal people has been significant." Researchers who work with Aboriginal Australians are now expected to obtain consent not only from the individuals concerned, but also from local and sometimes state-wide groups representing Aboriginal communities across Australia.

P. TWEEDIE/PANOS

Today's Australian Aboriginals are descended from the first humans to travel far from their African origins.

Sheila van Holst Pellekaan, a geneticist at the University of New South Wales in Sydney, says that she has encountered long delays in getting continued approval for her genetic studies of ancestry and disease among Aboriginal Australians, and can share only limited data with other researchers. Such obstacles, she says, mean that Aboriginals, who suffer from high rates of diabetes and heart disease, may miss out on advances in genetic medicine.

Willerslev says that he was not fully aware of these issues when his team set out to sequence Haddon's sample. Moreover, the sample came with little identifying information, so Willerslev's team had no idea whom to ask for permission to study it.

A Danish bioethical review board did not believe it was necessary to review the project because it viewed the hair as an archaeological specimen and not a biological one, Willerslev says. However, after his team sequenced the genome, an Australian colleague put Willerslev in touch with the Goldfields Land and Sea Council, a body based in Kalgoorlie, Western Australia, that represents the 5,000 or so Aboriginal Australians living in the region where Haddon collected the hair sample. In June, Willerslev flew to the region to describe his project to the organization's board and to seek its approval. He says that if the board had rejected his proposal, he would have ended the project and left the genome unpublished.

Craig Muller, the research manager at Goldfields Land and Sea Council, says that he researched the history of the man's hair sample and concluded that the man had donated it freely to Haddon. "Once that was made clear, nobody was bothered that there might be some underlying problem," says Muller.

"I hope that our study will set a precedent on how to potentially deal with these issues," says Willerslev, whose team has obtained similar approval to sequence the genome of the iconic Native American Sitting Bull from a lock of hair.

Despite Willerslev's efforts, "I would suggest there would be a certain amount of unrest in the indigenous communities", says van Holst Pellekaan. Greely agrees that Willerslev's team should have reached out to other Aboriginal groups.

"I think they did everything anyone could reasonably expect them to," counters Mark Stoneking, a molecular anthropologist at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. He published a complementary analysis of Aboriginal genomes last week[2], using DNA samples obtained by other scientists with the consent of the Aboriginal Australian individuals involved.

The study also raises broader consent issues over body parts of indigenous people held in museums, says Kowal. Many collections are returning bones to these groups, but the British Museum in London, for instance, generally excludes hair and nails from its repatriation policy. Such specimens are a valuable tool for studying the genomes of people from around the world, including populations that no longer exist, argues Willerslev.

Having a set of widely accepted guidelines for studying such samples would help to guide researchers, journals and funding agencies, says Stoneking. "Hopefully some sort of standards can be developed so everyone feels comfortable going ahead with this research," he says. ■

1. Rasmussen, M. *et al. Science* http://dx.doi.org/10.1126/science.1211177 (2011).
2. Reich, D. *et al. Am. J. Hum. Genet.* http://dx.doi.org/10.1016/j.ajhg.2011.09.005 (2011).
3. Reich, D. *et al. Nature* **468,** 1053–1060 (2010).

WAVES OF MIGRATION

Early human explorers charted a bold course

The first complete genome of an Aboriginal Australian is a portrait of a pioneer. Comparisons with other genomes indicate that Australia's original settlers parted company with other humans more than 60,000 years ago, suggesting that they were among the first to venture far beyond Africa[1].

Like other populations outside Africa, the genome carries small chunks of DNA that originally came from Neanderthals. More surprisingly, it shows that Aboriginals' ancestors also interbred with another archaic human population known as the Denisovans, only recently identified from 30,000–50,000-year-old DNA recovered from a finger bone found in a Siberian cave[3]. Until now, Papua New Guineans were the only modern humans whose ancestors were known to have interbred with Denisovans.

A separate study published last week, based on genetic markers in modern-day Aboriginal Australians, Asians and Pacific Islanders, paints a fuller picture of the Denisovans' genetic legacy. The research, led by Mark Stoneking at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, revealed a patchwork in which some populations, including Australian Aboriginals, bore varying levels of Denisovan DNA, whereas many of their neighbours, such as the residents of mainland Southeast Asia, contained none[2].

Stoneking says that this pattern suggests that an early wave of migration into Asia included the ancestors of contemporary Aboriginal Australians. This was followed by a second wave that gave rise to the current residents of mainland Asia. Some members of the first wave interbred with Denisovans. By the time the second wave of Asian migrants arrived, the Denisovans may have vanished. The study also suggests that the Denisovans' range once extended to Southeast Asia and perhaps Oceania.

"Put together, these two papers make an overwhelming case for multiple waves of migration," says David Reich, a population geneticist at Harvard Medical School in Boston, Massachusetts, and an author on the second study. **E.C.**