Updates: February 2022

Charles Vella PhD

Sonogenetics

- Currently: optogenetics = use of light to turn on brain cells

- In a new study published today (February 9) in *Nature Communications*, researchers report they've found a way to use ultrasound to noninvasively activate mouse neurons, both in culture and in the brains of living animals. The technique, which the authors call sonogenetics, elicits electrical activity in a subset of brain cells that have been genetically engineered to respond to sound waves.

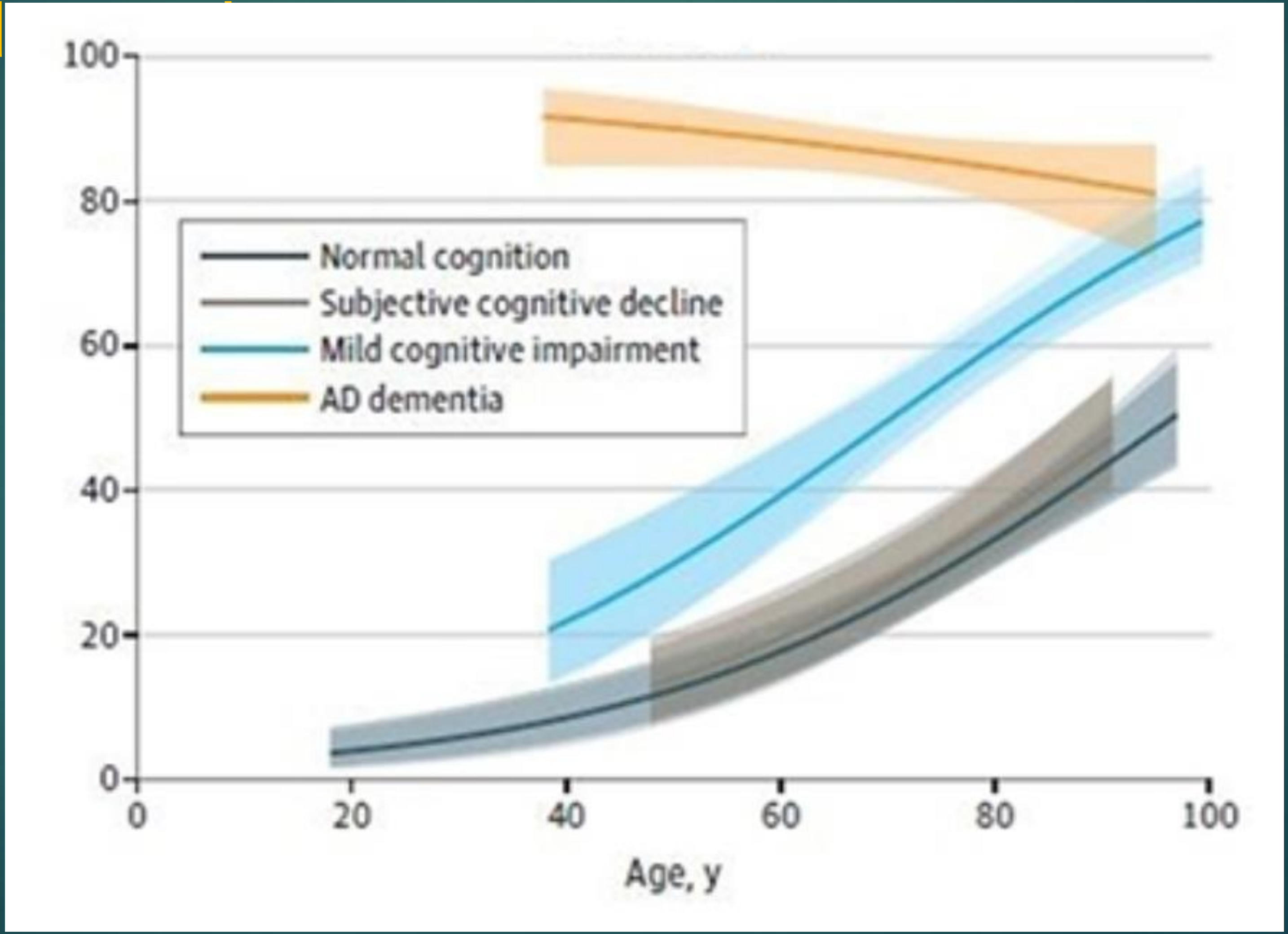
Not 10,000 steps

- JAMA: prospective study of 2100 middle aged people for 11 years with 1 year of step counter (from CARDIA study)
- 7000 steps: reduced chances of premature death by 50 to 70 percent (vs those who did less than 7K)
- More than 7000 burn calories
- Leveled off at 10 K; No benefit beyond 10,000
- Walking benefits frontal cortex: obsessive walkers included Darwin, Aristotle, Nietzsche, Wordsworth
- lower risk of premature all-cause mortality
- no association of step intensity
- Women’s Health Study reported a leveling at 7500 steps/d in older age (mean age, 72 years); as few as 4000 steps/d had approximately 30% lower risk

30% of normal 70 year olds have Beta Amyloid building

- N = 20,000: the largest study on amyloid prevalence to date estimates that 30% of cognitively normal people older than 70 have amyloid building up in their brains.
- 17% in cognitively sharp 50-year-olds, and 50%+ by age 95,
- Among people without dementia, amyloid prevalence rose with age, and was higher among ApoE4 carriers. ApoE4 carriers have steeper increases with age.

Amyloid Prevalence. Based on PET data, amyloid rose with age among people with normal or impaired cognition, but declined with age among people with d



ApoE2 & Education protective

- Across different ApoE genotypes. E4/E4 carriers started accumulating amyloid at the youngest age, followed by E3/E4, E2/E4, E3/E3, and E2/E3 carriers.
- Notably, the amyloid prevalence among E3/E4 carriers was 10 percent higher than it was among E2/E4 carriers across all groups without dementia, highlighting a protective effect of the E2 allele
- Among those without dementia, people with more education tended to have more amyloid, suggestive of cognitive reserve in the face of pathology. In people with AD dementia, educational level correlated with more amyloid, but only up to age 60.
- But sample only from Europe & US

Identical Twins Share Tau Trajectory, but Lifestyle Can Make a Difference

- Identical twins share the same womb, the same genome—and, it turns out, the same pattern of neurofibrillary tangles (Tau proteins).
- 2022 study compared the burden of tau tangles, and their regional distribution, among 39 pairs of identical twins who were in their 60s and 70s, some of whom also tested positive for Aβ plaques.
- For most of the twins, tau deposited in both siblings in a strikingly similar pattern, so much so that the researchers were able to identify a person's twin with 86 percent accuracy based solely on his or her tau-PET scan.
- Some twin pairs had discordant patterns of tau accumulation. Those were more likely seen in twins who differed in their Aβ status.
- Intriguingly, lifestyle factors also tracked with these differences, such that the twin who was less physically or socially active tended to have more tau tangles.

Anti-biotic resistant bacteria: human threat

- 1.3 million people died of anti-biotic resistant infections in 2019
- 3.65 million infections were questionable
- Killed more people than AIDS (680 k) or Malaria (627 k)

Use of bacterial phages as antibiotics

- Use of bacteria killing viruses/phages where antibiotics fail.
- Clinical improvement in 70% of patients
- Must find particular phage that will kill particular bacteria
- But bacteria evolve resistance to phages
- Have been used in Georgia and Poland for long time

Early excursions out of Africa

- Classic theory: MHs left Africa circa 60 Ka = final takeover of world
- Previous consensus in paleoanthropology held that settlements of modern humans in Europe around 46 to 40 Ka coincided with the demise of Neanderthals shortly thereafter.
- But increasing list of earlier MH excursions that proved to be dead ends
    - ▶ Apidima Cave, Greece (dated to 210 ka)
    - ▶ Misliya Cave, Israel mandible (180 ka)
    - ▶ N inherited mtDNA from MHs: A Neandertal found in 1937 in this cave in Germany had inherited modern human mtDNA; from a Neandertal thighbone found in 1937 in the Hohlenstein-Stadel cave (HST) in Germany; c 100 Ka

Cosimo Posth, et al., 2017

Multiple expansions: 210 to 50 Ka

- Israeli caves of Skhul and Qafzeh (90–130 ka)[1]
- Intermediate phalanx from the Al Wusta site in the Arabian Peninsula of 85 ka, showing a migration through the Bab el-Mandeb Strait in addition to the traditional passage sites along the Levantine corridor.
- 47 teeth from Fuyan Cave, SE China, dated 80-120 ka.
- Teeth from Sumatra (70 ka)
- Artefacts from northern Australia (65 ka)
- Cranial and mandibular fossils from Laos (50 Ka)

MH in Europe

- In Europe there was no record of modern humans above 46 ka.
- Among the oldest we have:
  - a tooth and six bone fragments from Bacho Kiro (Bulgaria) from 43-46 ka,
  - skull from Zlatý kůň (Czech Republic) from about 45 ka,
  - two teeth and the Uluzziense industry from Grotta del Cavallo (Italy, 43-45 ka),
  - Kent's Cavern 4 jaw (UK, 41-44 ka),
  - Oase-1 jaw (Romania, 38-42 ka).
  - In different places the lithic industry that accompanies the fossils is assigned to the initial Upper Paleolithic.

MHs in Europe

- The earliest evidence of Late Pleistocene *H. sapiens* settlement in Europe is constrained to ~45 ka to 43 ka ago based on
  - five isolated dental remains from
  - three Italian sites
    - Grotta Cavallo in Southern Apulia,
    - Riparo Bombrini in the western Ligurian Alps,
    - Grotta di Fumane in the western Lessini Mountains and
  - Bacho Kiro in Bulgaria.
- The latest Neanderthal remains in Europe are dated to 42 ka to 40 ka (& Gibraltar) ago, while their Mousterian lithic technologies ended by ~41 ka to 39 ka ago.

One of earliest MH incursion into Europe

- Multiple episodes of interbreeding between modern humans and Neanderthals likely occurred in Asia, and current paleogenetic data show that ancient gene flow between these groups may have also, to some degree, occurred in Europe,

- The newly published archeological and fossil evidence described here from layer E at Mandrin, France, documents an incursion of modern humans into Europe ~10 millennia earlier than previously identified

Modern human incursion into Neanderthal territories 54,000 years ago at Mandrin, France

- Findings at Grotte Mandrin, a cave in the Rhône Valley about 80 miles north of Marseille, provide fresh evidence that modern humans lived alongside Neanderthals, earlier than 45-43 Ka
- The earliest evidence of modern humans in Europe has been unearthed in a cave in southern France, showing they lived there at the same time as Neanderthals —
- However, level E where the aforementioned deciduous tooth appeared contained 1500 triangular objects of a very distinctive technology called Neronian, embedded in a short period of time (the layer is less than 20 cm thick) between clearly Mousterian levels.

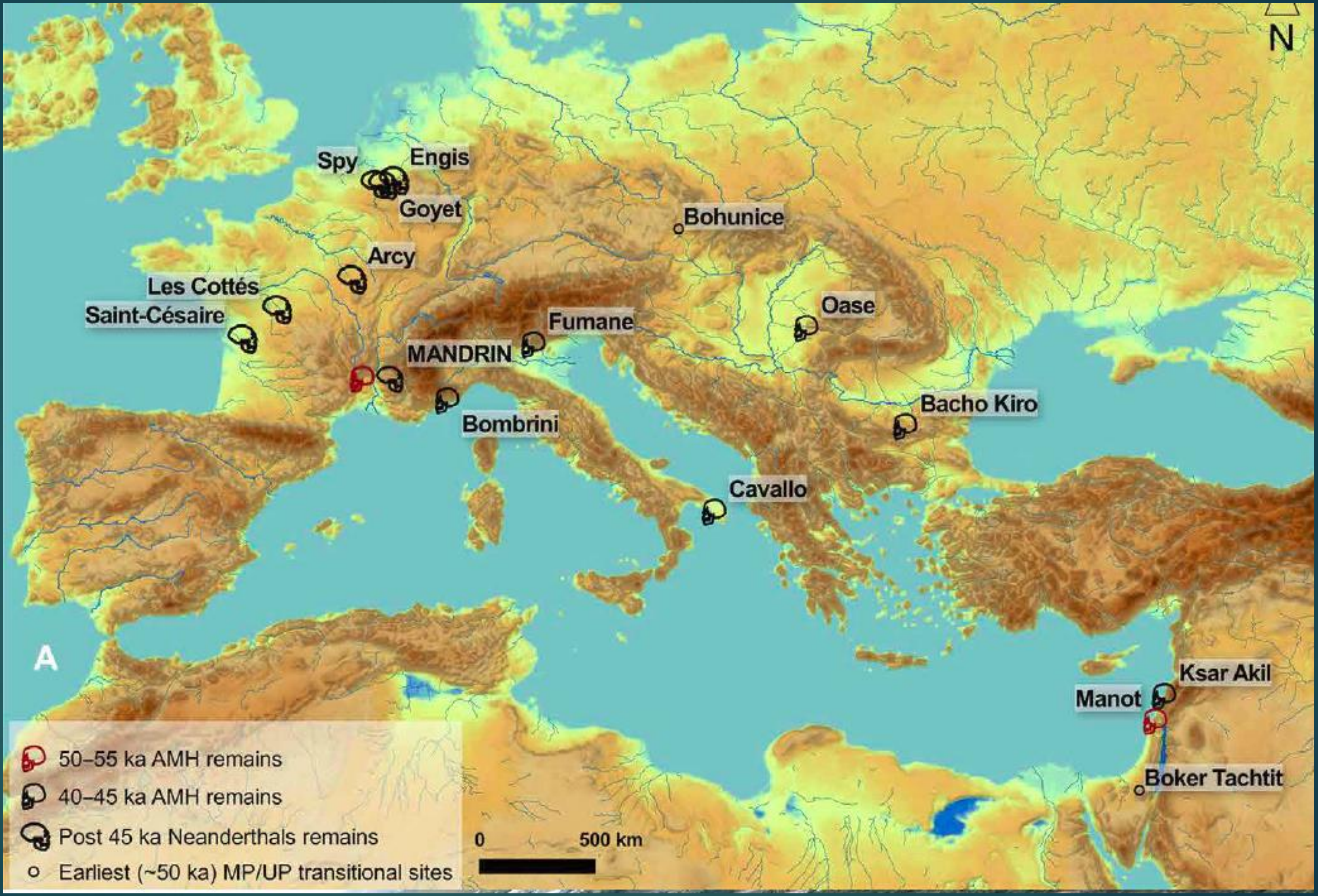
Ludovic Slimak, et al., *Science Advances*. 2022

Modern human incursion into Neanderthal territories 54,000 years ago at Mandrin, France

- A single *Homo sapiens* tooth and on distinctive fragments of MH flint points, found stratigraphically between layers containing Neanderthal remains associated with Mousterian industries..
- The discoveries push back the earliest date of our species — *Homo sapiens* — in Europe by roughly 10,000 years, to about 54,000 years ago (56.8 to 51.7 Ka.)
- Best evidence yet that Neanderthals and modern humans coexisted in Europe at times

This broken baby tooth may be the oldest known modern human fossil in Europe.

40-45 Ka
Europe



Grotte Mandrin in Rhône Valley, France

- Mandrin is like a kind of Neanderthalian Pompeii. 30 years of data
- The middle Rhône Valley: important natural corridor linking the Mediterranean Basin with the Northern European steppes.
- Overhanging the second most important river input to the Mediterranean Sea, represents a key for understanding these hominin successions at the Mediterranean basin scale.

30 years of research: Grotte Mandrin, a cave in the Rhône Valley

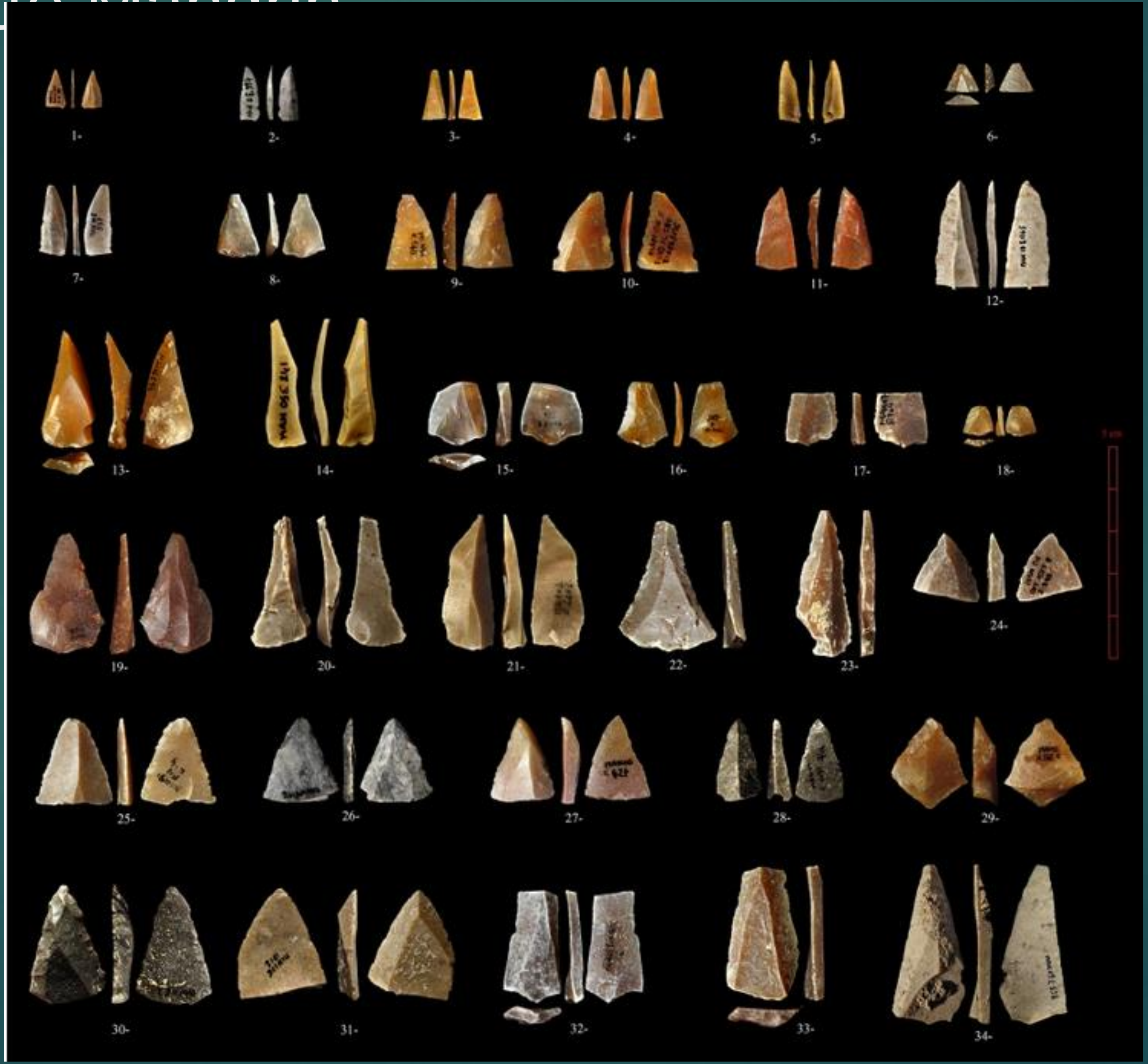
- 12 archeological layers (layers J to B1)
- Deposited between 80 to 35 Ka.
- 60,000 lithic objects
- more than 70,000 faunal remains dominated by horse, bison, and deer

