



Prof. Vagheesh Narasimhan – The University of Texas at Austin, USA


Human Evolution



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Darwin's predictions on human evolution



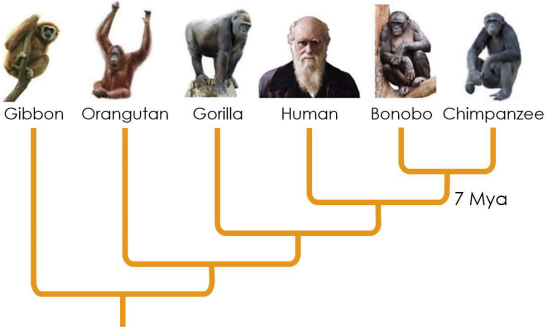
On the origin of species (1859)
 “In the distant future I see open fields for far more important researches. ...Light will be thrown on the origin of man and his history.”

Comparing early developmental stages of humans and other mammals (1871)
 “Without question, the mode of origin and the early stages of the development of man are identical with those of the animals immediately below him in the scale: without a doubt in these respects, he is far nearer to apes, than the apes are to the dog.”

On the geographic origin of *Homo sapiens*
 “In each great region of the world the living mammals are closely related to the extinct species of the same region. It is therefore probable that Africa was formerly inhabited by extinct apes closely allied to the gorilla and chimpanzee; and as these two species are now man's nearest allies, it is somewhat more probable that our early progenitors lived on the African continent than elsewhere.”

2

Our most basic understanding of human evolution comes from observations of the extant great apes



Gibbon Orangutan Gorilla Human Bonobo Chimpanzee

7 Mya

3

Futuyama DJ. & Kirkpatrick M. *Evolution*. Oxford University Press. 2017



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Our most basic understanding of human evolution comes from observations of the extant great apes

- > E.g., we're the only great apes with longer legs than arms
- > Additional changes in the pelvis and spine allow us to walk upright

Futuyma DJ. & Kirkpatrick M. *Evolution*. Oxford University Press. 2017

The hominin fossil record provides direct evidence of morphological change over time

Whilst the process of drawing relationships between fossils is not exact, they do provide a record of change over time that scientists can use to understand the evolutionary process

Futuyma DJ. & Kirkpatrick M. *Evolution*. Oxford University Press. 2017

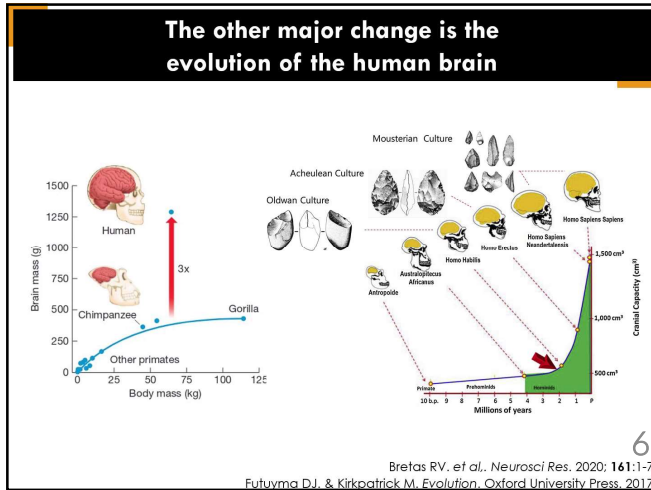
The evolution of bipedalism involves subtle changes in skeletal morphology

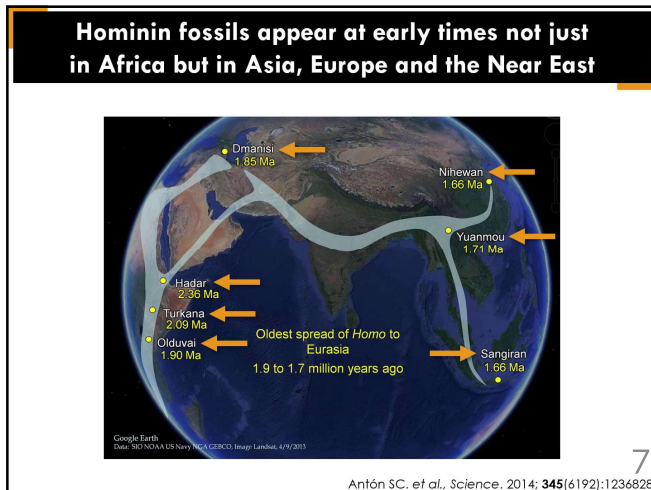
Stability improves over time

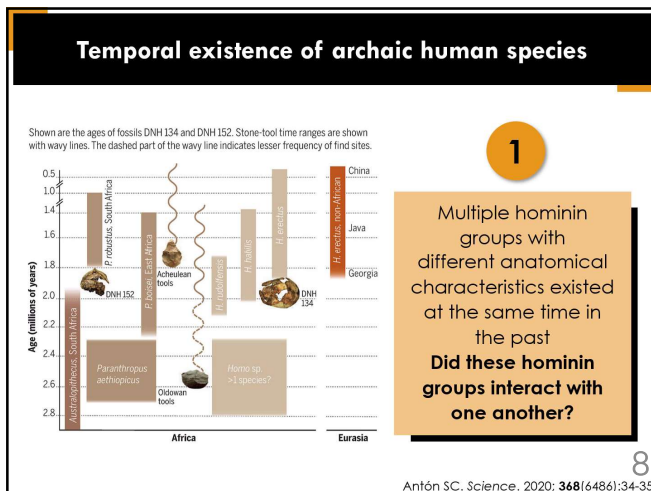
Pontzer H. *Curr Biol*. 2017; 27(12):R613-R621



