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**Editorial** 

# The 2022 Nobel Prize in Medicine for Paleogenomics Discovery the Genomes of Extinct Hominins and Human Evolution

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## Background

Ever since the first Neanderthal fossils were found in a mine in Germany in 1856, paleontologists have been puzzled by the research question: how those early humans were related to modern humans and what made them different. The release of the Neanderthal genome opened the door to finding answers. Ancient DNA suffers from chemical damage and is usually present at very low levels in samples. This DNA can easily be contaminated by the DNA of the scientists working with them, making it difficult to distinguish ancient genes from modern genes. Bacteria can also leave DNA in fossils, forcing scientists to learn how to isolate these genes (1). However, Dr. Paabo used the latest technology available to sequence DNA (Fig.1). When he needed more bones, he went the hard route of obtaining fossil fragments from other countries and designed "clean rooms," or laboratories with high standards of cleanliness that protected the specimens from contamination (1). In addition, when he and his team discovered fragments of DNA in fossils, they applied sophisticated statistical techniques to isolate modern genetic contaminants.



Fig. 1: Pääbo's seminal work provides a basis for explaining what makes us uniquely human (1)



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Svante Pääbo, biologist and evolutionary geneticist from Sweden, was born on April 20, 1955 in Stockholm. His father, Sune Bergström, a biochemist, also won the Nobel Prize in Medicine in 1982 along with Bengt Samuelsson and John R. Vane, for the discovery of Prostaglandin and related substances (1,2). As one of the founding fathers of Paleontology, Pääbo has worked extensively on the Neanderthal genome (3). Early in his career, Svante Pääbo was fascinated by the possibility of using modern genetic methods to study Neanderthal DNA. As a postdoctoral student with Alan Wilson, a pioneer in the field of evolutionary biology in America, Pääbo began developing methods for studying DNA from Neanderthals, an effort that spanned decades(3,4). In 1997, he was appointed as the director of the Genetic Department at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. He reported the successful sequencing of Neanderthal mitochondrial DNA (mtDNA) from a sample found in the Kleine Feldhofer Grotte near Düsseldorf (5).

In 2006, Pääbo presented a plan to reconstruct the entire Neanderthal genome. In 2007, he was selected as one of Time magazine's 100 most influential people of the year (1). In February 2009, at the annual meeting of the American Association for the Advancement of Science (AAAS) in Chicago, it was announced that the Max Planck Institute for Evolutionary Anthropology had completed the first draft of the Neanderthal genome. More than three billion base pairs were sequenced in collaboration with the American company "454 Life Sciences"(6,7).

This project, led by Pääbo, will shed light on the recent evolutionary history of modern humans. In March 2010, Pääbo and his colleagues published a report on DNA analysis of a finger bone found in the Denisova Cave in Siberia (8). This was the first time that an unknown hominid was discovered using DNA analysis. In May 2010, Pääbo and his colleagues published a draft of the Neanderthal genome sequence in the Science journal (1). In addition, they concluded that there might have been interbreeding between Neanderthals and Eurasian humans. In 2014, Paabo published the book "Neanderthal Man": In Search of Lost Genomes (Fig.2).



Fig. 2: Meet the family: Svante Pääbo has pioneered the painstaking study of ancient DNA. Photograph: Frank Vinken. www.theguardian.com

Importantly, Pääbo found that gene transfer from Denisova to intelligent humans also occurred after migration out of Africa about 70,000 years ago (7,8). Groups of Homo sapiens migrated from Africa to the Middle East of the Old Iranian plateau and present-day Iraq "Mesopotamia" and from there spread to other parts of the world. Modern Humans and Neanderthals coexisted for tens of thousands of years in large parts of Eurasia (9). Through his pioneering research, Svanet Pääbo founded an entirely new scientific discipline called "Paleogenomics". Powerful new methods for sequence analysis suggest that ancient hominins may have also mixed with Homo sapiens in Africa. However, no genomes have yet been sequenced from extinct hominins in Africa, due to the rapid degradation of ancient DNA in tropical climates. In 2020, Paabo determined that there were more severe effects on victims, including the need for hospitalization and vulnerability to Covid-19, through DNA analysis, expressed in genetic variants in the chromosomal region 3. These features are similar to the European Neanderthal heritage (9,10).

Finally, Swedish biologist Svante Pääbo won the 2022 Nobel Prize in Medicine for his discoveries (1).

#### **Conflict of Interest**

The authors declare that there is no conflict of interests.

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