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How to Clone a Mammoth: the science of de-extinction

Beth Shapiro Princeton University Press 978-0-691-15705-4

The conceit of this disturbing, thoughtful book is that it is a how-to manual, a cookbook for wannabe lords of (re)creation. Nine of the eleven chapters cover steps in the process of bringing an animal back from extinction, beginning with how to select an organism to resurrect, and ending with how to look after it once it is released into the wild. Along the way, the reader is treated to a sometimes dry exposition of the basic principles of recombinant DNA technology. Toggling between witty pop science and tedious genetics textbook, it is a bit of an uneven read, but well worth the effort, because Beth Shapiro knows whereof she speaks. She and her colleagues at the U. C. Santa Cruz 'Ancient DNA laboratory' study, among other things, the genetics of the mammoth, a cold-adapted relative of the elephant not seen on this planet for 37 centuries. A few years ago, Shapiro was contacted by the mayerick environmentalist Steward Brand, who recruited her to a network of scientists engaged in developing the basic genetic manipulation techniques required for de-extinction.

In 1968, in the first issue of the Whole Earth Catalog, his instruction manual for geeky DIY liberationists, Stewart Brand announced 'We are as gods and might as well get good at it.' [203] His line now, nearly half a century later, is that we *must* get good at exercising our Olympian powers as we hurtle ever-closer to ecological catastrophe. For Brand, de-extinction - along with nuclear energy and geoengineering (deliberately introducing reflective particles into the atmosphere to mitigate the greenhouse effect) - is one of the more promising technologies to help us ride out global warming. Every month the members of his 'Revive & Restore' organization connect via teleconference to share news of their progress towards the goal of resurrecting mammoths, dodos, passenger pigeons, etc. [123] Partly as a result of Brand's missionary zeal, most people Shapiro hangs out with 'believe that de-extinction is inevitable.' [xi] 'I'm nearly certain,' she says 'that someone will claim to have achieved de-extinction within the next several years.' [13]

So, how *does* an aspiring deity go about the astonishing business of reversing the extinction of the mammoth? First, Shapiro instructs us, find a well-preserved mammoth bone from which the whole genome can be sequenced. Then identify the differences between it and the genome of its nearest living relative, in this case the Asian elephant. Tweak the elephant genome to make the animal hairy, fatty, metabolically cold-tolerant, and in possession of enormous curly tusks. Engineer a cell containing the tweaked DNA. Turn the cell into an embryo. Implant the embryo into the womb of a female Asian elephant. Wait for a baby mammoth to be born. [pp. 11-12]

Each step of this process is at least theoretically achievable, given the current state of genetic technology. The devil, of course, is in the details, and most of the book is devoted to a thoughtful rehearsal of the difficulties and complexities of the undertaking, as well as the reservations Shapiro has about its desirability. She describes herself as an 'enthusiastic realist' about the project. This means that she lists the daunting obstacles in the path of de-extinction, as well as some of the compelling reasons we might want to call a halt to the whole endeavor, while at the same time cheerfully insisting that on balance it's a good thing, and will happen soon anyway whether we like it or not. She comes across as disarmingly modest and refreshingly cautious, and it is a relief to learn that the de-extinction project is in such sensible hands.

Shapiro teaches ecology at Santa Cruz, and one year she set her graduate students the task of choosing an extinct species to bring back. She was taken aback by the reasons the students gave for their choices. Every student selected a species that humans had wiped out, tempting Shapiro to make a diagnosis of liberal guilt. No-one chose anything small or undistinguished-looking, perhaps indicating a shallow aesthetic bent driving the choices. As for the students' stated motivations, they ranged from 'this species is scientifically interesting,' to 'this one will be good for tourism,' to 'this one will be relatively easy to engineer.' [19-20]

It is a little discouraging to learn that U.C. Santa Cruz graduate students in ecology, whom one used fondly to imagine as dreadlockadorned tree-dwellers, should be so, well, unecological. In fairness, her students did come up with one idea of ecosystem benefit: reintroduce the Yangtze River Dolphin in order to goad the Chinese government into cleaning up the Yangtze River, a chain of reasoning so expensive, wasteful, backwards and perverse as to seem quite politically plausible.

