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Taming the Wild

Only a handful of wild animal species have been successfully bred to get along with humans. The reason, scientists say, is found in their genes.

By Evan Ratliff

"Hello! How are you doing?" Lyudmila Trut says, reaching down to unlatch the door of a wire cage labeled "Mavrik." We're standing between two long rows of similar crates on a farm just outside the city of Novosibirsk, in southern Siberia, and the 76-year-old biologist's greeting is addressed not to me but to the cage's furry occupant. Although I don't speak Russian, I recognize in her voice the tone of maternal adoration that dog owners adopt when addressing their pets.

Mavrik, the object of Trut's attention, is about the size of a Shetland sheepdog, with chestnut orange fur and a white bib down his front. He plays his designated role in turn: wagging his tail, rolling on his back, panting eagerly in anticipation of attention. In adjacent cages lining either side of the narrow, open-sided shed, dozens of canids do the same, yelping and clamoring in an explosion of fur and unbridled excitement. "As you can see," Trut says above the din, "all of them want human contact." Today, however, Mavrik is the lucky recipient. Trut reaches in and scoops him up, then hands him over to me. Cradled in my arms, gently jawing my hand in his mouth, he's as docile as any lapdog.

Except that Mavrik, as it happens, is not a dog at all. He's a fox. Hidden away on this overgrown property, flanked by birch forests and barred by a rusty metal gate, he and several hundred of his relatives are the only population of domesticated silver foxes in the world. (Most of them are, indeed, silver or dark gray; Mavrik is rare in his chestnut fur.) And by "domesticated" I don't mean captured and tamed, or raised by humans and conditioned by food to tolerate the occasional petting. I mean bred for domestication, as tame as your tabby cat or your Labrador. In fact, says Anna Kukekova, a Cornell researcher who studies the foxes, "they remind me a lot of golden retrievers, who are basically not aware that there are good people, bad people, people that they have met before, and those they haven't." These foxes treat any human as a potential companion, a behavior that is the product of arguably the most extraordinary breeding experiment ever conducted.

It started more than a half century ago, when Trut was still a graduate student. Led by a biologist named Dmitry Belyaev, researchers at the nearby Institute of Cytology and Genetics gathered up 130 foxes from fur farms. They then began breeding them with the goal of re-creating the evolution of wolves into dogs, a transformation that began more than 15,000 years ago.

With each generation of fox kits, Belyaev and his colleagues tested their reactions to human contact, selecting

those most approachable to breed for the next generation. By the mid-1960s the experiment was working beyond what he could've imagined. They were producing foxes like Mavrik, not just unafraid of humans but actively seeking to bond with them. His team even repeated the experiment in two other species, mink and rats. "One huge thing that Belyaev showed was the timescale," says Gordon Lark, a University of Utah biologist who studies dog genetics. "If you told me the animal would now come sniff you at the front of the cage, I would say it's what I expect. But that they would become that friendly toward humans that quickly... wow."

Miraculously, Belyaev had compressed thousands of years of domestication into a few years. But he wasn't just looking to prove he could create friendly foxes. He had a hunch that he could use them to unlock domestication's molecular mysteries. Domesticated animals are known to share a common set of characteristics, a fact documented by Darwin in *The Variation of Animals and Plants Under Domestication*. They tend to be smaller, with floppier ears and curlier tails than their untamed progenitors. Such traits tend to make animals appear appealingly juvenile to humans. Their coats are sometimes spotted—piebald, in scientific terminology—while their wild ancestors' coats are solid. These and other traits, sometimes referred to as the domestication phenotype, exist in varying degrees across a remarkably wide range of species, from dogs, pigs, and cows to some nonmammals like chickens, and even a few fish.

Belyaev suspected that as the foxes became domesticated, they too might begin to show aspects of a domestication phenotype. He was right again: Selecting which foxes to breed based solely on how well they got along with humans seemed to alter their physical appearance along with their dispositions. After only nine generations, the researchers recorded fox kits born with floppier ears. Piebald patterns appeared on their coats. By this time the foxes were already whining and wagging their tails in response to a human presence, behaviors never seen in wild foxes.

