"Bringing Back the Passenger Pigeon" meeting convened at Harvard Medical School in Boston on Feb. 8, 2012

Report by Stewart Brand
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Participants

George Church - genomic engineer, Harvard Medical School

Beth Shapiro - evolutionary molecular biologist, University of California, Santa Cruz

Scott Edwards - Curator of Ornithology, Museum of Comparative Zoology, Harvard

Noel Snyder - ornithologist, California condor rescue

Joel Greenberg - writer, The Passenger Pigeon Project

David Blockstein - ornithologist, The Passenger Pigeon Project

Hank Greely - bioethicist, Stanford

Jamie Shreeve - Science Editor, *National Geographic*

Stewart Brand - co-convener, The Long Now Foundation

Ryan Phelan - co-convener, former CEO of DNA Direct

From back left: Scott Edwards, Stewart Brand, George Church, Hank Greely, Noel Snyder, Beth Shapiro, David Blockstein, Jamie Shreeve, Ryan Phelan, Joel Greenberg

The first purpose of the daylong meeting was to explore the technical plausibility of reviving the iconic extinct bird, *Ectopistes migratorius*, through genomic engineering. The last passenger pigeon remaining of the billions that once dominated the forests of eastern America died a century ago, in September 1914.

The second purpose of the meeting was to explore the potential cultural, social, political, and ecological ramifications of bringing the passenger pigeon back to life and perhaps restoring it to the wild. Also: if any extinct animal could be revived, would the passenger pigeon be the best candidate to start with? (Other candidates include the Carolina parakeet, heath hen, ivory-billed woodpecker, Labrador duck, great auk, and woolly mammoth.)

Stewart Brand suggested that the first campaign to bring back an extinct species will wind up framing, for good or ill, all subsequent attempts. He proposed that the ultimate goal be "deep ecological enrichment through extinct species revival." Genetic technology is moving so rapidly that amateurs may be able to revive extinct genelines within decades. It would be preferable to have a full set of publicly understood norms for proceeding responsibly in place by that time. Ryan Phelan noted that experiments in de-extinction may also provide new scientific knowledge that could be applied to helping save endangered species.

George Church and his "Multiplex Automated Genome Engineering" (MAGE) machine at the Wyss Institute, Boston.

George Church began by saying that the technical capabilities of reading and writing genetic code are increasing eightfold every year, with costs also dropping exponentially, and that rate is holding steady. We are now able to replace specific genes using "zinc finger nucleases," even in extremely difficult genomes. It's a form of enhanced homologous recombination. "You can make as little as one base pair change without touching the rest of the genome." In addition his lab has recently developed a technique called "Multiplex Automated Genome Engineering" (MAGE) that can engineer multiple changes over millions of base pairs by tricking replication. "You can take a piece of DNA out of your favorite organism, move it into e. coli, make a lot of changes---five changes every three hours, and then take that big piece of DNA and move it back. You can carefully craft the DNA in its normal place."

George Church's "lab in a box" Polonator G007

The whole process is made easier by a device his lab built which writes and reads DNA. It allows you to correct your results as you go along. You can even note the effects on organisms on the slide and then select the ones you want. For larger organisms, this form of “genome editing” can be tested on cells and tissues before you go for a whole bird. There has already been some genome engineering with chickens, to make them resistant to avian influenza. Working with primordial germ cells, you introduce the changes into the embryo in the egg---lots easier than trying to reach the embryo in a mammal. (Also the genome is simpler. Mice and humans have 3 billion base pairs; birds have 1.5 billion.)

The closest relative of the passenger pigeon is the band-tailed pigeon (*Patagioenas fasciata*), which is common in the American west. Church’s idea is to sequence both birds (there are hundreds of specimens of the passenger pigeon in museums), compare their genomes, and then gene by gene (trait by trait) transform the band-tailed genome into that of a passenger pigeon.

Band-tailed Pigeon

For example, a passenger pigeon has a much longer tail than a band-tailed pigeon. Once you’ve found the genome sequence that determines the tail length, you replace that sequence in the band-tailed pigeon with the tail-length sequence from the passenger pigeon. You take, say, twelve changes you want---a few for tail size, a few for color (red eye, peach-colored breast), a few that are behavioral---check that each set works in separate birds and then breed them conventionally until you get all twelve in one bird. “Identifying which genes to target may be the hardest part, especially the behavioral genes.”

David Blockstein commented that in captivity some pigeons can go from egg to next generation egg in as short as six months. Scott Edwards wondered if twelve gene changes might get you 80% of the way to a passenger pigeon, but it could take a thousand more to get you all the way. Beth Shapiro asked, “What is the threshold for making a species a species?” Jamie Shreeve suggested the term “proxy passenger pigeon” for the initial reconstructed bird. It would not yet be totally identical genomically to the original passenger pigeon but may embody its most significant characteristics.

Comparative tail lengths: passenger pigeon (left) and band-tailed pigeon (right)

The group then went across a courtyard to the Wyss Institute to view Church's spectacular hardware. The first was the Polonator G007 from Dover, perched on a table like an airport-lounge coffee machine. Church: "It's basically a whole lab in a box. You can read and write DNA. You can do biochemistry. You can do cell biology." In the next room was the current version of the MAGE machine, the size of a kitchen refrigerator on its side. "You can make up to a billion genomes a day for combinatorial exploration. "What would be the cost these days of building a passenger pigeon genomically? Church figured that if you did twelve strains in parallel, each with twelve mutations (constructs), you get 144 mutations. It might cost $100,000 per strain to get it into the bird. The whole process might take five years.

