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POLISH ACADEMY OF SCIENCES

RADA UPOWSZECHNIANIA NAUKI PAN

Genetics and genomics in the study of human evolution and prehistory

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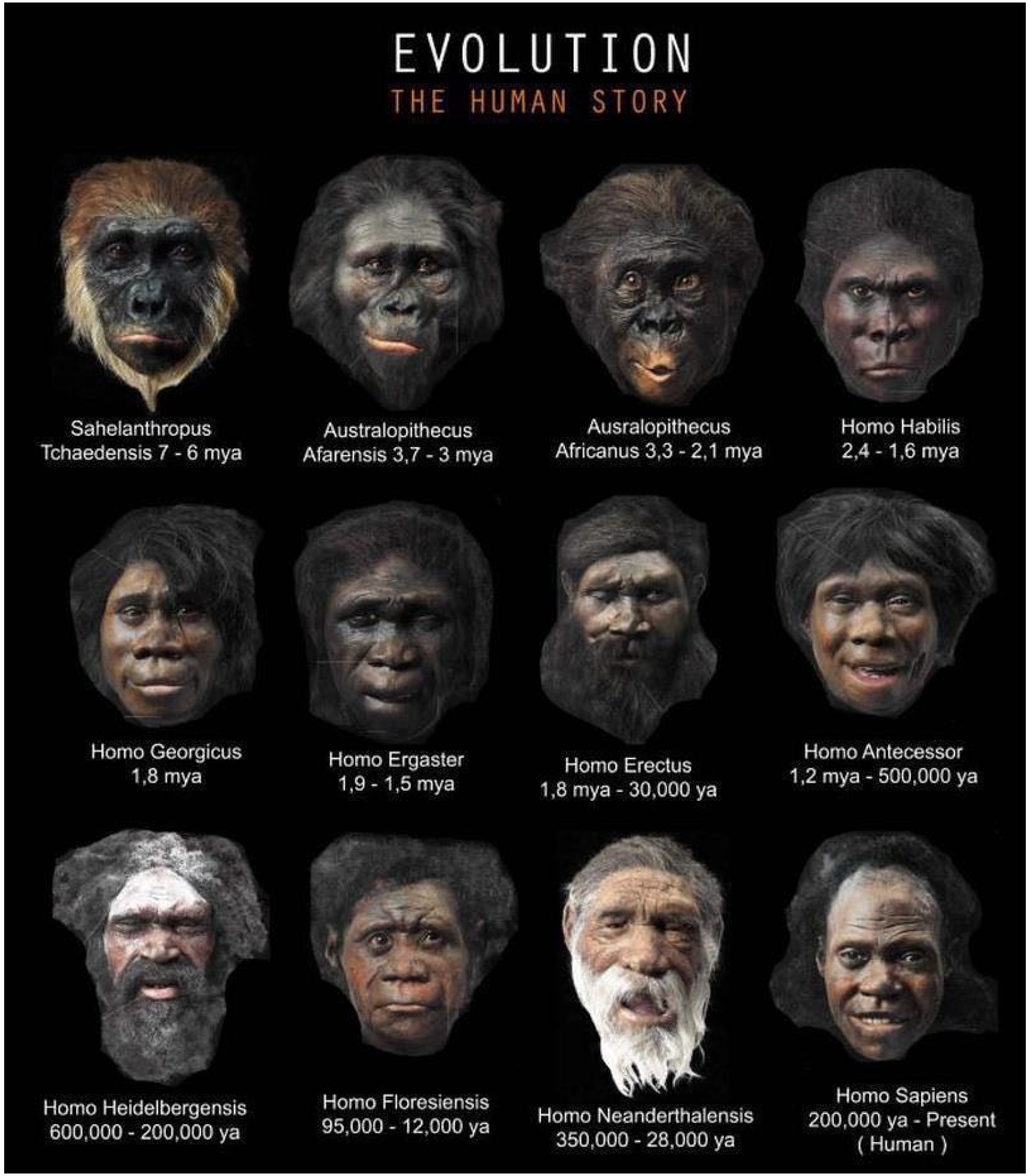
The presentation will be available

How do we know about the past?

- Fossil remains - paleontology
- Most of evolutionary history
- Fragmentary, require favorable conditions to be preserved



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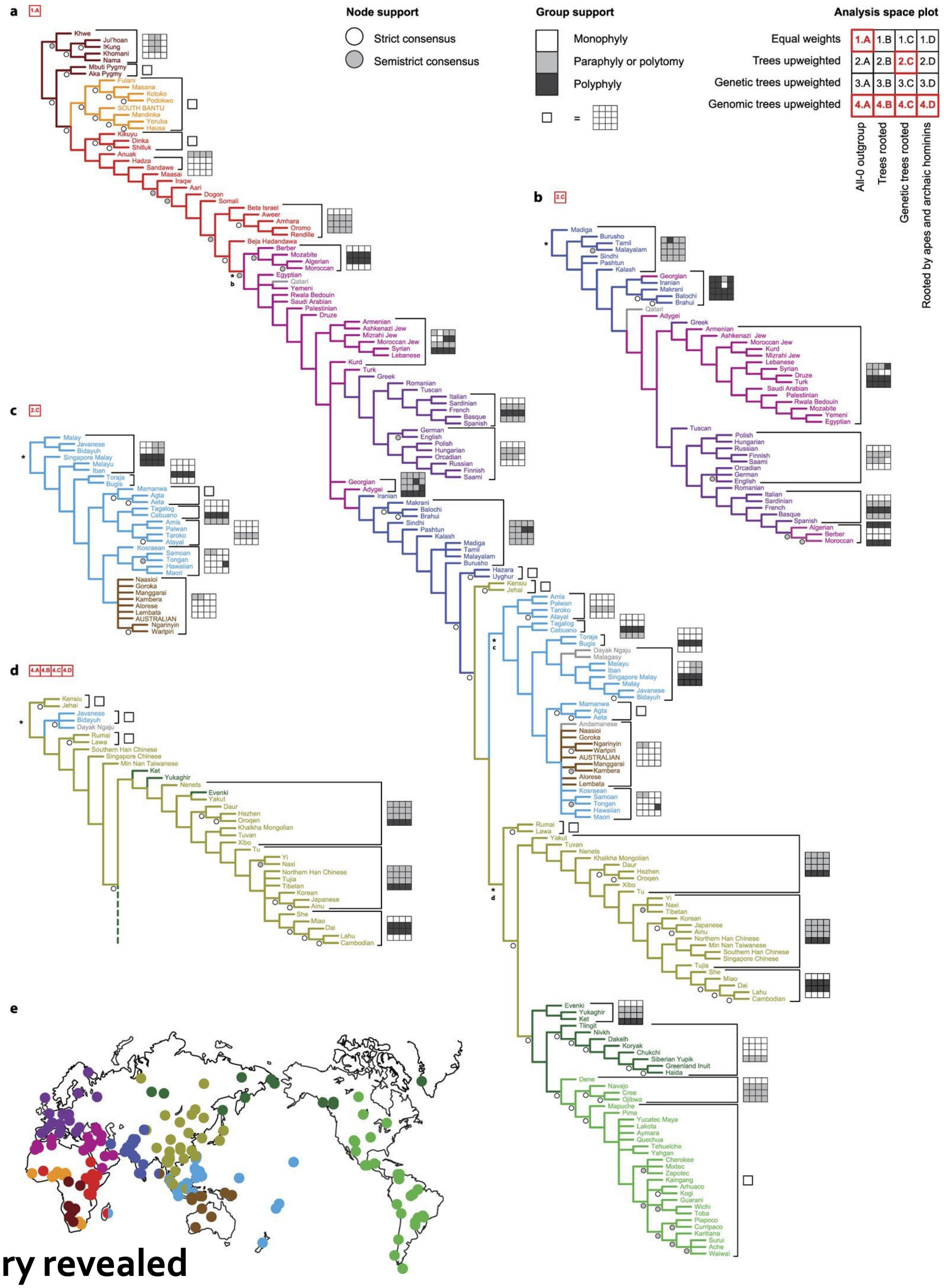
DNA as the source of information

- Comparative analysis of contemporary sequences
  - phylogenetic inference
  - population analysis (admixture, coalescence)



Human population history revealed by a supertree approach

Pavel Duda[1,2] & Jan Zrzavý[1]

SCIENTIFIC REPORTS | 6:29890 | DOI: 10.1038/srep29890

DNA as the source of information

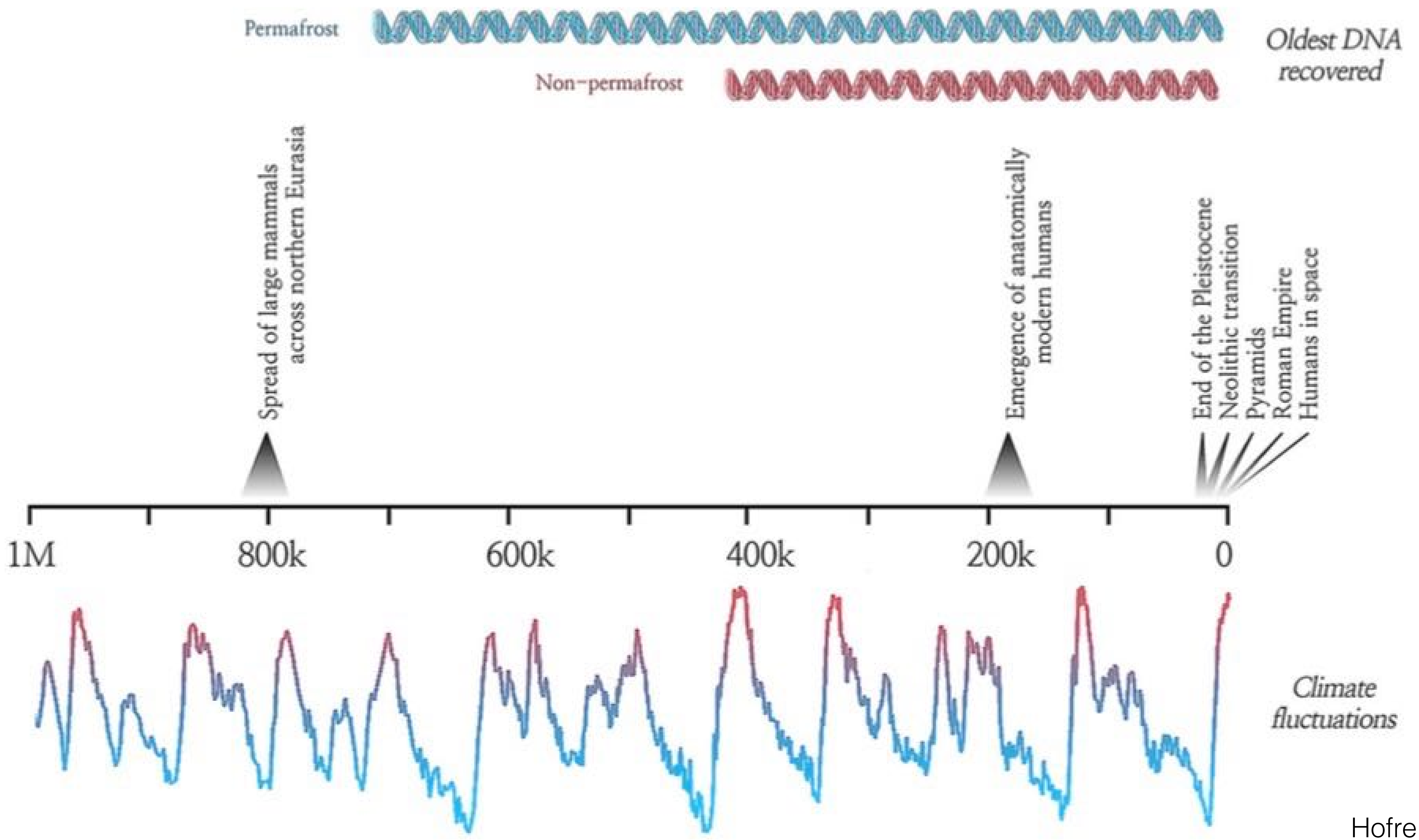
- Ancient DNA (aDNA)
    - partial and complete sequences
    - limits in hominids: ~400 kYA (thousands of years) (partial, mtDNA)
    - oldest complete hominin genome ~ 120 kYA (neanderthal)
    - oldest *H. sapiens* genome - 45 kYA (Ust'-Ishim, Siberia)
    - oldest complete genome - > 700 kYA years (a horse species) - preserved in permafrost

DNA pulled from this Neanderthal jawbone found in Belgium revealed fresh details about when these ancient human relatives moved across Europe and into Asia.

PHOTOGRAPH BY J. ELOY, AWEM, ARCHÉOLOGIE ANDENNAISE

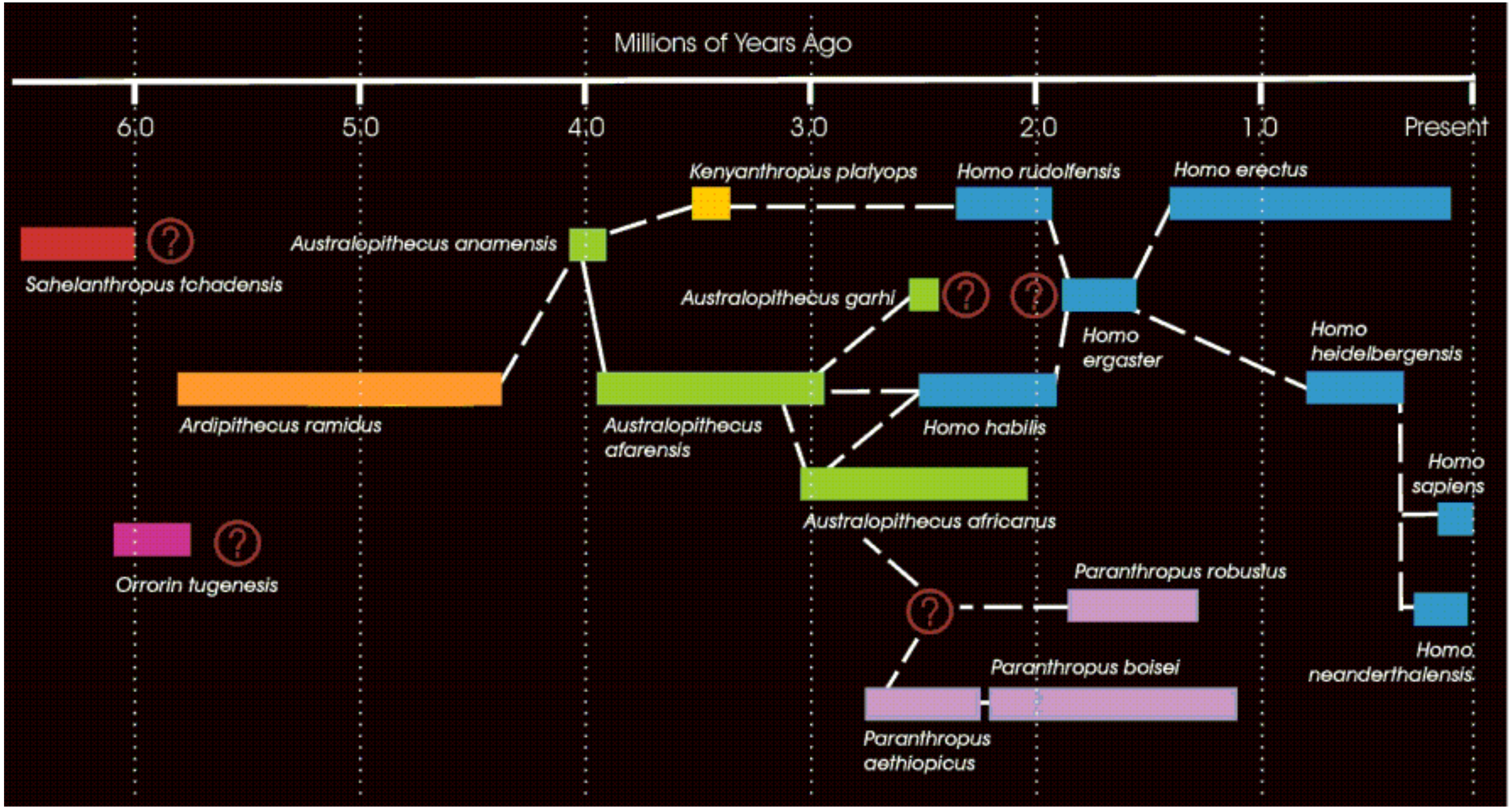
Bence Viola, MPI EVA, nature.com

aDNA



Hofreiter et al. 2014, Bioessays 36

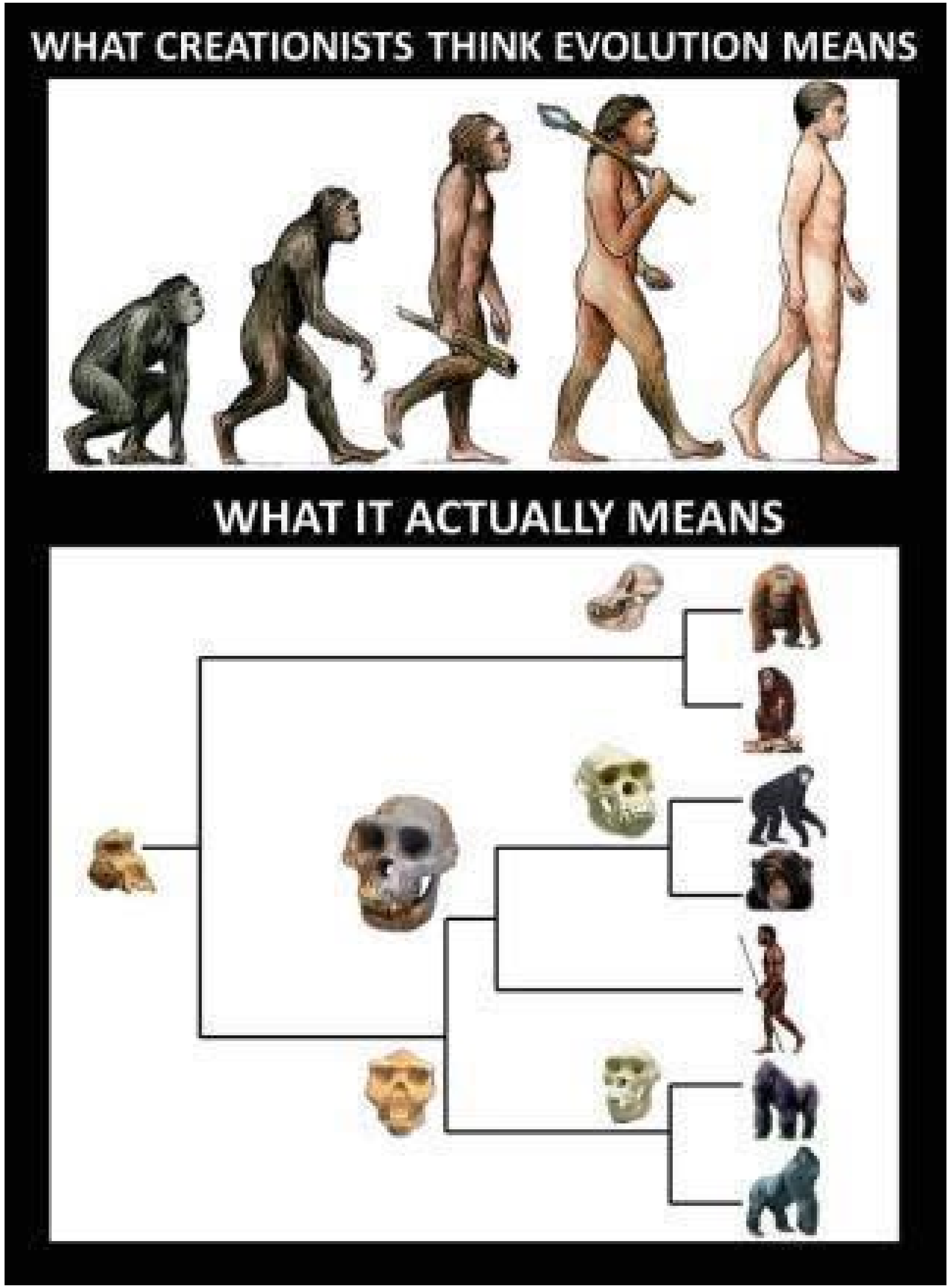
Ancestors?



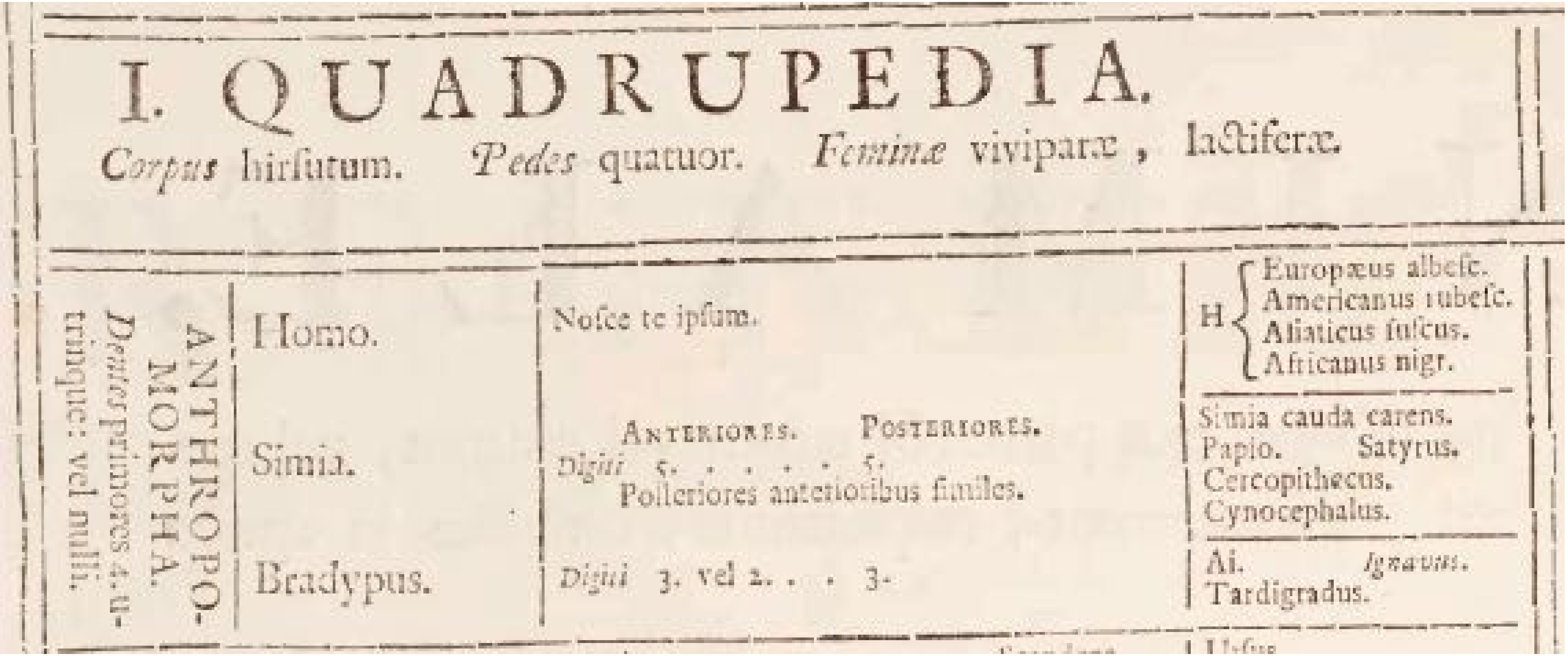
Multiple hominid fossils found. The relations are uncertain: ancestors or cousins?

The tree

- Evolution is not linear
- The status of many fossils often unclear - cannot be assigned to a particular branch
- There is no “missing link” - current paleontology has many fossils of transitory forms from ape-like to human-like



We are animals!



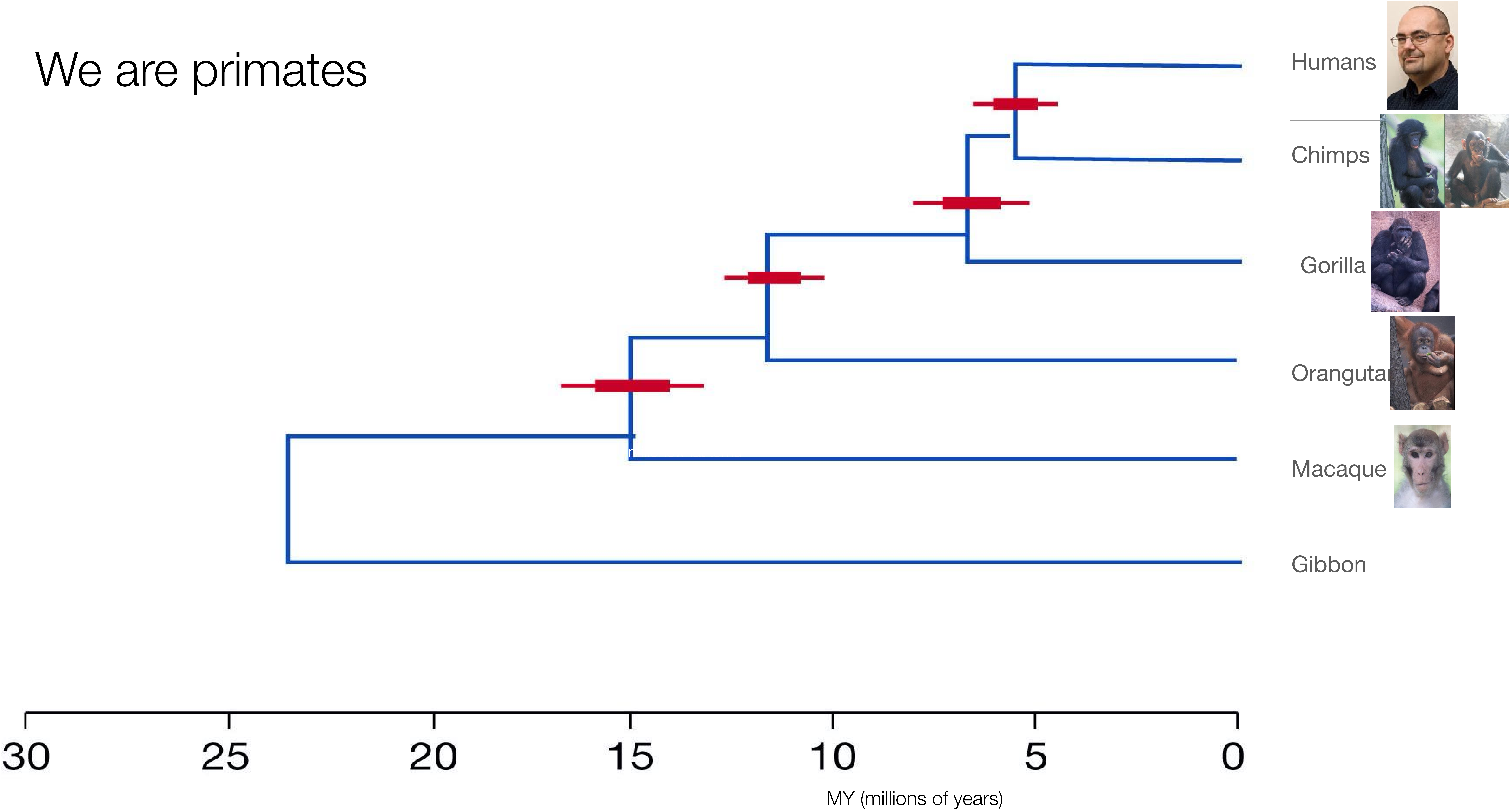
I. QUADRUPEDIA.

Corpus hirſutum. *Pedes* quatuor. *Feminæ* viviparæ, lactiferæ.

ANTHROPOMORPHA. *Dentes* primores 4. utrinque: vel nulli.	Homo.	Noſce te ipſum.	H. Europæus albeſc. Americanus rubeſc. Aſiaticus fuſcus. Africanus nigr.
	Simia.	ANTERIORES. POSTERIORES. *Digiti* 5. . . . . . 5. Poſteriores anterioribus ſimiles.	Simia cauda carens. Papio. Satyrus. Cercopithecus. Cynocephalus.
	Bradypus.	*Digiti* 3. vel 2. . . . 3.	Ai. *Ignavus.* Tardigradus.

Linnaeus, 1735 *Systema Naturae*

We are primates



Taxonomy

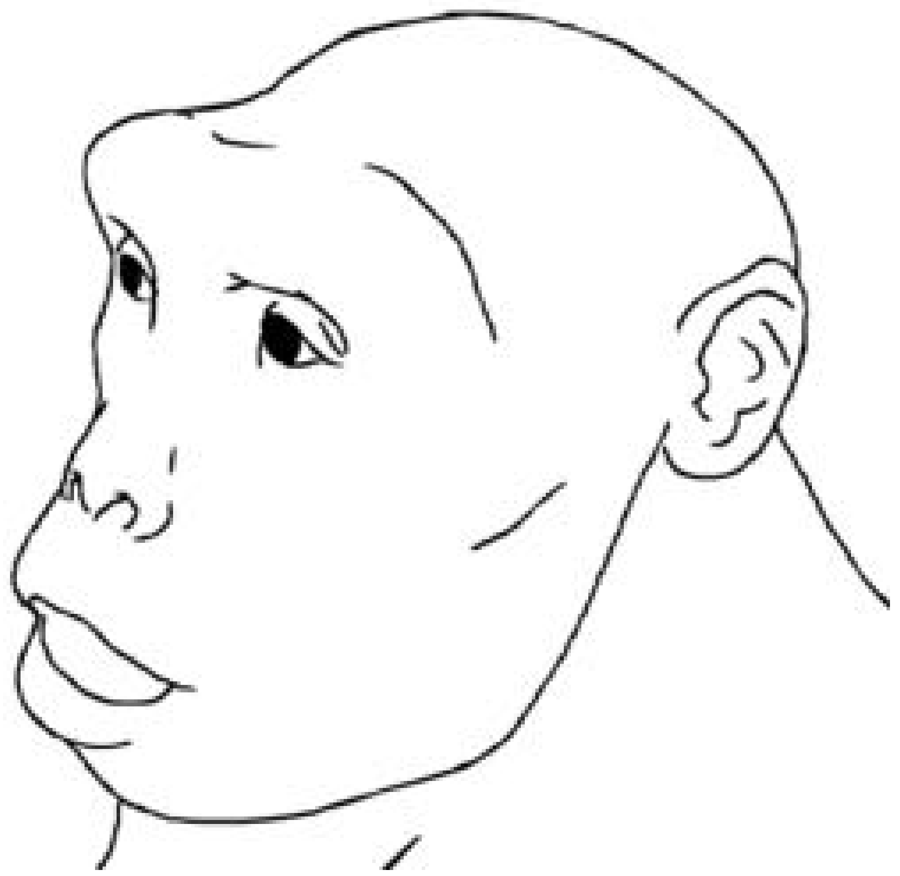
- **Hominids** - the family *Hominidae*:
  - currently: humans, chimpanzees (and bonobos), gorillas, orangutans
  - oldest traces: ~14-18 MYA (milion years ago) - branching from the gibbon lineage
  - subfamily *Homininae* - african hominids (minus orangutans)
- **Hominins** - humans and human ancestors, after separation from the chimpanzee lineage
  - In some taxonomies *Hominini* includes humans and chimpanzees

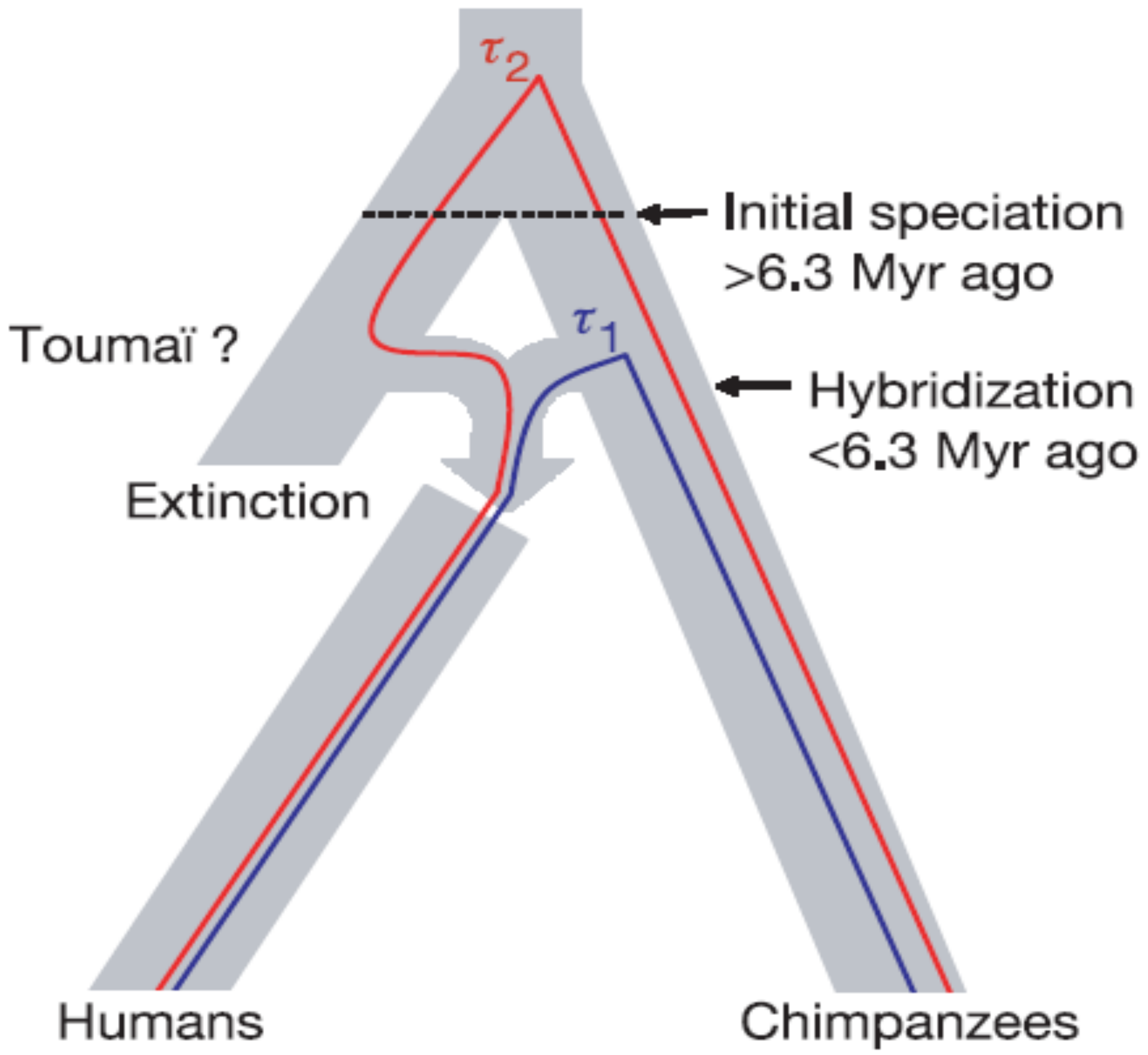
The last common ancestor of humans and chimpanzees

- 6 – 8 MYA – fossil record
  - Assignment of the fossils to a lineage often difficult
- 6 - 7 MYA – sequence analysis
  - Depends on the estimated mutation rates, underestimated until recently
- As distant from modern humans, as from modern chimpanzees!

