**Fact or Fiction?: Mammoths Can Be Brought Back from Extinction**

Is de-extinction a real possibility? Jun 10, 2014 By [David Biello](http://www.scientificamerican.com/author/david-biello)

In a petri dish in the bowels of Harvard Medical School scientists have tweaked three genes from the cells of an Asian elephant that help control the production of hemoglobin, the protein in blood that carries oxygen. Their goal is to make these genes more like those of an animal that last walked the planet thousands of years ago: the [woolly mammoth](http://blogs.scientificamerican.com/guest-blog/2013/03/18/cloning-woolly-mammoths-its-the-ecology-stupid/).

"Asian elephants are closer to mammoths than either is to African elephants, yet quite different in appearance and temperature range," notes Harvard geneticist and technology developer [George Church](http://www.scientificamerican.com/article.cfm?id=george-church-de-extinction-is-a-good-idea). "We are not trying to make an exact copy of a mammoth, but rather a cold-resistant elephant."

But what if the new—and fast advancing—techniques of genome editing allowed scientists to engineer not only cold-resistance traits but also other characteristics of the woolly mammoth into its living Asiatic relatives? Scientists have found mammoth cells preserved in permafrost. If they were to recover cells with intact DNA, they could theoretically “edit” an [Asian elephant’s genome](http://www.broadinstitute.org/scientific-community/science/projects/mammals-models/elephant/elephant-genome-project) to match the woolly mammoth’s. A single cell contains the complete genetic instruction set for its species, and by replicating that via editing a new individual can, theoretically, be created. But would [such a hybrid](http://www.scientificamerican.com/article/lost-species-revived-from-dna-and-restored-to-nature/)—scion of an Asian elephant mother and genetic tinkerers—count as a true woolly mammoth?

In other words, is [de-extinction](http://www.scientificamerican.com/podcast/episode/extinction-may-not-be-forever-13-03-31/) a real possibility?

The answer is yes. On January 6, 2000, a falling tree killed the last bucardo, a wild Iberian ibex, which is a goatlike animal. Her name was Celia. On July 30, 2003, Celia's clone was born. To make the clone scientists removed the nucleus of a cell from Celia intact and inserted it into the unfertilized egg cell of another kind of ibex. They then transferred the resulting embryo to the womb of a living goat. Nearly a year later they [delivered the clone](http://www.scientificamerican.com/article/de-extinction-to-bring-back-extinct-species-but-challenges-conservation/) by cutting her from her mother.

Although she lived for a scant seven minutes due to lung defects, Celia’s clone proved that not only is de-extinction real, "it has already happened," in the words of environmentalist Stewart Brand, whose San Francisco-based Long Now Foundation is funding some of this de-extinction research, including Church's effort as well as bids to bring back the passenger pigeon and heath hen, among other [candidate species](http://longnow.org/revive/candidates/). Nor is the bucardo alone in the annals of de-extinction. Several viruses have already been brought back, including the [flu variant responsible for the 1918 pandemic](http://www.cdc.gov/flu/about/qa/1918flupandemic.htm) that killed more than 20 million people worldwide.

And yet, the bucardo remains extinct. The lack of progress stems partly from a lack of funds, according to Alberto Fernández-Arias, the Spanish wildlife veterinarian who helped lead the bucardo cloning effort. But it also has to do with flaws in the method used to bring the species back to life. Researchers in Asia have been using the technique for a decade or more to try to [resurrect the mammoth](http://www.scientificamerican.com/article/de-extinction-to-bring-back-extinct-species-but-challenges-conservation/)—to no avail.

New genome editing techniques—in particular the CRISPR system Church and his team are using—offer new hope, however. In 1987 Japanese scientists found genetic sequences dubbed "clustered regularly interspaced short palindromic repeats" in [*Escherichia coli*](http://www.scientificamerican.com/podcast/episode/everything-you-ever-wanted-to-know-08-10-08/) bacteria. These CRISPRs, as they are known, were subsequently found to be ubiquitous in many bacteria, where they defend against viruses—a simple but effective immune system.

