Ancient DNA. What makes us human, and can we bring back a mammoth?

QB Workshop: June 1, 2023

Physicists – Big Bang?



Cell biologists/neuroscientists – emergence of multicellular life?



Biochemists – last common ancestor of your favorite protein?



Marsh GA, de Jong C, Barr JA, et al. 2012

What is ancient DNA?

"The study of DNA extracted from specimens that died decades, hundreds or thousands of years ago."

- International Society of Genetic Geneaology

How old is ancient DNA?



How old is ancient DNA?



The age of ancient DNA can vary significantly, depending on the preservation conditions and $\Box \quad \Box \quad \nabla$ the organism from which it is extracted. In general, ancient DNA refers to genetic material that is thousands to tens of thousands of years old.

For human remains, ancient DNA has been successfully recovered from individuals dating back tens of thousands of years, such as the remains of Neanderthals and Denisovans. These ancient hominin species lived hundreds of thousands of years ago and went extinct. By analyzing their DNA, scientists have been able to uncover valuable information about human evolution and the interactions between different hominin groups.

In some exceptional cases, ancient DNA has been recovered from much older specimens. For example, scientists have extracted DNA from the remains of ancient animals, such as mammoths and other Ice Age creatures, which can be tens of thousands of years old.

"Ancient" in ancient DNA terms – not too long ago! (relatively speaking)

"Ancient" in Ancient DNA terms – not long ago!



Ga = billion years



~560,000 – 780,000 years

~ 1 million years

~2 million years

How far back can we go?

Photo & Illustrations: Ludovic Orlando, Beth Zaiken

Q: Can we really learn much from a relatively short time scale?



2022 Nobel Prize Winner: Svante Pääbo

Q: Can we really learn much from a relatively short time scale?

A: It depends on what you want to learn. But yes.

Life on earth has undergone drastic change in the past ~100,000 years.

Extinction



Why have certain species become extinct? What have our ecosystems lost from their absence?

Life on earth has undergone drastic change in the past ~100,000 years.

Climate Change



Why did some species not survive past the ice age? How did species adapt to survive this change?

Life on earth has undergone drastic change in the past ~100,000 years.

Humans became human



What distinguishes a human from a neanderthal? Why are humans still around and other hominids not?



~560,000 - 780,000 years

~ 1 million years

~2 million years

What do these ancient DNA specimens have in common?

Photo & Illustrations: Ludovic Orlando, Beth Zaiken



Yukon Territory, Canada

Permafrost, Eastern Siberia

Kap København, Greenland

What do these locations have in common?

Photos: Vero Kherian, Alexander Kizyakov, Kurt Kjaer



Poinar et al. 2006



Anatomy & Physiology, Connexions



Anatomy & Physiology, Connexions





Cold Spring Harbor



This can introduce complications in sequencing. Uracil can be read as Thymine by some polymerases. This causes the complementary PCR strand to read "A" instead of the "G" they should have.



Rohland et al. 2007



Rohland et al. 2007

Ancient DNA Boom. Why now?



De-extinction

01 COLOSSAL ANNOUNCES \$60M SERIES A

Why bring back the mammoth at all? – Restore an ecosystem



Why bring back the mammoth at all? - Lower the temperature



<u>Pleistocene Park Soil Temperature</u>

Season 2012 / 2013

Source: Science Reports (2020)

• How do we do it?





Asian Elephant (99.6% similar)

Culture elephant cells and edit them to contain mammoth DNA



I AFRICAN ELEPHANT CELLS



REPLACEMENT PROGRAMMED DNA

Mammoth gene expression in Asian Elephant cells **Relative Gene Expression** Mammoth gene 3 Mammoth gene 1 Mammoth gene 2 Mammoth gene 4

SCNT: Somatic cell nuclear transfer





A question for you:

Should we bring back the mammoth?

And release them into Alaska?

Maybe a more palettable example? The Dodo



© Encyclopædia Britannica, Inc.