Driving those changes, Belyaev postulated, was a collection of genes that conferred a propensity to tameness—a genotype that the foxes perhaps shared with any species that could be domesticated. Here on the fox farm, Kukekova and Trut are searching for precisely those genes today. Elsewhere, researchers are delving into the DNA of pigs, chickens, horses, and other domesticated species, looking to pinpoint the genetic differences that came to distinguish them from their ancestors. The research, accelerated by the recent advances in rapid genome sequencing, aims to answer a fundamental biological question: "How is it possible to make this huge transformation from wild animals into domestic animals?" says Leif Andersson, a professor of genome biology at Uppsala University, in Sweden. The answer has implications for understanding not just how we domesticated animals, but how we tamed the wild in ourselves as well.

The exercise of dominion over plants and animals is arguably the most consequential event in human history. Along with cultivated agriculture, the ability to raise and manage domesticated fauna—of which wolves were likely the first, but chickens, cattle, and other food species the most important—altered the human diet, paving the way for settlements and eventually nation-states to flourish. By putting humans in close contact with animals, domestication also created vectors for the diseases that shaped society.

Yet the process by which it all happened has remained stubbornly impenetrable. Animal bones and stone carvings can sometimes shed light on the *when* and *where* each species came to live side by side with humans. More difficult to untangle is the *how*. Did a few curious boar creep closer to human populations, feeding off their garbage and with each successive generation becoming a little more a part of our diet? Did humans

capture red jungle fowl, the ancestor of the modern chicken, straight from the wild—or did the fowl make the first approach? Out of 148 large mammal species on Earth, why have no more than 15 ever been domesticated? Why have we been able to tame and breed horses for thousands of years, but never their close relative the zebra, despite numerous attempts?

In fact, scientists have even struggled to define domestication precisely. We all know that individual animals can be trained to exist in close contact with humans. A tiger cub fed by hand, imprinting on its captors, may grow up to treat them like family. But that tiger's offspring, at birth, will be just as wild as its ancestors. Domestication, by contrast, is not a quality trained into an individual, but one bred into an entire population through generations of living in proximity to humans. Many if not most of the species' wild instincts have long since been lost. Domestication, in other words, is mostly in the genes.

Yet the borders between domesticated and wild are often fluid. A growing body of evidence shows that historically, domesticated animals likely played a large part in their own taming, habituating themselves to humans before we took an active role in the process. "My working hypothesis," says Greger Larson, an expert on genetics and domestication at Durham University in the United Kingdom, "is that with most of the early animals—dogs first, then pigs, sheep, and goats—there was probably a long period of time of unintentional management by humans." The word domestication "implies something top down, something that humans did intentionally," he says. "But the complex story is so much more interesting."

The fox-farm experiment's role in unraveling that complexity is all the more remarkable for how it began. The Soviet biology establishment of the mid-20th century, led under Joseph Stalin by the infamous agronomist Trofim Lysenko, outlawed research into Mendelian genetics. But Dmitry Belyaev and his older brother Nikolay, both biologists, were intrigued by the possibilities of the science. "It was his brother's influence that caused him to have this special interest in genetics," Trut says of her mentor. "But these were the times when genetics was considered fake science." When the brothers flouted the prohibition and continued to conduct Mendelian-based studies, Belyaev lost his job as director of the Department of Fur Breeding. Nikolay's fate was more tragic: He was exiled to a labor camp, where he eventually died.

Secretly, Belyaev remained dedicated to genetic science, disguising his work as research in animal physiology. He was particularly consumed with the question of how such an incredible diversity of dogs could have arisen from their wolf ancestors. The answer, he knew, must lie at the molecular level. But even outside the Soviet Union, in the 1950s, the technology to sequence an animal's genome—and thereby try to understand how its genes had changed through history—was an impossible dream. So Belyaev decided to reproduce history himself. The silver fox, a fellow canid and close cousin of dogs that had never been domesticated, seemed the perfect choice.

Lyudmila Trut's first job as a grad student, in 1958, was to travel around to Soviet fur farms and select the calmest foxes she could find, to serve as the base population for Belyaev's experiment. The prohibition on genetic studies had thawed since Stalin's death in 1953, and Belyaev set up shop in Siberia at the newly minted Institute of Cytology and Genetics. Still, he was careful to frame the study only in terms of physiology, leaving out any mention of genes. Trut recalls that when Soviet leader Nikita Khrushchev arrived to inspect the institute, he was overheard to say, "What, are those geneticists still around? Were they not destroyed?" Protected by the careful politics of Belyaev's boss and favorable articles on genetics written by Khrushchev's journalist daughter, the fox-farm experiment quietly began.

