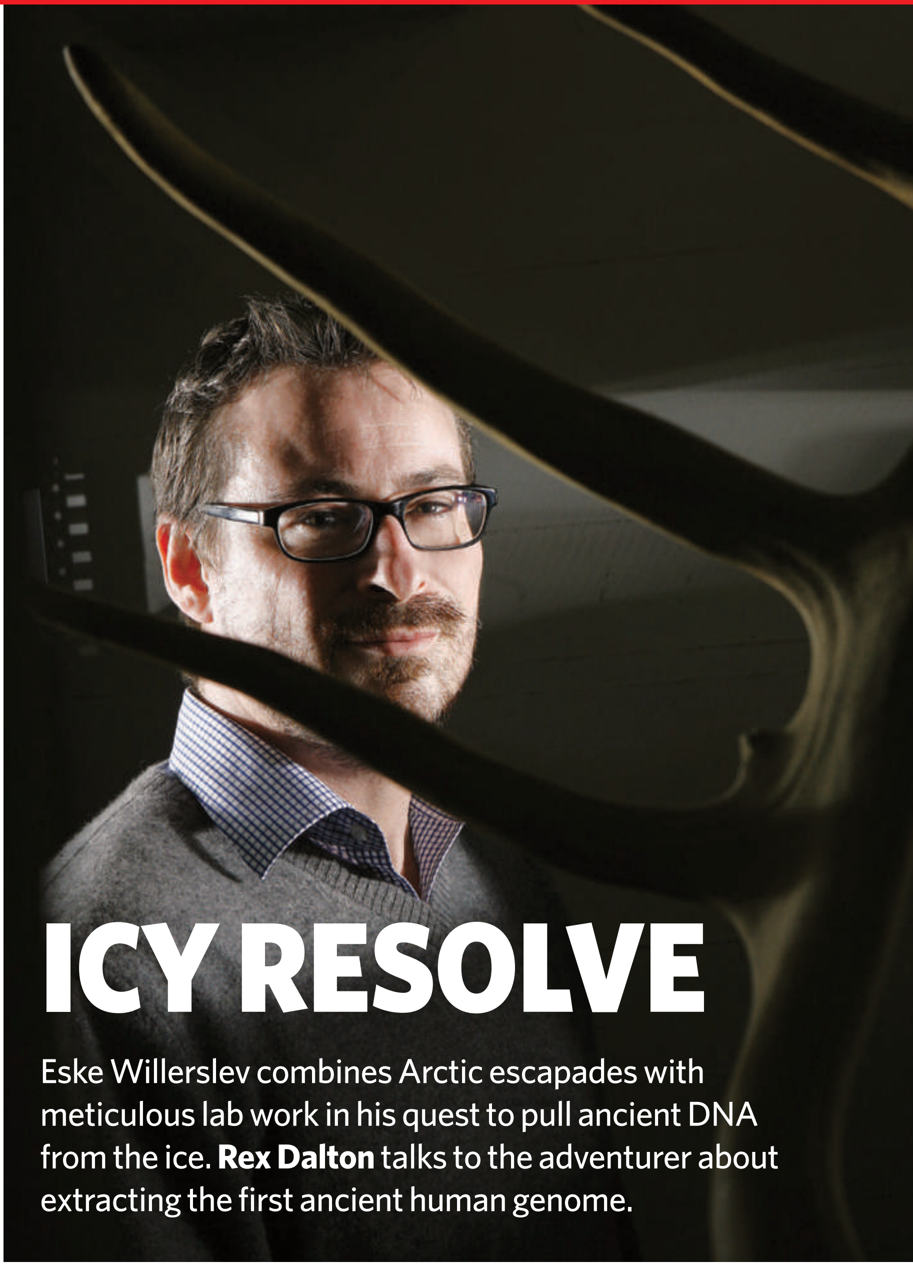

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ICY RESOLVE

Eske Willerslev combines Arctic escapades with meticulous lab work in his quest to pull ancient DNA from the ice. **Rex Dalton** talks to the adventurer about extracting the first ancient human genome.

All Eske Willerslev wanted was a scrap of something human: some hair, a bone, a tooth.