Sahelanthropus tchadensis - Toumaï

- Skull fragment
- Dating: ~ 6-7 MYA
- Close to a last common ancestor (LCA) of humans and chimps?
- Around the same time as the LCA
- Some traits more chimp-like (cranial proportions), some more hominin-like



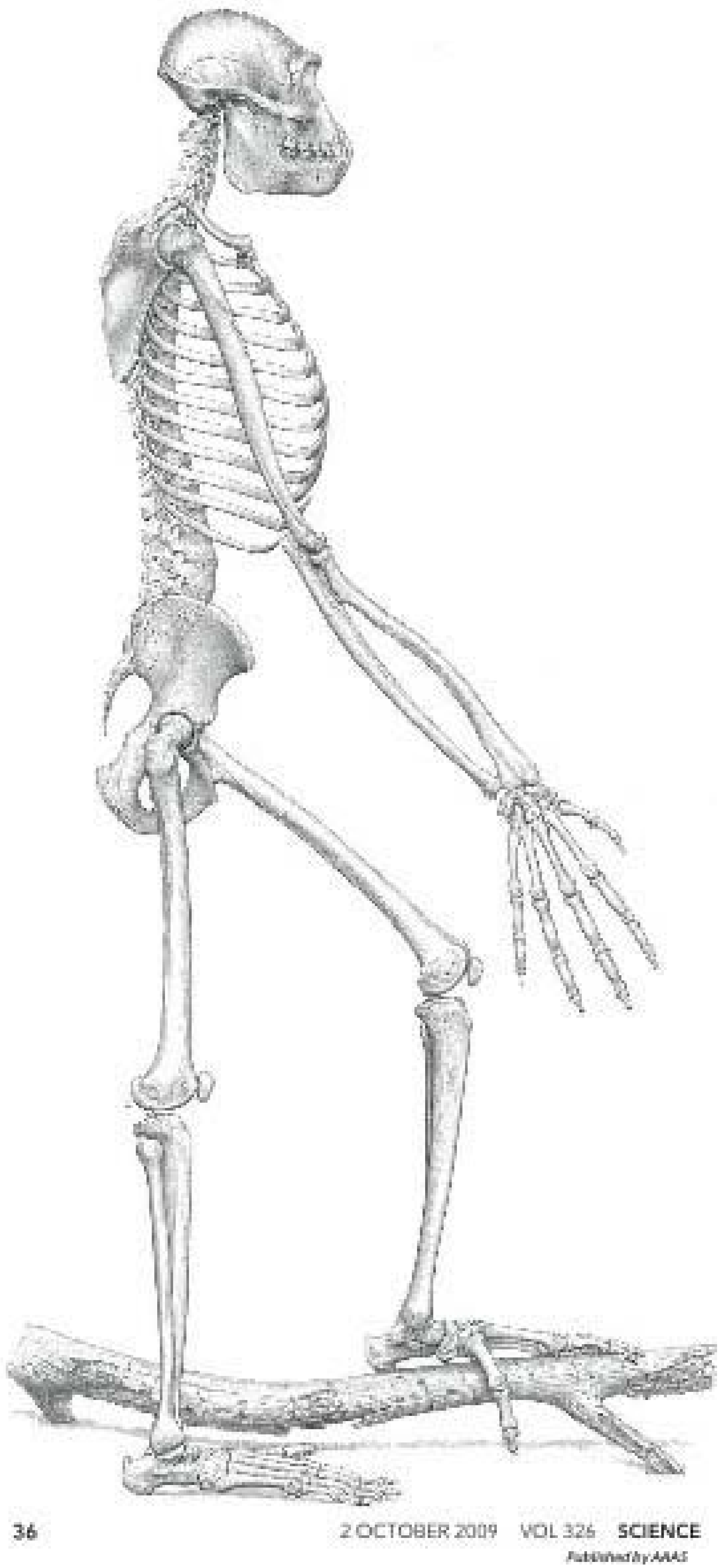


Orrorin tugenensis

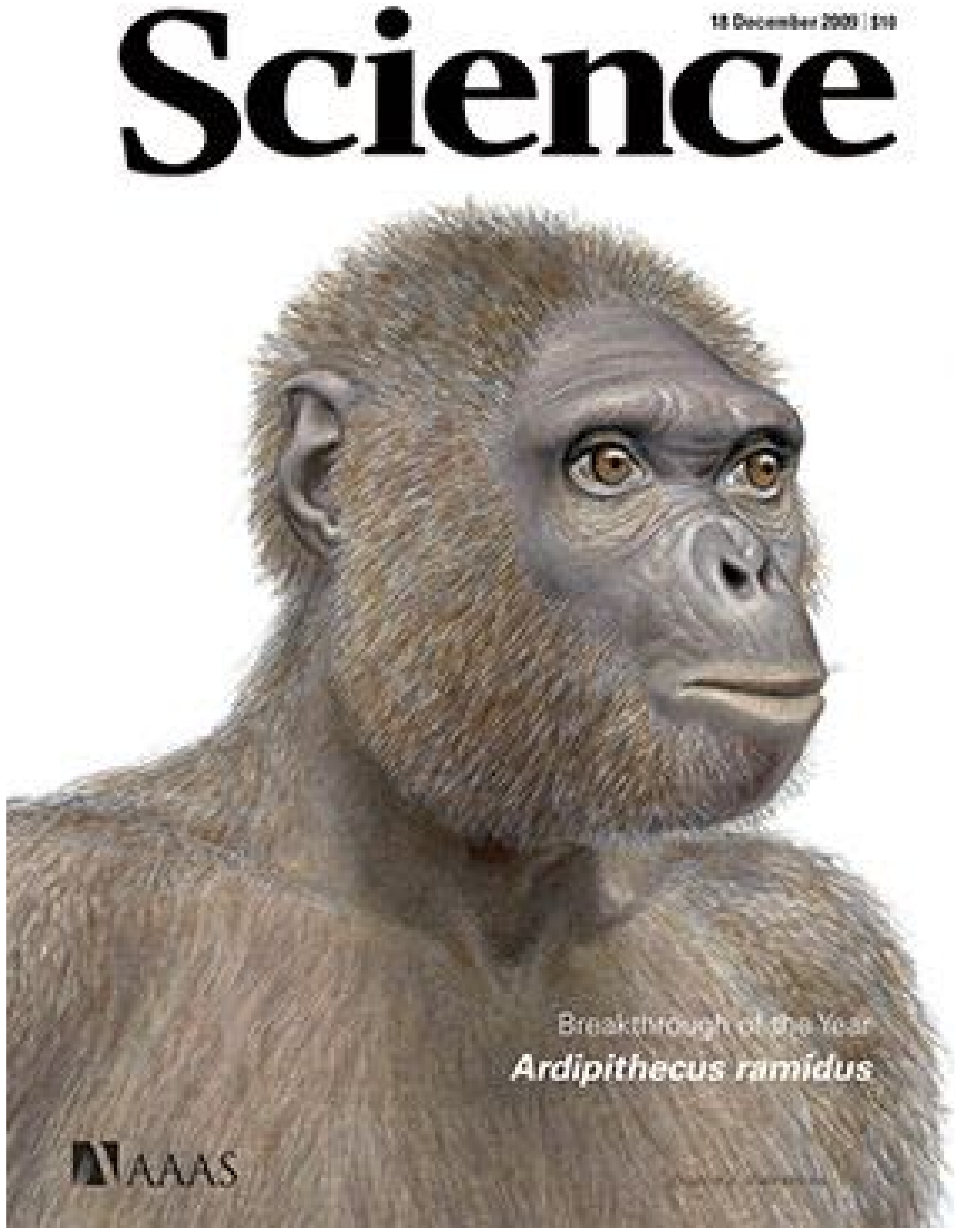
- Discovered in 2001 ("the millenium man")
- ~5-6 MYA
- Was it a real hominin?
  - Some traits even more "human like" than in *Australopithecus*
  - still could be a parallel lineage
- Partially bipedal
- Habitat - forests and forest border

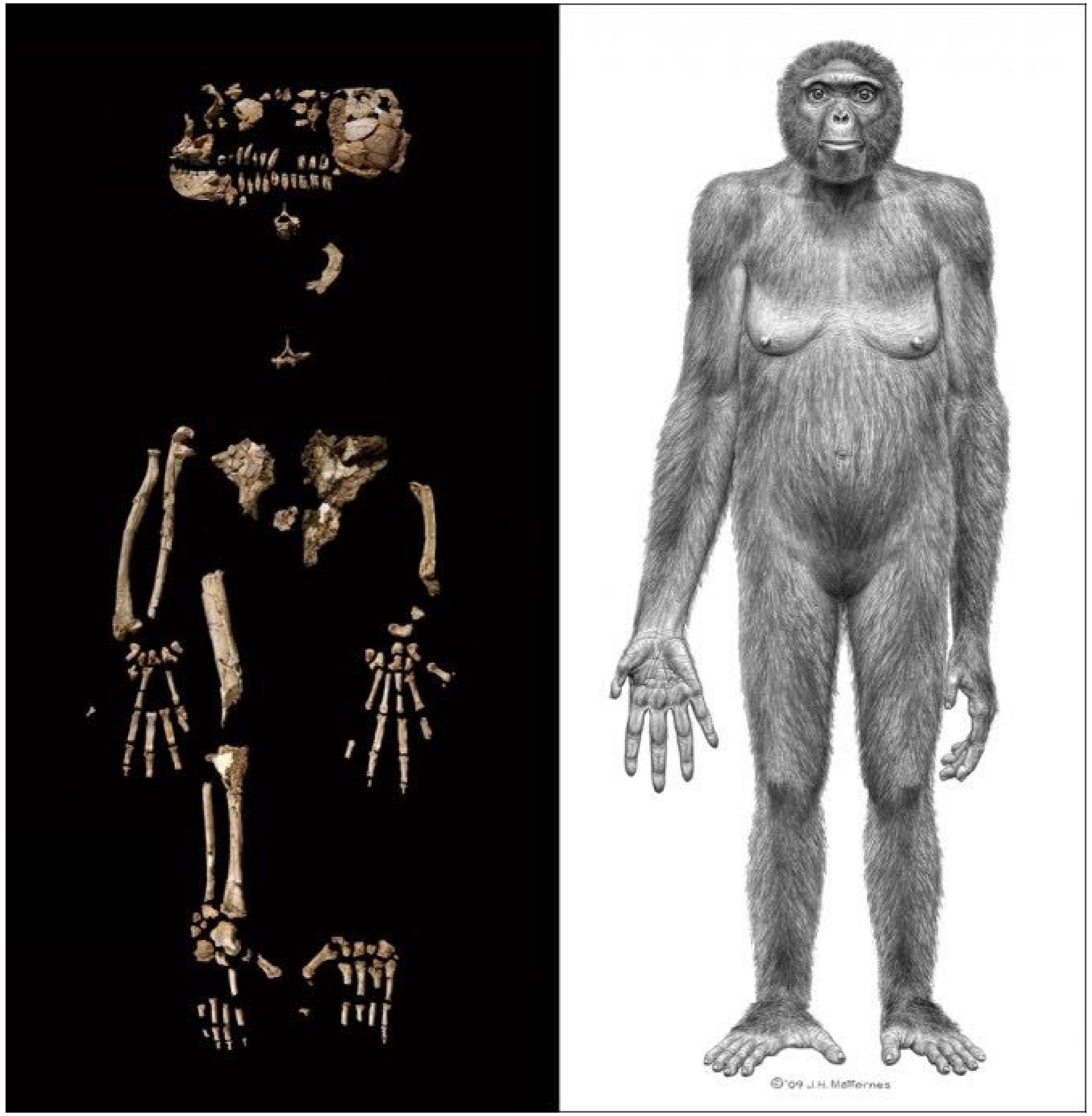
Ardipithecus ramidus - Ardi

- Discovered 1994, published 2009
- 4.4 MYA
- Oldest true hominin
- Partially bipedal
- Ancestor of *Australopithecus* (?)

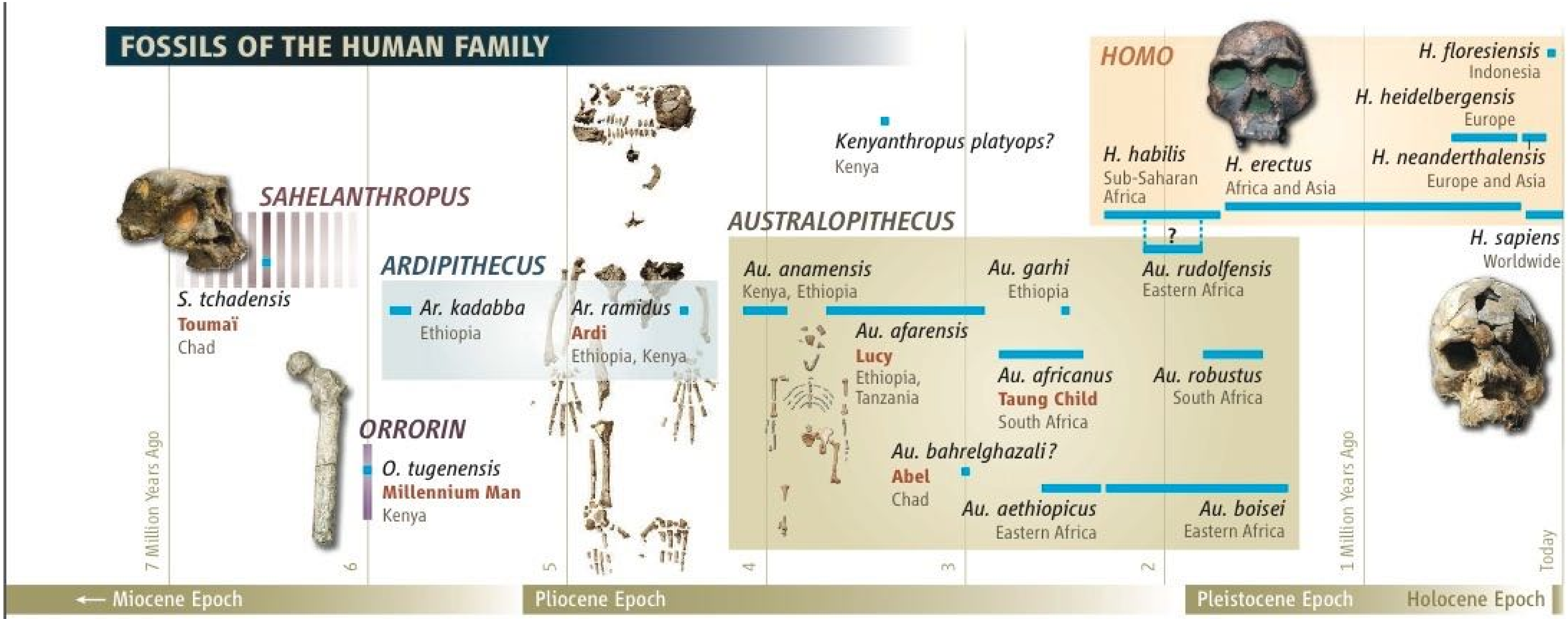


Ardipithecus ramidus - Ardi





Ardipithecus et al.

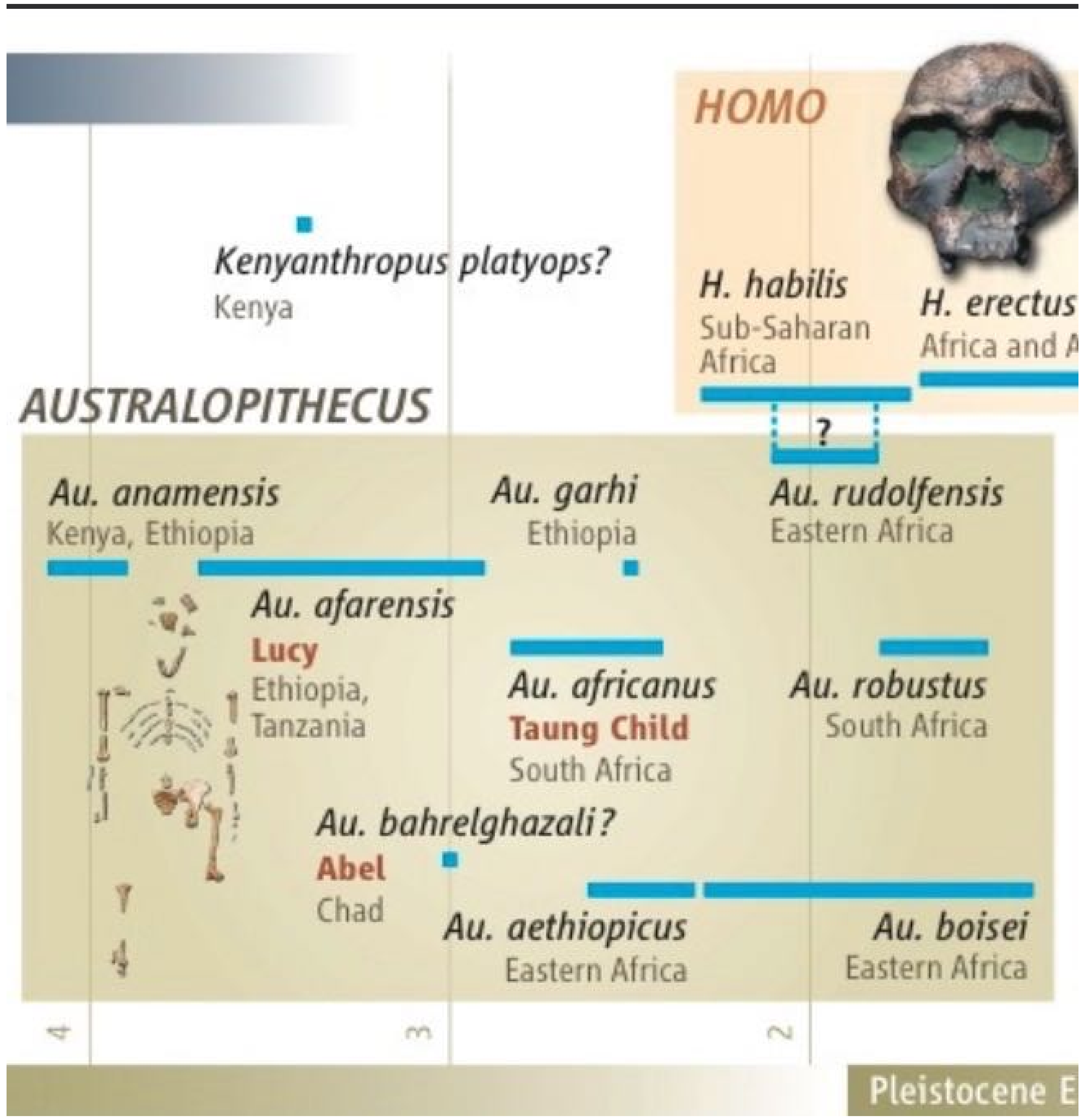


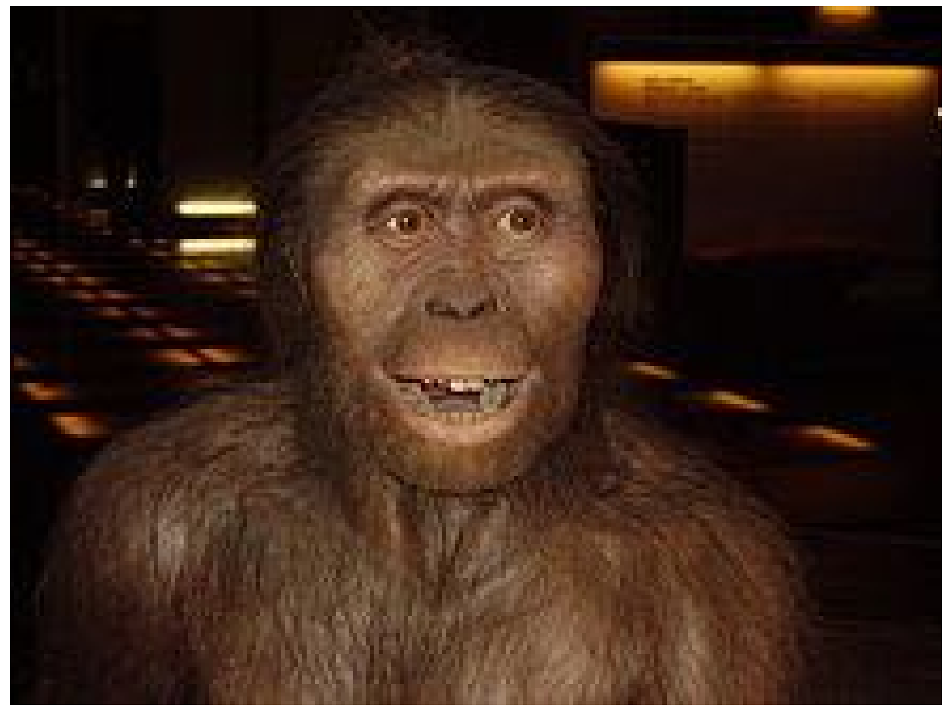
Filling a gap. *Ardipithecus* provides a link between earlier and later hominins, as seen in this timeline showing important hominin fossils and taxa.

www.sciencemag.org **SCIENCE** VOL 326 2 OCTOBER 2009
Published by AAAS

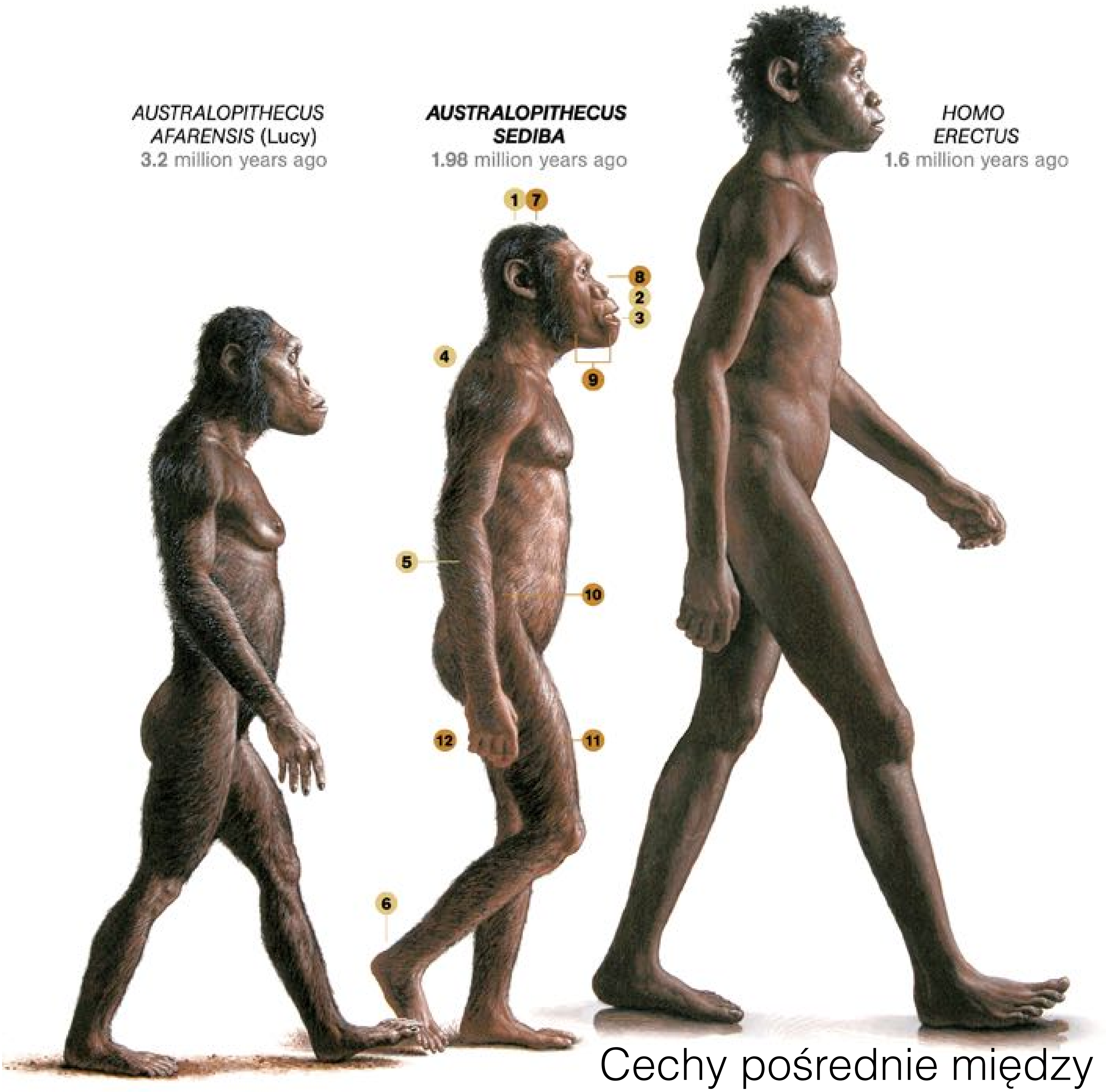
Australopithecus

- Many differen species
  - gracile
  - massive (*Paranthropus*)
- 4 – 2 MYA





Australopithecus sediba - a late australopithecus



SIMILARITIES WITH AUSTRALOPITHS

1. Small brain size
2. Long, high cheekbones
3. Primitive molar cusps
4. Small body size
5. Long upper limbs
6. Primitive heel bone

SIMILARITIES WITH *HOMO*

7. Front of brain reorganized
8. Projecting nose
9. Smaller teeth and chewing muscles
10. Hips less flared, similar to humans
11. Longer legs
12. Hand with precision grip

Opisany w 2010,
Wiek: ~ 2 mln. lat

Cechy pośrednie między innymi *Australopithecus* a *Homo*

The genus *Homo*

- Origin ~2.3 MY
- The Olduvai culture, stone tools (1.9 MYA) – *Homo habilis*
- *Homo erectus, H. ergaster* ("pithecantropus") – 1.5 MYA, extinct only ~ 70 kYA (thousand years ago)
    - **First to leave Africa**
    - Used fire
    - Hunters (weapons - javelins)
    - Social groups
    - Only one species survived: *H. sapiens*

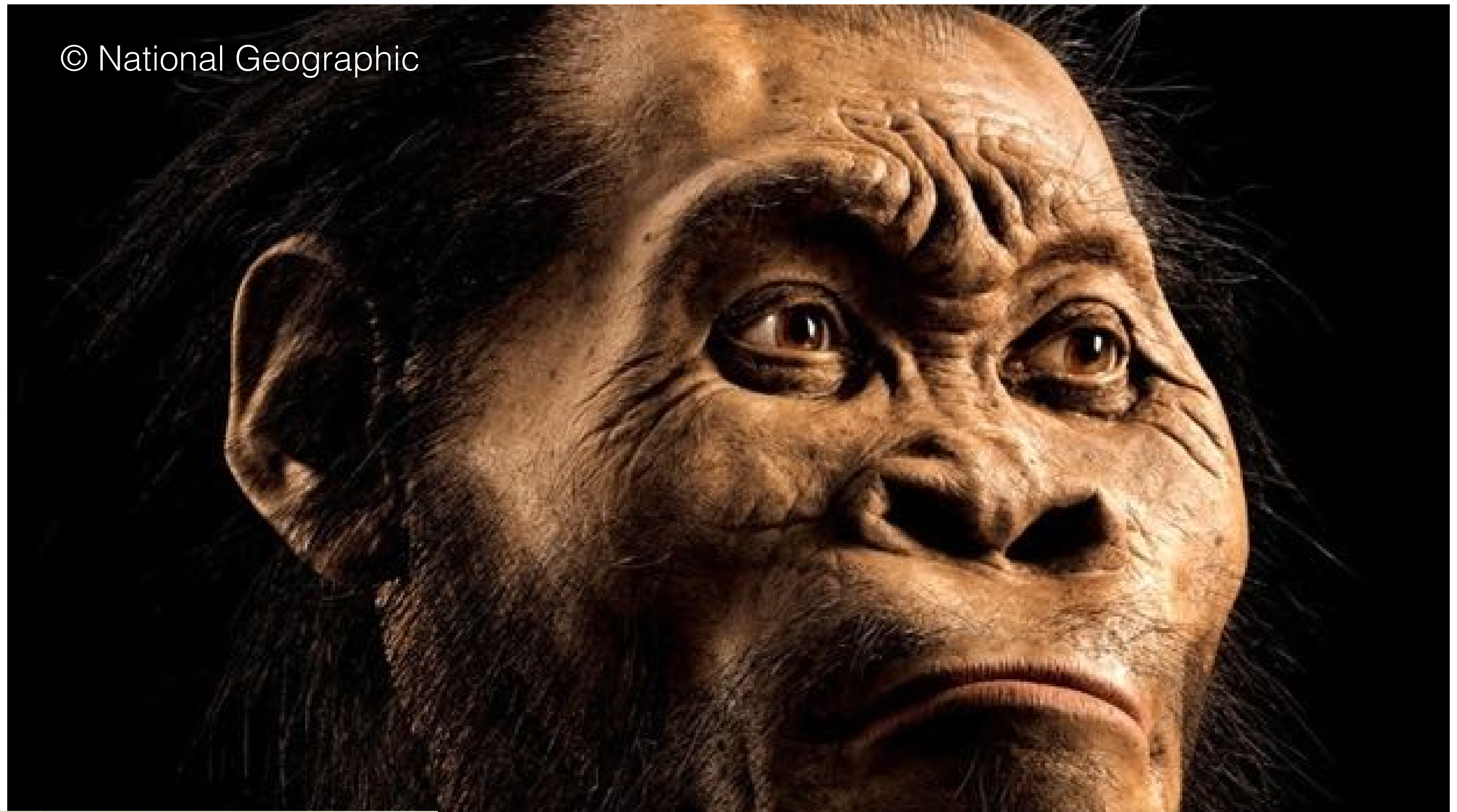
Olduvai tools
British Museum

Homo - how many species

- Fossils found in Georgia (Dmanisi) (~1.8 MYA) *H. habilis, H. ergaster* and *H. rudolfensis* together
- Were they simply different morphs of *H. erectus?*
- No genetic data (too old)

Homo naledi

- Described in 2015, Dinaledi Cave, South Africa
- Likely a burial site
- At first believed to be old, but recent dating suggests not older than 600-300 kYA
- No DNA
- Did it mix with *H. sapiens?*



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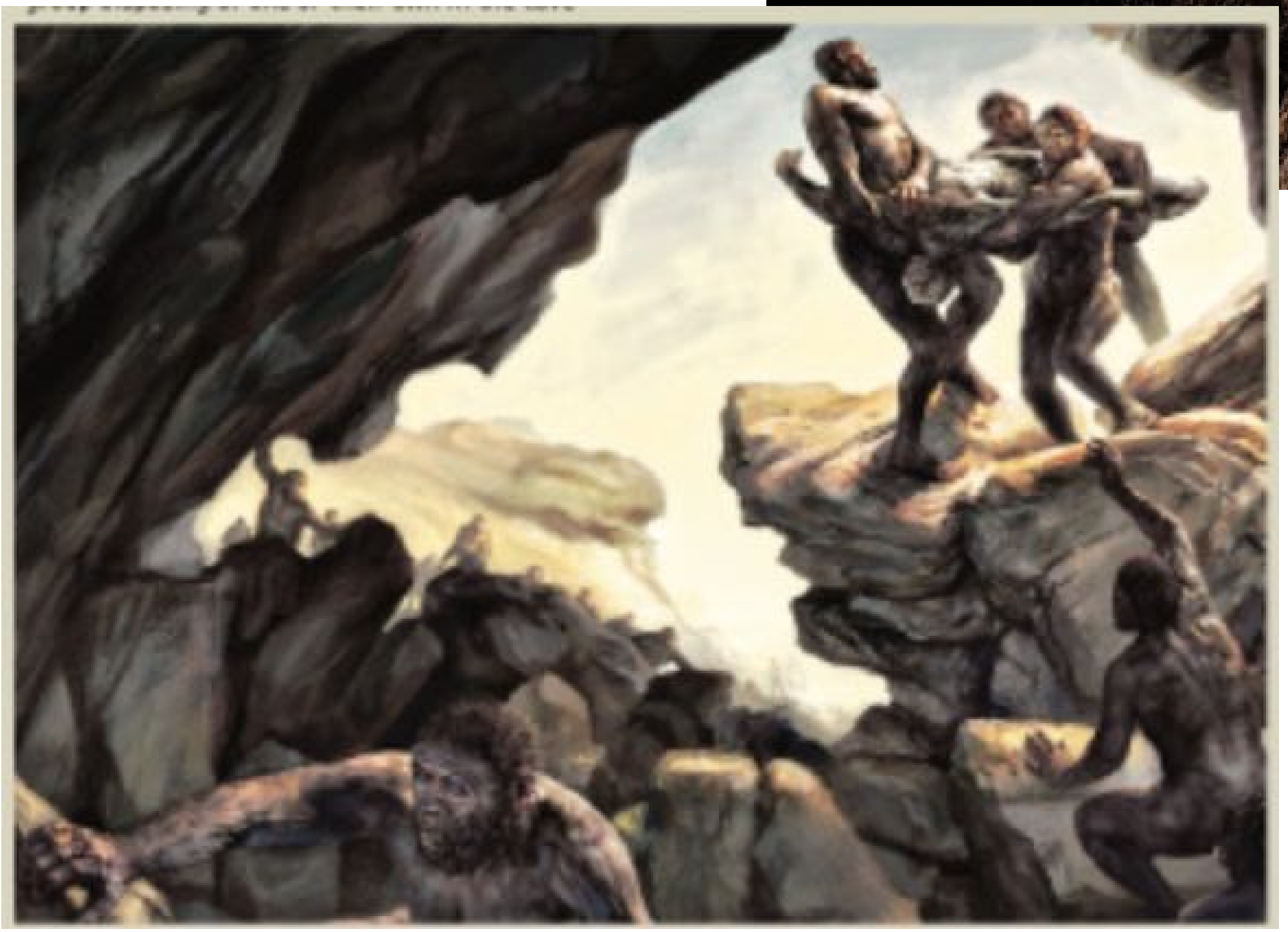


We are all African

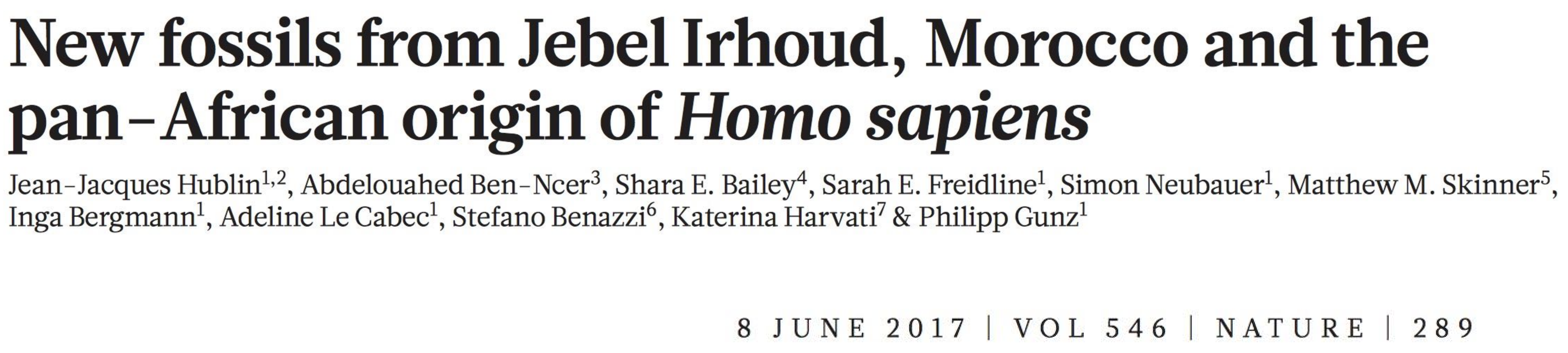
Australopithecus afarensis (Lucy)
oldest *Homo* (a jawbone ~ 2.3 MYA)

Australopithecus, Homo habilis, H. erectus, H. sapiens

Australopithecus africanus
A. sediba

The first *H. sapiens*

- About 500-400 kYA - divergence of human and neanderthal lineages
- ~ 190 kYA - anatomically modern *H. sapiens* - Ethiopia
- ~ 300 kYA - oldest *H. sapiens* (anatomically primitive) - Morocco.
- *H. sapiens* had a wide distribution in Africa!