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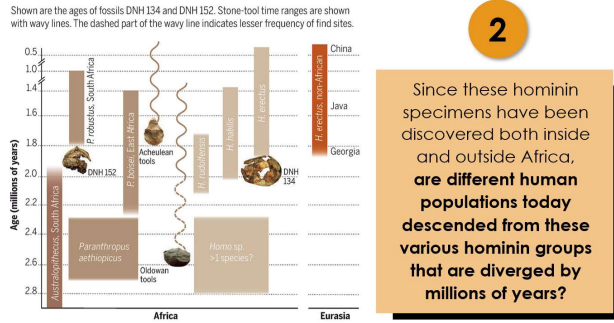






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Temporal existence of archaic human species



2

Since these hominin specimens have been discovered both inside and outside Africa, **are different human populations today descended from these various hominin groups that are diverged by millions of years?**

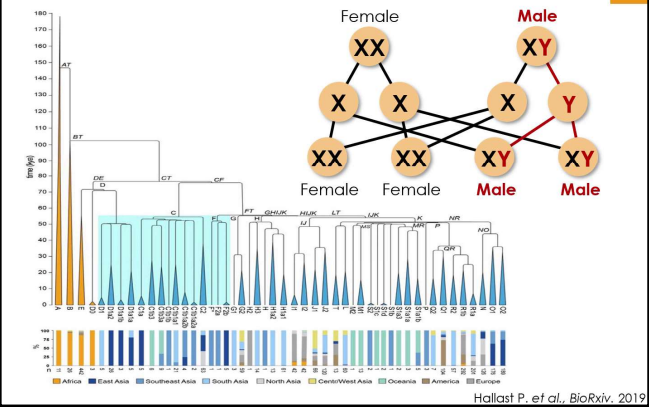
Antón SC. *Science*, 2020; 368(6486):34-35

Answering these questions via genetic sequencing

We can answer these questions using DNA data from modern human populations from all over the world

9

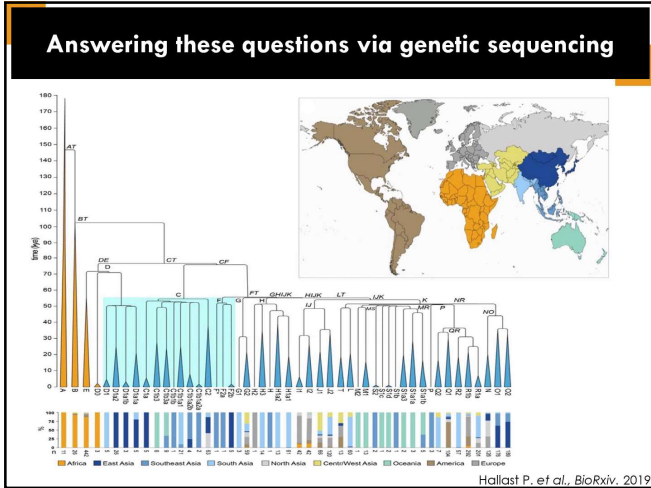
Answering these questions via genetic sequencing



Hallast P. et al., *BioRxiv*, 2019



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Ancient DNA adds a time dimension to human genomic data

Ancient DNA

- › Allows us to examine genetic changes in the sample, that can be tens of thousands, if not hundreds of thousands of years old

- › The process begins with archaeological excavation of ancient human remains
- › Collaboration between DNA researchers and archaeologists is important

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Ancient DNA adds a time dimension to human genomic data

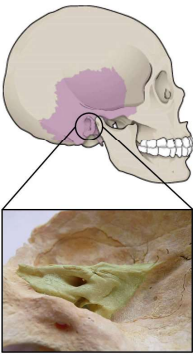
- › Environmental DNA risks contaminating ancient DNA samples
- › Samples are excavated using PPE (Personal Protective Equipment)

Shinde VS. et al., PLoS One. 2018; 13(2):e0192299



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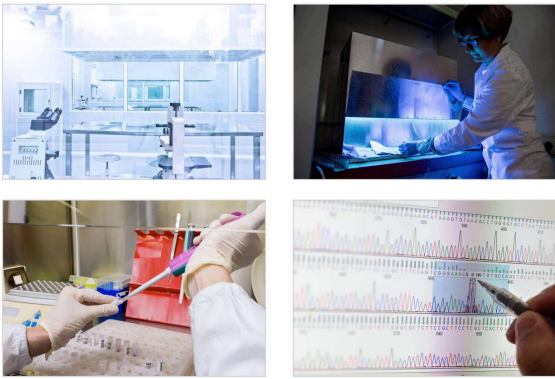
Ancient DNA adds a time dimension to human genomic data



Petrous bone

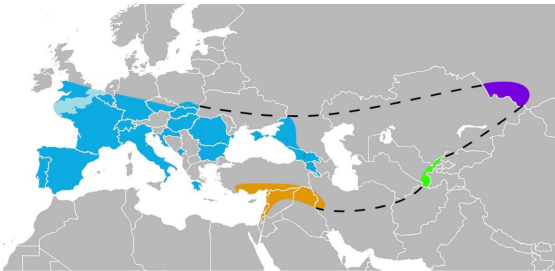
- > Makes up part of the inner ear
- > Dense bone
- > Does not remodel
- > Tends to contain well preserved DNA, this may be due to higher cellular density, or the physical isolation of the area within the skull cavity
- > 75mg of bone powder sampled