For this, the Danish evolutionary biologist flew to Greenland's most remote northern tundra in 2006. At Nord military station, he learned that the helicopter that was to take him and his team to an archaeology site had just crashed in a storm. Undeterred, he commandeered a plane, which had to land in the rocky outback. Then there were six frigid weeks of probing remnants of human camps — all without finding the specimen he sought.

So two years later, Willerslev could laugh when he found the hair he was seeking a 10-minute bicycle ride away from his lab in Copenhagen, in the basement of the Natural History Museum of Denmark. From that tuft, which had been extracted from permafrost some 20 years earlier, Willerslev and his team have now secured the first complete ancient human genome[1] (see page 757) — that of a palaeo-Eskimo some 4,000 years old, whose ancestors had trekked from Siberia around the Arctic circle in pursuit of game.

The accomplishment comes less than a decade after the first genome from a living human was deciphered, and at a time when the ancient-DNA field still struggles to eliminate contamination from samples. With it, the 38-year-old has cemented a reputation for conjuring prehistoric genetic gems from frozen ground. "I never quite fully appreciated Eske's willpower until this project," says Thomas Gilbert, an evolutionary biologist who works with him at the University of Copenhagen. "Now, if he said he was going to walk on water, I think he might."

"It is a lot of fun having Eske around," adds Morten Meldgaard, director of the Natural History Museum. "He takes things to another level."

By comparing the ancient Eskimo sequence to modern human genomes from Arctic populations and elsewhere, Willerslev's team has deduced that the palaeo-Eskimo was a male member of the Arctic Saqqaq, the first known culture to settle in Greenland. The team shows that the Saqqaq are closest genetically to the Chukchis from Siberia, and that beginning about 5,500 years ago, this man's ancestors migrated from Siberia east through Alaska and Canada to Greenland, settling there about 1,500 years later. The genome settles a debate about Saqqaq origins, showing that they are descended from separate migrations from those that gave rise to today's Inuit Greenlanders and natives of North America. It also suggests that the man was dark skinned, brown-eyed and possibly going bald.

Worldwide, there are just a handful of laboratories seeking to wrest ancient genomes out of bone, teeth or even petrified faeces. In the past five years, though, Willerslev and the Center for GeoGenetics he directs have become leaders of the pack.

In 2003, Willerslev reported the recovery from permafrost cores of the oldest known DNA at the time — a collection of plant and animal sequences dating from 10,000 to 400,000 years ago and including mammoth and bison[2]. By 2007, his group had showed how DNA extracted from ice cores could describe ancient plants and animals from an estimated 450,000–800,000 years ago, painting a scene of a Greenland once rich with forest[3]. The next year, he and collaborators reported DNA from fossilized human faeces at what is thought to be the oldest inhabited site in North America, Oregon's Paisley Caves, dating a human presence there to some 12,300 years ago[4].

Sequencing the roughly 3 billion base pairs of an ancient, fragmented human genome — and showing convincingly that it is not tainted with the near-identical DNA of modern humans — was the biggest challenge yet. What made this possible is Willerslev's exacting requirement for technical detail and his willingness to go to extremes in pursuit of pristine DNA. The best place to find it is entombed in ice, where it is preserved by the cold and protected from contamination. And Willerslev's background made him want to go looking for it.

Frozen feats

As a boy, Willerslev frequently journeyed beyond the upmarket suburb of Copenhagen where he lived. His father, a history professor at the University of Copenhagen, took him and his identical twin brother, Rane, on his trips to study Swedish migrations of the 1800s, and the twins spent summers at the family's cabin in a Swedish forest. "Our father was pretty tough — into icy waters and chopping wood," says Rane Willerslev, now an ethnologist at the Arrhus University in Denmark. "We did everything together," he says, speaking of his brother. "It was always competitive."

In 1993, the twins embarked on a summer

E. WILLERSLEV

ANDREAS MIKKEL HANSEN

Eske Willerslev in Siberia (above) and examining a Greenland ice core (far right).

fossil-collecting trek in eastern Siberia that extended into a five-month winter sojourn with Russian trappers. Moving by cross-country skis, hauling gear in dog sleds, Eske Willerslev hunted moose, set traps and skinned mink and sable. "Physically and mentally, I was done by Christmas," he recalled, "but it was weeks later before I got out." The pair eventually escaped in a Russian tank-like vehicle.

