

We are all Africans: what mtDNA and Y chromosome mutations reveal about human origins and migrations

Gyan Bhanot

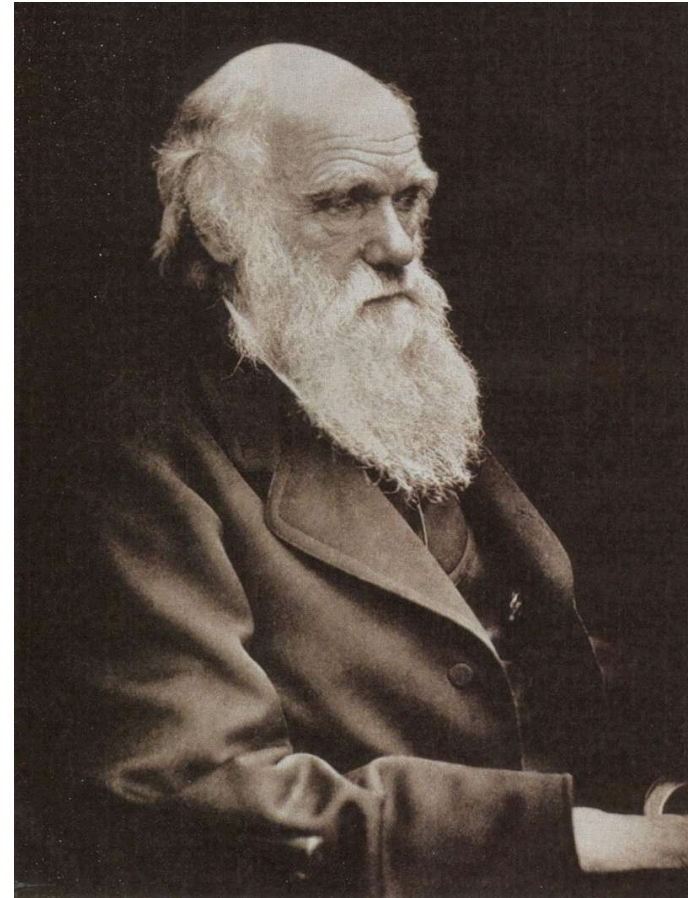
*Rutgers University
Cancer Institute of New Jersey
Institute for Advanced Study, Princeton*

gyanbhanot@gmail.com

*University of Hawaii 03/20/2008; Brown University 03/31/2008, Bar Ilan Hebrew University 09/11/2008,
Cornell University, 10/16/2009*

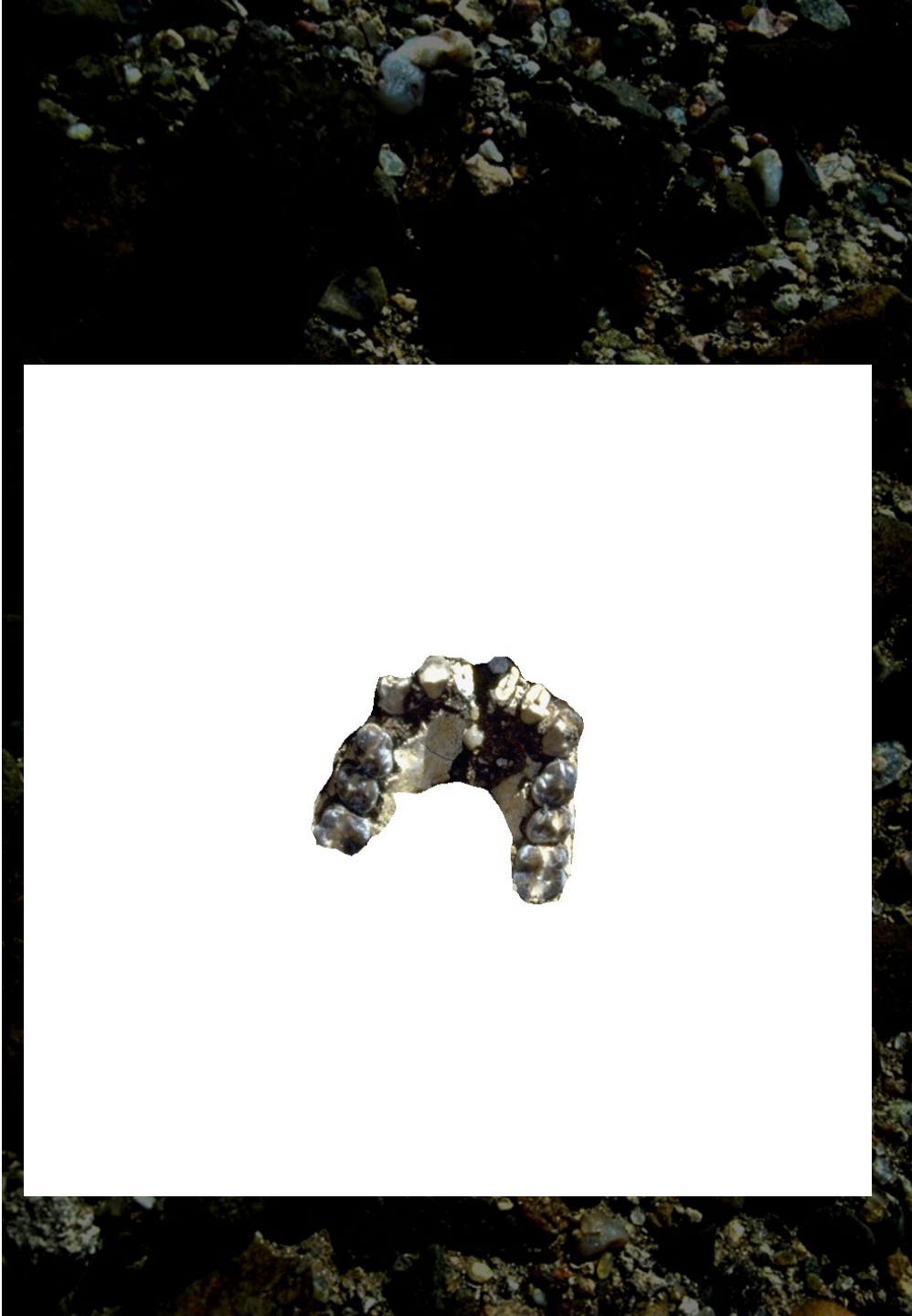
Nothing in Biology Makes Sense Except in the Light of Evolution

Theodosius Dobzhansky (1900-1975)

