ANNALS OF EVOLUTION

SLEEPING WITH THE ENEMY

What happened between the Neanderthals and us?

BY ELIZABETH KOLBERT

The Max Planck Institute for Evolutionary Anthropology, in Leipzig, is a large, mostly glass building shaped a bit like a banana. The institute sits at the southern edge of the city, in a neighborhood that still very much bears the stamp of its East German past. If you walk down the street in one direction, you come to a block of Soviet-style apartment buildings; in the other, to a huge hall with a golden steeple, which used to be known as the Soviet Pavilion. (The pavilion is now empty.) In the lobby of the institute there's a cafeteria and an exhibit on great apes. A TV in the cafeteria plays a live feed of the orangutans at the Leipzig Zoo.

Svante Pääbo heads the institute's department of evolutionary genetics. He is tall and lanky, with a long face, a narrow chin, and bushy eyebrows, which he often raises to emphasize some sort of irony. Pääbo's office is dominated by a life-size model of a Neanderthal skeleton, propped up so that its feet dangle over the floor, and by a larger-than-life-size portrait that his graduate students presented to him on his fiftieth birthday. Each of the students painted a piece of the portrait, the over-all effect of which is a surprisingly good likeness of Pääbo, but in mismatched colors that make it look as if he had a skin disease.

At any given moment, Pääbo has at least half a dozen research efforts in progress. When I visited him in May, he had one team analyzing DNA that had been obtained from a forty- or fifty-thousand-year-old finger bone found in Siberia, and another trying to extract DNA from a cache of equally ancient bones from China. A third team was slicing open the brains of mice that had been genetically engineered to produce a human protein.

In Pääbo's mind, at least, these research efforts all hang together. They are attempts to solve a single problem in evolutionary genetics, which might, rather dizzyingly, be posed as: What made us the sort of animal that could create a transgenic mouse?

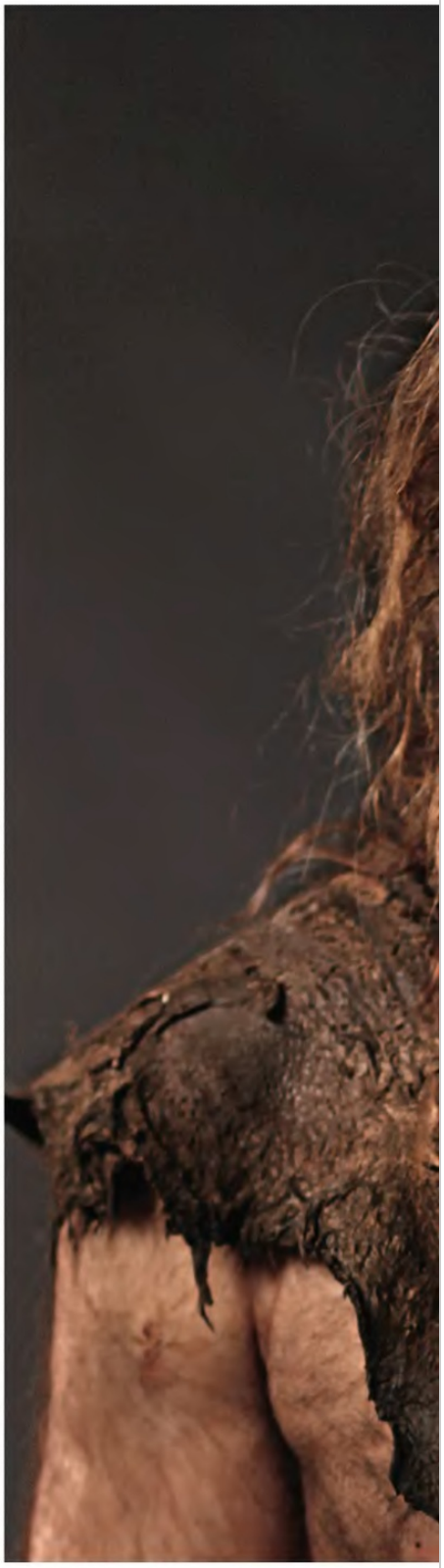
The question of what defines the human has, of course, been kicking around since Socrates, and probably a lot longer. If it has yet to be satisfactorily resolved, then this, Pääbo suspects, is because it has never been properly framed. "The challenge is to address the questions that are answerable," he told me.

Pääbo's most ambitious project to date, which he has assembled an international consortium to assist him with, is an attempt to sequence the entire genome of the Neanderthal. The project is about halfway complete and has already yielded some unsettling results, including the news, announced by Pääbo last year, that modern humans, before doing in the Neanderthals, must have interbred with them.

Once the Neanderthal genome is complete, scientists will be able to lay it gene by gene—indeed, base by base—against the human, and see where they diverge. At that point, Pääbo believes, an answer to the age-old question will finally be at hand. Neanderthals were very closely related to modern humans—so closely that we shared our prehistoric beds with them—and yet clearly they were *not* humans. Somewhere among the genetic disparities must lie the mutation or, more probably, mutations that define us. Pääbo already has a team scanning the two genomes, drawing up lists of likely candidates.

"I want to know what changed in fully modern humans, compared with Neanderthals, that made a difference," he said. "What made it possible for us to build up these enormous societies, and spread around the globe, and develop the technology that I think no one can doubt is unique to humans. There has to be a genetic basis for that, and it is hiding somewhere in these lists."

Pääbo, who is now fifty-six, grew up in Stockholm. His mother, a chemist, was an Estonian refugee. For a time, she worked in the laboratory of a biochemist named Sune Bergström, who later won a



Svante Pääbo's genome-sequencing project hopes

ATELIER DAYNÈS; PHOTOGRAPH: S. ENTRESSANGLE

to point up the differences that enabled humans, unlike the Neanderthals, with whom they interbred, to build complex societies.

Nobel Prize. Pääbo was the product of a lab affair between the two, and, although he knew who his father was, he wasn't supposed to discuss it. Bergström had a wife and another son; Pääbo's mother, meanwhile, never married. Every Saturday, Bergström would visit Pääbo and take him for a walk in the woods, or somewhere else where he didn't think he'd be recognized.

