ORIGIN OF MODERN HUMANS

Paleoanthropology: How Old Is the Oldest Human?

Jean-Jacques Hublin

Figure 1. The LD 350-1 mandible in hands of its discover, Chalachew Seyoum.
The Ledi-Geraru area provides an invaluable material documenting a critical period of hominin evolution for which the East African fossil record is still very scarce. (Photo credit: Brian Villmoare.)

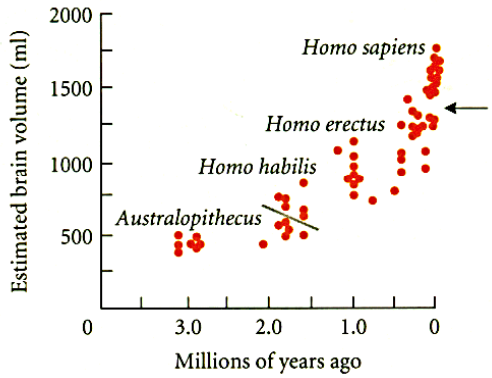
A 2.8 Ma old mandible unearthed in Ethiopia fills the gap between ape-like australopithecines and representatives of the genus *Homo*. It pushes the origin of large-brained hominins further back in time and highlights the complexity of the human evolutionary tree.

Current Biology *25*, R448–R469, June 1, 2015

APPEARANCE OF THE GENUS *HOMO*

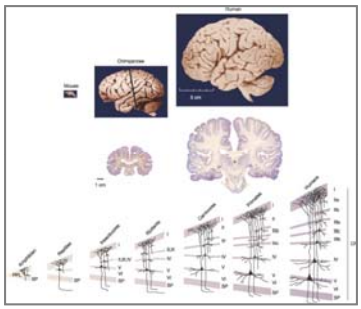
- **Increasingly large brain**
  - *habilis* - 650-800 cc
  - *erectus* - 900-1200 cc
  - *sapiens* - 1200-1400 cc
- **Stone tool use**
- **Number of biological species???**

***Homo habilis* 1.9 mya**



Molecular insights into human brain evolution

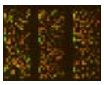
Robert Sean Hill and Christopher A. Walsh

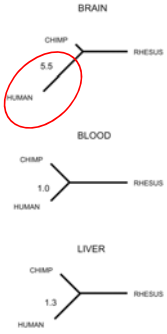


Differences in cerebral cortical size are associated with differences in the cerebral cortex circuit diagram.

Nature **437**, 64-67 (1 September 2005)

Intra- and Interspecific Variation in Primate Gene Expression Patterns





- **Enard et al. used an AFFIMETRIX gene chip with 12,000 human genes to analyze differences in expression patterns among 3 primates.**
- **No significant differences were noted in blood or liver assays *BUT* large differences were observed in brain expression patterns.**
- **Rapid evolution of gene expression patterns in the human brain.**

FROM: Enard et al., *Science* April 12, 2002 296:340-343

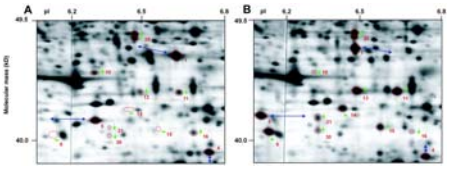


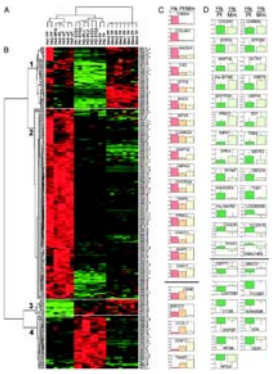
Table 1. Brain protein pattern differences between humans and chimpanzees as analyzed by 2D gel electrophoresis. Differences between humans and chimpanzees were scored if confirmed in three individual human-chimpanzee pairs and were analyzed in the same way as in a larger mouse study comparing *M. musculus* and *M. spretus*. **Qualitative differences** represent changes in electrophoretic mobility of spots, which likely result from amino acid substitutions, whereas **quantitative differences** reflect changes in the amount of protein.