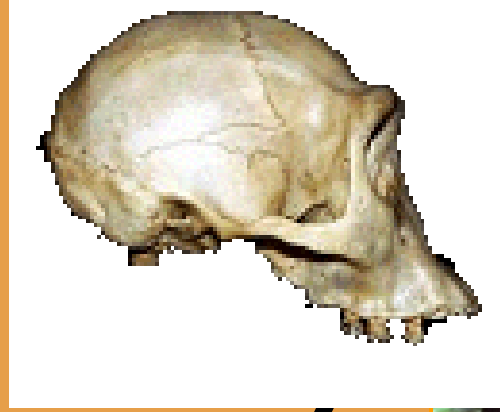


Inferences from Fossils









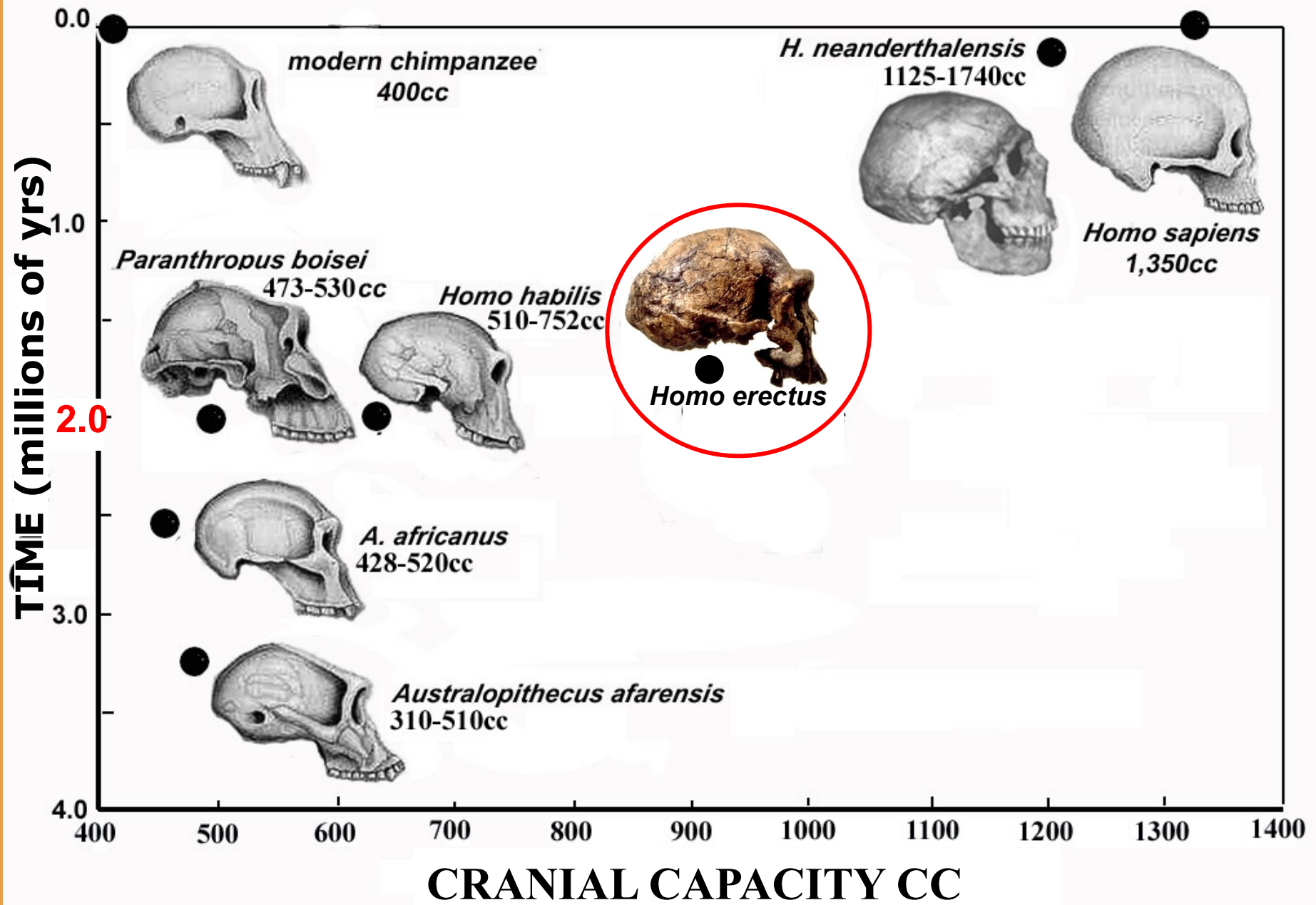
Homo sapiens

chimps & bonobos

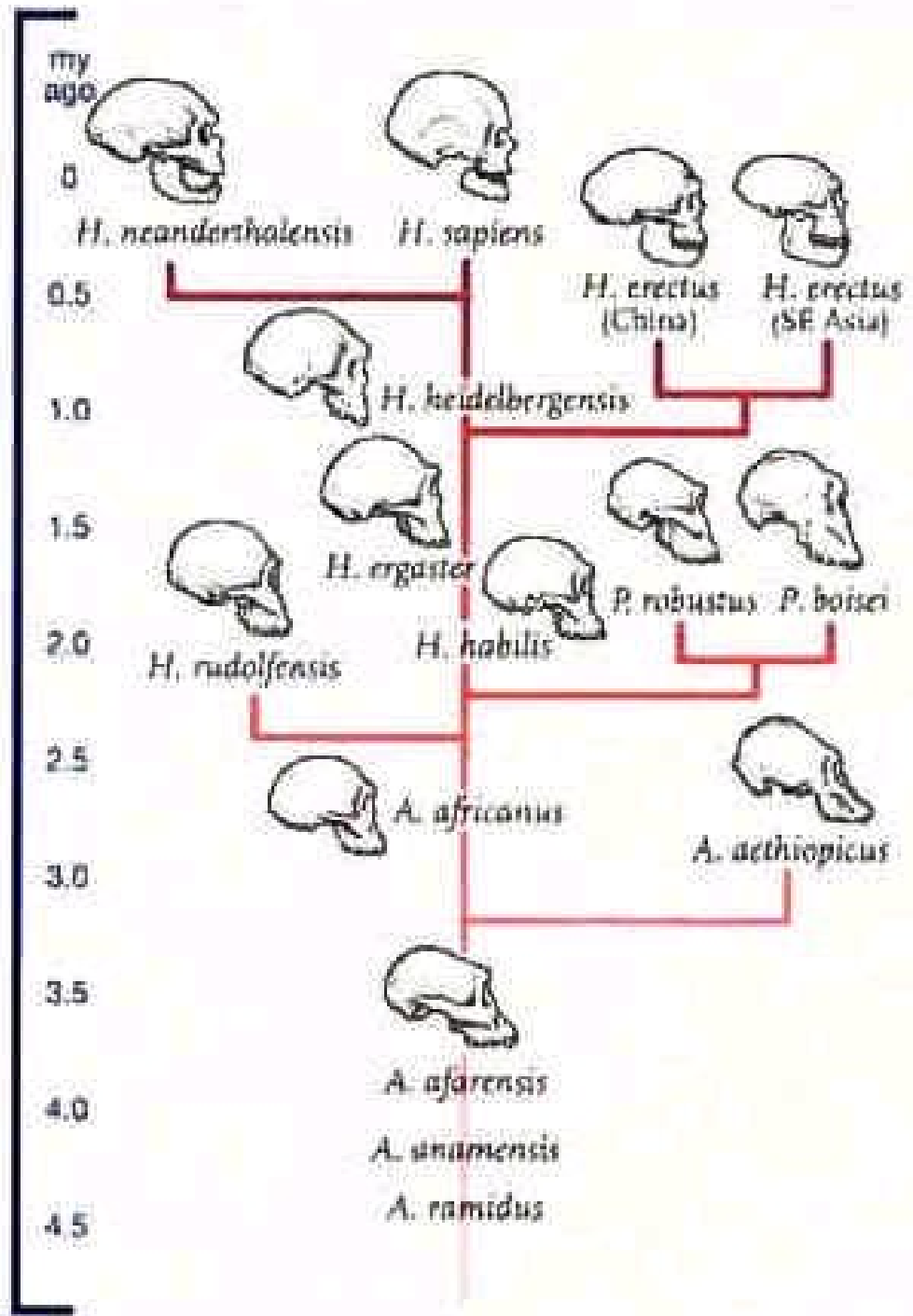
TMRCA = 5 MYA



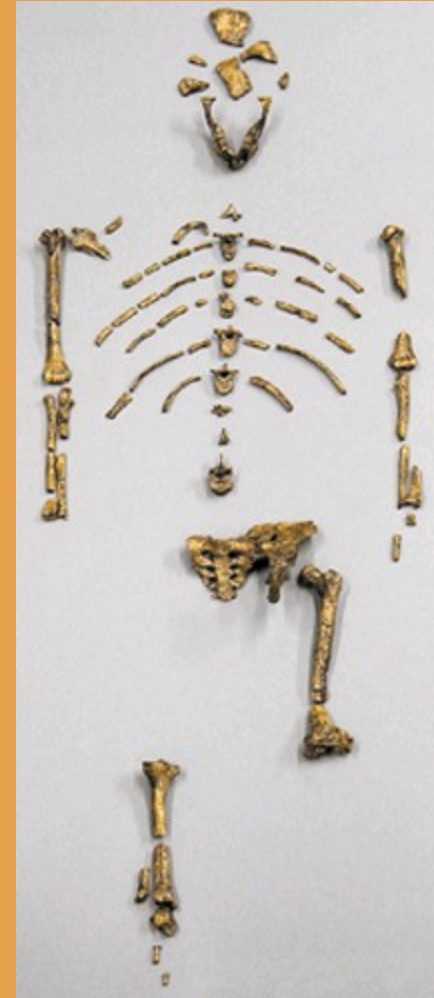
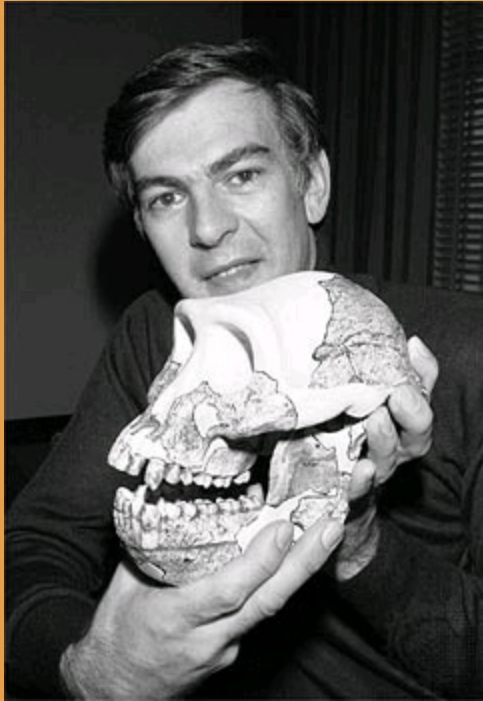
Courtesy of Meave Leakey



CRANIAL CAPACITY CC



Donald Johanson and “Lucy”



D. Johanson:

‘Lucy: The Beginnings of Humankind’

R. Leakey, R. Lewin:

‘People of the Lake: Mankind & Its Beginnings’

Every creature alive today had
ancestors

Not all fossils had descendants

How Evolved are YOU?

- True or False?
 - The first living organisms were like bacteria
 - The Coelacanth is the living fossil of the first four limbed vertebrate
 - Humans evolved from chimpanzees
 - Modern hunter-gathers resemble humans before the advent of agriculture
 - The Basque are a paleolithic relict population
 - The Australian aboriginals are like the original people that migrated “Out of Africa” 50-70 kybp.
- **ALL ARE FALSE !**
- **Fallacy of the Contemporary Ancestor:**
 - Misguided anthropocentric view regards humans as the pinnacle of evolution. ***Evolution has no direction or goal !***
- If evolution = genetic change, humans are **less** evolved than monkeys or mice - they have lower genetic diversity (**and perhaps “civilization” is driving them to phenotypic identity as well**)

Fallacy of Linear Evolution

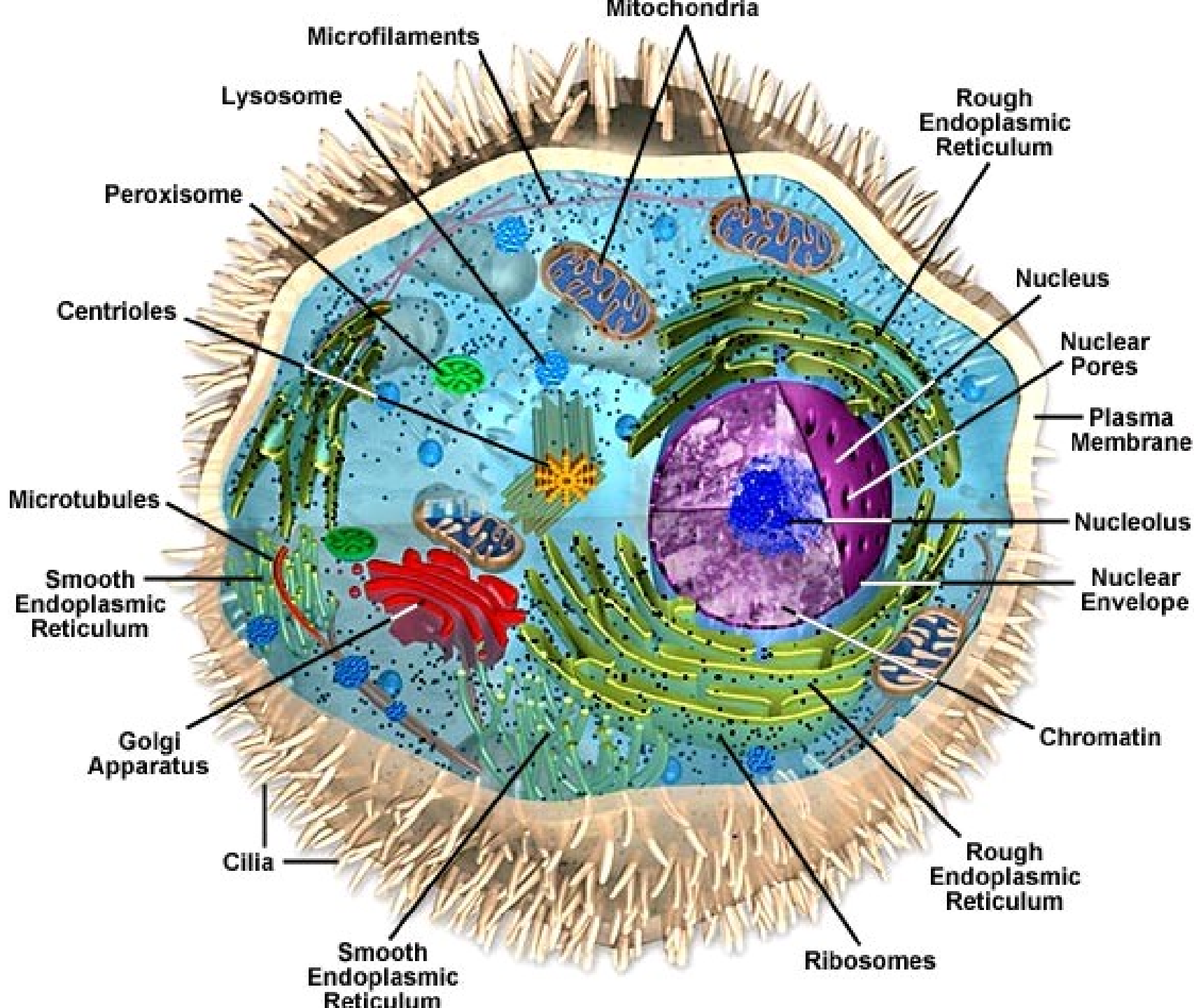
- Examples of Stupid & Dangerous questions:
 - What is the genetic basis for low IQ?
 - Which languages/species are the “most evolved”?
 - What is the ancestral biological homeland of population X?
 - Genetic diversity cannot be traced to a single time and place.
Different segments of genome converge to different ancestors.
 - Nordic people have Irish mtDNA. Are they Irish?
 - Where did my ancestors live, a thousand years ago?
 - After n generations, we have 2^n ancestors.
 - n=30 (600-900 ybp): Ancestors $\sim 10^9$
 - n=40 (800-1200 ybp): Ancestors $\sim 10^{12}$
 - **OUR ANCESTORS LIVED EVERYWHERE !**

Inferences from Genetics

Sequencing cost: 6 Giga Bases = 2 human
genomes = \$10,000

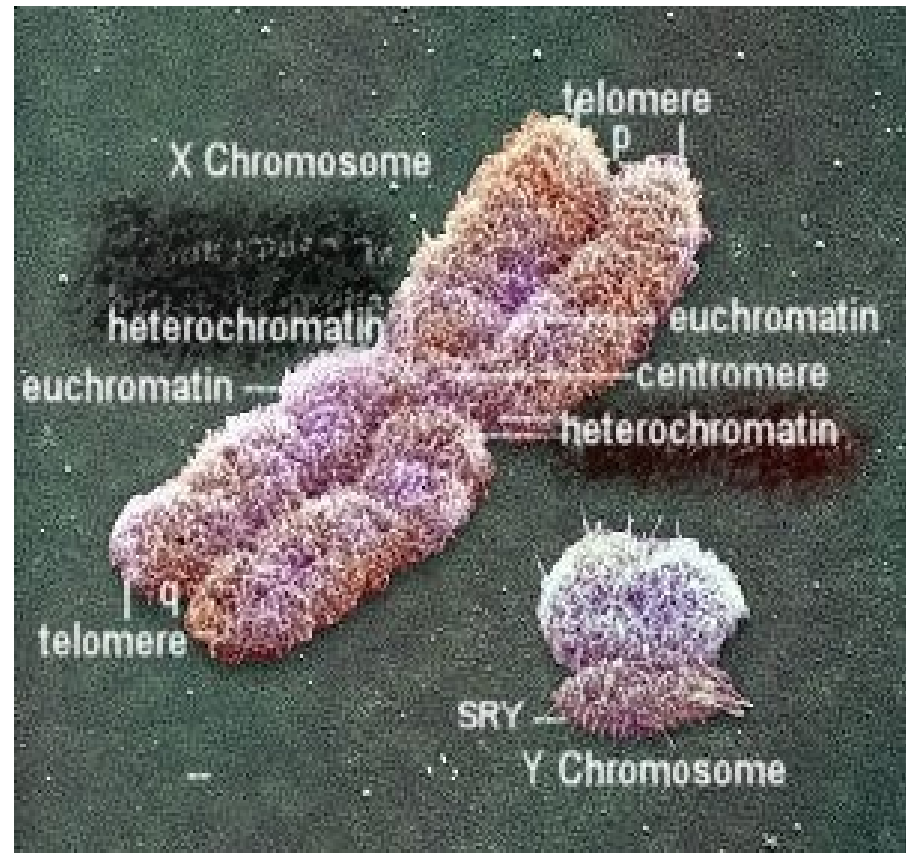
Biology 101

- Life starts as a single cell with 46 chromosomes, 23 from the female egg and 23 from the male sperm
- The cell divides and differentiates into $\sim 10^{13}$ - 10^{14} cells (our bodies).
- We regenerate our bodies ~ 500 fold in a lifetime: 10^7 new cells per second !
- Cells multiply by Mitosis : [demo](#)
- Meiosis produces germ line cells: [demo](#)