New fossils from Jebel Irhoud, Morocco and the pan-African origin of *Homo sapiens*

Jean-Jacques Hublin[1,2], Abdelouahed Ben-Ncer[3], Shara E. Bailey[4], Sarah E. Freidline[1], Simon Neubauer[1], Matthew M. Skinner[5], Inga Bergmann[1], Adeline Le Cabec[1], Stefano Benazzi[6], Katerina Harvati[7] & Philipp Gunz[1]

8 JUNE 2017 | VOL 546 | NATURE | 289

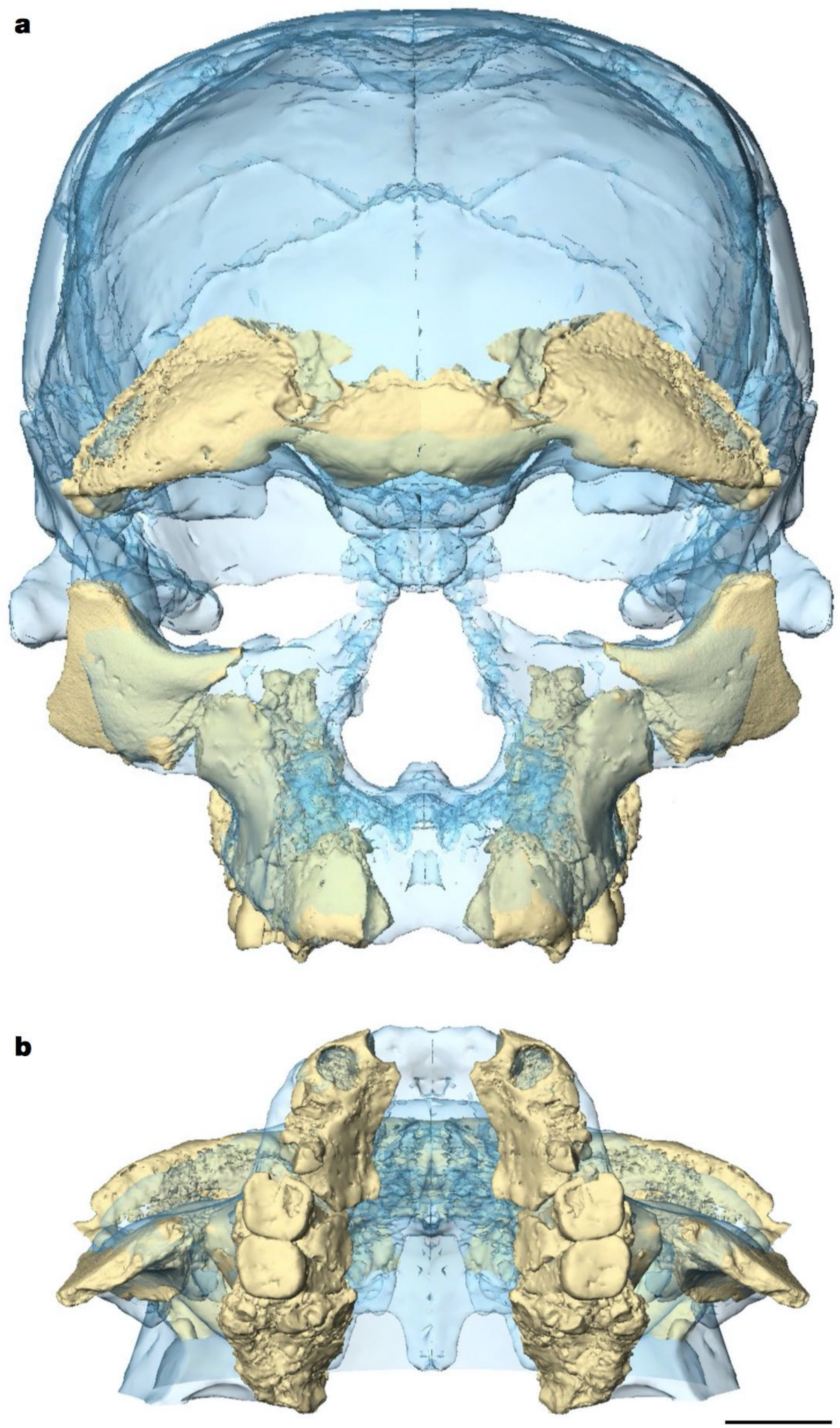
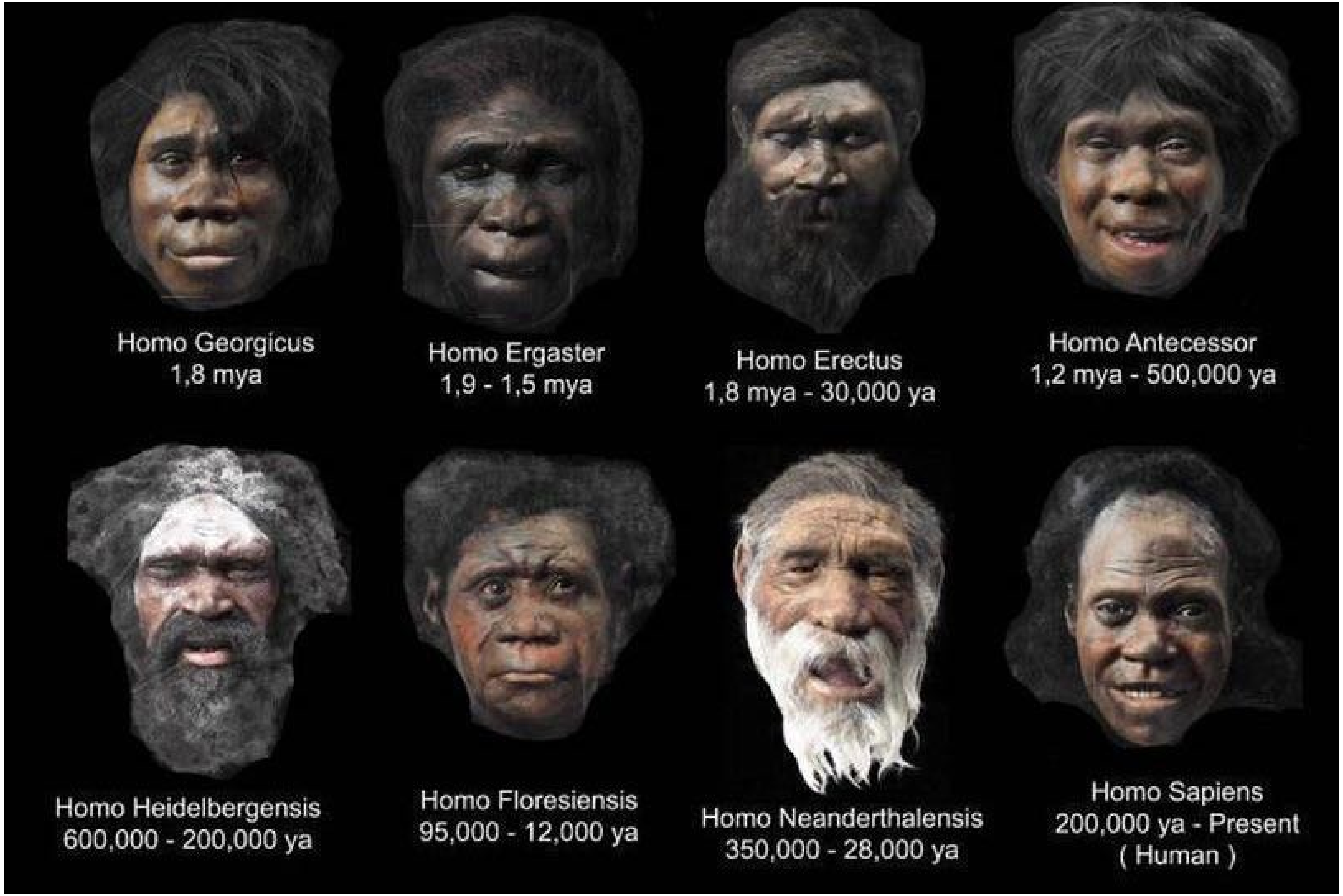


Figure 1 | Facial reconstruction of Irhoud 10. a, b, Frontal (**a**) and basal (**b**) views. This superimposition of Irhoud 10 (beige) and Irhoud 1 (light blue) represents one possible alignment of the facial bones of Irhoud 10.

The first migrations ~2 MYA

Ancestors or cousins?



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The questions

- Who were the ancestors of modern human populations
- Do we come from the first hominids that left Africa?
  - Eg. *H. antecessor* - 800 kYA in western Europe (Spain)

The multiregional model

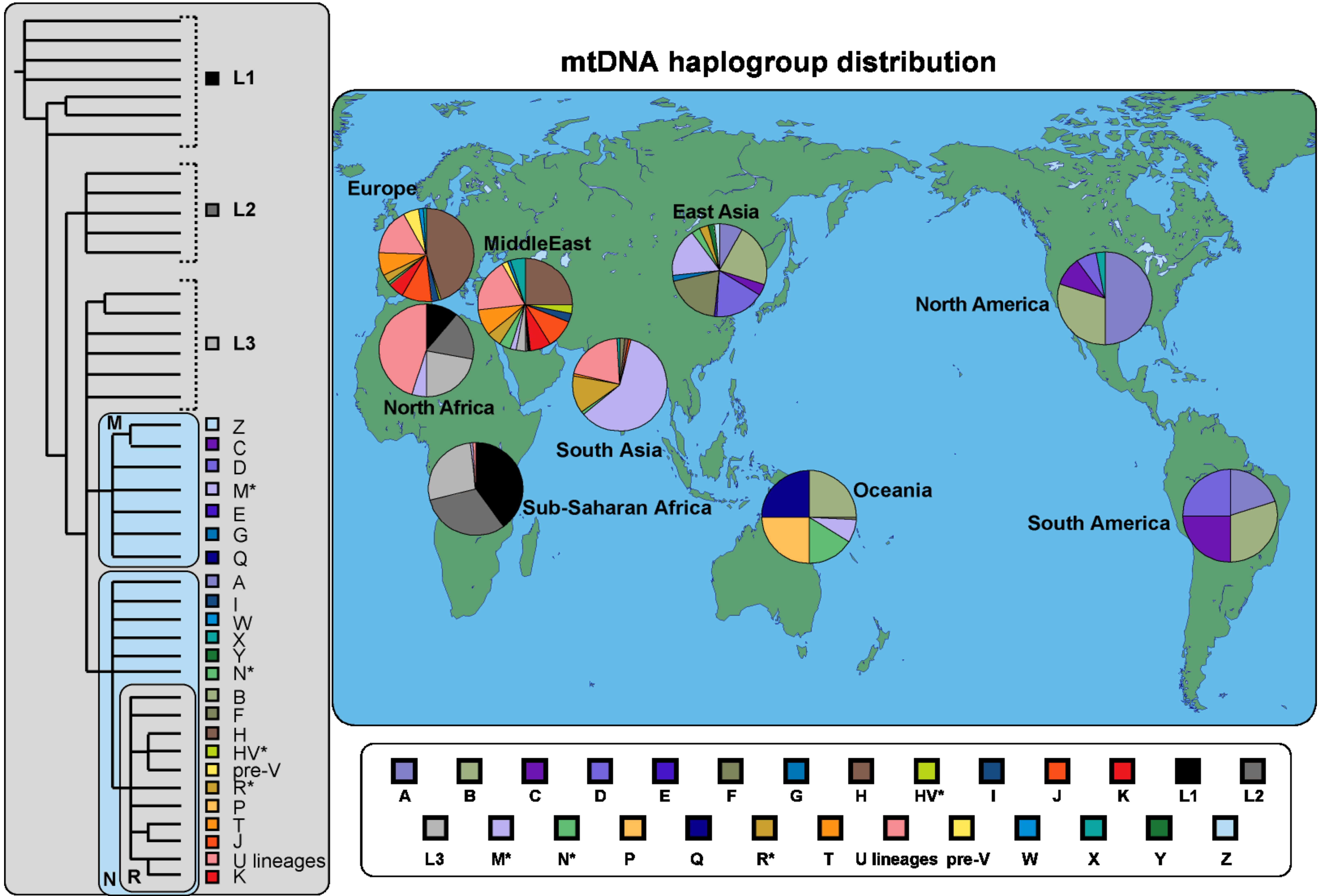
- The human ancestors that left Africa more than 1.5 MYA evolved separately on different continents

- Constant genetic flow between the regions

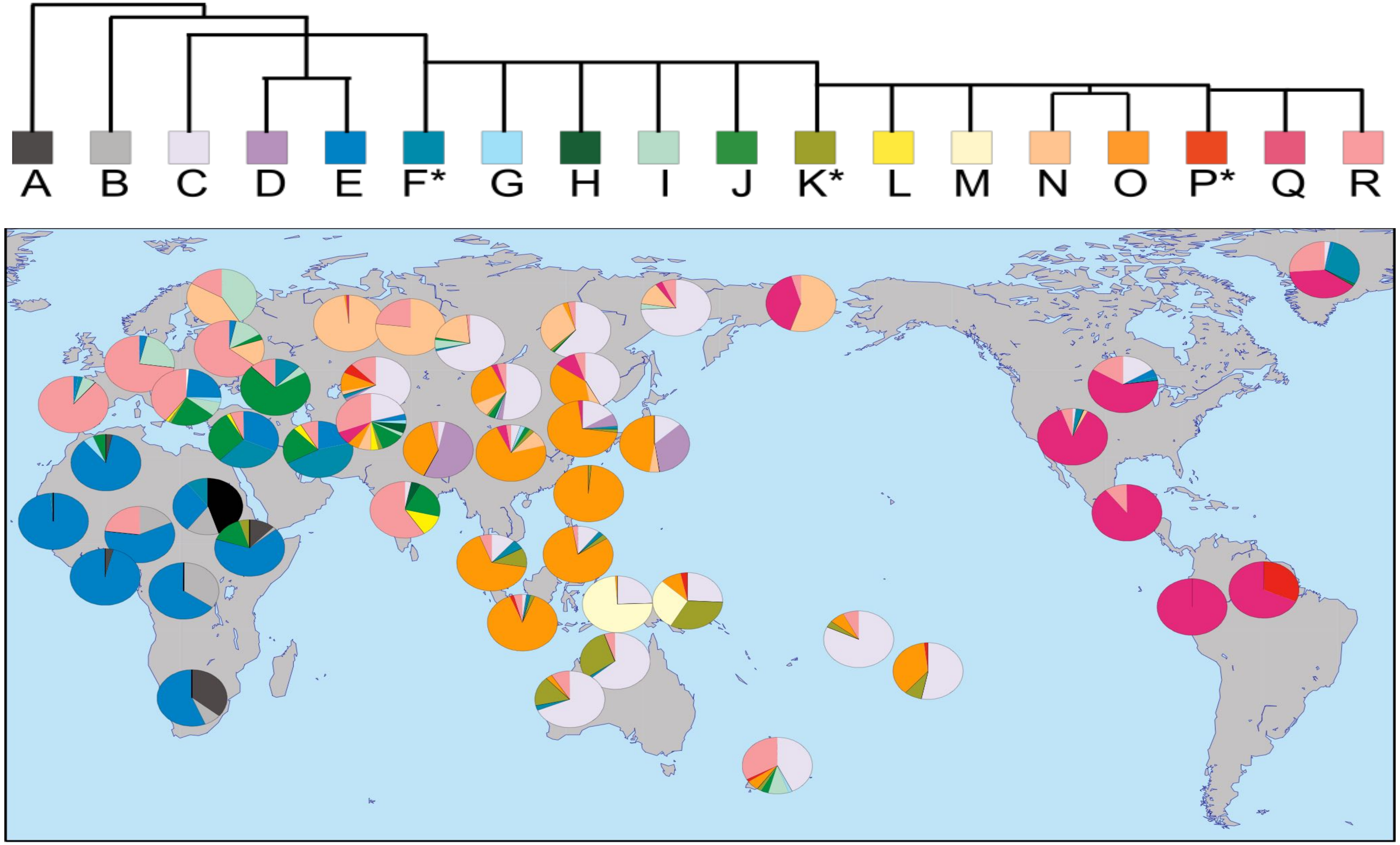
The first genetic studies - mtDNA

- A small DNA molecule (13 genes, 16.5kb)
- Maternally inherited - easy to follow evolutionary changes
  - Variants evolve linked together as haplotypes that form larger haplogroups
  - No recombination in every generation
- Multicopy - easy to isolate

The mtDNA haplogroup tree



The Y chromosome haplogroup tree - another uniparental genome segment



Jobling & Tyler-Smith (2003) Nature Rev. Genet. 4, 598-612

The OoA (OAR) modell

- “Out of Africa (replacement)”
- Modern humans descend from a population that ~ 200 kYA still lived in Africa, and started migrating ~100 kYA to other continent
- That was already modern *H. sapiens*
- The new migrants replaced the previous hominins
- All modern humans come from the last migration wave, not from the earlier migrants

What is OAR about

- Not the African origin
  - all models, based on fossil evidence place human origins in Africa
- We don’t come from a single woman (“the mitochondrial Eve”)
  - we come from one population, mtDNA is not the only lineage, requires unbroken female-to-female lineage
  - modern genomic techniques estimate the effective size of this population at ~30 000 individuals
- **The ancestral population of modern humans lived in Africa recently (~200-300 kYA) they were already modern *H. sapiens***
  - Earlier migrating hominins were not our ancestors

THE MIGRATION OF ANATOMICALLY MODERN HUMANS

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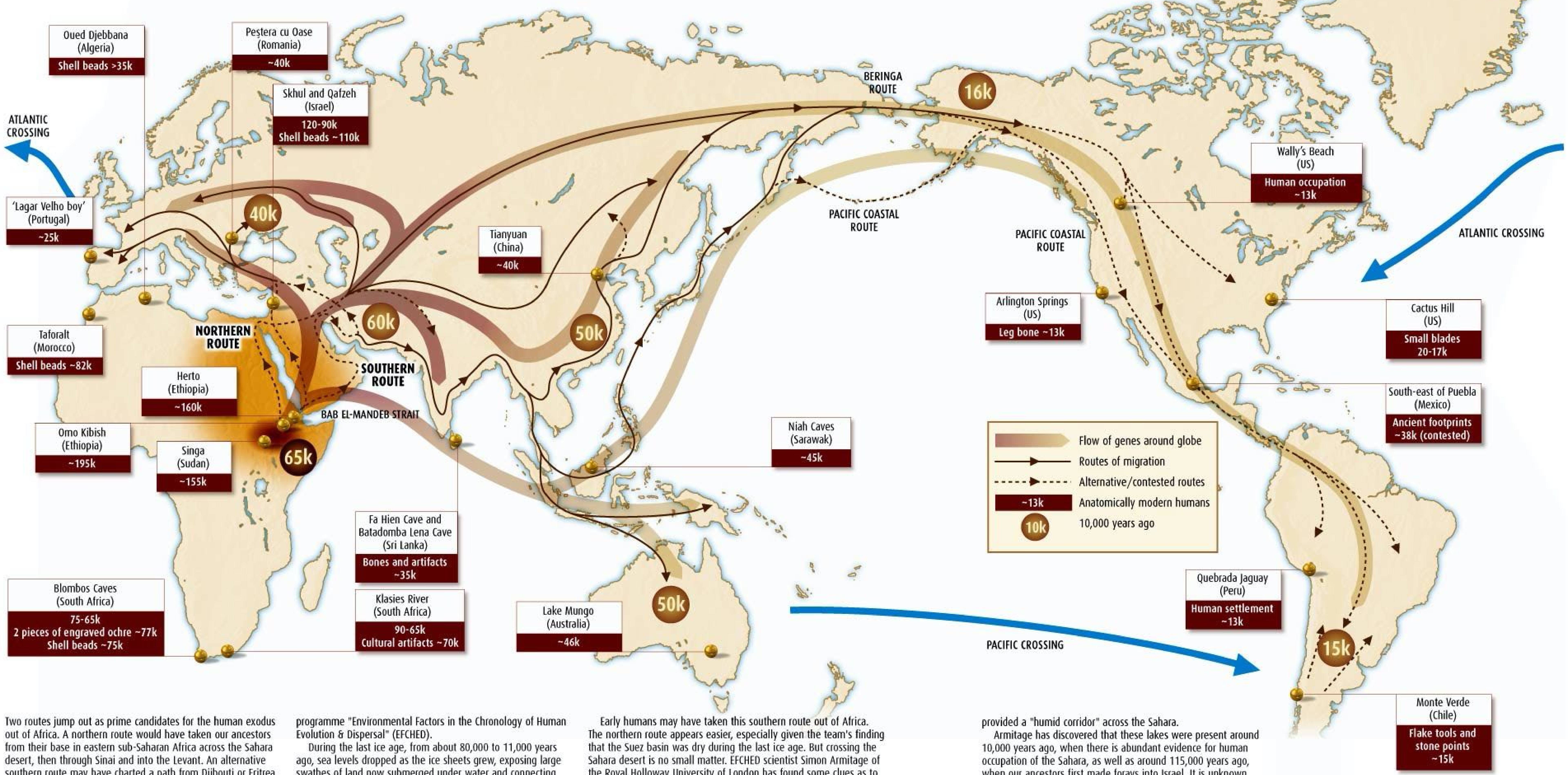
Evidence from fossils, ancient artefacts and genetic analyses combine to tell a compelling story

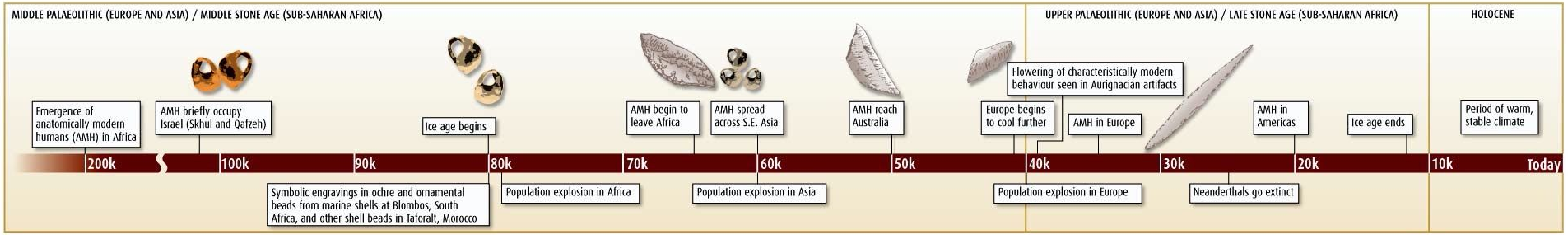


Two routes jump out as prime candidates for the human exodus out of Africa. A northern route would have taken our ancestors from their base in eastern sub-Saharan Africa across the Sahara desert, then through Sinai and into the Levant. An alternative southern route may have charted a path from Djibouti or Eritrea in the Horn of Africa across the Bab el-Mandeb strait and into Yemen and around the Arabian peninsula. The plausibility of these two routes as gateways out of Africa has been studied as part of the UK's Natural Environment Research Council's programme "Environmental Factors in the Chronology of Human Evolution & Dispersal" (EFCHED).

During the last ice age, from about 80,000 to 11,000 years ago, sea levels dropped as the ice sheets grew, exposing large swathes of land now submerged under water and connecting regions now separated by the sea. By reconstructing ancient shorelines, the EFCHED team found that the Bab el-Mandeb strait, now around 30 kilometres wide and one of the world's busiest shipping lanes, was then a narrow, shallow channel.

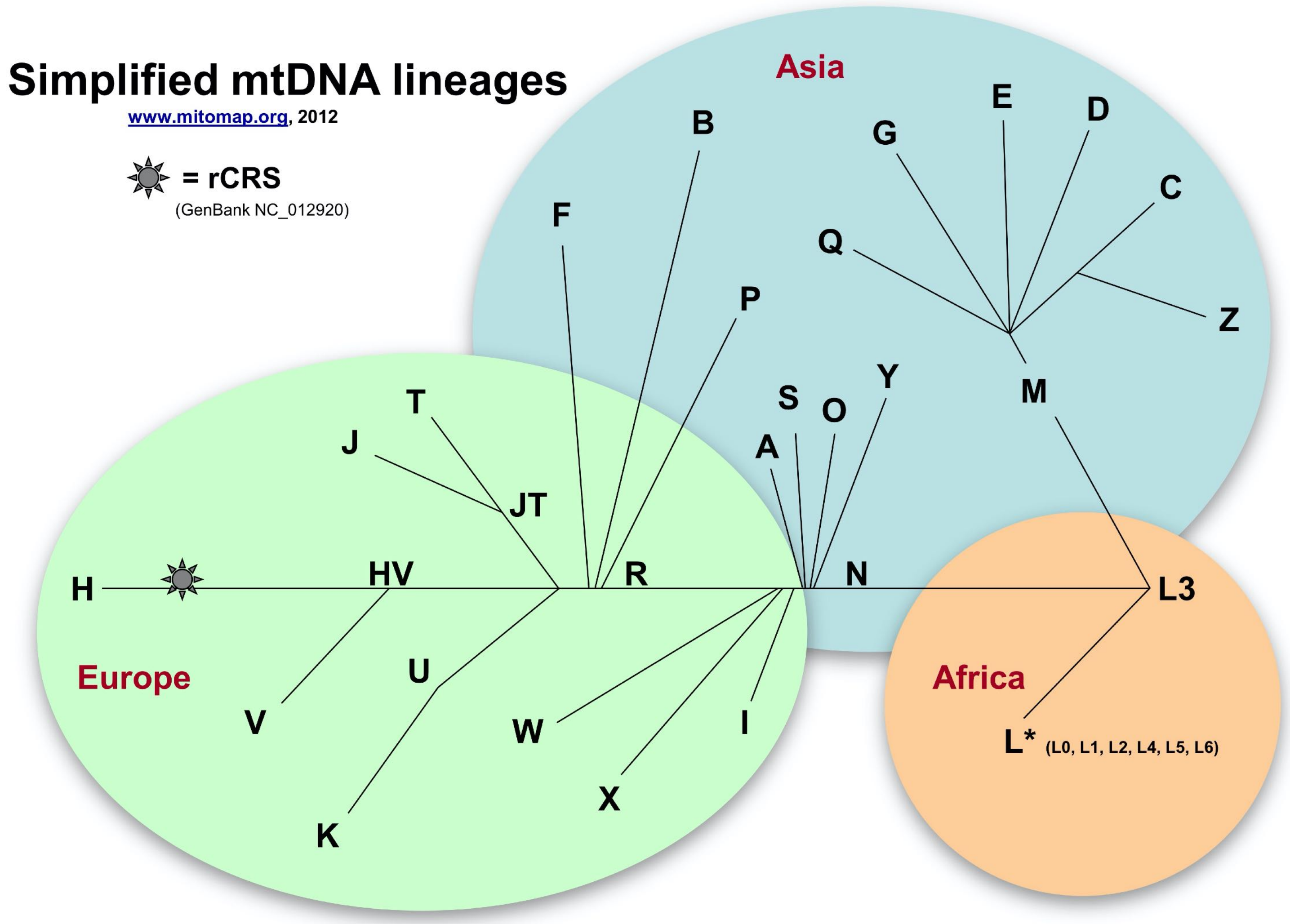
Early humans may have taken this southern route out of Africa. The northern route appears easier, especially given the team's finding that the Suez basin was dry during the last ice age. But crossing the Sahara desert is no small matter. EFCHED scientist Simon Armitage of the Royal Holloway University of London has found some clues as to how this might have been possible. During the past 150,000 years, North Africa has experienced abrupt switches between dry, arid conditions and a humid climate. During the longer wetter periods huge lakes existed in both Chad and Libya, which would have provided a "humid corridor" across the Sahara.

Armitage has discovered that these lakes were present around 10,000 years ago, when there is abundant evidence for human occupation of the Sahara, as well as around 115,000 years ago, when our ancestors first made forays into Israel. It is unknown whether another humid corridor appeared between about 65,000 and 50,000 years ago, the most likely time frame for the human exodus. Moreover, accumulating evidence is pointing to the southern route as the most likely jumping-off point.



