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Bringing Them Back to Life

The revival of an extinct species is no longer a fantasy.
But is it a good idea?

By Carl Zimmer

On July 30, 2003, a team of Spanish and French scientists reversed time. They brought an animal back from extinction, if only to watch it become extinct again. The animal they revived was a kind of wild goat known as a *bucardo,* or Pyrenean ibex. The bucardo *(Capra pyrenaica pyrenaica)* was a large, handsome creature, reaching up to 220 pounds and sporting long, gently curved horns. For thousands of years it lived high in the Pyrenees, the mountain range that divides France from Spain, where it clambered along cliffs, nibbling on leaves and stems and enduring harsh winters.

Then came the guns. Hunters drove down the bucardo population over several centuries. In 1989 Spanish scientists did a survey and concluded that there were only a dozen or so individuals left. Ten years later a single bucardo remained: a female nicknamed Celia. A team from the Ordesa and Monte Perdido National Park, led by wildlife veterinarian Alberto Fernández-Arias, caught the animal in a trap, clipped a radio collar around her neck, and released her back into the wild. Nine months later the radio collar let out a long, steady beep: the signal that Celia had died. They found her crushed beneath a fallen tree. With her death, the bucardo became officially extinct.

But Celia’s cells lived on, preserved in labs in Zaragoza and Madrid. Over the next few years a team of reproductive physiologists led by José Folch injected nuclei from those cells into goat eggs emptied of their own DNA, then implanted the eggs in surrogate mothers. After 57 implantations, only seven animals had become pregnant. And of those seven pregnancies, six ended in miscarriages. But one mother—a hybrid between a Spanish ibex and a goat—carried a clone of Celia to term. Folch and his colleagues performed a cesarean section and delivered the 4.5-pound clone. As Fernández-Arias held the newborn bucardo in his arms, he could see that she was struggling to take in air, her tongue jutting grotesquely out of her mouth. Despite the efforts to help her breathe, after a mere ten minutes Celia’s clone died. A necropsy later revealed that one of her lungs had grown a gigantic extra lobe as solid as a piece of liver. There was nothing anyone could have done.

The dodo and the great auk, the thylacine and the Chinese river dolphin, the passenger pigeon and the imperial woodpecker—the bucardo is only one in the long list of animals humans have driven extinct, sometimes deliberately. And with many more species now endangered, the bucardo will have much more company in the years to come. Fernández-Arias belongs to a small but passionate group of researchers who believe that cloning can help reverse that trend.

The notion of bringing vanished species back to life—some call it de-extinction—has hovered at the boundary between reality and science fiction for more than two decades, ever since novelist Michael Crichton unleashed the dinosaurs of Jurassic Park on the world. For most of that time the science of de-extinction has lagged far behind the fantasy. Celia’s clone is the closest that anyone has gotten to true de-extinction. Since witnessing those fleeting minutes of the clone’s life, Fernández-Arias, now the head of the government of Aragon’s Hunting, Fishing and Wetlands department, has been waiting for the moment when science would finally catch up, and humans might gain the ability to bring back an animal they had driven extinct.

“We are at that moment,” he told me.

I met Fernández-Arias last autumn at a closed-session scientific meeting at the National Geographic Society’s headquarters in Washington, D.C. For the first time in history a group of geneticists, wildlife biologists, conservationists, and ethicists had gathered to discuss the possibility of de-extinction. Could it be done? Should it be done? One by one, they stood up to present remarkable advances in manipulating stem cells, in recovering ancient DNA, in reconstructing lost genomes. As the meeting unfolded, the scientists became increasingly excited. A consensus was emerging: De-extinction is now within reach.

"It's gone very much further, very much more rapidly than anyone ever would've imagined," says Ross MacPhee, a curator of mammalogy at the American Museum of Natural History in New York. "What we really need to think about is why we would want to do this in the first place, to actually bring back a species."

In *Jurassic Park* dinosaurs are resurrected for their entertainment value. The disastrous consequences that follow have cast a shadow over the notion of de-extinction, at least in the popular imagination. But people tend to forget that Jurassic Park was pure fantasy. In reality the only species we can hope to revive now are those that died within the past few tens of thousands of years and left behind remains that harbor intact cells or, at the very least, enough ancient DNA to reconstruct the creature's genome. Because of the natural rates of decay, we can never hope to retrieve the full genome of *Tyrannosaurus rex,* which vanished about 65 million years ago. The species theoretically capable of being revived all disappeared while humanity was rapidly climbing toward world domination. And especially in recent years we humans were the ones who wiped them out, by hunting them, destroying their habitats, or spreading diseases. This suggests another reason for bringing them back.