Ancient DNA adds a time dimension to human genomic data



A draft sequence of the Neanderthal genome was first reported in 2010

Known historic Neanderthal range in Europe, Southwest Asia, Uzbekistan, and the Altai Mountains



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A draft sequence of the Neanderthal genome was first reported in 2010

Neanderthal reconstruction (left) next to a modern human skeleton (right)

Neanderthal stone tools retrieved from Teixoneres Cave, Spain

Picin A. et al., J. Archae Sci Rep. 2020; 29:102145
Sawyer G.J. and Maley B. Anat Rec B New Anat. 2005; 283(1):23-31

A draft sequence of the Neanderthal genome was first reported in 2010

1 Did modern humans and Neanderthals interact?

2 Did modern humans and Neanderthals mix genetically?

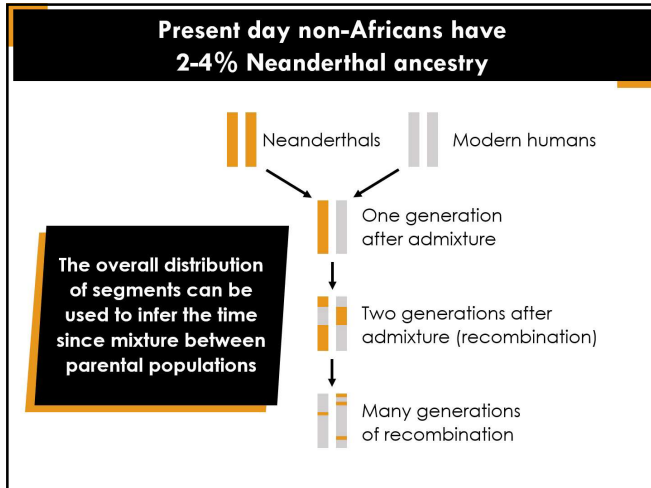
Present day non-Africans have 2-4% Neanderthal ancestry

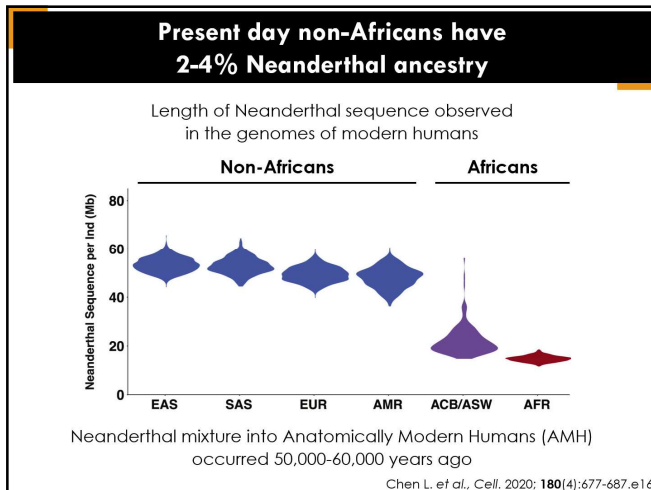
- › With Neanderthal DNA sequences, statistical methods could be used to identify segments of Neanderthal ancestry in modern human DNA
 - › Approx. 2-4% of non-African ancestry comes from Neanderthals
- › It is possible to estimate the time period when this ancestry entered the genomes of non-Africans
- › This is done by analyzing the length distribution of Neanderthal segments in modern human genomes

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The mysterious skull from Peștera cu Oase

1 Was this the only interbreeding event that occurred between these two groups?

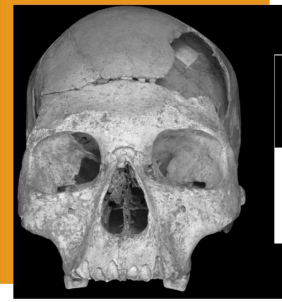
Neanderthals occupied many sites across Europe, it is not unthinkable that AMH often encountered Neanderthals after the initial interbreeding event

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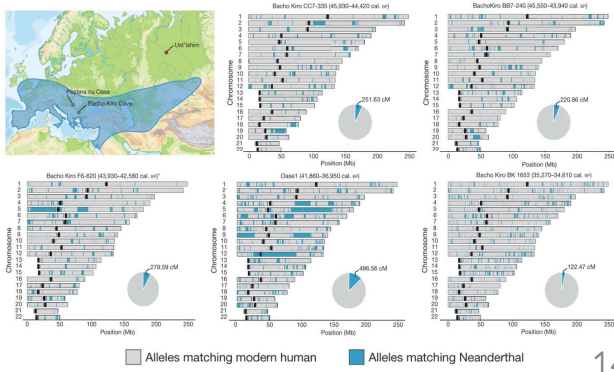
The mysterious skull from Peștera cu Oase



- › Discovered in the 80s, radiocarbon dated to ~40,000 years ago
- › The skull exhibited strange features of both archaic and AMH morphological characteristics
- › Paleoanthropologists scoffed at the idea that it was admixture, and said it's probably an AMH with Mendelian disease

Rougier H. et al., PNAS. 2007; 104(4):1165-1170

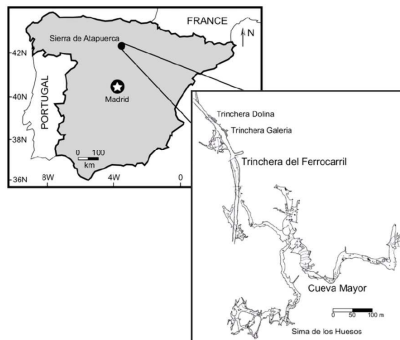
Samples close to the mixing time have close Neanderthal ancestors