Comparison	Analyzed spots	Differences	
		Qualitative	Quantitative
Human-chimpanzee	538	41 (7.6%)	169 (31.4%)
M. musculus-M. spretus	8767	668 (7.6%)	656 (7.5%)

FROM: Enard et al., *Science* April 12, 2002 296:340-343

Elevated gene expression levels distinguish human from non-human primate brains

Caceres *et al.* (*PNAS* 2003) identified 169 genes that exhibited gene expression differences between human and chimpanzee lineages. 91 of these genes differentiated in the human lineage. **Most differences involved up-regulation with higher expression levels humans.**



Expression profiling in primates reveals a rapid evolution of human transcription factors
Yoav Gilad *et al.*

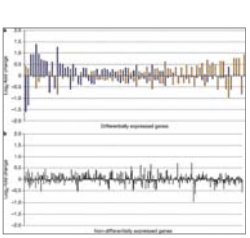
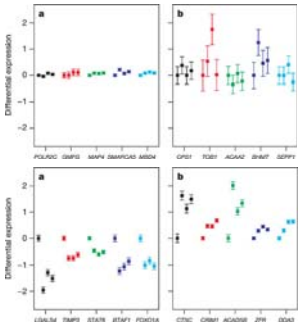


Table 1 | Inter-species differentially expressed genes

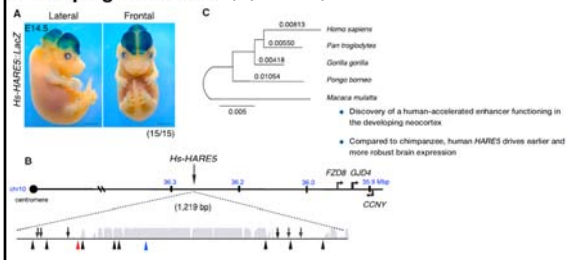
	Chimpanzee	Orangutan	Rhesus macaque
Human	110	128	176
Chimpanzee	-	150	141
Orangutan	-	-	129



humans, chimpanzees, orangutans and rhesus macaque (left to right)

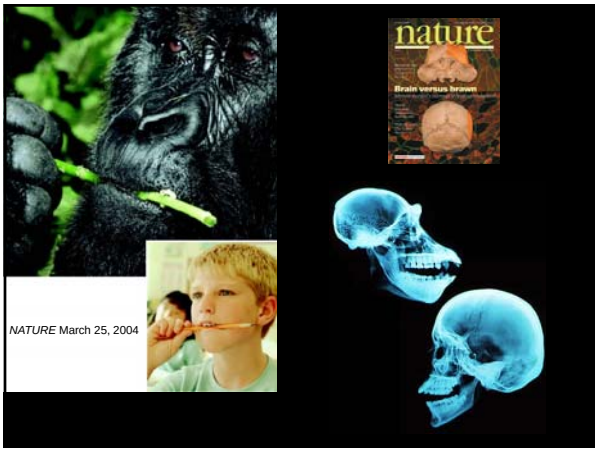
Nature **440**, 242-245 (9 March 2006)

Human-Chimpanzee Differences in a *FZD8* Enhancer Alter Cell-Cycle Dynamics in the Developing Neocortex (Boyd *et al.* 2015)



The neocortex expanded spectacularly during human evolution, giving rise to distinctively human anatomical and cognitive capabilities **Yet to date, just a handful of genetic loci have been associated with human-specific brain traits** and none have been shown to functionally impact corticogenesis in an evolutionarily divergent fashion. In this study, we report the discovery of the first human-accelerated enhancer that functions in brain development… **Our study suggests the intriguing hypothesis that evolutionary changes in HARE5 sequence and activity contributed to the origin of unique features of the human brain.**

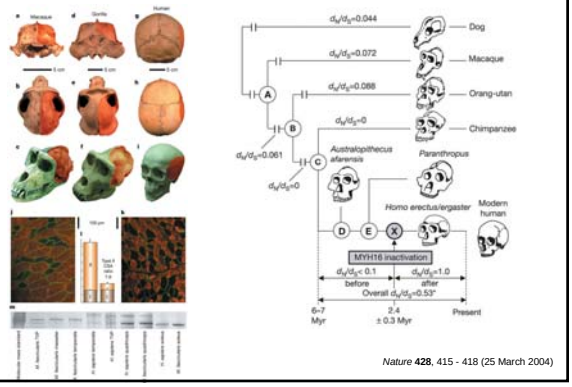
Current Biology 25, 772-779, March 16, 2015



NATURE March 25, 2004

Myosin gene mutation correlates with anatomical changes in the human lineage

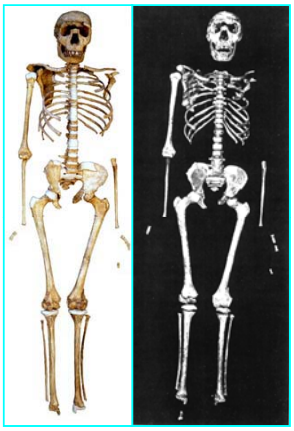
STEDMAN et al.