By 1964 the fourth generation was already beginning to live up to the researchers' hopes. Trut can still remember the moment when she first saw a fox wag its tail at her approach. Before long, the most tame among them were so doglike that they would leap into researchers' arms and lick their faces. At times the extent of the animals' tameness surprised even the researchers. Once, in the 1970s, a worker took one of the foxes home temporarily as a pet. When Trut visited him, she found the owner taking his fox for walks, unleashed, "just like a dog. I said 'Don't do that, we'll lose it, and it belongs to the institute!'" she recalls. "He said 'just wait,' then he whistled and said, 'Coca!' It came right back."

Simultaneously, more of the foxes began to show signs of the domestication phenotype: floppy ears retained longer in development and characteristic white spots on their coats. "At the beginning of the 1980s, we observed a kind of explosion-like change of the external appearance," says Trut. The research had expanded to include rats in 1972, followed by mink and—for a brief period—river otters. The otters proved difficult to breed and the experiment was eventually abandoned, but the scientists were able to shape the behavior of the other two species in parallel with the foxes.

Just as the genetic tools became available to accomplish Belyaev's end goal of tracing that connection to the animal's DNA, however, the project fell on hard times. With the collapse of the Soviet Union, scientific funds began to dwindle, and the researchers could do little more than keep the fox population alive. When Belyaev died of cancer in 1985, Trut took over the research and fought to keep it funded. But by the beginning of the 21st century, she was in danger of having to shut down the experiment.

Around the same time, Anna Kukekova, a Russian-born postdoc in molecular genetics at Cornell, read about the project's struggles. She had been fascinated with the fox-farm work for years, and now decided to focus her own research on the experiment. With help from Utah's Gordon Lark and a grant from the National Institutes of Health (NIH), she joined Trut's effort to try and finish what Belyaev had started.

Not all the foxes on the farm in Novosibirsk, it turns out, are as friendly as Mavrik. Across the small road from him and his fellow tame foxes is an identical-looking shed full of wire crates, each holding one of what the researchers refer to as the "aggressive foxes." To study the biology of tameness, the scientists needed to create a group of decidedly untame animals. So in a mirror image of the friendly foxes, the kits in the aggressive population are rated according to the hostility of their behavior. Only the most aggressive are bred for the next generation. Here are the evil twins of the tail-wagging Mavrik, straight out of a B-grade horror film: hissing, baring their teeth, snapping at the front of their cages when any human approaches.

"I'd like to draw your attention to this fox," says Trut, pointing to one snarling creature nearby. "You can see how aggressive she is. She was born to an aggressive mother but brought up by a tame mother." The switch, the result of the aggressive mother being unable to feed its kit, serendipitously proved a point: The foxes' response to humans is more nature than it is nurture. "Here," she says, "it's the genetics that change."

Identifying the precise genetic footprint involved in tameness, however, is proving extremely tricky science. First the researchers need to find the genes responsible for creating friendly and aggressive behaviors. Such general behavior traits, however, are actually amalgamations of more specific ones—fear, boldness, passivity, curiosity—that must be teased apart, measured, and traced to individual genes or sets of genes working in combination. Once those genes are identified, the researchers can test whether the ones influencing behavior

are also behind the floppy ears and piebald coats and other features that characterize domesticated species. One theory among the scientists in Novosibirsk is that the genes guiding the animals' behavior do so by altering chemicals in their brains. Changes to those neurochemicals, in turn, have "downstream" impacts on the animals' physical appearance.

For now, though, Kukekova is focused on the first step: linking tame behavior to genes. Toward the end of every summer, she travels from Cornell to Novosibirsk to evaluate the year's newborn kits. Each researcher's interaction with a kit is standardized and videotaped: opening a cage, reaching a hand in, touching the fox. Later, Kukekova reviews the tapes, using objective measures to quantify the foxes' postures, vocalizations, and other behaviors. Those data are layered on top of a pedigree—records that keep track of tame, aggressive, and "crossed" foxes (those with parents from each group).

The joint American-Russian research team then extracts DNA from blood samples of each fox in the study and scans for stark differences in the genomes of those that scored as aggressive or tame in the behavioral measures. In a paper in press in *Behavior Genetics*, the group reports finding two regions that are widely divergent in the two behavioral types and might thus harbor key domestication genes. Increasingly, it appears that domestication is driven not by a single gene but a suite of genetic changes. "Domestication," the paper concludes, "appears to be a very complex phenotype."