Beth Shapiro reported on her experience sequencing "ancient DNA" from woolly mammoths, bison and horse bones, dodos, and passenger pigeons. Along with DNA reads from the target species you get contamination from creatures in the soil, things that colonize the bone, from people, and from mysterious sources. Of the reads they got from one well-preserved, frozen woolly mammoth, some 45% were "alignable" with current elephant DNA. That's considered very good. What other groups got from Neanderthals was only 0.1% - 2% alignable with primates.

The genetic reads she got from passenger pigeon specimens are in between---about 25%, which is plenty to work with. Samples were taken from toe pads, the base of feathers, and muscle tissue, from nine specimens so far. Her research has focussed on traces of historic population dynamics discoverable in the genomes of animals such as bison. A reduction in genetic diversity would suggest that the population was getting smaller, potentially heading toward a bottleneck, and that crisis can be roughly dated. Studying nine specimens of passenger pigeons from the Royal Ontario Museum showed that they had very high genetic diversity.

She now has a great many short reads from the passenger pigeon genome, but they have yet to be mapped against a similar living genome. Her group has been using the common rock pigeon. A band-tailed pigeon would be better. Getting more DNA samples from more passenger pigeon specimens would help. The goal is a complete and annotated genome. The cost of their passenger pigeon work so far ("not including person time") has been about $10,000. The cost of thoroughly sequencing the band-tailed pigeon (there are some in captivity) might be about $60,000, Shapiro concluded.

Any attempt to restore revived passenger pigeons to the wild will have to operate with good knowledge about what elements led to their extinction in the first place, because those elements must be anticipated and overcome this time around, or there's little hope. (It may be that 21st-century genomic analysis and attempts to rewild the bird have the side-benefit of revealing the true causes of the original extinction.)

Passenger pigeon nest and customary single egg

David Blockstein probed the standard explanations of the precipitous decline of the bird population from billions to thousands in 25 years---massive hunting, habitat loss, mysterious disease---and he made the case for constrained reproduction. The bird seemed to mate most successfully only in huge groups, and it laid a single egg on a flimsy, conspicuous nest. Its ecological success may have depended too exclusively on "predator satiation"---overwhelming predators with sheer numbers---and when that was compromised, the rest of its defenses may have been too feeble. "Once its population dropped below a certain level, the passenger pigeon may have been ecologically extinct long before the last birds died."

Joel Greenberg argued that the literature indicates that there were many small groups who nested successfully. Even more than with their overwhelming numbers, the pigeons evaded predators (including Indians) by roosting, nesting, and feeding in different places every year. Once Americans had the telegraph to spread the word about where the birds were massing each year, that former advantage turned into the pigeon's greatest vulnerability.

Noel Snyder drew on his decades of experience saving the California condor (22 birds left in 1987; 400 alive now, half of them back in the wild) to consider potential problems with captive breeding and release to the wild of reconstructed passenger pigeons. "Politics can often overwhelm everything else that you're trying to do." California condors are still not safe in the wild because gun enthusiasts refuse to use non-lead bullets, and the condors keep being poisoned by lead in carcasses that hunters leave. The very problem that caused the near extinction of the bird has not been corrected.

Scott Edwards opined that the passenger pigeon may be a pretty good candidate for re-establishment in the wild. It's small enough to reproduce rapidly. Being nomadic and irruptive (migrates in large numbers), it can find and occupy favorable habitats. There are 309 species of pigeons, which suggests they adapt and speciate readily. Much of the eastern deciduous forest has grown back since the 1880s, and commercial hunting has stopped.

Hank Greely addressed "the ethical, legal, and social issues that this project might raise." He thinks that quite different issues will arise in its two phases---1) recreating the passenger pigeon and 2) releasing it into the wild.

The passgenger pigeon's famously alert, red eye and peach-colored breast. (Photo by Joel Sartore)

The issues with the first phase should be minor. "Some will think it's wrong because they think we're playing God. Others will think it's wrong because they think we're usurping the deity they call Nature." Visceral reactions like that could come from both left and right. But any potential ecological risks from recreating the species don't matter so long as it is kept in a controlled environment. Some will worry that if you can revive extinct species, then you undercut efforts to keep endangered species from going extinct. (A similar argument was made against seat belts in cars---people will feel invulnerable and drive more dangerously.)

Once you consider releasing the birds, now the question is, what are the risks? The habitat the bird was once native to has been replaced by different forests and many more people. Will it cause eco-disruption? Could it be a disease vector? You may get political opposition from farmers or from hunters. Would the bird have to go through the exhaustive bureaucratic process that GMO crops face? (Is it really a transgenic organism? All its genes are pigeon genes, edited precisely.) The Environmental Protection Agency would get involved, and Environmental Impact Reports would be required. One advantage of recreating the bird genetically and breeding it in captivity for years is that you would gain a lot of information to help manage its reintroduction to the wild.

Brand proposed that, as the project chugs along, the public will have years to comprehend and discuss the prospects of bringing back an extinct species. "This generation gets to rethink extinction, gets to rethink habitat loss and habitat restoration, and gets to ponder the role of biotechnology in protecting biodiversity. Welcome to a very interesting century."

The group finished by contemplating next steps. Jamie Shreeve urged moving ahead on the proposed genetic technique to see if it works and how it can be improved. Plans for a "Revive and Restore" conference in the Fall of 2012 were discussed---perhaps hosted by National Geographic, perhaps by Stanford. As for near-term public visibility of the proposed scheme to Bring Back the Passenger Pigeon (or other extinct species), the group agreed that everyone at the meeting should feel free to raise the subject with anyone while at the same time being careful to lower expectations. The de-extinction idea is being explored; there are LOTS of reasons it may not work.

Financial report: The cost of the meeting was about $10,000, mostly for travel and lodging, and was provided by Ryan Phelan. The meeting room we owe to Harvard Medical School.