Nature **428**, 415 - 418 (25 March 2004)

Homo (Kenyanthropus) rudolfensis
2.5 – 1.9 mya

Homo ergaster
1.8 – 1.4 mya



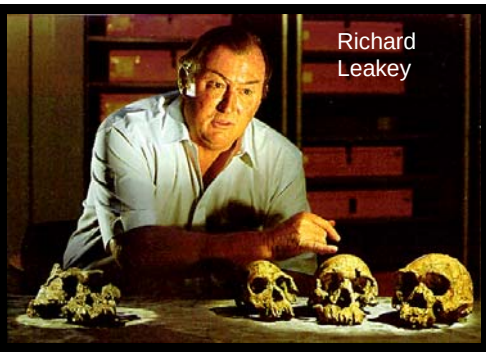
"Turkana boy"

- 10-12 years old
- 1.6 million years ago
- Kenya
- called early African *H. erectus* or *H. ergaster*

"Turkana boy"

10-12 years old

1.6 million years ago



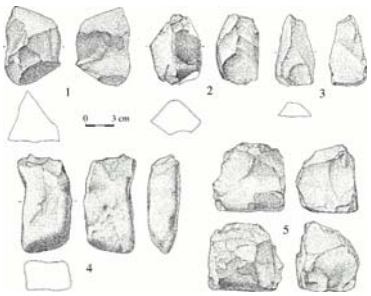
Eastern Africa - Lake Turkana region

coexistence of different hominids

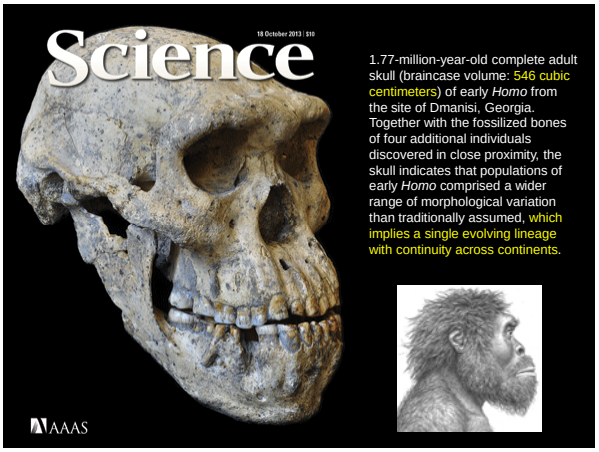
DMANISI, REPUBLIC OF GEORGIA

- **1.7 mya**
- **Shortly after the origin of *Homo*, there is a migration out of Africa.**

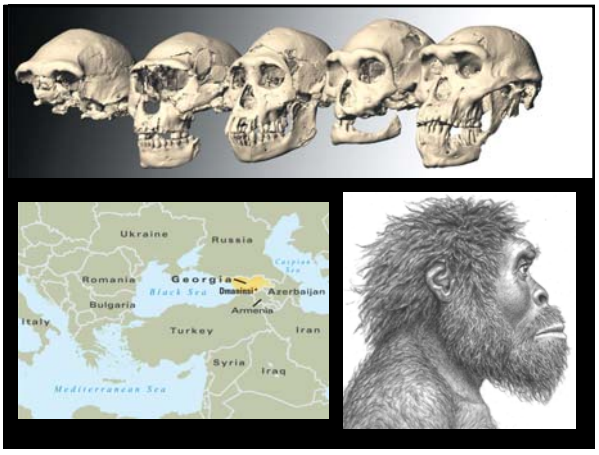
DMANISI STONE TOOLS



clearly not close to anatomically modern *H. sapiens* - like Turkana boy



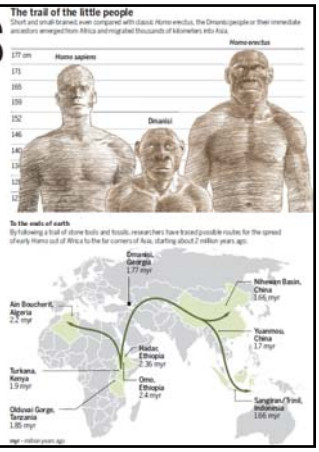
1.77-million-year-old complete adult skull (braincase volume: 546 cubic centimeters) of early *Homo* from the site of Dmanisi, Georgia. Together with the fossilized bones of four additional individuals discovered in close proximity, the skull indicates that populations of early *Homo* comprised a wider range of morphological variation than traditionally assumed, which implies a single evolving lineage with continuity across continents.