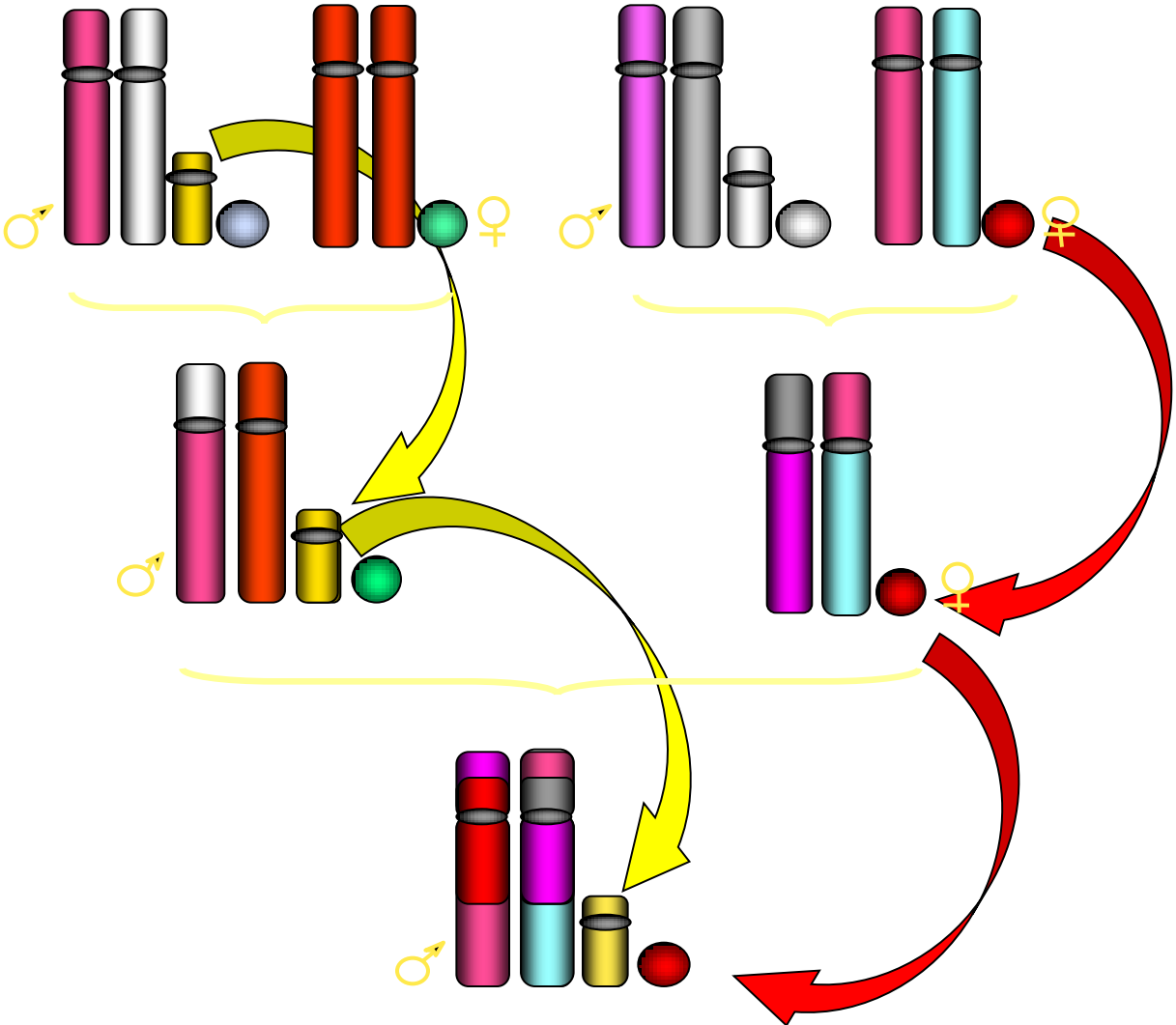


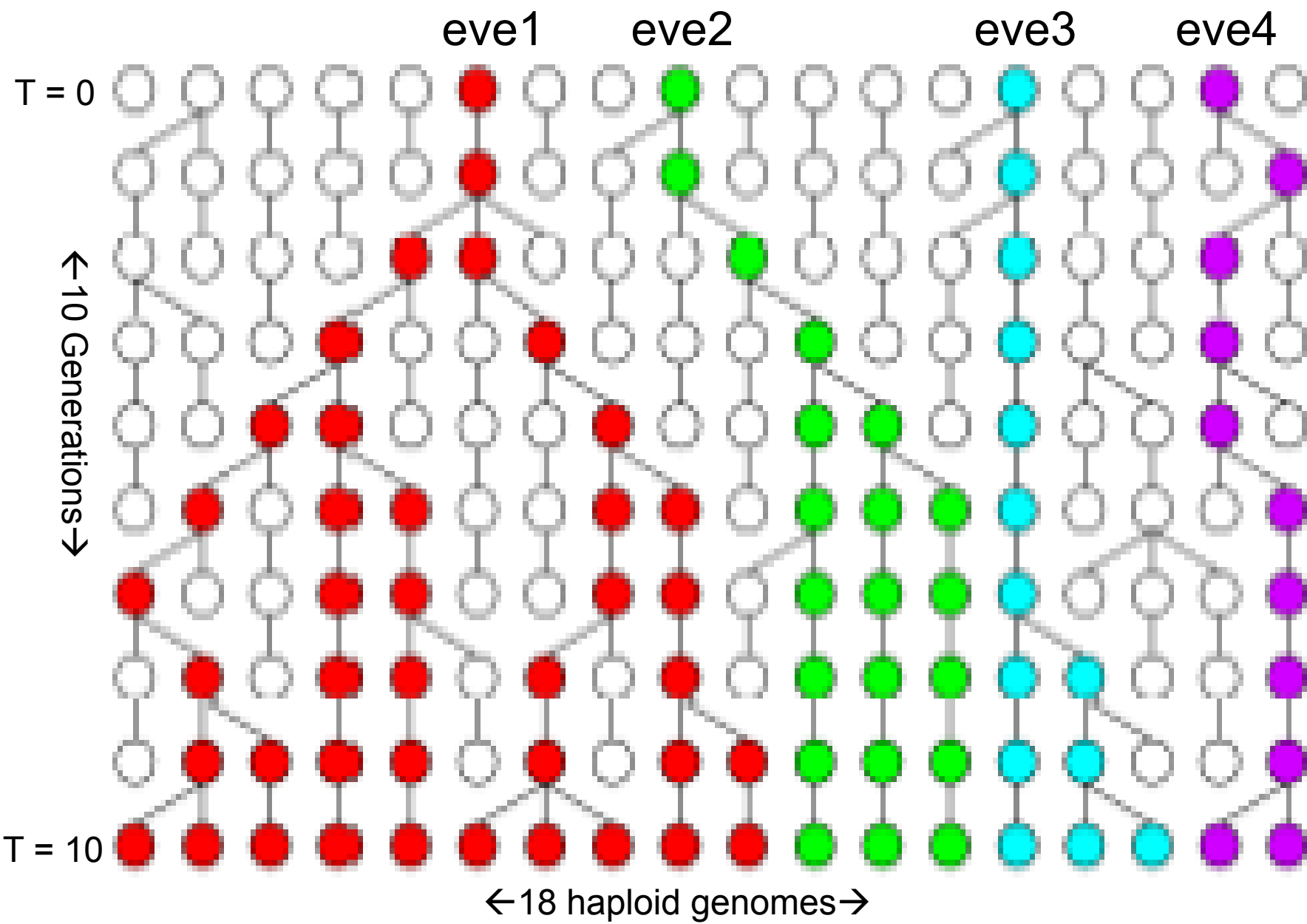
The Human Y Chromosome

- ~58 MB, paternal inheritance, 90% non-recombining
- few coding genes
- Palindromic, self recombination in male meiosis.
- Few variants (~5000)
- Derived from X about 300,000,000 years ago.



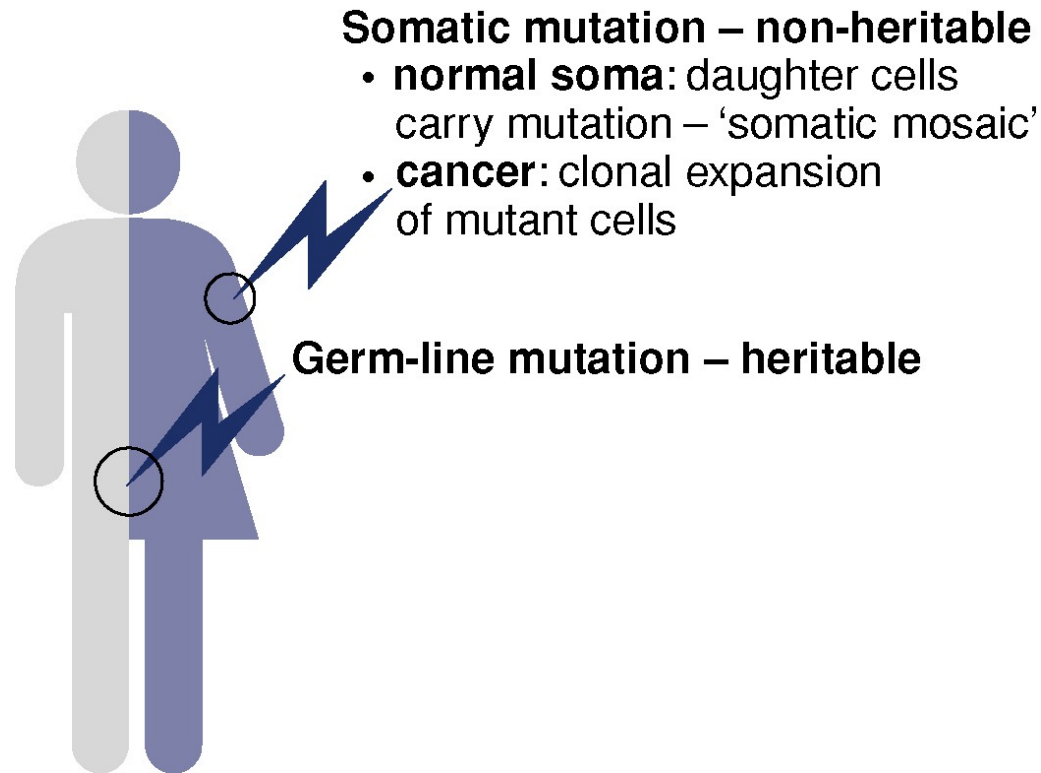
Uniparental Inheritance of Y & mtDNA



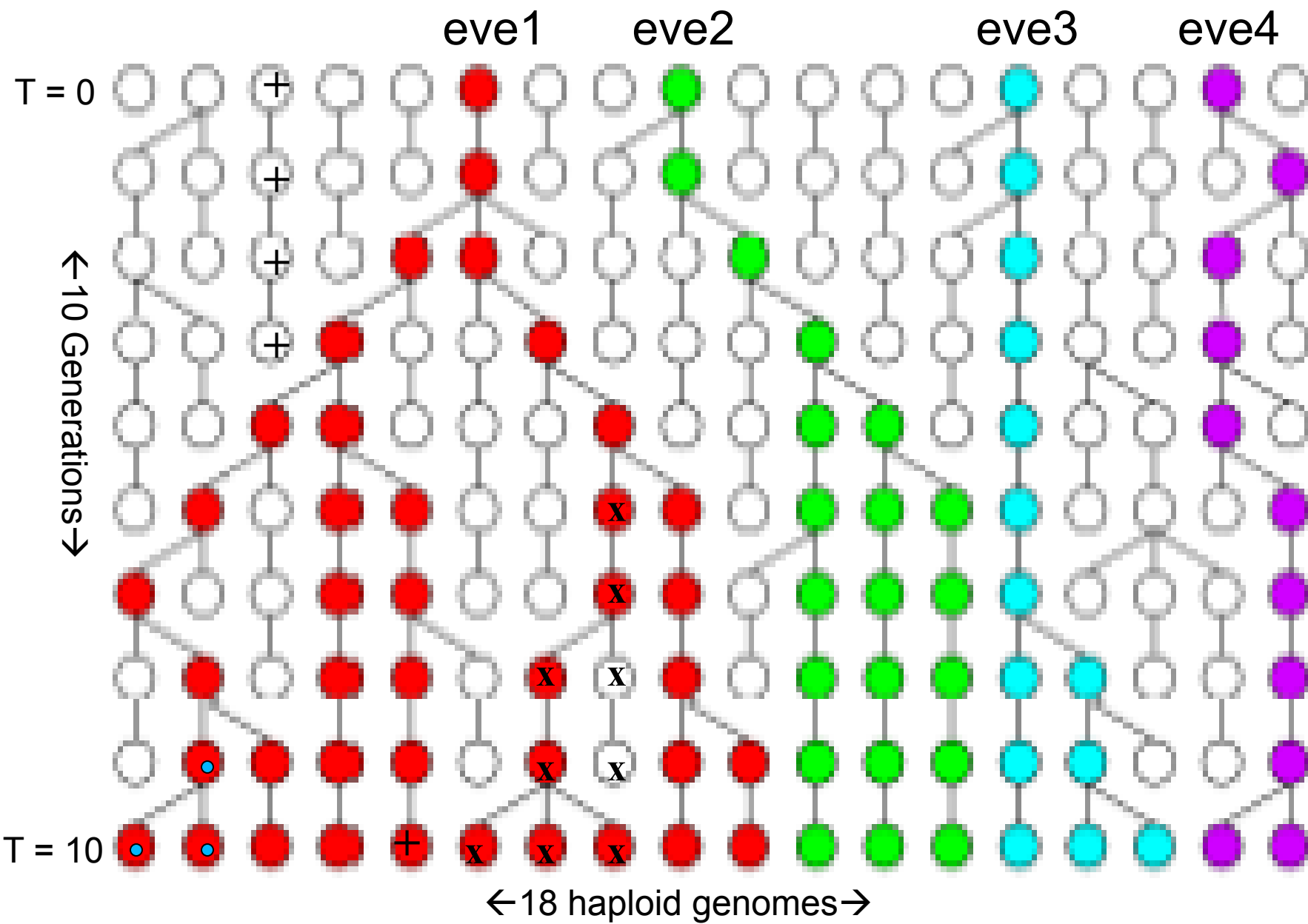


Mutations mark the tree of evolution

Scientists try to read this record !

