Revive & Restore (2012–)

Revive & Restore is a California-based nonprofit that uses genetic engineering to help solve conservation problems, such as saving endangered species and increasing the biodiversity of ecosystems. To facilitate their solutions, Revive & Restore utilizes genetic engineering, which is the process of making changes to an organism's DNA, or the set of instructions for how an organism develops and functions. One of their broad solutions is genetic rescue, which involves imbuing populations of endangered species with a wider variety of traits to make them more adaptable to a changing environment. Their other solution is de-extinction, which takes a more radical approach by attempting to recreate extinct species that performed important roles in their ecosystems. While scientists working with Revive & Restore have helped advance genome editing technology on a theoretical and technical level, their research has also prompted practical and ethical concerns over the extent of permissible human interference with nature, even when attempting to conserve it.

Husband and wife Stewart Brand and Ryan Phelan founded Revive & Restore in 2012. Brand trained as a biologist at Stanford University in Stanford, California, and is an entrepreneur who created two health-care companies, including Direct Medical Knowledge, which WebMD purchased in the late 1990s, and DNA Direct, a genetic testing company. Phelan met Brand when she applied for a job to work at a magazine that he started, called Whole Earth Catalog. After marrying in 1983, they moved to San Francisco, California, and became involved in a number of conservation projects.

Revive & Restore's de-extinction projects focus on reversing global species losses by devising new technologies capable of recreating extinct species altogether. While some researchers generally have described de-extinction as an approach that could bring extinct species back to life, the researchers at Revive & Restore use a method of genetic engineering technology that does not aim to actually yield a perfect recreation of the extinct species. Instead, they use technologies that enable them to edit DNA to such a degree that they can create species similar those that are extinct. One of those technologies is Multiplex Automated Genome Engineering, or MAGE, which lets genetic engineers alter multiple sites in an organism's genome at once to eventually resemble the genomes of their extinct relatives more closely. Revive & Restore expects their researchers will be able to harness those technologies to create modified animals that will fulfill their de-extinction conservation goals.

Revive & Restore also uses a genetic engineering technology known as CRISPR-cas9, which is a genome editing tool derived from bacteria that allows for scientists to cut out specific sequences of DNA and replace them with other sequences. Revive & Restore suggests that altering the genomes of certain members of an endangered species can cause the population to become more genetically diverse by adding genes that code for traits the population might not carry. Genetic diversity is a measure of how many different kinds of traits exist within a population or species. In general, greater genetic diversity tends to make populations of organisms more adaptable to changing environmental conditions. That is because with greater genetic diversity, there is a higher probability that more organisms within the population are carrying traits that could make them better suited to different environments. Revive & Restore suggests that having greater genetic diversity within a population can make it easier for the population to adapt to unpredictable conditions such as climate change or habitat loss. In combination with de-extinction, their goal is to use biotechnology and genetic engineering to empower conservation efforts from a new approach.

The first de-extinction project that Revive & Restore attempted was the passenger pigeon. In February 2012, Phelan organized a workshop to bring de-extinction researchers together at the Wyss Institute for Biologically Inspired Engineering at Harvard University in Cambridge, Massachusetts.

There, the scientists discussed the feasibility of de-extincting the passenger pigeon, a bird that was once abundant along North America's east coast but driven to extinction by hunters in 1914. Conservationists have historically associated the extinction of the passenger pigeon as the catalyst for the US conservation movements, largely because it was the first species to go extinct primarily due to human activity. Additionally, the passenger pigeon was also an important species in its ecosystem. Large flocks of passenger pigeons would regularly create random disturbances in the forests they inhabited by breaking branches, which inadvertently created areas of the forest with more sun exposure and diversified the types of environments other species could inhabit.

In order to de-extinct the passenger pigeon, Revive & Restore planned to edit the genome of the passenger pigeon's closest living relative, the band-tailed pigeon, so that it looked and functioned the way passenger pigeons once had. While the de-extinction process would not produce an exact replica of a passenger pigeon, it would theoretically generate an organism that could perform its ecological functions and initiate those same disturbances within the forests. However, the project to de-extinct the passenger pigeon is still ongoing as of 2020.

Revive & Restore continued to apply the theory behind de-extinction to other species. In 2015, they announced plans to de-extinct the woolly mammoth, a species that died out around 4,000 years ago. Like the utility of the passenger pigeon, woolly mammoths played a critical role in their Arctic ecosystem by trampling the ground and causing a form of healthy destruction that created a more diverse habitat for a wider variety of species to occupy. However, scientists like Sergey Zimov, a researcher of ecology in Russia, believe that reintroducing mammoth-like creatures could diminish the Arctic permafrost, which is a thick layer of frozen soil found across tundra. A mammoth or similar animal could cause the permafrost to melt and release significant amounts of greenhouse gases that are trapped within the ice, thereby further potentially contributing to global warming. When they were alive, mammoths trampled and cleared away snow, exposing the permafrost to cold winter air that kept it permanently frozen. Without large grazing animals like mammoths presently in the Arctic, snow covers the permafrost and prevents it from freezing entirely, making it thaw more easily when temperatures increase.

