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Rajesh Ramachandran

ASSOCIATED PROFESSOR, IISER, MOHALI

This year's Nobel Prize in Physiology or Medicine goes to Prof. Svante Pääbo, Director of the Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany. Pääbo's Nobel journey is

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Venkatraman Ramakrishnan, a physicist by training who received the prize in chemistry for his biological studies on ribosomes.

Pääbo researched the biology of adenoviruses and the immune system; He later switched to genetics and genomics, with a particular focus on paleoanthropology, to receive the Nobel Prize for what appeared to be a “non-medical” subject, but one that has enormous medical implications.

Pääbo is one of the founders of the branch of science called paleogenetics, which deals with the characterization of ancient genomes. Pääbo focused on “high-risk, high-reward” research, studying human evolution with a particular focus on the Neanderthal genome and discovering a previously unknown hominin named Denisovan.

Pääbo devoted much time and effort to prehistoric caves in search of ancient human remains. Its success also underscores the importance of basic scientific research in the modern world.

The human race is originally from Africa and has made several migrations out of Africa ranging from 50,000 to 70,000 years ago. Homo sapiens, modern man, arose in Africa 3,00,000 years ago. Our closest cousins, the Neanderthals, evolved in Europe and western Asia around 4,00,000 years ago and remained there until 30,000 years ago before becoming extinct. The migration of Homo sapiens from Africa occurred 40,000 years ago to western Asia and then to the rest of the world. Homo sapiens and Neanderthals overlapped spatially and temporally across much of Eurasia for thousands of years. The lack of any Neanderthal data 30,000 years ago had led to speculation that Homo sapiens would wipe out the Neanderthals through competition.

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But what was our relationship to the extinct Neanderthals? To answer this would require sequencing of genomic DNA recovered from archaic specimens. While at the University of Munich, Pääbo undertook the challenging task of sequencing ancient mitochondrial DNA from 40,000-year-old Neanderthal bone remains and found that Neanderthals were genetically different from modern humans and chimpanzees.

Pääbo continued to compile the ever-challenging task of building the Neanderthal genome and published the entire genome in 2010. Genome analysis suggested the independent origin of this human race outside of Africa. However, the lineage of their ancestors stretches back to Africa. Paabo's study uncovered the possibility of Homo sapiens interbreeding with Neanderthals, leading to their genomic dilution, which has left traces of their genome of up to 4 percent in

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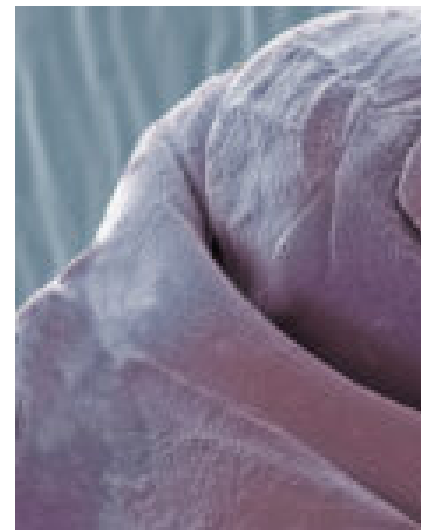
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modern humans. Genome comparison studies showed that the most recent common ancestor of Neanderthals and Homo sapiens may have lived around 8,00,000 years ago.

In 2008, Pääbo sequenced the DNA of a well-preserved 40,000-year-old finger bone discovered in the Denisova Cave in Siberia. The results were sensational as the DNA sequence was unique compared to Neanderthals and modern day humans. Pääbo discovered a previously unknown hominin, Denisova. Further studies showed that gene flow also occurred between Denisova and Homo sapiens. This trait is evident in human populations in Melanesia and other parts of Southeast Asia, where some individual genomes carry up to 6 percent Denisovan DNA.

Pääbo's discoveries have led to a new understanding of human evolutionary history. At least two distinct and later extinct populations of hominins lived in Eurasia when Homo sapiens migrated from Africa. The Neanderthals lived in western Eurasia while their contemporary Denisovans thrived in the eastern part of the continent. The final eastward spread of Homo sapiens outside of Africa was about 40,000 years ago; They encountered and interbred with Neanderthals and Denisovans.

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Studies and discoveries by Pääbo established an entirely new scientific discipline – paleogenomics. These lines of evidence further strengthened the scientific community's understanding of human evolution and migration.

Modern and robust DNA sequence analysis methods support the view that archaic hominins interbred with Homo sapiens in Africa. However, the tropical climate of Africa hampers the discovery of ancient DNA obtained from the bone remains of extinct hominins on that continent.

Pääbo's discoveries of archaic gene sequences from our extinct relatives suggest the influence of modern human physiology. For example, the EPAS1 gene, which confers a survival advantage at high altitudes – prevalent among Tibetans today – is associated with Denisovans. Several Neanderthal genes are responsible for our immunological response to various infections.

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Although Homo sapiens could perform complex tasks such as creative toolmaking, figurative art, voyages across the seas, social organization, and communication, they often lacked the physical stamina and bulk found in Neanderthals. Successful interbreeding of Homo sapiens and Neanderthals would have allowed better survival in the harsh Eurasian climate. The genetic connection between Homo sapiens and our closest extinct relatives, Neanderthals and Denisovans, was unknown until established by Pääbo's epic work. In addition to his discoveries, the focus is on analyzing the functional implications of differences between Homo sapiens, Neanderthals and Denisovans, with the primary goal of learning more about how humans evolved into a successful species.

The emigration of Homo sapiens from Africa is an important issue in human evolutionary history. The current belief that our species originated in Africa and spread to colonize much of Eurasia before colonizing the rest of the world is also well supported by Indian studies. Studies by the Indian Statistical Institute and other research laboratories have supported the idea that India was an important corridor for early human dispersal as early as 1,00,000 years ago, although the exact time frame of human settlement in India remains unknown.

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A study by the Center for Cellular and Molecular Biology, Hyderabad has proven that the Andamanese tribe is more closely related to Asian populations than to African populations, while the Nicobarese today have genetic links to populations across Asia.

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