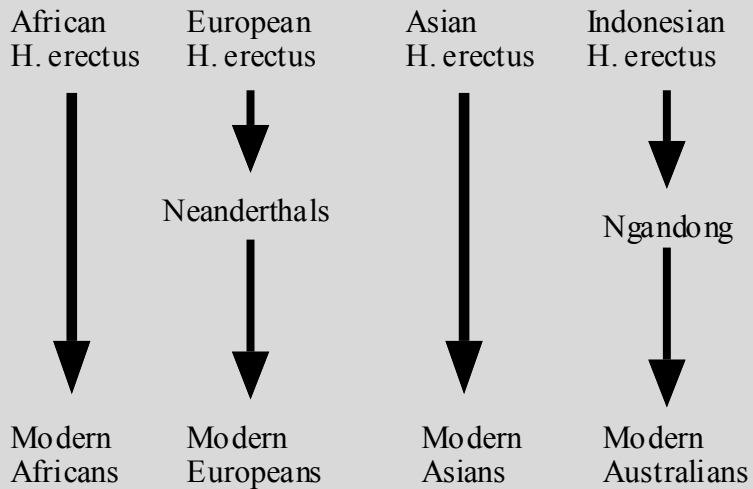


Mutation clues

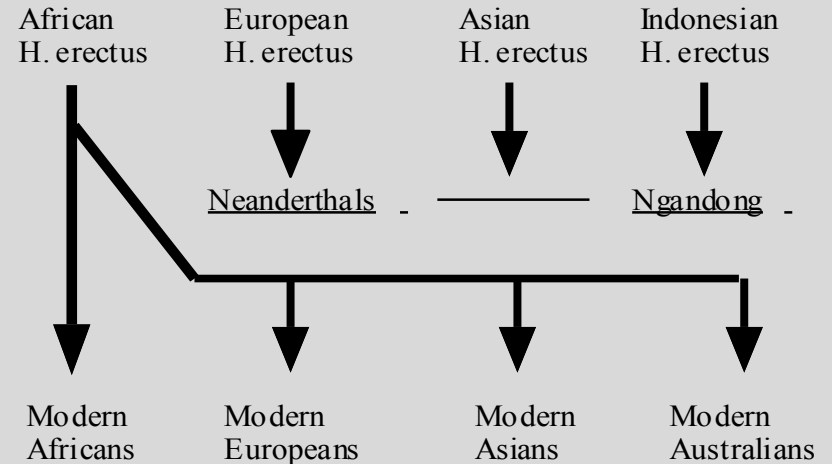


Two Main Models of Human Evolution

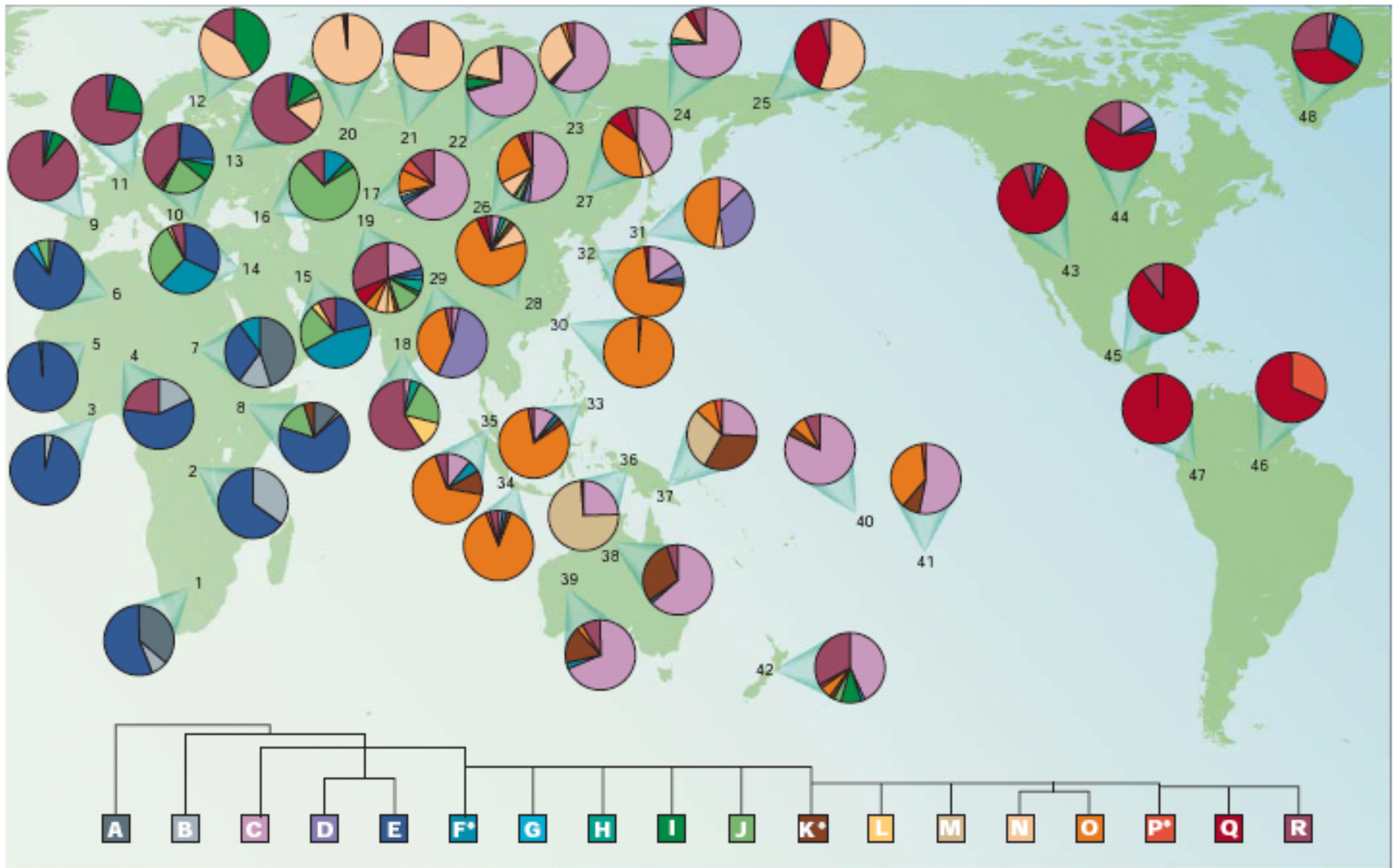
MULTIREGIONAL HYPOTHESIS



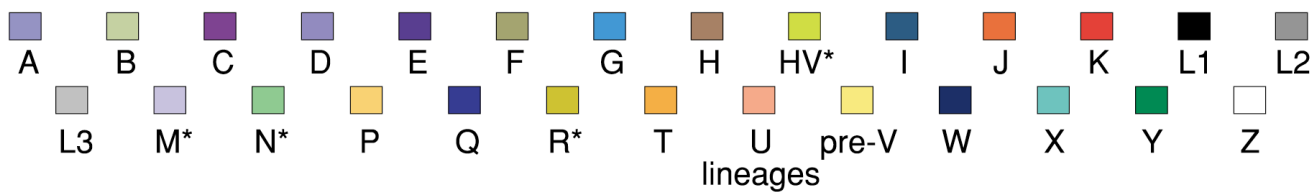
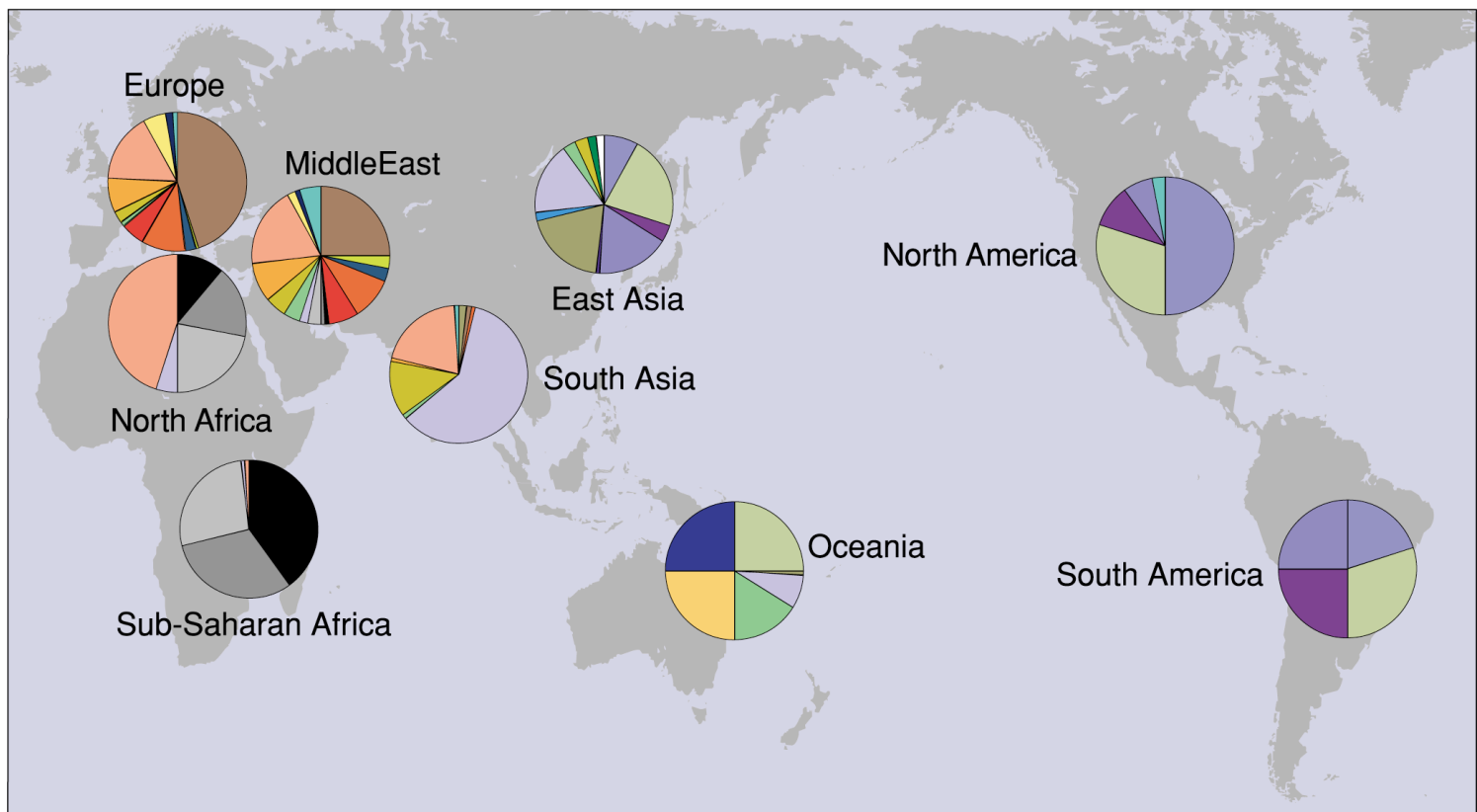
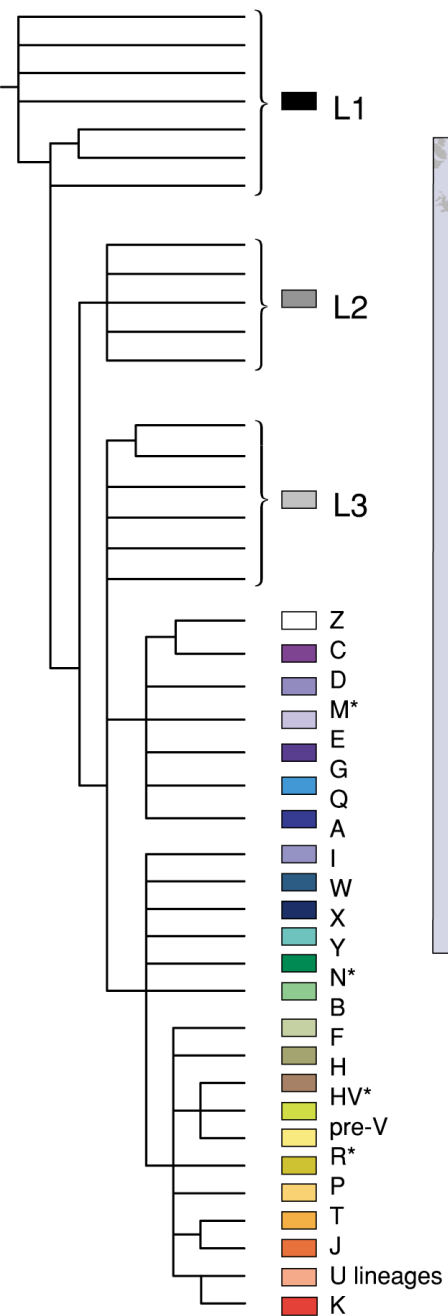
OUT-OF-AFRICA HYPOTHESIS



Distribution of Y Chr Groups



mtDNA haplogroup distribution






A LANDMARK STUDY OF THE HUMAN JOURNEY

Who was **your** first ancestor? New DNA studies say that all humans descended from an African ancestor who lived only 60,000 years ago. Uncover the specific paths that led from him to you—the ultimate human history, as written in our genes.

INTERACTIVE ATLAS OF THE HUMAN JOURNEY
EXPLORE THE ATLAS ►

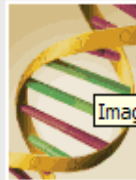
YOUR GENETIC JOURNEY



Explore your own genetic journey with Dr. Spencer Wells. DNA analysis includes a depiction of your ancient ancestors and an interactive map tracing your genetic lineage around the world and through the ages.

Interested in learning more? Find out **how to become part of the Genographic Project** and discover your own deep ancestry.

GENETICS OVERVIEW



The human story is written in our genes. **Image: DNA Strand** and explore the basics of genetics, from chromosomes and DNA to natural selection and genetic drift.

NEWS

- **Global Gene Project to Trace Humanity's Migrations**
- **Project Receives Approval From University Review Board**

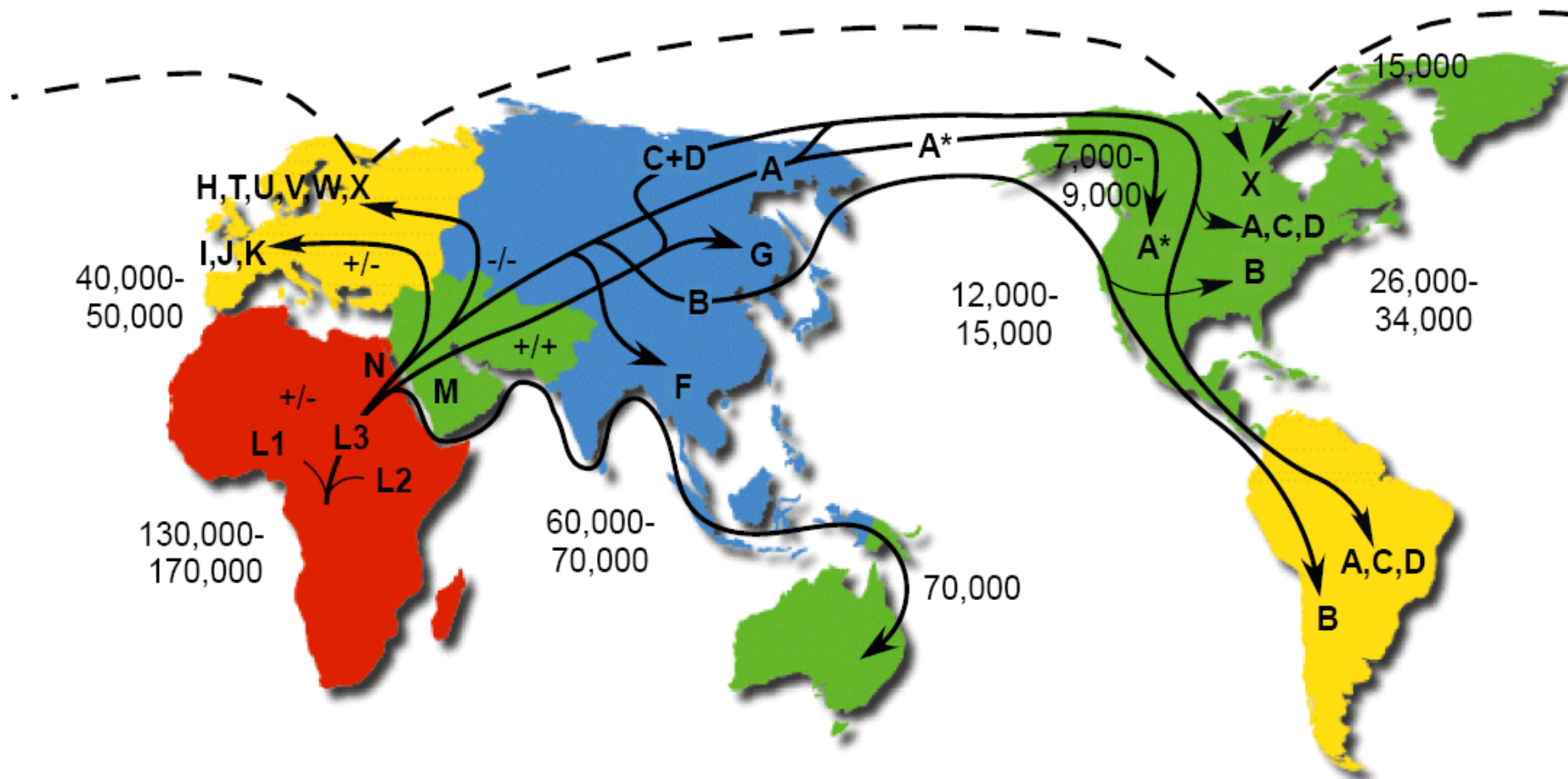
ALSO SEE

Video: Indigenous Representatives Talk About Their Migratory Histories (Download Windows Media)