"If we're talking about species we drove extinct, then I think we have an obligation to try to do this," says Michael Archer, a paleontologist at the University of New South Wales who has championed de-extinction for years. Some people protest that reviving a species that no longer exists amounts to playing God. Archer scoffs at the notion. "I think we played God when we exterminated these animals."

Other scientists who favor de-extinction argue that there will be concrete benefits. Biological diversity is a storehouse of natural invention. Most pharmaceutical drugs, for example, were not invented from scratch—they were derived from natural compounds found in wild plant species, which are also vulnerable to extinction. Some extinct animals also performed vital services in their ecosystems, which might benefit from their return. Siberia, for example, was home 12,000 years ago to mammoths and other big grazing mammals. Back then, the landscape was not moss-dominated tundra but grassy steppes. Sergey Zimov, a Russian ecologist and director of the Northeast Science Station in Cherskiy in the Republic of Sakha, has long argued that this was no coincidence: The mammoths and numerous herbivores maintained the grassland by breaking up the soil and fertilizing it with their manure. Once they were gone, moss took over and transformed the grassland into less productive tundra.

In recent years Zimov has tried to turn back time on the tundra by bringing horses, muskoxen, and other big mammals to a region of Siberia he calls Pleistocene Park. And he would be happy to have woolly mammoths roam free there. "But only my grandchildren will see them," he says. "A mouse breeds very fast. Mammoths breed very slow. Be prepared to wait."

When Fernández-Arias first tried to bring back the bucardo ten years ago, the tools at his disposal were, in hindsight, woefully crude. It had been only seven years since the birth of Dolly the sheep, the first cloned mammal. In those early days scientists would clone an animal by taking one of its cells and inserting its DNA into an egg that had been emptied of its own genetic material. An electric shock was enough to get the egg to start dividing, after which the scientists would place the developing embryo in a surrogate mother. The vast majority of those pregnancies failed, and the few animals that were born were often beset with health problems.

Over the past decade scientists have improved their success with cloning animals, shifting the technology from high-risk science to workaday business. Researchers have also developed the ability to induce adult animal cells to return to an embryo-like state. These can be coaxed to develop into any type of cell—including eggs or sperm. The eggs can then be further manipulated to develop into full-fledged embryos.

Such technical sleights of hand make it far easier to conjure a vanished species back to life. Scientists and explorers have been talking for decades about bringing back the mammoth. Their first—and so far only—achievement was to find well-preserved mammoths in the Siberian tundra. Now, armed with the new cloning technologies, researchers at the Sooam Biotech Research Foundation in Seoul have teamed up with mammoth experts from North-Eastern Federal University in the Siberian city of Yakutsk. Last summer they traveled up the Yana River, drilling tunnels into the frozen cliffs along the river with giant hoses. In one of those tunnels they found chunks of mammoth tissue, including bone marrow, hair, skin, and fat. The tissue is now in Seoul, where the Sooam scientists are examining it.

"If we dream about it, the ideal case would be finding a viable cell, a cell that's alive," says Sooam's Insung Hwang, who organized the Yana River expedition. If the Sooam researchers do find such a cell, they could coax it to produce millions of cells. These could be reprogrammed to grow into embryos, which could then be implanted in surrogate elephants, the mammoth's closest living relatives.

Most scientists doubt that any living cell could have survived freezing on the open tundra. But Hwang and his colleagues have a Plan B: capture an intact nucleus of a mammoth cell, which is far more likely to have been preserved than the cell itself. Cloning a mammoth from nothing but an intact nucleus, however, will be a lot trickier. The Sooam researchers will need to transfer the nucleus into an elephant egg that has had its own nucleus removed. This will require harvesting eggs from an elephant—a feat no one has yet accomplished. If the DNA inside the nucleus is well preserved enough to take control of the egg, it just might start dividing into a mammoth embryo. If the scientists can get past that hurdle, they still have the formidable task of transplanting the embryo into an elephant's womb. Then, as Zimov cautions, they will need patience. If all goes well, it will still be almost two years before they can see if the elephant will give birth to a healthy mammoth.

"The thing that I always say is, if you don't try, how would you know that it's impossible?" says Hwang.

In 1813, while traveling along the Ohio River from Hardensburgh to Louisville, John James Audubon witnessed one of the most miraculous natural phenomena of his time: a flock of passenger pigeons *(Ectopistes migratorius)* blanketing the sky. "The air was literally filled with Pigeons," he later wrote. "The light of noon-day was obscured as by an eclipse, the dung fell in spots, not unlike melting flakes of snow; and the continued buzz of wings had a tendency to lull my senses to repose."