THE WANDERERS

Fossils of the first human ancestors to trek out of Africa reveal primitive features and a brutal way of life

By Ann Gibbons, in Dmanisi, Georgia

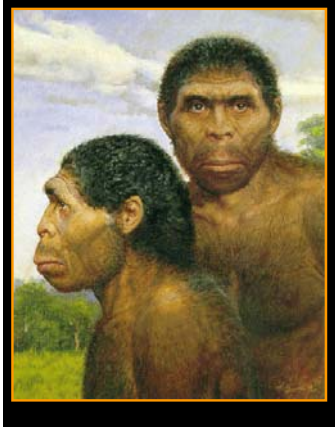


"By now, the fossils have made it clear that these pioneers were startlingly primitive, with small bodies about 1.5 meters tall, simple tools, and brains one-third to one-half the size of modern humans."

Asian *Homo erectus*

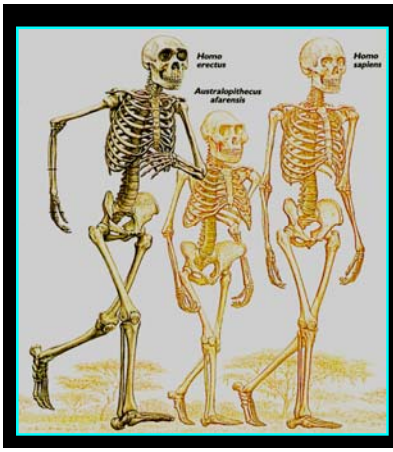
"Java Man"
0.75 mya

Peking Man
China
0.77 mya



RECONSTRUCTION of Indonesian

H. erectus



Brain Size:

A. afarensis

500cc

H. erectus

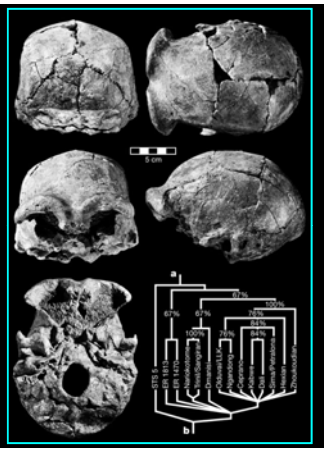
900 – 1200 cc

H. sapiens

1100 – 1400 cc

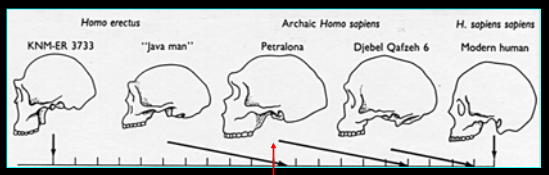
'Daka' Ethiopian Skull

- 1 million-year-old remains from Ethiopia show clear link between Asian *Homo erectus* and African *H. erectus* (widespread paleospecies)
- intermediate between earlier and later African fossils



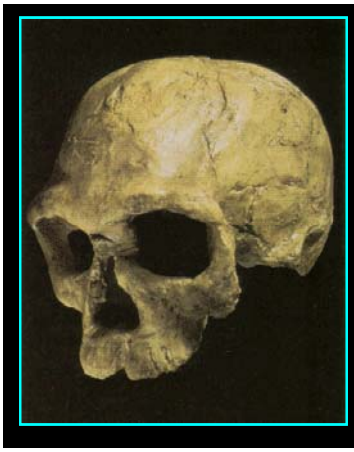
- **There is a growing realization that there may have been a high degree of sexual dimorphism in this archaic lineage compared to more modern groups.**

- Comparison of two *H. erectus* skulls found in Kenya showing the huge variation in size



