The future of ancient DNA-Can we remake extinct species?

Where is the science of ancient DNA taking us?

Michael Hofreiter, of the University of York, best known for his work on ancient horses, cattle, and cave bears, says he's not comfortable with predicting the future of ancient DNA. And no wonder. Pressed into service as a forecaster at a recent <u>Royal Society meeting on ancient DNA</u>, Hofreiter pointed out that nobody would have predicted as recently as 5 years ago that by the end of 2013, we would possess complete genomes not only from today's version of *Homo sap*, but also the <u>modern human genome from 24,000 years ago that I wrote about here last week</u>–plus complete genomes of two of our recent forebears. (That's the Neandertals and those mystery Siberians called Denisovans, known only from a teen girl's finger bone and a couple of teeth from other individuals.)

Nor was it foreseeable that these new human genomes and other paleontological studies would force so much rethinking of human evolution. This revisionism has involved a somewhat shocked recognition that the human desire to move around and play around are not recent inventions. Judging from headlines, that came as a surprise to some.

The bad news: What's not possible with ancient DNA

First, Hofreiter shared the bad news about what is probably **not** forthcoming from studies of ancient DNA.

- No dinosaur genomes.
- No genome, probably, from *Homo floresiensis*, the hobbit from the Indonesian island of Flores, whose bones lay for thousands of years in <u>the worst possible conditions for DNA preservation: hot</u> <u>and wet</u>. Hofreiter hedged a bit here because recovery and analysis of ancient DNA has improved so much.
- No DNA much older than about a million years, with an outside chance of older DNA fragments from very cold environments.

And now the good news about the future of ancient DNA

What we probably will see, according to Hofreiter, is lots more paleogenomes, quite a safe bet. Many more human genomes but also animals, domestic and otherwise, and plants, and microbes, especially bacteria. And the more paleogenomes there are, the more scientists can figure out evolutionary relationships among species–although that won't always be possible.

What can be done with paleogenomes? Phylogenetics-tracing evolutionary relationships among groups of organisms.

Also phenotype studies. With a good quality genome a scientist can discern observable

traits–biochemistry, something of what an organism looked like, how it developed, what diseases it was susceptible to, sometimes even behavior. Hofreiter noted that much was made of the <u>2007 news that</u> <u>some Neandertals were redheads</u> (although Neandertal genes for red hair were not the same as ours.) But, he also noted, there are lots of genes more interesting than hair color, for example hemoglobin.

In fact, a genome yields the DNA sequence of any protein the ancient organism could construct, including information on amino acid substitutions that might make the protein function in a different way (or not at all.) But figuring out function requires other sorts of scientists to be part of the paleo team, Hofreiter said. Scientists such as biochemists and physiologists will be essential "so we can figure out what the hell the ancient genomes we get mean in terms of the physiology of the animal and the adaptations of the animal."

Paleogenomes also make it possible to infer gene flow, which is a decorous term for interbreeding. Now we know, for example, that human genetic history has been a network rather than the lineal descent that was for so long conventional wisdom. Studies of gene flow would be a major contribution to understanding the evolution of species, but according to Hofreiter, they are only possible with a lot of genomic data.

The future of ancient DNA technology

That we have paleogenomes of so many species already–animal, vegetable, and microbial–is due entirely to technology that didn't exist 5 years ago, technology that has achieved DNA sequencing speeds formerly unimaginable and at much lower cost.

Another technical development will be ways of fishing out sequences where there's a lot of environmental clutter. Hofreiter is particularly enthusiastic about <u>hybridization capture</u>. He says this approach makes it possible to get very small DNA fragments, which in turn makes it possible to go farther back in time.

Paleogenomics has expanded way beyond trying to extract DNA from fossil bones and teeth. The substrates now include soft tissue, hair, parchment, and even calculus, those deposits of calcium salts and microbes that the dental hygienist scrapes off your teeth. Plus, always good for a snicker, the fossilized feces known as coprolites. Hofreiter also expects to see complete paleogenomes extracted from eggshells.

Regenerating an ancient species?

And, finally, the question everybody wants the answer to: Will it be possible to generate a viable organism from ancient DNA?

Hofreiter has good news and bad news about that, too. If scientists start with a living relative of an extinct species and modify its genome by exchanging parts of the modern genome with the corresponding sequences from an ancient genome, probably in cell culture, his answer is "Maybe". It might be possible that the resulting organism would function like the extinct species phenotypically and ecologically even though many parts of its genome would still be the same as in the living species used as a starter organism.

But will it be possible to make an organism using just the genomic information obtained from an extinct

species alone, with no material from a modern species? For example, if scientists started with a modern cell without a genome and added sequence information from an ancient genome? Would this result in a living organism?

Here his answer was "No." Which perhaps is just as well.

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