The view based on mtDNA and chr Y, ca. 2000

- The story of out of Africa migrations
- Branching into separate lineages

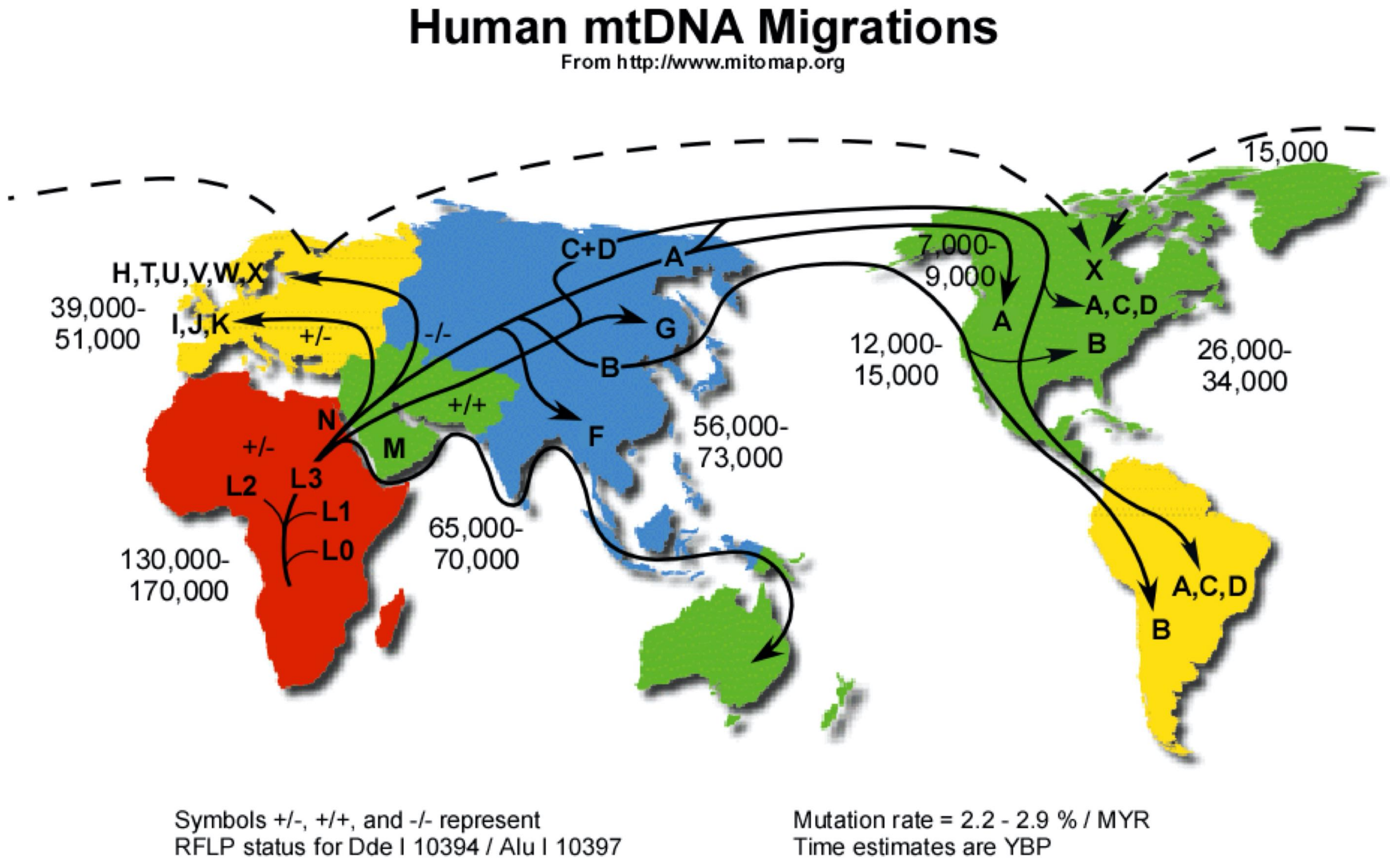


Simplified mtDNA lineages

www.mitomap.org, 2012

✸ = rCRS

(GenBank NC_012920)



Human mtDNA Migrations

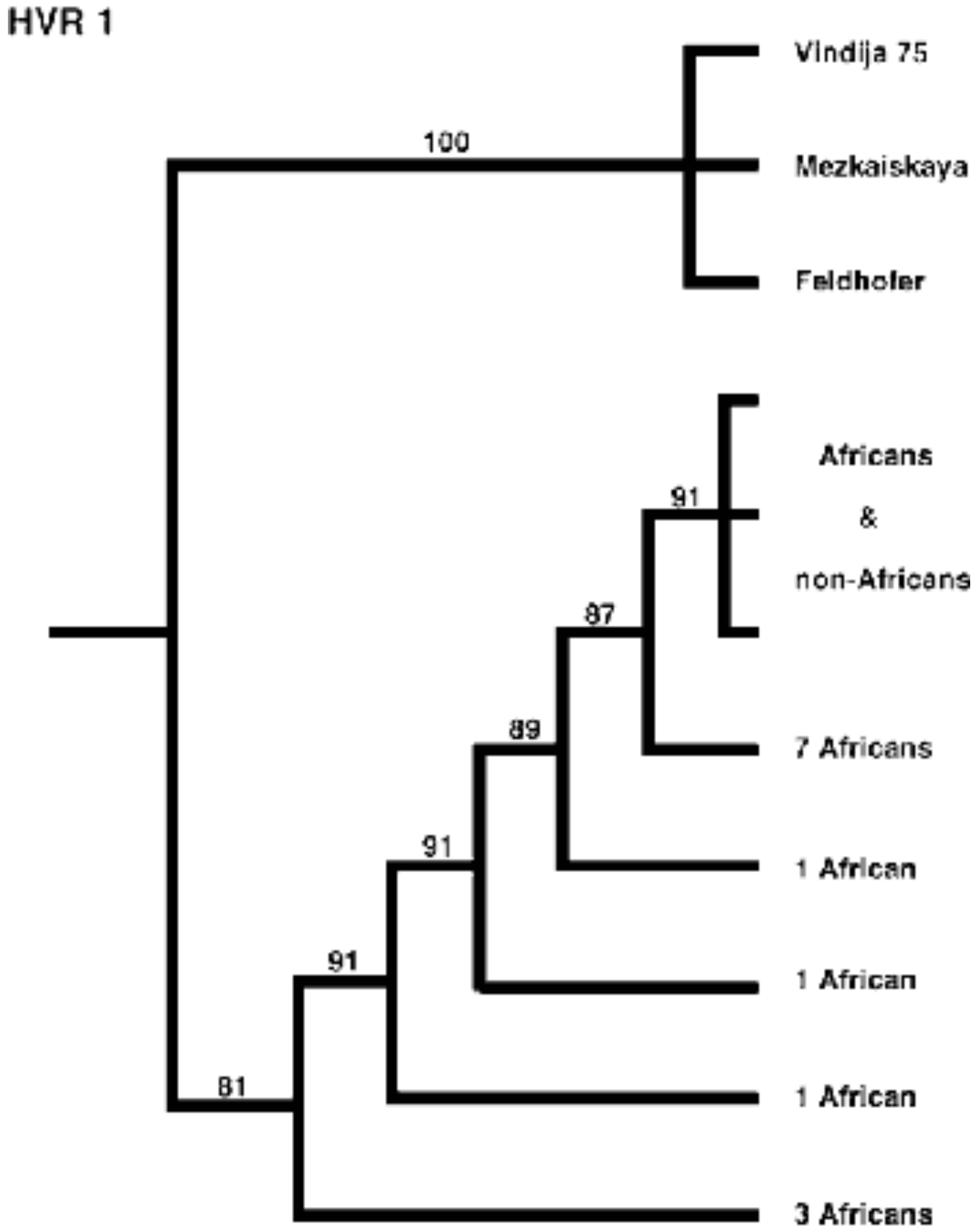
From http://www.mitomap.org

Symbols +/-, +/+, and -/- represent RFLP status for Dde I 10394 / Alu I 10397

Mutation rate = 2.2 - 2.9 % / MYR
Time estimates are YBP

mtDNA and neanderthals

- The neanderthal mtDNA are outside of the human clade
    - Lineages diverged before humans left Africa
- Not our ancestors



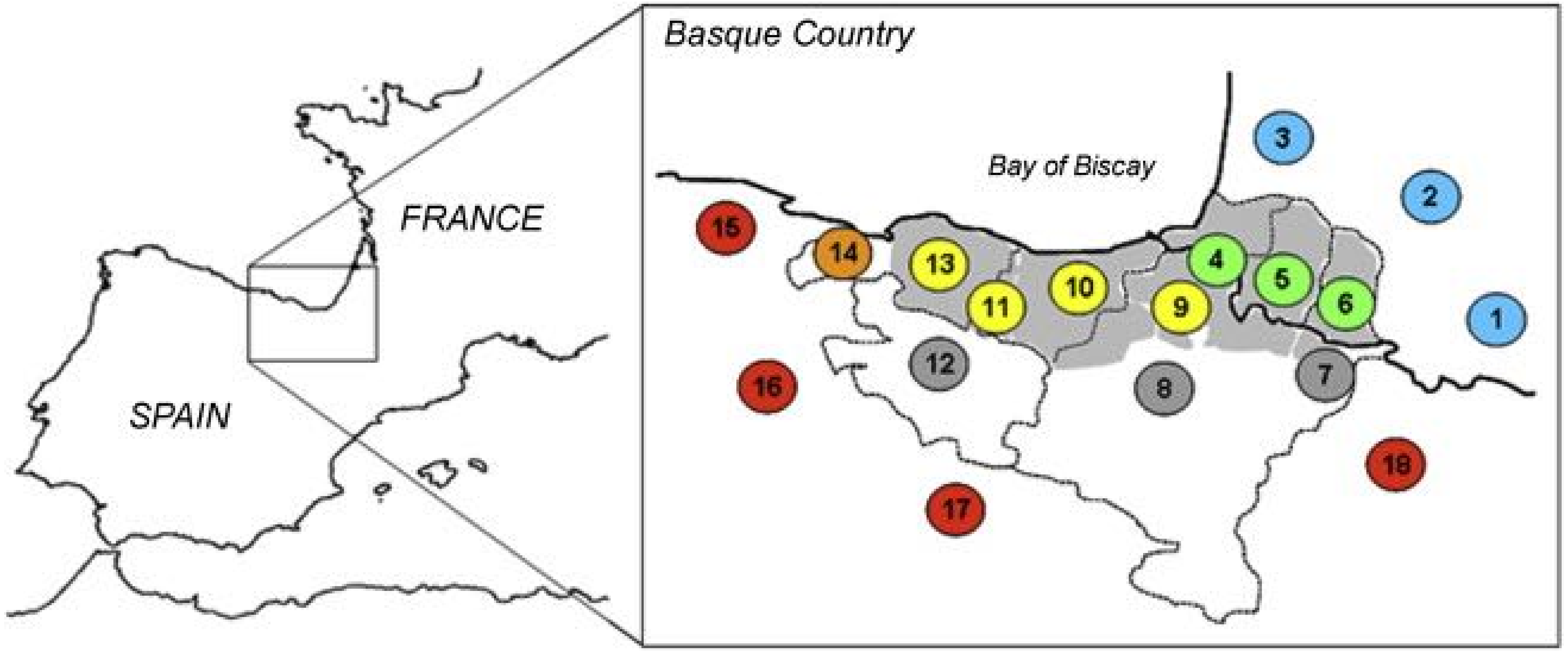
Knight A. (2003): Journal of Human Evolution, 44:627-32.

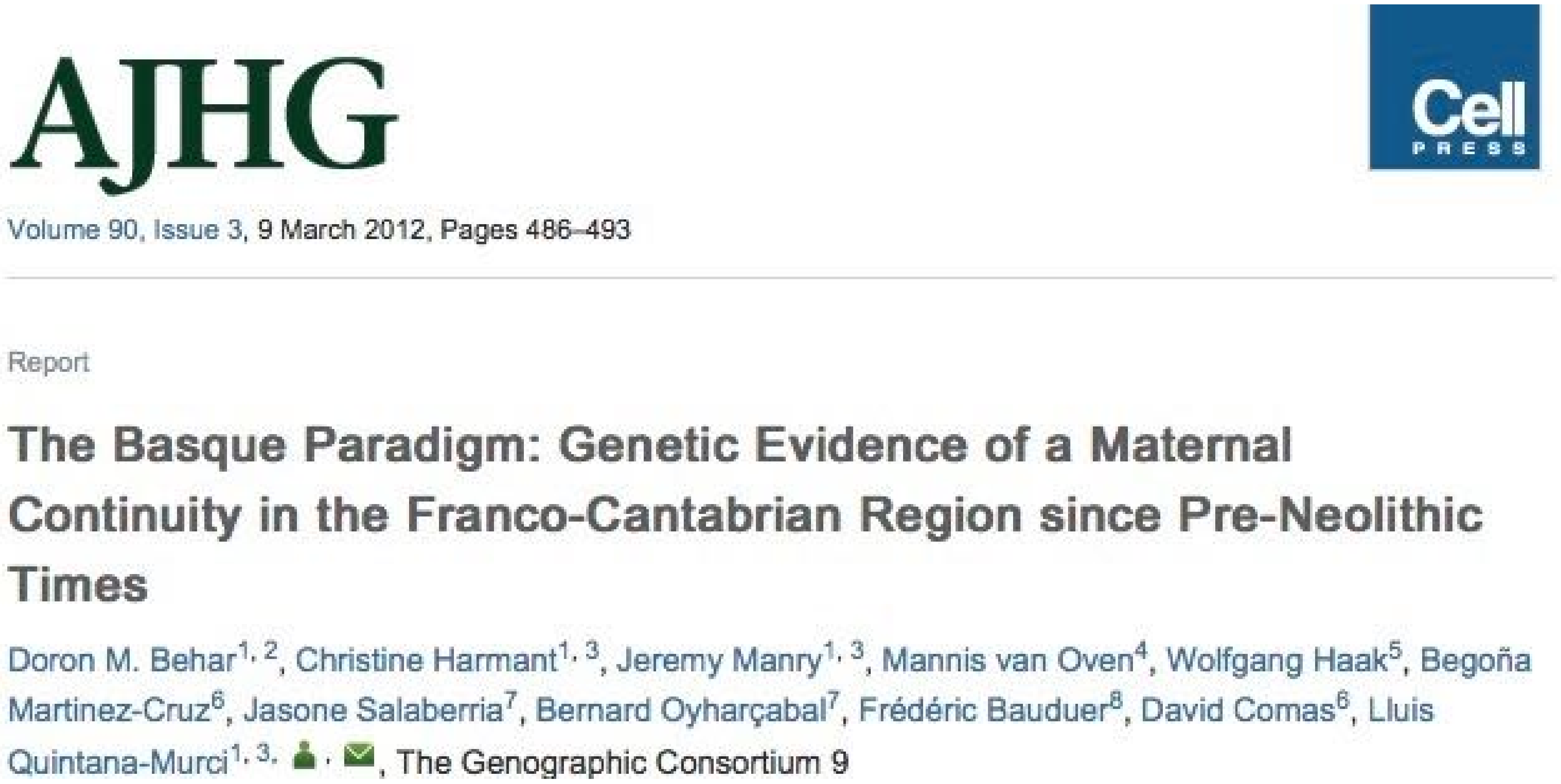
The prehistory of Europe

- First humans arrived ~ 45-50 kYA from Africa via the basal Eurasian population
  - hunter-gatherers, Cro-Magnon humans
- Glacial periods - migrations to souther refugia (18-10 kYA)
- The neolithic farmer migration from the Middle East (10 - 7 kYA)
  - how did it spread - replacement or cultural diffusion?
- Later migrations
  - indoeuropean groups ~5-3 kYA

The only descendants of first Europeans?

- The only traces of pre-neolithic mtDNAs in Basques
- The Basque language - an isolate, not indoeuropean




AJHG

Volume 90, Issue 3, 9 March 2012, Pages 486–493

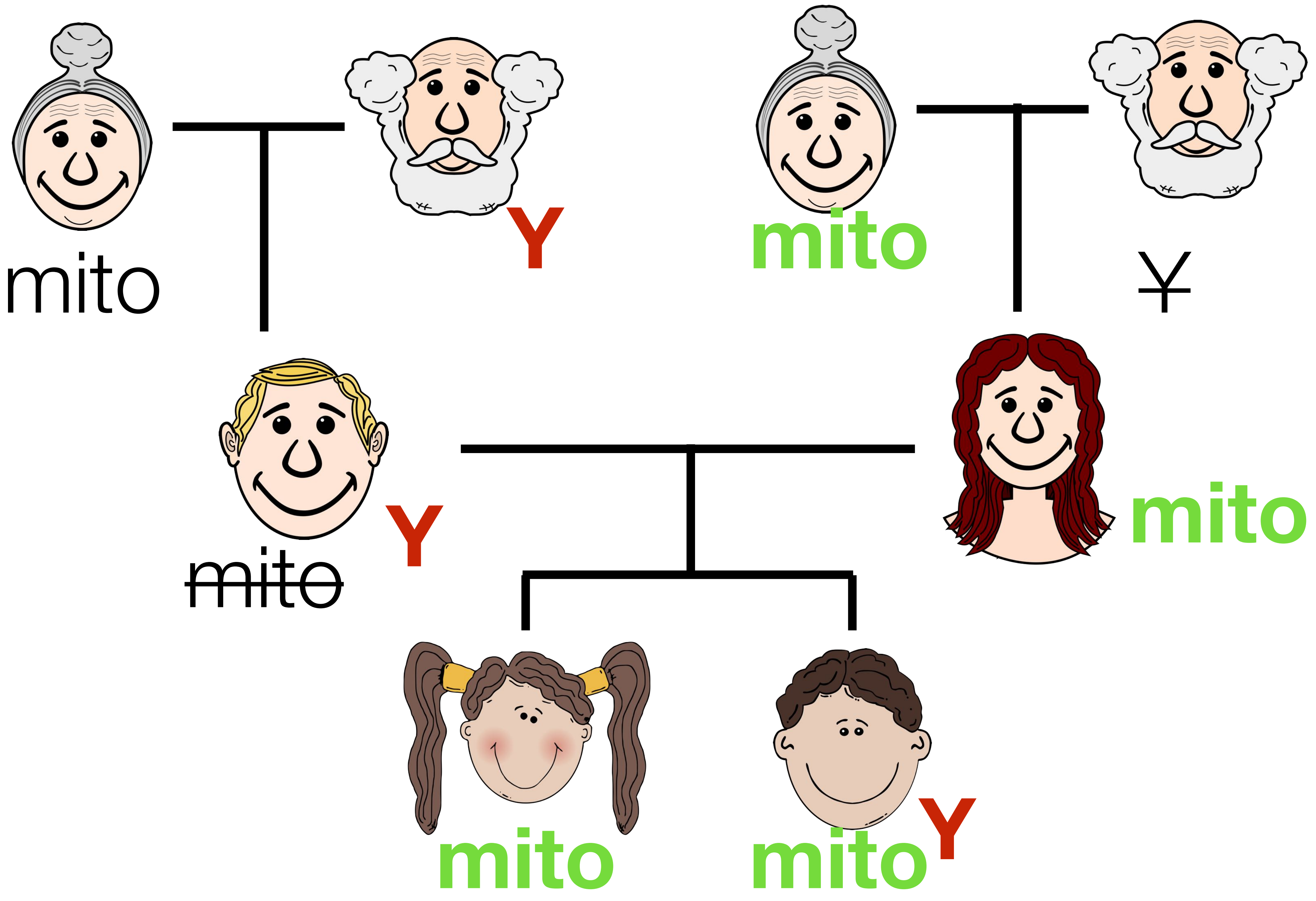
Report

The Basque Paradigm: Genetic Evidence of a Maternal Continuity in the Franco-Cantabrian Region since Pre-Neolithic Times

Doron M. Behar[1, 2], Christine Harmant[1, 3], Jeremy Manry[1, 3], Mannis van Oven[4], Wolfgang Haak[5], Begoña Martinez-Cruz[6], Jasone Salaberria[7], Bernard Oyharçabal[7], Frédéric Bauduer[8], David Comas[6], Lluis Quintana-Murci[1, 3], ✉, The Genographic Consortium 9

mtDNA and chr. Y - the whole story?

- Using uniparentally inherited genome segments makes analysis simple
- But a lot of information is lost

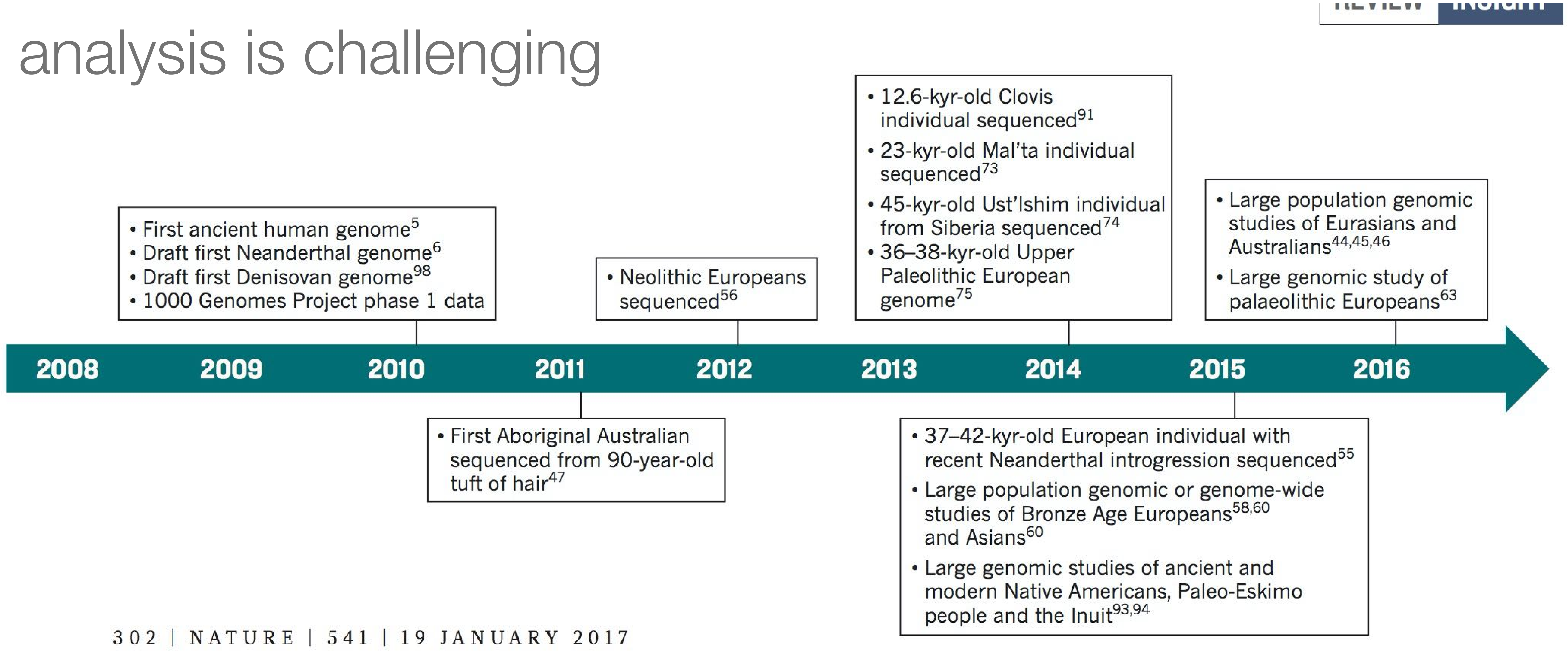


The genome era

- In the 21st century NGS genomic sequencing allowed to gather information on the whole genome diversity of modern humans

- Advances in aDNA - whole-genome data on samples up to 100 kYA

- Lots of new data, but analysis is challenging



- First ancient human genome[5]
- Draft first Neanderthal genome[6]
- Draft first Denisovan genome[98]
- 1000 Genomes Project phase 1 data

- First Aboriginal Australian sequenced from 90-year-old tuft of hair[47]

- Neolithic Europeans sequenced[56]

- 12.6-kyr-old Clovis individual sequenced[91]
- 23-kyr-old Mal'ta individual sequenced[73]
- 45-kyr-old Ust'Ishim individual from Siberia sequenced[74]
- 36–38-kyr-old Upper Paleolithic European genome[75]

- 37–42-kyr-old European individual with recent Neanderthal introgression sequenced[55]
- Large population genomic or genome-wide studies of Bronze Age Europeans[58,60] and Asians[60]
- Large genomic studies of ancient and modern Native Americans, Paleo-Eskimo people and the Inuit[93,94]

- Large population genomic studies of Eurasians and Australians[44,45,46]
- Large genomic study of palaeolithic Europeans[63]

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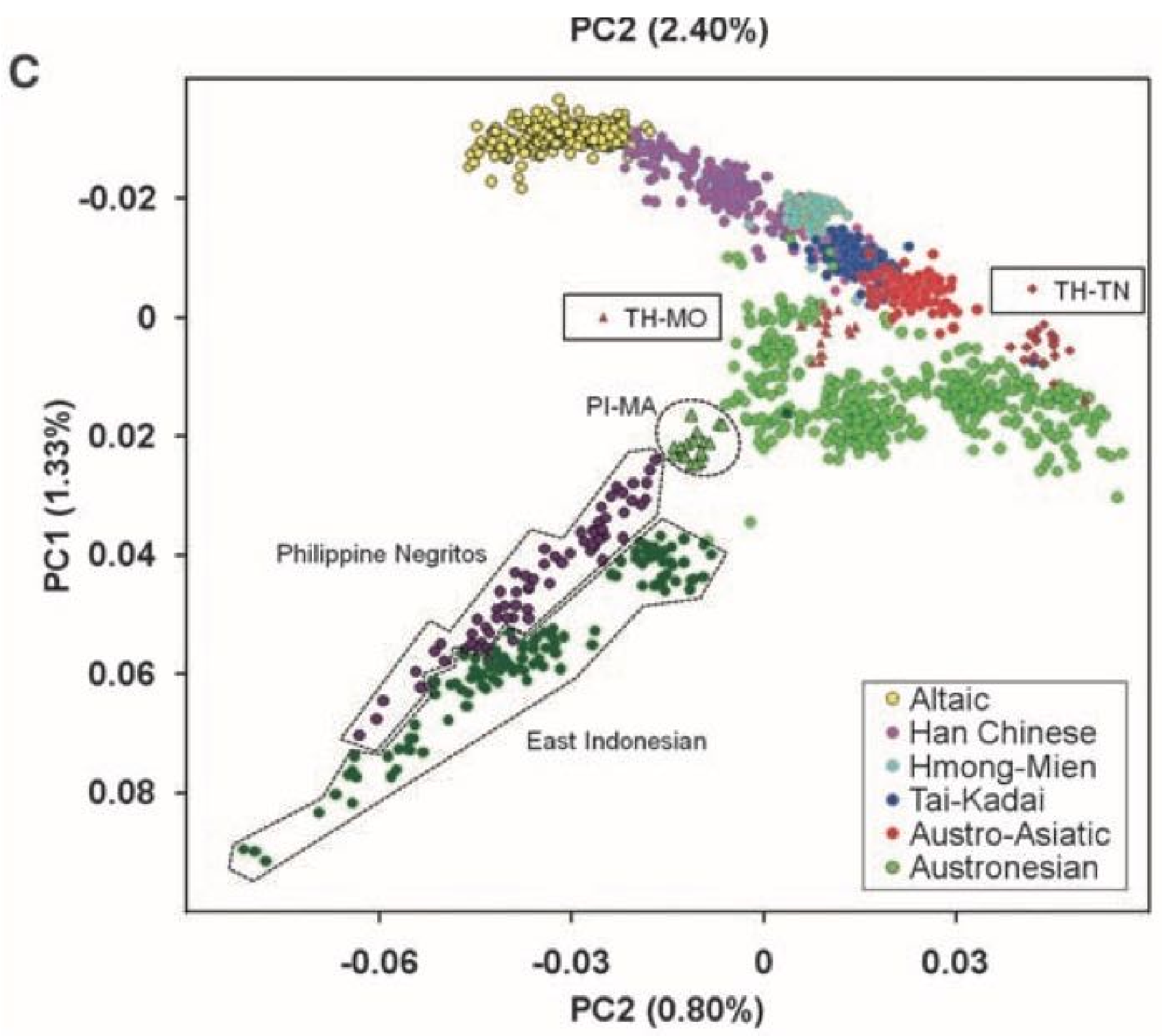
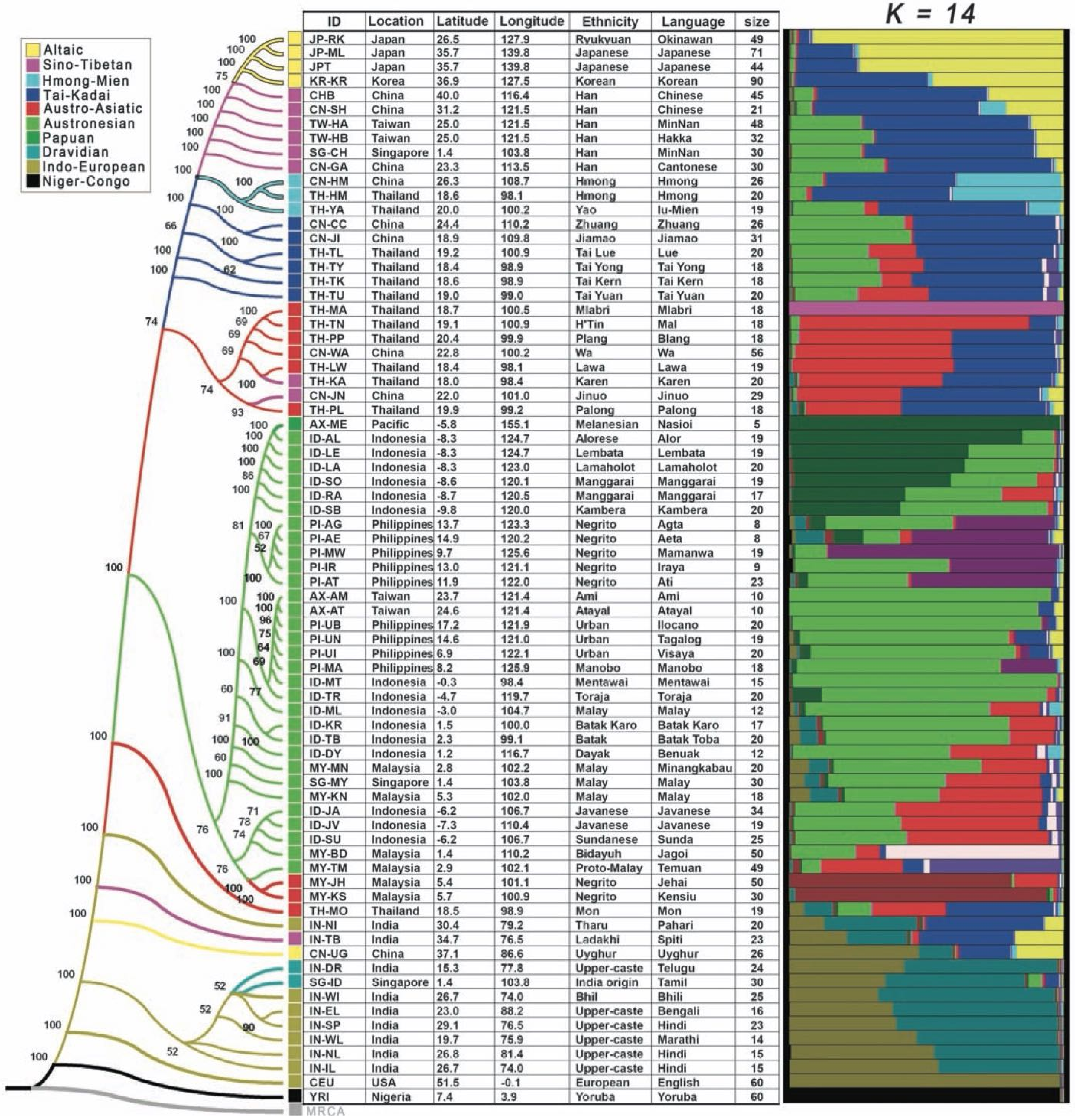
Analysis methods

- Admixture analysis: presents the contribution of *K* source populations to each individual in the sample (programs: ADMIXTURE, STRUCTURE)
- Clustering methods: PCA and MDS
- Data - whole genome sequencing or SNP arrays





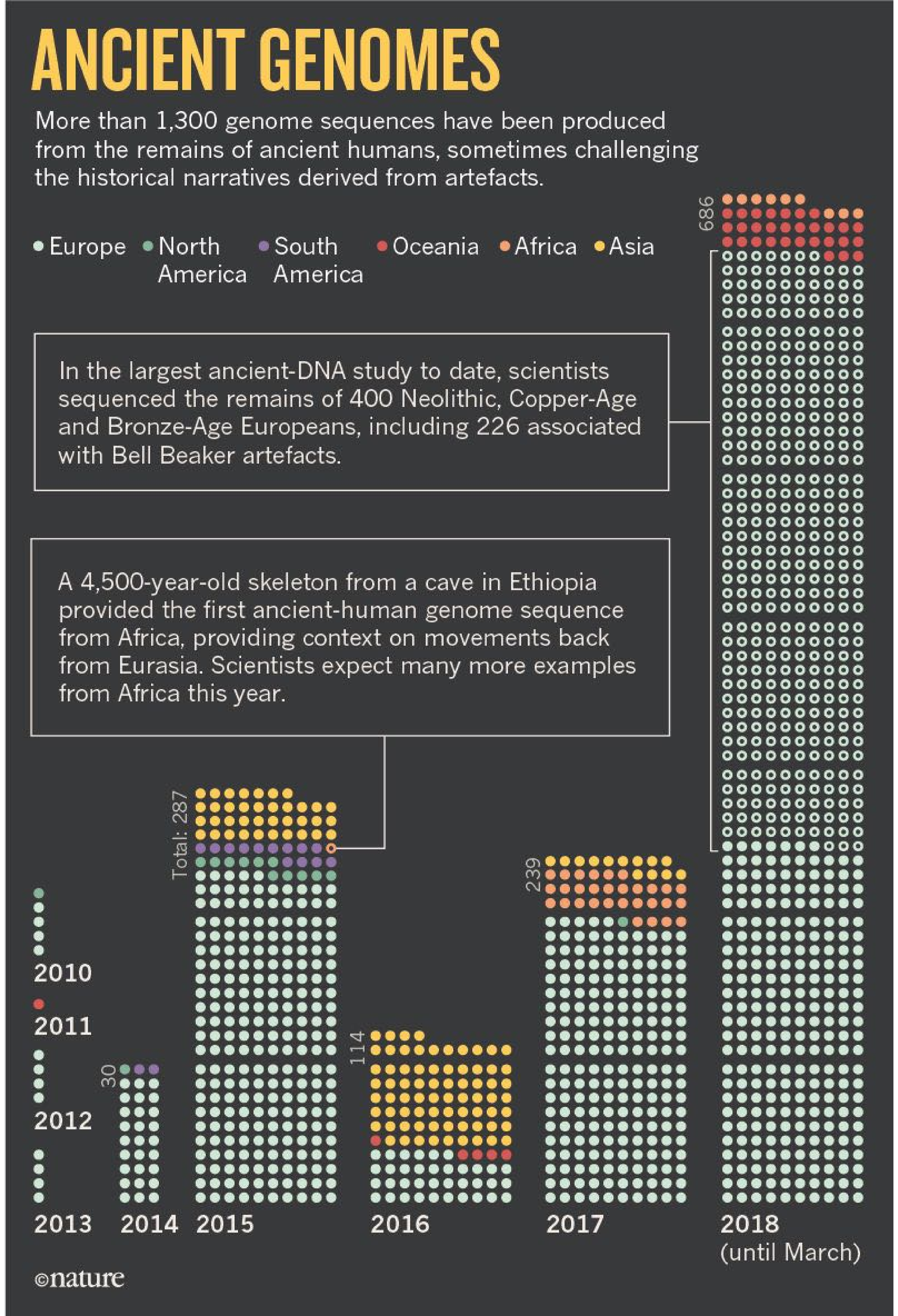
ID	Location	Latitude	Longitude	Ethnicity	Language	size
JP-RK	Japan	26.5	127.9	Ryukyuan	Okinawan	49
JP-ML	Japan	35.7	139.8	Japanese	Japanese	71
JPT	Japan	35.7	139.8	Japanese	Japanese	44
KR-KR	Korea	36.9	127.5	Korean	Korean	90
CHB	China	40.0	116.4	Han	Chinese	45
CN-SH	China	31.2	121.5	Han	Chinese	21
TW-HA	Taiwan	25.0	121.5	Han	MinNan	48
TW-HB	Taiwan	25.0	121.5	Han	Hakka	32
SG-CH	Singapore	1.4	103.8	Han	MinNan	30
CN-GA	China	23.3	113.5	Han	Cantonese	30
CN-HM	China	26.3	108.7	Hmong	Hmong	26
TH-HM	Thailand	18.6	98.1	Hmong	Hmong	20
TH-YA	Thailand	20.0	100.2	Yao	Iu-Mien	19
CN-CC	China	24.4	110.2	Zhuang	Zhuang	26
CN-JI	China	18.9	109.8	Jiamao	Jiamao	31
TH-TL	Thailand	19.2	100.9	Tai Lue	Lue	20
TH-TY	Thailand	18.4	98.9	Tai Yong	Tai Yong	18
TH-TK	Thailand	18.6	98.9	Tai Kern	Tai Kern	18
TH-TU	Thailand	19.0	99.0	Tai Yuan	Tai Yuan	20
TH-MA	Thailand	18.7	100.5	Mlabri	Mlabri	18
TH-TN	Thailand	19.1	100.9	H'Tin	Mal	18
TH-PP	Thailand	20.4	99.9	Plang	Blang	18
CN-WA	China	22.8	100.2	Wa	Wa	56
TH-LW	Thailand	18.4	98.1	Lawa	Lawa	19
TH-KA	Thailand	18.0	98.4	Karen	Karen	20
CN-JN	China	22.0	101.0	Jinuo	Jinuo	29
TH-PL	Thailand	19.9	99.2	Palong	Palong	18
AX-ME	Pacific	-5.8	155.1	Melanesian	Nasioi	5
ID-AL	Indonesia	-8.3	124.7	Alorese	Alor	19
ID-LE	Indonesia	-8.3	124.7	Lembata	Lembata	19
ID-LA	Indonesia	-8.3	123.0	Lamaholot	Lamaholot	20
ID-SO	Indonesia	-8.6	120.1	Manggarai	Manggarai	19
ID-RA	Indonesia	-8.7	120.5	Manggarai	Manggarai	17
ID-SB	Indonesia	-9.8	120.0	Kambera	Kambera	20
PI-AG	Philippines	13.7	123.3	Negrito	Agta	8
PI-AE	Philippines	14.9	120.2	Negrito	Aeta	8
PI-MW	Philippines	9.7	125.6	Negrito	Mamanwa	19
PI-IR	Philippines	13.0	121.1	Negrito	Iraya	9
PI-AT	Philippines	11.9	122.0	Negrito	Ati	23
AX-AM	Taiwan	23.7	121.4	Ami	Ami	10
AX-AT	Taiwan	24.6	121.4	Atayal	Atayal	10
PI-UB	Philippines	17.2	121.9	Urban	Ilocano	20
PI-UN	Philippines	14.6	121.0	Urban	Tagalog	19
PI-UI	Philippines	6.9	122.1	Urban	Visaya	20
PI-MA	Philippines	8.2	125.9	Manobo	Manobo	18
ID-MT	Indonesia	-0.3	98.4	Mentawai	Mentawai	15
ID-TR	Indonesia	-4.7	119.7	Toraja	Toraja	20
ID-ML	Indonesia	-3.0	104.7	Malay	Malay	12
ID-KR	Indonesia	1.5	100.0	Batak Karo	Batak Karo	17
ID-TB	Indonesia	2.3	99.1	Batak	Batak Toba	20
ID-DY	Indonesia	1.2	116.7	Dayak	Benuak	12
MY-MN	Malaysia	2.8	102.2	Malay	Minangkabau	20
SG-MY	Singapore	1.4	103.8	Malay	Malay	30
MY-KN	Malaysia	5.3	102.0	Malay	Malay	18
ID-JA	Indonesia	-6.2	106.7	Javanese	Javanese	34
ID-JV	Indonesia	-7.3	110.4	Javanese	Javanese	19
ID-SU	Indonesia	-6.2	106.7	Sundanese	Sunda	25
MY-BD	Malaysia	1.4	110.2	Bidayuh	Jagoi	50
MY-TM	Malaysia	2.9	102.1	Proto-Malay	Temuan	49
MY-JH	Malaysia	5.4	101.1	Negrito	Jehai	50
MY-KS	Malaysia	5.7	100.9	Negrito	Kensiu	30
TH-MO	Thailand	18.5	98.9	Mon	Mon	19
IN-NI	India	30.4	79.2	Tharu	Pahari	20
IN-TB	India	34.7	76.5	Ladakhi	Spiti	23
CN-UG	China	37.1	86.6	Uyghur	Uyghur	26
IN-DR	India	15.3	77.8	Upper-caste	Telugu	24
SG-ID	Singapore	1.4	103.8	India origin	Tamil	30
IN-WI	India	26.7	74.0	Bhil	Bhili	25
IN-EL	India	23.0	88.2	Upper-caste	Bengali	16
IN-SP	India	29.1	76.5	Upper-caste	Hindi	23
IN-WL	India	19.7	75.9	Upper-caste	Marathi	14
IN-NL	India	26.8	81.4	Upper-caste	Hindi	15
IN-IL	India	26.7	74.0	Upper-caste	Hindi	15
CEU	USA	51.5	-0.1	European	English	60
YRI	Nigeria	7.4	3.9	Yoruba	Yoruba	60