Shapiro's vision of de-extinction is focused *entirely* on the larger ecological benefits to be reaped from the exercise. For her the goal is not to satisfy scientific curiosity or stimulate tourism, but to reintroduce keystone species in order to initiate a cascade of effects congenial to restoring pre-human levels of biodiversity. One controversial proposal for environmental regeneration involves the reintroduction of large herbivores into the wild, on the grounds that their big feet trample and turn over the soil, their excrement transports seeds and fertilizes the ground, their selective grazing of woody plants opens up space for more diverse flora, and so on. [161] Some advocates for this 'rewilding' argue for the release of exotic megafauna, such as Asian and African elephants, from American zoos, in order that they might take up the empty ecological niches of longextinct species. Shapiro persuasively integrates de-extinction into the rewilding project, arguing that it makes more sense to genetically reengineer hairy mammoths to do the job than to hope against reason that tropical elephants will learn to enjoy winter snow.

Stewart Brand's current favorite candidate for resurrection is the passenger pigeon. The attraction for him seems to be its status as an icon of human destructiveness. Enormous flocks of passenger pigeons once darkened the North American skies. One such flock, witnessed by the ornithologist John Audubon, took three days to pass overhead. It was said that a single bullet fired directly upwards could bring down fifty or more birds. Hunted for cheap meat and pillow feathers, passenger pigeons declined catastrophically at the turn of the twentieth century. The last one, a female named Martha, expired in Cincinnati Zoo on September 1st, 1914.

The narrative arc of the passenger pigeon story is undeniably dramatic. There were so many of them. And then, because of human greed, there was only one. In our remorse, we gave the last passenger pigeon a name, and recorded the exact date of her passing. Despite the poignancy of Martha's demise, one gets the impression that Shapiro does not share Brand's enthusiasm for the species: "Flocking in the billions, hungry passenger pigeons could destroy the entire seed crop of a forest stand in very little time," she observes. "When they nested, as many as five hundred birds would nest in a single tree, and when they left the nests, they tended to leave behind dead trees covered in bird droppings." Yuck. It's one thing to mourn the passing of the last passenger pigeon. It turns out to be quite another to contemplate a vast flock of de-extinct birds sweeping through the suburbs and farmlands of twenty-first-century America, leaving in its wake a trail of tree-skeletons dripping with shit. [37]

Desirability aside, many of the practical difficulties attendant upon deextinction may be summed up with a single word: epigenetics. Formally speaking, 'epigenetics' refers to everything outside of the gene itself that might affect its expression, from chemicals attached to DNA that turn genes on and off, to the ecosystems in which whole organisms live and reproduce. It takes more than the correct DNA sequence to make a functioning animal. An egg cell, for example, doesn't just provide a nice warm place for an embryo to grow; it is a complex system of stimulants and suppressants that initiates the orderly development of the organism. A mismatch between egg and DNA throws the whole process off, and so the closer-related the surrogate species is to the 'target' species, the better the chances of success. The line of descent leading to Asian elephants and mammoths diverged some seven or eight million years ago, at about the same time as the human line split off from the other great apes. Using an elephant womb to grow a mammoth baby, in other words, would be a bit like a woman gestating a chimp.

Shapiro makes the alien womb problem particularly vivid with the example of the Steller's sea cow, a large marine mammal that was hunted to extinction by hungry sailors in the eighteenth century. The nearest relative of the Steller's sea cow is a dugong. This makes the dugong uterus the obvious candidate for resurrecting the Steller's sea cow if not for one impediment: 'a newborn calf will be somewhere in the range of three to six meters long. Longer, at birth, than his surrogate mom.' [46] The image of a de-extinct fetus bursting the boundaries of its surrogate parent may be an apt symbol of the combined folly, grandeur, and difficulty of the whole enterprise.

The epigenetic problems with de-extinction do not end with the birth of a healthy infant. Baby Asian elephants dine off the feces of their mothers in order to ingest the microbes needed to break down the woody plants on which they will feed for the rest of their lives. Mammoths did the same thing. "Will it be necessary to reconstruct mammoth gut microbes?" Shapiro asks. [13] Having created a healthy mammoth baby and fed it de-extinct dung, scientists will then have to repeat the trick again and again, using subtly different DNA sequences, in order to generate the genetic diversity needed for a sustainable living population. Finally, once they have a herd of not-completelyidentical baby mammoths able to digest the toughest shrubbery, they will then have somehow to teach the poor little beasts their natural behaviors – without anyone really having a clue what those might be.