"Officially, at home, he worked on Saturday," Pääbo told me. "It was really crazy. His wife knew. But they never talked about it. She never tried to call him at work on Saturdays." As a child, Pääbo wasn't particularly bothered by the whole arrangement; later, he occasionally threatened to knock on Bergström's door. "I would say, 'You have to tell your son—your other son—because he will find out sometime,'" he recalled. Bergström would promise to do this, but never followed through. (As a result, Bergström's other son did not learn that Pääbo existed until shortly before Bergström's death, in 2004.)

From an early age, Pääbo was interested in old things. He discovered that around fallen trees it was sometimes possible to find bits of pottery made by prehistoric Swedes, and he filled his room with potsherds. When he was a teenager, his mother took him to visit the Pyramids, and he was entranced. He enrolled at Uppsala University, planning to become an Egyptologist.

"I really wanted to discover mummies, like Indiana Jones," he said. Mostly, though, the coursework turned out to involve parsing hieroglyphics, and instead of finding it swashbuckling Pääbo thought it was boring. Inspired by his father, he switched first to medicine, then to cell biology.

In the early nineteen-eighties, Pääbo was doing doctoral research on viruses when he once again began fantasizing about mummies. At least as far as he could tell, no one had ever tried to obtain DNA from an ancient corpse. It occurred to him that if this was possible, then a whole new way of studying history would open up.

Suspecting that his dissertation adviser would find the idea silly (or worse), Pääbo conducted his mummy research in secret, at night. With the help of one of his former Egyptology professors, he managed to obtain some samples from the Egyptian Museum in what was then East Berlin. In 1984, he published his results in an obscure East German journal. He had, he wrote, been able to detect DNA in the cells of a mummified child who'd been dead for more than two thousand years. Among the questions that Pääbo thought mummy DNA could answer were what caused pharaonic dynasties to change and who Tutankhamun's mom was.

While Pääbo was preparing a version of his mummy paper for publication in English, a group of scientists from the University of California at Berkeley announced that they had succeeded in sequencing a snippet of DNA from a zebralike animal known as a quagga, which had been hunted to extinction in the eighteen-eighties. (The DNA came from a hundred-and-forty-year-old quagga hide preserved at the National History Museum in Mainz.) The leader of the team, Allan Wilson, was an eminent biochemist who had, among other things, come up with a way to study evolution using the concept of a "molecular clock." Pääbo sent Wilson the galleys of his mummy paper. Impressed, Wilson replied asking if there was any space in Pääbo's lab; he might like to spend a sabbatical there. Pääbo had to write back that he could not offer Wilson space in his lab, because, regrettably, he didn't have a lab—or even, at that point, a Ph.D.

Pääbo's mummy paper became the cover article in *Nature*. It was also written up in the *Times*, which called his achievement "the most dramatic of a series of recent accomplishments using molecular biology." Pääbo's colleagues in Sweden, though, remained skeptical. They urged him to forget about shrivelled corpses and stick to viruses.

"Everybody told me that it was really stupid to leave that important area for something which looked like a hobby of some sort," he said. Ignoring them, Pääbo moved to Berkeley, to work for Wilson.

"He just kind of glided in," Mary-Claire King, who had also been a student of Wilson's, and who is now a professor of genome sciences at the University of Washington, recalled. According to King, Pääbo and Wilson, who died in 1991, turned out to share much more than an interest in ancient DNA.

"Each of them thought of very big ideas," she told me. "And each of them was very good at translating those ideas into testable hypotheses. And then each of them was very good at developing the technology that's necessary to test the hypotheses. And to have all three of those capacities is really remarkable." Also, although "they were both very data-driven, neither was afraid to say outrageous things about their data, and neither was afraid to be wrong."

DNA is often compared to a text, a comparison that's apt as long as the definition of "text" encompasses writing that doesn't make sense. DNA consists of molecules known as nucleotides knit together in the shape of a ladder—the famous double helix. Each nucleotide contains one of four bases: adenine, thymine, guanine, and cytosine, which are designated by the letters A, T, G, and C, so that a stretch of the human genome might be represented as ACCTCCTCTAATGTCA. (This is an actual sequence, from chromosome 10; the comparable sequence in an elephant is ACCTCCCCTAATGTCA.) The human genome is three billion bases—or, really, base pairs—long. As far as can be determined, most of it is junk.

With the exception of red blood cells, every cell in an organism contains a complete copy of its DNA. It also contains many copies—hundreds to thousands—of an abridged form of DNA known as mitochondrial DNA, or mtDNA. But as soon as the organism dies the long chains of nucleotides begin to break down. Much of the damage is done in the first few hours, by enzymes inside the creature's own body. After a while, all that remains is snippets, and after a longer while—how long seems to depend on the conditions of decomposition—these snippets, too, disintegrate. "Maybe in the permafrost you could go back five hundred thousand years," Pääbo told me. "But it's certainly on this side of a million." Five hundred thousand years ago, the dinosaurs had been dead for more than sixty-four million years, so the whole "Jurassic Park" fantasy is, sadly, just that. On the other hand, five hundred thousand years ago modern humans did not yet exist.

When Pääbo arrived in California, he was still interested in finding a way to use genetics to study human history. He'd discovered, however, a big problem with trying to locate fragments of ancient Egyptian DNA: they look an awful lot like—indeed, identical to—fragments of contemporary human DNA. Thus a sin-

gle microscopic particle of his own skin, or of someone else's, even some long-dead museum curator's, could nullify months of work.

"It became clear that human contamination was a huge problem," he explained. (Eventually, Pääbo concluded that the sequences he had obtained for his original mummy paper had probably been corrupted in this way.) As a sort of warmup exercise, he began working on extinct animals. He analyzed scraps of mtDNA from giant ground sloths, which disappeared about twelve thousand years ago, and from mammoths, which vanished around the same time, and from Tasmanian tigers, which were hunted to extinction by the nineteen-thirties. He extracted mtDNA from moas, the giant flightless birds that populated New Zealand before the arrival of the Maori, and found that moas were more closely related to birds from Australia than to kiwis, the flightless birds that inhabit New Zealand today. "That was a blow to New Zealand self-esteem," he recalled. He also probed plenty of remains that yielded no usable DNA, including bones from the La Brea tar pits and fossilized insects preserved in amber. In the process of this work, Pääbo more or less invented the field of paleogenetics.