Petralona Skull – 250,000 years old

- ***H. erectus* or archaic *H. sapiens*?**



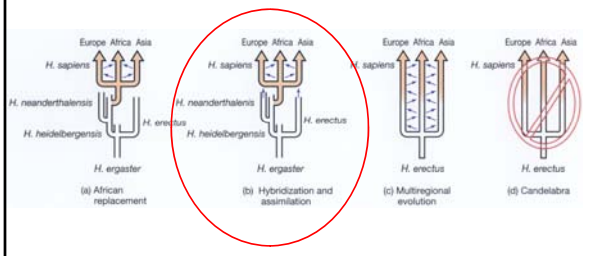
JEBEL IRHOUD 1

MOROCO

100,000 – 200,000 YEARS OLD

H. erectus* or *H. sapiens?

COMPETING HYPOTHESES FOR THE DEVELOPMENT OF MODERN HUMANS

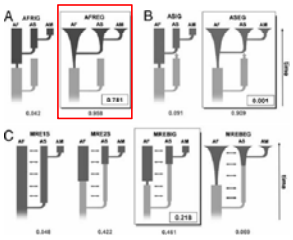


COMPETING HYPOTHESES FOR THE DEVELOPMENT OF MODERN HUMANS

- **Multiregional model: archaic *H. sapiens* (or *H. erectus*) dispersed throughout the Old World and simultaneously evolved to modern form with abundant gene flow.**
- **Replacement Model (Out – of– Africa): single group that relatively recently dispersed from Africa, evolved into modern form and replaced all archaic forms, including Neanderthals.**
- **Hybridization & Assimilation Model: This model suggests that archaic lineages spread out from Africa early, followed later by a second wave of dispersal from a more derived lineage. Some amount of hybridization accompanied the replacement of the archaic lineages.**

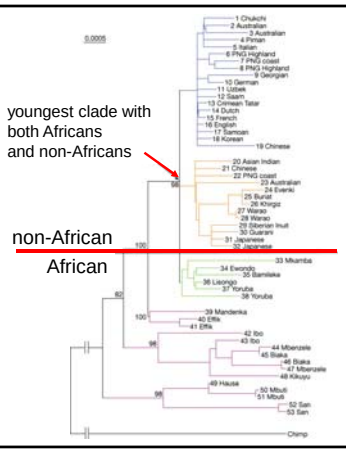
Statistical evaluation of alternative models of human evolution

Fangundes et al. 2007 PNAS 17614-17619



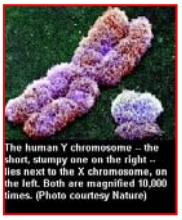
Using DNA data from **50 nuclear loci** sequenced in African, Asian and Native American samples…**a simple African replacement model with exponential growth has a higher probability (78%) as compared with alternative multiregional evolution or assimilation scenarios.** A Bayesian analysis of the data under this best supported model points to an origin of our species **141 thousand years ago (Kya), an exit out-of-Africa 51 Kya, and a recent colonization of the Americas 10.5 Kya.** We also find that the African replacement model explains not only the shallow ancestry of mtDNA or Y-chromosomes but also the occurrence of deep lineages at some autosomal loci, which has been formerly interpreted as a sign of interbreeding with *Homo erectus*.

Recent comparisons of ENTIRE mtDNA genome indicate a recent (0.2 mya), African origin of anatomically modern humans.



Y CHROMOSOME STUDIES

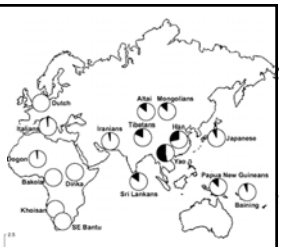
Dorit et al. 1995	173,000
Hammer et al. 1995	188,000

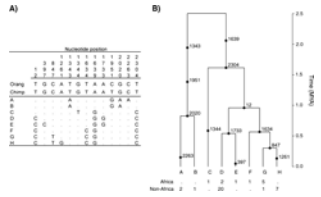

The human Y chromosome -- the short, stumpy one on the right -- lies next to the X chromosome, on the left. Both are magnified 10,000 times. (Photo courtesy Nature)

- mtDNA and Y chromosome studies yield similar dates for the MRCA of modern humans.
- Taken together, these studies strongly suggest that the ***multiregional model*** cannot be correct.

Evidence for Archaic Asian Ancestry on the Human X Chromosome

Garrigan et al (2005) Mol. Biol. Evol. 22:189-192





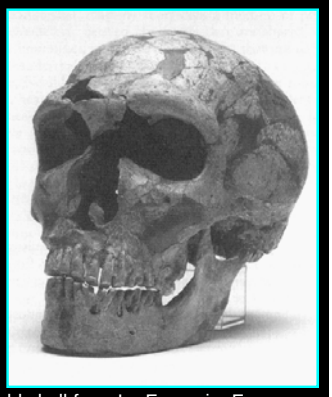
Geographical distribution of the archaic *RRM2P4* lineage in 17 population samples

WHAT ABOUT NEANDERTHALS???

H. sapiens neanderthalensis
50,000 years ago
France

H. sapiens sapiens
Present

- Neanderthal fossils are found from 400,000 to about 30,000 years ago in Europe and western Asia.