Human mtDNA Migrations

<http://www.mitomap.org/mitomap/WorldMigrations.pdf>

Copyright 2002 © Mitomap.org



+/-, +/+, or -/- = Dde I 10394 / Alu I 10397
* = Rsa I 16329

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

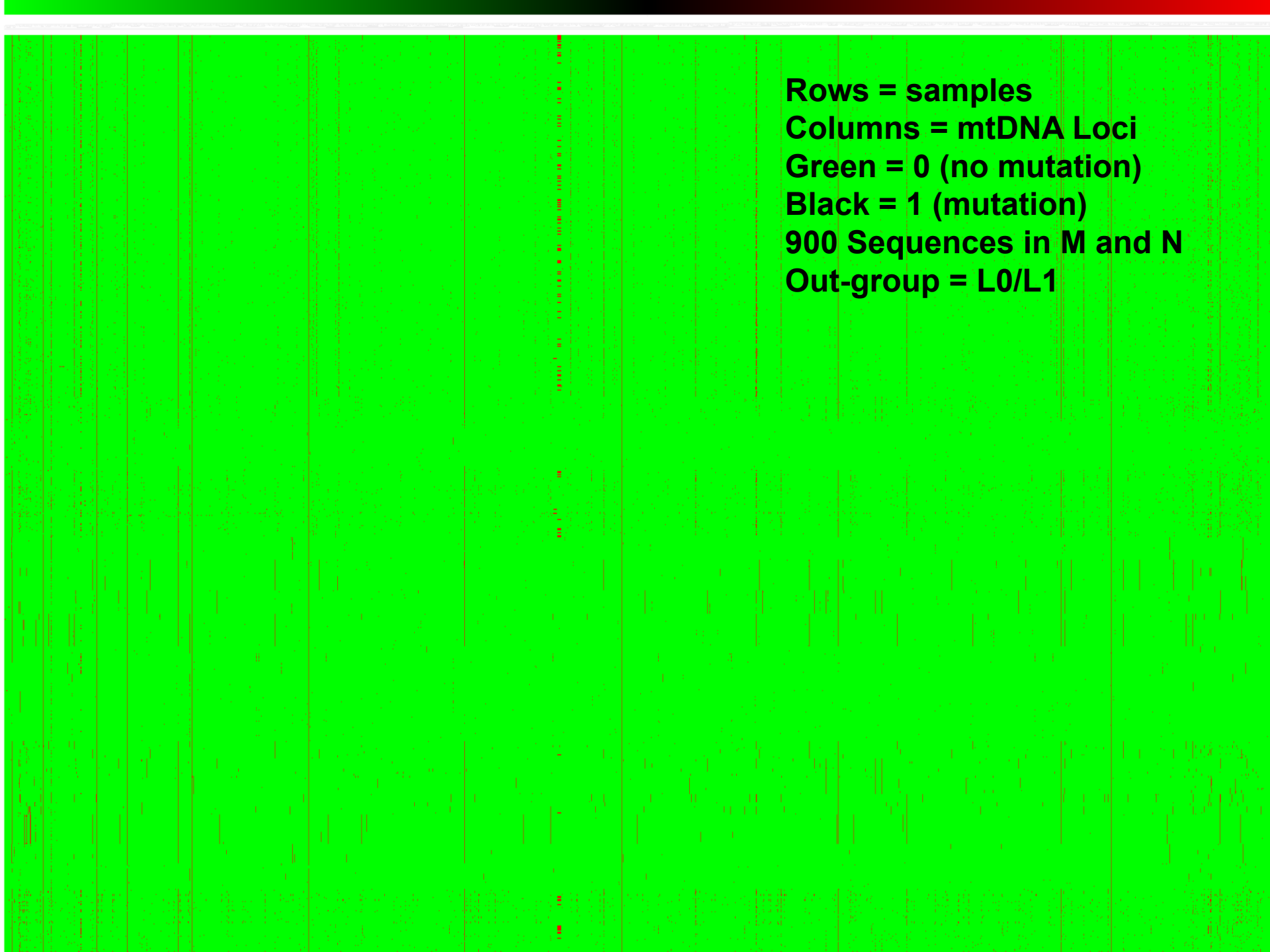
Geographic Location of MRCA of Selected Loci

Chr 11	β Globin 2670 b Hemoglobinopathies	326 Samples	African root	Harding et al 1997
Chr 18	LPL 9734 b Cardiovascular Diseases	71 Samples	Africa and elsewhere	Clark et al 1998
Chr 16	MC1R 954 b Skin pigment	356 Samples	Africa and elsewhere	Harding et al
X	PDHA1 4200 b Neurological Diseases	35 Samples	Africa	Harris and Hey, 1999

Table 1. The ethnicities of the mtDNA data analyzed in this study

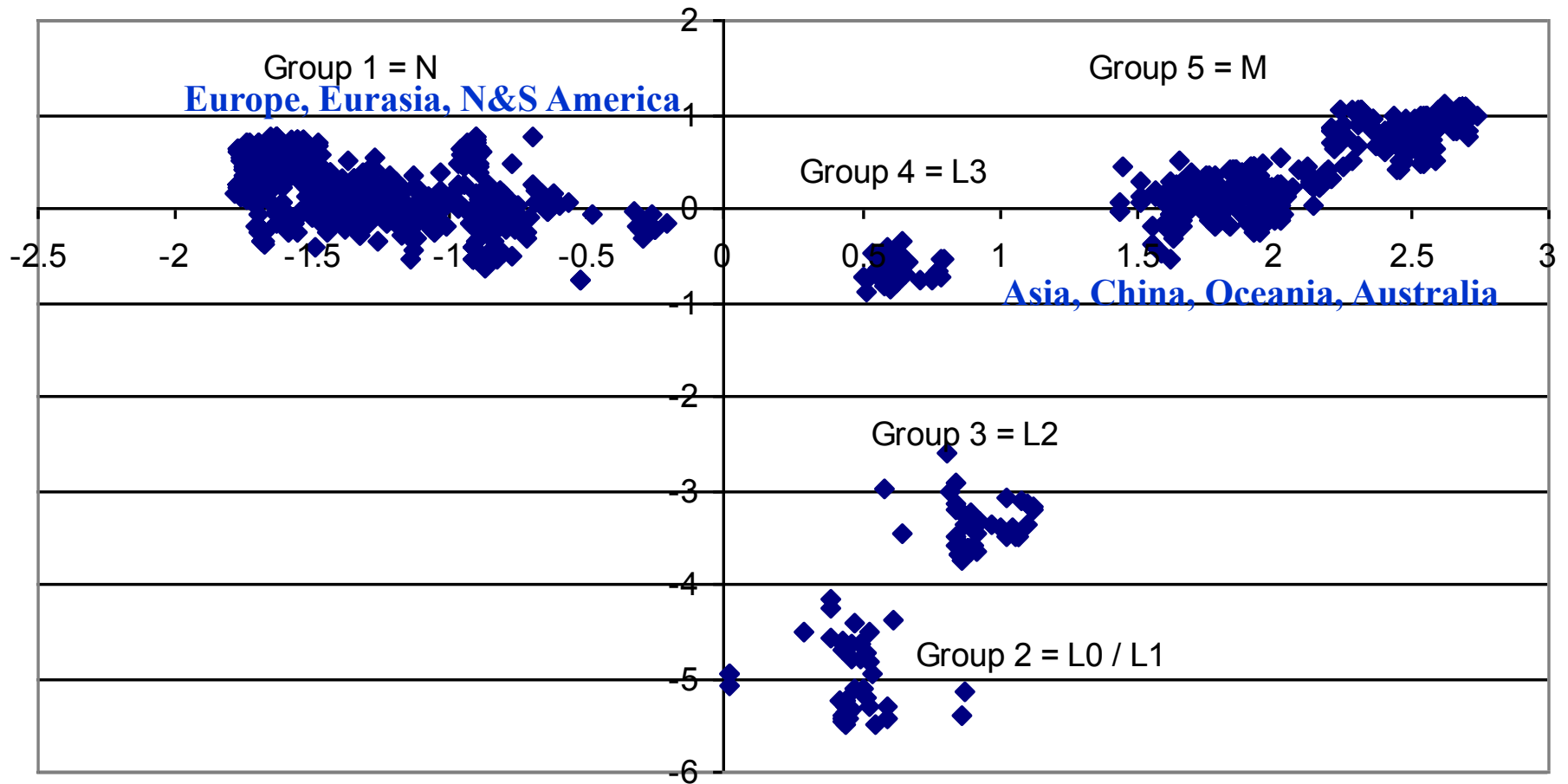
Population	Ethnicity	Size
<i>Africa</i>		146
<i>America</i>		9
<i>Asia</i>	China	50
	India	98
	Japanese	674
	Malaysia	14
	Taiwan	12
	Other areas	86
<i>Australia</i>		48
<i>Europe</i>	Caucasian	258
	Finland	194
	Italy	63
	Other areas	67
<i>Unspecified areas</i>		18
Total		1737

G. Alexe, R. Vijaya-Satya, D. Platt, M. Seiler, T. Bhanot, S. Hui, M. Tanaka, A. Levine, G. Bhanot, ‘Principal Component Analysis and Clustering Reveal Alternate Phylogeny for the N and M Clades’, J of Molecular Evolution, 2008.



Rows = samples
Columns = mtDNA Loci
Green = 0 (no mutation)
Black = 1 (mutation)
900 Sequences in M and N
Out-group = L0/L1