"Frankly, it was a problem that I wouldn't have tackled myself, because I thought it was too difficult," Maynard Olson, an emeritus professor at the University of Washington and one of the founders of the Human Genome Project, told me. "Pääbo brought very high standards to this area, and took the field of ancient DNA study from its 'Jurassic Park' origins to a real science, which is a major accomplishment."

"There's nothing unique about most of science," Ed Green, a professor of biomolecular engineering at the University of California at Santa Cruz who works on the Neanderthal Genome Project, said. "If you don't do it, somebody else is going to do it a few months later. Svante is one of the rare people in science for whom that is not true. There wouldn't even be a field of ancient DNA as we know it without him."

"It's a nice rarity in science when people take not only unique but also productive paths," Craig Venter, who led a rival effort to the Human Genome Project, told me. "And Svante has clearly done both. I have immense respect for him and what he's done."

While Pääbo was living in California, he sometimes went to Germany to visit a woman who was attending graduate school at the University of Munich. "I had many relationships with men, but I also had girlfriends now and again," he told me. The relationship ended; shortly afterward, the University of Munich offered Pääbo an assistant professorship. With no pressing reason to move to Germany, he demurred. The offer was increased to a full professorship: "So then I said, 'Germany isn't that bad after all. I'll go there for a few years.' "

Pääbo was still in Munich several years later when he got a call from the Rhenish State Museum, in Bonn. The museum houses the bones of the first Neanderthal to be identified as such, which was discovered in the summer of 1856. What did Pääbo think the odds were that he could extract usable DNA? He had no way of determining what kind of shape the bones were in until he dissolved them.

"I didn't know what to tell them, so I said, 'There's a five-per-cent chance that it works,' " he recalled. A few months later, he received a small chunk of the Neanderthal's right humerus.

The first Neanderthal was found in a limestone cave about forty-five miles north of Bonn, in an area known as the Neander Valley, or, in German, *das Neandertal.* Although the cave is gone—the limestone was long ago quarried into building blocks—the area is now a sort of Neanderthal theme park, with its own museum, hiking trails, and a garden planted with the kinds of shrubs that would have been encountered during an ice age. In the museum, Neanderthals are portrayed as kindly, if not particularly telegenic, humans. By the entrance to the building, there's a model of an elderly Neanderthal leaning on a stick. He is smiling benignantly and resembles an unkempt Yogi Berra. Next to him is one of the museum's most popular attractions—a booth called the Morphing-Station. For three euros, visitors to the station can get a normal profile shot of themselves and, facing that, a second shot that has been doctored. In the second, the chin recedes, the forehead slopes, and the back of the head bulges out. Kids love to see themselves—or, better yet, their siblings—morphed into Neanderthals. They find it screamingly funny.

When the first Neanderthal bones showed up in the Neander Valley, they were treated as rubbish (and almost certainly damaged in the process). The fragments—a skullcap, four arm bones, two thighbones, and part of a pelvis—were later salvaged by a local businessman, who, thinking they belonged to a cave bear, passed them on to a fossil collector. The fossil collector realized that he was dealing with something much stranger

"Your mother and I are separating because I want what's best for the country and your mother doesn't."

than a bear. He declared the remains to be traces of a "primitive member of our race."

As it happened, this was right around the time that Darwin published "On the Origin of Species," and the fragments soon got caught up in the debate over the origin of humans. Opponents of evolution insisted that they belonged to an ordinary person. One theory held that it was a Cossack who had wandered into the region in the tumult following the Napoleonic Wars. The reason the bones looked odd—Neanderthal femurs are distinctly bowed—was that the Cossack had spent too long on his horse. Another attributed the remains to a man with rickets: the man had been in so much pain from his disease that he'd kept his forehead perpetually tensed—hence the protruding brow ridge. (What a man with rickets and in constant pain was doing climbing into a cave was never really explained.)

Over the next decades, bones resembling those from the Neander Valley—thicker than those of modern humans, with strangely shaped skulls—were discovered at several more sites, including two in Belgium and one in France. Meanwhile, a skull that had been unearthed years earlier in Gibraltar was shown to look much like the one from Germany. Clearly, all these remains could not be explained by stories of disoriented Cossacks or rachitic spelunkers. But evolutionists, too, were perplexed by them. Neanderthals had very large skulls—larger, on average, than people today. This made it hard to fit them into an account of evolution that started with small-brained apes and led, through progressively bigger brains, up to humans. In "The Descent of Man," which appeared in 1871, Darwin mentioned Neanderthals only in passing. "It must be admitted that some skulls of very high antiquity, such as the famous one of Neanderthal, are well developed and capacious," he noted.

In 1908, a nearly complete Neanderthal skeleton was discovered in a cave near La Chapelle-aux-Saints, in southern France. The skeleton was sent to a paleontologist named Marcellin Boule, at Paris's National Museum of Natural History. In a series of monographs, Boule invented what might be called the cartoon version of the Neanderthals—bent-kneed, hunched over, and brutish. Neanderthal bones, Boule wrote, displayed a

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From the cistern in the dome the daylight drips
While the calls to prayer
From the quarter's seven minarets—
Overlapping tape loops of Submission—slip
Down through the arching crescent lunettes
Cut into the air
As if the vault itself had loosened its grip.

I am on my back, listening to the tattoo
Of clogs crisscrossing
The sopping white marble floor inlaid
With veins of still darker matters to pursue.
A skittish gleam accents, like eyeshade,
A fountain's boss in
The corner alcove, where hot and cold make do

In a basin Tony Curtis and Franz Liszt
Both stared into once.
(Stardom is a predictable fate:
The point is forgotten but somehow still missed.)
Gods, whenever they annunciate,
Long for romance
That ironclad heroes peering through the mist

Or mousy adolescent girls both provide.
The same unlikely
Places—a battlefield or grotto—
Are returned to, while again the hollow-eyed
Ogle in flagrante devoto
And obey, shyly,
The scrambled revelations so true-and-tried.