As it happens, 2,800 miles to the west in Leipzig, Germany, another laboratory is at the exact same juncture in understanding domestication genes in rats. Frank Albert, a researcher at the Max Planck Institute for Evolutionary Anthropology, obtained 30 descendants of Belyaev's rats (15 tame, 15 aggressive) in two wooden boxes from Siberia in 2004. "What we found were regions of the genome that influence tameness and aggression," says Albert. "But we don't know which genes cause these signals." Like Kukekova's group, he says, "we are in the process of whittling down the number."

Once either group is able to pinpoint one or more of the specific genetic pathways involved, they or other researchers can look for parallel genes in other domesticated species. "In a perfect situation, we'd like to define specific genes involved in tame and aggressive behaviors," says Kukekova. "Even when we find those, we will not know if they are the genes for domestication until we compare them in other animals."

Ultimately, the biggest payoff of the research may come from finding similar genes in the most thoroughly domesticated species of all: human beings. "Understanding what has changed in these animals is going to be incredibly informative," says Elaine Ostrander, of the National Human Genome Research Institute at NIH. "Everyone is waiting with great excitement for what they come out with."

Not all domestication researchers believe that Belyaev's silver foxes will unlock the secrets of domestication. Uppsala University's Leif Andersson, who studies the genetics of farm animals—and who lauds Belyaev and his fellow researchers' contribution to the field—believes that the relationship between tameness and the domestication phenotype may prove to be less direct than the fox study implies. "You select on one trait and you see changes in other traits," Andersson says, but "there has never been proven a causal relationship."

To understand how Andersson's view differs from that of the researchers in Novosibirsk, it's helpful to try and imagine how the two theories might have played out historically. Both would agree that the animals most likely

to be domesticated were those predisposed to human contact. Some mutation, or collection of mutations, in their DNA caused them to be less afraid of humans, and thus willing to live closer to them. Perhaps they fed off human refuse or benefited from inadvertent shelter from predators. At some point humans saw some benefit in return from these animal neighbors and began helping that process along, actively selecting for the most amenable ones and breeding them. "At the beginning of the domestication process, only natural selection was at work," as Trut puts it. "Down the road, this natural selection was replaced with artificial selection."

Where Andersson differs is in what happened next. If Belyaev and Trut are correct, the self-selection and then human selection of less fearful animals carried with it other components of the domestication phenotype, such as curly tails and smaller bodies. In Andersson's view, that theory understates the role humans played in selecting those other traits. Sure, curiosity and lack of fear may have started the process, but once animals were under human control, they were also protected from wild predators. Random mutations for physical traits that might quickly have been weeded out in the wild, like white spots on a dark coat, were allowed to persist. Then they flourished, in part because, well, people liked them. "It wasn't that the animals behaved differently," as Andersson says, "it's just that they were cute."

In 2009 Andersson bolstered his theory by comparing mutations in coat-color genes between several varieties of domesticated and wild pigs. The results, he reported, "demonstrate that early farmers intentionally selected pigs with novel coat coloring. Their motivations could have been as simple as a preference for the exotic or selection for reduced camouflage."

In his own hunt for domestication genes, Andersson is taking a close look at the most populous domesticated animal on Earth: the chicken. Their ancestors, red jungle fowl, roamed freely in the jungles of India, Nepal, and other parts of South and Southeast Asia. Somewhere around 8,000 years ago, humans started breeding them for food. Last year Andersson and his colleagues compared the full genomes of domesticated chickens with those of zoo-based populations of red jungle fowl. They identified a mutation, in a gene known as *TSHR*, that was found only in domestic populations. The implication is that *TSHR* thereby played some role in domestication, and now the team is working to determine exactly what the *TSHR* mutation controls. Andersson hypothesizes that it could play a role in the birds' reproductive cycles, allowing chickens to breed more frequently in captivity than red jungle fowl do in the wild—a trait early farmers would have been eager to perpetuate. The same difference exists between wolves, which reproduce once a year and in the same season, and dogs, which can breed multiple times a year, in any season.

If Andersson's theory is correct, it may turn out to have intriguing implications for our own species. Harvard biologist Richard Wrangham has theorized that we, too, went through a domestication process that altered our biology. "The question of what is the difference between the domestic pig and a wild boar, or the distinction between a broiler chicken and a wild jungle fowl," Andersson told me, "is very similar to the question of what is the difference between a human and a chimpanzee."