When Audubon reached Louisville before sunset, the pigeons were still passing overhead—and continued to do so for the next three days. "The people were all in arms," wrote Audubon. "The banks of the Ohio were crowded with men and boys, incessantly shooting at the pilgrims... Multitudes were thus destroyed."

In 1813 it would have been hard to imagine a species less likely to become extinct. Yet by the end of the century the red-breasted passenger pigeon was in catastrophic decline, the forests it depended upon shrinking, and its numbers dwindling from relentless hunting. In 1900 the last confirmed wild bird was shot by a boy with a BB gun. Fourteen years later, just a century and a year after Audubon marveled at their abundance, the one remaining captive passenger pigeon, a female named Martha, died at the Cincinnati Zoo.

The writer and environmentalist Stewart Brand, best known for founding the *Whole Earth Catalog* in the late 1960s, grew up in Illinois hiking in forests that just a few decades before had been aroar with the sound of the passenger pigeons' wings. "Its habitat was my habitat," he says. Two years ago Brand and his wife, Ryan Phelan, founder of the genetic-testing company DNA Direct, began to wonder if it might be possible to bring the species back to life. One night over dinner with Harvard biologist George Church, a master at manipulating DNA, they discovered that he was thinking along the same lines.

Church knew that standard cloning methods wouldn't work, since bird embryos develop inside shells and no museum specimen of the passenger pigeon (including Martha herself, now in the Smithsonian) would likely contain a fully intact, functional genome. But he could envision a different way of re-creating the bird. Preserved specimens contain fragments of DNA. By piecing together the fragments, scientists can now read the roughly one billion letters in the passenger pigeon genome. Church can't yet synthesize an entire animal genome from scratch, but he has invented technology that allows him to make sizable chunks of DNA of any sequence he wants. He could theoretically manufacture genes for passenger pigeon traits—a gene for its long tail, for example—and splice them into the genome of a stem cell from a common rock pigeon.

Rock pigeon stem cells containing this doctored genome could be transformed into germ cells, the precursors to eggs and sperm. These could then be injected into rock pigeon eggs, where they would migrate to the developing embryos' sex organs. Squabs hatched from these eggs would look like normal rock pigeons—but they would be carrying eggs and sperm loaded with doctored DNA. When the squabs reached maturity and mated, their eggs would hatch squabs carrying unique passenger pigeon traits. These birds could then be further interbred, the scientists selecting for birds that were more and more like the vanished species.

Church's genome-retooling method could theoretically work on any species with a close living relative and a genome capable of being reconstructed. So even if the Sooam team fails to find an intact mammoth nucleus, someone might still bring the species back. Scientists already have the technology for reconstructing most of the genes it takes to make a mammoth, which could be inserted into an elephant stem cell. And there is no shortage of raw material for further experiments emerging from the Siberian permafrost. "With mammoths, it's really a dime a dozen up there," says Hendrik Poinar, an expert on mammoth DNA at McMaster University in Ontario. “It’s just a matter of finances now.”

Though the revival of a mammoth or a passenger pigeon is no longer mere fantasy, the reality is still years away. For another extinct species, the time frame may be much shorter. Indeed, there’s at least a chance it may be back among the living before this story is published.

The animal in question is the obsession of a group of Australian scientists led by Michael Archer, who call their endeavor the Lazarus Project. Archer previously directed a highly publicized attempt to clone the thylacine, an iconic marsupial carnivore that went extinct in the 1930s. That effort managed to capture only some fragments of the thylacine’s DNA. Wary of the feverish expectations that such high-profile experiments attract, Archer and his Lazarus Project collaborators kept quiet about their efforts until they had some preliminary results to offer.

That time has come. Early in January, Archer and his colleagues revealed that they were trying to revive two closely related species of Australian frog. Until their disappearance in the mid-1980s, the species shared a unique—and utterly astonishing—method of reproduction. The female frogs released a cloud of eggs, which the males fertilized, whereupon the females swallowed the eggs whole. A hormone in the eggs triggered the female to stop making stomach acid; her stomach, in effect, became a womb. A few weeks later the female opened her mouth and regurgitated her fully formed babies. This miraculous reproductive feat gave the frogs their common names: the northern *(Rheobatrachus vitellinus)* and southern *(Rheobatrachus silus)* gastric brooding frogs.

Unfortunately, not long after researchers began to study the species, they vanished. “The frogs were there one minute, and when scientists came back, they were gone,” says Andrew French, a cloning expert at the University of Melbourne and a member of the Lazarus Project.