Specifically, the enzyme known as [Cas9](http://arep.med.harvard.edu/pdf/Mali_nmet_13.pdf) (for CRISPR-associated system 9) can attach itself to specific DNA in a virus and cut it, following the lead of an RNA guide. That cut kills the pathogen or at least disables it. And now geneticists, armed with the right RNA sequence to guide Cas9 exactly where they want it to go (an outcome still not always guaranteed), can unleash this editor from the *Streptococcus pyogenes* bacteria to add or subtract code from many genes, such as those that produce hemoglobin in the Asian elephant genome or even genes in human cells. Moreover, with the right RNA guide CRISPR can edit up to five genes at once—a number that keeps growing as scientists continue to experiment. And RNA is quick and cheap to make with machines.

Combined with Church's own technique— a combination of robotics and genetic experimentation known as "multiplex automated genome engineering," or MAGE—the entire five billon or so base pairs of the Asian elephant genome can be broken down into their constituent parts and then reassembled in the image of a [mammoth's genetic code](http://www.scientificamerican.com/article/woolly-mammoth-genome-sequenced/). As it stands, Church and his team have tinkered with three genes and hope to test their viability in organs soon. "We need to construct and characterize Asian elephant stem cells and organs derived from these [stem cells]," he says.

This new technique is not confined to just resurrecting extinct species. Yeast, tobacco, rice, wheat, rats, rabbits, frogs and fruit flies are just a few of the 20 or so organisms to have their genes altered this way to date. The tinkering could prove profound: Church has suggested that the genes that protect certain [extremophile bacteria](http://www.scientificamerican.com/article/cheating-dna-death-how-an/) against the harmful effects of radiation could be added to the human genome to enable long-distance space travel, to take one far-out example.

Such genome editing could also be used to add much needed genetic diversity back into species with precariously small populations, such as the cheetah or [Sumatran rhino](http://www.onearth.org/articles/2014/03/in-the-case-of-saving-the-sumatran-rhino-is-incest-best). By taking DNA from dead individuals and incorporating it into the genomes of survivors, what were gene puddles might be restored to gene pools.

Such species play critical roles in their home ranges, helping shape entire forests or savannas. And that's the hope for a resurrected bucardo or woolly mammoth as well. The mammoth steppe of Siberia might be brought back one day, along with the great herds of woolly proboscideans. The woolly Asian elephant hybrids Church envisions might even help stave off the new global warming human society is presently engineering by sequestering CO2 in a restored Siberian steppe, according to Russian geophysicist Sergey Zimov**,** who has lead efforts to create such a [Pleistocene Park](http://www.pleistocenepark.ru/en/) in northeastern Siberia. Of course, introduction of any species, even one that used to live in a particular place, could prove difficult because it would have to coexist with plants, humans and other animals that have adapted to living in an area without the introduced species.

Ultimately, given the primary focus of genetic advances like CRISPR, the easiest species to resurrect would not be the recently [vanished passenger pigeon](http://www.scientificamerican.com/article/lost-species-revived-from-dna-and-restored-to-nature/) or the mammoth—it would be the Neandertal. There appear to be just slightly more than 30,000 genetic mutations that differentiate us from them—and *Homo sapiens* is the complicated organism best understood by human geneticists.

But resurrecting an extinct hominid opens a new dimension to the ethical concerns around this scientific potential. "Neandertals were sentient human beings," [wrote evolutionary geneticist Svante Pääbo](http://www.nytimes.com/2014/04/25/opinion/neanderthals-are-people-too.html) of the Max Planck Institute for Evolutionary Anthropology in Germany in a recent *New York Times* op–ed. "In a civilized society we would never create a human being in order to satisfy scientific curiosity," he observed. Pääbo and his colleagues were the first to sequence the Neandertal genome.

Such [de-extinction](http://blogs.scientificamerican.com/culturing-science/2013/03/15/deextinction/)—whether of Neandertal or mammoth—may never come to pass, but the technologies that make it possible could help prevent extinction in the first place by restoring genetic vigor to imperiled species. And with human activities currently fueling a [new mass extinction](http://www.scientificamerican.com/podcast/episode/sixth-extinction-wipes-out-animals-08-10-09/), perhaps it is good that de-extinction continues to edge further away from fiction and closer to fact. Or, as Church notes of the fact of de-extinction: "I'm skeptical that there will be a [clean defining moment](http://longnow.org/revive/tedxdeextinction/tedxdeextinction-2013/)."