Hajdinjak M. et al., Nature, 2021; 592(7853):253-257

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Ancient DNA recovered from Sima De Los Huesos (Northern Spain) dating to ~430,000 years ago



Garcia N. et al., PLoS One. 2015; 10(12):e0142895
Meyer M. et al., Nature. 2016; 531(7595):504-7

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Ancient DNA recovered from Sima De Los Huesos (Northern Spain) dating to ~430,000 years ago

Anatomical evidence labelled these samples as *Homo heidelbergensis*



Garcia N. and Arsuaga J.L. *Quaternary Sci Rev.* 2011; **30**(11):1413-1419
Meyer M. et al., *Nature.* 2016; **531**(7595):504-7

DNA evidence suggests that this population were early Neanderthals

Original morphological consensus

Using the ancient DNA data

Ancient DNA analysis suggests *Homo heidelbergensis* was a lineage more closely related to Neanderthals than humans, in contrast to the original morphological consensus

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Futuyama DJ. & Kirkpatrick M. *Evolution.* Oxford University Press. 2017
Meyer M. et al., *Nature.* 2016; **531**(7595):504-7

The discovery of the Denisovans: an archaic hominin without any real fossil evidence



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Reich D. et al., *Nature.* 2010; **468**(7327):1053-60




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The discovery of the Denisovans: an archaic hominin without any real fossil evidence

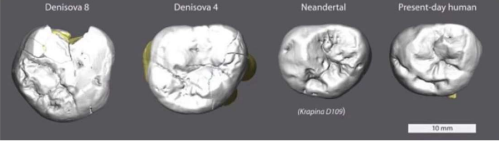
Bone fragment sequenced



Denisova Cave




Denisovan molars are much larger than Neanderthals & humans



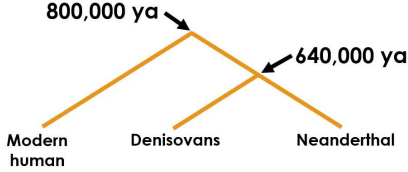
Sawyer S. et al., PNAS, 2015; 112(51):15694-700
Reich D. et al., Nature, 2010; 468(7327):1053-60

The discovery of the Denisovans: an archaic hominin without any real fossil evidence

Bone fragment sequenced



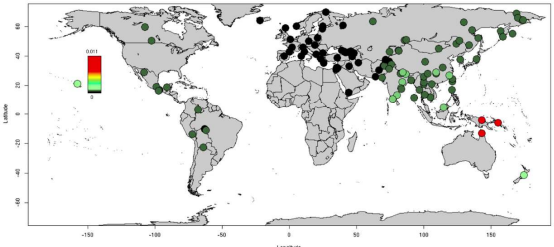
DNA sequencing of the fingerbone revealed a hominin species that diverged from humans and Neanderthals quite some time ago



Reich D. et al., Nature, 2010; 468(7327):1053-60

Indigenous individuals from Oceania derive up to 5% of their ancestry from Denisovans

Sequences seen in Oceanians are quite diverged from the genome sequence obtained from Denisova Cave



Present day individuals from Oceania (Papuan, Australians and South-East Asians) have up to 5% of their ancestry derived from Denisovans, who are diverged from Neanderthals by around 400,000 years or more

Sankararaman S. et al., Curr Biol, 2016; 26(9):1241-7



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Admixture is ubiquitous in human history

- › Denisova Cave is rich in bone deposits from many species
- › Some of these bones are not identifiable morphologically
- › ZooMS: a type of collagen peptide mass fingerprinting



- › Subsequent DNA sequencing of hominin bones

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Brown S. et al., *Sci Rep.* 2016; 6:23559

Multiple admixture events between Denisovans and Neanderthals

99% of the genome looks as follows

Match to Neanderthal reference

Match to Denisovan reference

Five 1MB long chunks look as follows

Match to Neanderthal reference

Match to Denisovan reference

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Slon V. et al., *Nature*, 2018; 561(7721):113-116

Multiple admixture events between Denisovans and Neanderthals

- › Admixture between hominin groups was ubiquitous in our evolutionary history
- › Evidence of interbreeding between:
 - › Humans and Neanderthals
 - › Humans and Denisovans
 - › Neanderthals and Denisovans

Slon V. et al., *Nature*, 2018; 561(7721):113-116



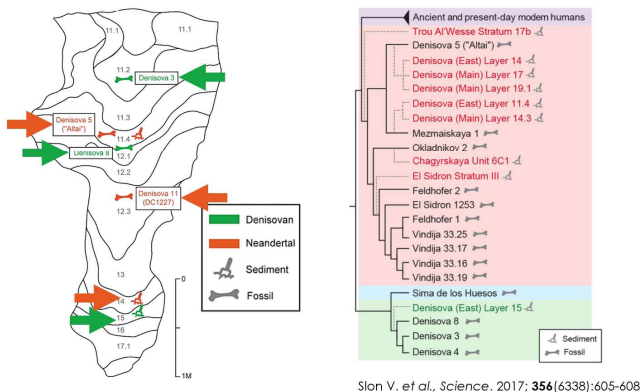
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Ancient DNA from sediments can be used to study the occupation of sites over time

- › Ancient DNA extracted from sediments allows for phylogenetic analysis in the absence of bone material
- › Researchers dig trenches at cave sites, and look for evidence of human occupation at different times

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Ancient DNA from sediments can be used to study the occupation of sites over time