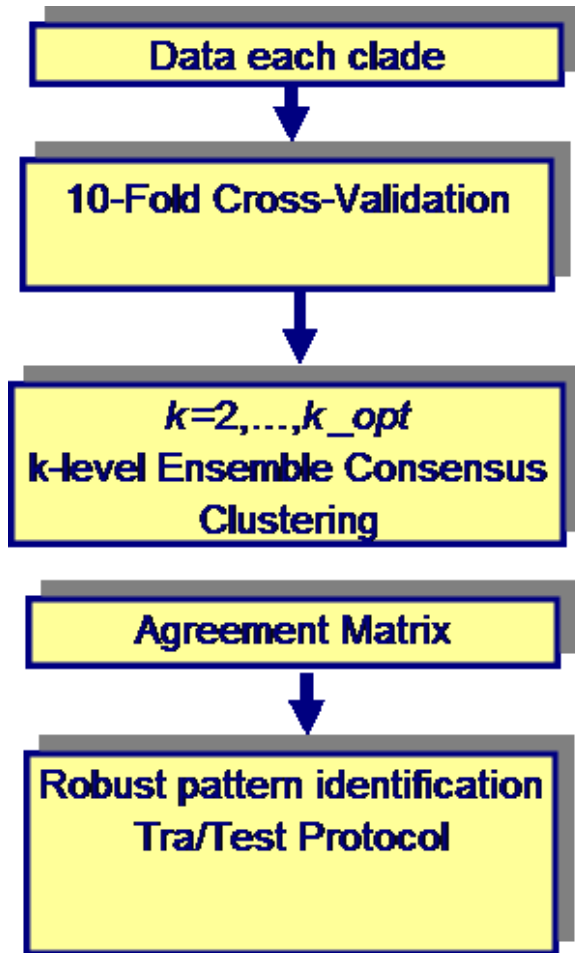
Principal Component Analysis



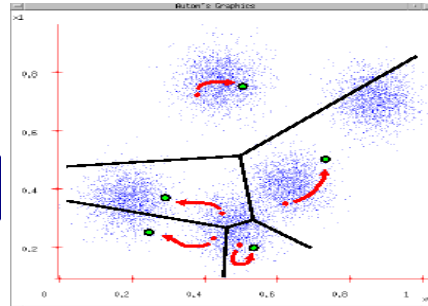
1737 mtDNA sequences

~20% variation

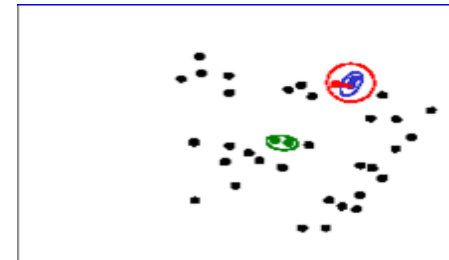
Haplogroups within Clades



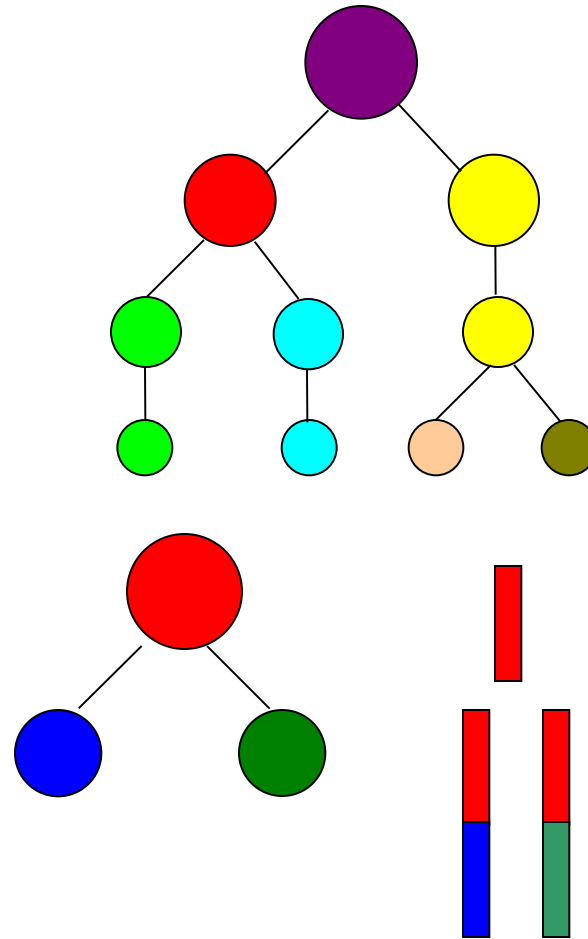
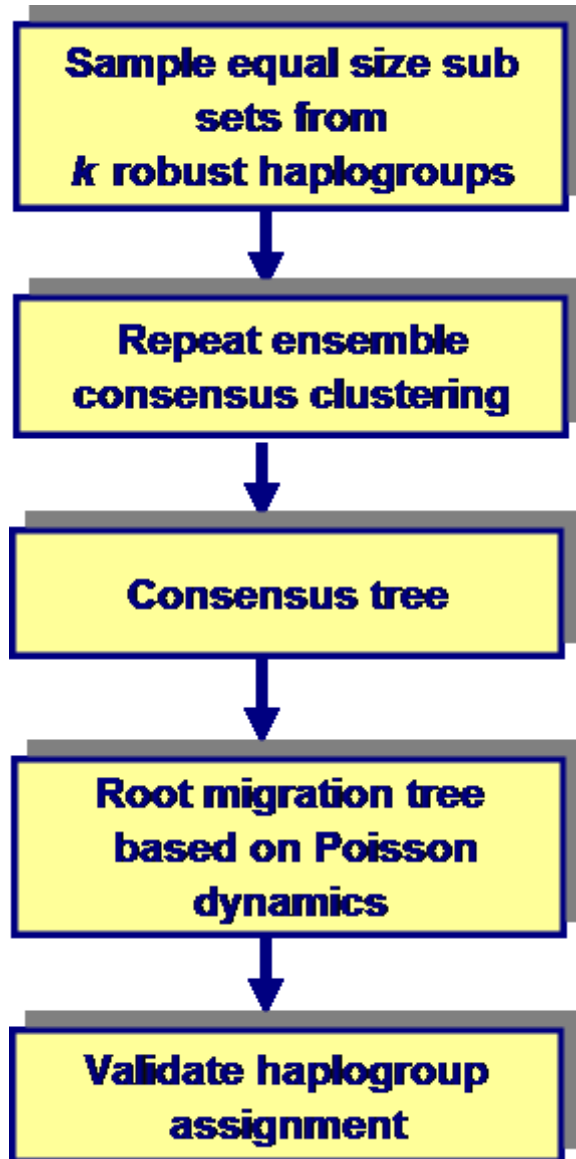
e.g., Partitioning / relocation



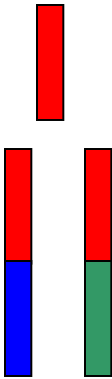
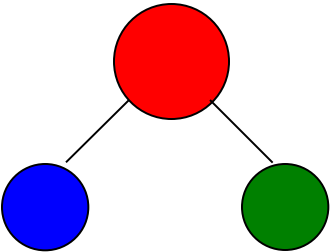
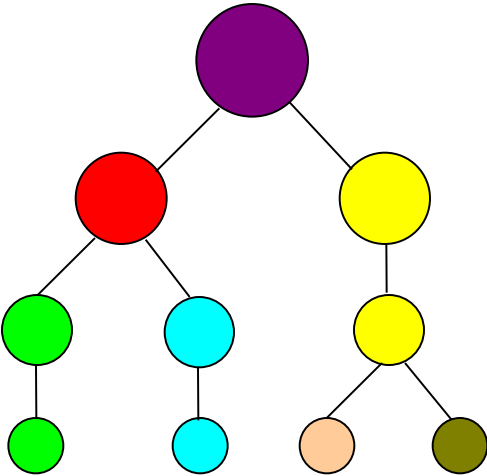
Agglomerative



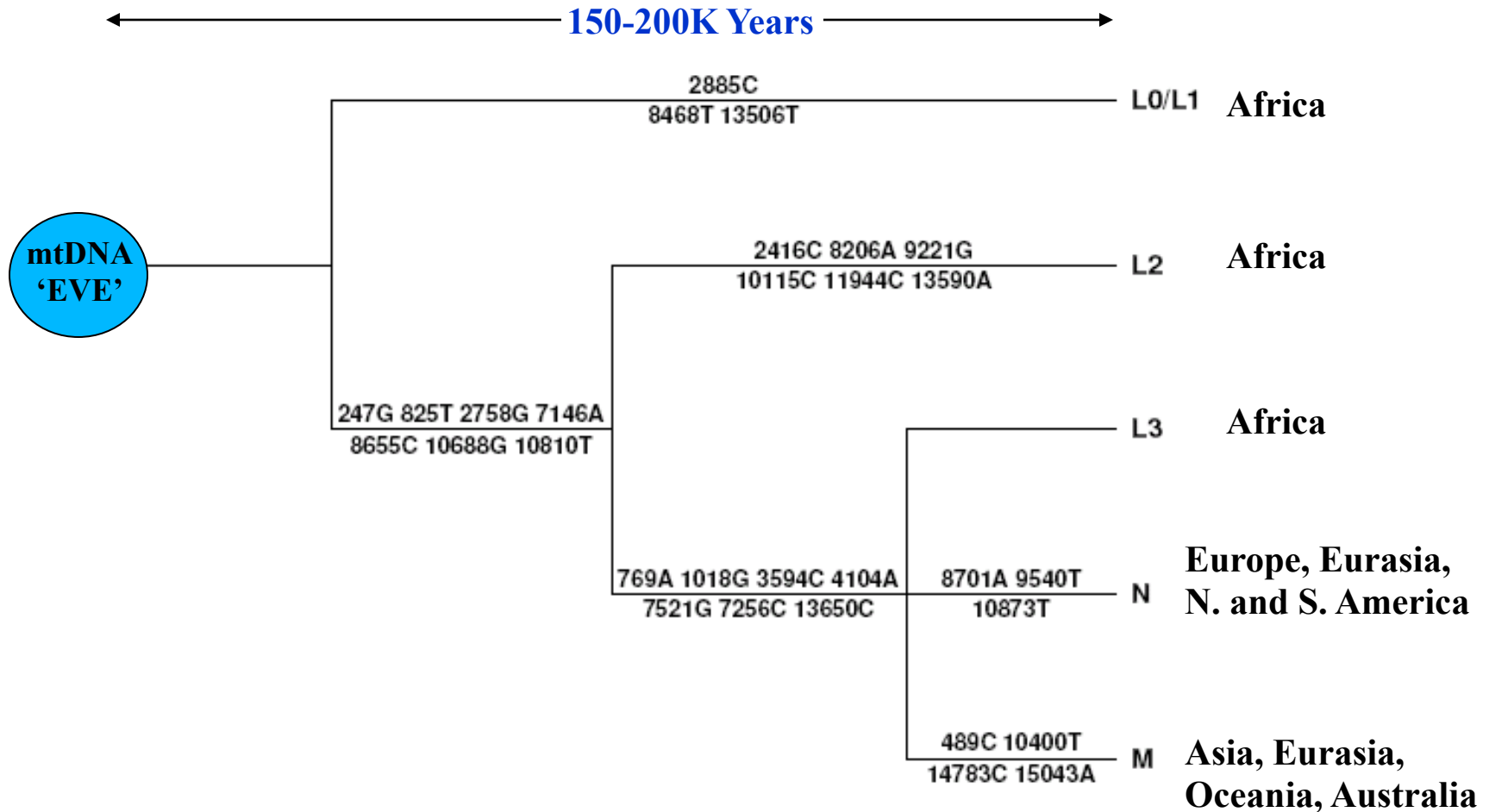
Clustering Reveals tree



Divide the Data into 2,3,4... k_{opt} clusters



Major mtDNA CLADES



Cann et al. (1987) Nature 325(6099):31-6.
 Ingman et al. (2000) Nature 408(6813):708-13
 Alexe et al, 2008. submitted

1-2-3 PCs for N Clade. Note location of B and A/J/T/U/H

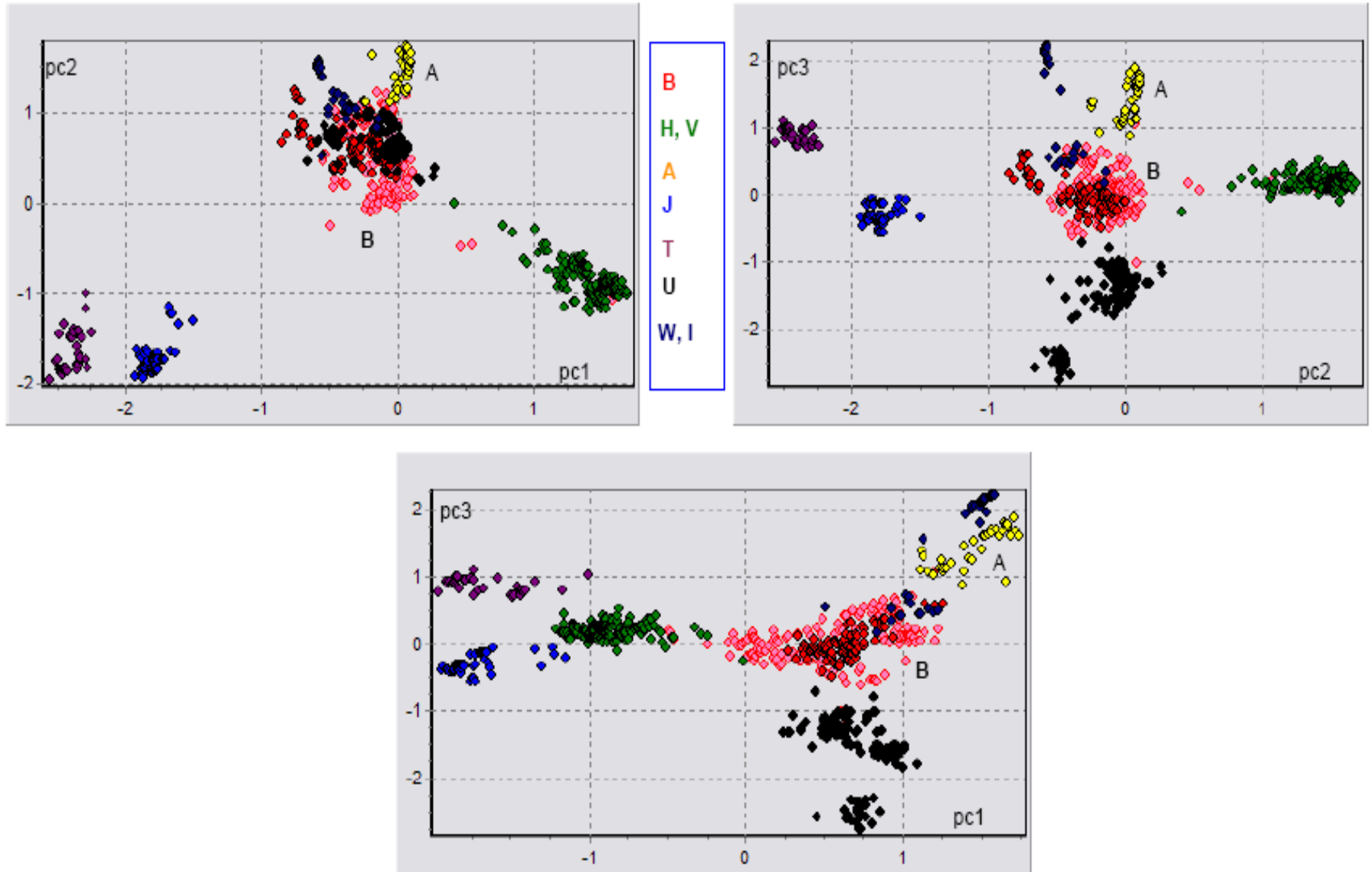
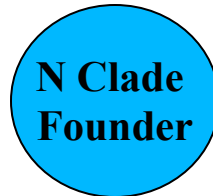