This site was already well known for its Mousterian levels, which indicate intermittent Neanderthal occupation over almost 40,000 years. The cave has been studied since the 1990s, with 3 meters excavated In 2006, layer E yielded a trove of precisely sharpened stone points and animal bones. Six years later, they found a partial molar—a baby tooth. They spent 15 years excavating this layer,

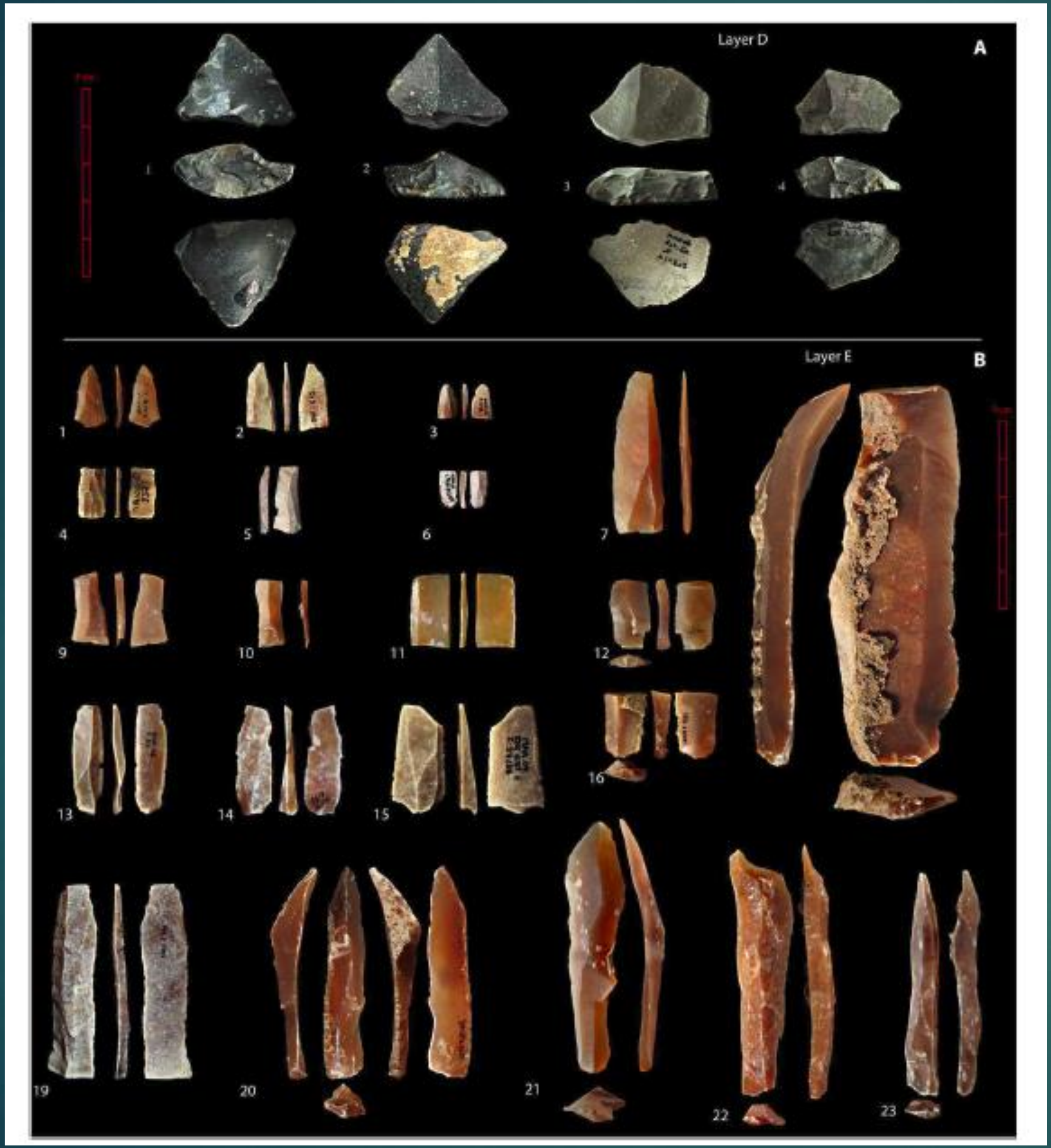
A flint point, thought to be the tip of an arrowhead, found during an excavation of Grotte Mandrin.

The points were made with the distinctive flint-knapping techniques called Neronian after the Grotte de Néron, 30 miles north of Grotte Mandrin

- Layer E's stone tools are smaller, more precisely made, and more standardized than the tools from the layers bearing Neanderthal teeth, which resemble Neanderthals' characteristic Mousterian tools



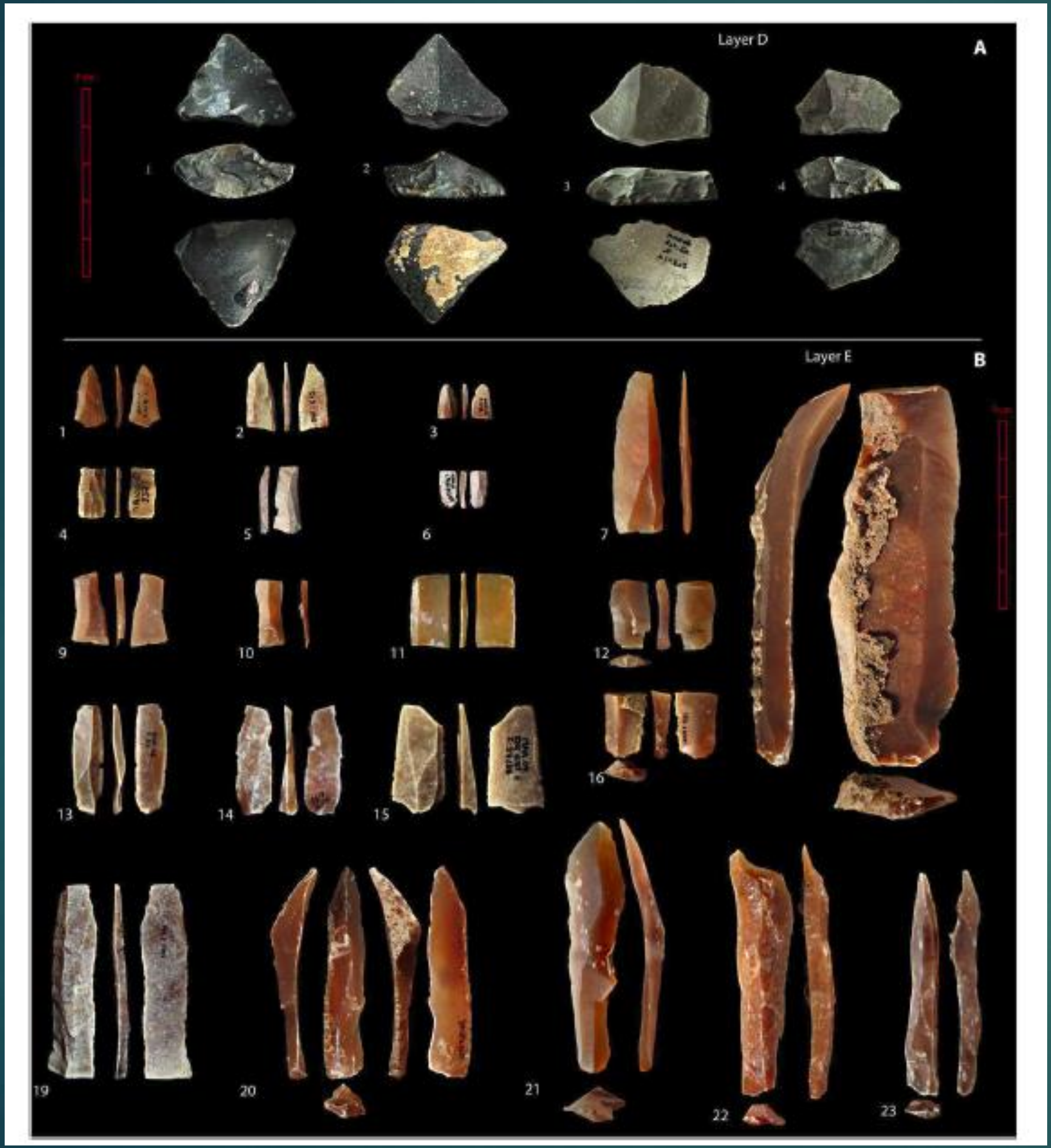
identical to flint points made by early modern humans in Lebanon,



Mandrin N layer D and MH layer E lithic industries.

A) Layer D: post–Neronian I Mousterian. Pseudo-Levallois points with truncated back in black exotic flints coming from ~70 to 90 km northeast of the site.

B) (**B**) Mandrin layer E: Neronian. Blades, bladelets, and bladelets by-products. Numbers 1 to 21, bladelets; number 18, crested bladelet; number 22, blade.



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Neronian artifacts from layer E:

Top to Bottom:

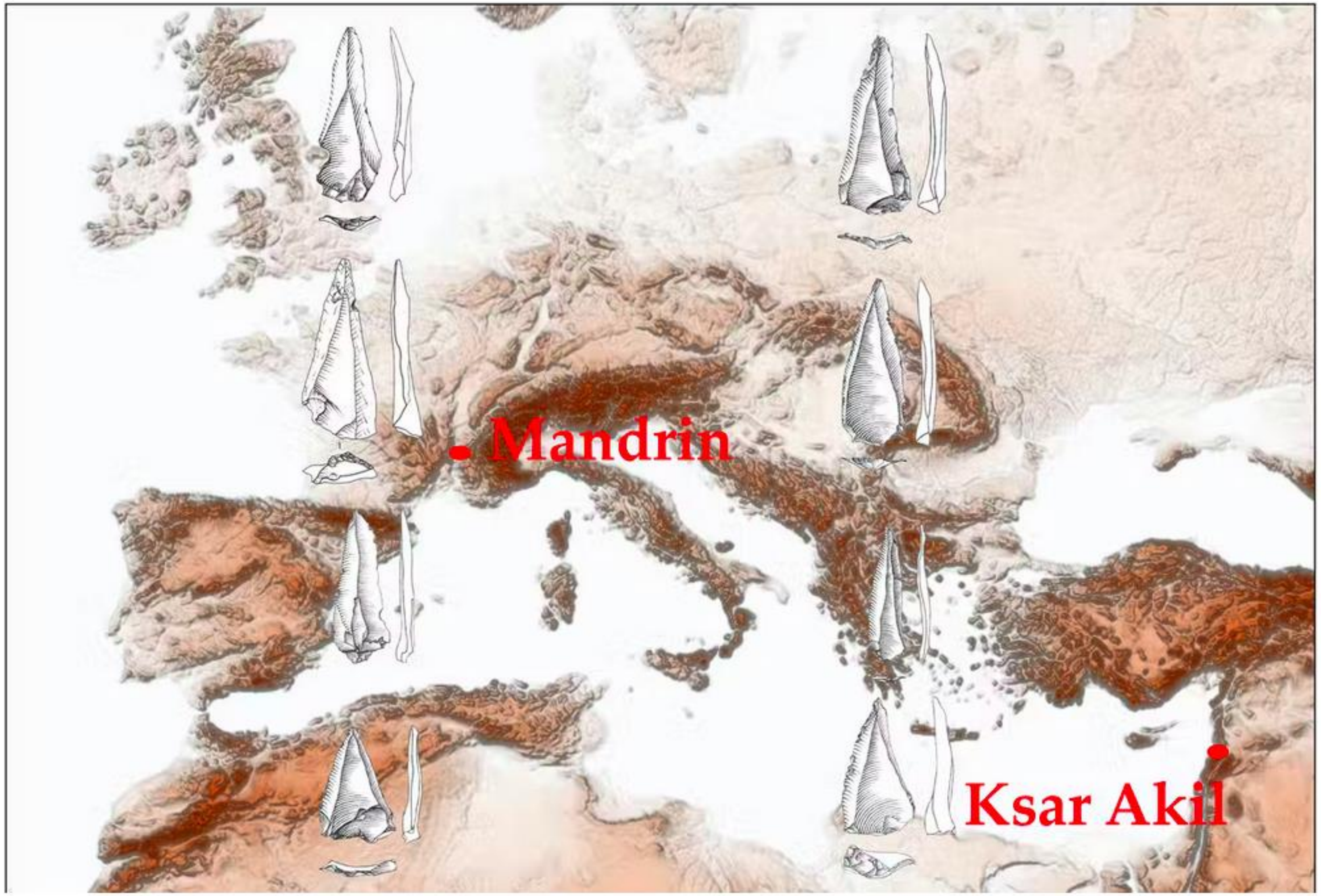
Pointed bone point with lateral notches,

Worked red deer canine,

Eagle talon with cutmarks,

Pebble with an engraved line separating the rock in two subequal parts

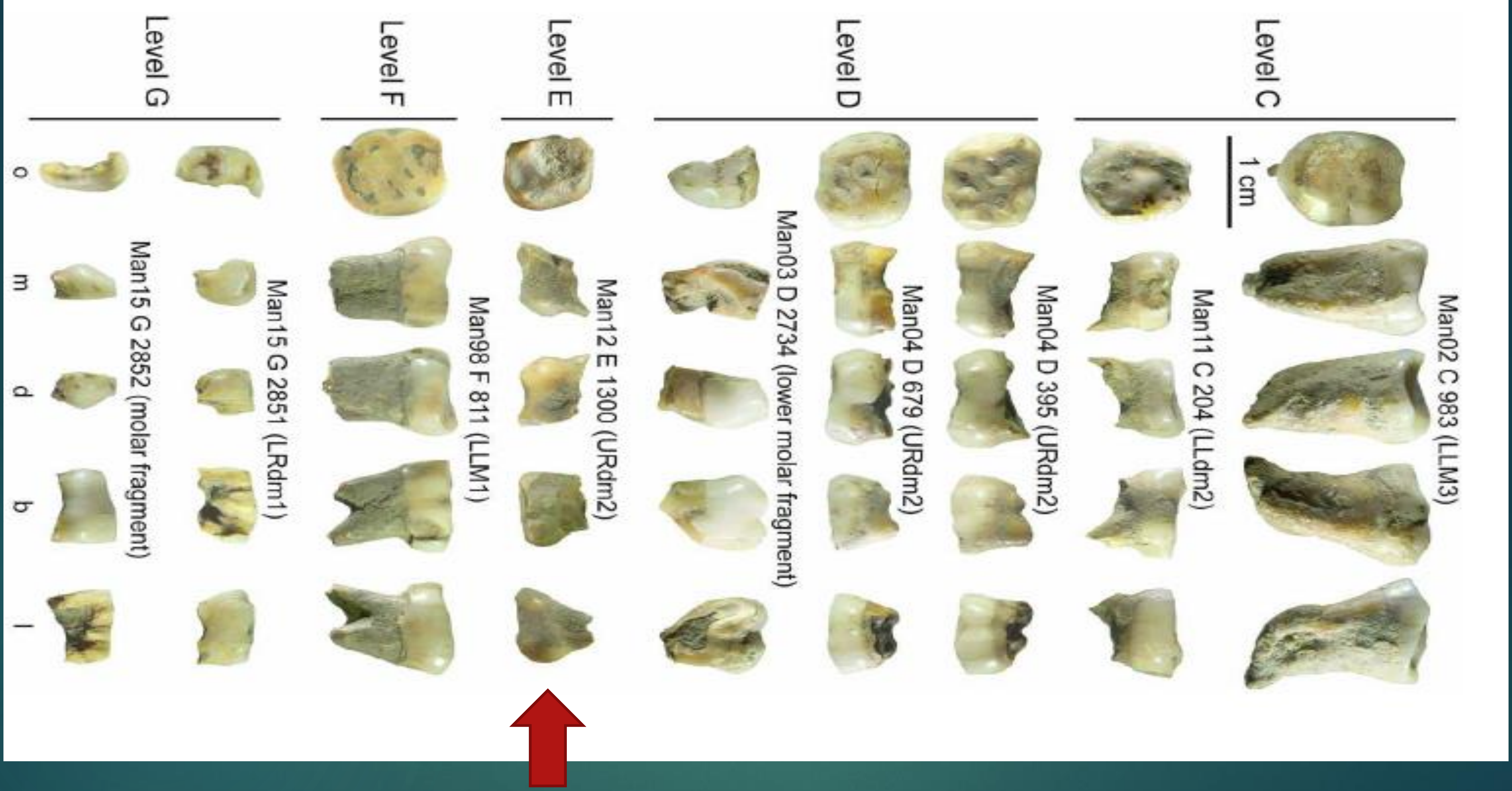
Two sites for Neronian MH points: France, Lebanon