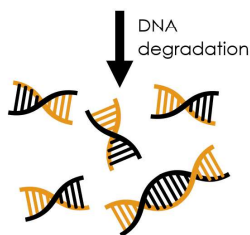


Slon V. et al., Science, 2017; 356(6338):605-608

Paleoproteomics extends the ability to obtain genetic information from much deeper in time

A limitation of using ancient DNA

- › DNA fragments can become too short to utilize for population genetic analysis
- › The oldest genetic sequence information came from an organism that lived ~one million years ago



A frozen mammoth discovered in the permafrost zone of Siberia

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Paleoproteomics extends the ability to obtain genetic information from much deeper in time

To overcome this limitation, genetic information could be attained from proteins, which are much more stable in their nature

Phylogenetic tree built off of 6 collagen proteins from dentin

Chen F. et al., *Nature*, 2019; 569(7756):409-412
Zhang D. et al., *Science*, 2020; 370(6516):584-587

The major genetic risk factor for severe Covid-19 is inherited from Neanderthals

How might this interbreeding impact human health?

Covid-19 risk factors

Zeberg H. and Pääbo S. *Nature*, 2020; 587(7835):610-612

The major genetic risk factor for severe Covid-19 is inherited from Neanderthals

The major genetic risk factor for severe COVID-19 is inherited from Neanderthals

<https://doi.org/10.1038/s41586-020-2818-3> Hugo Zeberg^{1,2} & Svante Pääbo^{1,2}

- › A locus on chromosome 3 was discovered where a particular set of alleles could make an individual 2-3x more likely to have severe Covid-19
- › This set of alleles is inherited from Neanderthals
- › Present in ~50% of individuals from South Asia
- › ~16% of individuals in Europe

Zeberg H. and Pääbo S. *Nature*, 2020; 587(7835):610-612



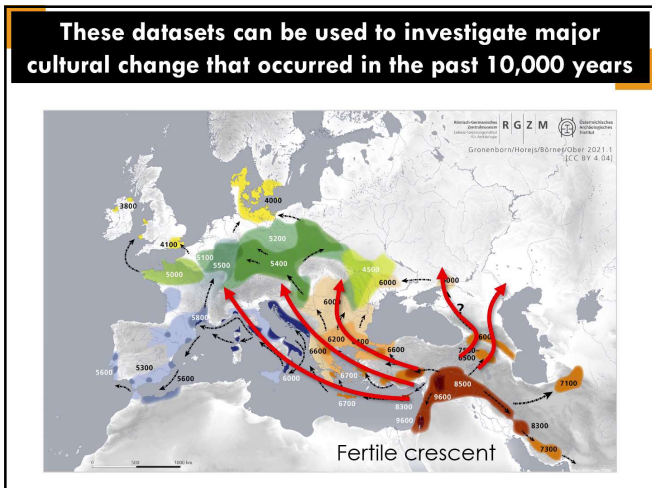
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These datasets can be used to investigate major cultural change that occurred in the past 10,000 years

The most important cultural change in human history is perhaps the transition from hunting-gathering to farming

This transition resulted in much larger population sizes, and humans living in much closer proximity to each other, as well as domesticated animals

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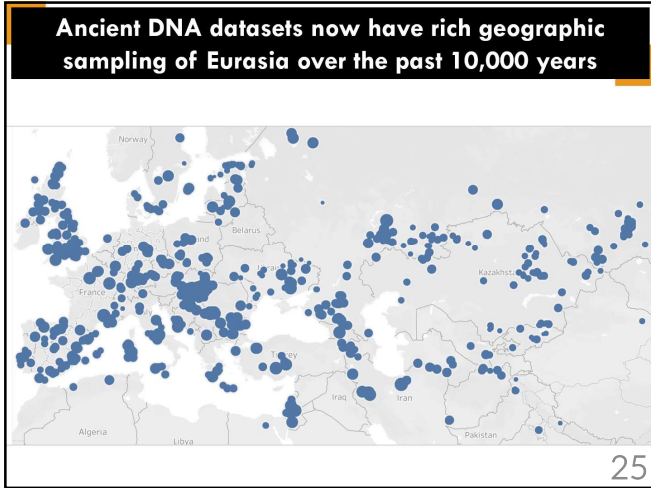


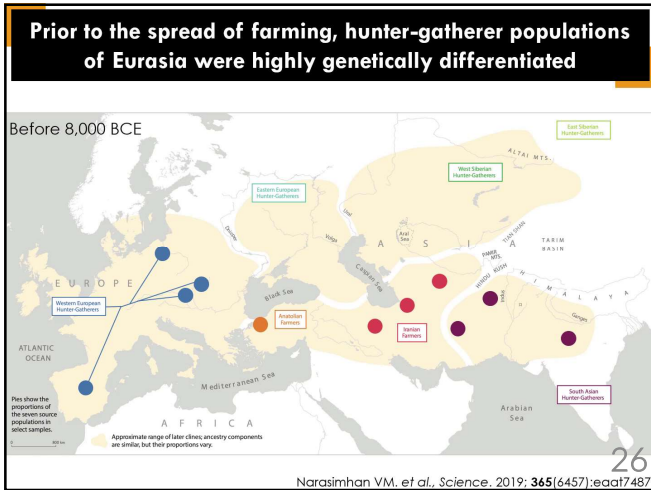
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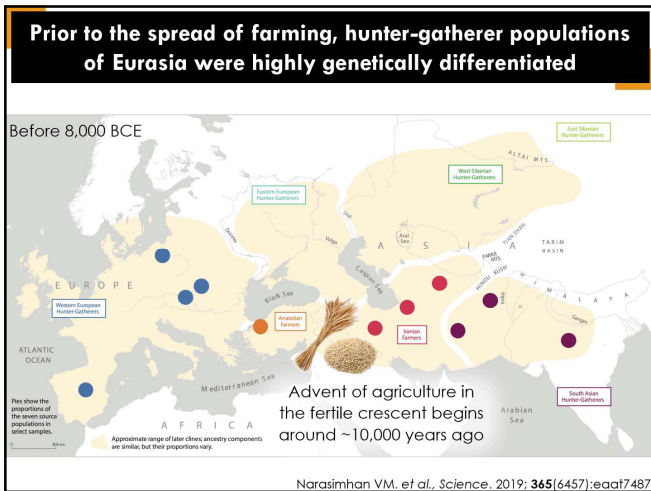
Do these cultural transformations occur due to the cultural exchange of information, or due to the dramatic movement of human populations that occurred in the past 10,000 years?