To illustrate this problem, Shapiro recounts the story of the California condor, down to a mere 22 individuals in the early 1980s. An intensive program of captive hatching was initiated. The incubated condor chicks had to be raised by humans. How were the humans going to teach the birds to be birds? The answer the surrogate parents came up with was both heroic and absurd. They made puppets resembling the heads of California condors. After watching videos of condor parents interacting with their young, they then used the puppets to implement "an appropriately strict, condor-like parenting style."

This *Sesame Street* approach to interspecies pedagogy enjoyed only limited success, and the human-raised condors apparently turned into

the avian equivalent of sullen teenagers: "Rather than shy away from humans, they preferred to play with garbage, hang about on roofs chewing on loose tiles, and stare disdainfully at rock climbers from above," Shapiro drily remarks. [179] California condors now number in the hundreds, but the populations still require a lot of management, including annual veterinary visits to clean their blood of contaminants in the food chain.

It is greatly to Beth Shapiro's credit that she presents so many of the downsides and obstacles to the de-extinction game. After she gave a TEDx talk about de-extinction in 2013, she got both hate mail and fan mail, and so she is now a veteran of the standard objections. The 'moral hazard' argument – once de-extinction is a possibility, we will cease to worry about wiping things out – she thinks is an overly pessimistic view of human nature. She does admit that de-extinction might cause animal suffering, but she offers our growing understanding of the needs of animals in captivity as a solution. To the argument that resurrected species have nowhere to go, she responds with the hope that de-extinction 'may act as a beacon for new investment and new solutions, which would equally benefit existing conservation projects.' [198] The 'playing God' objection is simply tedious old hat, and she points out that we have been manipulating nature from the time of the domestication of the grey wolf some 30,000 years ago. She cheerfully concedes that 'the product of deextinction won't be the same as the original species,' but doesn't see this as a problem, given that ecological restoration is the aim of the whole enterprise: "We don't need to create exact replicas of extinct species to achieve this goal," she says. "Instead we can engineer species that are alive today so that they can act as proxies for extinct species." [205]

It is clear from the lucid honesty of this book, however, that an astounding amount of waste and expense will be involved. "We'll need hundreds, even thousands, of elephant eggs for this work," Shapiro says. "Elephants are struggling to make enough elephants sustain healthy populations; the last thing they need is for us to be snooping around their ovaries stealing their precious few mature eggs." For Shapiro, this would be a deal-breaker, if it were not for the fact that "there may be another way" (an oft-repeated sentiment in the book). In 1998, a group of scientists managed to get a genetically-engineered mouse to produce "a slightly misshapen elephant egg." [150]. So, if we get tons of mice to produce tons of elephant eggs, we might be able to turn at least a few cells containing genetically-re-engineered mammoth DNA into viable embryos, which we will then try and implant into elephant wombs. Even with an endless supply of elephant eggs, the chances of success are vanishingly slim. The one "successful" de-extinction on record was of a bucardo, a species of mountain goat that went extinct in 2000. Cells from the ear of 'Celia,' the last bucardo, were defrosted and transferred into 782 eggs of domestic goats. 407 of these developed into embryos. Of these, 208 were transferred into surrogate hosts. Seven pregnancies were established. Only one lasted to term. The resulting baby bucardo lived for less than ten minutes. To anyone unfamiliar with the submerged iceberg of heroic failures and mindnumbing repetitions on which the tip of scientific achievement is built, these odds seem laughable. But biology has overcome these odds before, and doubtless will again.

For all that Shapiro makes such a good, sensible, balanced case, it is still possible to walk away from her book with an uneasy feeling. Some sufferers from ecological anxiety, including myself, cannot relinquish the forlornly Luddite conviction that the challenge is to figure out how to reduce human impact by doing *less*. Mammoth de-extinction is a rather fantastical and extreme example of the opposite impulse. But maybe Steward Brand and his fellow enthusiasts are right. We need to undo the damage that we have done. And so far, we seem to be absolutely incapable of simply unpicking it, and going backwards, even to the 1990s, let alone anything remotely resembling pre-industrial levels of consumption and pollution. Given the insatiability of human curiosity and appetite, perhaps the only way to go backwards is to go forwards, full-bore, into the science fiction future.