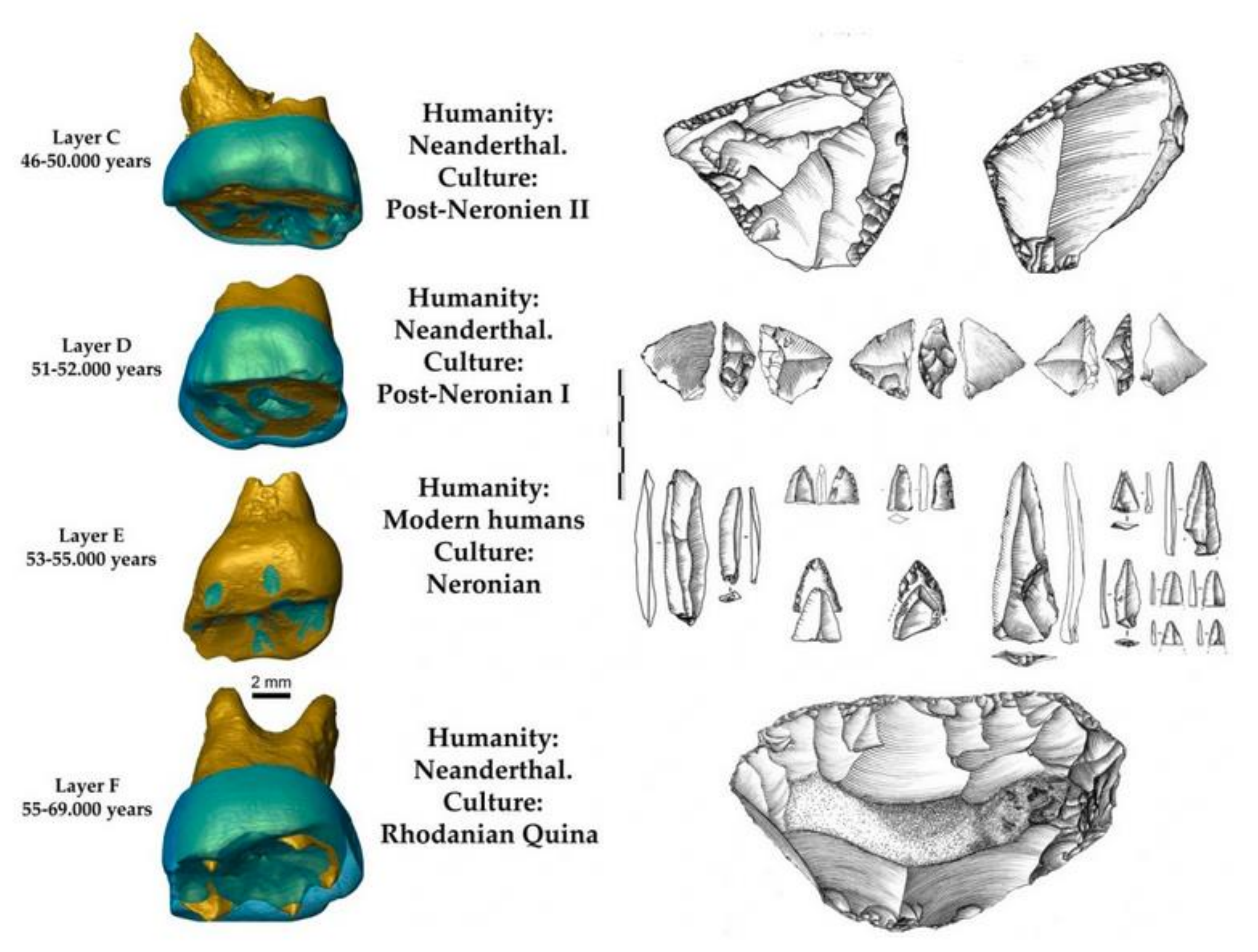
On opposite sides of the Mediterranean, similar stone points were made by *Homo sapiens* around the same time. Laure Metz and Ludovic Slimak, CC BY-ND

Earlier co-existence of Ns and MHs

- Radiocarbon analysis and luminescence dating established that the modern human layer in Grotte Mandrin is between 51,700 and 56,800 years old.
- That's roughly between 10,000 and 12,000 years before the previously accepted date for our species to have first set foot in Europe.
- These findings challenge the narrative that the arrival of Homo sapiens in Europe triggered the extinction of Neanderthals.
- We've often thought that the arrival of modern humans in Europe led to the pretty rapid demise of Neanderthals, but this new evidence suggests that both the appearance of modern humans in Europe and disappearance of Neanderthals is much more complex



MH tooth squarer outline than those of Neanderthals. All the teeth from layers ab
and below layer E had distinctly Neanderthal characteristics.



- One modern human tooth (deciduous maxillary second molar crown) in sediments that were sandwiched between sediments that held Neanderthal teeth and on dozens of distinctive flint points made by

Reading soot like tree rings

- Discovery of sooted vault fragments in 2006, and the team recovered thousands, year after year, in every archaeological layer of Mandrin.
- Thin layers of mineral deposits form along the walls of rock shelters like Grotte Mandrin, recording the passage of wet and dry seasons, a bit like tree rings.
- These mineral layers can trap soot from fires burning inside the caves, offering microscopic records of campfires past.
- This new technique, known as fuliginochronology, was first described in 2018 by Ségolène Vandevelde.
- These patterns can be read like tree rings to tell us with what frequency and duration the groups visited the site, demonstrating that human groups came to Mandrin some 500 times over 80,000 years.

Reading soot

- Vandevelde was then able to determine how much time separated the last Neanderthal fire from the first modern human fire in the cave, showing that it was only a maximum of a year between Neanderthals using Grotte Mandrin and modern humans moving in.

- Tiny chunks of mineral fell from the cave wall into each excavated layer. The sequence of soot layers in wall chunks from layer E overlapped with the sequence in chunks from the layer immediately beneath it, which held Neanderthal tools. That suggests only a brief period passed between the formation of the layers and therefore between the exit of the Neanderthals and the entrance of moderns—perhaps no more than a single calendar year.

Fire evidence

- Analysis of the soot on the cave's ceiling can be matched with the remains of fires in the sediments and suggests Grotte Mandrin was first occupied by modern humans perhaps a year after it was abandoned by Neanderthals.
- It's not known, however, just why the cave and its surrounding territory changed hands between the two species, and the researchers have found no direct evidence that they interacted. But flints in the modern human layer came from 60 miles away, so it seems they were familiar with the area's resources and may have had Neanderthal scouts or contacts

Alternation at Mandrin

- After modern humans first moved into the shelter, they and Neanderthals took turns for another 10,000 years.

- Pattern of small wave intrusions of MHs rather than tidal wave

- Therefore, this tooth indicates that, after a period of Neanderthal occupation of the cave between 80 and 54 ka ago, a group of *Sapiens* was there only one year after the previous Neanderthals, judging by the periodic marks left by the deposits of calcite in the cave

Taking turns

- Later, one or two generations of *sapiens they* remained for about 40 years and disappeared.
- Then Neanderthals return to occupy the place for another 12,000 years
- And, after them, modern humans again.
- Cave was occupied at least 500 times by the 2 groups over 80,000 years.
- The study of the industries of the different levels does not show exchange of cultural traditions between Neanderthal groups, nor between Neanderthals and modern humans, which indicates rapid replacement of some human groups with others in this area.

4 Replacements

- At least four alternating phases of replacement, with no obvious processes of cultural exchange:
- Neanderthals occupying the area around Mandrin from 80 Ka up to ~54 ka (Mandrin layers J to F),
- A modern human incursion for a year at around 54 ka (56.8 to 51.7 ka; Mandrin E)
- Followed by Neanderthal reoccupations over 12 K (Mandrin D-C2-C1-B3-B2), 55 to 44 Ka
- A second & final modern human phase for from ~44.1 ka to 41.5 ka. (Mandrin B1) onward.
- Complex historical process during which both populations replaced each other rapidly or even abruptly, at least twice, in the same territory.

Early MH incursion

- The study also suggests this modern human group was part of an incursion from the eastern Mediterranean coast that didn’t last long before they again vanished from Europe — one of the early waves of *Homo sapiens* migrating to the continent. They may have numbered a few hundred, including women and children.

- The clearest evidence is a single baby tooth from a modern human child, aged between 2 and 6, that was found in a layer of clay and sand sediments on the floor of the cave.

- It was sandwiched between sediment layers that held Neanderthal teeth, among other remains; and because Neanderthals and *Homo sapiens* had distinctly different teeth, the evidence is unquestionable

Need DNA

- Findings upend the idea that most of the European continent was the exclusive domain of Neanderthals until 45,000 years ago.

- Did not do DNA of tooth to prove it was MH (because collateral analysis of horse tooth failed).

- Need more solid skeletal or genetic evidence.

- Conclusion that tooth is MH is still theoretical until the DNA is done

Chimpanzees observed treating wounds of others, using crushed insects

- The project began in 2019, when an adult female chimpanzee named Suzee was observed inspecting a wound on the foot of her adolescent son.
- Suzee then suddenly caught an insect out of the air, put it in her mouth, apparently squeezed it, and then applied it to her son’s wound.
- After extracting the insect from the wound, she applied it two more times.
- The scene unfolded in Loango national park on Gabon’s Atlantic coast, where researchers are studying a group of 45 central chimpanzees, an endangered species. Over the following 15 months, scientists saw chimpanzees administer the same treatment on themselves at least 19 times.
- And on two other occasions they observed injured chimpanzees being treated in the same way by one or several fellow apes.

Ancient skull belonged to a cousin of the ape common ancestor

- New extinct ape species Nyanzapithecus alesi

- Infant ape: the most complete extinct ape skull in the fossil record so far.

- in the Napudet area of northern Kenya, the fossil – nicknamed Alesi – is 13 million years old.

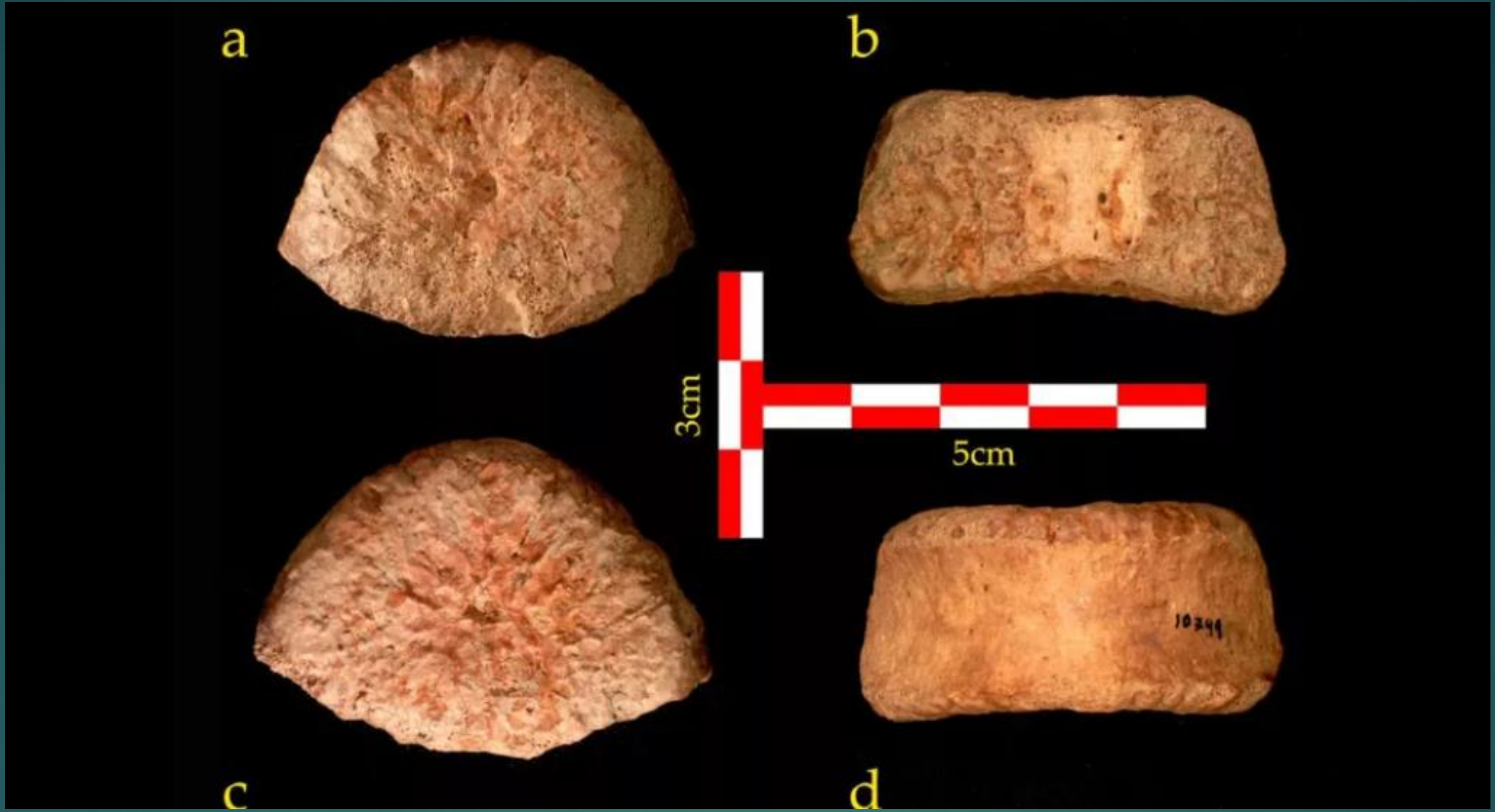
- It is the first relatively complete ape skull from the period between 14 and 10 million years ago.
- links *Nyanzapithecus* to apes, because *N. alesi* clearly has well-developed bony ear tubes – an important ape feature. *N. alesi* and its close relatives probably evolved some time just before the common ancestor of all living apes.

The earliest Pleistocene record of a large-bodied hominin from the Levant supports two out-of-Africa dispersal events

- Report on the earliest large-bodied hominin remains from the Levantine corridor: a juvenile vertebra (UB 10749) from the 1.5 Ma Pleistocene site of ‘Ubeidiya, Israel, discovered during a reanalysis of the faunal remains.
- UB 10749 is a complete lower lumbar vertebral body, with morphological characteristics consistent with *Homo* sp.
- Analysis indicates that UB-10749 was a 6- to 12-year-old child at death, displaying delayed ossification pattern compared with modern humans. Its predicted adult size is comparable to other early Pleistocene large-bodied hominins from Africa.
- Supports at least two distinct out-of-Africa dispersal events.

A Barash, et al., 2022

Hominin Vertebra discovered at Ubeidiya, Israel



A 1.5 million-year-old vertebra from an extinct human species unearthed in Israel suggests that ancient humans may have migrated from Africa in multiple waves; second-oldest archaeological site outside Africa - 6-12 yo 100 lb : suggests a large body size as adult; larger than 1.8 yo Dmanisi erecti

Lithics: Acheulean at Ubeidiya, Oldowan at Dmanisi: 2 different migrations

New Denisovan skull? 3 pieces

PA1486
(No.7/XJY 6a)
occipital bone,

PA1490
(No.10/XJY 6b)
right parietal
bone, and

PA1498
(No.17/XJY 15)
left temporal
bone—which
originated from
the same young
adult individual.

Xiu-Jie Wu, et al., 2022

Xujiayao 6 or XJY 6: 160,000-year-old fossil may be the first Denisovan skull we've found

- First reconstruction of a fairly complete posterior cranium, Xujiayao 6 (XJY 6), confidently dated to ~200–160 ka, which facilitated an assessment of its overall cranial size.

- The earliest human with a “modern” brain size. It could represent an unknown group of ancient humans, or perhaps one of the enigmatic Denisovans

- Conservatively estimate the XJY 6 endocranial volume to be ~1700 cc (1555–1781 cc).

Xujiayao 6 or XJY 6

- Bones come from Xujiayao, an archaeological site in northern China that was first excavated in the 1970s.
- Down the years, the site has yielded 21 fragments of hominin skeletons, ranging from teeth and bits of jawbone to pieces of skull. These fragments represent at least 10 individuals
- Sediment in which it was found is between 160 to 200 Ka.

- Xujiayao 6 is “the earliest evidence of a brain size that falls in the upper range of Neanderthals and modern *Homo sapiens*”

Big brains

- Lynne Schepartz at the University of the Witwatersrand in Johannesburg, South Africa. “We are long past the days when brain size was the famous ‘cerebral Rubicon’ used to assign human status”.
- Big brains aren’t necessarily linked to intelligence. “Human populations in colder environments have larger brains,” she says, but that is because of “thermal packaging” that keeps the neurons warmer and thus able to function.
- Wu thinks new species.
- but Bence Viola: If Xujiayao 6 is a Denisovan, its large brain could be explained: if they were indeed big-bodied, their brains would be proportionately large as well.
- Similar to the Harbin cranium (Dragon man)
- XJY 6, together with Xuchang 1, *Homo floresiensis*, *Homo luzonensis*, and *Homo naledi*, challenge the general pattern that brain size gradually increases over geological time.

Cooperative Carnivores in the Fossil Record
By Pat Lee Shipman

- Pat Shipman: Cooperation in carnivores
- Fossil evidence indicates that *Homo erectus* cared for their sick, elderly, and disabled, demonstrating a closely knit social structure and cooperative behavior.

- The wild dog *Canis{Xenocyon) lycaonoides* had a cooperative pack structure, which is necessary for large predators that get most of their food from even larger prey.

- *H. erectus* also shows evidence of such a hypercarnivorous lifestyle: large body size, tool use for slicing meat, and strong sociality.
- Cooperation was a key adaptation for large hunters.

Dmanisi, 1.8 Ma & African KNM-ER 1808 : *H. erectus* was cooperative

KNM-ER 1808: a *H. erectus* with hypervitaminosis A in a caring community

- *H. erectus* specimen found in Kenya known as KNM-ER 1808, which is dated to 1.65 million years.
- The KNM-ER 1808 fossils were marked by an extraordinary overgrowth of pathological bone tissue around the limb bones, diagnosed as a probable case of hypervitaminosis A.
- This disease is sometimes caused by overzealous parents who feed their children excessive amounts of vitamins.
- It also occurs in extraordinary circumstances when an individual consumes an extreme amount of raw carnivore liver at one sitting, or smaller amounts over a period of time.

KNM-ER 1808

- Carnivores concentrate the vitamin A from their prey in the stellate cells of their livers, making carnivore liver poisonous to species not adapted to this diet.
- The measured content of vitamin A in a single gram of adult polar bear liver can be 20 to 100 times the recommended daily allowance for humans.
- Before dying, sufferers of hypervitaminosis A experience weakness, headache, sloughing off of skin, joint pain, and loss of hair and teeth.
- But the pathological condition of the fossil bones showed that *H. erectus* had shifted to a predominantly meat-eating diet and that this particular individual probably died of hypervitaminosis A.
- He would have needed extensive care while disabled for months or years as he grew up to a quarter inch of pathological bone in many places on his limbs.

Dmanisi’s cooperative carnivores: survival of the friendliest

- Dmanisi preserves many carnivores: giant cheetahs, two kinds of saber-toothed cats, a small wolf, a lynx, several kinds of bear, giant hyenas, and a jaguar as big as a lion. There was also an extinct canid, *Canis*, a probable ancestor of the living African hunting dog, and *H. erectus*
- What is so curious is that these canids apparently migrated from Eurasia into Africa through Georgia while *H. erectus* expanded its territory from Africa into Eurasia through Georgia at the same time.
- And both the canid and the hominin show evidence of cooperative behavior with other conspecifics. These co-occurrences are more than simply an odd coincidence; they may tell us something important about survival and sociality among predatory species.

H. erectus

- Animals with weights over about 21–25 kilograms—about as big as or bigger than a Dalmatian. The energetic requirements of larger carnivores can be met only by eating more than 70 percent meat derived from prey much bigger than themselves. This strategy is known as *hypercarnivory* and requires pack hunting and extreme sociality to succeed.

- These two partial skeletons of *H. erectus*—one from Kenya and one from Dmanisi—indicate fairly large body size, tool use, strong sociality, and prolonged care for other members of the group.
- In sum, our ancestors were very probably hypercarnivorous.

No sustained increase in zooarchaeological evidence for carnivory after the appearance of *Homo erectus*

- Many quintessential human traits (e.g., larger brains) first appear in *Homo erectus*.
- The evolution of these traits is commonly linked to a major dietary shift involving increased consumption of meat.
- Early archaeological sites preserving evidence of carnivory predate the appearance of *H. erectus*, but larger, well-preserved sites only appear after the arrival of *H. erectus*.
- This qualitative pattern is a key tenet of the “meat made us human” viewpoint,
- Data from sites across eastern Africa have not been quantitatively synthesized to test this hypothesis.
- New analysis shows no sustained increase in the relative amount of evidence for carnivory after the appearance of *H. erectus*, calling into question the primacy of carnivory in shaping its evolutionary history.