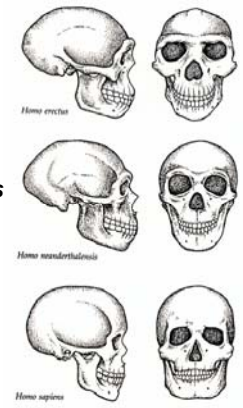


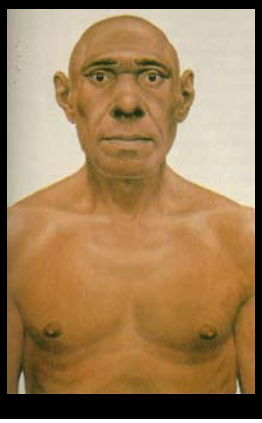
50,000 year old skull from La Ferassie, France

Homo erectus

Homo neanderthalensis

Homo sapiens

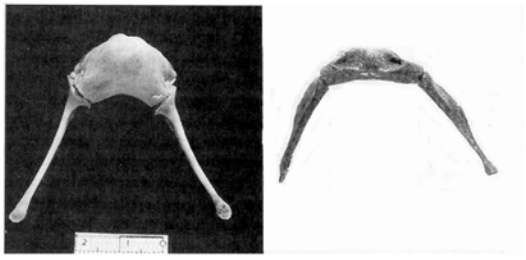




RECONSTRUCTION BASED ON SKULLS FROM SHANIDAR CAVE IN IRAQ

- Prominent brow ridge
- Large bulbous nose
- Powerful build
- Possible advanced culture: sophisticated tools, burials, language?

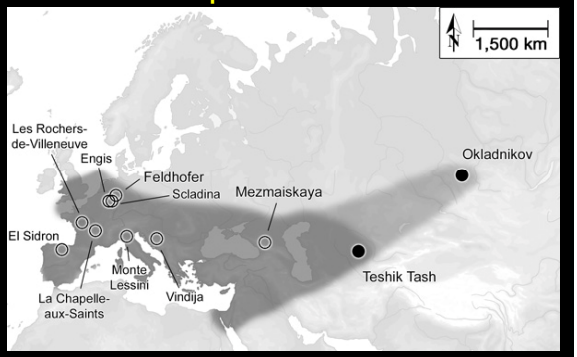
HYOID BONES CLOSELY RESEMBLE MODERN HUMANS



Chimpanzee Neanderthal

Sympatry *H. neanderthalensis* and *H. sapiens*

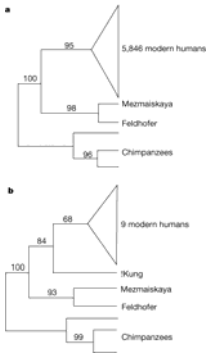
Ancient DNA samples from *H. neanderthalensis*



Krause et al. *Nature* **449**, 902-904 (18 October 2007)

mtDNA SEQUNCE ANALYSIS FROM NEANDERTHAL BONE (>30, 000 YEARS OLD)

- **Neanderthal sequences are 3 times as divergent from modern human sequences than are the most divergent modern humans.**
- **It is unlikely that Neanderthals were assimilated into human populations.**



1% to 4% of the DNA of Europeans and Asians, but not of Africans, was shared with Neandertals and concluded that modern humans interbred with Neandertals at low levels (*Science*, 7 May 2010, pp. 680, 710)

Denisova human

This view of the Altai Mountains is from just above Denisova Cave, where the fragment of bone analysed by Krause *et al.* was discovered. The excavation field camp is visible in the valley below.

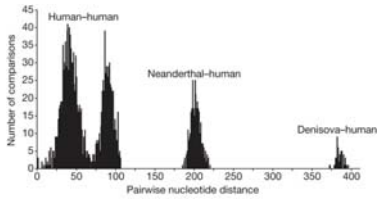
HUMAN EVOLUTION

Stranger from Siberia

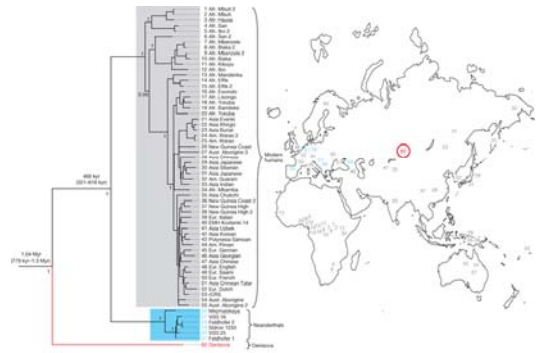
Terence A. Brown

The sequencing of ancient DNA is generating dramatic results. The sequence from a bone fragment has revealed the existence of an unknown type of extinct human ancestor that lived in Asia 40,000 years ago.