Human beings are not simply domesticated chimpanzees, but understanding the genetics of domestication in chickens, dogs, and pigs may still tell us a surprising amount about the sources of our own social behavior. That's one reason the fox-farm research being conducted by Kukekova is underwritten by the NIH. "There are over 14,000 genes expressed in the brain, and not many are understood," she points out. Ferreting out which of those genes are related to social behavior is a tricky business; obviously one cannot perform breeding experiments on humans, and studies purporting to find innate differences in behavior among people or

populations are at the very least problematic.

But delving into the DNA of our closest companions can deliver some tantalizing insights. In 2009 UCLA biologist Robert Wayne led a study comparing the wolf and dog genomes. The finding that made headlines was that dogs originated from gray wolves not in East Asia, as other researchers had argued, but in the Middle East. Less noticed by the press was a brief aside in which Wayne and his colleagues identified a particular short DNA sequence, located near a gene called *WBSCR17*, that was very different in the two species. That region of the genome, they suggested, could be a potential target for "genes that are important in the early domestication of dogs." In humans, the researchers went on to note, *WBSCR17* is at least partly responsible for a rare genetic disorder called Williams-Beuren syndrome. Williams-Beuren is characterized by elfin features, a shortened nose bridge, and "exceptional gregariousness"—its sufferers are often overly friendly and trusting of strangers.

After the paper was published, Wayne says, "the number one email we got was from parents of children suffering from Williams-Beuren. They said, 'Actually our children remind us of dogs in terms of their ability to read behavior and their lack of social barriers in their behavior.'" The elfin traits also seemed to correspond to aspects of the domestication phenotype. Wayne cautions against making one-to-one parallels between domestication genes and something as genetically complex as Williams-Beuren. The researchers are "intrigued," he says, and hoping to explore the connection further.

In 2003 a young researcher at Duke University named Brian Hare traveled out to Novosibirsk. Hare is known for his work cataloging the unique behaviors of dogs and wolves, showing the ways in which dogs have evolved to follow human cues like pointing and eye movements. When he conducted similar tests on fox kits in Siberia, he found that they did just as well as puppies of the same age. The results, while preliminary, suggest that selecting against fear and aggression—what Hare calls "emotional reactivity"—has created foxes that are not just tame but that also have the doglike ability to engage with humans using their social cues.

"They didn't select for a smarter fox but for a nice fox," says Hare. "But they ended up getting a smart fox." This research also has implications for the origins of human social behavior. "Are we domesticated in the sense of dogs? No. But I am comfortable saying that the first thing that has to happen to get a human from an apelike ancestor is a substantial increase in tolerance toward one another. There had to be a change in our social system."

Hare's research came to mind on my last afternoon in Novosibirsk, as Kukekova, my translator Luda Mekertycheva, and I played with Mavrik in a pen behind the fox farm's research house. We watched him chase a ball and wrestle with another fox, then run back so we could grab him up and let him lick our faces. But we all had flights to catch, and after an hour, Kukekova carried him back toward the sheds. Mavrik seemed to sense that he was headed back to his cage and whined with increasing agitation. Here was an animal biologically conditioned for human attention, as much as any dog is. Now that we'd provided it, I suddenly felt guilty for taking it away.

The fox-farm experiment is, of course, just that: a scientific experiment. For decades the project has been forced to manage their population by selling off to real fur farms those foxes not friendly or aggressive enough to be research candidates. For the scientists, deciding which ones stay and which ones go is a harrowing process; Trut says she has long since passed on the job to others and stays away from the farm during selection

time. "It is very difficult emotionally," she told me.

In recent years the institute has been working to obtain permits to sell the surplus tame foxes as pets, both domestically and in other countries. It would be a way not just to find a better home for the unwanted foxes, they suggest, but also to raise money for the research to continue. "The situation today is we are just doing our best to preserve our population," Trut says. "We do some genetic work with our partners in America. But this experiment has many more questions to resolve."

As for Mavrik, Luda Mekertycheva was so enthralled by the chestnut-colored fox and another playmate that she decided to adopt them. They arrived at her dacha outside of Moscow a few months later, and not long after, she emailed me an update. "Mavrik and Peter jump on my back when I kneel to give them food, sit when I pet them, and take vitamins from my hand," she wrote. "I love them a lot."

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