W. Andrew Barr, et al. 2022

Carnivory sampling error

- New Analysis: a quantitative synthesis of the zooarchaeological record of eastern Africa from 2.6 to 1.2 Ma.

- Sampling error: The prevalence of hominin carnivory are all strongly related to how well the fossil record has been sampled

- When correcting for sampling effort, there is no sustained increase in the amount of evidence for hominin carnivory between 2.6 and 1.2 Ma.

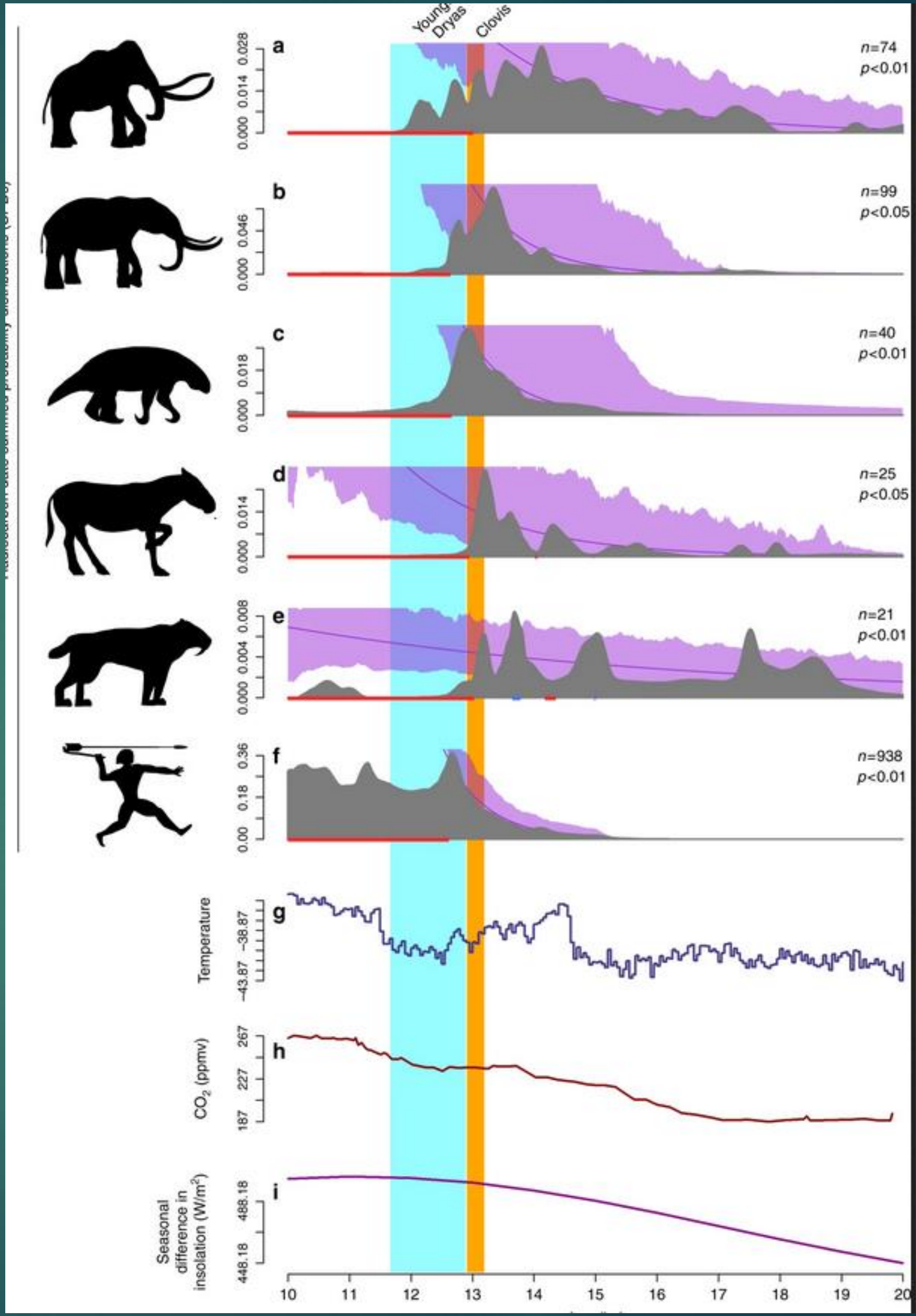
- These findings undercut evolutionary narratives linking anatomical and behavioral traits to increased meat consumption in *H. erectus*, suggesting that other factors are likely responsible for the appearance of its human-like traits.

Paleogenetics, Pt 5:
Genetics of African Origins
Genetics of Non-African Population Migrations

Charles J Vella, Feb. 2022

Doug sent:

- Massive megafauna (over 44kg) extinction directly after human arrival in N.A.
- Extinction of 70% of megafauna taxa & 100% of megafauna of S.A. origin. e.g. look at horses, which we seem to have eaten rapidly.
- But whether MHs were sole cause?: Megafauna lasted a few 1000 years after our arrival, so likely we weren't the only cause.



KhoeSan

Not so isolated: Khoisan tribes have European DNA

Ariadne Van Zandbergen/Alamy

N DNA in KhoeSan

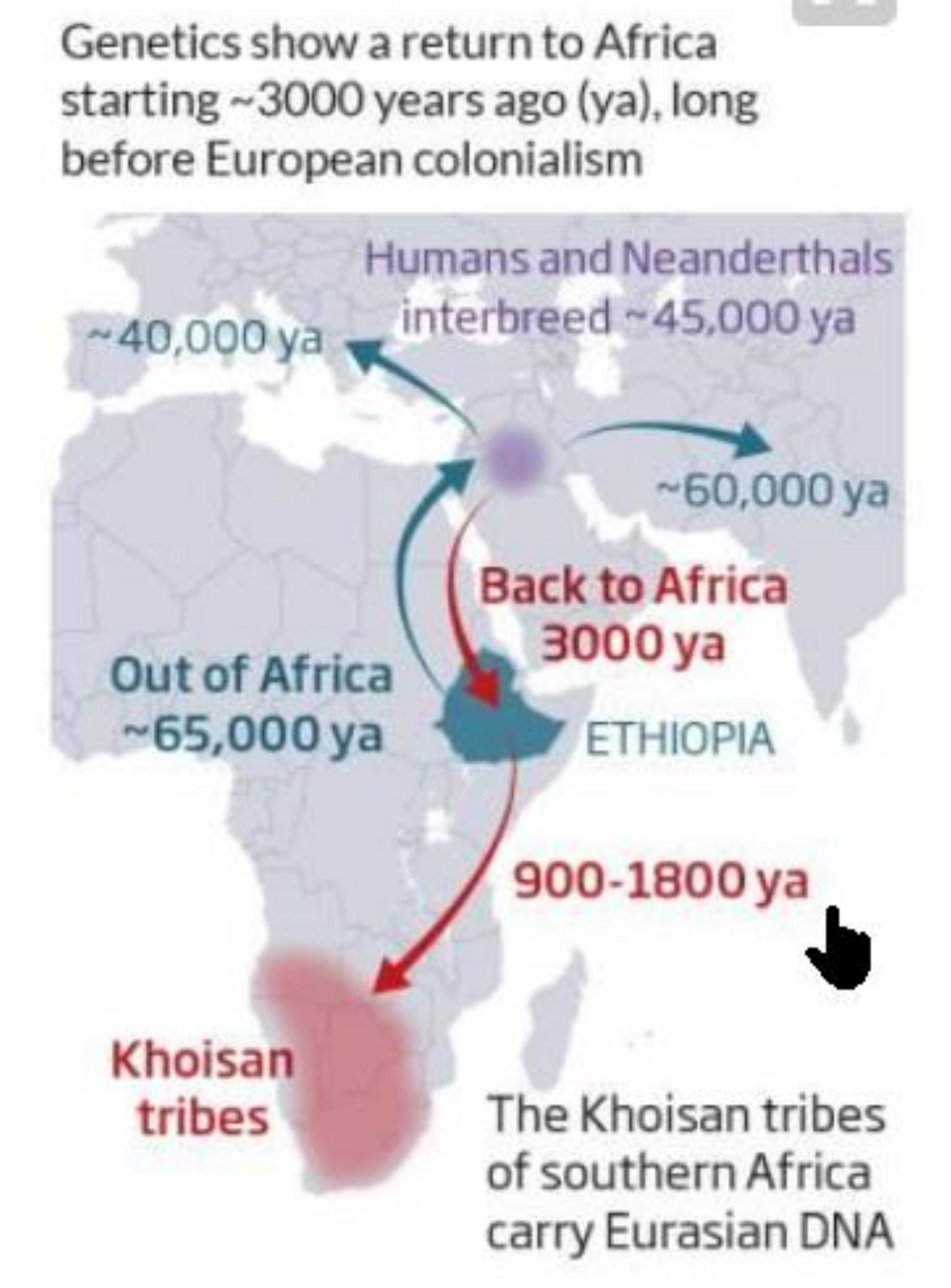
- The KhoeSan tribes of southern Africa are hunter-gatherers and pastoralists who speak unique click languages. Their extraordinarily diverse gene pool split from everyone else's before the African exodus.
- According to conventional thinking, the KhoeSan tribes of southern Africa, have lived in near-isolation from the rest of humanity for thousands of years. In fact, the study shows that some of their DNA matches most closely people from modern-day southern Europe, including Spain and Italy.
- Because Eurasian people also carry traces of Neanderthal DNA, the finding also shows – for the first time – that genetic material from our extinct cousin may be widespread in African populations.

Schuster, SC, et al., 2010

Some Africans have N DNA:

~ 3000 ya MHs with Neandertal DNA returned to Africa

Today there is N DNA in some KhoeSan tribes of S Africa



N DNA in KhoeSan

- This DNA made their way into the KhoeSan DNA sometime between 900 and 1800 years ago.

- A subset of the KhoeSan, known as the Khoe-Kwadi speakers, arrived in southern Africa from east Africa around 2200 years ago. the proportion of Eurasian DNA was highest in Khoe-Kwadi tribes, who have up to 14 per cent of western Eurasian ancestry.

- What is more, when they looked at the east African tribes from which the Khoe-Kwadi descended, they found a much stronger proportion of Eurasian DNA – up to 50 per cent.

- Neanderthal traces have also been found in the Yoruba

Denisovan mtDNA

- However, according to the nuclear DNA (nDNA) of Denisova 3—Denisovans and Neanderthals were more closely related to each other than they were to modern humans.
- Using the percent distance from human–chimpanzee last common ancestor, Denisovans/Neanderthals split from modern humans about 804,000 years ago, and from each other 640,000 years ago.
- Using a mutation rate of $1\text{x}10^{-9}$ or $0.5\text{x}10^{-9}$ per base pair (bp) per year, the Neanderthal/Denisovan split occurred around either 236–190 or 473–381 Ka respectively.

Denisovan mtDNA

- The more divergent Denisovan mtDNA has been interpreted as evidence of admixture between Denisovans and an unknown archaic human population, possibly a relict *H. erectus* or *H. erectus*-like population about 53,000 years ago.

- Alternatively, divergent mtDNA could have also resulted from the persistence of an ancient mtDNA lineage which only went extinct in modern humans and Neanderthals through genetic drift.

- Modern humans contributed mtDNA to the Neanderthal lineage, but not to the Denisovan mitochondrial genomes yet sequenced.

D mtDNA

- The mtDNA sequence from the femur of a 430 Ka *H. heidelbergensis* from the Sima de los Huesos Cave in Spain:
  - was found to be related to those of Neanderthals and Denisovans,
  - but was closer to Denisovans,
  - authors posited that this mtDNA represents an archaic sequence which was subsequently lost in Neanderthals due to replacement by a modern-human-related sequence.

Origin of MHs Debate as of 2011: Stringer vs Wolpoff

- From 1984, for 27 years, Chris Stringer and Milford Wolpoff fought about where and how MHs originated.

- Stringer, a paleoanthropologist at the Natural History Museum in London, held that modern humans came out of Africa,
  - spread around the world,
  - and replaced, rather than mated with, the archaic humans they met.

- Wolpoff, of the University of Michigan, Ann Arbor, argued that a single, worldwide species of human, including archaic forms outside of Africa,
  - met, mingled and had offspring,
  - and so produced *Homo sapiens*.
  - Their battle was long and bitter.

Ann Gibbons 2011

Origins

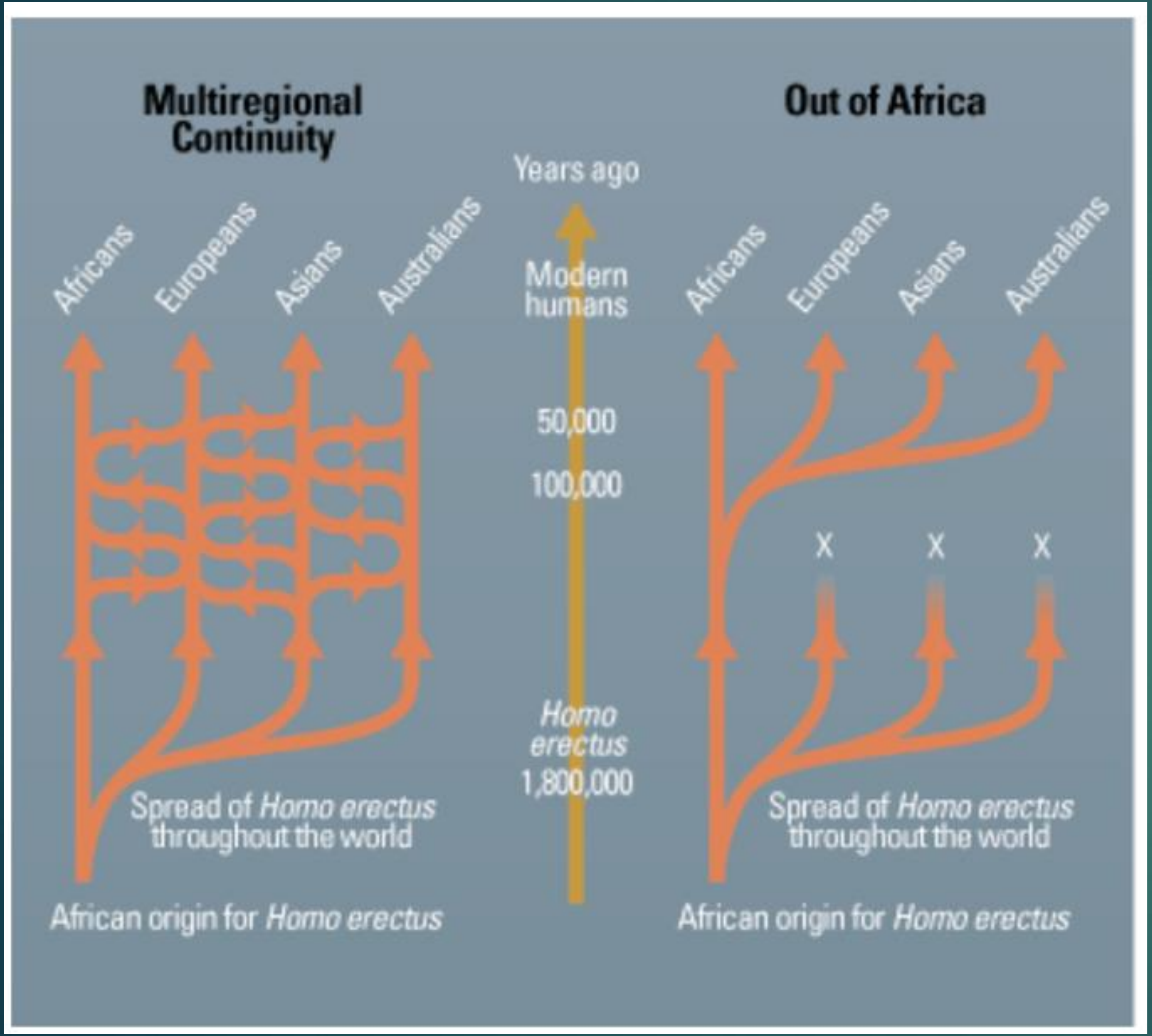
- Then in 2010, nuclear genomes of Ns and Ds came out.
- Allowed test of above models.
- There were at least two instances of interbreeding between archaic and modern humans, raising the question of whether *H. sapiens* at that point was a distinct species;
- Genomes appeared to refute the complete replacement concept of the Out of Africa model;
- Out of Africa, but with low levels of admixture

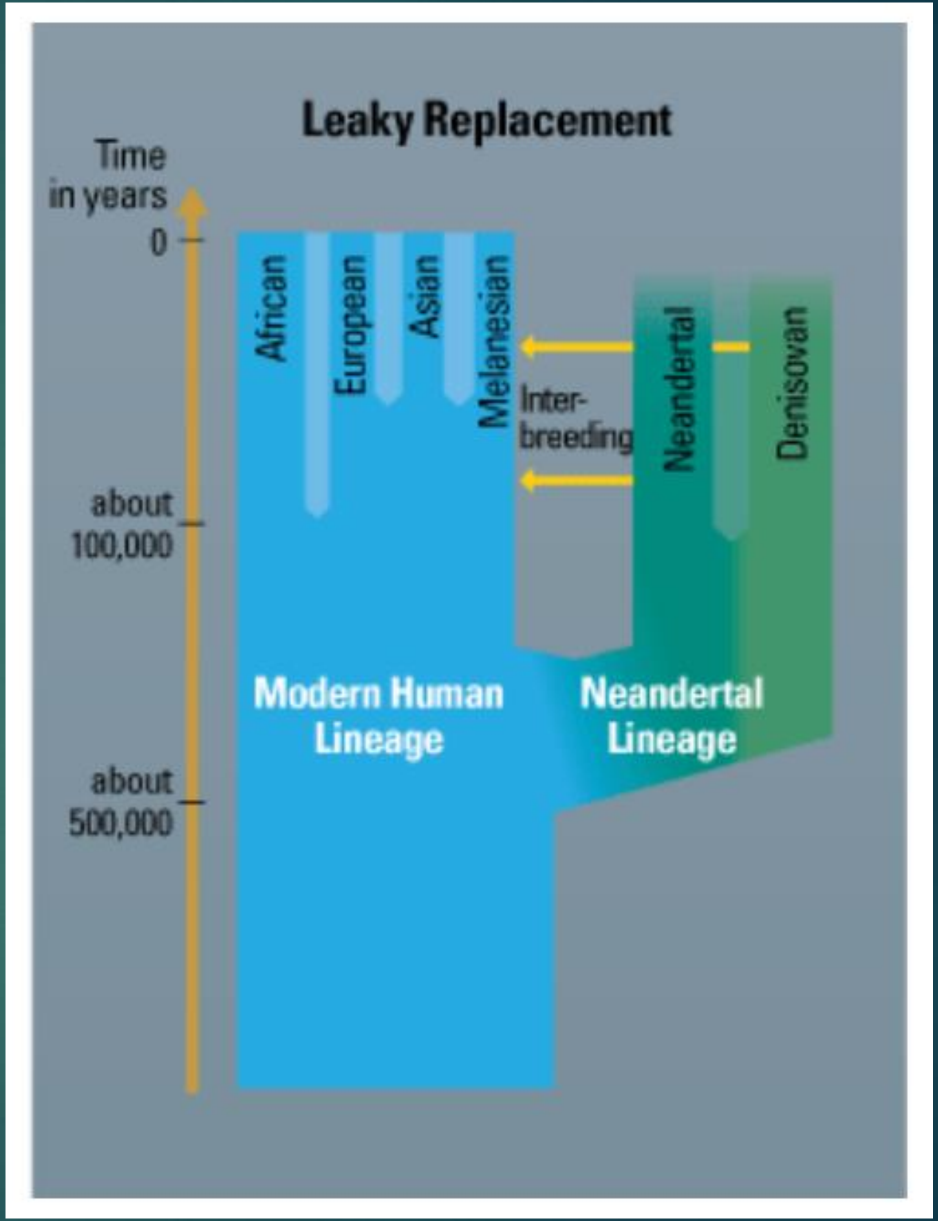
Origin of MHs Debate

- Genomic data did not prove the classic multiregionalism model correct either.
- They suggest only a small amount of interbreeding, presumably at the margins where invading moderns met archaic groups that were the worldwide descendants of *H. erectus*
- Svante Pääbo: best model as replacement with hybridization, or ‘leaky replacement.
- New picture most resembles so-called assimilation models, which got relatively little attention over the years, a la Fred Smith

Origins

- In 1984, Mitochondrial Eve: mother of all in Africa, circa 200 Ka
- Studies of living people—from Y DNA in nucleus & mtDNA—consistently found that Africans were the most diverse genetically.
- This suggests that modern humans arose in Africa, where they had more time to accumulate mutations


Multiregional Continuity
Out of Africa
Years ago
Africans
Europeans
Asians
Australians
Modern humans
50,000
100,000
Homo erectus
1,800,000
X
X
X
Spread of Homo erectus throughout the world
African origin for Homo erectus
Africans
Europeans
Asians
Australians
Spread of Homo erectus throughout the world
African origin for Homo erectus


Leaky Replacement
Time in years
0
about 100,000
about 500,000
African
European
Asian
Melanesian
Inter-breeding
Neandertal
Denisovan
Modern Human Lineage
Neandertal Lineage

John D. Hawks: Multiregionalist, Molecular genetics

- Professor of Anthropology at the University of Wisconsin–Madison.