- Pairwise nucleotide differences from all pairs of complete mtDNAs from 54 present-day and one Pleistocene modern human, six Neanderthals and the Denisova hominin are shown.



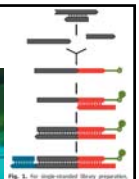
The complete mitochondrial DNA genome of an unknown hominin from southern Siberia

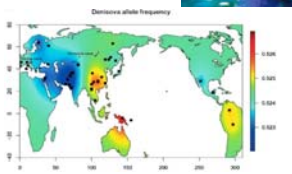


NATURE|Vol 464|8 April 2010

This replica of a tiny finger bone from Denisova Cave yielded an entire genome. *Photo: Max Planck Institute for Evolutionary Anthropology*

A Crystal-Clear View Of an Extinct Girl's Genome





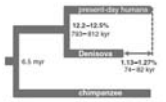


Fig. 2. Average sequence divergence and branch length differences between the Denisovan genome and 11 present-day humans represented as a tree. Divergence is reported as fraction of the branch leading from human to the common ancestor with chimpanzee, and in years, if one assumes a human-chimpanzee divergence of 6.5 million years ago.

Science AAAS

A High-Coverage Genome Sequence from an Archaic Denisovan Individual
Matthias Meyer *et al.*
Science **338**, 222 (2012);
DOI: 10.1126/science.1224344

Location of the Middle Pleistocene site of **Sima de los Huesos** (yellow) as well as Late Pleistocene sites that have yielded **Neanderthal** DNA (red) and **Denisovan** DNA (blue).

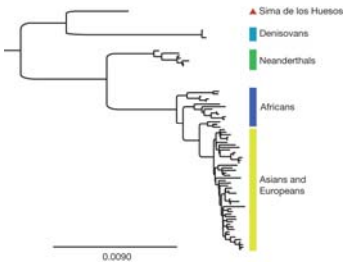
Svante Paabo

A mitochondrial genome sequence of a hominin from Sima de los Huesos

nature

M Meyer *et al. Nature* **000**, 1-4 (2013) doi:10.1038/nature12788

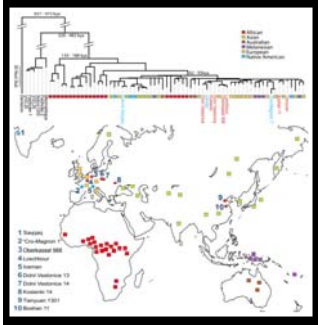
Bayesian phylogenetic tree of hominin mitochondrial relationships based on the Sima de los Huesos mtDNA sequence determined using the inclusive filtering criteria.



nature

M Meyer *et al. Nature* **000**, 1-4 (2013) doi:10.1038/nature12788

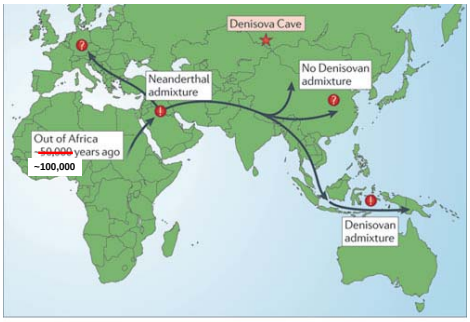
A Revised Timescale for Human Evolution Based on Ancient Mitochondrial Genomes
Fu et al.



Denisova	657 – 973 kya
Neanderthal	326 – 482 kya
Modern Humans	134 – 188 kya
Out-of-Africa	62 – 95 kya

Cell Press
Source: Current Biology - Volume 23, Issue 7 - Pages 553-559 (DOI:10.1016/j.cub.2013.02.044)

Learning about human population history from ancient and modern genomes
Mark Stoneking & Johannes Krause

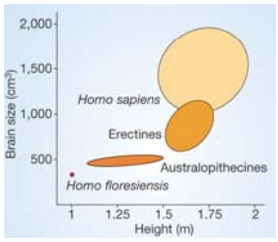


Nature Reviews Genetics **12, 603-614 (September 2011)**
Nature Reviews | Genetics

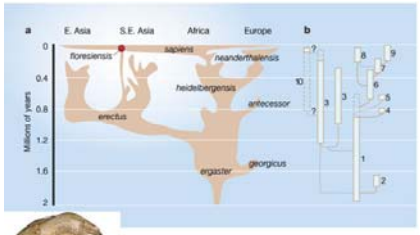
Palaeoanthropology: Human evolution writ small

We are the only living species of the genus *Homo*. Given the startling results of a cave excavation in Southeast Asia, it seems that we coexisted with another species until much more recently than had been thought.