Mapping Human Genetic Diversity in Asia
The HUGO Pan-Asian SNP Consortium

SCIENCE VOL 326 11 DECEMBER 2009

Ancient genomes

- First complete ancient human genome: 2010
- Currently - hundreds of sequences from humans and other hominins



ANCIENT GENOMES

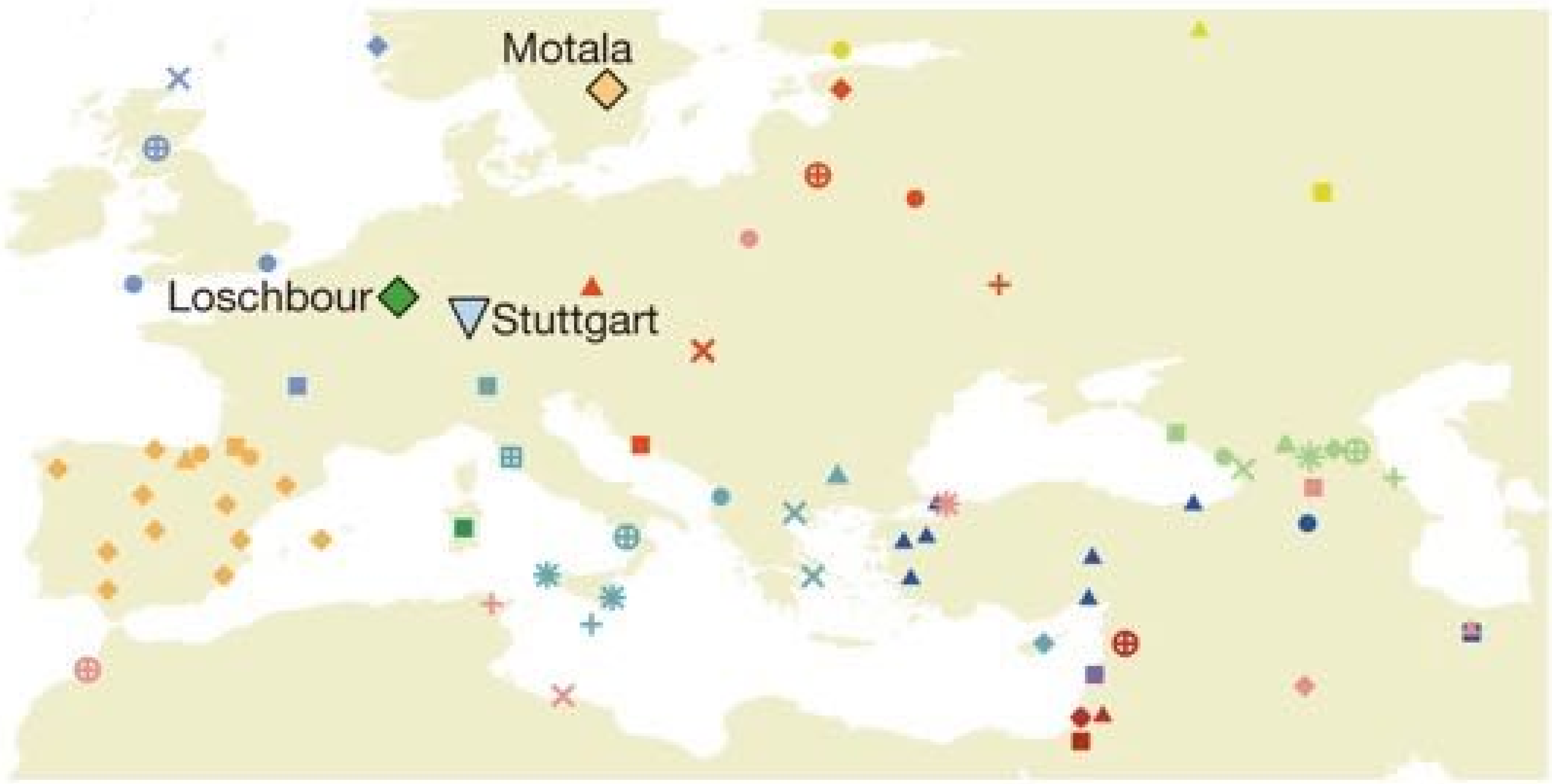
More than 1,300 genome sequences have been produced from the remains of ancient humans, sometimes challenging the historical narratives derived from artefacts.

In the largest ancient-DNA study to date, scientists sequenced the remains of 400 Neolithic, Copper-Age and Bronze-Age Europeans, including 226 associated with Bell Beaker artefacts.

A 4,500-year-old skeleton from a cave in Ethiopia provided the first ancient-human genome sequence from Africa, providing context on movements back from Eurasia. Scientists expect many more examples from Africa this year.

The european mosaic

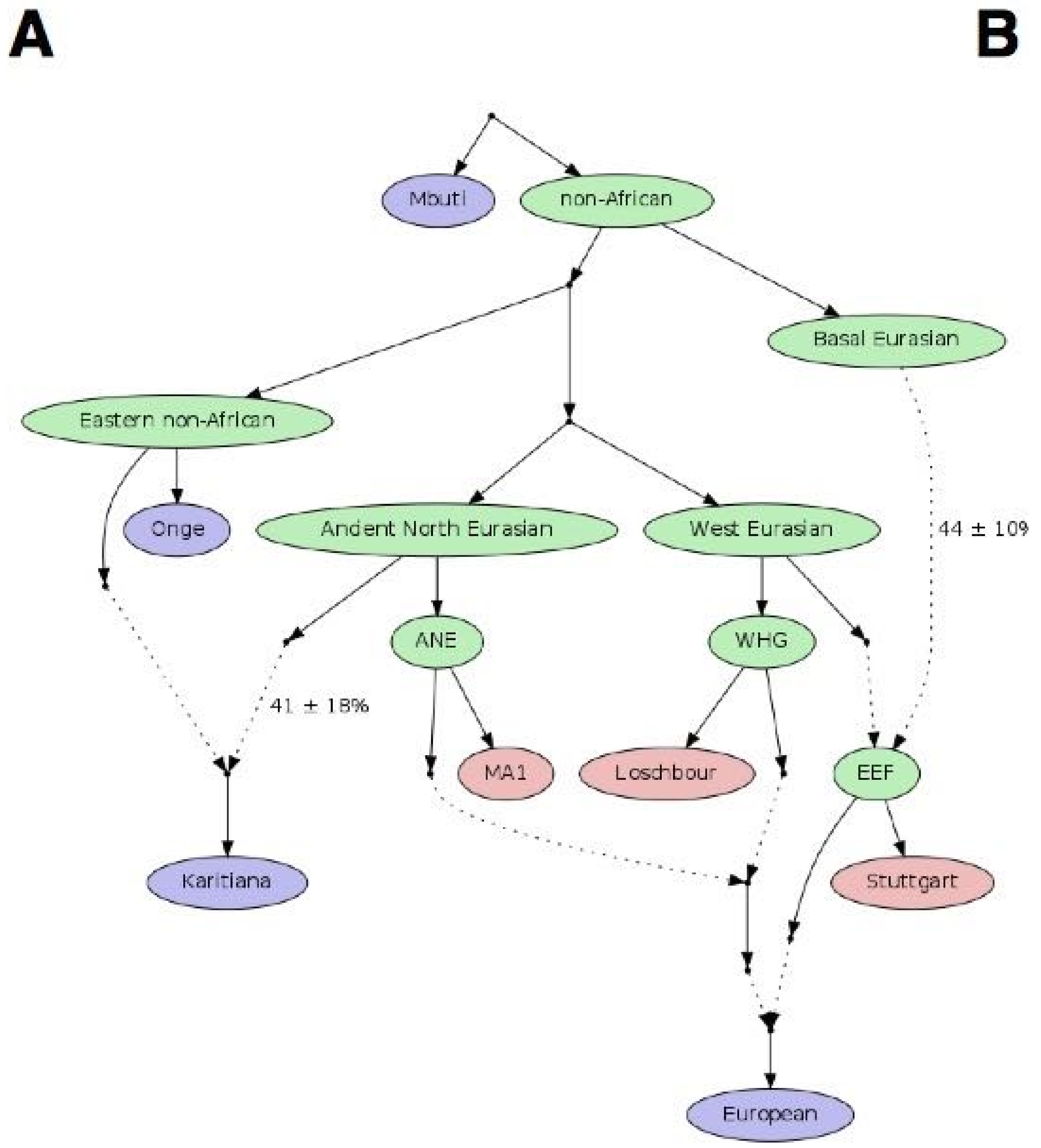
Map of west Eurasian populations.



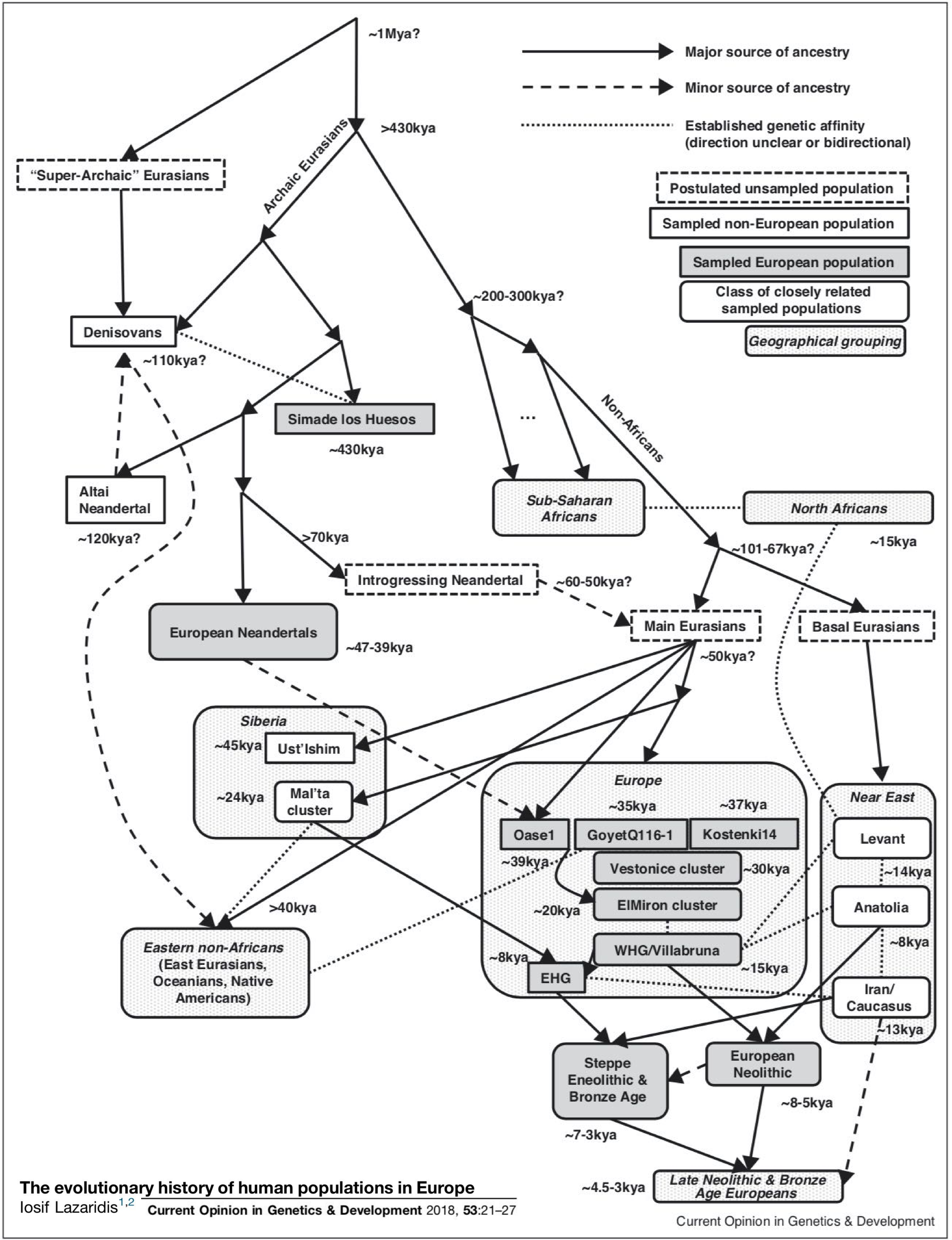
I Lazaridis *et al.* *Nature* **513**, 409-413 (2014) doi:10.1038/nature13673

The european mosaic

- 2015: at least three source populations for modern European genomes
  - **WHG - western hunter-gatherers**
    - the first to arrive from Africa, dark skinned, Cro-Magnon man
  - **EEF - early eastern farmers**, neolithic farmer migration from the fertile crescent through Anatolia
    - fair skin
  - **ANE - ancient north eurasia** (central Siberia), also contributed to genomes in modern Siberia and Native Americans, Mal'ta–Buret' culture


A
B
Mbuti
non-African
Basal Eurasian
Eastern non-African
Onge
Ancient North Eurasian
West Eurasian
44 ± 10%
ANE
WHG
41 ± 18%
MA1
Loschbour
EEF
Karitiana
Stuttgart
European

European prehistory, current view

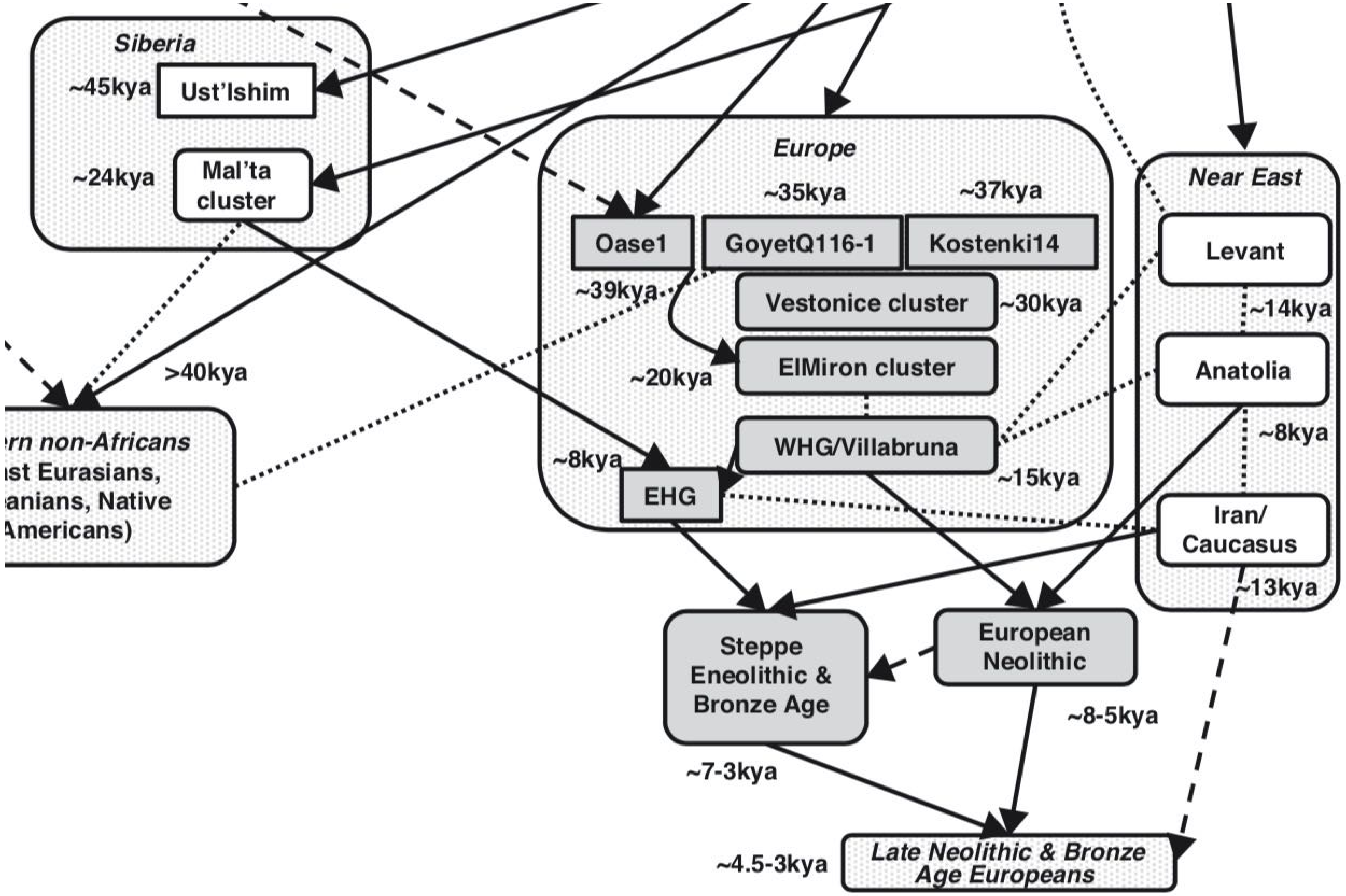


The evolutionary history of human populations in Europe
Iosif Lazaridis[1,2] **Current Opinion in Genetics & Development** 2018, **53**:21–27

Current Opinion in Genetics & Development

European prehistory, current view

- In Europe: palaeolithic WHG + EEF from Anatolia gave European neolithic population
- In the steppes and Caucasus eurasian hunter-gatherers mixed with ANE to give EHG (eastern hunter-gatherers)
- EHG people mixed with EEF from the Caucasus and Iran to give the steppe population (Yamnaya)
- The steppe people invaded Europe mixing (or displacing) neolithic Europeans



Current Opinion in Genetics & Development

Ötzi - a neolithic european

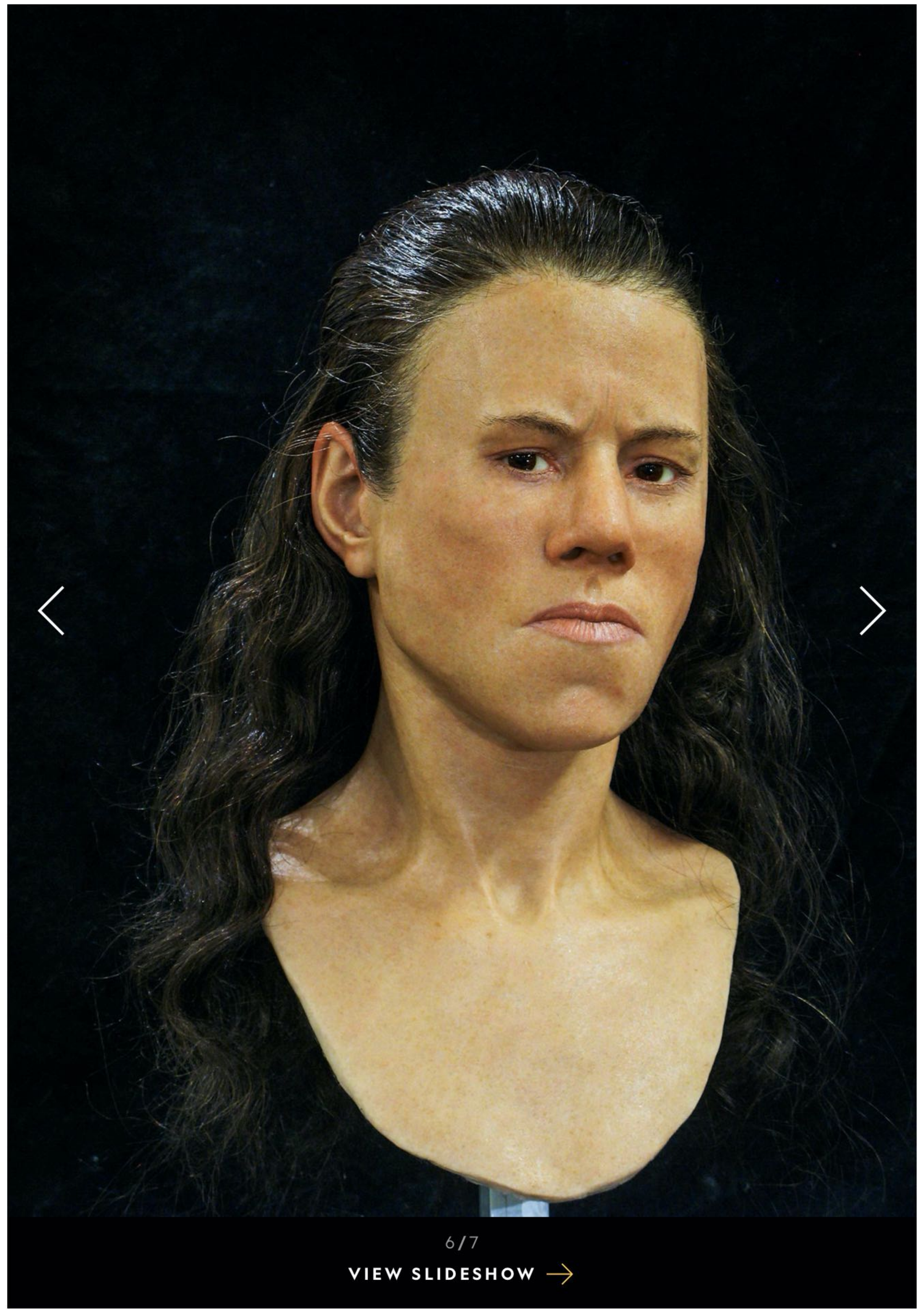
- Body found in the glacier in Austria (South Tirol)
- ~5.3 kYA
- Had WHG and EEF ancestry, but no ANE (which came with the steppe migration)

A hunter-gatherer woman, Sweden, ~7 kYA

Researchers used skeletal remains and ancient DNA to reconstruct the burial of a woman who lived in what is now southern Sweden 7,000 years ago.

PHOTOGRAPH BY GERT GERMERAAD, TRELLEBORGS MUSEUM

A neolithic farmer, Greece ~ 9 kYA



Facial features have "smoothed out" over millennia, and humans look less masculine today, says reconstructor Oscar Nilsson, who recreated this face of a teenager who lived in Greece 9,000 years ago.

PHOTOGRAPH BY OSCAR NILSSON

The bell beaker invasion

- Bell beaker culture spread westwards betwee 2750 and 2500 BCE (4.7-4.5 kYA)
- Analysis of 400 human aDNA samples, including 226 from the bell beaker culture (02.2018)

ARTICLE

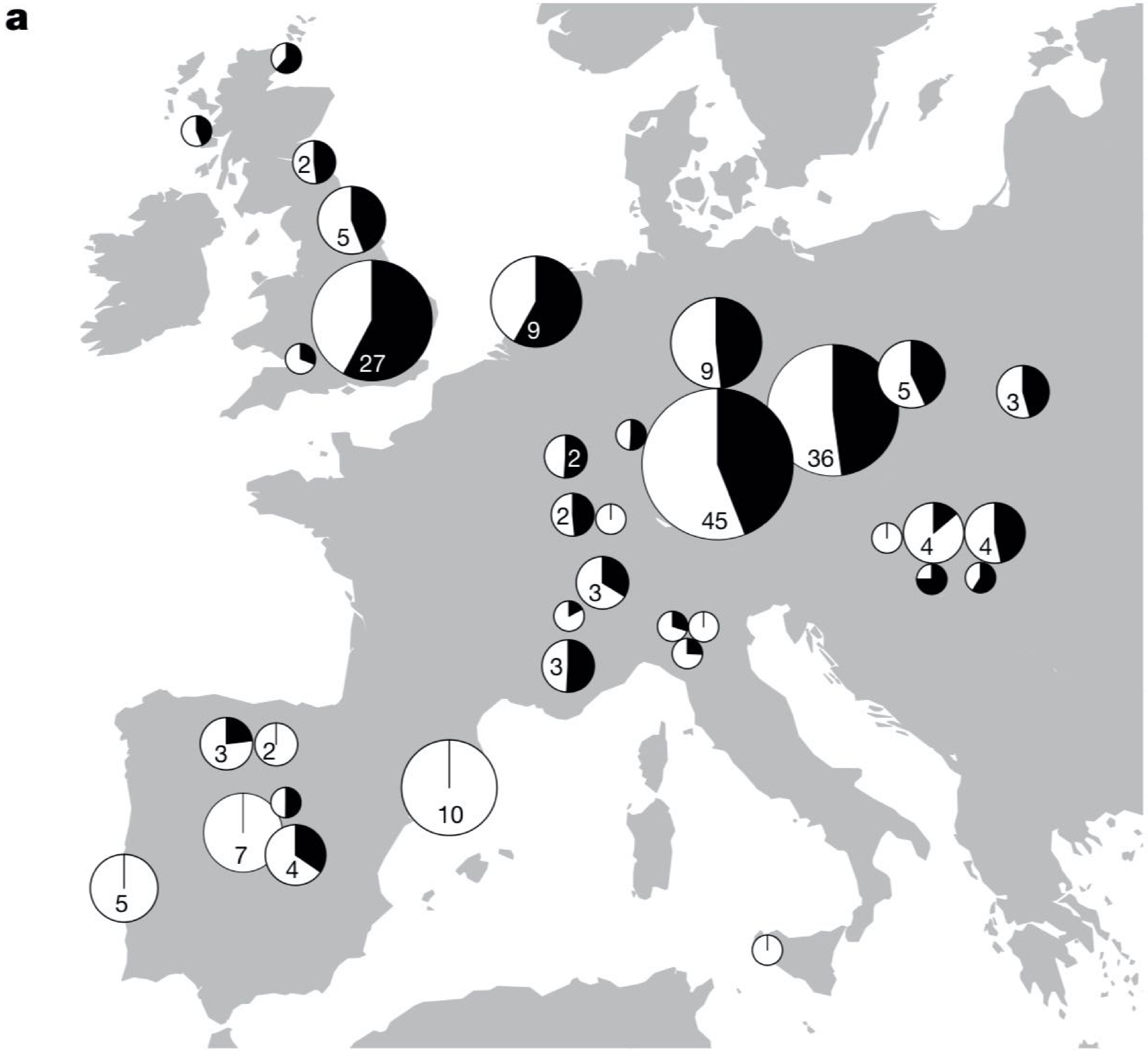
doi:10.1038/nature25738

The Beaker phenomenon and the genomic transformation of northwest Europe

Ashmolean Museum/Univ. Oxford/Bridgeman

The bell beaker story

- In central and eastern Europe the bell beaker people mixed with the previous populations, replacing some of their genes
- In southern Europe the genetic composition of the inhabitants remained unchanged - culture spread without demographic replacement




ARTICLE

doi:10.1038/nature25738

The Beaker phenomenon and the genomic transformation of northwest Europe

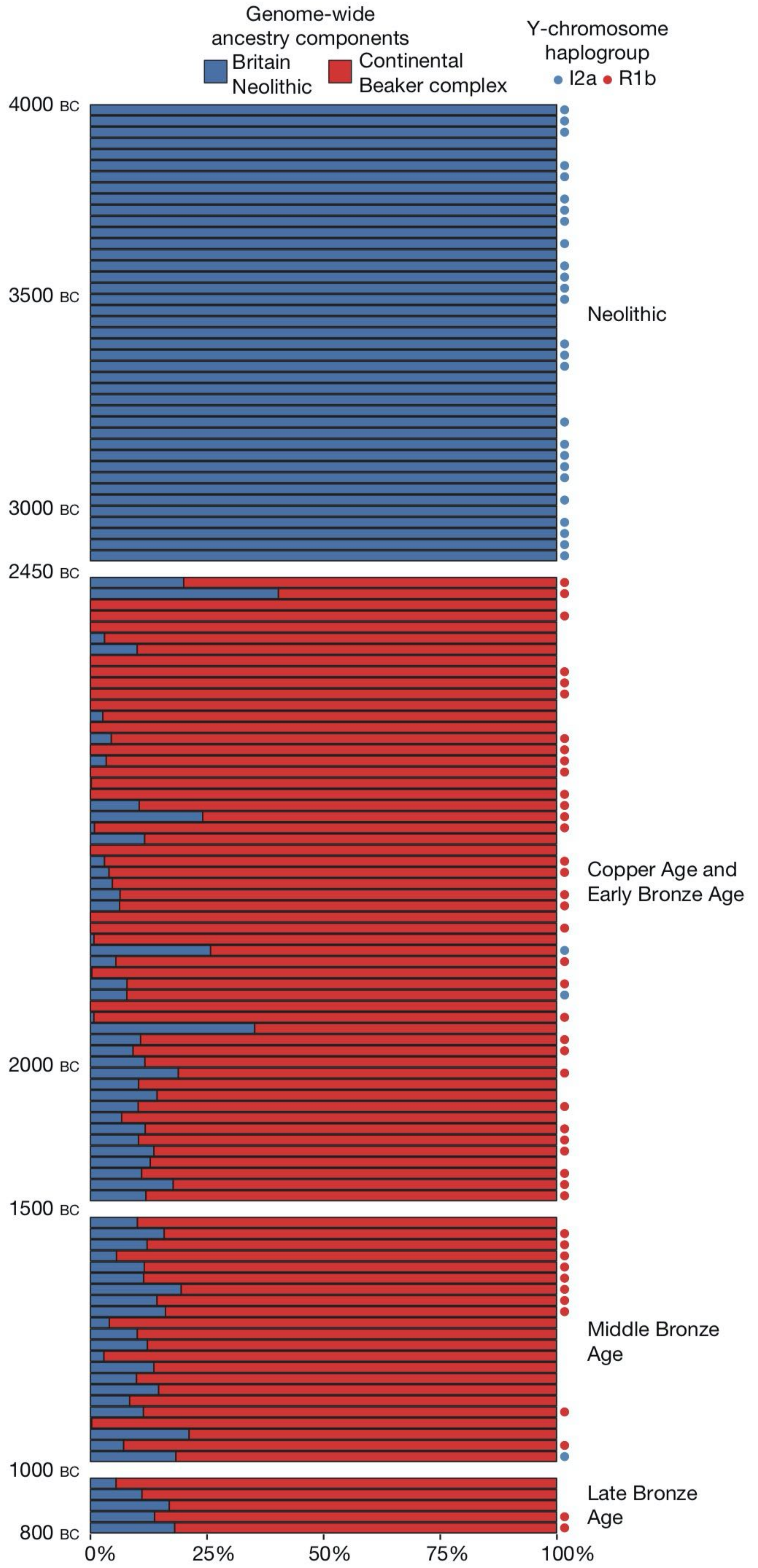
The bell beaker invasion in British Isles

- In the British Isles the bell beaker people completely replaced the earlier neolithic inhabitants with genomes similar to the continental peoples

ARTICLE

doi:10.1038/nature25738

The Beaker phenomenon and the genomic transformation of northwest Europe



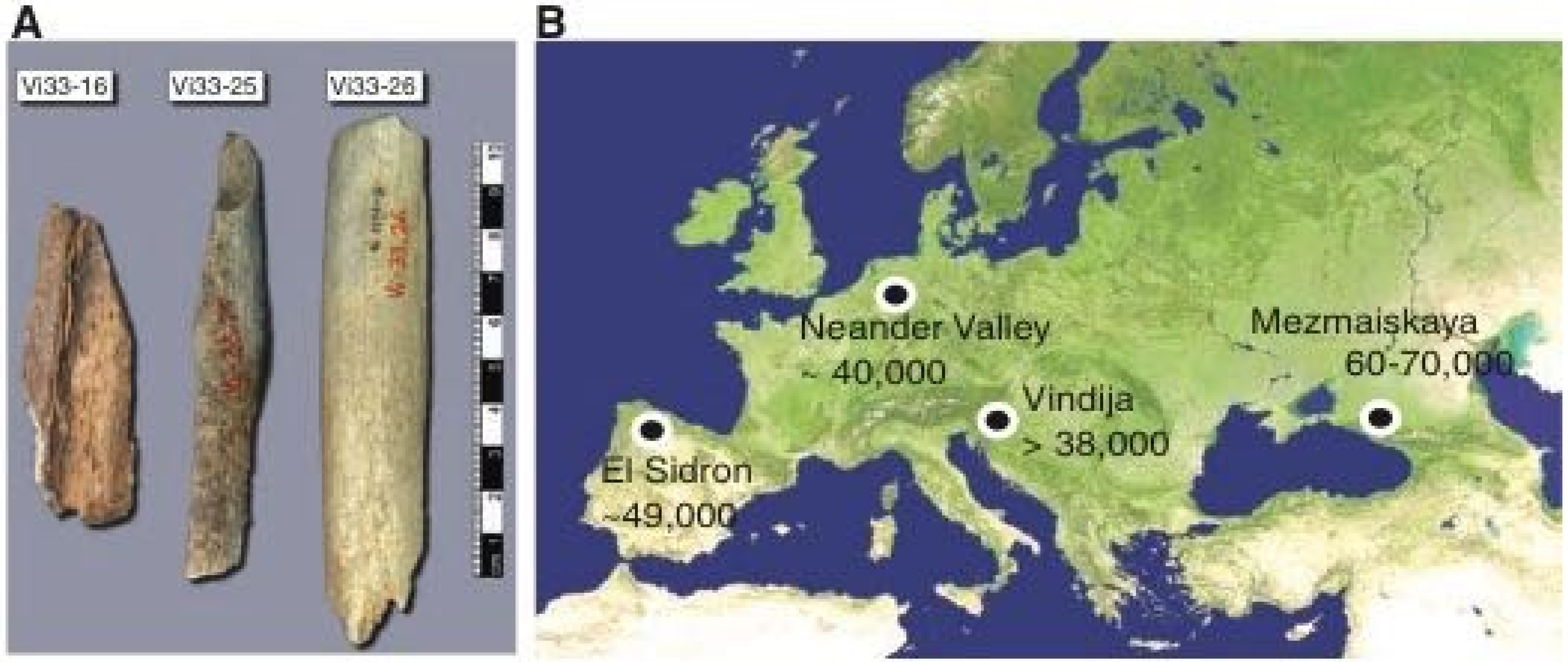
A beaker culture man, England, ~4.4 kYA

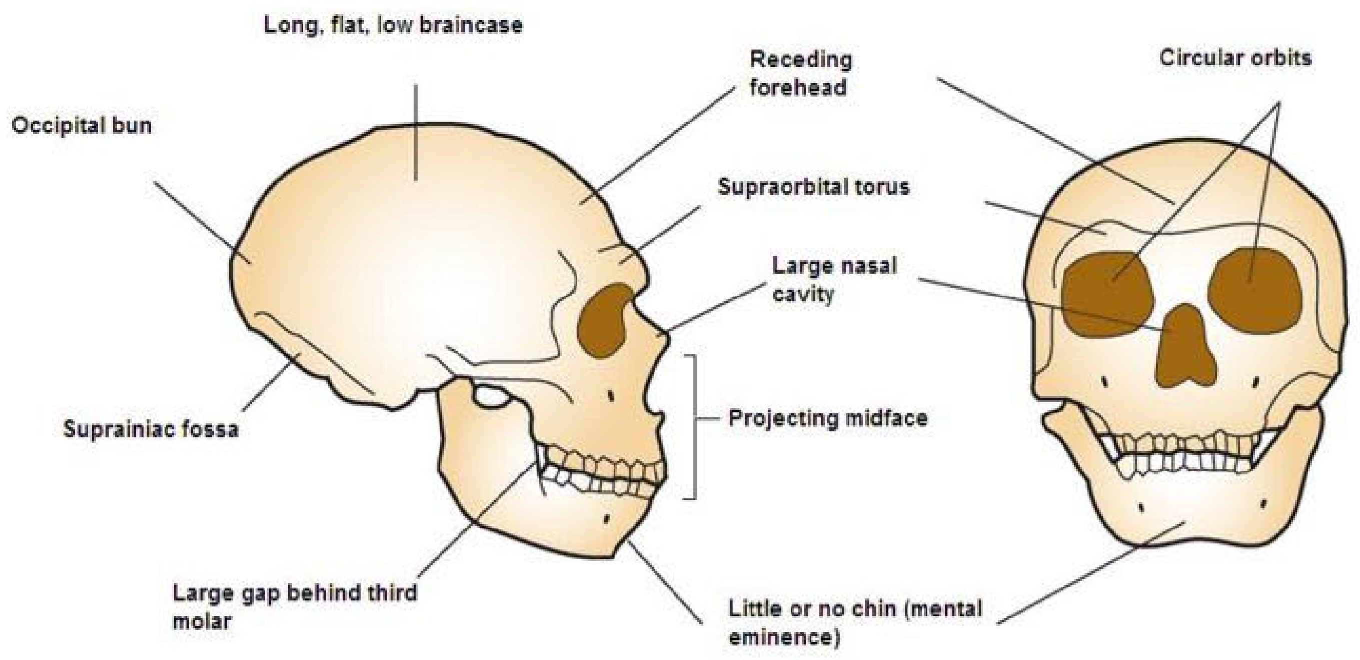
Ditchling Road Man, named for the road-widening project that revealed his remains in 1921, was part of the first wave of farmers from continental Europe that arrived in Britain with their distinctive Beaker pottery around 2,400 B.C. His remains show that he suffered several periods of malnutrition while growing up, which may have slightly stunted his growth. Ditchling Road Man died between the ages of 25 and 35 and was buried with a Beaker vessel by his feet and a small number of snail shells next to his mouth.

