Proteins in ancient skeletons could provide key insights into human evolution

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Credit: Andrea Piacquadio from Pexels

Humankind's genetic links to long-extinct relatives are being mapped in a rapidly expanding research field called paleoproteomics.

They are a fixture of almost every novelty T-shirt shop: humorous

pictorials of human evolution, five figures in silhouette—from ape to human—usually with the last replaced by a skateboarder, Darth Vader or maybe even a barcode.

Whatever these fashion statements say about people's sense of humor, they reveal a fascination with human evolution.

Protein power

Now, researchers are on the cusp of acquiring much more knowledge about humankind's family tree. And it's all down to proteins.

Analyzing the proteins in ancient materials, a field known as paleoproteomics, allows insights beyond the bounds of DNA scrutiny and is a fast-growing research area that also touches on biology, paleontology and archaeology.

Prehistoric proteins can survive in a range of environmental conditions.

"We can retrieve ancient proteins from temperate environments—so from the latitudes close to ours," said Dr. Enrico Cappellini, a paleoproteomics expert at the University of Copenhagen in Denmark. "Then we started to see that we could retrieve proteins from species that come from tropical environments."

Cappellini leads a project that received EU funding to advance paleoproteomics research into the evolution of hominids, a broad group that includes all Great Apes and their ancestors.

Called BACKWARD, the project is still very much heading forward. It runs for five years until the end of 2026.

In July 2023, in an article posted to *bioRxiv*, Cappellini and colleagues

revealed the oldest genetic data ever collected from a hominin, a category that is narrower than hominid and includes species regarded as human or directly ancestral to humans.

The information came from a distant human cousin who lived in Africa 2 million years ago. The sequenced proteins were extracted from the enamel of four teeth found in a cave 40 kilometers northwest of Johannesburg in South Africa's Cradle of Humankind, a World Heritage Site.

Reverse engineering

While DNA carries genetic information, proteins are the expression of that genetic information.

This means that the amino acid sequence of a protein can be reverse-engineered by scientists to gain information on the DNA.

And proteins can survive for much longer than DNA.

This longevity is crucial for researchers because they say learning more about the historical lineage of the human species requires looking at the Middle Pleistocene period, which was between 777,000 and 126,000 years ago.

"In the Middle Pleistocene we have very little DNA preservation," said Dr. Frido Welker, an expert in human evolution also at the University of Copenhagen. "Proteins, therefore, are a potential molecular solution to get some genetic information."

Welker leads a separate EU-funded project to improve the extraction and computational analysis of ancient skeletal proteins while limiting destruction of hominin fossils.

Called PROSPER, the five-year initiative runs through November 2025. The research focuses on ancient proteins and proteomes, which are large sets of proteins.

The goal is to enable scientists to extract enough proteins from ancient skeletons to address evolutionary questions about time periods longer ago than around 130,000 years, according to Welker.

"There are many avenues to explore—chemically, computationally and others—that hopefully will allow us to get access to larger, more informative proteomes," he said.

Beyond DNA

Decades of advances in DNA sequencing technology have enabled scientists to extract genetic material from very old human skeletons and compare it with those of modern humans.

This has provided major insights into the genetic history of extinct hominins, such as the similarity between human DNA and that of Neanderthals.

In 2010, ancient DNA even enabled scientists to identify a previously unknown species of hominin—the Denisovans.

But DNA simply doesn't survive long enough to offer the potential that proteins do in opening up vast new sources of prehistorical data.

PROSPER will also look to improve understanding of sample taints, which can occur when ancient skeletal remains are dug up and handled by humans.

"Contamination is a real issue when studying ancient biomolecules," said

Welker. "We need to think about strategies on how to identify contamination and how to remove it from our datasets or our samples."

Archaic orangutans

Welker and Cappellini are at the forefront of worldwide research in this field.

In 2019, both were among scientists who made a major protein removal from a now extinct large ape species called Gigantopithecus blacki, which lived from around 2 million to 350,000 years ago.

The group extracted proteins from a 1.9-million-year-old molar in a cave in a subtropical part of southern China.

Gigantopithecus blacki roamed forested areas of Southeast Asia. Its evolutionary relationship with other Great Ape species was unclear.

The protein sequences that Welker, Cappellini and their colleagues discovered suggested that the Gigantopithecus group was closely related to orangutans, with a common ancestor from around 10–12 million years ago.

Perhaps most importantly, it showed that proteomes that are around 2 million years old can be retrieved from samples preserved in tropical conditions.

This opened the possibility of extending biomolecular research in hominid and hominin evolution far beyond previous limits.

"After this—and this is part of the BACKWARD project—we said we should also look at material from Africa," said Cappellini.

Large numbers of hominin fossils have been discovered around the world, with the Cradle of Humankind and the area around the Great Rift Valley in East Africa being particularly rich sites.

"The analysis of this material is extremely challenging because the amount of protein we recover is extremely limited," said Cappellini.

If paleoproteomics can unlock the secrets of these ancient humans, a great deal more will be learned about their evolutionary relationships, spread from Africa across the globe and association with activities in the archaeological record such as fire making.

That in turn would almost certainly provide more key insights into humankind's own ancient history.

More information:

- BACKWARD
- PROSPER

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