Congestive, crotch-scented vapor has congealed
Into beads that skid
Along suction-knots and shadow-ends
Abutting my slab. Eager for an ordeal
The illustrated brochure commends
As a bath to rid
The body of its filth both real and unreal,

I have bought their boast, "We make you feel reborn,"
For fifty euros.
Pinched and idly gestured toward a plinth
Two centuries of customers have careworn
To a shallow trough not quite my length,
I'm forced to burrow
Into a pose much more flagellant than faun.

The sodden towel is too heavy now to hold
Itself across me—
And there is the pasha's bay window,
The shrivelled bulblet, the whole ill-shaped scaffold
Of surplus fact and innuendo,
From the beer belly
To the congenital heart flutter's toehold.

The attendant walks up and down on my back,
Pacing the problem,
Then kneads, then reams, then applies a foam
He scrubs in until it causes an attack
Of radiance, the world's palindrome
Suddenly solemn,
Suddenly seeming to surrender its knack

For never allowing us simply to want
What we already
Have, or are, or perhaps could have been.
His hand signal to get up seems like a taunt.
I lie there, my fist under my chin,
Senses unsteady,
Something gradually, like a tiny font,

Coming into focus. I sit up and start
To notice small bits
Of grit when I run my hand over
My chest. But wasn't this debris the chief part
Of the package deal? The makeover
And its benefits?
In the fog I can't really see what trademark

Schmutz the Oriental Luxury Service
Has failed to wash off.
So I put it in my mouth and taste
Two dank gobbets—salty, glairy and grayish—
I should have recognized as the waste
That was my old self,
A loofah having scraped it from each crevice

And bulge, from every salacious thought and deed.
Every good one, too.
It is the past, not just what is wrong,
It is the embarrassments we still breast-feed,
That we absent-mindedly so long
To shed. A new *you*,
Oneself an innate second person succeeds.

How do the saints feel when they fall to their knees,
God coming to light?
Less ecstatic than ashamed, I fear,
Of bodies never worthy of being seized.
Encumbered by the weight of a tear,
In hopeless hindsight
They see all that the flesh can never appease,

All that the flesh is obliged to mortify.
Here I am laid out,
Looking up to where nothing appears,
Hardly wondering why nothing satisfies
And yet saddened that it's all so clear.
Tulip waterspouts
Trickle. Reservoirs deep underground reply.

—*J. D. McClatchy*

"distinctly simian arrangement," while the shape of their skulls indicated "the predominance of functions of a purely vegetative or bestial kind." Boule's conclusions were studied and then echoed by many of his contemporaries; the British anthropologist Sir Grafton Elliot Smith, for instance, described Neanderthals as walking with "a half-stooping slouch" upon "legs of a peculiarly ungraceful form." (Smith also claimed that Neanderthals' "unattractiveness" was "further emphasized by a shaggy covering of hair over most of the body," although there was—and still is—no clear evidence that they were hairy.)

In the nineteen-fifties, a pair of anatomists, Williams Straus and Alexander Cave, decided to reëxamine the skeleton from La Chapelle. What Boule had taken for the Neanderthal's natural posture, Straus and Cave determined, was probably a function of arthritis. Neanderthals did not walk with a slouch, or with bent knees. Indeed, given a shave and a new suit, the pair wrote, a Neanderthal probably would attract no more attention on a New York City subway "than some of its other denizens." More recent scholarship has tended to support the idea that Neanderthals, if not quite up to negotiating the I.R.T., certainly walked upright, with a gait we would recognize more or less as our own. The version of Neanderthals offered by the Neanderthal Museum—another cartoon—is imbued with cheerful dignity. Neanderthals are presented as living in tepees, wearing what look like leather yoga pants, and gazing contemplatively over the frozen landscape. "Neanderthal man was not some prehistoric Rambo," one of the display tags admonishes. "He was an intelligent individual."

Pääbo announced his plan to sequence the entire Neanderthal genome in July, 2006, just in time for the hundred-and-fiftieth anniversary of the Neanderthal's discovery. The announcement was made together with an American company, 454 Life Sciences, which had developed a so-called "high throughput" sequencing machine that, with the help of tiny resin spheres, could replicate tens of thousands of DNA snippets at a time. Both inside and outside the genetics profession, the plan was viewed as wildly ambitious, and the project made international news. "A

"I wish I had that kind of energy."

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STUDY WITH A LOT OF BALLS," the headline in *The Economist* declared.

By this point, a complete version of the human genome had been published. So, too, had versions of the chimpanzee, mouse, and rat genomes. But humans, chimps, mice, and rats are all living organisms, while Neanderthals have been extinct for thirty thousand years. The first hurdle was simply finding enough Neanderthal DNA to sequence. The chunk of the original Neanderthal that Pääbo had received had yielded shreds of genetic information, but nowhere near the quantities needed to assemble—or reassemble—an entire genome. So Pääbo was placing his hopes on another set of bones, from Croatia. (The Croatian bones turned out to have belonged to three individuals, all of them women; the original Neanderthal was probably a man.)

Toward the end of 2006, Pääbo and his team reported that, using a piece of Croatian bone, they had succeeded in sequencing a million base pairs of the Neanderthal genome. (Just like the human genome, the full Neanderthal genome consists of roughly three billion base pairs.) Extrapolating from this, they estimated that to complete the project would take roughly two years and six thousand "runs" on a 454 Life Sciences machine. But later analysis revealed that the million base pairs had probably been contaminated by human DNA, a finding that led some geneticists to question whether Pääbo had rushed to publish results that he should have known were wrong. Meanwhile, subsequent bones yielded a much lower proportion of Neanderthal DNA and a much higher percentage of microbial DNA. (Something like eighty per cent of the DNA that has been sequenced for the Neanderthal Genome Project belongs to microorganisms and, as far as the project is concerned, is useless.) This meant the initial estimates of the labor involved in finishing the genome were probably far too low. "There were times when one despaired," Pääbo told me. No sooner would one problem be resolved than another materialized. "It was an emotional roller coaster," Ed Green, the biomolecular engineer from Santa Cruz, recalled.