- Multiregionalist

- Molecular genetics

- Hawks predicted introgression including the Neanderthal admixture hypothesis which was eventually proven by the Neanderthal genome project in May 2010.

Rise of Humans: Great Scientific Debates

Professor John Hawks

Teaching Company

Origin of MHs Debate

- Meanwhile, ancient DNA technology also took off.
- Pääbo's group sequenced first a few bits of Neandertal mitochondrial DNA in 1997, then the entire mitochondrial genomes of several Neandertals—and found them to be distinct from those of living people.
- So this ancient DNA, too, argued against the idea of mixing between Neandertals and moderns.
- Over the years the replacement model became the leading theory, with only a stubborn few, including Wolpoff, holding to multiregionalism.

Origin of MHs Debate

- A few paleoanthropologists proposed middle-of-the-road models, i.e. Fred Smith:
  - most of our ancestors arose in Africa but interbred with local populations as they spread out around the globe, with archaic people contributing to about 10% of living people's genomes.

- At the University of Hamburg in Germany, Gunter Brauer similarly proposed replacement with hybridization, but with a trivial amount of interbreeding.

- But neither model got much traction. Over time, the two more extreme models moved toward the middle, with most multiregionalists recognizing that the chief ancestors of modern humans arose in Africa

Origin of MHs Debate

- Then in May 2010 came the Neandertals' complete nuclear genome, sequenced from the bones of three female Neandertals who lived in Croatia more than 38,000 years ago.

- Pääbo's team found that a small amount—1% to 4%—of the nuclear DNA of Europeans and Asians, but not of Africans, can be traced to Neandertals.

- The most likely model to explain this, Pääbo says, was that early modern humans arose in Africa but interbred with Neandertals in the Middle East or Arabia before spreading into Asia and Europe, about 50,000 to 80,000 years ago

Origins: Denisovans

- In December 2010, the team published in *Nature* the complete nuclear genome of a girl's pinky finger from Denisova Cave, Siberia.
- At 30-50 KA, neither a Neandertal's nor a modern human's: a new group, Denisovans, more closely related to Ns.
- Denisovans/Neanderthals split from modern humans about 760 to 550 Ka ago

Origin of MHs Debate

- After Neandertal and Denisovan populations split from each other about 200,000 years ago, modern humans interbred with Neandertals as they left Africa in the past 100,000 years.

- Neandertals left their mark in the genomes of living Asians and Europeans

- Later, a subset of this group of moderns—who carried some Neandertal DNA—headed east toward Melanesia and interbred with the Denisovans in Asia on the way.

- As a result, Melanesians inherited DNA from both Neandertals and Denisovans, with as much as 8% of their DNA coming from archaic people,

Origin of MHs Debate

- This means *H. sapiens* mixed it up with at least two different archaic peoples, in at least two distinct times and places.

- To some, that's starting to sound a lot like a newer version multiregionalism.

- “It's hard to explain how good I feel about this,” said Wolpoff, who says that seeing complete replacement falsified twice in 1 year was beyond his wildest expectations.”

Origin of MHs Debate

- Yet the interbreeding with archaic humans seemed limited—from 1% to 6% of some living people's genomes. Stringer and many others did not consider it full-scale multiregional continuity.

- Low levels of interbreeding suggest that either archaic people mated with moderns only rarely—or their hybrid offspring had low fitness and so produced few viable offspring.

- Reich notes that at least 90% of our genomes are inherited from African ancestors who replaced the archaic people on other continents but hybridized with them around the margins.

- And that scenario most closely backs the assimilation models proposed by Smith and Brauer.

Reich, 2010

- Denisovans are a sister group of Neanderthals with a population divergence time of one-half to two-thirds of the time to the common ancestor of Neanderthals and humans.

- After the divergence of the Denisovans from Neanderthals, there was gene flow from Neanderthals into MHs (& vice versa).

- Later there was admixture between the Denisovans and the MH ancestors of Melanesians

Reich, 2010

- The population history indicated by the D nuclear genome is different from that indicated by the mtDNA phylogeny.

- There are two possible explanations for this.

- One possible explanation:
  - both Ns & Ds descend from a common ancestral population that separated earlier from ancestors of present-day humans.

  - Such a scenario would predict a closer relationship between the Denisova individual and Neanderthals than between either of them and present-day humans.

Reich, 2010: A common ancestral population

- Another theory is that the mtDNA lineage was introduced into Denisovan ancestors by admixture from another archaic hominin lineage for which we have no data.

- Another idea is that the discordance is the result of ‘incomplete lineage sorting’, (the random assortment of genetic lineages due to genetic drift) which may have allowed a divergent mtDNA lineage to survive in Denisovans by chance while becoming lost in Neanderthals and modern humans. A large ancestral population size makes incomplete lineage sorting more likely to occur.

Reich, 2010: Denisova 4 tooth

- In 2000, a hominin tooth (Denisova 4) was discovered in layer 11.1 of the south gallery of Denisova.

- Its mtDNA genome differs at only two positions from the mtDNA of the finger bone, making it D, whereas it differs at about 380 positions from both Neanderthal and present-day humans.

- The tooth and the finger bone are both Denisovan but derive from two different individuals

Reich, 2010: Conclusions

- The Denisovans have:
  - some exceptionally archaic mtDNA
  - Different morphological dental features
  - Nuclear DNA indicates the Denisova population is a sister group to Neanderthals.
  - D and Ns split before Ns developed their final facial morphology

Sima mtDNA

- Pääbo notes that previously published full nuclear genomes of Neanderthals and Denisovans suggest that the two had a common ancestor that lived up to 700,000 years ago.

- Sima de los Huesos hominins could represent a founder population that once lived all over Eurasia and gave rise to the two groups.

- Both may have then carried the mitochondrial sequence seen in the caves.
- But these mitochondrial lineages go extinct whenever a female does not give birth to a daughter, so the Neanderthals could have simply lost that sequence while it lived on in Denisovan women.

Sima mtDNA

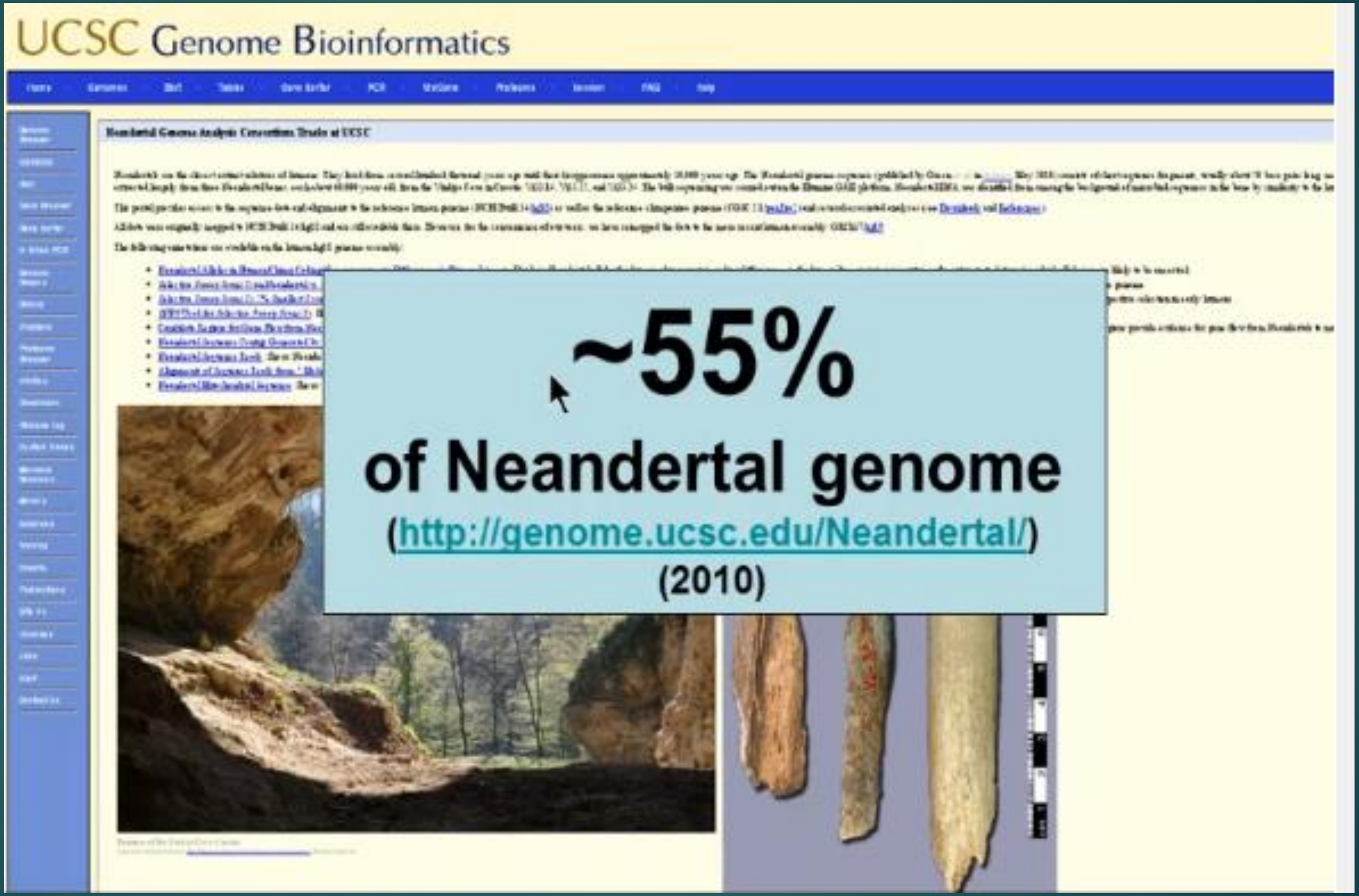
- "I've got my own twist on it," says Chris Stringer, who has previously argued that the Sima de los Huesos hominins are indeed early Neanderthals
- **He thinks that the newly decoded mitochondrial genome ma**y have come from another distinct group of hominins.
- Not far from the caves, researchers have discovered hominin bones from about 800,000 years ago that have been attributed to an archaic hominin called *Homo antecessor*, thought to be a European descendant of *Homo erectus*.
- Stringer proposes that this species interbred with a population that was ancestral to both Denisovans and Sima de los Huesos hominins, introducing the newly decoded mitochondrial lineage to both populations
- Pääbo's team suggests that Denisovans seem to have interbred with a mysterious hominin group

C. Stringer *Evol. Anthropol.* 21, 101–107; 2012

2010: Draft sequence of the Neandertal genome (Green *et al.*, *Science* **328**, 710 (2010))

2010: Three Neandertal Bones: combined the DNA from all 3 bones to get first draft genome of N

2010



UCSC Genome Bioinformatics

~55%

of Neandertal genome

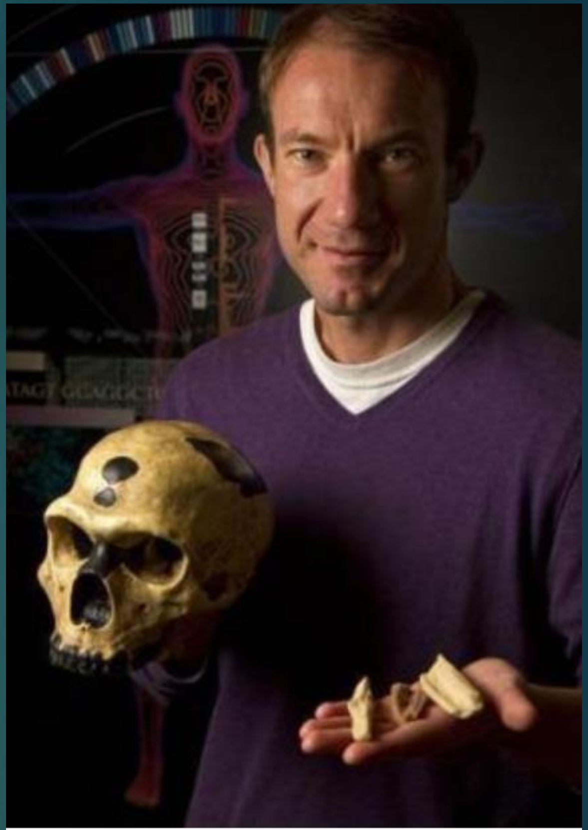
(http://genome.ucsc.edu/Neandertal/)

(2010)

Richard Edward Green:
1-4% Neandertal DNA in modern humans

- Computational biologist; UC Santa Cruz
- Student of Svante Pääbo
- 2010: proved gene flow from Neanderthals to modern humans between 50-80K ago
- Directs the Neanderthal Genome Project
- 2010: Found 1 to 4 % of the genomes of non-Africans is derived from Neanderthals, meaning that the admixture occurred early on, probably in the Middle East; data from 3 female bones from Vindiga Cave, Croatia, 38-44 K; from 3.5% of DNA; 95% was bacterial
- New: proportion of Neanderthal-derived DNA in people outside Africa is 1.5–2.1%; introgression before HMs in Europe, circa 50-60K

- Green *et al.*, *Science* **328**, 710 (2010)



Richard E. (Ed) Green, a computational biologist in
he Baskin School of Engineering at UC Santa

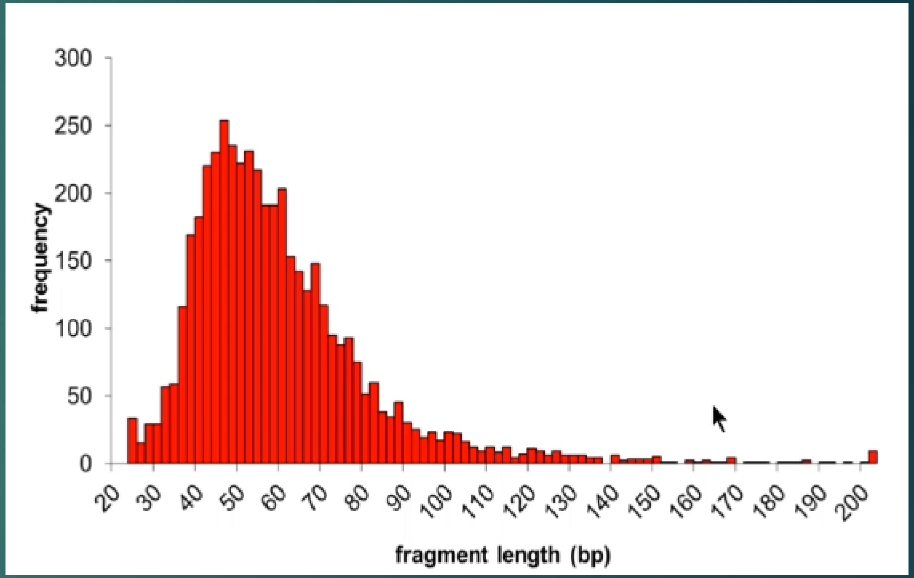
2010: 3 N bones from Vindija, Croatia

Tim White concluded that Vindija bone was N

First N nuclear DNA by Pääbo lab

Vindija Cave, Croatia

Vi 33.16; AMS date: 38, 310 +/- 2,130 BP



40-50 bp fragments vs 20,000 bp in current MH

Vindija Cave

- Distribution of N DNA fragments: one very degraded 38 Ka bone, very small fragments, 60-70 basepairs
- Vast majority of DNA is not N; from bacteria and fungi that colonized bone after N death
- Best bone: 4% endogenous N DNA
- Eventually screened many bones