To bring the frogs back, the project scientists are using state-of-the-art cloning methods to introduce gastric brooding frog nuclei into eggs of living Australian marsh frogs and barred frogs that have had their own genetic material removed. It’s slow going, because frog eggs begin to lose their potency after just a few hours and cannot be frozen and revived. The scientists need fresh eggs, which the frogs produce only once a year, during their short breeding season.

Nevertheless, they’ve made progress. “Suffice it to say, we actually have embryos now of this extinct animal,” says Archer. “We’re pretty far down this track.” The Lazarus Project scientists are confident that they just need to get more high-quality eggs to keep moving forward. “At this point it’s just a numbers game,” says French.

The matchless oddity of the gastric brooding frogs’ reproduction drives home what we lose when a species becomes extinct. But does that mean we should bring them back? Would the world be that much richer for having female frogs that grow little frogs in their stomachs? There are tangible benefits, French argues, such as the insights the frogs might be able to provide about reproduction—insights that might someday lead to treatments for pregnant women who have trouble carrying babies to term. But for many scientists, de-extinction is a distraction from the pressing work required to stave off mass extinctions.

“There is clearly a terrible urgency to saving threatened species and habitats,” says John Wiens, an evolutionary biologist at Stony Brook University in New York. “As far as I can see, there is little urgency for bringing back extinct ones. Why invest millions of dollars in bringing a handful of species back from the dead, when there are millions still waiting to be discovered, described, and protected?”

De-extinction advocates counter that the cloning and genomic engineering technologies being developed for de-extinction could also help preserve endangered species, especially ones that don’t breed easily in captivity. And though cutting-edge biotechnology can be expensive when it’s first developed, it has a way of becoming very cheap very fast. “Maybe some people thought polio vaccines were a distraction from iron lungs,” says George Church. “It’s hard in advance to say what’s distraction and what’s salvation.”

But what would we be willing to call salvation? Even if Church and his colleagues manage to retrofit every passenger pigeon–specific trait into a rock pigeon, would the resulting creature truly be a passenger pigeon or just an engineered curiosity? If Archer and French do produce a single gastric brooding frog—if they haven’t already—does that mean they’ve revived the species? If that frog doesn’t have a mate, then it becomes an amphibian version of Celia, and its species is as good as extinct. Would it be enough to keep a population of the frogs in a lab or perhaps in a zoo, where people could gawk at it? Or would it need to be introduced back into the wild to be truly de-extinct?

“The history of putting species back after they’ve gone extinct in the wild is fraught with difficulty,” says conservation biologist Stuart Pimm of Duke University. A huge effort went into restoring the Arabian oryx to the wild, for example. But after the animals were returned to a refuge in central Oman in 1982, almost all were wiped out by poachers. “We had the animals, and we put them back, and the world wasn’t ready,” says Pimm. “Having the species solves only a tiny, tiny part of the problem.”

Hunting is not the only threat that would face recovered species. For many, there’s no place left to call home. The Chinese river dolphin became extinct due to pollution and other pressures from the human population on the Yangtze River. Things are just as bad there today. Around the world frogs are getting decimated by a human-spread pathogen called the chytrid fungus. If Australian biologists someday release gastric brooding frogs into their old mountain streams, they could promptly become extinct again.

“Without an environment to put re-created species back into, the whole exercise is futile and a gross waste of money,” says Glenn Albrecht, director of the Institute for Social Sustainability at Murdoch University in Australia.

Even if de-extinction proved a complete logistical success, the questions would not end. Passenger pigeons might find the rebounding forests of the eastern United States a welcoming home. But wouldn’t that be, in effect, the introduction of a genetically engineered organism into the environment? Could passenger pigeons become a reservoir for a virus that might wipe out another bird species? And how would the residents of Chicago, New York, or Washington, D.C., feel about a new pigeon species arriving in their cities, darkening their skies, and covering their streets with snowstorms of dung?

De-extinction advocates are pondering these questions, and most believe they need to be resolved before any major project moves forward. Hank Greely, a leading bioethicist at Stanford University, has taken a keen interest in investigating the ethical and legal implications of de-extinction. And yet for Greely, as for many others, the very fact that science has advanced to the point that such a spectacular feat is possible is a compelling reason to embrace de-extinction, not to shun it.

“What intrigues me is just that it’s really cool,” Greely says. “A saber-toothed cat? It would be neat to see one of those.”

Carl Zimmer’s award-winning blog, the Loom, is hosted by *National Geographic*. Robb Kendrick also used 19th-century tintype photography in a story on 21st-century cowboys in the December 2007 issue.