About two years into the project, a new puzzle arose. Pääbo had assembled an international team to help analyze the data the sequencing machines were generating—essentially, long lists of A's, T's, G's, and C's. Sifting through the data, one of the members of this team, David Reich, a geneticist at Harvard Medical School, noticed something odd. The Neanderthal sequences, as expected, were very similar to human sequences. But they were more similar to some humans than to others. Specifically, Europeans and Asians shared more DNA with Neanderthals than did Africans. "We tried to make this result go away," Reich told me. "We thought, This must be wrong."

For the past twenty-five years or so, the study of human evolution has been dominated by the theory known in the popular press as "Out of Africa" and in academic circles as the "recent single-origin" or "replacement" hypothesis. This theory holds that all modern humans are descended from a small population that lived in Africa roughly two hundred thousand years ago. (Not long before he died, Pääbo's adviser Allan Wilson developed one of the key lines of evidence for the theory, based on a comparison of mitochondrial DNA from contemporary humans.) Around a hundred and twenty thousand years ago, a subset of the population migrated into the Middle East, and by fifty thousand years ago a further subset pushed into Eurasia. As they moved north and east, modern humans encountered Neanderthals and other so-called "archaic humans," who already inhabited those regions. The modern humans "replaced" the archaic humans, which is a nice way of saying they drove them into extinction. This model of migration and "replacement" implies that the relationship between Neanderthals and humans should be the same for all people alive today, regardless of where they come from.

Many members of Pääbo's team suspected another case of contamination. At various points, the samples had been handled by Europeans; perhaps they had got their DNA mixed in with the Neanderthals'. Several tests were run to assess this possibility. The results were all negative. "We kept seeing this pattern, and the more data we got, the more statistically overwhelming it became," Reich told me. Gradually, the other team members started to come around. In a paper published in *Science*, in May, 2010, they introduced what Pääbo has come to refer to as the "leaky replacement" hypothesis. (The paper was later voted the journal's outstanding article of the year, and the team received a twenty-five-thousand-dollar prize.) Before modern humans "replaced" the Neanderthals, they had sex with them. The liaisons produced children, who helped to people Europe, Asia, and the New World.

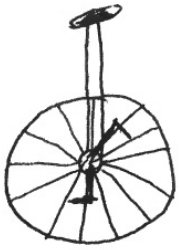
The leaky-replacement hypothesis—assuming for the moment that it is correct—provides further evidence of the closeness of Neanderthals to modern humans. Not only did the two interbreed; the resulting hybrid offspring were functional enough to be integrated into human society. Some of these hybrids survived to have kids of their own, who, in turn, had kids, and so on to the present day. Even now, at least thirty thousand years after the fact, the signal is discernible: all non-Africans, from the New Guineans to the French to the Han Chinese, carry somewhere between one and four per cent Neanderthal DNA.

One of Pääbo's favorite words in English is "cool." When he finally came around to the idea that Neanderthals bequeathed some of their genes to modern humans, he told me, "I thought it was very cool. It means that they are not totally extinct—that they live on a little bit in us."

The Leipzig Zoo lies on the opposite side of the city from the Institute for Evolutionary Anthropology, but the institute has its own lab building on the grounds, as well as specially designed testing rooms inside the ape house, which is known as Pongoland. Since none of our very closest relatives survive (except as little bits in us), researchers have to rely on our next closest kin, chimpanzees and bonobos, and our somewhat more distant cousins—gorillas and orangutans—to perform live experiments. (The same or, at least, analogous experiments are usually also performed on small children, to see how they compare.) One morning, I went to the zoo, hoping to watch an experiment in progress. That day, a BBC crew was also visiting Pongoland, to film a program on animal intelligence, and when I arrived at the ape house I found it strewn with camera cases marked "Animal Einsteins."

For the benefit of the cameras, a researcher named Héctor Marín Manrique was preparing to reënact a series of experiments he'd performed earlier in a more purely scientific spirit. A female orangutan named Dokana was led into one of the testing rooms. Like most orangutans, she had copper-colored fur and a world-weary expression. In the first experiment, which involved red juice and skinny tubes of plastic, Dokana showed that she could distinguish a functional drinking straw from a non-functional one. In the second, which involved more red juice and more plastic, she showed that she understood the *idea* of a straw by extracting a rod from a length of piping and using the pipe to drink through. Finally, in a Mensa-level show of pongid ingenuity, Dokana managed to get at a peanut that Manrique had placed at the bottom of a long plastic cylinder. (The cylinder was fixed to the wall, so it couldn't be knocked over.) She fist-walked over to her drinking water, took some water in her mouth, fist-walked back, and spit into the cylinder. She repeated the process until the peanut floated within reach. Later, I saw this experiment re-staged with some five-year-old children, using little plastic containers of candy in place of peanuts. Even though a full watering can had been left conspicuously nearby, only one of the kids—a girl—managed to work her way to the floating option, and this was after a great deal of prompting. ("How would water help me?" one of the boys asked, just before giving up.)

One way to try to answer the question "What makes us human?" is to ask "What makes us different from apes?," or, to be more precise, from nonhuman apes, since, of course, humans *are* apes. As just about every human by now knows—and as the experiments with Dokana once again confirm—nonhuman apes are extremely clever. They're capable of making inferences, of solving complex puzzles, and of understanding what others are (and are not) likely to know. When researchers from Leipzig performed a battery of tests on chimpanzees, orangutans, and two-and-a-half-year-old children, they found that the chimps, the orangutans, and the kids performed comparably on a wide range of tasks that involved understanding of the physical world. For example, if an experimenter placed a reward inside one of three cups, and then moved the cups around, the apes found the goody just as often as the kids—indeed, in the case of chimps, more often. The apes seemed to grasp quantity as well as the kids did—they consistently chose the dish containing more treats, even when the choice involved using what might loosely be called math—and also seemed to have just as good a grasp of causality. (The apes, for instance, understood that a cup that rattled when shaken was more likely to contain food than one that did not.) And they were equally skillful at manipulating simple tools.



Where the kids routinely outscored the apes was in tasks that involved reading social cues. When the children were given a hint about where to find a reward—someone pointing to or looking at the right container—they took it. The apes either didn't understand that they were being offered help or couldn't follow the cue. Similarly, when the children were shown how to obtain a reward, by, say, ripping open a box, they had no trouble grasping the point and imitating the behavior. The apes, once again, were flummoxed. Admittedly, the kids had a big advantage in the social realm, since the experimenters belonged to their own species. But, in general, apes seem to lack the impulse toward collective problem-solving that's so central to human society.