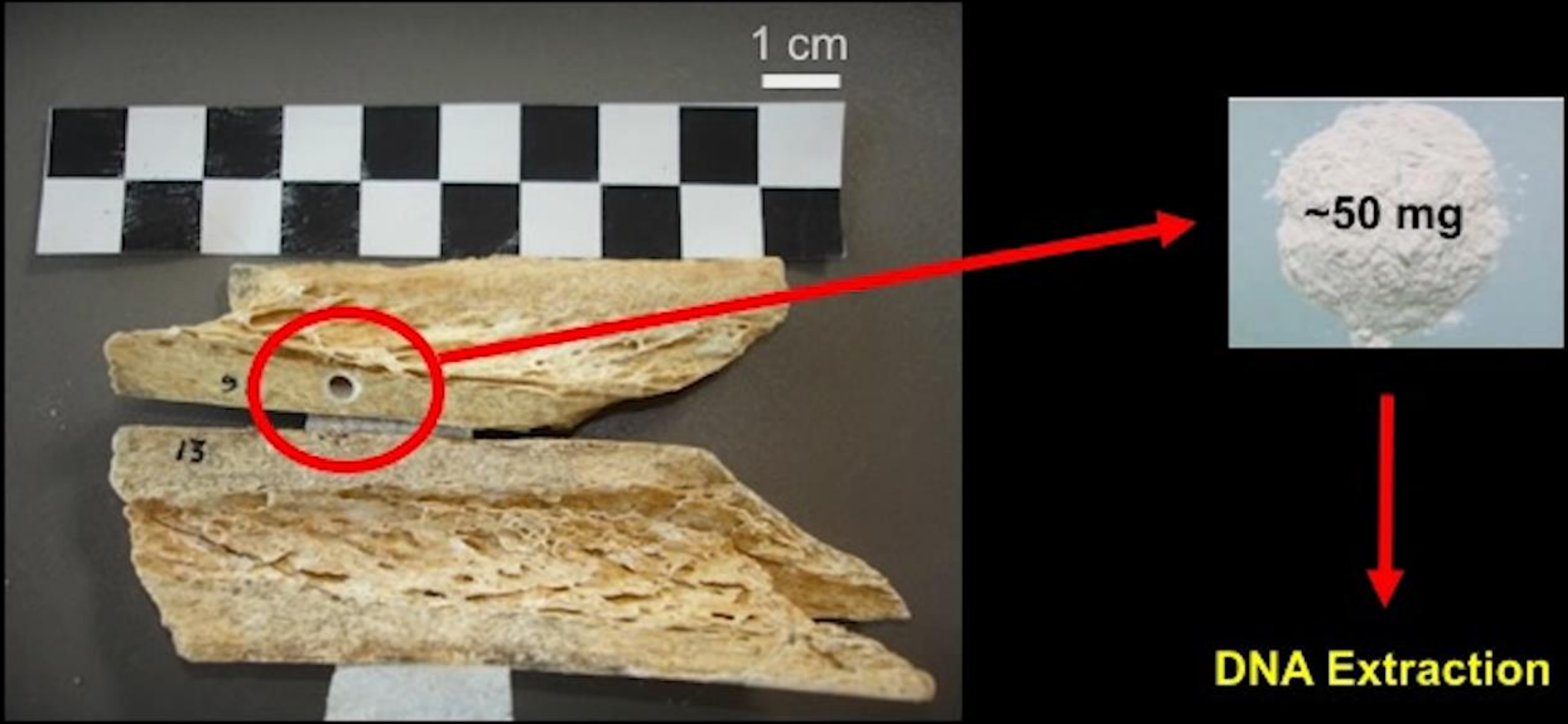
Tibia fragment from Vindiga: First bone for N genome;
Was first tossed in box of animal bones

3 Vindija Cave tibia bone fragments that first produced N DNA

Three
full N
Genomes:
1.2 x
coverage
in 2010

Originally thought to be a faunal bone and tossed in box with animal bones

Vindija is 10 miles from Krapina in Croatia



DNA Extraction

Genome Sequencing

First N nuclear DNA extracted from this Vindiga bone
Goal: 3.2 billion bases Neandertal DNA (1-fold coverage) by end of 2008.

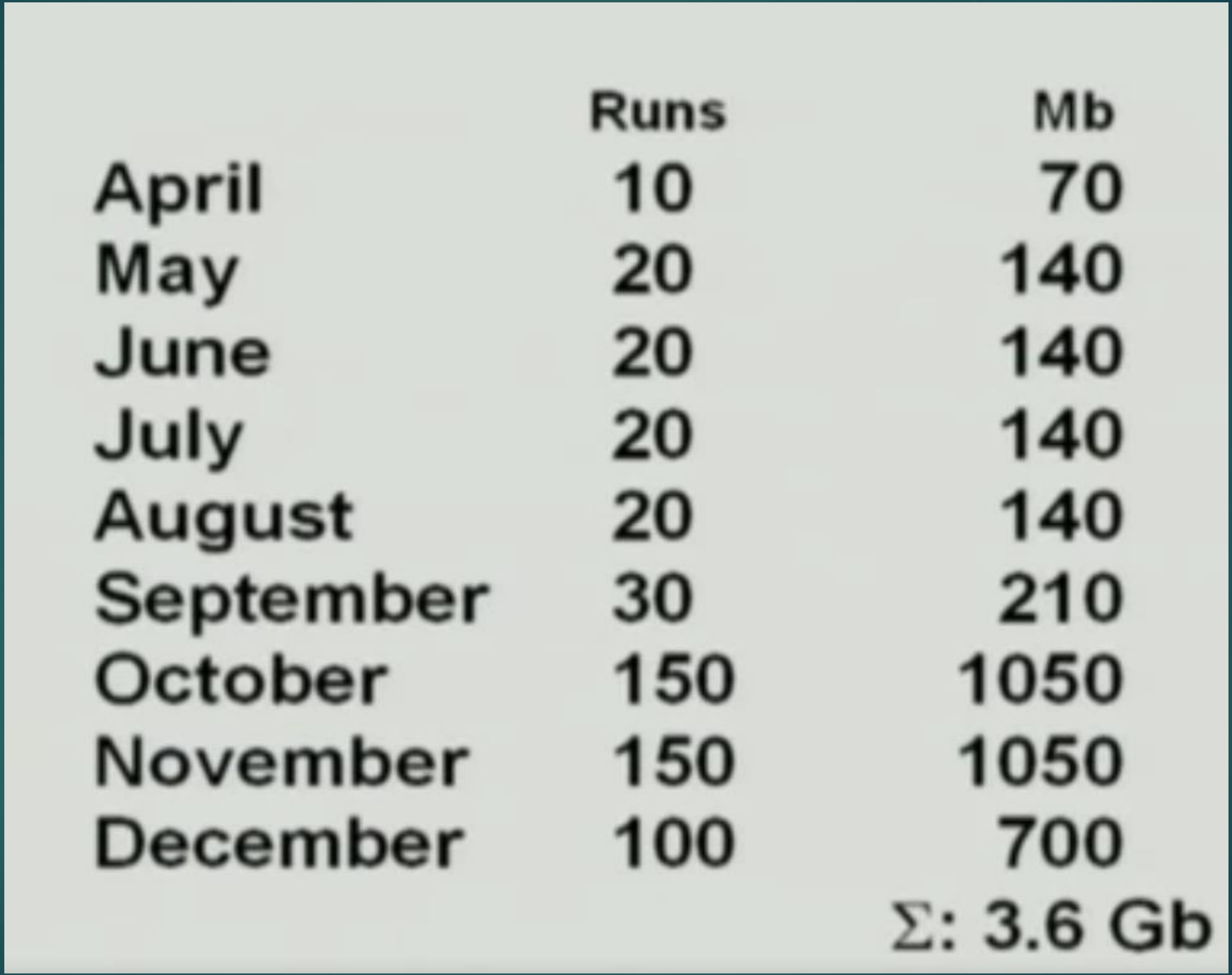
Original nuclear DNA extraction amount:

El Sidron - 760 Mb
Feldhofer - 650 Mb
Vindija - 4.0 Gb

% hominin DNA

El Sidròn	0.1 - 0.4
Feldhofer	0.2 - 0.5
Vindija	0.2 - 5.0

9 months of work



	Runs	Mb
April	10	70
May	20	140
June	20	140
July	20	140
August	20	140
September	30	210
October	150	1050
November	150	1050
December	100	700
		Σ: 3.6 Gb

All full current N genomes

Most of N diversity is in Western Asia; N's were a central Asian population, that occasionally entered Europe

Neanderthal mtDNA

- The Neanderthal mtDNA sequences were substantially different from modern human mtDNA (Krings et al. 1997, 1999). Researchers compared the Neanderthal to modern human and chimpanzee sequences.

- Most human sequences differ from each other by on average 8 substitutions, while the human and chimpanzee sequences differ by about 55 substitutions.

- The Neanderthal and modern human sequences differed by approximately 27.2 substitutions.

- Using this mtDNA information, the last common ancestor of Neanderthals and modern humans dates to approximately 550 to 690 Ka, which is about four times older than the modern human mtDNA pool.

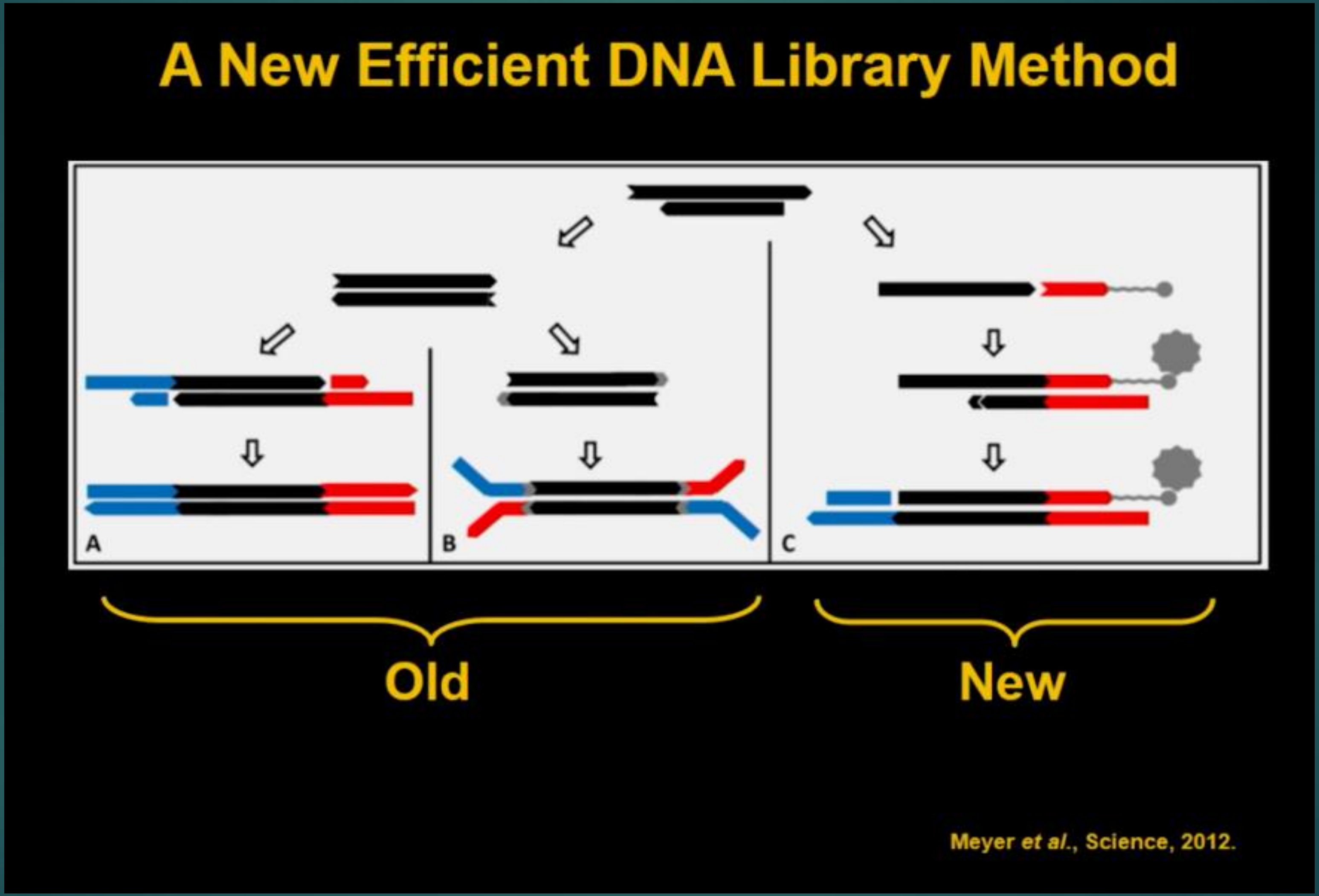
2012 - M. Meyer: discovery of single DNA strand method

- To tackle the problem of limited endogenous aDNA quantities, Meyer et al. developed a single-stranded DNA library preparation method for a Denisovan sample in 2012.

- Their approach substantially increased the number of ancient molecules that could be incorporated into the DNA sequencing libraries, thereby yielding enough DNA sequence to obtain the first high-quality ancient genome, with 30× coverage of a single individual.

- This study provided further evidence for hominin admixture.

M. Meyer, 2012: Double vs single DNA strands



A New Efficient DNA Library Method

Meyer *et al.*, Science, 2012.

Paleogenetic Studies:

- 2012: Full sequence of the Denisovan genome
- (Matthias Meyer, et al., A High-Coverage Genome Sequence from an Archaic Denisovan Individual *Science* (30 August 2012)

Paleogenetic Studies

- 2013: The complete genome sequence of a Neanderthal from the Altai Mountains
- Kay Prüfer, et al., *Nature, 2013*

Paleogenetic Studies:

- 2013: A mitochondrial genome sequence of a hominin from Sima de los Huesos,
- Matthias Meyer, et al., *Nature*, 2013

Paleogenetic Studies:

- 2013; 2nd oldest ancient DNA
- Genome from a 780-560 Ka horse leg bone
- 25 DNA letters, SNPs, from the Canadian Yukon Territory

2013: 735 K year old horse genome

- Samples from a horse leg bone from 735 KA have yielded the 2ND oldest full genome known to date.
- Cold is good. Frozen is even better, because liquid water isn't present to degrade DNA molecules.
- The six-inch (15-centimeter) horse leg bone originated in the Yukon Territory of western Canada in permafrost in 2003.
- Sequenced 12 billion DNA (mostly bacterial) molecules, of which 40 million were of horse origin
- Suggests that the Equus lineage giving rise to all contemporary horses, zebras and donkeys originated 4.0-4.5 million years before present

Orlando, L., *et al.*, *Nature*, 2013

2nd Oldest DNA: Dawson, in Canada’s Yukon Territory

700 Ka frozen sediment; bone near ash layer at 680-700 Ka; DNA of complete horse

2nd Oldest genome: 735 ± 88 kyr

- In 2003, recovery of a metapodial horse fossil at the Thistle Creek site in west-central Yukon Territory, Canada.
- The fossil was from an interglacial organic unit associated with the Gold Run volcanic ash, dated to 735 ± 88 kyr

Paleogenetic Studies:

- 2014: The genomic landscape of Neanderthal ancestry in present-day humans, S. Sankararaman, et al., *Nature*, 2014:

- The antiquity of Neanderthal gene flow into modern humans means that genomic regions that derive from Neanderthals in any one human today are usually less than a hundred kilobases in size.

- Study of Neanderthal haplotypes in the genomes of 1,004 present-day humans:
- Regions that harbor a high frequency of Neanderthal alleles are enriched for genes affecting keratin filaments, suggesting that Neanderthal alleles may have helped modern humans to adapt to non-African environments.

Negative consequences of N alleles in MHs

- There are Neanderthal-derived alleles that confer risk for disease, suggesting that Neanderthal alleles continue to shape human biology.
- Genes that are more highly expressed in testes than in any other tissue are especially reduced in Neanderthal ancestry,
- There is an approximately fivefold reduction of Neanderthal ancestry on the X chromosome, which is known from studies of diverse species to be especially dense in male hybrid sterility genes.
- These results suggest that part of the explanation for genomic regions of reduced Neanderthal ancestry is Neanderthal alleles that caused decreased fertility in males when moved to a modern human genetic background.

Paleogenetic Studies:

- 2014: Resurrecting Surviving Neandertal Lineages from Modern Human Genomes, B. Vernot and J. M. Akey, *Science*, 2014:
- Identified Neandertal lineages that persist in the DNA of modern humans, in whole-genome sequences from 379 European and 286 East Asian individuals, recovering more than 15 gigabases of introgressed sequence that spans ~20% of the Neandertal genome.
- Analyses of surviving archaic lineages suggest that:
  - there were fitness costs to hybridization,
  - admixture occurred both before and after divergence of non-African modern humans,
  - Neandertals were a source of adaptive variation for loci involved in skin phenotypes.

DNA discoveries

- *Kennewick Man*: 2013-2015, an 8,000-year-old skeleton found in Washington state in 1996, was genetically closest to Native Americans. The revelation ended a 20-year legal battle and allowed tribes to rebury the bones.

- *Anzick-1:* 2014, an infant buried with Clovis tools. confirmed that Native Americans mostly descend from Siberians

- *Neanderthals*: 2016 – Oldest hominin DNA of 430,000-year-old Neanderthal ancestors found in Spain's *Sima de los Huesos* cave

DNA discoveries

- Ice Age Immigrants **(*Eurasia 7,000-45,000 years ago*):**
  - **a**DNA from 51 individuals reveals the earliest modern humans to reach Europe went extinct;
  - those arriving in subsequent waves, starting 37,000 years ago, left modern descendants

- 2016: Migrants of Near Easterners into Europe roughly 14,000 years ago, detected for the first time by aDNA analysis.

DNA discoveries

- 2015: Before the Black Death (*Eurasia 3,000-5,000 years ago*):
  - In 2015, geneticists discovered from plague-causing *Yersina pestis* bacteria in the teeth of Bronze Age Eurasians, revealing that less-contagious strains infected people millennia before historically documented pandemics.
  - The bubonic types responsible for the medieval Black Death and recent outbreaks emerged about 3,000 years ago from a mutation that made *Y. pestis* flea-borne.

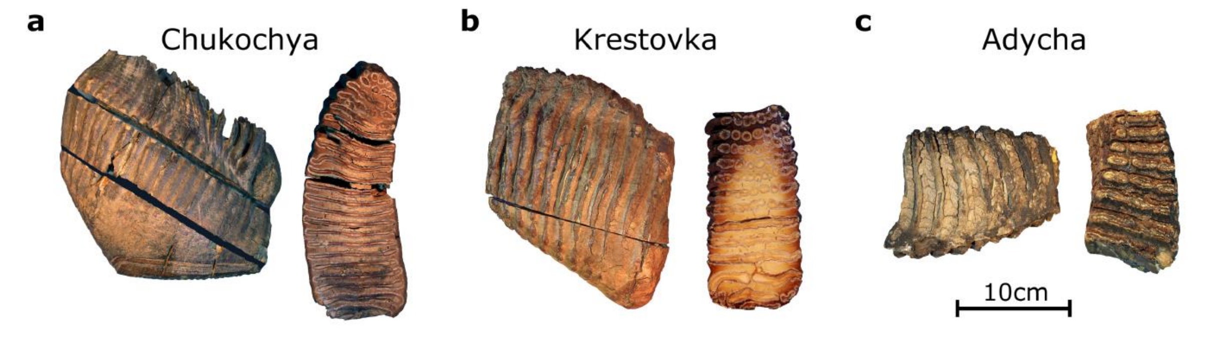
- First Farmers (*Middle East and Europe 3,000-14,000 years ago*)
  - Analyses of hundreds of genomes show how early Middle Eastern farmers spread to Europe, mixed with hunter-gatherers and adapted to agricultural diets, including through a lactase gene mutation that allowed people to drink milk after childhood.