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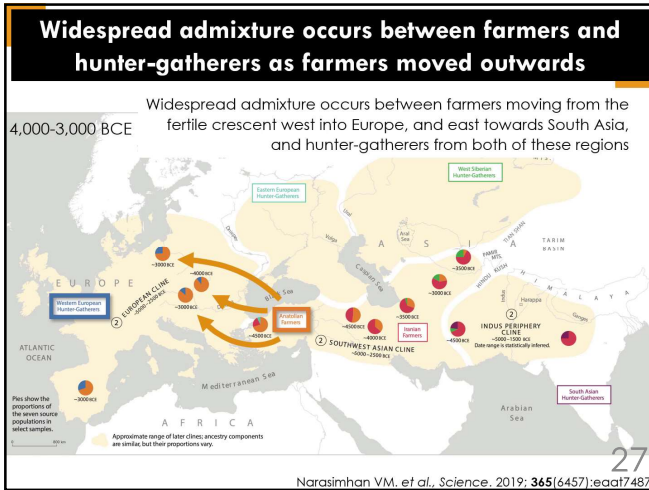


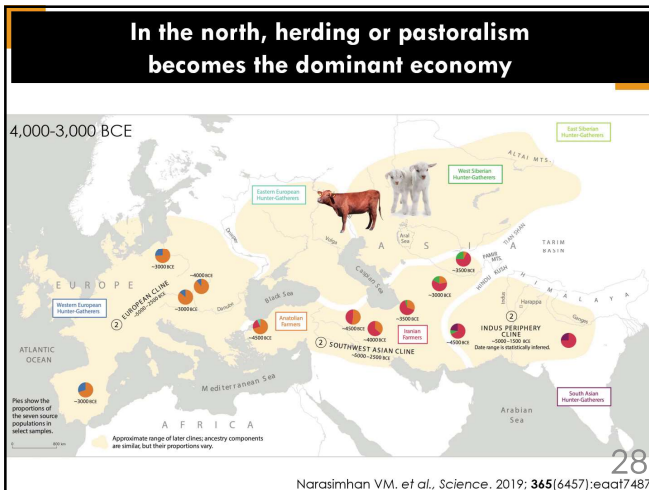


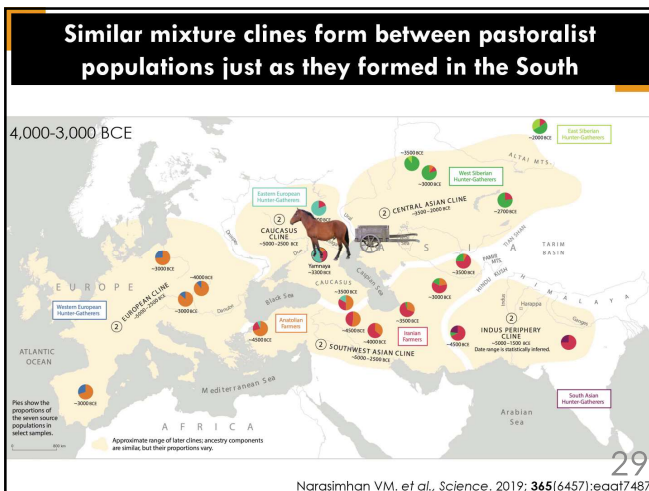




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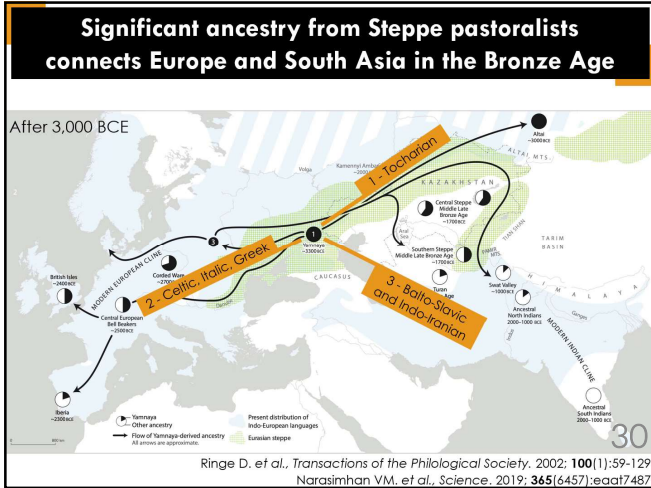