"Chimps do a lot of incredibly smart things," Michael Tomasello, who heads up the institute's department of developmental and comparative psychology, told me. "But the main difference we've seen is 'putting our heads together.' If you were at the zoo today, you would never have seen two chimps carry something heavy together. They don't have this kind of collaborative project."

Pääbo usually works late, and most nights he has dinner at the institute, where the cafeteria stays open until 7 P.M. One evening, though, he offered to knock off early and show me around downtown Leipzig. We visited the church where Bach is buried, and ended up at Auerbachs Keller, the bar to which Mephistopheles brings Faust in the fifth scene of Goethe's play. (The bar was supposedly Goethe's favorite hangout when he was a university student.) Pääbo's wife, Linda Vigilant, an American primatologist who also works at the institute, joined us. Pääbo and Vigilant first met in the nineteen-eighties, in Berkeley, but they didn't get together until both moved to Leipzig, in the late nineties. (Vigilant was then married to another geneticist, who works at the institute, too.) Pääbo and Vigilant have a

six-year-old son, and Vigilant has two older sons from her previous marriage.

I had been to the zoo, and I asked Pääbo about a hypothetical experiment. If he had the opportunity to subject Neanderthals to the sorts of tests I'd seen in Pongoland, what would he do? Did he think he'd be able to talk to them? He sat back in his chair and folded his arms across his chest.

"One is so tempted to speculate," he said. "So I try to resist it by refusing questions such as 'Do I think they would have spoken?' Because, honestly, I don't know, and in some sense you can speculate with just as much justification as I can."

By now, scores of Neanderthal sites have been excavated, from western Spain to central Russia and from Israel to Wales. They give lots of hints about what Neanderthals were like, at least for those inclined to speculate. Neanderthals were extremely tough—this is attested to by the thickness of their bones—and probably capable of beating modern humans to a pulp. They were adept at making stone tools, though they seem to have spent tens of thousands of years making the same tools over and over, with only marginal variation. At least on some occasions, they buried their dead. Also on some occasions, they appear to have killed and eaten each other. Wear on their incisors suggests that they spent a lot of time grasping animal skins with their teeth, which in turn suggests that they processed hides into some sort of leather. Neanderthal skeletons very often show evidence of disease or disfigurement. The original Neanderthal, from Mettmann, for example, seems to have suffered and recovered from two serious injuries, one to his head and the other to his left arm. The Neanderthal whose nearly complete skeleton was found in La Chapelle endured, in addition to arthritis, a broken rib and kneecap. Both individuals survived into their fifties, which indicates that Neanderthals had the capacity for collective action, or, if you prefer, empathy. They must—at least sometimes—have cared for their wounded.

From the archeological record, it's inferred that Neanderthals evolved in Europe or western Asia and spread out from there, stopping when they reached water or some other significant obstacle. (During the ice ages, sea levels were a lot lower than they are now, so there was no English Channel to cross.) This is one of the most basic ways modern humans differ from Neanderthals and, in Pääbo's view, also one of the most intriguing. By about forty-five thousand years ago, modern humans had already reached Australia, a journey that, even mid-ice age, meant crossing open water. Archaic humans like *Homo erectus* "spread like many other mammals in the Old World," Pääbo told me. "They never came to Madagascar, never to Australia. Neither did Neanderthals. It's only fully modern humans who start this thing of venturing out on the ocean where you don't see land. Part of that is technology, of course; you have to have ships to do it. But there is also, I like to think or say, some madness there. You know? How many people must have sailed out and vanished on the Pacific before you found Easter Island? I mean, it's ridiculous. And why do you do that? Is it for the glory? For immortality? For curiosity? And now we go to Mars. We never stop." If the defining characteristic of modern humans is this sort of Faustian restlessness, then, by Pääbo's account, there must be some sort of Faustian gene. Several times, he told me that he thought it should be possible to identify the basis for this "madness" by comparing Neanderthal and human DNA.

"If we one day will know that some freak mutation made the human insanity and exploration thing possible, it will be amazing to think that it was this little inversion on this chromosome that made all this happen and changed the whole ecosystem of the planet and made us dominate everything," he said at one point. At another, he said, "We are crazy in some way. What drives it? That I would really like to understand. That would be really, really cool to know."

According to the most recent estimates, Neanderthals and modern humans share a common ancestor who lived about four hundred thousand years ago. (It is unclear who that ancestor was, though one possibility is the somewhat shadowy hominid known, after a jawbone found near Heidelberg, as *Homo heidelbergensis*.) The common ancestor of chimps and humans, by contrast, lived some five million to seven million years ago. This means that Neanderthals and humans had less than one-tenth the time to accumulate genetic differences.

Mapping these differences is, in principle, pretty straightforward—no harder, say, than comparing rival editions of "Hamlet." In practice, it's quite a bit more complicated. To begin with, there's really no such thing as *the* human genome; everyone has his or her own genome, and they vary substantially—between you and the person sitting next to you on the subway, the differences are likely to amount to some three million base pairs. Some of these variations correspond to observable physiological differences—the color of your eyes, say, or your likelihood of developing heart disease—and some have no known significance. To a first approximation, a human and a Neanderthal chosen at random would also vary by three million base pairs. The trick is ascertaining which of these millions of variations divide us from them. Pääbo estimates that when the Neanderthal Genome Project is completed, the list of base-pair changes that are at once unique to humans and shared by all humans will number around a hundred thousand. Somewhere in this long list will lie the change—or changes—that made us human to begin with. Identifying these key mutations is where the transgenic mice come in.

From an experimental viewpoint, the best way to test whether any particular change is significant would be to produce a human with the Neanderthal version of the sequence. This would involve manipulating a human stem cell, implanting the genetically modified embryo into a surrogate mother, and then watching the resulting child grow up. For obvious reasons, such Island of Dr. Moreau-like research on humans is not permitted, nor is it necessarily even possible. For similar reasons, such experimentation isn't allowed on chimpanzees. But it is allowed on mice. Dozens of strains of mice have been altered to carry humanized DNA sequences, and new ones are being created all the time, more or less to order.