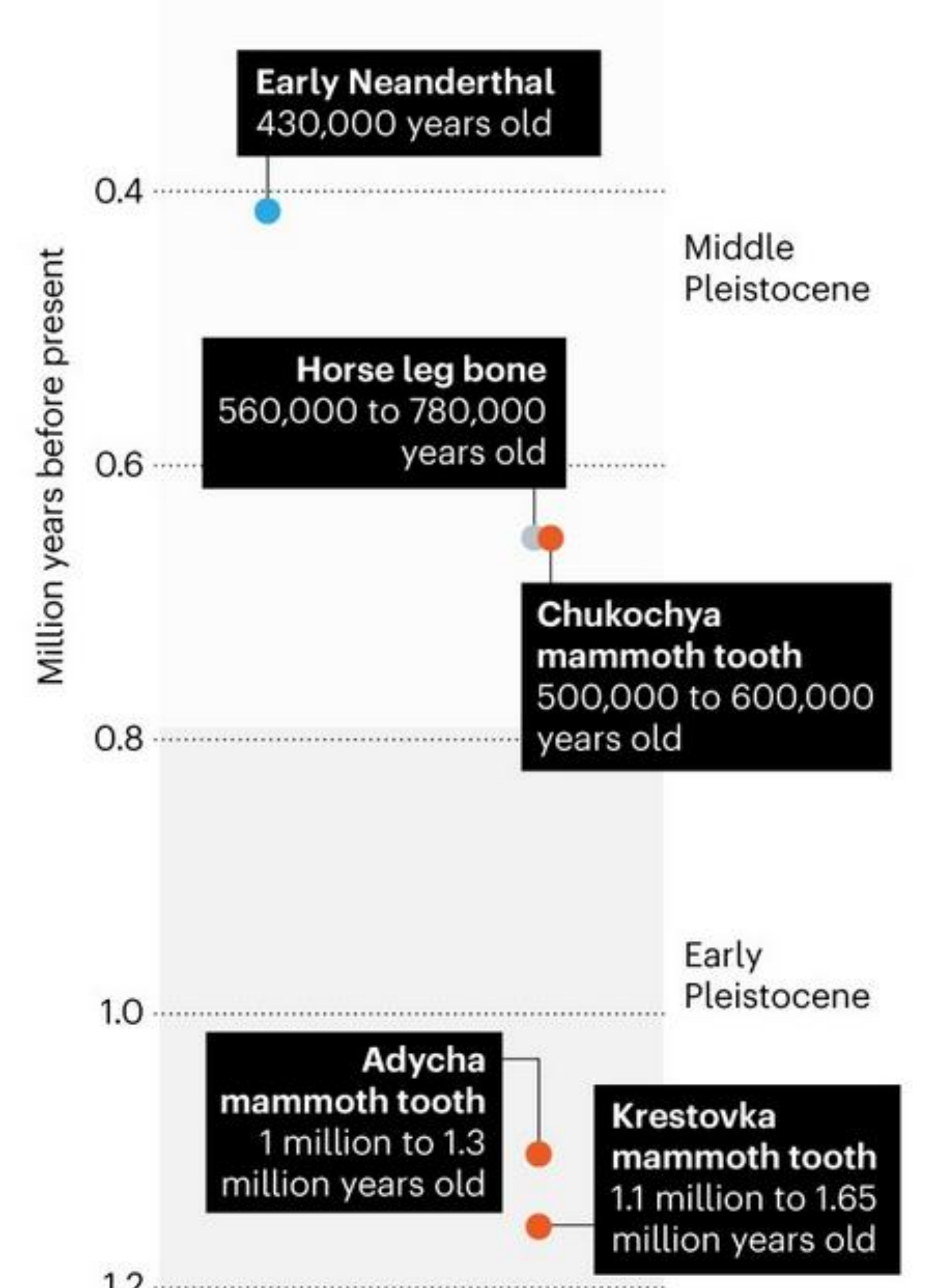
Oldest DNA genome: 1.6 Ma mammoth

- 2021: Permafrost-preserved mammoth teeth, 1.6 million years old, identify a new kind of mammoth in E. Siberia.
- Genomic DNA extracted from a trio of tooth specimens excavated in the 1970s: The samples sequenced,
  - one from an early woolly mammoth (*Mammuthus primigenius*) and
  - two assigned to a precursor known as steppe mammoths (*Mammuthus trogontherii*), had been excavated by the Russian palaeontologist Andrei Sher.

Tom van der Valk, et al., 2021

Three Most ancient genomes





Oldest Mammoth

- Analysis of the DNA suggested that the
  - Krestovka sample was 1.65 Ma, 49 M base pairs
  - Adycha sample around 1.3 Ma, 884 M base pairs
  - Chukochya sample, a 600 Ka, 3.7 Billion base pairs of DNA, more than the length of its 3.1-billion-base-pair genome.

Mammoths

- Krestovka is new species, half woolly and half Columbian mammoth;

- The idea that new species can form through mixing — and not just splitting from a single parent species — is gaining currency among evolutionary biologists.

- But this is the first evidence for ‘hybrid speciation’ from ancient DNA.

Oldest proteins

- In 2016, researchers reported protein sequences from 3.8-million-year-old ostrich eggshells from Tanzania

- In 2019 another team decoded proteins from a 1.77-million-year-old rhinoceros tooth from Georgia.

- In 2013, 3.4-million-year-old camel found in the Arctic

- In 2017, *Lufengosaurus* — a long-necked herbivore dinosaur, 195 million years.

Oldest proteins

- 160 Ka Denisovan jawbone and N-D Hybrid Denny, 90 Ka

- Protein sequences tend to be much less informative about an organism’s ancestry than DNA.

- As for the likely age limit of ancient DNA = 2.6 million years = age limit of the permafrost.

- I am waiting for *H. erectus* in deep cold cave.

Ancient Genomics of Modern Humans: The First Decade

- Since the mid-2000s, high-throughput sequencing has allowed sequencing of ancient DNA fragments across their entire length

- This led to the first genome-wide ancient DNA studies of modern humans, which appeared starting in 2010.

- These studies revealed that ancient populations often had ancestry not fully represented in present-day populations

- Ancient DNA would become critical for reconstructing the genetic history and evolution of modern humans.

Pontus Skoglund & I. Mathieson, 2018

First Decade

- Eight years after the first sequencing of an ancient human genome,
  - whole-genome shotgun data from hundreds of ancient modern humans are available
  - plus capture data from more than 1,000, dating as far back as 45,000 years before present

Hypothesis testing of population history

- This ancient DNA revolution has allowed direct testing of hypotheses and models of human population history and evolution that were formulated in the pre-paleogenomic era based on anthropology, archaeology, and DNA from present-day people.

- Some of these hypotheses, such as the out-of-Africa model, have been corroborated, others have been disproved.

- Ancient DNA allows us to directly study the past, rather than extrapolating information from present-day genomic variation, and could overturn many of our most closely held beliefs about human population history.

Support for Out of Africa theory

Origins and Genetic Diversity of MHs

- Evidence for Out-of-Africa Theory: Human genetic diversity (by the number of mutations) indicates that Africa has most genetic diversity in the world.
  - Example: two chromosomes of a person with recent African ancestry show greater sequence divergence than any two chromosomes, ancient or modern, from any two non-African people
  - Evidence: a population history where a relatively recent ancestral population carrying a subset of African diversity was the founder of the out-of-Africa expansion of modern humans.
  - Evidence: all living humans today are more closely related to each other than they are to archaic humans, such as Neanderthals.

Support for Out of Africa theory

- While no ancient genomes from earlier than ~8,100 BP have been obtained from Africa, there is far more Eurasian genomic evidence.
- All sequenced ancient humans from outside of Africa before ~50 Ka are archaic—they all fall outside present-day human genetic variation in the majority of the genome.
- By contrast, all ancient genomes from modern non-African humans form a related group with present-day non-Africans relative to present-day Africans.
- Evidence vs Multiregionalism theory: above evidence reject models of regional continuity of archaic human populations in Eurasia in favor of models dominated by replacement.

Gene Flow evidence

- aDNA has also revealed at least two independent episodes of gene flow from archaic humans into the ancestors of modern humans.
  - Neanderthals contributed ~2% of the ancestry of people of non-Africans ancestry today,
  - Denisovan population contributed up to 5% of the ancestry of present-day Oceanian populations and likely also to the ancestry of East Asians.
- These contributions imply that not all present-day non-African ancestry is nested within African variation, referred to by Svante Pääbo as a “leaky replacement” model of Eurasian human population history

Origin and Diversification of Non-African Populations

- The ancestral out-of-Africa population was most closely related to:
    - present-day and ancient eastern African populations
    - but shows a complex pattern of affinities to African lineages,
    - There is evidence of gene flow as recently as 50 Ka, which suggests that the ancestors of present-day non-Africans were once part of a structured, largely African, metapopulation.

Non-Africans

- As modern humans expanded across the Eurasian continent, they diversified into multiple lineages.

- One signal of this expansion is the observation that, in present-day populations, genetic diversity successively decreases
  - from Africa to Eurasia,
  - from west to east across Eurasia, and then
  - again in Oceania and America.

- This has been interpreted as the signature of a serial founder effect, where the expansion of modern humans was driven by the outward migration of groups with successively smaller effective population sizes owing to repeated bottlenecks

European vs Asian genetic diversity: divergence dates of non-African population lineages

- However, ancient DNA has revealed that in Europe,
  - this pattern does not date back to the original Eurasian expansion
  - but is a more recent phenomenon, since European populations as recently as 5,000 BP had much lower diversity than present-day populations.

- Instead, the recent high diversity in Europe is the result of Holocene (after 12 Ka) migrations and admixture.

- In Eurasia, several anatomically modern human genomes date to close to the time of the diversification of non-African lineages (60 Ka+)

Eurasian Gene flow dates

- First, directly dated ancient samples allow calibration of the human mutation rate over the relevant timescale.

- Analysis of the 45,000-BP Ust'-Ishim individual supports an autosomal mutation rate of ~0.43×10^{-9} per base per year and a Y-chromosome mutation rate of 0.76×10^{-9} per base per year.

- This autosomal mutation rate implies a split time between eastern and western Eurasians of ~47 to 60 Ka.

Most common African ancestors: 60-90 Ka

- Most recent common ancestor of African and non-African Y-chromosome lineages dates to ~75 Ka, with non-African lineages diversifying around 47,000–55,000 Ka.

- Ancient samples also allow direct calibration of the mitochondrial mutation rate, indicating that the most recent common ancestors of African and non-African lineages date to 62-95 Ka, with diversification of non-African mitochondrial clades around 45-55 Ka..

- These are an upper bound on the time of the most recent gene flow between those populations.

Date of N introgression

- Second, the rate of breakdown of Neanderthal segments of the genome since admixture suggests that this N-MH gene flow took place around 50-60 Ka.

- Since Neanderthal ancestry is shared among all known non-African modern human genomes, most of the ancestors of these populations must have been present at a single time and in a single region (perhaps southwestern Asia) to receive the same Neanderthal ancestry, implying that the divergence of non-African lineages cannot be older than the Neanderthal introgression.

Date of D introgression

- By contrast, Denisovan ancestry is restricted largely to present-day Oceania and is approximately 90% as old as Neanderthal ancestry (44-50 Ka).

- The dates of Neanderthal and Denisovan introgression must bracket the earliest divergences among non-African populations.

- The third line of evidence for the time of diversification of non-African lineages comes from the 45 Ka Ust'-Ishim individual, a modern human, who is consistent with being close to the divergence between Upper Paleolithic Europeans and the ancestors of East Asians and Aboriginal Australians.

East-West division ~45-55 Ka

- These lines of evidence strongly suggest that the mean divergence of the western Eurasian Upper Paleolithic lineage and the East Asian/Oceanian lineage can be fairly tightly constrained to the period 45 -55 Ka.

- These estimates of the divergences of non-African population lineages are in tension with recent evidence of putative modern humans at very early dates, specifically remains dated to ~80–120 Ka from Fuyan Cave in China and ~63-73 Ka from Sumatra, as well as artifacts from ~65 Ka at the Madjedbebe site in Australia.

No descendants of earlier migrations

- Because these latter finds significantly predate the diversification of extant lineages, early populations in these regions cannot have contributed substantial ancestry to any present-day populations.
- Indeed, these population lineages went extinct.
- For example, the population to which the Oase individual did not contribute detectably to present-day populations.

Basal Eurasian lineage

- Another key component of present-day non-African ancestry is the deeply diverging basal Eurasian lineage, most anciently observed around 13 Ka in the Caucasus Mountains, the Levant, and northern Iran and now ubiquitous in western Eurasia.

- This lineage is an outgroup to all other known Eurasian lineages, including the deep Ust'-Ishim and Oase lineages, and therefore likely diverged before 50 Ka.

Basal Eurasian lineage

- In addition, this lineage carried relatively little or no Neanderthal ancestry, which may explain why present-day Europeans have less Neanderthal ancestry than present-day East Asians.

- The location of the hypothetical population that harbored basal Eurasian ancestry between 13-50 Ka remains unknown but would likely be in northern Africa or southwestern Asia.

Holocene History and Human Population Structure

- While the broad patterns of present-day genetic diversity outside Africa were formed by
  - the out-of-Africa bottleneck and
  - subsequent divergence,
  - much of the finer-scale structure is the result of relatively recent population movements after 12 Ka.

- Europe and Western Eurasia: Europe has provided the best example of the ability of ancient DNA to explain the genetic structure of modern humans.

Genetic structure of Europe

- Empirically, genetic structure in Europe is continuous,
  - forming clines that were originally interpreted by Cavalli-Sforza
  - as the signature of a Neolithic expansion of agriculturalists through a landscape of the original resident Mesolithic hunter–gatherer populations.

- However, it was later shown, again using present day genetic data, that exactly the same sort of patterns could arise without major expansions—as the product of an interconnected but spatially structured population evolving with ongoing gene flow but without major waves of expansions and admixture (isolation by distance - accrual of local genetic variation under geographically limited dispersal) .

Need for ancient DNA to resolve historical population dynamics

- Thus, the processes that drove the observed population structure could not be resolved using present-day data alone, since both migration and isolation by distance could, in principle, explain the data.

- We now know that:
  - the agricultural expansion suggested by Cavalli-Sforza took place
  - but did not produce the major present-day clines in Europe in the manner originally proposed.
  - Cline = gradual change of a character or feature (phenotype) in a species over a geographical area

Genetic history of migrations

- Instead, European genetic history is marked by multiple migrations, and patterns of genetic diversity in present-day Europe have been shaped by the admixture of at least three, not two, distinct ancestral populations.

- Anatomically modern humans were widely distributed in Europe by at least 42-47 Ka.

- The oldest genomic data from a modern human in Europe are from the Oase 1 dated to 37-42 Ka. This individual, who had a direct Neanderthal ancestor in the past four to six generations and did not contribute detectable ancestry to later Upper Paleolithic populations.

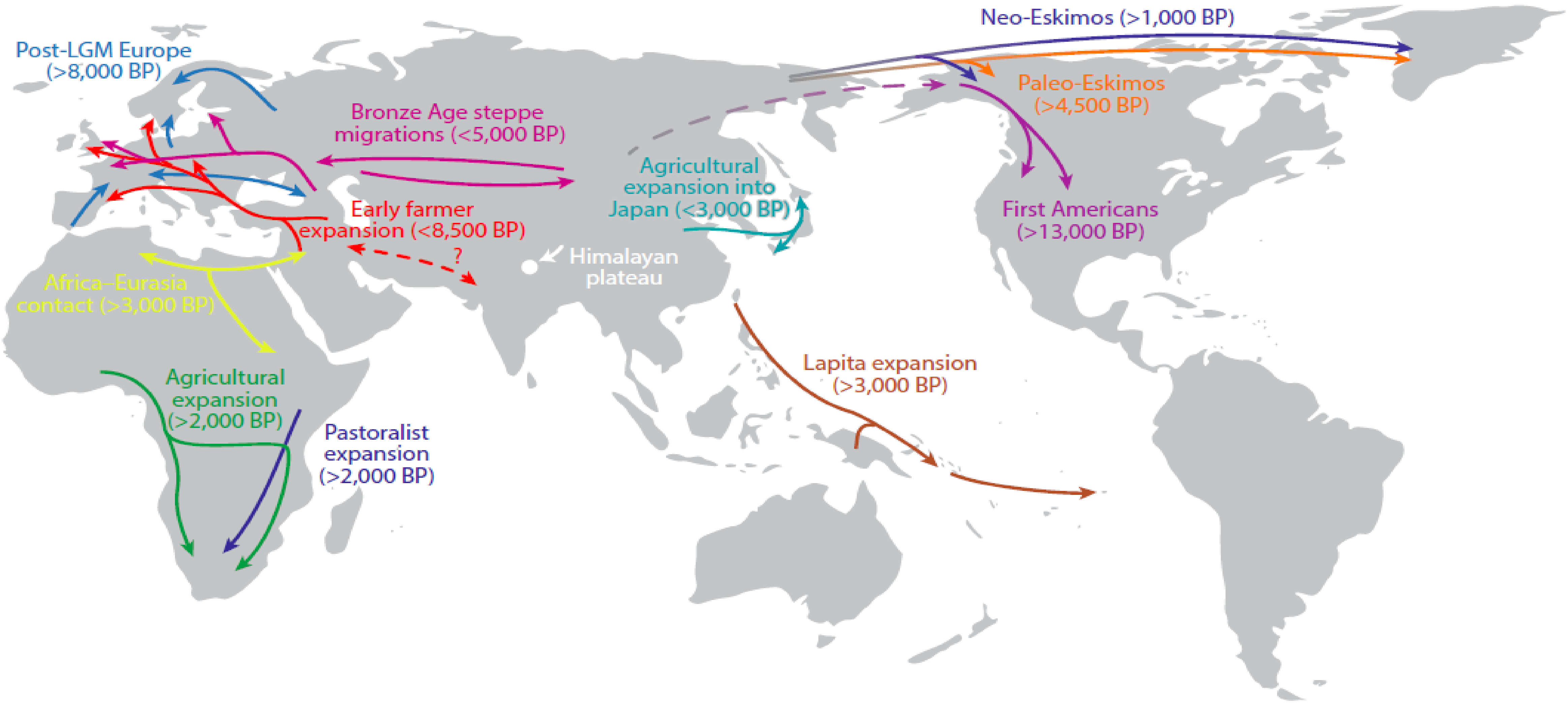


Figure 4

Major Holocene population movements and expansions that have been demonstrated using ancient DNA. Abbreviations: BP, years before present; LGM, Last Glacial Maximum.