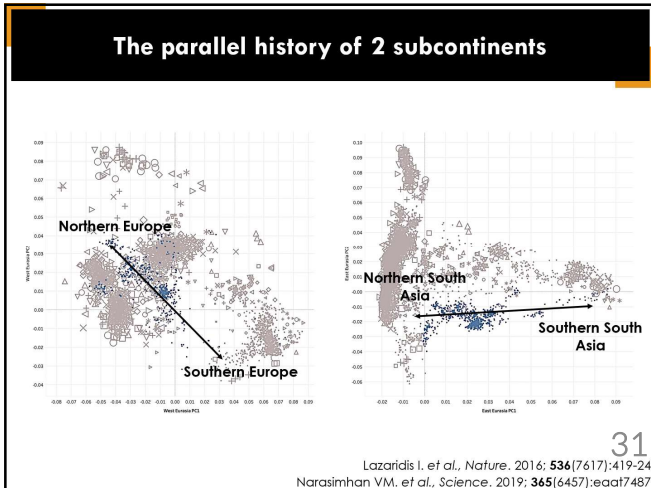


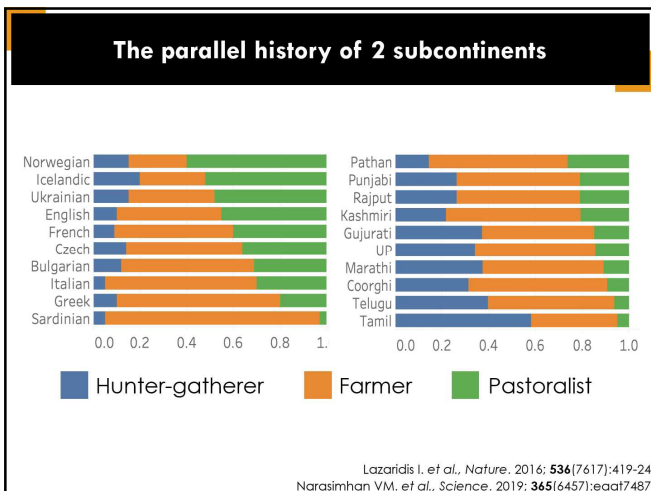




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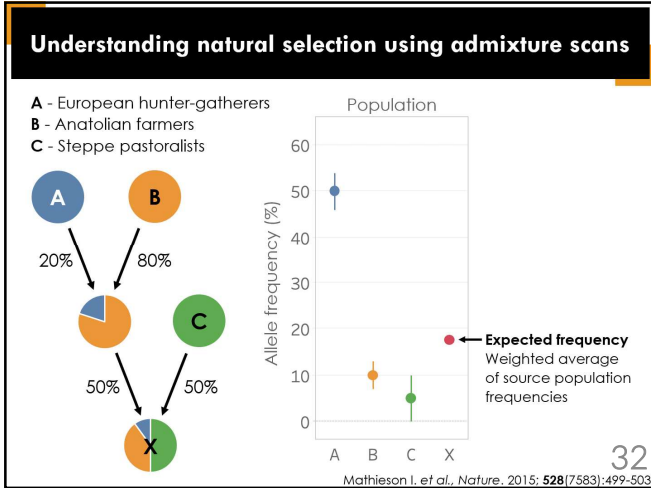


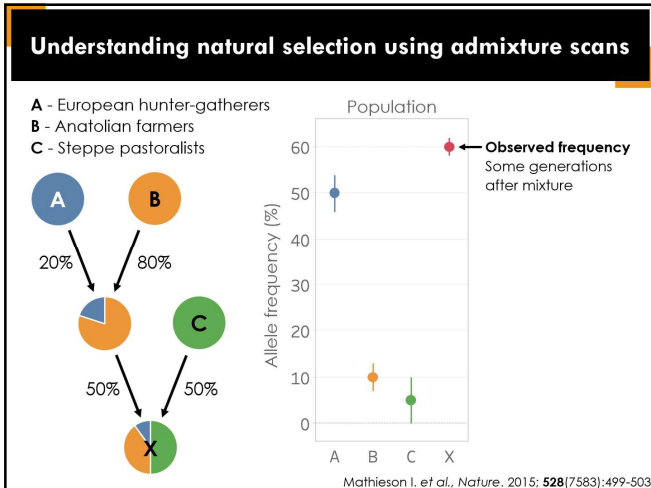






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Signals of selection observed over the past 10,000 years

