## Recipe for a Resurrection Bringing extinct species back to life is no longer considered science fiction. But is it a good idea? By Tom Mueller

Last November, when a team led by Teruhiko Wakayama, a reproductive biologist based in Kobe, Japan, reported it had cloned mice that had been frozen for 16 years, the scientists conjectured that the same techniques might open the door to cloning mammoths and other extinct species preserved in permafrost.

"I laughed when Steven Spielberg said that cloning extinct animals was inevitable," says Hendrik Poinar of McMaster University, an authority on ancient DNA who served as a scientific consultant for a film about the making of *Jurassic Park*. "But I'm not laughing anymore. This is going to happen. It's just a matter of working out the details."

As Poinar himself admits, however, the details are daunting. The two fundamental steps involved in cloning an extinct animal, are to recover its complete DNA sequence—in the case of mammoths, estimated to be more than 4.5 billion base pairs long—and to express this data in flesh and blood. The publication of the partial mammoth genome is a good start on the first problem, though the remaining 30 percent of the genome would have to be recovered and the entire genome re-sequenced several more times to weed out errors that have crept into the ancient DNA over the centuries as it degraded. Scientists would also have to package the DNA into chromosomes—and at present they don't even know how many chromosomes the mammoth had. Yet none of these tasks appears insurmountable, especially in light of recent technical advances, such as a new generation of high-speed sequencers and a simple, inexpensive technique for recovering high-quality DNA from mammoth hair. "It's a simple question of time and money, not of technology anymore," says Schuster.

Transforming this data into a woolly mammoth will be far trickier, though the existence of close living relatives, the African and Asian elephants, helps. The Penn State team used the African elephant genome as a guide to reassemble the pieces of mammoth DNA they'd recovered from hair samples. Since this ancient DNA is far too fragmented to use to create an organism, one way to make living mammoth genetic material might be to modify elephant chromosomes at each of the estimated 400,000 sites where they differ from the mammoth's, effectively rewriting an elephant's cells into a mammoth's. If researchers can figure out how mammoth DNA was organized into chromosomes, another strategy would be to synthesize the entire genome from scratch, although so far the largest genome to be synthesized was only a thousandth the size of the mammoth's.

Once scientists have functional mammoth chromosomes in hand, they could wrap them in a membrane to create an artificial cell nucleus. Then they could follow the approach pioneered in creating Dolly, the sheep cloned in 1996 by scientists at the Roslin Institute in Scotland: Remove the nucleus of an elephant's egg and replace it with the rebuilt mammoth nucleus, electrically stimulate the egg to trigger initial cell division into an embryo, and eventually transfer the embryo into an elephant's womb for gestation. Each of these steps has significant question marks of its own. No one knows, for example, just how to build a mammoth nucleus. Harvesting an elephant egg is difficult, and bringing a mammoth fetus to term in an elephant uterus is fraught with uncertainties.

Some scientists are tackling a less daunting challenge: cloning endangered or recently extinct animals. The San Diego Zoo and the Audubon Center for Research of Endangered Species in New Orleans both maintain "frozen zoos," where the DNA of a growing number of endangered species is stored in tanks of liquid nitrogen at minus 320° Fahrenheit. In 2003 scientists at Advanced Cell Technology used cells stored at the San Diego facility to successfully clone across the species barrier. They created two bantengs, an endangered Southeast Asian ox, by inserting banteng DNA into domestic cow eggs and placing the resulting embryos in cow fostermothers. There is talk of using similar methods to clone endangered giant pandas, African bongo antelopes, and Sumatran tigers. Ultimately scientists hope to re-create extinct species like the Pyrenean ibex and the thylacine, or Tasmanian tiger.

Today the thorniest questions about cloning extinct species may be less technical than ethical. "Mammoths, like elephants, were intelligent, highly social animals," says Adrian Lister, paleontologist and mammoth expert at the Natural History Museum in London. "Cloning would give you a single animal, which would live all alone in a park, a zoo, or a lab—not in its native habitat, which no longer exists. You're basically creating a curio." Tom Gilbert, an expert in ancient DNA at Copenhagen University who with Schuster and Webb pioneered the harvesting of mammoth DNA from hair, admits that as a student of mammoths, he'd be the first to go see one trundle across a paddock. But he questions both the utility and the wisdom of cloning extinct species. "If you can do a mammoth, you can do anything else that's dead, including your grandmother. But in a world in global warming and with limited resources for research, do you really want to bring back your dead grandmother?"

## Oddbox by bOb gOnZalez



## Science in the News #8 Name:

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