In 2016, Revive & Restore submitted a proposal to the US Fish and Wildlife Service for permission to apply genetic rescue techniques in an attempt to save the black-footed ferret, an endangered species living in the western US. The species was first listed as endangered in 1967, after ferret populations were decimated by local ranchers. Ecologists had previously believed black-footed ferrets were extinct until researchers found a small population in the 1980s. Scientists managed to capture twenty-six black-footed ferrets and began a captive breeding program to introduce them back into the wild and increase their numbers. While researchers have successfully introduced over 300 ferrets back into the wild as of 2020, those wild populations are not very genetically diverse because the population all descended from a very small group of black-footed ferrets. Their low genetic diversity makes wild ferret populations more susceptible to diseases which could drive them to extinction once more.

Revive & Restore made plans to restore genetic diversity to black-footed ferret populations using cryopreserved ferret cells from the San Diego Frozen Zoo, which keeps a large reserve of cryopreserved DNA from species around the world. Revive & Restore researchers suggested they could clone the DNA of ferrets from thirty years ago and implant that DNA into the egg cell of a domestic ferret, a close relative of the black-footed ferret. They could then use a domestic ferret to act as a surrogate for a black-footed ferret in order to create a hybrid organism of the two species that carries unique black-footed ferret DNA. They would then introduce individuals from the hybrid population back into wild black-footed ferret populations in order to spread the different genes to other ferrets and increase that population's genetic diversity. In 2018, the US Fish and Wildlife Service approved Revive & Restore to begin testing genomic technologies in order to solve the genetic diversity problem of wild black-footed ferrets.

On top of de-extinction and genetic rescue projects, Revive & Restore led projects to promote the use of biotechnology in conservation in other ways. In 2018, Revive & Restore launched a project focusing on saving the endangered horseshoe crab, a species heavily relied on by the pharmaceutical industry because a compound within the crab's blood can effectively detect bacterial contamination. Revive & Restore released a study confirming the effectiveness of rFC, a synthetic alternative to

horseshoe crab blood that the pharmaceutical industry could use instead, thereby sparing the crabs. As a result of their discovery, a pharmaceutical business named Eli Lilly and Company pledged to switch to rFC instead of horseshoe crab blood. As of 2020, Revive & Restore continues to advocate for more companies to make the switch.

Additionally, in 2018, Revive & Restore launched its Catalyst Science Fund with the intent to fund other projects with similar goals. The fund launched in collaboration with Promega, a Wisconsin-based biotechnology manufacturer that pledged three million dollars to the Catalyst Science Fund. Since its launch, the Catalyst Science Fund has awarded grants to several projects focused on helping species such as coral, Asian elephants, sea stars, and additional efforts for black-footed ferrets.

The topic of de-extinction made media headlines numerous times during the 2010s. In March 2013, Revive & Restore hosted a TED conference called TEDxDeExtinction in collaboration with National Geographic to publicize the conversation on de-extinction. A series of speakers with experience in history and technology related to de-extinction delivered talks discussing how de-extinction would work and why they felt it could become a necessity. Supporters largely saw de-extinction as a way to make up for past mistakes that drove species like the passenger pigeon to extinction while revitalizing ecosystems. On the other hand, critics claimed that de-extinction was inadequate because it would not address many human activities that continue to drive species toward extinction.

Additionally, skeptics such as Stuart Pimm, a conservation biology researcher, worried that species created through de-extinction could actually end up harming a habitat more than helping it. Because the organisms created through de-extinction are not genetically identical to the extinct ones, he suggests it will be hard for an animal to adopt the exact niches that were once done by the extinct species, especially without parents or a herd teaching them social behaviors. Additionally, the ecosystems that those organisms are being introduced into may have already evolved to exist without them. Because of that, introducing new organisms may disrupt the balance evolved in their absence. Lastly, Susan Clayton, a researcher of conservation psychology, among other critics, suggested that if extinction suddenly seems like a reversible process, it may decrease support for conservation because people may believe that they have no responsibility in any further extinctions. For critics like Pimm and Clayton, the risks of de-extinction may outweigh the benefits.

Revive & Restore has promoted the applications of biotechnology while producing substantial debates over the obligation for humans to correct the consequences of their own actions in nature. Revive & Restore has pushed the limits of genome editing technology by undergoing projects like the de-extinction of the passenger pigeon and the woolly mammoth, and by using biotechnology to help endangered species like the black-footed ferret and horseshoe crab. If successful, researchers suggest that de-extinction and genetic rescue technologies may help slow the rising rates of biodiversity loss, and in cases such as the woolly mammoth, could also help mitigate the effects of climate change. Although there is a potential risk, as of 2020 Revive & Restore continues to present their ideas at annual international science conferences such as the International Union for the Conservation of Nature, which calls itself a global authority on the measures needed to safeguard the planet.

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