COURTESY ROYAL PAVILION & MUSEUMS, BRIGHTON & HOVE

The neanderthals

- Earliest neanderthal fossils found in Asia, ~ 400 kYA
- Lived in Europe until ~30 kYA
- First humans came to Europe 50-45 kYA
- Neanderthals and humans lived in Europe together. Did they mix?
- mtDNA did not indicate any admixture





A reconstruction of a Neanderthal is standing a the Neandertal Museum. The Neandertal Museum, which is located between Mettmann and Dusseldorf, North Rhine-Westphalia, contains the pre- and early history of human beings and of the Neanderthals, who were named after the place of discovery of the fossil Neandertal 1. Picture from 23 August 2013.

A neanderthal woman, England, ~40 kYA

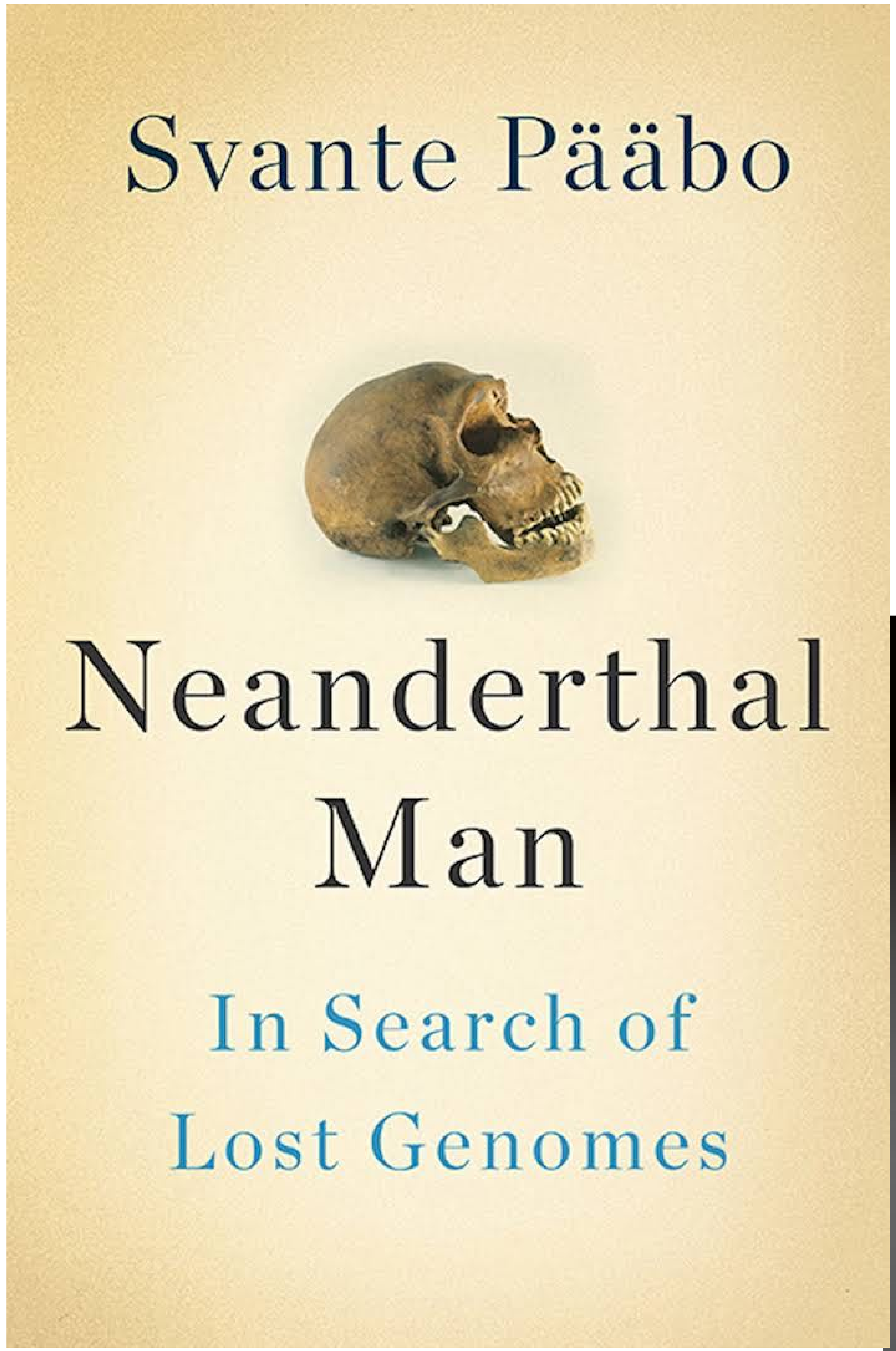
- Note the fair skin and reddish hair
- All *H. sapiens* at that time had black skin and hair
- Skin and hair color can be deduced from genomic sequence (analysis of ~12-20 loci)

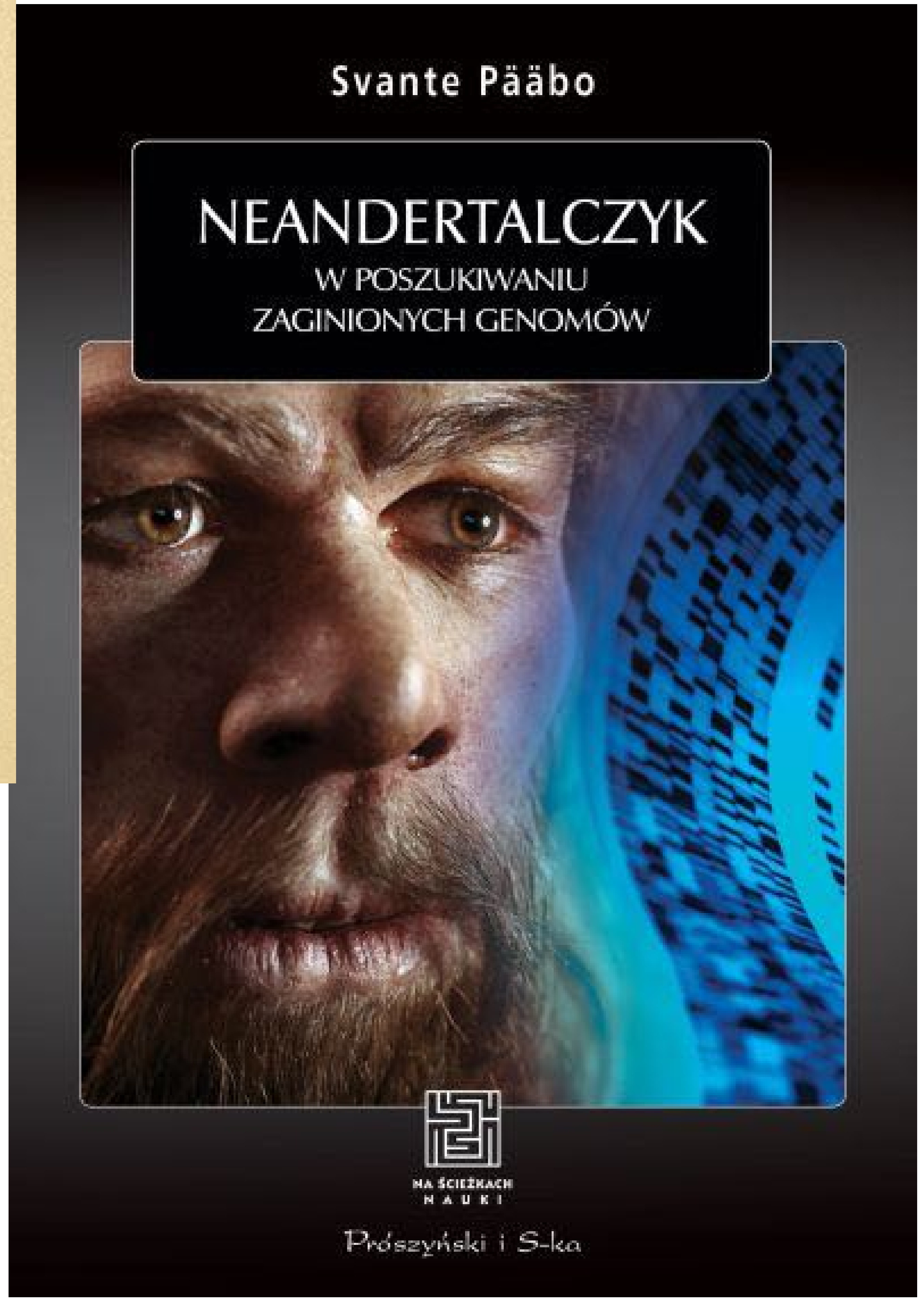
Artifacts from southern England show that both Neanderthals, such as this woman, and modern humans were residents of what is now southern England some 40,000 years ago.

COURTESY ROYAL PAVILION & MUSEUMS, BRIGHTON & HOVE

The neanderthal genome

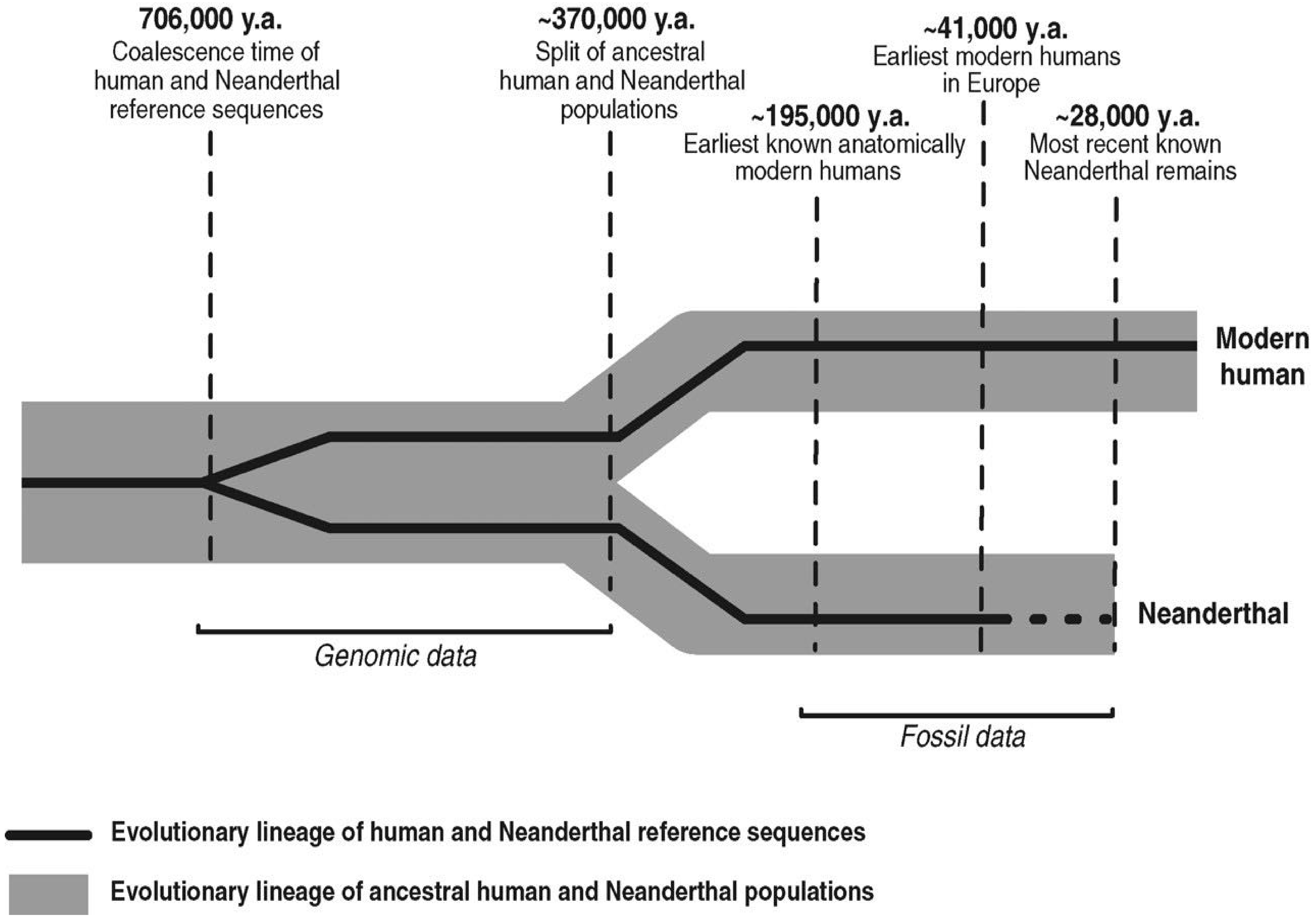
- ~ 10^6 bp of nuclear DNA (2006)
- 60% of genome (2010)
- Currently up to 99% of genome with 50x coverage from multiple individuals (starting material ~40 mg of bone!)





Restults of the nDNA analysis

- The lineages were completely separated long before human out of Africa migration
- Traces of mixing between neanderthals and *Homo sapiens*



Human-neanderthal crosses

- Traces of neanderthal alleles in all populations, except Africa
- ~ 2-4% of Eurasian genomes
  - not the same 4% in different individuals, ~40% of introgressing population genome reconstructed
- Eurasians mixed with neanderthals after leaving Africa
- The admixed DNA amount decreased from the palaeolithic - negative selection
- Some regions in human genome devoid of neanderthal DNA - incompatibility (eg. on chromosome X) - nascent genetic barrier

Can different species interbreed

- Yes (the definition is not complete)
- Example brown and polar bears (distance similar to human-neanderthal

A hybrid of brown and polar bear
Rothschild Museum, Tring
© wikipedia

Neanderthals and us

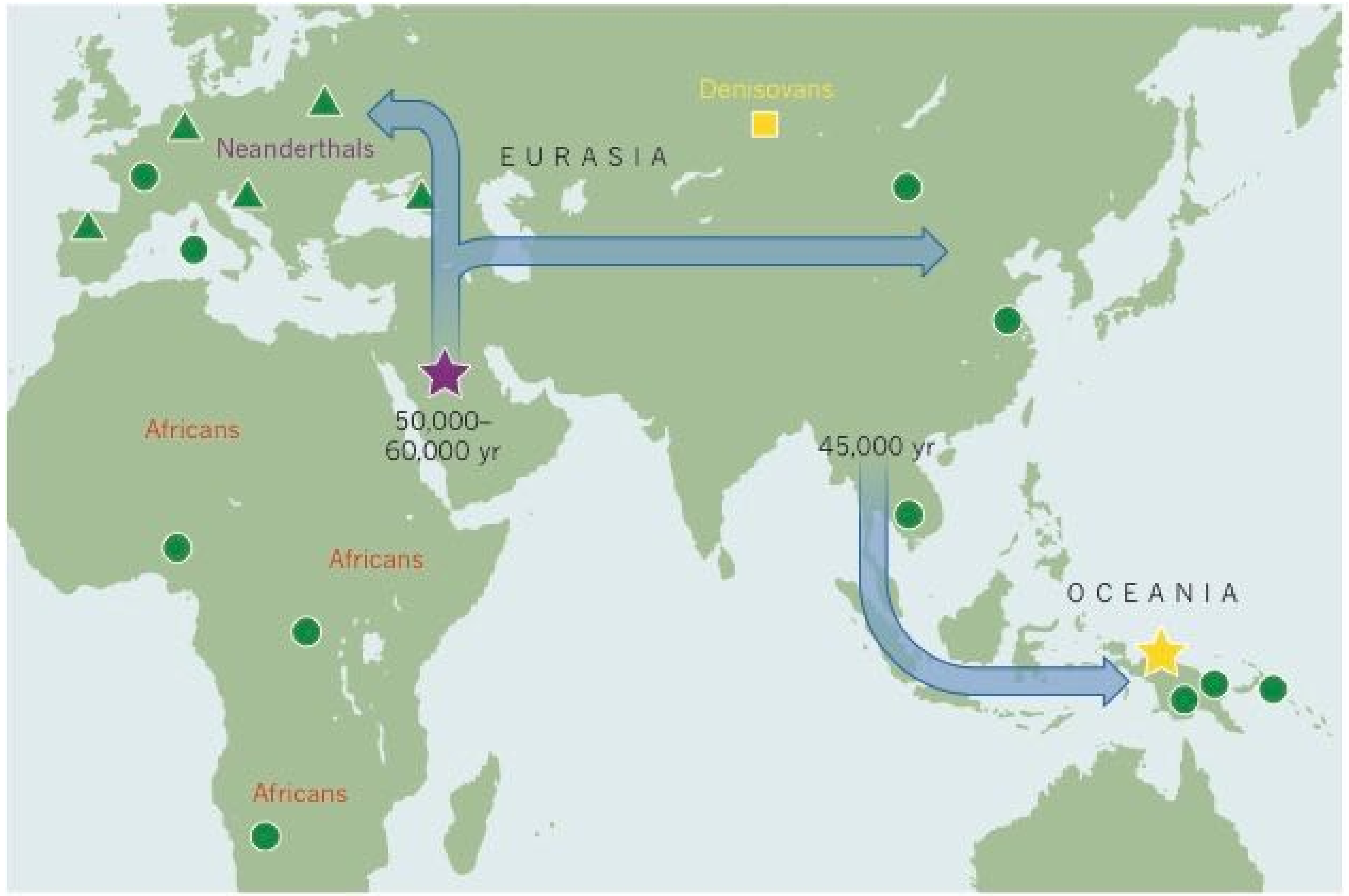
- Humans and neanderthals continued interbreeding in Europe ~ 40 kYA - the second wave of admixture
- In modern populations we see traces of the first admixture wave, but not the second
- Neanderthal genomes also show traces of human admixture

DNA taken from a 40,000-year-old modern human jawbone from the cave Pestera cu Oase in Romania reveals that this man had a Neandertal ancestor as recently as four to six generations back.

IMAGE, SVANTE PAABO, MAX PLANCK INSTITUTE FOR EVOLUTIONARY ANTHROPOLOGY

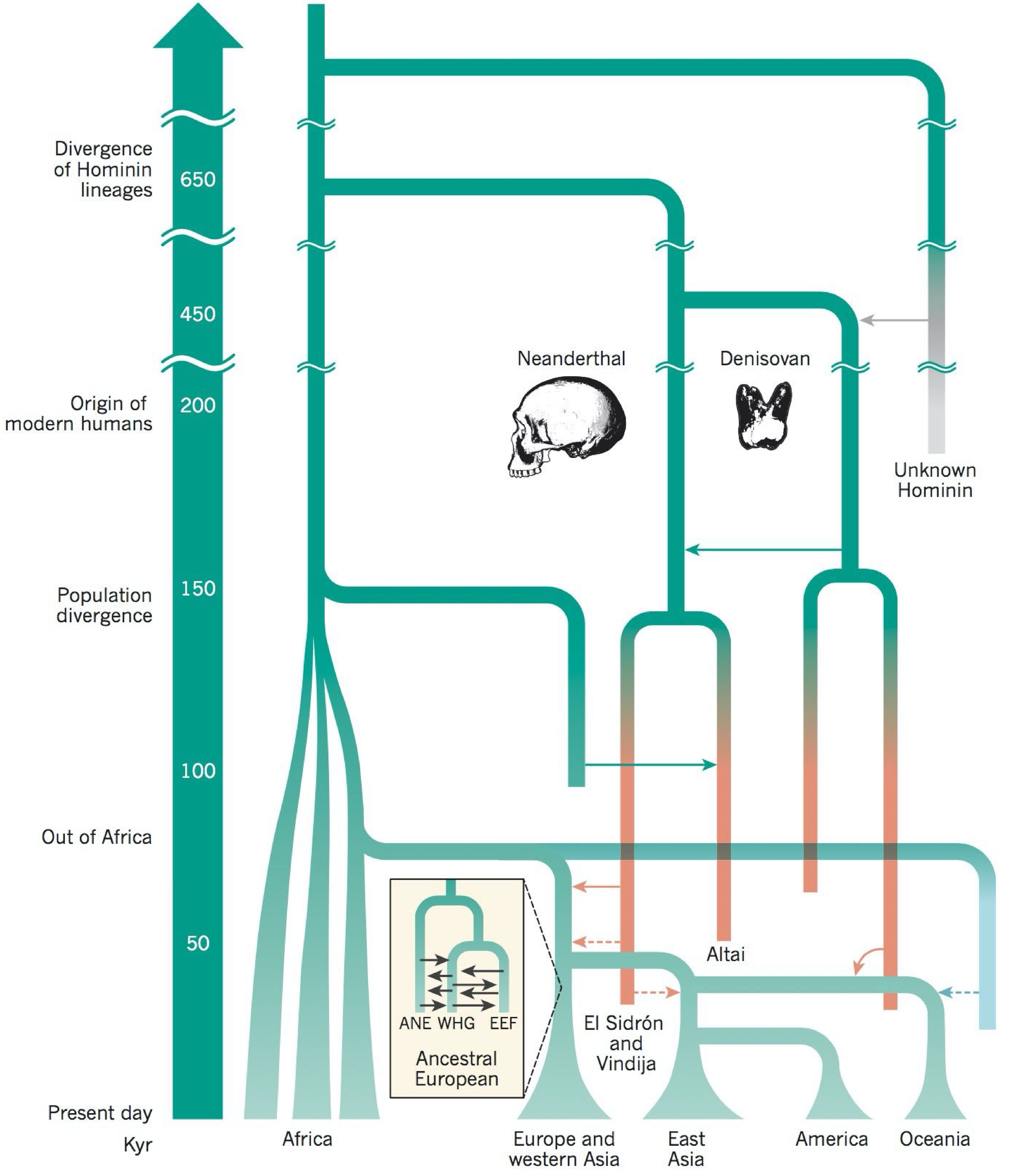
Not only neanderthals

- Bones from the Denisova Cave (Altai mountains)
- Contemporary with neanderthals, probably a sister species
- Traces of intermixing with humans in south-east Asia and Oceania



What happened in the Denisova Cave

- A complete Denisovan genome (2013) suggests gene flow between *H. sapiens, H. neanderthalensis* and probably a third, unidentified hominid



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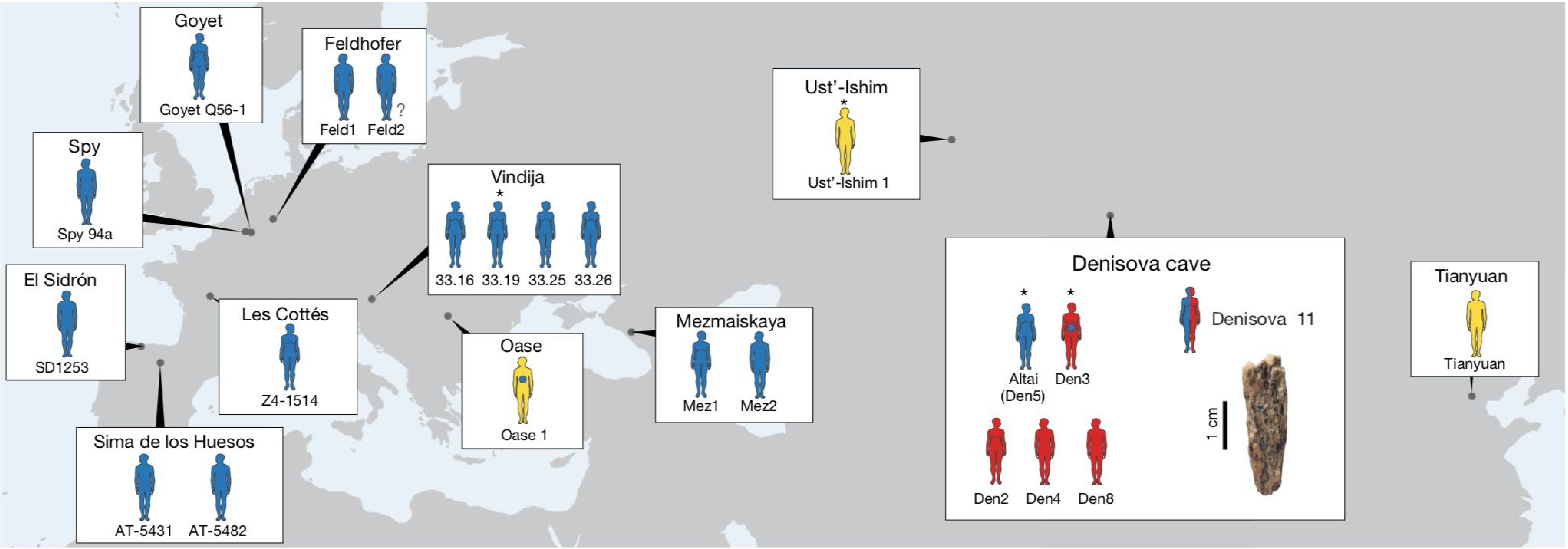
Eurasia, 40 000 kYA



🟦 Neandertalczycy

🟥 Denisowianie

🟨 *H. sapiens*

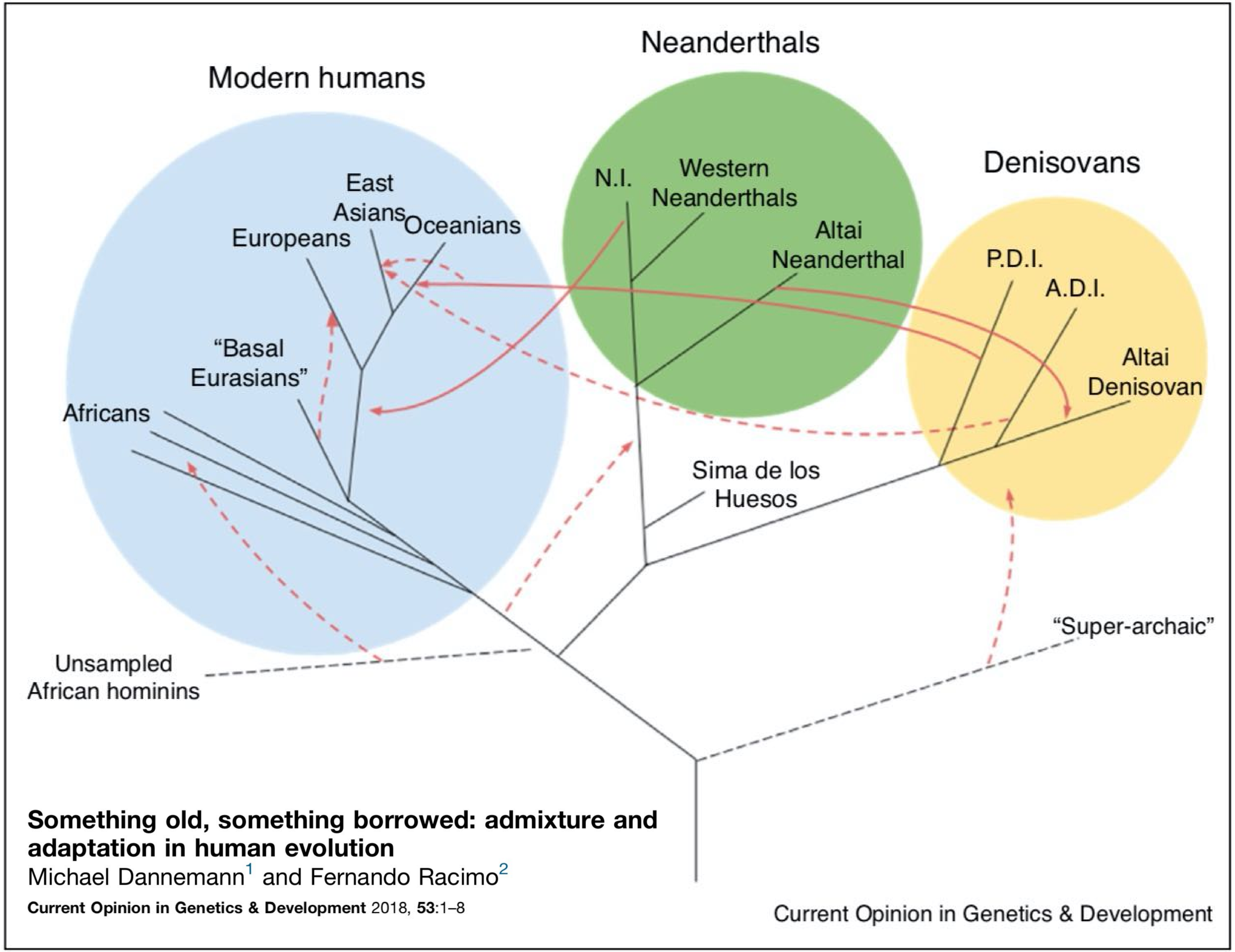
The genome of the offspring of a Neanderthal mother and a Denisovan father

Viviane Slon[1,7]*, Fabrizio Mafessoni[1,7], Benjamin Vernot[1,7], Cesare de Filippo[1], Steffi Grote[1], Bence Viola[2,3], Mateja Hajdinjak[1], Stéphane Peyrégne[1], Sarah Nagel[1], Samantha Brown[4], Katerina Douka[4,5], Tom Higham[5], Maxim B. Kozlikin[3], Michael V. Shunkov[3,6], Anatoly P. Derevianko[3], Janet Kelso[1], Matthias Meyer[1], Kay Prüfer[1] & Svante Pääbo[1]*

6 SEPTEMBER 2018 | VOL 561 | NATURE | 113

The admixture

- N.I.: Introgressing Neanderthal population
- P.D.I.: Papuan-Introgressing Denisovan population
- A.D.I.: Asian- Introgressing Denisovan population



Something old, something borrowed: admixture and adaptation in human evolution
Michael Dannemann[1] and Fernando Racimo[2]
Current Opinion in Genetics & Development 2018, **53**:1–8

The adaptations from admixture

- Adaptation to altitude in Tibetans - allele of the *EPAS1* gene (in the hypoxia response pathway)
- This *EPAS1* haplotype is frequent in Tibetans, but absent in their close relatives - Han Chinese
- This haplotype is found in the Denisovan genome

Altitude adaptation in Tibetans caused by introgression of Denisovan-like DNA

Emilia Huerta-Sánchez[1,2,3]*, Xin Jin[1,4]*, Asan[1,5,6]*, Zhuoma Bianba[7]*, Benjamin M. Peter[2], Nicolas Vinckenbosch[2], Yu Liang[1,5,6], Xin Yi[1,5,6], Mingze He[1,8], Mehmet Somel[9], Peixiang Ni[1], Bo Wang[1], Xiaohua Ou[1], Huasang[1], Jiangbai Luosang[1], Zha Xi Ping Cuo[10], Kui Li[11], Guoyi Gao[12], Ye Yin[1], Wei Wang[1], Xiuqing Zhang[1,13,14], Xun Xu[1], Huanming Yang[1,15,16], Yingrui Li[1], Jian Wang[1,16], Jun Wang[1,15,17,18,19] & Rasmus Nielsen[1,2,20,21]

