

Nobel Prize awarded to Svante Pääbo for study of ancient human DNA

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This year's Nobel Prize for Physiology or Medicine has been awarded to Swedish geneticist Svante Pääbo, of the Max Planck Institute for Evolutionary Anthropology (MPI-EVA) in Leipzig, Germany. The Nobel Assembly cited his pioneering work in deciphering the genetic codes of ancient humans, including Neanderthals and Denisovans, the latter first identified by Pääbo's research, thus contributing to the study of human evolution.

The Assembly's citation states, "Through his groundbreaking discoveries, Pääbo opened a new window to our evolutionary past, revealing an unexpected complexity in the evolution and admixture of ancient hominins, as well as providing the basis for an improved understanding of genetic features that make us uniquely human."

These accomplishments were made possible by research the geneticist led resulting in the development of techniques to sequence ancient DNA despite tens of thousands of years of degradation, and the separation of ancient DNA from modern contamination, thus founding the field of paleogenetics.

Pääbo announced the first sequencing of ancient human DNA, from mitochondria (organelles within cells), in 1997, from a roughly 40,000-year-old Neanderthal, which had been found near Dusseldorf in the 1850s. Mitochondria, known as cells' "powerhouses," have their own DNA, which is much shorter than the cell's nuclear genetic material and, therefore, easier to sequence.

With further refinement of the necessary methods, Pääbo and colleagues accomplished the sequencing of the full Neanderthal genome in 2010. The oldest ancient human DNA that has so far reconstructed is from 430,000-year-old remains from Spain.

Paleogenetic research benefited greatly from the

sequencing of modern human DNA by the Human Genome Project. In order to identify ancient genetic sequences it is essential to have the modern code for comparison.

The ability to sequence ancient DNA adds a powerful tool in the study of human evolution and biological evolution more generally. Previously, paleontologists have had to rely on the comparison of the physical characteristics of fossils in the attempt to identify degrees of similarity and difference as clues to the relationships between extinct animals indicating evolutionary pathways. Obviously, fossils do not reproduce. Therefore, the degrees of genetic relationships, key to the modern definition of species, are not discernable. Paleogenetics provides an independent source of data regarding genetic similarities and differences that help illuminate the course of evolution.

Pääbo's research resulted in the discovery that the modern *Homo sapiens*, who had originated in Africa between approximately 300,000 and 200,000 years ago, interbred with both Neanderthals, in Europe and the Near East, and Denisovans in Siberia, during periods of coexistence when the moderns expanded into Eurasia, roughly 50,000 or 60,000 years ago. Neanderthals disappear as a distinct population about 30,000 years ago.

The conclusion that these groups interbred is based on the persistence of small portions of genetic material from the latter two groups in modern Eurasian populations. Notably, such admixture is not present in modern Africans, indicating there was no significant "back migration" from Eurasia. Modern humans of European or Asian descent retain 1 to 4 percent of Neanderthal DNA. Fragments of Denisovan DNA are also found in many modern populations, as high as 6

percent in some Southeast Asian populations.

This important conclusion demonstrated that these three groups were not different species (i.e., were not genetically isolated), as some have thought. Neanderthals and modern humans shared a common ancestor approximately 600,000 years ago. Subsequently, after dispersion, each group evolved in geographically distinct regions over hundreds of thousands of years and, therefore, had developed some differences in response to varying environmental factors and genetic drift. Nevertheless, despite the long period of significant separation, their basic common adaptation, primarily the reliance on culture and language, limited the degree of divergence. Therefore, when migration brought segments of these populations in contact, they were able to interbreed successfully and produce viable offspring.

A significant follow-on finding is that contrary to some extreme interpretations, modern *Homo sapiens* did not drive the archaic groups to extinction in bloody massacres or by outcompeting them for resources, due to the former's supposed intellectual superiority. While such behaviors cannot be entirely ruled out, nor can relative differences in intelligence, in a significant proportion of inter-group encounters the participants engaged in some form of productive interaction. These exchanges were apparently not exclusively genetic. For example, tool assemblages of some late Neanderthal populations, known as Chatelperronian, were altered by adoption of aspects of modern human technology, presumably from nearby groups.

Further benefits of this new field of research include the ability to trace the migrations and interactions of various more recent populations of humans and to examine, for example, the development of variations in the immune systems of various populations. Some of these adaptations may have provided advantages to these ancient populations, such as high-altitude adaptation, which have been passed on to modern people living on the Tibetan Plateau, apparently derived from Denisovan ancestors. Some genetic traits inherited from ancient humans may not be so salubrious. Dr. Pääbo and a colleague announced in 2021 that a certain segment of DNA inherited from Neanderthals may result in carriers suffering more severe symptoms from COVID-19.

Recent genetic research that benefits from the study of ancient DNA also highlights differences between archaic (Neanderthal and Denisovan) and modern humans. Newly published work identified a gene variant found in the latter but not the former that appears to promote greater neuronal growth in laboratory trials, suggesting that modern humans may indeed have had some intellectual advantage over their ancient cousins.

In all cases, however, the growing body of knowledge derived from the study of ancient DNA contributes to our understanding of human biology, including the potential for improved health outcomes. The recognition of the value of this research is fully justified.



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