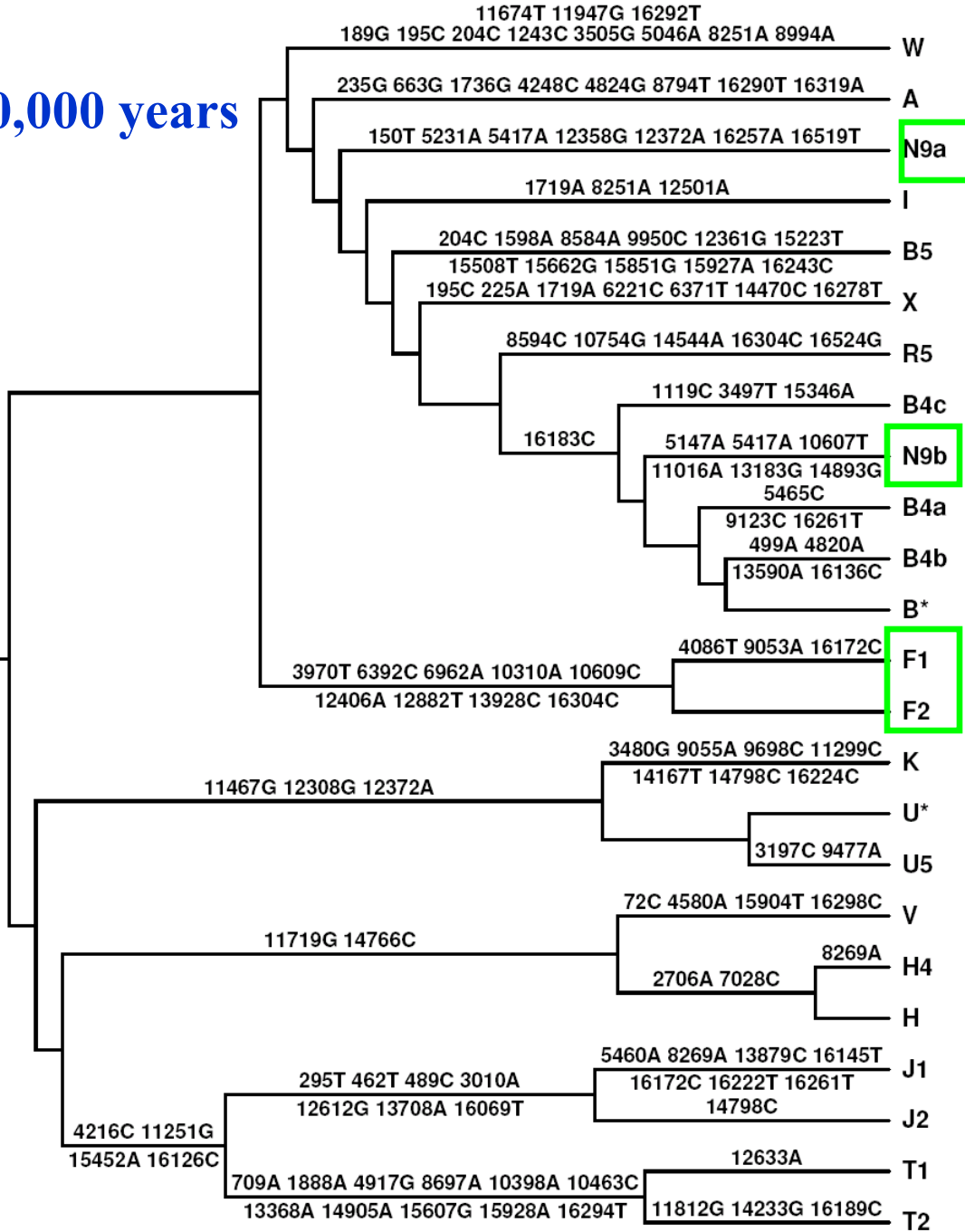
Figure 5a. N-Clade PCA projections. The mnemonic in the middle assigns colors to the haplogroup labels for the samples in this clade. Note that B and A are much closer than B and any of J/T/H/U/V. The inference is that B and A separated later than B and J/T/H/U/V.

N Clade Tree
Time depth ~ 60,000 years

Eastern Migration



Western Migration



Asia, N. & S. America

Europe, Eurasia Americas

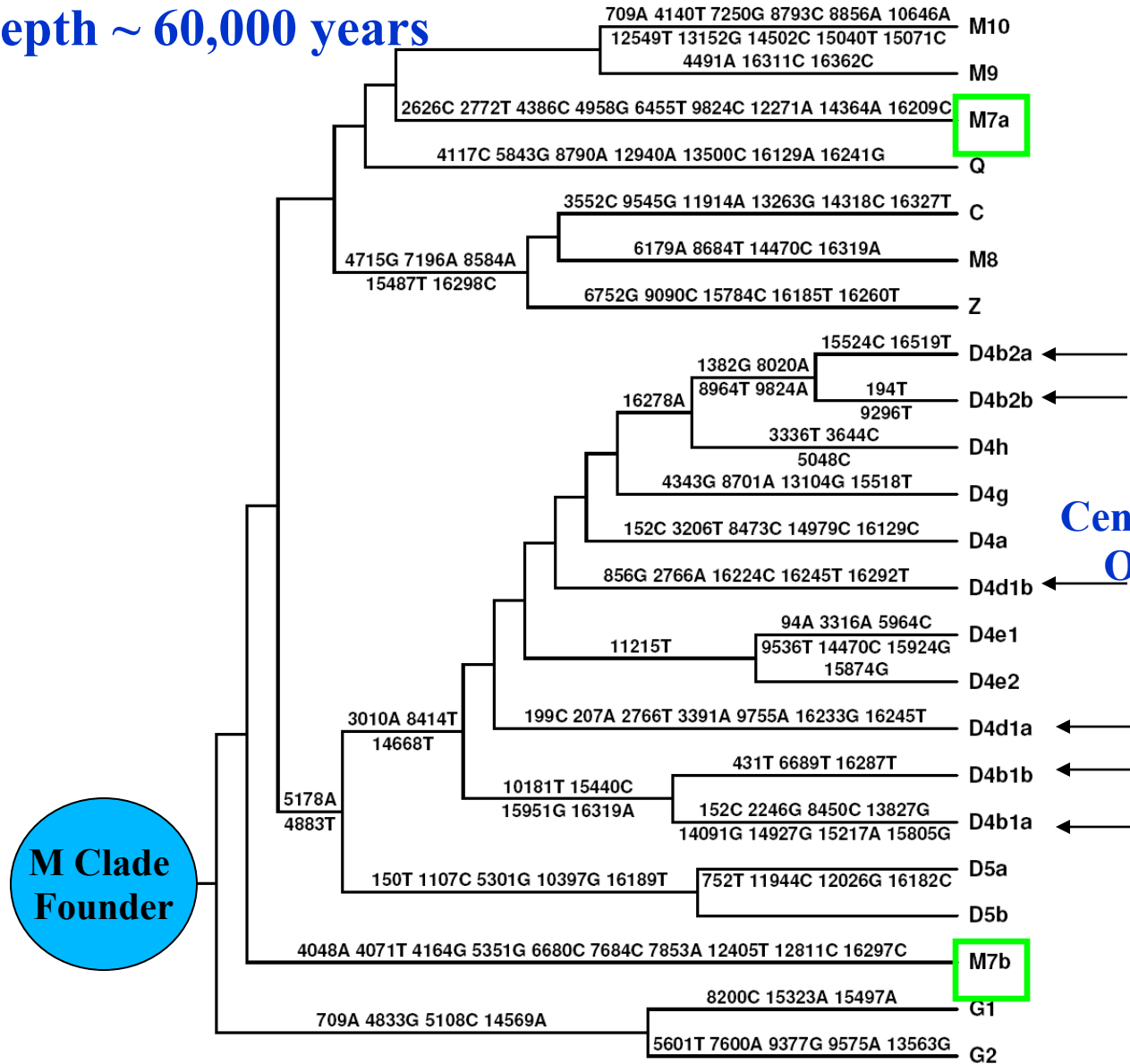
Haplogroup JT → J and T

- **Haplogroup T** originated in Mesopotamia ~ 10,000 ybp and moved northwards. High concentrations around the eastern Baltic Sea.
- **Haplogroup J**: Defined by a mutation ~ 45,000 ybp in the DNA of a woman who lived in the Caucasus region. Further mutations in the J line are identified as J1a1 (27,000 yrs ago), J2a (19,000 yrs ago), J2b2 (16,000 years ago), J2b3 (5,800 yrs ago), etc.
- **Haplogroup J and T associated with the spread of farming and herding in Europe during the Neolithic Era (8,000-10,000 yrs ago). All other West Eurasian-origin groups (H, V, U, K, W, I, X) were previously given to hunting and gathering.**

**SNP 5417, M7a/M7b, homoplasy
Jomon/Yayoi**

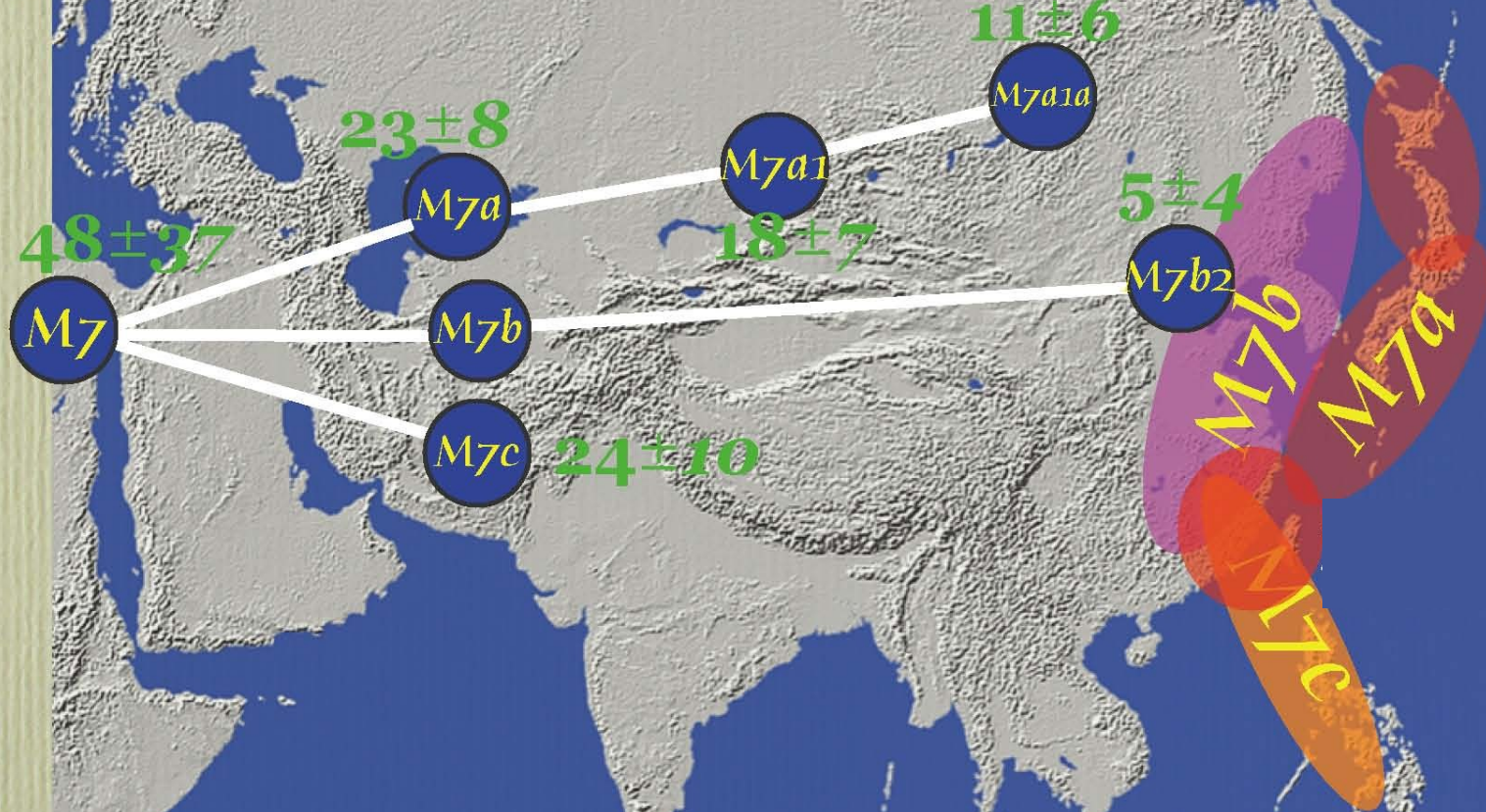
M Clade Tree

Time depth ~ 60,000 years



**Central and South Asia,
Oceania, Australia,
N. & S. America**

SNP 6455 and 9824 in M7a and M7b

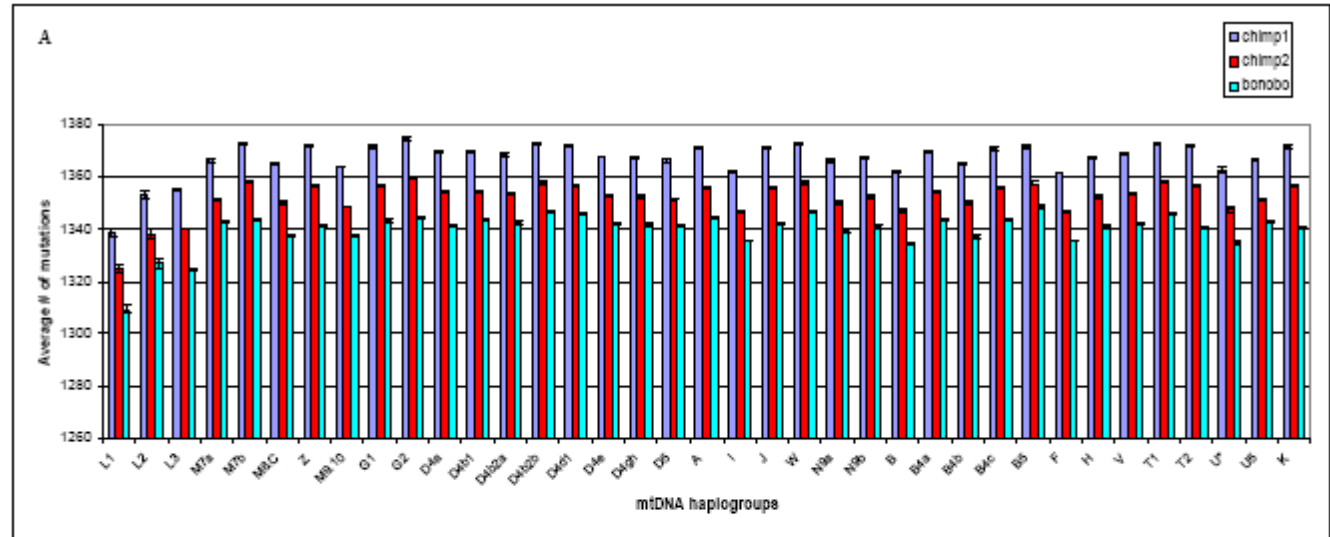


Divergence of haplogroup M7 into subhaplogroups M7a, M7b, and M7c

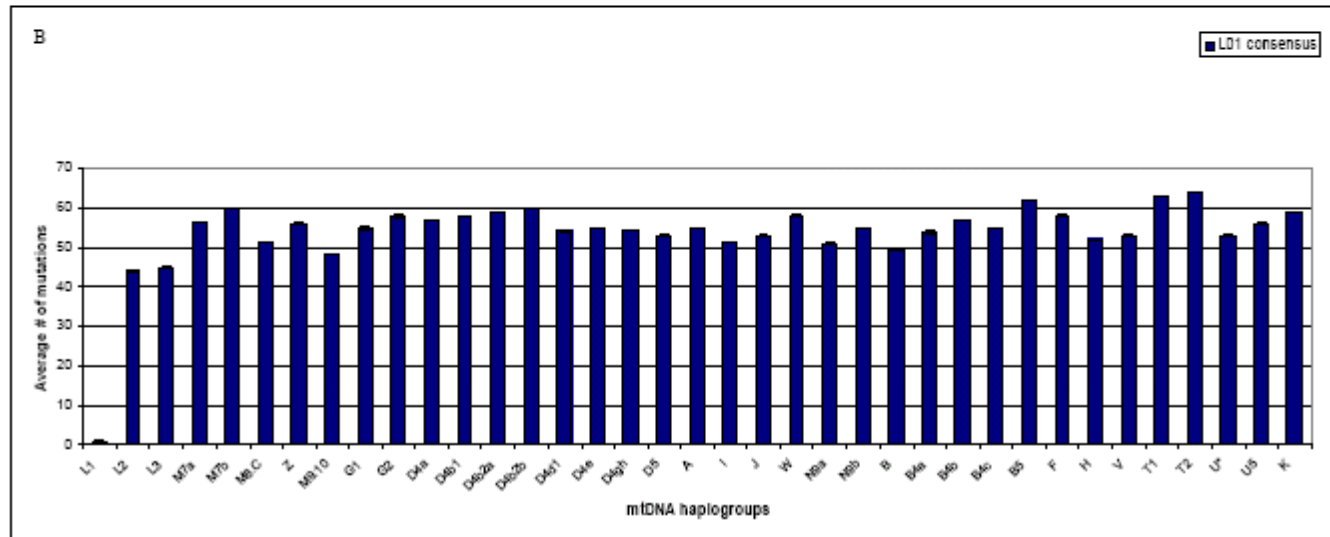
How Long Ago Did 'mtDNA Eve' Live?