Several years ago, Pääbo and a colleague, Wolfgang Enard, became interested in a gene known as FOXP2, which in humans is associated with language. (People who have a faulty copy of the gene—an extremely rare occurrence—are capable of speech, but what they say

is, to strangers, mostly incomprehensible.) Pääbo and Enard had some mice bred with a humanized version of the gene, and then studied them from just about every possible angle. The altered mice, it turned out, squeaked at a lower pitch than their un-humanized peers. They also exhibited measurable differences in neural development. (While I was in Leipzig, I watched a graduate student cut the heads off some of the altered mice and then slice up their brains, like radishes.) The Neanderthals' FOXP2 gene, it turns out, is in almost all ways identical to humans', but there is one suggestive base-pair difference. When this difference was discovered, it prompted Pääbo to order up a new round of transgenic mice, which, at the time of my visit, had just been born and were being raised under sterile conditions in the basement.

Genes that seem to play a role in speech are obvious places to look for human-specific changes. But one of the main points of sequencing the Neanderthal genome is that the most obvious places to look may not be the right ones.

"The great advantage with genomics in this form is that it's unbiased," Pääbo told me. "If you go after candidate genes, you're inherently saying what you think the most important thing is. Language, many people would say. But perhaps we will be surprised—perhaps it's something else that was really crucial." Recently, Pääbo has become interested in a gene known as RUNX2, which is involved in bone formation. When members of his team analyzed the human and Neanderthal genomes mathematically, RUNX2 emerged as a place where significant changes in the human lineage seem to have occurred. People who have faulty copies of the RUNX2 gene often develop a condition, known as cleidocranial dysplasia, whose symptoms include such Neanderthal-like features as a flared rib cage. Two genes that have been implicated in autism, CADPS2 and AUTS2, also appear to have changed substantially between Neanderthals and humans. This is interesting because one of the symptoms of autism is an inability to read social cues.

One afternoon, when I wandered into his office, Pääbo showed me a photograph of a skullcap that had recently been discovered by an amateur collector about half an hour from Leipzig. From the photograph, which had been e-mailed to him, Pääbo had decided that the skullcap could be quite ancient—from an early Neanderthal, or even a *Homo heidelbergensis*. He'd also decided that he had to have it. The skullcap had been found at a quarry in a pool of water—perhaps, he theorized, these conditions had preserved it, so that if he got to it soon, he'd be able to extract some DNA. But the skull had already been promised to a professor of anthropology in Mainz. How could he persuade the professor to give him enough bone to test?

Pääbo called everyone he knew who he thought might know the professor. He had his secretary contact the professor's secretary to get the professor's private

cell-phone number, and joked—or maybe only half joked—that he'd be willing to sleep with the professor if that would help. The frenzy of phoning back and forth across Germany lasted for more than an hour and a half, until Pääbo finally talked to one of the researchers in his own lab. The researcher had seen the actual skullcap and concluded that it probably wasn't very old at all. Pääbo immediately lost interest in it.

With old bones, you never really know what you're going to get. A few years ago, Pääbo managed to get hold of a bit of tooth from one of the so-called "hobbit" skeletons found on the island of Flores, in Indonesia. (The "hobbits," who were discovered in 2004, are generally believed to have been diminutive archaic humans—*Homo floresiensis*—though some scientists have argued that they were just modern humans who suffered from microcephaly.) The tooth, which was about seventeen thousand years old, yielded no DNA.

Then, about a year and a half ago, Pääbo obtained a fragment of finger bone that had been unearthed in a cave in southern Siberia along with a weird, vaguely human-looking molar. The finger bone—about the size of a pencil eraser—was believed to be more than forty thousand years old. Pääbo assumed that it came either from a modern human or from a Neanderthal. If it proved to be the latter, then the site would be the farthest east that Neanderthal remains had been found.

In contrast to the hobbit tooth, the finger fragment yielded astonishingly large amounts of DNA. When the analysis of the first bits was completed, Pääbo happened to be in the United States. He called his office, and one of his colleagues said to him, "Are you sitting down?" The DNA showed that the digit could not have belonged to a Neanderthal or to a modern human. Instead, its owner must have been part of some entirely different and previously unsuspected type of hominid. In a paper published in December, 2010, in *Nature*, Pääbo and his team dubbed this group the Denisovans, after the Denisova Cave, where the bone had been found. "GIVING ACCEPTED PREHISTORIC HISTORY THE FINGER," ran the headline on the story in the Sydney *Morning Herald*. Amazingly—or perhaps, by now, predictably—modern humans must have interbred with Denisovans, too, because contemporary New Guineans carry up to six per cent Denisovan DNA. (Why this is true of New Guineans but not native Siberians or Asians is unclear, but presumably has to do with patterns of human migration.)

It has been understood for a long time that modern humans and Neanderthals were contemporaries. The discovery of the hobbits and now the Denisovans shows that humans shared the planet with at least two additional creatures like ourselves. And it seems likely that as DNA from more ancient remains is analyzed still other human relatives will be found; as Chris Stringer, a prominent British paleoanthropologist, told me, "I'm sure we've got more surprises to come."

"If these other forms of humans had survived two thousand generations more, which is not so much, then how would that have influenced our view of the living world?" Pääbo said, once the excitement over the skullcap had passed and we were sitting over coffee. "We now make this very clear distinction between humans and animals. But it might not be as clear. That is sort of an interesting thing to philosophize about." It's also interesting to think about why we're the ones who survived.

Over the decades, many theories have been offered to explain what caused the demise of the Neanderthals, ranging from climate change to simple bad luck. In recent years, though, it's become increasingly clear that, as Pääbo put it to me, "their bad luck was us." Again and again, the archeological evidence in Europe indicates, once modern humans showed up in a region where Neanderthals were living, the Neanderthals in that region vanished. Perhaps the Neanderthals were actively pursued, or perhaps they were just outcompeted. The Neanderthals' "bad luck" is presumably the same misfortune that the hobbits and the Denisovans encountered, and similar to the tragedy suffered by the giant marsupials that once browsed Australia, and the varied megafauna that used to inhabit North America, and the moas that lived in New Zealand. And it is precisely the same bad luck that has brought so many species—including every one of the great apes—to the edge of oblivion today.