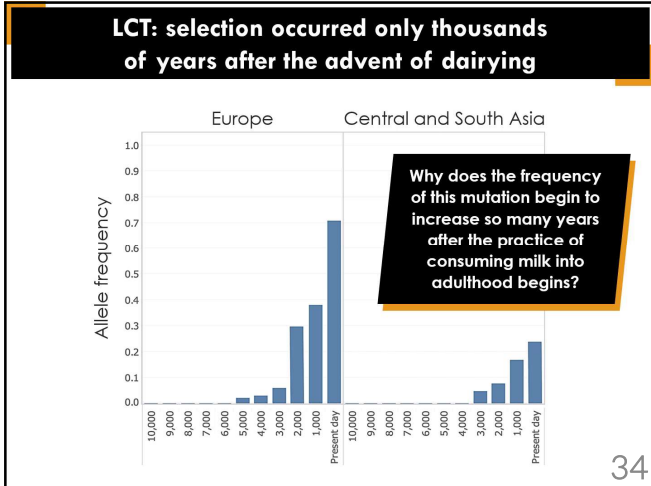
Epoch	Gene Name	Chr	Pos	Category	Function
Neolithic period	BDNF	1	27679936	Diet	Body weight, Appetite
	PTPRV	1	202151566	Diet	Obesity, Circulating glucose levels
	FTO	16	54231250	Diet	Obesity
	ENSA	1	150596411	Diet	Insulin secretion
	MAF	16	80057803	Diet	Insulin secretion
	PGAP3	17	37834541	Diet	Serum alkaline phosphatase levels
	FUT2	19	49206603	Blood group / Immune	ABO secretor status; Resistance to Norovirus infection
	IL3R1C2	2	102824201	Immune	Interleukin receptor; Inflammatory response
	FAM49B	8	130981907	Immune	Resistance to Salmonella infection
	PP1L2	22	22027348	Immune	Resistance to HIV infection
Bronze Age	SLC45A2	5	33954511	Pigmentation	Light eye color
	OCA2/HERC2	15	28386626	Pigmentation	Light skin pigmentation
	MR1	1	181018799	Immune	MHC locus; bacterial sensing
	KIR family	19	55324566	Immune	Natural killer cell pathogen detection
	AGT	1	230836065	Cardiovascular	Blood pressure regulator
	ABCG1	21	43679554	Cardiovascular	HDL level regulator
	MARK3	14	103867320	Rare disease	Childhood blindness
Historical Period	HYDIN	16	71096248	Rare disease	Sperm motility / infertility
	LCT	2	136555659	Vitamin D	Lactase persistence
	DHCR7	11	71153459	Vitamin D	7-dehydrocholesterol for conversion to vitamin D3
	FAO5L2	11	61571478	Diet	Lipid metabolism
	SLC45A2	5	33954511	Pigmentation	Light skin pigmentation
TLR family	4	38776107	Immune	Macrophage pathogen detection	
SH2B3	12	112007756	Immune	NOD2/bacterial signaling	

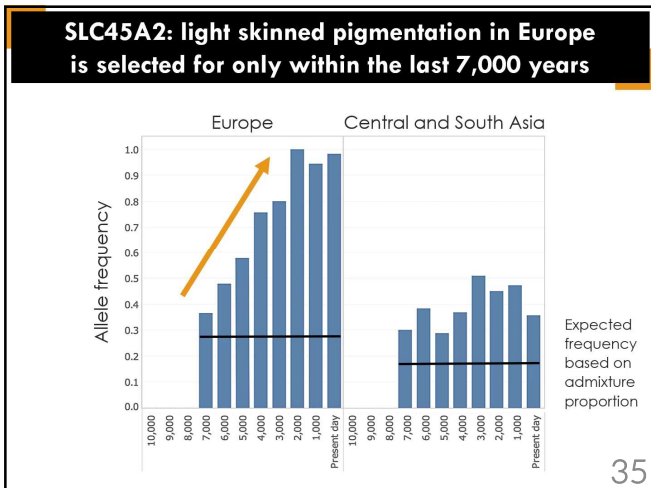
Le MK. et al., BioRxiv, 2022

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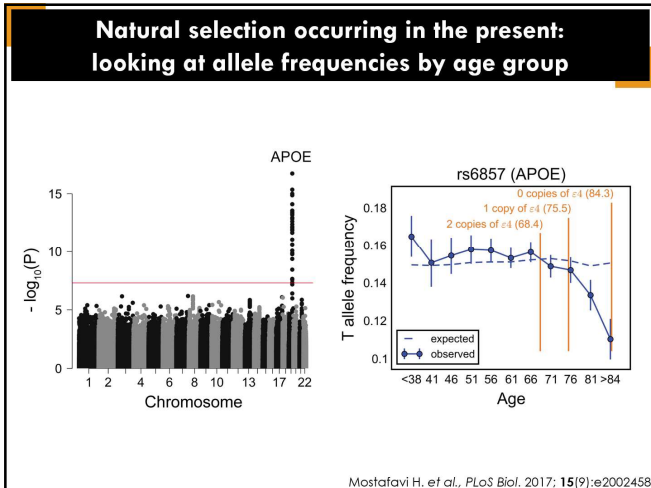
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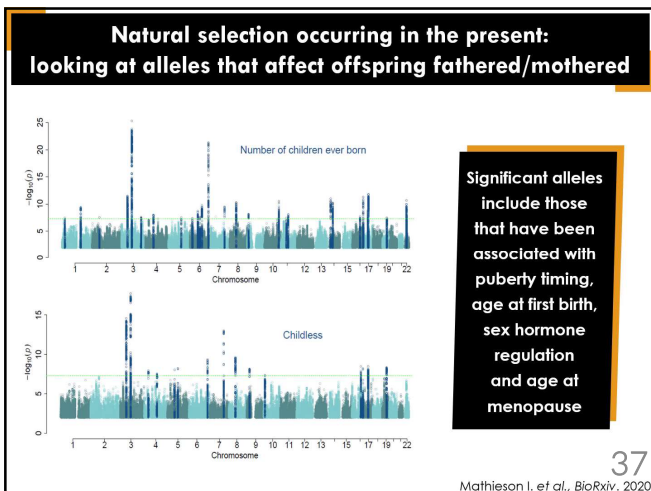
Natural selection occurring in the present: looking at allele frequencies by age group

One way that scientists can identify natural selection is by looking for alleles that change in frequency depending on age

E.g., alleles that confer longevity, or those that result in deleterious consequences if carried on at particular frequencies

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Thank you!

- › Human evolution is a very exciting area of scientific research
- › It has been approached through many means, including the study of changes in morphological characteristics over time
- › Ancient DNA has revolutionized the study of human evolution
- › Interbreeding between archaic hominid groups is evident
- › DNA sequencing has allowed us to study the many cultural transformations that have occurred over the past 10,000 years
- › Modern day genetic sequences can show us how natural selection is continuing to influence human evolution to this day

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