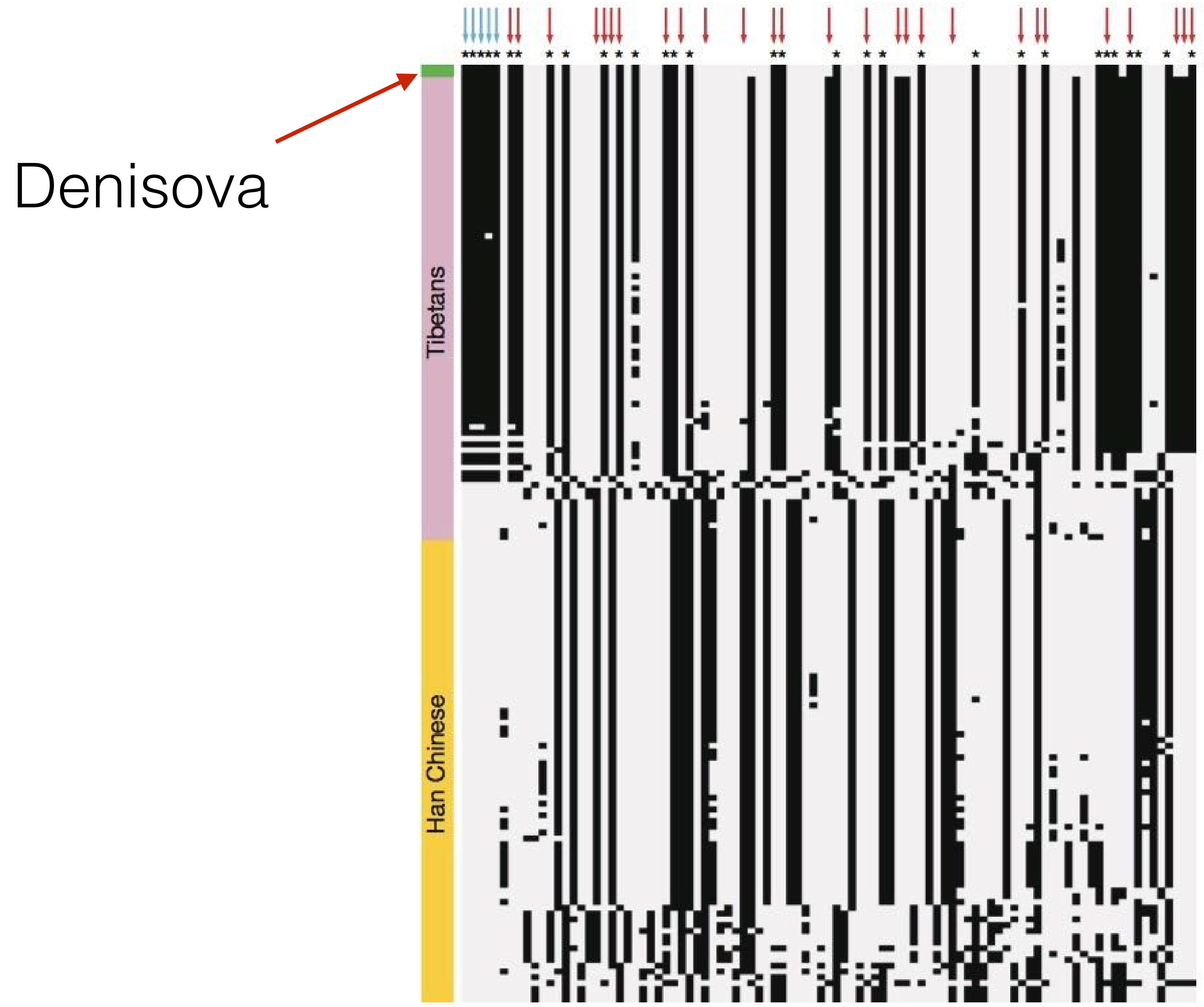


Figure 2 | Haplotype pattern in a region defined by SNPs that are at high frequency in Tibetans and at low frequency in Han Chinese. Each column is a polymorphic genomic location (95 in total), each row is a phased haplotype (80 Han and 80 Tibetan haplotypes), and the coloured column on the left denotes the population identity of the individuals. Haplotypes of the Denisovan individual are shown in the top two rows (green). The black cells represent the presence of the derived allele and the grey space represents the presence of the ancestral allele (see Methods). The first and last columns correspond to the

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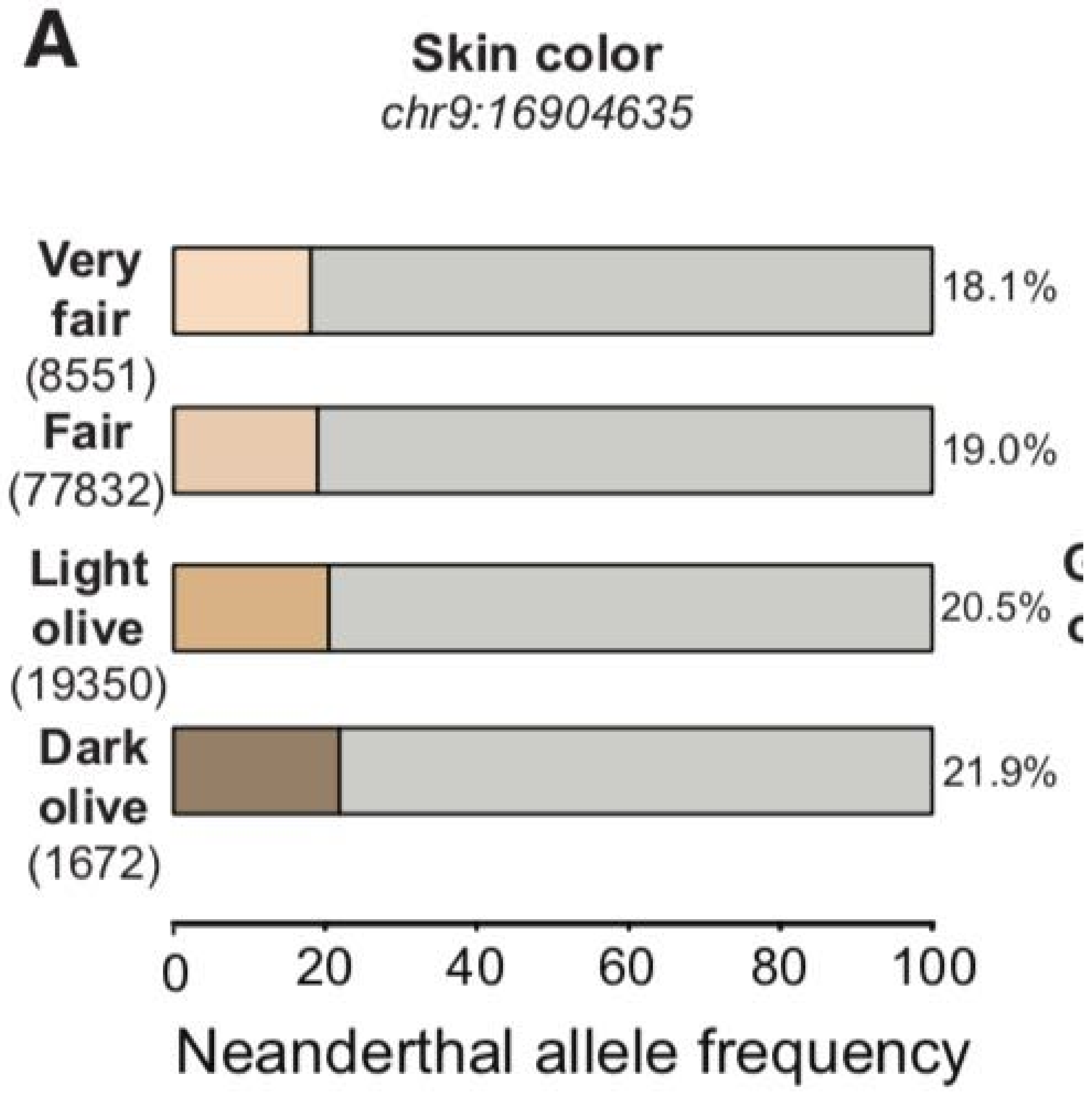
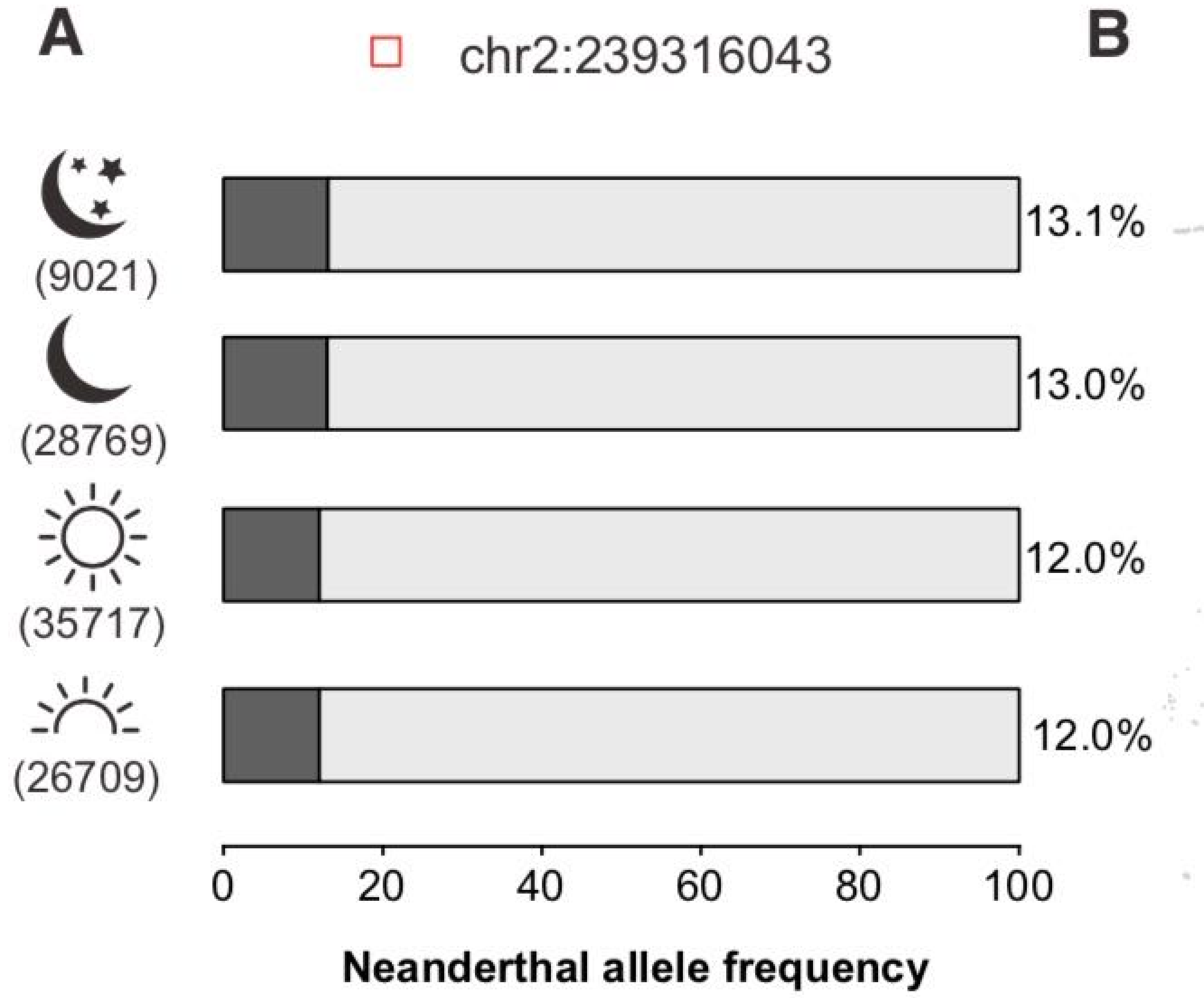
What did neanderthals leave us?

- The neanderthal population was diverse with regard to skin color, eye and hair color, etc.
- Some (but not all) of these alleles may contribute to human variation
- Immune system alleles - adaptation to non-African pathogens, but also autoimmune disease
- Chronotype variation, circadian rhythms, mood. Could be linked to depression
- Neanderthals were longer adapting to lower sun exposure





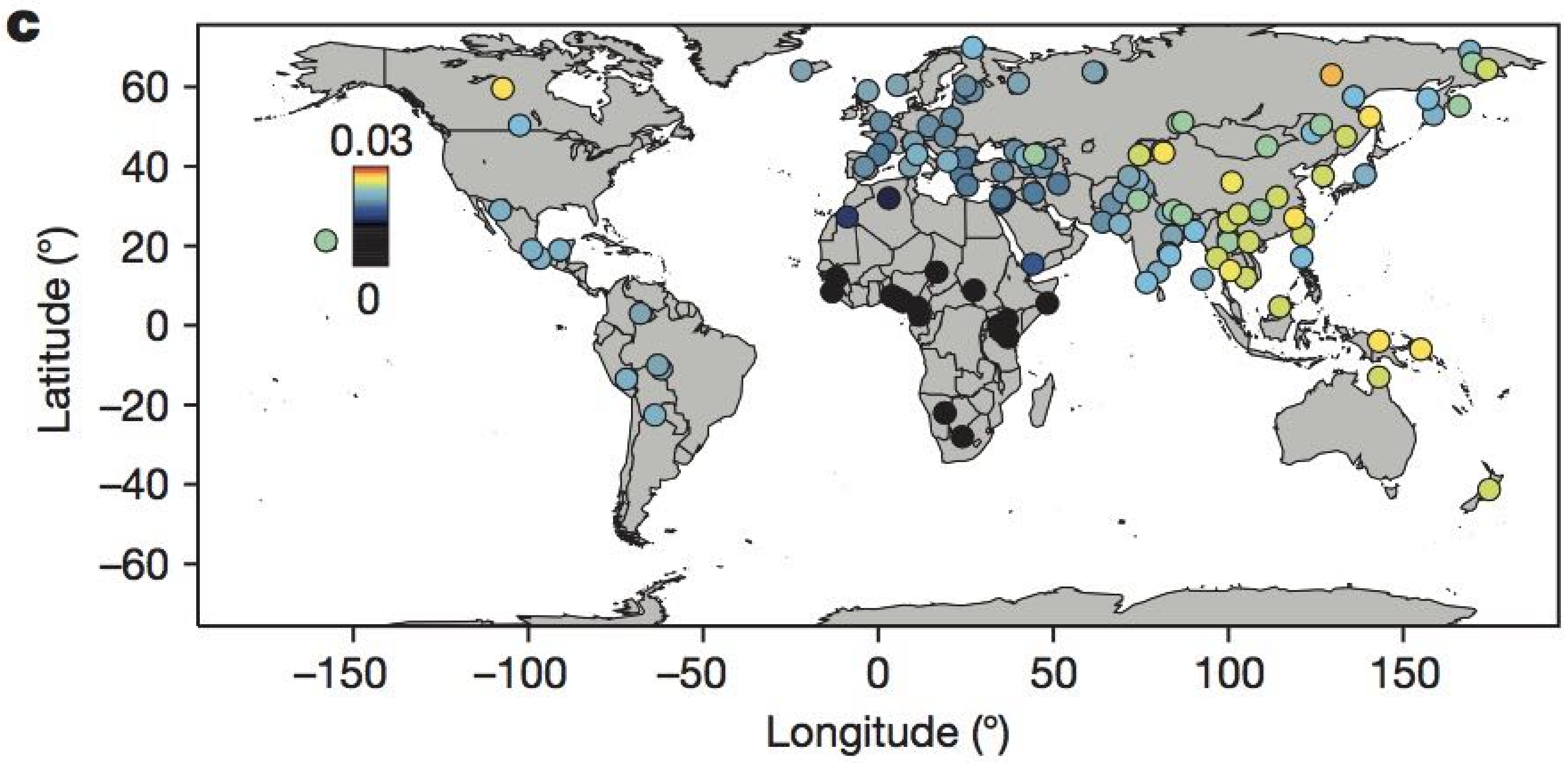
The Contribution of Neanderthals to Phenotypic Variation in Modern Humans

Michael Dannemann[1] and Janet Kelso[1,*]

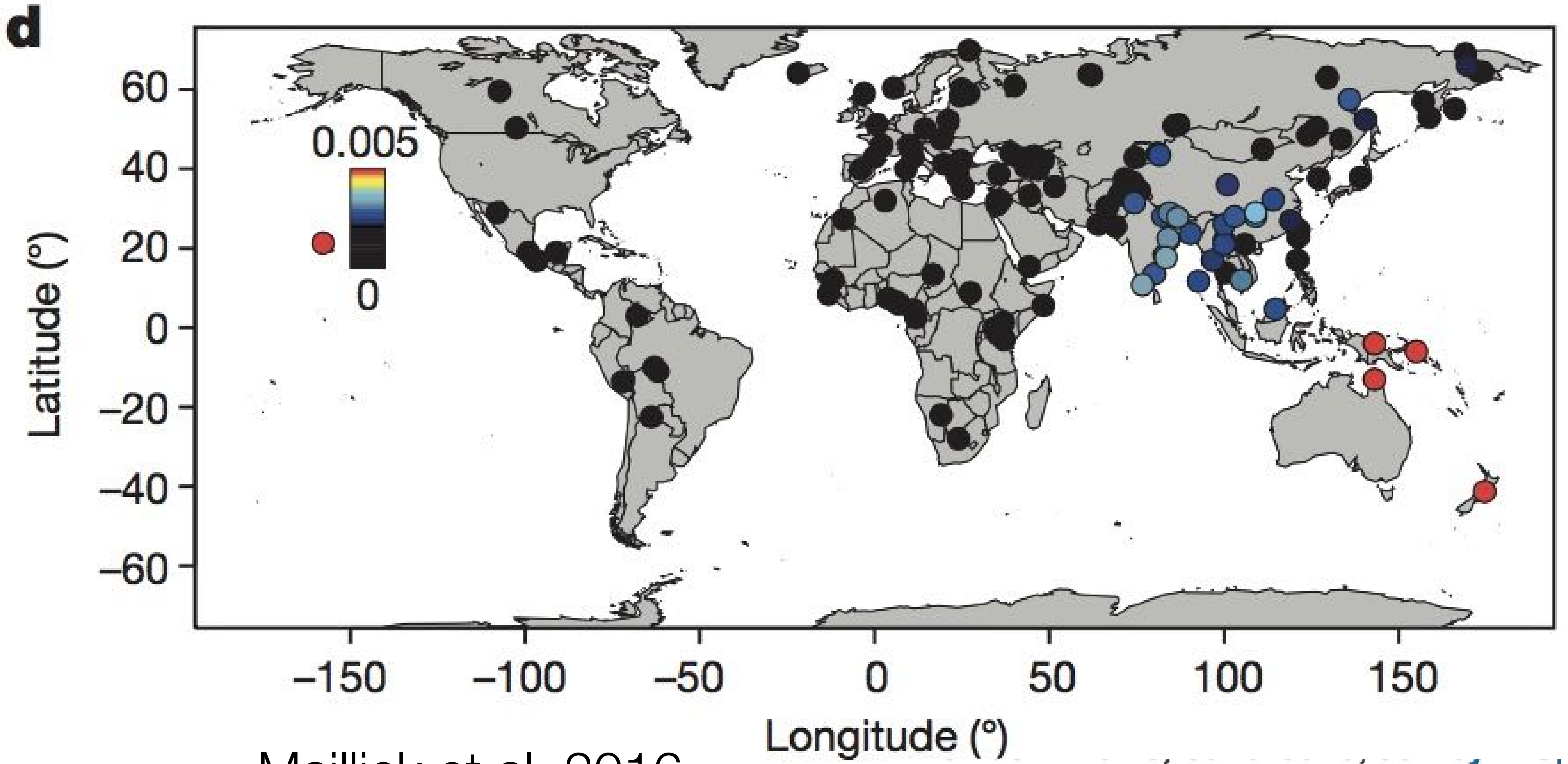
The American Journal of Human Genetics *101*, 578–589, October 5, 2017

The neanderthal and denisovian contribution

- Neanderthal admixture



- Denisovian admixture



Maillick et al. 2016

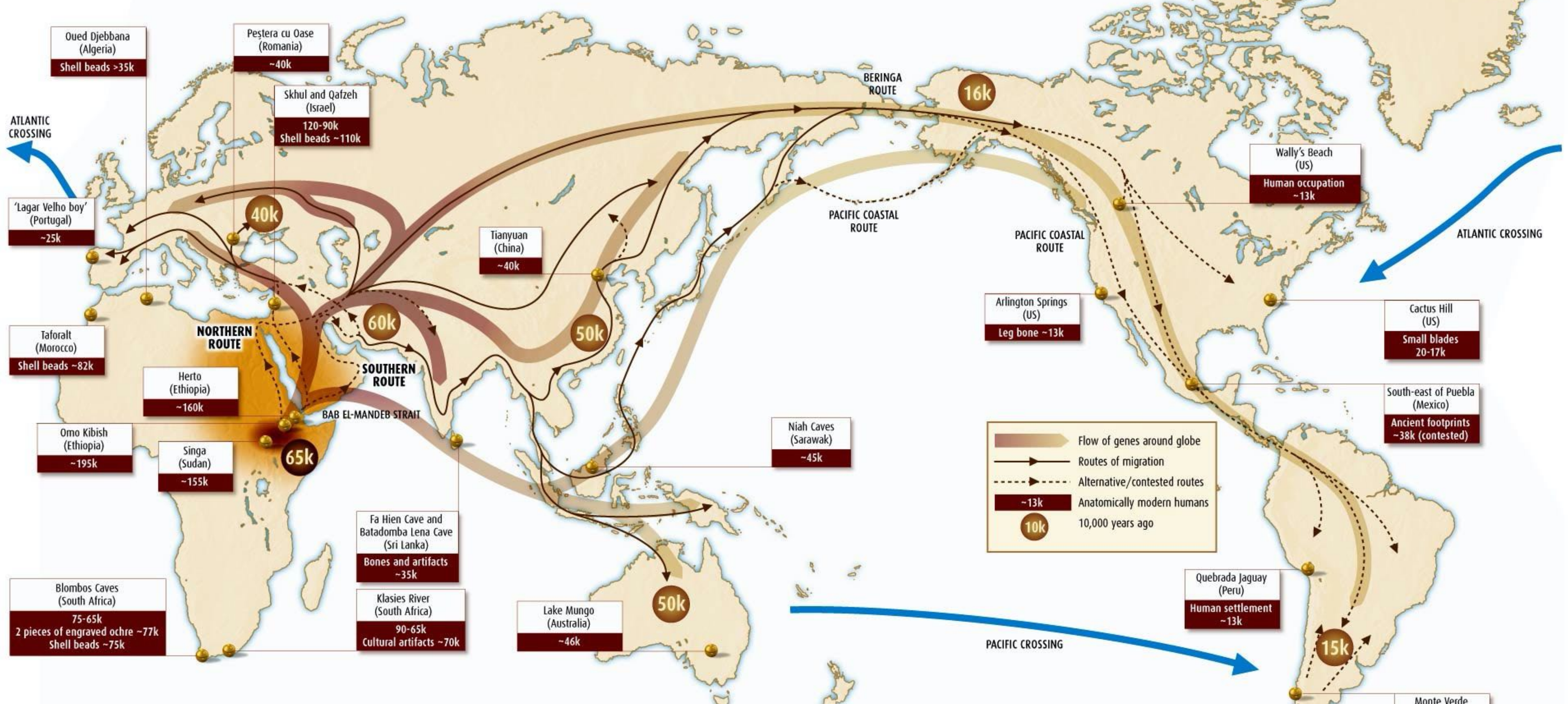
Nature (2016) | doi:10.1038/nature18964

How many human migrations

- *H. sapiens* remains ~80-100 kYA found in China - before the migrations
- The first wave ~120 kYA - to Australia and Oceania
- The second wave ~ 80 kYA - Eurasia
- But the modern genomes indicate a single migration wave?

THE MIGRATION OF ANATOMICALLY MODERN HUMANS

Evidence from fossils, ancient artefacts and genetic analyses combine to tell a compelling story

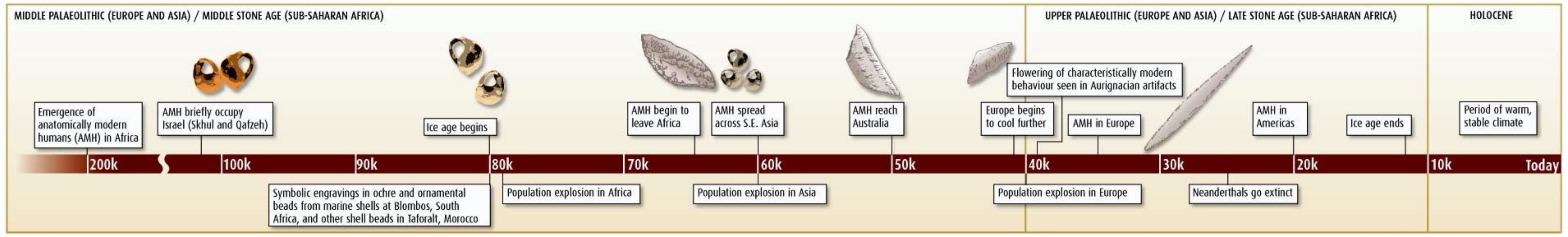


Two routes jump out as prime candidates for the human exodus out of Africa. A northern route would have taken our ancestors from their base in eastern sub-Saharan Africa across the Sahara desert, then through Sinai and into the Levant. An alternative southern route may have charted a path from Djibouti or Eritrea in the Horn of Africa across the Bab el-Mandeb strait and into Yemen and around the Arabian peninsula. The plausibility of these two routes as gateways out of Africa has been studied as part of the UK's Natural Environment Research Council's programme "Environmental Factors in the Chronology of Human Evolution & Dispersal" (EFCHED).

During the last ice age, from about 80,000 to 11,000 years ago, sea levels dropped as the ice sheets grew, exposing large swathes of land now submerged under water and connecting regions now separated by the sea. By reconstructing ancient shorelines, the EFCHED team found that the Bab el-Mandeb strait, now around 30 kilometres wide and one of the world's busiest shipping lanes, was then a narrow, shallow channel.

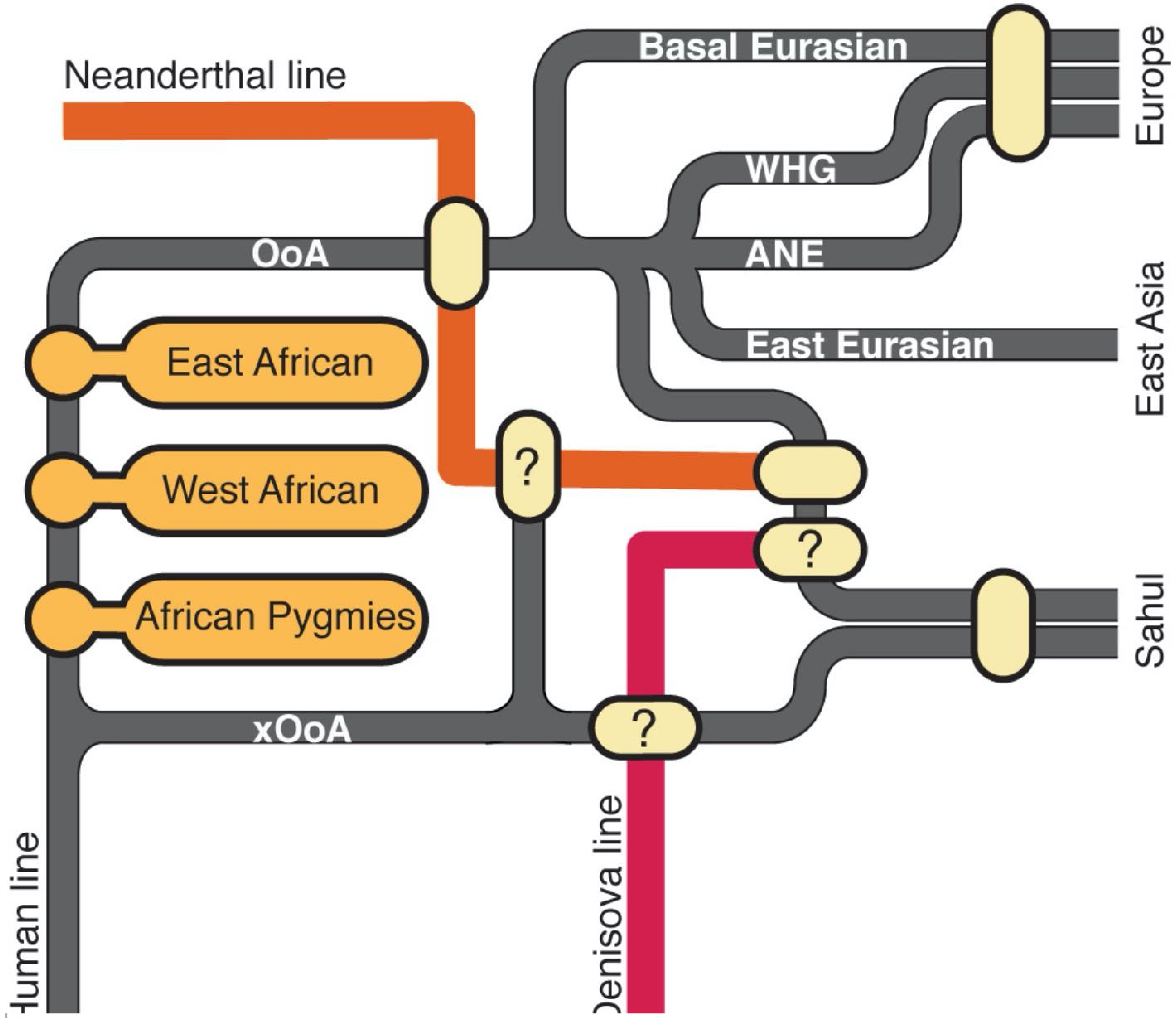
Early humans may have taken this southern route out of Africa. The northern route appears easier, especially given the team's finding that the Suez basin was dry during the last ice age. But crossing the Sahara desert is no small matter. EFCHED scientist Simon Armitage of the Royal Holloway University of London has found some clues as to how this might have been possible. During the past 150,000 years, North Africa has experienced abrupt switches between dry, arid conditions and a humid climate. During the longer wetter periods huge lakes existed in both Chad and Libya, which would have provided a "humid corridor" across the Sahara.

Armitage has discovered that these lakes were present around 10,000 years ago, when there is abundant evidence for human occupation of the Sahara, as well as around 115,000 years ago, when our ancestors first made forays into Israel. It is unknown whether another humid corridor appeared between about 65,000 and 50,000 years ago, the most likely time frame for the human exodus. Moreover, accumulating evidence is pointing to the southern route as the most likely jumping-off point.



One of the models

- The first wave (xOoA): reached south-east Asia, but later went extinct. Mixed with Denisovians and neanderthals
- The second wave (OoA) - the ancestors of modern non-African populations
- xOoA and OoA mixed before xOoA people disappeared
- Through xOoA the denisovian and neanderthal admixture is higher in some populations in south-east Asia



From

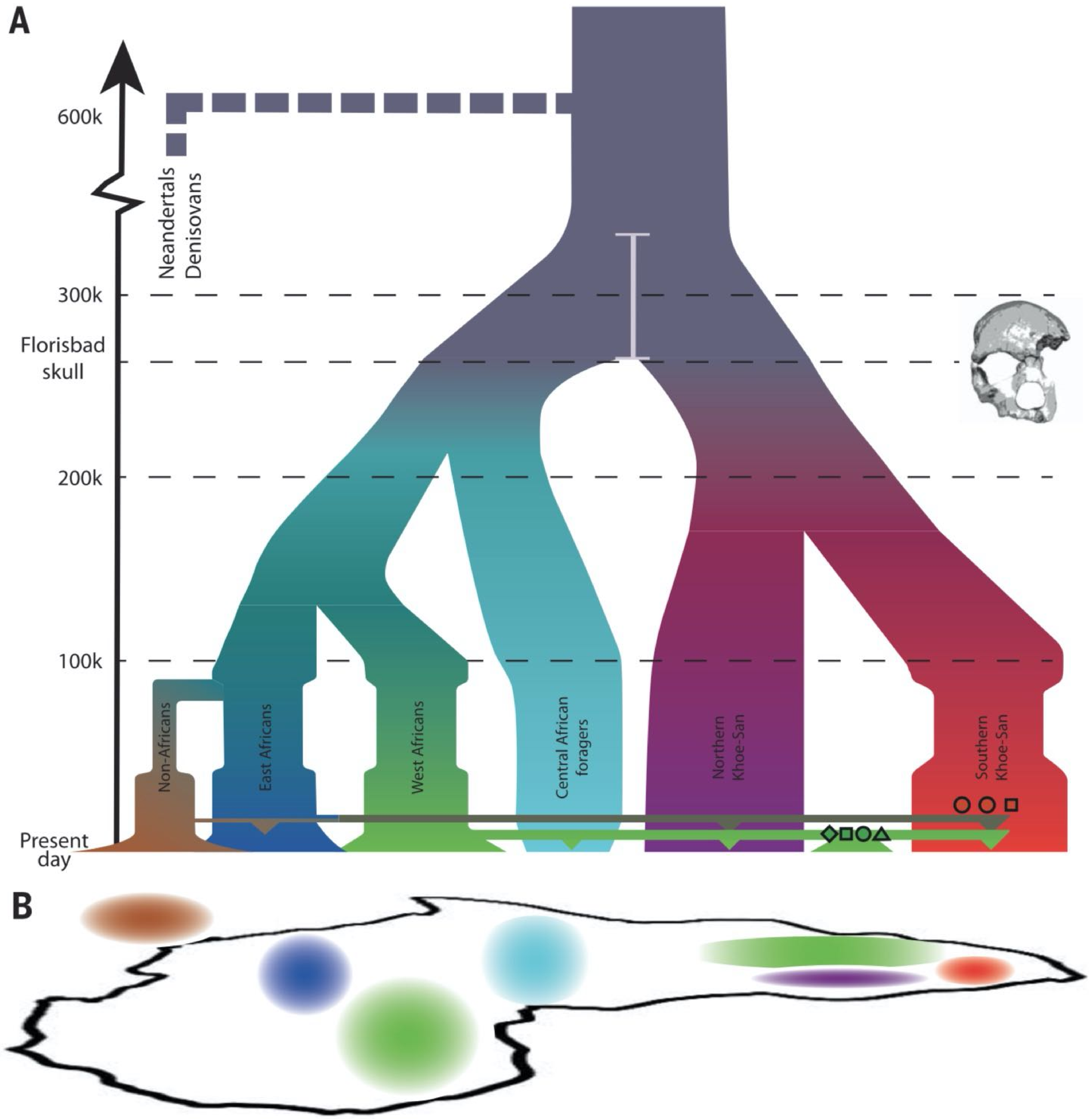
Genomic analyses inform on migration events during the peopling of Eurasia

Luca Pagani, Daniel John Lawson, Evelyn Jagoda, Alexander Mörseburg, Anders Eriksson, Mario Mitt, Florian Clemente, Georgi Hudjashov, Michael DeGiorgio, Lauri Saag, Jeffrey D. Wall, Alexia Cardona, Reedik Mägi, Melissa A. Wilson Sayres, Sarah Kaewert, Charlotte Inchley, Christiana L. Scheib, Mari Järve, Monika Karmin, Guy S. Jacobs, Tiago Antao, Florin Mircea Iliescu, Alena Kushniarevich, Qasim Ayub, Chris Tyler-Smith + *et al.*

Nature (2016) | doi:10.1038/nature19792

“Out of Africa”? Not really.