"To me, the mystery is not the extinction of the Neanderthals," Jean-Jacques Hublin, the director of the Institute for Evolutionary Anthropology's department of human evolution, told me. "To me the mystery is what makes modern humans such a successful group that they have been replacing not just the Neanderthals but *everything*. We don't have much evi-

dence that the Neanderthals or other archaic humans ever led to an extinction of a species of mammal or anything else. For modern humans, there are hundreds of examples, and we do it very well."

One of the largest assemblages of Neanderthal bones ever found—remains from seven individuals—was discovered about a century ago at a spot known as La Ferrassie, in southwestern France. La Ferrassie is in the Dordogne, not far from La Chapelle and within half an hour's drive of dozens of other important archeological sites, including the painted caves at Lascaux. Over the summer, a team that included one of Pääbo's colleagues was excavating at La Ferrassie, and I decided to go down and have a look. I arrived at the dig's headquarters—a converted tobacco barn—just in time for a dinner of bœuf bourguignonne, which was served on makeshift tables in the back yard.

The next day, I drove out to La Ferrassie with some of the team's archeologists. The site lies in a sleepy rural area, right by the side of the road. Many thousands of years ago, La Ferrassie was a huge limestone cave, but one of the walls has since fallen in, and now it is open on two sides. A massive ledge of rock juts out about twenty feet off the ground, like half of a vaulted ceiling. The site is ringed by a wire fence and hung with tarps, which give it the aspect of a crime scene.

The day was hot and dusty. Half a dozen students crouched in a long trench, picking at the dirt with trowels. Along the side of the trench, I could see bits of bone sticking out from the reddish soil. The bones toward the bottom, I was told, had been tossed there by Neanderthals. The bones near the top were the leavings of modern humans, who occupied La Ferrassie once the Neanderthals were gone. The Neanderthal skeletons from the site had long since been removed, but there was still hope that some stray bit, like a tooth, might be found. Each bone fragment that was unearthed, along with every flake of flint and anything else that might even remotely be of interest, was set aside to be taken back to the headquarters to be sorted and tagged.

After watching the students chip away for a while, I retreated to the shade. I tried to imagine what life had been like for the Neanderthals at La Ferrassie. Though the area is now wooded, then it would have been tundra. There would have been elk roaming the valley, and reindeer and wild cattle and mammoths. Beyond these stray facts, not much came to me. I put the question to the archeologists I had driven out with.

"It was cold," Shannon McPherron, of the Max Planck Institute, volunteered.

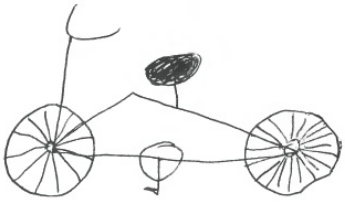
"And smelly," Dennis Sandgathe, of Canada's Simon Fraser University, said.

"Probably hungry," Harold Dibble, of the University of Pennsylvania, added.

"No one would have been very old," Sandgathe said.

Later on, back at the barn, I picked through the bits and pieces that had been dug up over the past few days. There were hundreds of fragments of animal bone, each of which had been cleaned and numbered and placed in its own little plastic bag, and hundreds of flakes of flint. Most of the flakes were probably the detritus of toolmaking—the Stone Age equivalent of wood shavings—but some, I learned, were the tools themselves. Once I was shown what to look for, I could see the bevelled edges that the Neanderthals had crafted. One tool in particular stood out: a palm-size flint shaped like a teardrop. In archeological terms, it was a hand axe, though it probably was not used as an axe in the contemporary sense of the word. It had been found near the bottom of the trench, so it was estimated to be about seventy thousand years old. I took it out of its plastic bag and turned it over. It was almost perfectly symmetrical and—to a human eye, at least—quite beautiful. I said that I thought the Neanderthal who had fashioned it must have had a keen sense of design. McPherron objected.

"We know the end of the story," he told me. "We know what modern culture looks like, and so then what we do is we want to explain how we got here. And there's a tendency to overinterpret the past by projecting the present onto it. So when you see a beautiful hand axe and you say, 'Look at the craftsmanship on this; it's virtually an object of art,' that's your perspective today. But you can't assume what you're trying to prove."



Among the hundreds of thousands of Neanderthal artifacts that have been unearthed, almost none represent unambiguous attempts at art or adornment, and those which have been interpreted this way—for instance, ivory pendants discovered in a cave in central France—are the subject of endless, often abstruse disputes. (Many archeologists believe that the pendants were created by Neanderthals who had come into contact with modern humans and were trying to imitate them, but, relying on the most recent dating techniques, some argue that the pendants were, in fact, created by modern humans.) This paucity has led some to propose that Neanderthals were not capable of art or—what amounts to much the same thing—not interested in it. They simply did not possess what, genomically speaking, might be called the aesthetic mutation.

On my last day in the Dordogne, I decided to visit a nearby human site known for its extraordinary images. The site, Grotte des Combarelles, is a long, very narrow cave that zigzags through a limestone cliff. Hundreds of feet in, the walls of the cave are covered with engravings—a mammoth curling its trunk, a wild horse lifting its head, a reindeer leaning forward, apparently to drink. In very recent times, the floor of the Grotte des Combarelles has been dug out, so that a person can walk in it, and the tunnel is dimly lit by electric lights. But when the etchings were originally created, some twelve or thirteen thousand years ago, the only way to gain access to the site would have been to crawl, and the only way to see in the absolute dark would have been to carry fire. As I crept along through the gloom, past engravings of wisent and aurochs and woolly rhinos, it occurred to me that I really had no clue what would drive someone to wriggle through a pitch-black tunnel to cover the walls with images that only another, similarly driven soul would see. Yet it also struck me that so much of what is distinctively human was here on display—creativity, daring, "madness." And then there were the animals pictured on the walls—the aurochs and mammoths and rhinos. These were the beasts that Paleolithic Europeans had hunted, and then, one by one, as with the Neanderthals, obliterated. ♦