Human history

Why are humans around today and not Neandertals?

First: how do we distinguish modern humans and Neandertals?



Krings et al. 1997

Why are humans around today and not Neanderthals? **Or Denisovans?**

ARTICLE

doi:10.1038/nature09710

Genetic history of an archaic hominin group from Denisova Cave in Siberia

David Reich^{1,2}*, Richard E. Green^{3,4}*, Martin Kircher³*, Johannes Krause^{3,5}*, Nick Patterson²*, Eric Y. Durand⁶*, Bence Viola^{3,7}*, Adrian W. Briggs^{1,3}, Udo Stenzel³, Philip L. F. Johnson⁸, Tomislav Maricic³, Jeffrey M. Good⁹, Tomas Marques–Bonet^{10,11}, Can Alkan¹⁰, Qiaomei Fu^{3,12}, Swapan Mallick^{1,2}, Heng Li², Matthias Meyer³, Evan E. Eichler¹⁰, Mark Stoneking³, Michael Richards^{7,13}, Sahra Talamo⁷, Michael V. Shunkov¹⁴, Anatoli P. Derevianko¹⁴, Jean–Jacques Hublin⁷, Janet Kelso³, Montgomery Slatkin⁶ & Svante Pääbo³

How do we distinguish modern humans and Neandertals AND Denisovans?



Reich et al. 2010

How do we distinguish modern humans and Neandertals AND Denisovans?



Reich et al. 2010

Some differences can be characterized biochemically: smell!

Reich D. et al. 2010 - OR1K1. Arginine > Cysteine.



de March C.A. et al. 2023

Some differences can be characterized biochemically: smell!



de March C.A. et al. 2023

Other differences explained by what elements modern humans have left behind

"Introgression Deserts" – regions in the genome depleted of archaic DNA. Buisan et al. 2022



Other differences explained by what elements modern humans have left behind

"Introgression Deserts" – regions in the genome depleted of archaic DNA. *Buisan et al. 2022*



Veller et al. 2023

Other differences can be explained by what genetic elements modern humans have left behind

FOXP2: speech and language development

Buisan et al. 2022

Despite our differences, Denisovans, Neandertals, and Humans all shared a home



Zavala E. et al. 2021

Despite our differences, Denisovans, Neandertals, and Humans all shared a home



Zavala E. et al. 2021

Don't forget – when studying ancient human remains. These are someone's ancestors

First attempt at defining "Ancient DNA Ethics" falls extremely short

Perspective

Ethics of DNA research on human remains: five globally applicable guidelines

October 2021

Recommendations for Sustainable Ancient DNA Research in the Global South: Voices From a New Generation of Paleogenomicists

Maria C. Ávila-Arcos¹*[†], Constanza de la Fuente Castro²*[†], Maria A. Nieves-Colón³*[†] and Maanasa Raghavan²*[†]

March 2022

HGG Advances

COMMENTARY

April 2023

Community partnerships are fundamental to ethical ancient DNA research

Researchers demonstrate the power of community involvement in ancient DNA work



Characterize the African genetic ancestry of Mexico, working together with Afro-Mexican communities.

Generate genome-wide genotype from hundreds of Afro-descendants.

We will characterize ancient genomes from archaeological remains likely belonging to enslaved Africans brought to Mexico during the slave trade.

Dr. María C. Ávila Arcos International Laboratory for Human Genome Research

Paraphrased from lab website: <u>https://liigh.unam.mx/mavila/</u>

Researchers demonstrate the power of community involvement in ancient DNA work





From lab website: https://liigh.unam.mx/mavila/

Feeling connected to a past we cannot remember



Ginkgo Bioworks

CURRENT & FORTHCOMING EXHIBITIONS

Gene Cultures

MIT Museum

Cambridge, USA

October 2, 2022 – September 2024

'Leucadendron grandiflorum (Salisb.) R. Br.'

Extras

Sandblasting a bone that will undergo "ancient DNA extraction"