Tools associated with
H. floresiensis



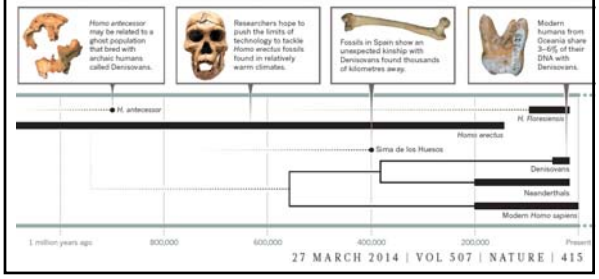
Co-occurrence of *H. sapiens* and *H. erectus* as recently as 19,000 years ago?



The
Neanderthal
in the **family**

By Ewen Callaway

HIDDEN HERITAGE *The study of ancient DNA is revealing connections between archaic humans — and the traces they left behind in modern genomes.*



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Neanderthals had outsize effect on human biology

From skin disorders to the immune system, sex with archaic species changed Homo sapiens.

A small, but significant, portion of modern human genomes has roots in archaic forms.

- Europeans and Asians have 2-4% Neanderthal DNA.
- Melanesians and Aboriginal Australians have up to 5% Denisovan DNA.

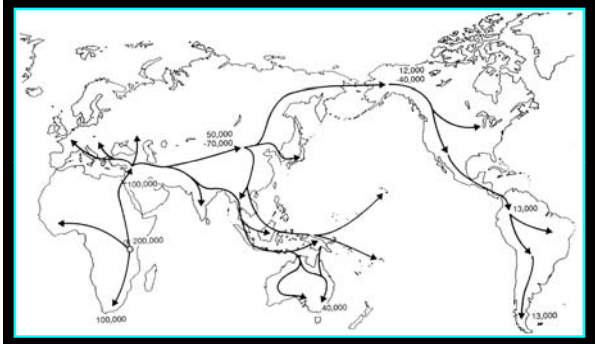
A number of phenotypic traits are associated with these archaic genes including an increased or decreased risk of:

- Osteoporosis, blood-coagulation disorders, Nicotine addiction, depression, obesity skin disorders

Specific genes include:

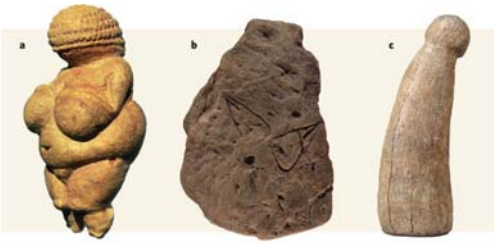
- Toll-like receptors involved in immunity (Neanderthals & Denisovans)
- EPAS1 involved in high altitude adaptation (Denisovans)

RECONSTRUCTING THE PATH OF HUMAN MIGRATION



- **Cave Paintings ~35,000 years ago**

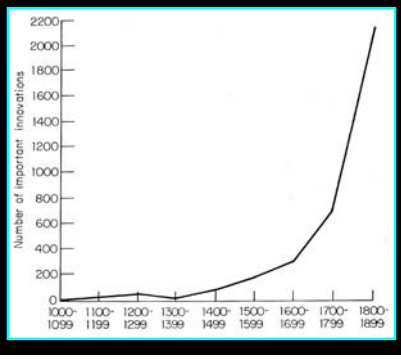
35,000 year-old statues



More….

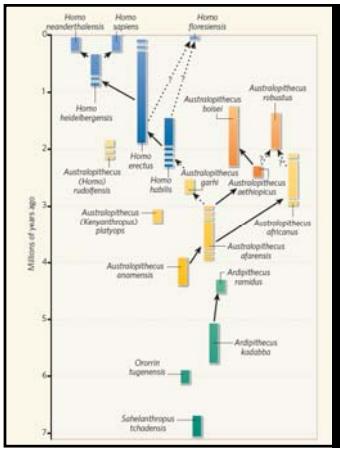
NATURE|Vol 459|14 May 2009

RAPID INCREASE IN TECHNOLOGY, ART, AND MUSIC DEMONSTRATES CULTURAL EVOLUTION IN MODERN HUMANS.



HUMANS ARE UNIQUE IN THEIR EXTREMELY HIGH RATE OF CULTURAL EVOLUTION

- To what extent is an interaction between cultural evolution and phenotypic evolution possible?



- ***H. floresiensis*** **~18,000**
- **Denisova ~40,000**
- **H. neanderthalensis ~30,000**

Possibly 4 separate lineages as recently as 40,000 years ago

NATURE|Vol 459|7 May 2009