- Most earlier studies underestimated the diversity in Africa
- *H. sapiens* was widespread in Africa when anatomically modern humans evolved
- aDNA studies in Africa only beginning (2017-18)



C

Split method	Human-Neandertal (Nean-BBayA)	Human-Neandertal (Nean-San)	Human-Neandertal (Nean-Dinka)	Deep Human (Dinka-BBayA)	Deep Human (Dinka-San)	Deep Human (Mandenka-BBayA)	Deep Human (Mandenka-San)	NKSP-SKSP (San-BBayA)	Out of AFR (Dinka-Sardinian)
G-PhoCS	545 ± 9	534 ± 8	535 ± 9	336 ± 7	282 ± 7	356 ± 7	298 ± 7	185 ± 6	115 ± 6
TT-method	660 ± 33	639 ± 26	632 ± 28	265 ± 5	255 ± 5	256 ± 6	261 ± 5	156 ± 5	76 ± 6

Southern African ancient genomes estimate modern human divergence to 350,000 to 260,000 years ago

Carina M. Schlebusch, Helena Malmström, Torsten Günther, Per Sjödin, Alexandra Coutinho, Hanna Edlund, Arielle R. Munters, Mário Vicente, Maryna Steyn, Himla Soodyall, Marlize Lombard and Mattias Jakobsson

Science **358** (6363), 652-655.
DOI: 10.1126/science.aao6266originally published online September 28, 2017

The diversity of modern humans is low

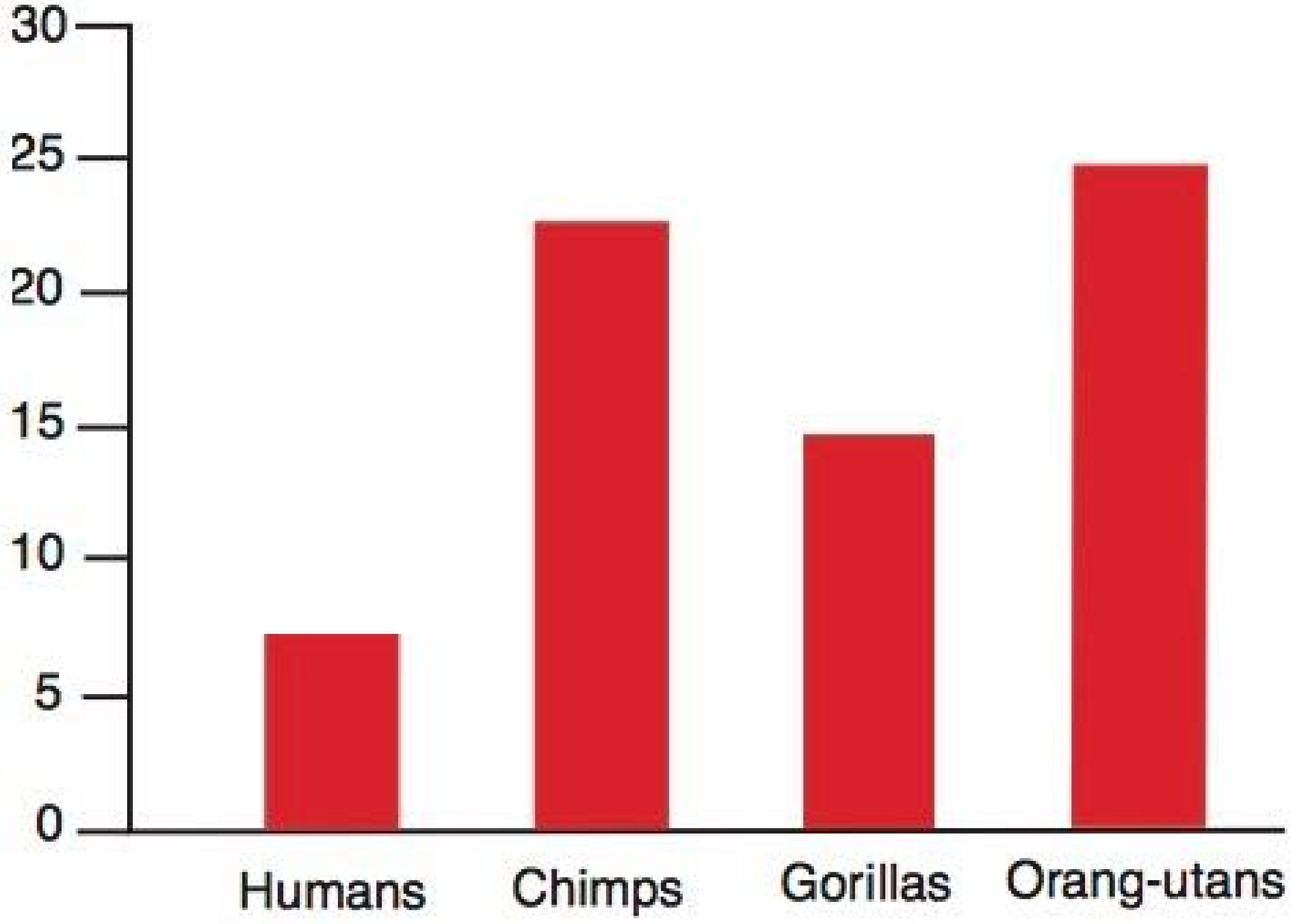
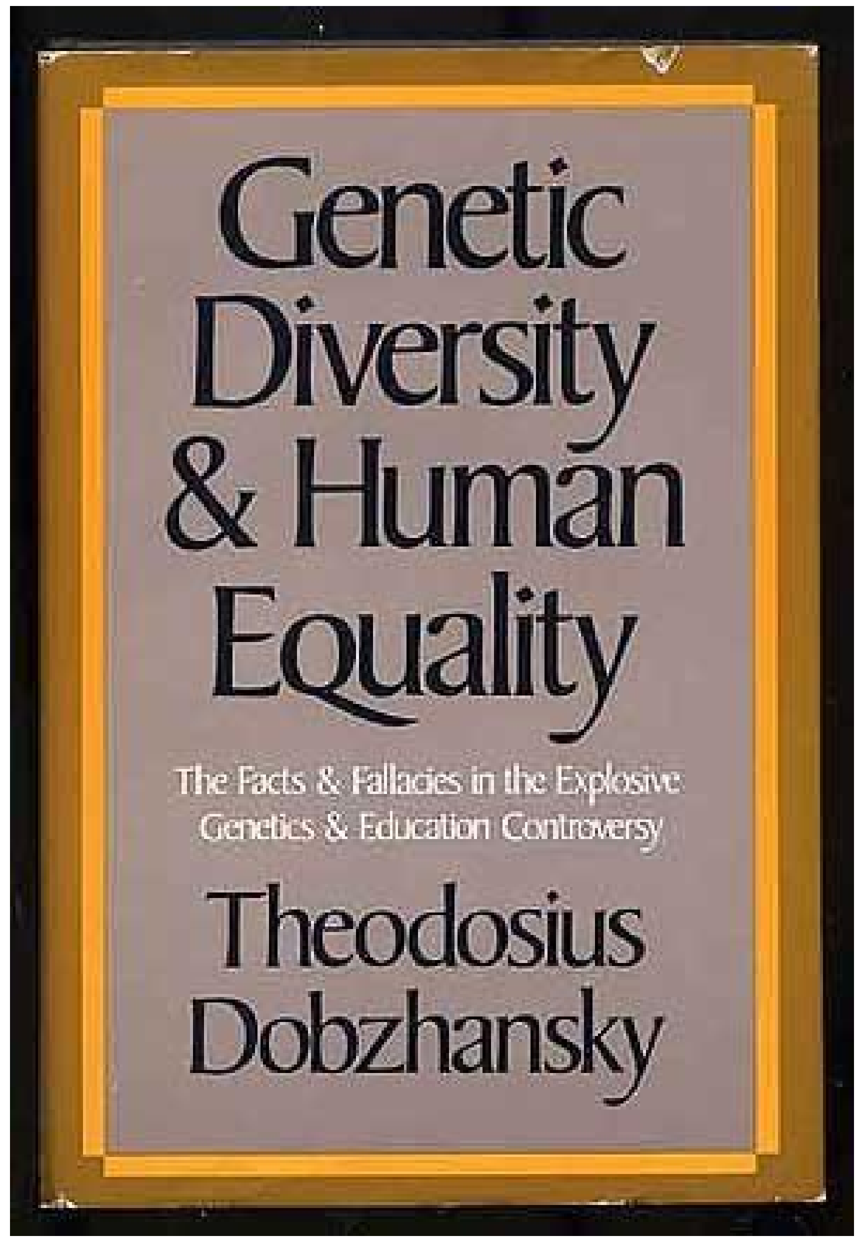


Fig. 11 DNA sequence diversity within humans and great apes. Values are based on the number of variable positions within each species taking the number of sequences determined into account (Watterson's diversity estimator, θ_w).

Kassemann & Pääbo, 2002, J. Int. Med. 251:1-18

Diversity, equality, racism

- Genetic diversity among humans is a fact (even though it is low)
- It does not correspond to traditional notion of continental races
  - it can show history of particular ethnic groups
  - most, if not all populations show traces of mixing and migration
- Equality is about embracing diversity, not negating its existence



Genetic Diversity & Human Equality

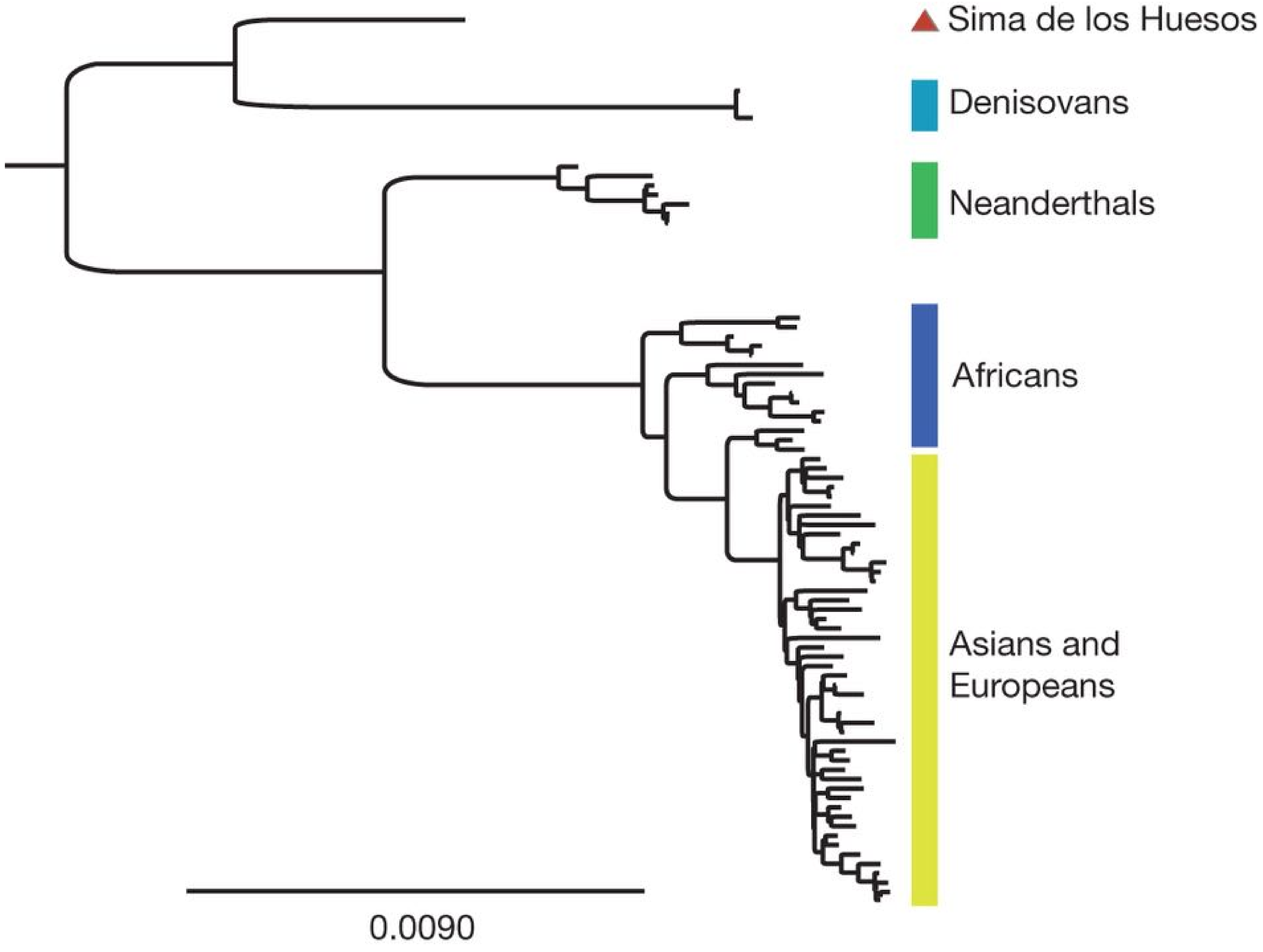
The Facts & Fallacies in the Explosive Genetics & Education Controversy

Theodosius Dobzhansky

1973

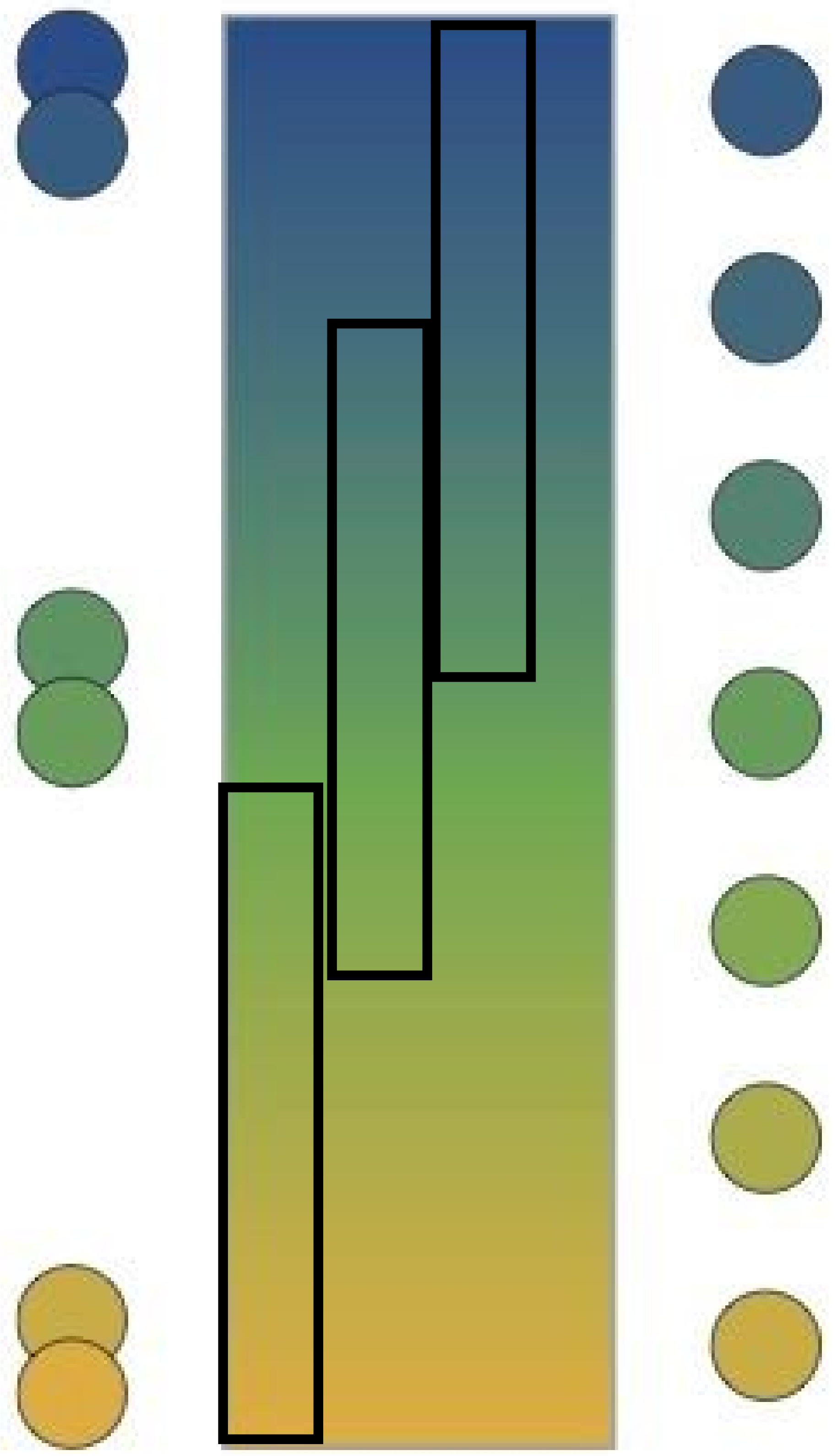
Taxonomy

- Taxonomically we are all African
- Greates diversity within Africa
- Two Africans can differ more than one of them from a non-African



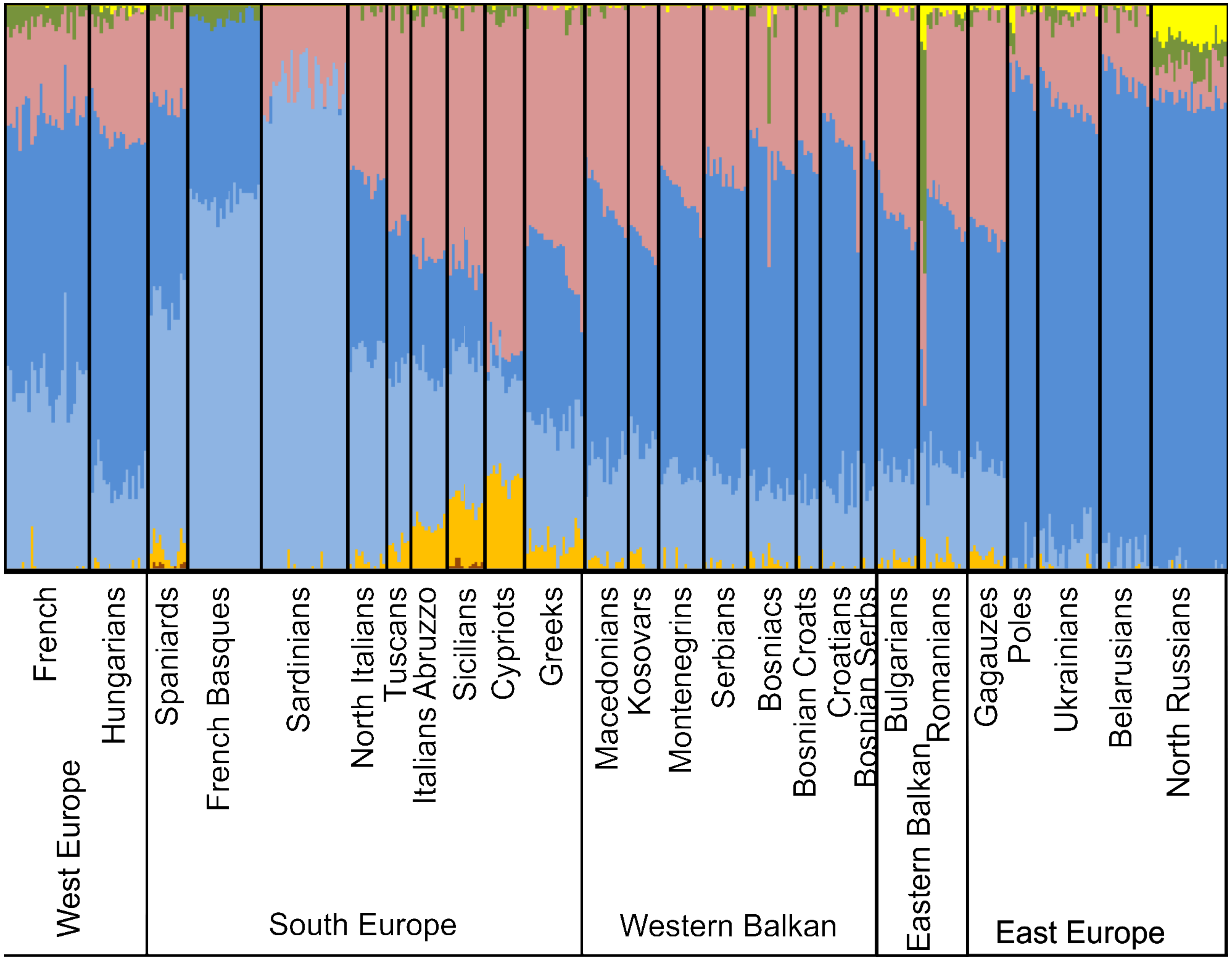
Diversity and “races”

- There are genetic markers that can distinguish ethnic groups
  - they form gradients, not distinct clusters
  - they do not correspond to traditional races
  - different genes and analyses tell different stories
- Division of this continuous diversity into separate groups is a cultural phenomenon
  - two individuals from the same group can be more different, than two individuals from different groups



Pure identity?

- Closely related groups are indistinguishable
- But that's where the conflict often occurs




Standing at the Gateway to Europe - The Genetic Structure of Western Balkan Populations Based on Autosomal and Haploid Markers

Lejla Kovacevic[1,2,3]*, Kristiina Tambets[1], Anne-Mai Ilumäe[1], Alena Kushniarevich[1], Bayazit Yunusbayev[1,3], Anu Solnik[1], Tamer Bego[4], Dragan Primorac[5], Vedrana Skaro[6], Andreja Leskovac[7], Zlatko Jakovski[8], Katja Drobnic[9], Helle-Viivi Tolk[1], Sandra Kovacevic[10], Pavao Rudan[11], Ene Metspalu[1], Damir Marjanovic[2,5]

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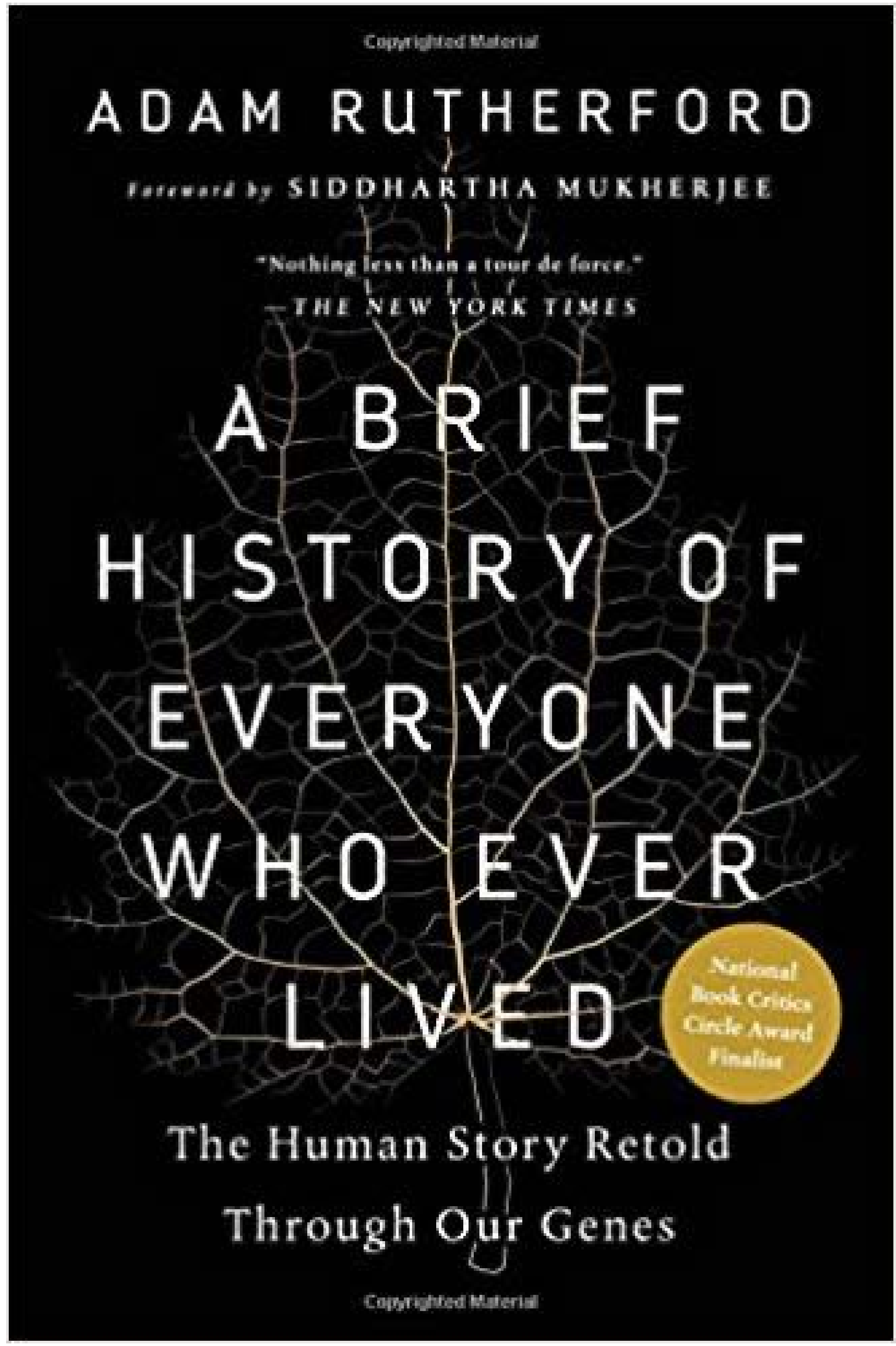
Additional reading



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Foreword by SIDDHARTHA MUKHERJEE

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—THE NEW YORK TIMES

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National Book Critics Circle Award Finalist

The Human Story Retold Through Our Genes

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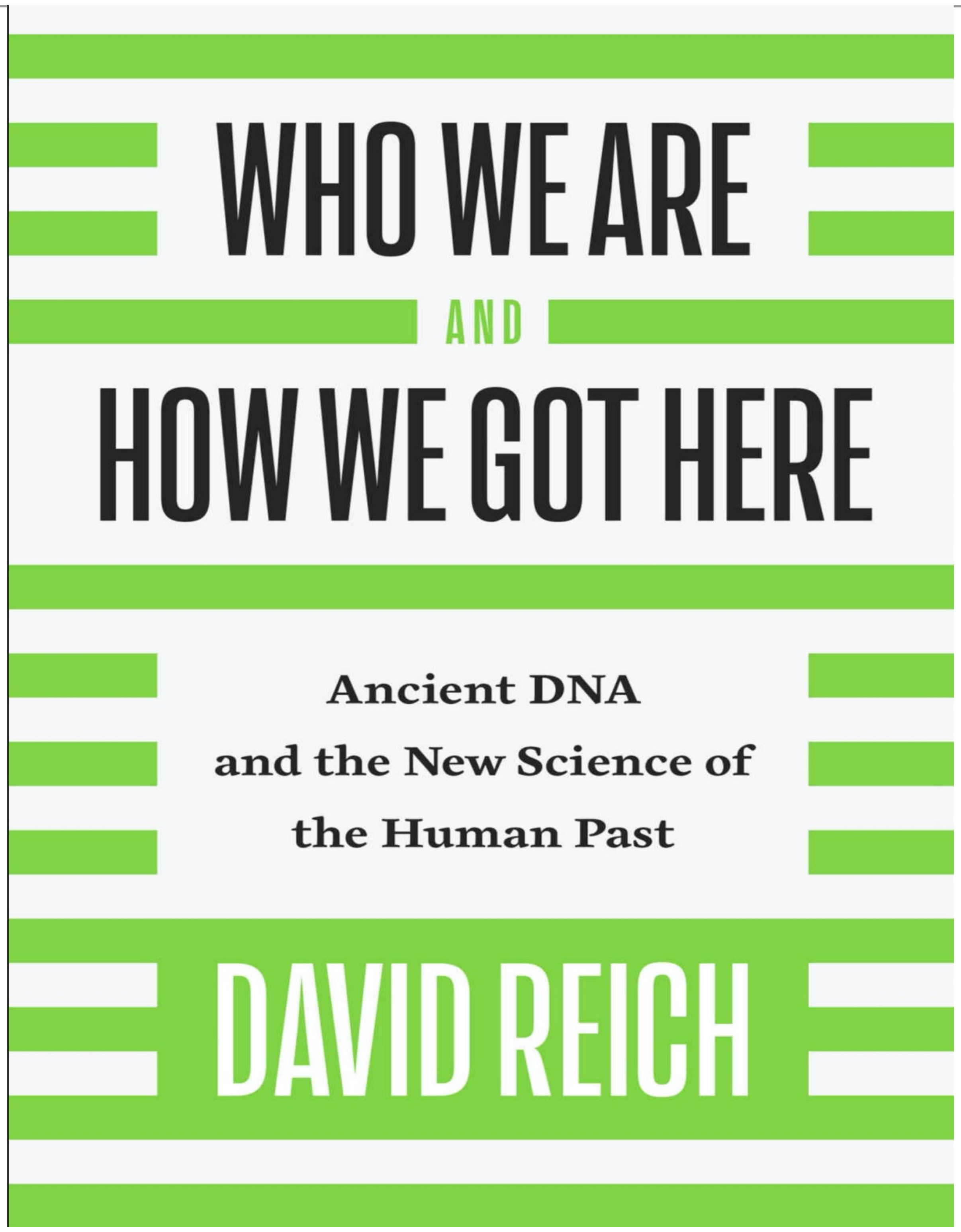
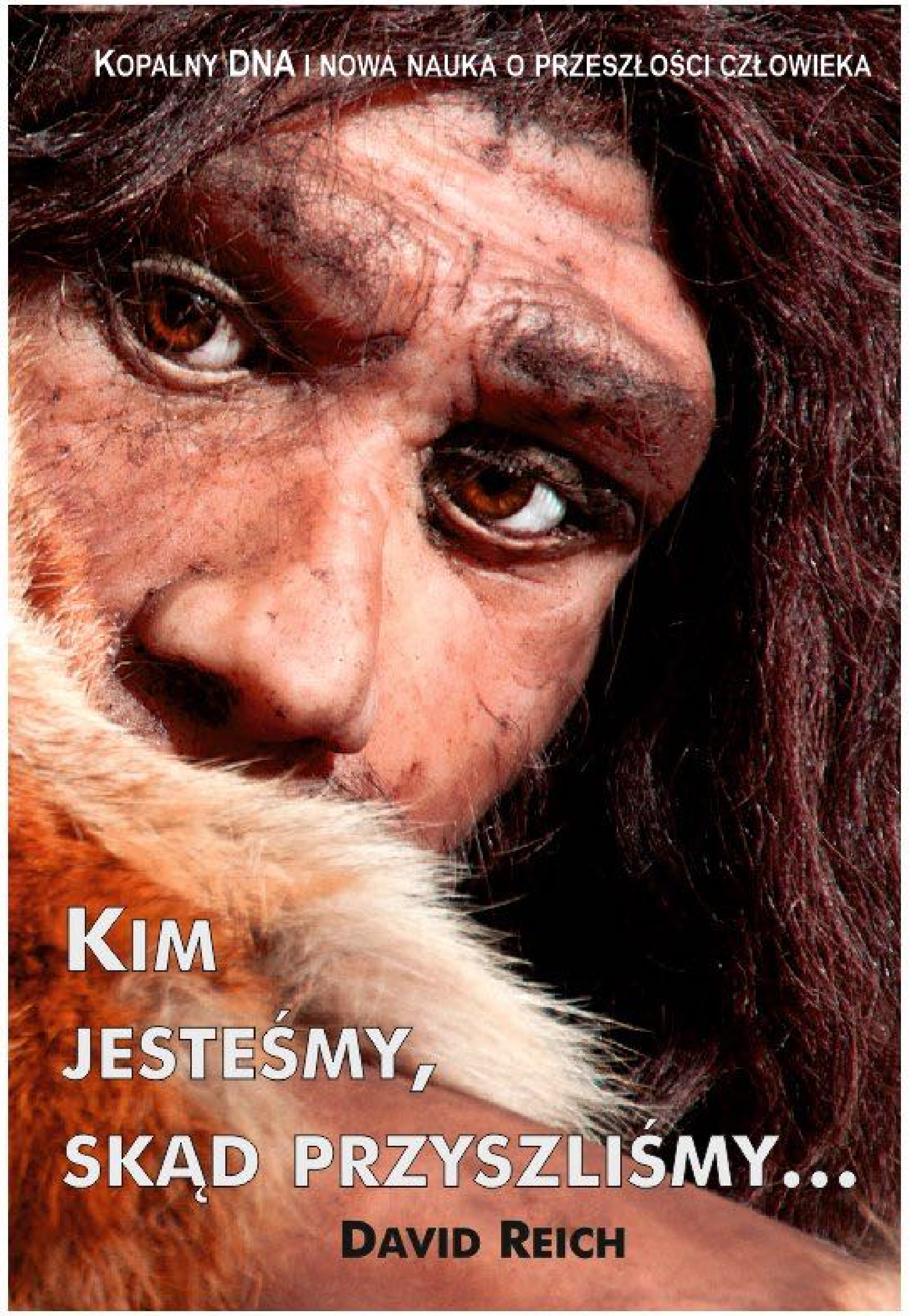
OPOWIEŚCI ZAPISANE W NASZYCH GENACH



WHO WE ARE AND HOW WE GOT HERE

Ancient DNA
and the New Science of
the Human Past

DAVID REICH



KOPALNY DNA I NOWA NAUKA O PRZESZŁOŚCI CZŁOWIEKA

KIM JESTEŚMY, SKĄD PRZYSZLIŚMY...

DAVID REICH