Post Glacial replacements

- During the Upper Paleolithic, a major transformation occurred around 30 – 35 Ka and was likely associated with
  - the replacement of the Aurignacian with the Gravettian culture in western Europe.
- As the Last Glacial Maximum (LGM) came to an end and the ice sheets receded, Europe was repopulated, possibly from southern European and central Eurasian refugia.
- Another transformation may have taken place during a warm period around 14.5 Ka, replacing the original re-colonizers with a population that would come to form the Mesolithic populations of Europe .

Three genetic Mesolithic groups

- These Mesolithic populations were outside the genetic diversity of present-day Europe and themselves display an east-to-west cline.

- First Farmers (Anatolian Neolithic group):
  - Starting from the southeast around 8.5 Ka,
  - the hunter gatherers of Europe was marginalized
  - as a new type of ancestry related to that found in Neolithic northwest Anatolia and, ultimately, to early farming populations of the Levant and northern Iran expanded throughout Europe.

First Decade: Hunter gatherers then farmers

- This farmer population rapidly reached the extreme edges of Europe, with direct evidence of their presence in Iberia at 7.3 Ka, in Ireland at 5.1 Ka, and in Scandinavia at 4.9 Ka.

- This Anatolian Neolithic ancestry was highly differentiated from the hunter–gatherer ancestry of the populations that previously inhabited Europe.
- Across Europe, its appearance was closely linked in time and space to the adoption of an agricultural lifestyle, and it is now clear that this change in lifestyle was driven, at least in part, by the migration.

First Decade of aDNA research

- However, the Anatolian Neolithic migrants did not completely replace the hunter–gatherer populations.
- Over the next 4,000 years, the two populations merged,
- By 4.5 Ka, almost all European populations were admixed between these two ancestries, typically with 10–25% hunter–gatherer ancestry.
- This mixture process occurred independently in different parts of Europe, likely driven by local hunter–gatherer populations who lived in close proximity to farming groups.

First Decade: Yamnaya migration into Europe

- The next substantial change is closely associated with ancestry that by around 5,000 BP extended over a region of more than 2,000 miles of the Eurasian steppe, including in individuals associated with the Yamnaya cultural complex in far eastern Europe and with the Afanasievo culture in the central Asian Altai mountains.
- This steppe ancestry is itself a mixture between ancestry that is related to Mesolithic hunter–gatherers of eastern Europe and ancestry that is related to both present-day populations and Mesolithic hunter–gatherers from the Caucasus mountains, and also to the populations of Neolithic and Copper Age Iran.
- Steppe ancestry appeared in southeastern Europe by 6,000 BP, northeastern Europe around 5,000 BP, and central Europe at the time of the Corded Ware complex around 4,600 BP.

First Decade of aDNA research

- These dates are reasonably tight constraints, because in each case there is no evidence of steppe ancestry in individuals immediately preceding these dates.
- Gene flow on the steppe was extensive and bidirectional, as shown by the eastward flow of Anatolian Neolithic ancestry and the westward flow of East Asian ancestry [found in individuals associated with the Iron Age Scythian culture close to the Black Sea around 2,500 BP].
- Copper and Bronze Age population movements, as well as later movements in the Iron Age and historical period, further distributed steppe ancestry around Europe.

3 European Genetic Groups

- Present-day western European populations can thus be modeled as mixtures of three differing genetic groups:
    - Mesolithic hunter–gatherer,
    - Anatolian Neolithic farmers, and
    - Steppe Yamnaya
- East-to-west gene flow also brought new ancestry—related to populations from Copper Age Iran—to the Levant during the Copper and Bronze ages.

Start here March 23

Ancestry of present-day Europeans

- The geographic structure of these population transformations gave rise to the population structure of present-day Europe.

- For example, Anatolian Neolithic ancestry is highest in southern European populations such as Sardinians and lowest in northern European populations.

- Steppe ancestry is at high frequency in north-central Europeans and at low frequency in the south. Isolation by distance may have contributed to these patterns to some extent, but the contribution must have been small. In much of Europe, extreme population discontinuity was the norm.

Siberia

- The 24 Ka Mal’ta genome showed surprisingly strong affinities to both western Eurasian and Native American populations

- Populations related to Mal’ta contributed 10–20% of the ancestry of present-day Europeans and 30–40% of the ancestry of Native Americans.

- That the Mal’ta individual falls on the western lineage of the 45,000–55,000-year-old original divergence of Eurasian populations suggests that estimates of Native American divergence from East Asians and Siberians around 20,000 BP may be too ancient

Mal’ta lineage

- The Mal’ta lineage is basal to all western Eurasian Paleolithic genomes
- Mal’ta lineage persisted locally through the LGM.
- The major Native American population lineage may have formed after the LGM.
- This leaves open the possibility of a relatively late separation from Siberian ancestors and entry into Beringia.

America: Anzick-1

- Archaeological evidence supports a human presence in the Americas at least 14,500 Ka.

- All present-day Native Americans can trace part of their ancestry to a single population that existed at least 12,600 Ka.

- The most controversial hypotheses about the peopling of the Americas, including the Solutrean hypothesis of a European origin, were largely dispelled by the sequencing of a 12,600-BP individual from western Montana buried in association with Clovis stone tools.

- This individual, known as Anzick-1, falls within present-day Native American diversity and was more closely related to present-day populations from Central and South America than to geographically closer populations from North America.

America: North vs South

- This >12.5 Ka divergence of a northern Native American lineage has been confirmed by analyses of younger remains from North America
- Diversification of Native American mitochondrial lineages around 12 – 18 Ka suggests that northern and southern lineages diverged during this time.
- Native American lineage must have split from Siberian ancestors around 25,000 Ka at the earliest (more likely around 20 Ka or later) and at least before the divergence of northern and southern Native American lineages (13-18 Ka).
- However, a genetic affinity between Amazonian and Australo-Melanesian populations suggests that we still do not have the full picture of the ancestry of the first Americans.

Americas

- The expansion into the Americas was done by different populations, with some subpopulations retaining greater affinity to an unknown northeastern Asian population related to present-day Australo-Melanesians.

- Discovery that the ~40,000-year-old Tianyuan individual from eastern China also had affinity to the Amazonian populations supports the presence of ancient subgroups in Siberia contributing to the Amazonian and Australo-Melanesian connection

Americas: Paleo and Neo Eskimo migrations

- The first ancient modern human genome sequence ever published was from an individual dated to ~4 Ka associated with the Saqqaq culture of Greenland.
- This individual's affinity to the Koryak and Chukchi populations of northeast Siberia rather than present-day Inuit in Greenland suggested that the Saqqaq ancestors were from a separate migration to North America than those of the present-day Inuit.
- Since then, this model of separate Paleo- and Neo-Eskimo migrations into the Americas has been largely confirmed by direct evidence of additional Paleo-Eskimo (associated with the Middle and Late Dorset culture) and Neo-Eskimo (associated with the Thule culture) genomes.

Africa – The Bantu

- Poor preservation conditions make it more challenging to recover ancient DNA from Africa than from colder parts of the world.

- The first ancient African genome sequence was from a 4.5 Ka individual from Mota Cave in highland Ethiopia.

- There was a profound impact of the agricultural expansion associated with western African–like ancestry and Bantu languages.

- Archaeological evidence suggests that this expansion followed the earliest evidence of agriculture in western Mali around 4.5 Ka and brought farming to eastern Africa by ~2 Ka as well as to southern Africa by ~1.5 Ka.

Africa: Bantu expansion

- The Bantu expansion disrupted a long-standing group of hunter–gatherers that stretched from Ethiopia to South Africa and had existed since at least ~8.1 Ka.
- In Malawi, a hunter–gatherer population that survived at least until 2.5 Ka contributed almost no ancestry to present-day Bantu-speaking groups in Malawi, suggesting a complete or near-complete replacement.
- In other parts of Africa, present-day populations carry more genetic ancestry from preagricultural populations, including the Hadza of Tanzania, the Khoe-San of southern Africa, and the Aari in Ethiopia.

Africa & Eurasia

- There was extensive Holocene gene flow between northern Africa, eastern Africa, and the Levant.

- Northeastern African populations also have additional ancestry related to Neolithic Levantine and Iranian populations, also seen in prehistoric Egypt.

- These connections emphasize the extent of Holocene interactions between Africa and Eurasia.

East Asia

- Ancient DNA data from Asia are sparse.

- Only 13 genetic samples from East Asia: ~40 Ka Tianyuan individual & autosomal genomic data are limited to eight individuals dated to 1 to 3 Ka from Tibet, two individuals dated to 7,700 BP from the Devil's Gate site north of the Korean peninsula, and low-coverage data from two individuals associated with the Final Jomon culture of Japan, dated to around 3,000 BP.

- The Tibetan and Devil's Gate individuals appear to be relatively similar to present-day populations in their respective regions, indicating long-term population continuity that would be unusual in the context of western Eurasia.

Asia

- This mirrors the pattern of admixture between hunter–gatherer and farming populations seen in Neolithic Europe and raises the question of whether this pattern was universal in agricultural expansions.

- There are no published ancient DNA studies from South or Southeast Asia, another challenging region in terms of ancient DNA preservation.

- However, data from neighboring regions provide clues to the population history of this region.

Oceania

- Archaeological evidence: anatomically MHs were established beyond the Wallace line in Oceania by at least 40 to 50 Ka.

- Genetic data: present day Aboriginal Australian and Papuan ancestry derives from a single founding population, which also contributed part of the ancestry of populations in Island Southeast Asia and the Pacific.

- However, many Pacific populations show evidence of mixture related to a later migration around 3.5 Ka of mainland-East-Asian-ancestry populations associated with the Lapita culture, the spread of Austronesian languages, and food production.

Oceania

- Lapita culture: a prehistoric Austronesian people who left evidence of their livelihood on several Pacific Islands, esp. pottery

- Ancient DNA from~3 Ka remains in Vanuatu and Tonga showed that individuals associated with the Lapita culture had <u>very little or no ancestry from Papuan or Australian populations</u> and instead <u>derived all of their ancestry from populations related to present-day Taiwanese populations.</u>

Oceania

- By contrast, all present-day Pacific populations surveyed have 25% or more ancestry from (primarily male) Papuan ancestors.

- The extreme eastern ends of this Austronesian expansion were the Polynesian islands of Hawaii and Rapa Nui (Easter Island)—both of which are more than 2,000 miles from the American continent.

- Some data, such as the presence of Native American ancestry on Rapa Nui today, suggest the possibility of contact between Polynesia and South America, although direct ancient DNA data suggest that this ancestry may postdate European contact.

Functional Variation & Phenotypes

- Ancient DNA can illuminate the evolutionary history of human phenotypic diversity.

- In particular, ancient DNA should be valuable for identifying and quantifying the contribution of natural selection to phenotypic variation.

- Ancient DNA allows us to directly detect rapid changes in allele frequencies over time = the immediate results of selection.

Diet and Lactase Persistence:

- Diet-related genes are a common target of natural selection, and analysis of ancient DNA has documented selection at several loci in Holocene Europe and at taste receptor genes in the past 2,000 years in southern Africa.

- However, by far the clearest evidence of natural selection, from both ancient and modern DNA, is for lactase persistence—the ability to digest lactose and therefore milk in adulthood.

Diet and Lactase Persistence:

- In Europe, this phenotype is determined largely by a single-base mutation in the *MCM6* gene, upstream of *LCT*, which shows one of the strongest signals of a hard selective sweep in the entire genome.
- This particular SNP has attracted more ancient DNA studies than any other.

First Decade: Functional Variation & Phenotypes

- One potential issue with ancient DNA data for this SNP is that, because it is common in present-day populations and is a C>T mutation, contamination or deamination damage can easily lead to false positive inference of the derived allele.
- Nonetheless, ancient DNA has clearly shown that the lactase persistence allele did not become common until relatively recently.
  - rare or absent in Early Neolithic farming populations (8.5 – 4 Ka),
  - present but rare in Europe and on the steppe around 4.5 Ka,
  - and still rare well into the Bronze Age (up to 3 Ka).

Functional Variation & Phenotypes

- The following rapid increase in the frequency of the persistence allele (to ~70% in northern Europe today) thus came many thousands of years after evidence of dairying appears in the archaeological record.
- This delay suggests that milk consumption may have been restricted largely to children, limited to fermented products that contain less lactose, or assisted by the gut microbiome, or that any side effects might simply have been tolerated.
- It remains unknown why the *MCM6* gene was so strongly selected and why strong selection was limited to northern Europe.

Depigmentation: Early Europeans were dark skinned

- The evolution of light skin pigmentation is another case where ancient DNA evidence has provided new insight into the history of the trait.

- Depigmentation as humans moved into high-latitude environments is thought to be an adaptation to lower levels of UV radiation.

- A main conclusion from ancient DNA studies is that UP Eurasians and Mesolithic western Europeans carried ancestral (i.e., relatively dark skin) alleles at the two loci that are most important for light skin pigmentation in present-day Europe, *SLC24A5* and *SLC45A2* .

Pigmentation

- In the Mesolithic, both of these light skin alleles were present in eastern Europe and Anatolia.
- The newer *SLC24A5* allele was introduced to Europe at high frequency by the Anatolian Neolithic migration, while the newer *SLC45A2* allele was introduced at lower frequency and subsequently selected.
- Both of these alleles are now virtually fixed in Europe.
- Other depigmentation alleles, including alleles at *TYR* and *GRM5*, also appear to have been selected over this period, implying a gradual depigmentation of European populations over the Holocene.

Pigmentation: lighter in last 5 Ka

- Specific combination of pigmentation alleles that is common in western Europe today is relatively recent and reached its current high frequency only within the past 5,000 years.

- Similarly, signals of selection in southern Africa in the past 2,000 years may also be linked to relatively recent changes in pigmentation.

- Non-skin pigmentation alleles associated with eye and hair color have also been tracked using ancient DNA.

- In particular, the SNP rs12913832 at the *HERC2/OCA2* locus is strongly associated with light (particularly blue) eye color in Europe.

Pigmentation

- The derived light eye color allele is first seen in hunter–gatherers from present-day Italy and Georgia around 13 to 14 Ka and appears to have become almost fixed in parts of northern and western Europe by around 8 Ka.

- This rapid increase in frequency seems likely to have been driven by selection.

- Direct evidence of more recent natural selection comes from time-series data in eastern and central Europe showing that the present-day distribution of the allele is driven by both admixture and adaptation

Immune System

- Ancient DNA: history of genes involved in the immune system, which exhibit complex patterns of population differentiation.
- In Europe, several immune-associated genes have been shown to be under selection in the past 10,000 years.
- However, in contrast to genes associated with skin pigmentation, the selected variations have been at high frequency for a relatively long time.
- For example, Mesolithic hunter–gatherers carried many derived variants at immune genes.

Immune System,

- In the Americas, ancient DNA has been used to assess evidence of positive selection before and after European contact at specific HLA alleles.
- In some cases, it is possible to recover pathogen DNA from ancient samples—
  - presence of an early version of plague in Bronze Age Europe
  - use this kind of data to correlate genetic changes in humans with the presence of specific pathogens.

Height

- Increasing focus on polygenic adaptation as an important mode of evolution in humans.
- Genetic variants underlying several traits—most clearly height—have been influenced by polygenic selection acting on multiple loci that each have a small effect.
- In particular, height-increasing variants have been driven by selection to higher frequency in northern European populations relative to southern European populations.
- Similarly, but on a larger scale, variants that increase height (in Europeans) tend to be at higher frequency in western Eurasia relative to East Asia, a pattern that is also likely driven by selection.

Height

- This selection occurred in both European hunter–gatherers and the ancestors of Bronze Age steppe populations—who may therefore have been selected for increased height at some point during or after the LGM.
- Variation in steppe ancestry is correlated with mean height in present-day European populations; but needs more evidence
- With ancient sample sizes now reaching thousands and genome-wide association study sample sizes reaching hundreds of thousands, the power of ancient DNA to explain patterns of complex trait variation in present-day populations will dramatically increase in the near future.

Functional Archaic Admixture

- Admixture from archaic humans may have helped modern humans expanding outside of Africa adapt to the unfamiliar environments of Eurasia.
- A haplotype at *EPAS1* that was shared with the Denisovan genome, is present at high frequency in present-day Tibetans, and appears to be an adaptation to life at high altitudes.
- However, most archaic human ancestry is not adaptive but appears to have been selected against.

Functional Archaic Admixture

- There are three lines of evidence for this selection against archaic ancestry:
    - Archaic haplotypes are depleted in more conserved parts of the genome (those that are survival related),
    - archaic haplotypes have decreased in frequency over time,
    - archaic variants are less likely to have functional consequences.

Functional Archaic Admixture

- Within European-ancestry populations, there is some evidence that archaic variants contribute significantly but with a small effect size to several phenotypes, including risk of depression, mood, skin and hair structure, and height.

- Proportions of Neanderthal ancestry vary by only a small amount within Eurasia [~2.2% in Europe compared with ~2.4% in East Asia and this ancestry probably derives from the same Neanderthal population,

First Decade of aDNA research

- Ancient DNA has greatly increased our knowledge about the <u>expansion and diversification of the ancestors of present-day non-Africans around 50 Ka</u>.

- However, we still <u>know relatively little about the population from which this expansion began</u>.

- Two pieces of <u>evidence suggest that it was part of a structured population that was the source for most of the ancestry of present-day people</u>:

First Decade of aDNA research

- first, evidence of relatively recent (~50 Ka) gene flow between the ancestors of present-day non-African and eastern, central, and western African populations,

- second, the observation that some African lineages are more closely related to present-day non-African populations than others.

First Decade of aDNA research

- The exact structure and location of this structured source population are unknown;
  - may have been geographically restricted to the African continent or
  - may well have extended into southwestern Asia, (secure evidence of an AMH presence by 120 Ka)

- Although conditions for ancient DNA preservation in this hot region are poor, techniques for ancientDNA extraction are continually improving, and DNA recovery is not implausible, i.e. Sima de los Huesos at 430 Ka.

First Decade of aDNA research

- A key challenge for ancient DNA retrieval
  - Relatively little idea of where to look
  - Lack DNA from early modern humans, on the order of 100 to 200 Ka
- These data would likely be transformative for our understanding of the origin and evolution of our species.
- Finally, archaic human genomes have proved extremely useful for tracking the history of modern humans,

First Decade of aDNA research

- For example, if we had no Denisovan genome sequence, it would be difficult to tell whether present-day Oceanians had ancestry from a separate out-of-Africa migration or an unknown archaic human population, and the timing of their ancestors’ isolation from the ancestors of present-day East Asian populations would be unclear.

- Discussion of Holocene ancient DNA results often focuses on what they can tell us about the spread of language—for example, the spread of Indo-European languages.

First Decade of aDNA research

- On the other hand, for cultural features that appear in the archaeological record, ancient DNA allows us to almost directly assess links between culture and genetic history.

- In particular, we have direct evidence—in Africa, far eastern Asia, and Europe —that expansions of agriculture were associated with movements of people, as inferred from the concurrent expansion of distinctive genetic ancestries.

- In almost all of these cases, the agricultural population merged with the existing preagricultural hunter-gatherer population.