"I didn't think my Siberian trapping experience would add to my scientific career, but it did," says Willerslev. "It taught me how far to push the body and mind. I find I can work twice as long as some colleagues."

Willerslev applied that stamina to his academic work at the University of Copenhagen, where as a master's and doctoral student he showed that it was possible to extract ancient DNA from debris in polar ice cores[5] and permafrost[2]. Captivated by the field, he moved to the University of Oxford, UK, in 2003 for a fellowship in the lab of Alan Cooper, a prominent member of the ancient-DNA field.

"My Siberian experience taught me how far to push the body and mind."
— Eske Willerslev

In 2005, Willerslev returned to Copenhagen to establish Denmark's first ancient-DNA lab, which grew into the Center for GeoGenetics. A year ago, he won a 50-million-Danish-krone (US$9-million) excellence grant from the Danish National Research Foundation, along with a 25-million-krone government grant to build up and equip the centre.

Willerslev has been ruthless about keeping contamination at bay. He prowled museums at home and abroad looking for usable ancient specimens. It was fear of contamination that prompted his team to risk the flight to northern Greenland — to a location so inhospitable that, they hoped, no modern archaeologists would have reached it.

The hair clump that they eventually used for the ancient-human genome project had been discovered in 1986 on the western shore of Greenland's Disko Bay, on an archaeology dig directed by Meldgaard's father. It had been stored in a specimen case at room temperature and handled very little. Willerslev says that it is easier to capture pristine ancient DNA from hair than from bone and teeth. Hair doesn't as readily absorb contaminants, and its surface can be bleached clean.

Well preserved

Shortly after securing the hair, Gilbert, Willerslev and their colleagues sequenced the roughly 16,000 base pairs of the mitochondrial genome, work that was published in 2008 (ref. 6). Usually, researchers have an easier time finding mitochondrial DNA in ancient specimens, because it is more abundant and survives more readily than that from the nucleus. But permafrost seemed to have maintained large amounts of nuclear DNA in the Saqqaq sample too. "About three weeks after the mitochondrial genome publication, I recall waking in the middle of the night, thinking: We can do the whole genome," Willerslev says.

To guard against contamination, a co-author of the genome study, Rasmus Nielsen of the University of California, Berkeley, tagged the millions of fragments of extracted DNA with a barcode-like sequence to distinguish them from stray modern human DNA. The genome sequencing was completed in two and a half months last year at a cost of about $500,000 by teaming up with Jun Wang, deputy director at the Beijing Genomics Institute (BGI) at Shenzen, China. Willerslev contacted the institute after learning it had 120 of the newest Illumina sequencing machines. The collaboration has since blossomed: late last year, the Sino-Danish Genomics Center was established at the BGI.

By the end of the summer, the group had sequenced the ancient genome roughly ten times over on average, equivalent to the coverage achieved for the Human Genome Project. Then it was discovered that the data included artefacts from the sequencing process. "A cheapskate might have been happy with ten times coverage," says Gilbert. "Eske wanted higher quality." Willerslev decided to refine and re-sequence. The published genome has been sequenced 20 times on average over nearly 80% of its length. This level of rigour helps to ensure that any differences between the ancient and modern sequences are true differences, rather than sequencing errors, or degraded or contaminating DNA.

To identify the origins of the ancient man, the team had to compare his sequence with some from living populations. They turned to researchers such as Richard Villems, a population geneticist at University of Tartu in Estonia, who studies migrations worldwide and whose freezers are stocked with human specimens. "The ancestry really gives you a geographical context," says Villems. "This is important for Eske and me. We both are field men."

And the field is where Willerslev is heading next. This summer, he will return to Greenland, seeking DNA from more humans and hoping to map out broader migration patterns across the north. He is also ready to take on the next technical challenge: "I hope to do a complete ancient genome from a non-frozen specimen," he says, with all the additional contamination problems this could entail.

Few doubt he can do it. "I think he's the best in his field," says Dennis Jenkins, an archaeologist at the University of Oregon in Eugene who sought Willerslev's expertise to date the human faeces in Oregon's caves. "When you provide him with samples, you get results." ■

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