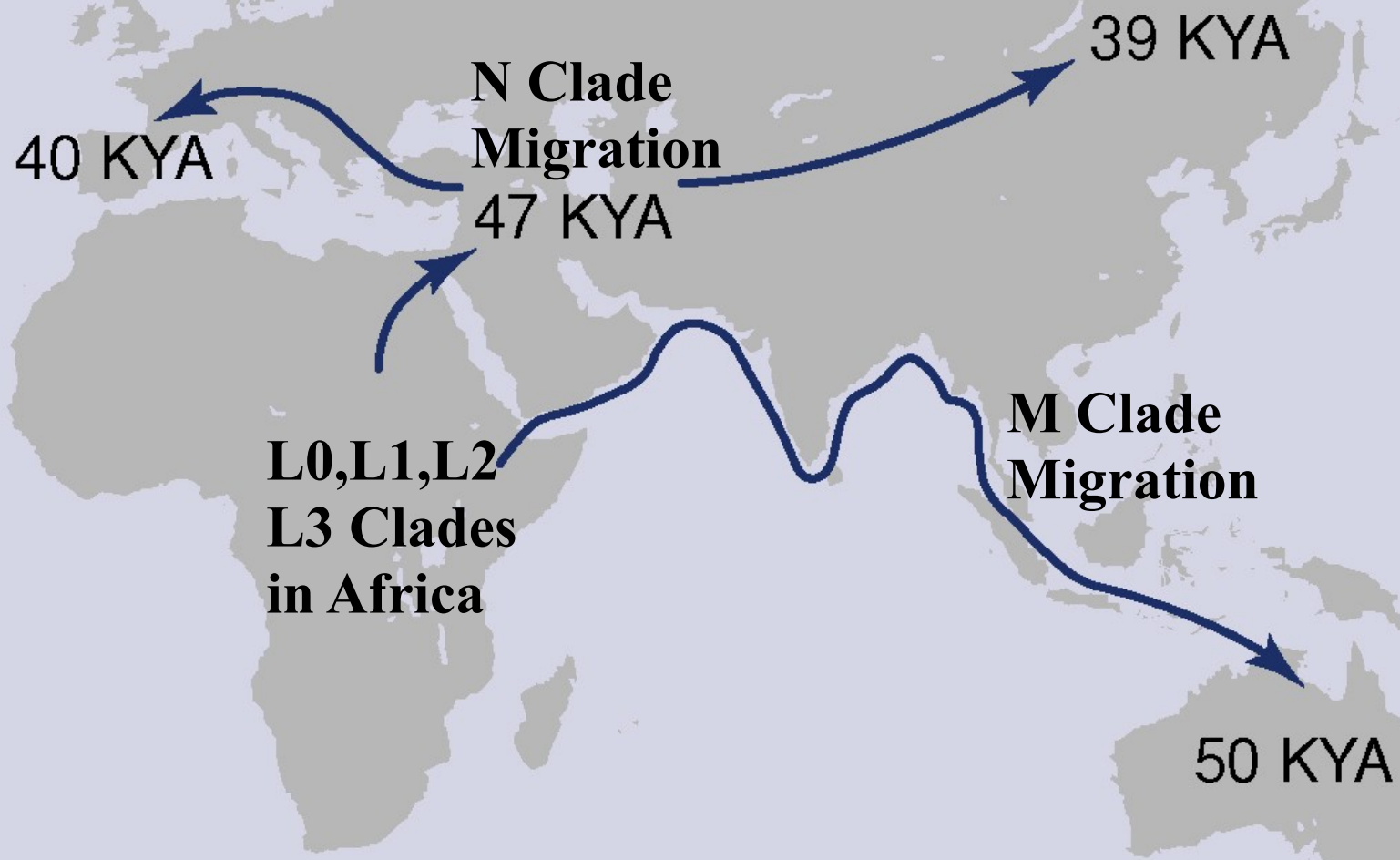
$$T_{H-C}/T_{H-H} = 24.3 \pm 1.7 \rightarrow T_{H-H} = 206K \pm 14K \text{ if } T_{H-C} = 10^6$$

Humans-Chimp/Bonobo

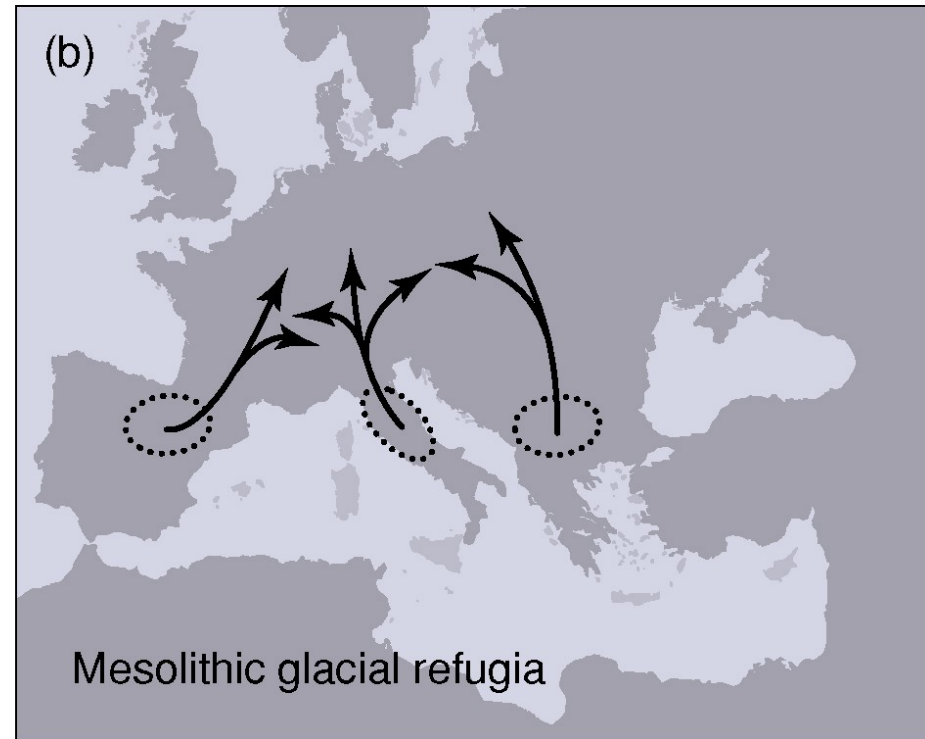
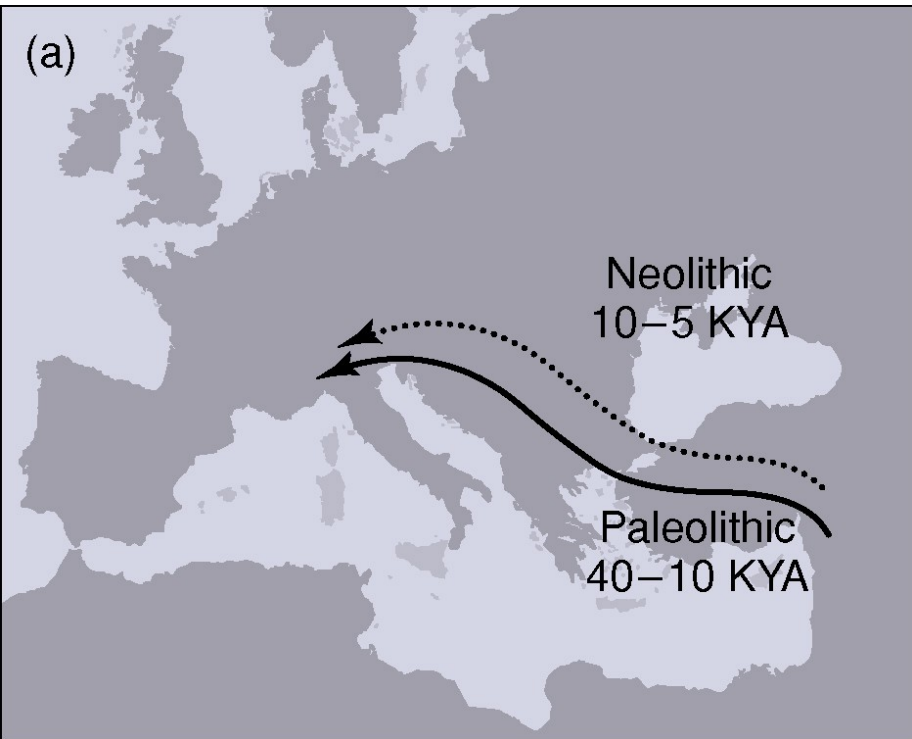


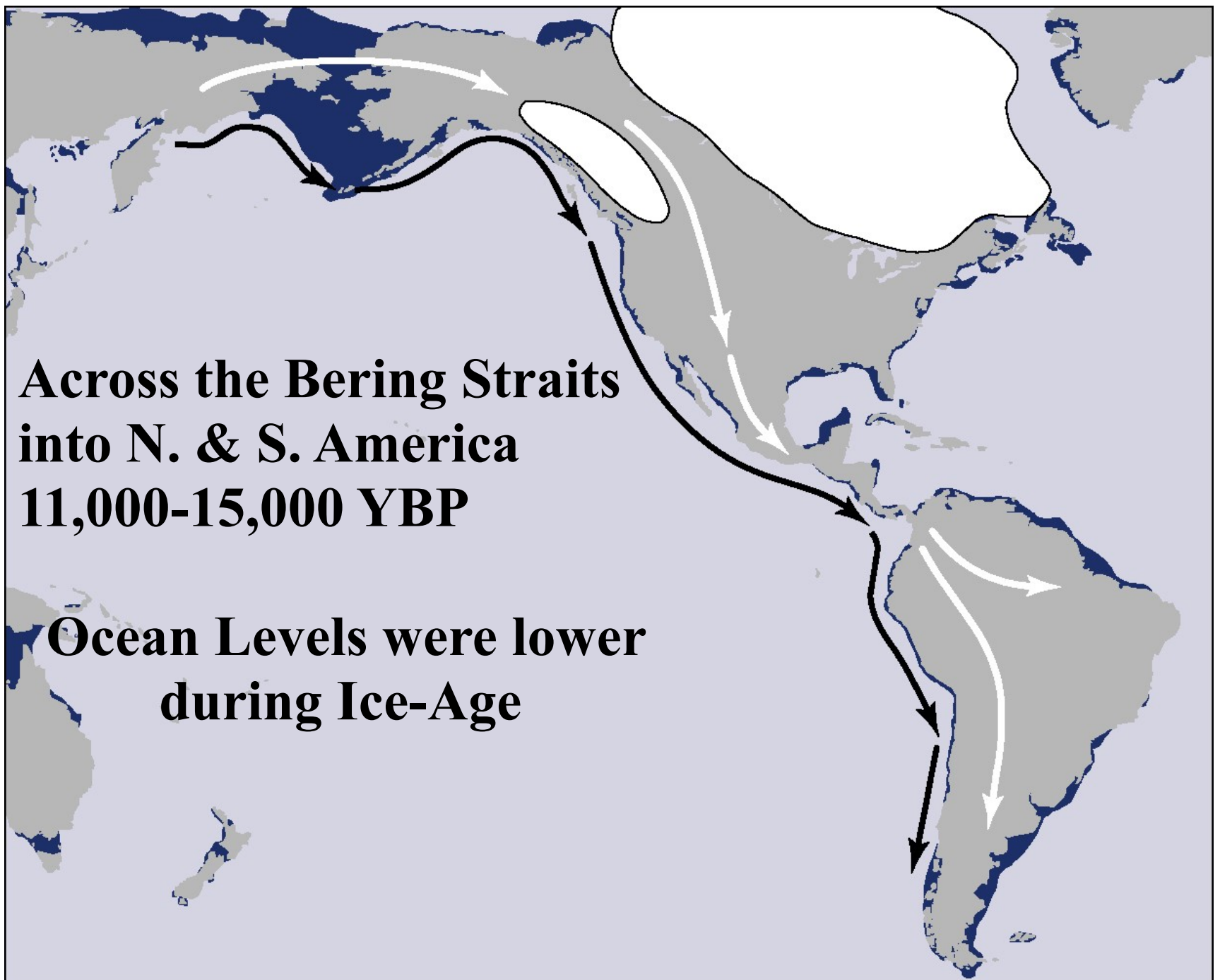
Human-Human





mtDNA and migrations into Europe

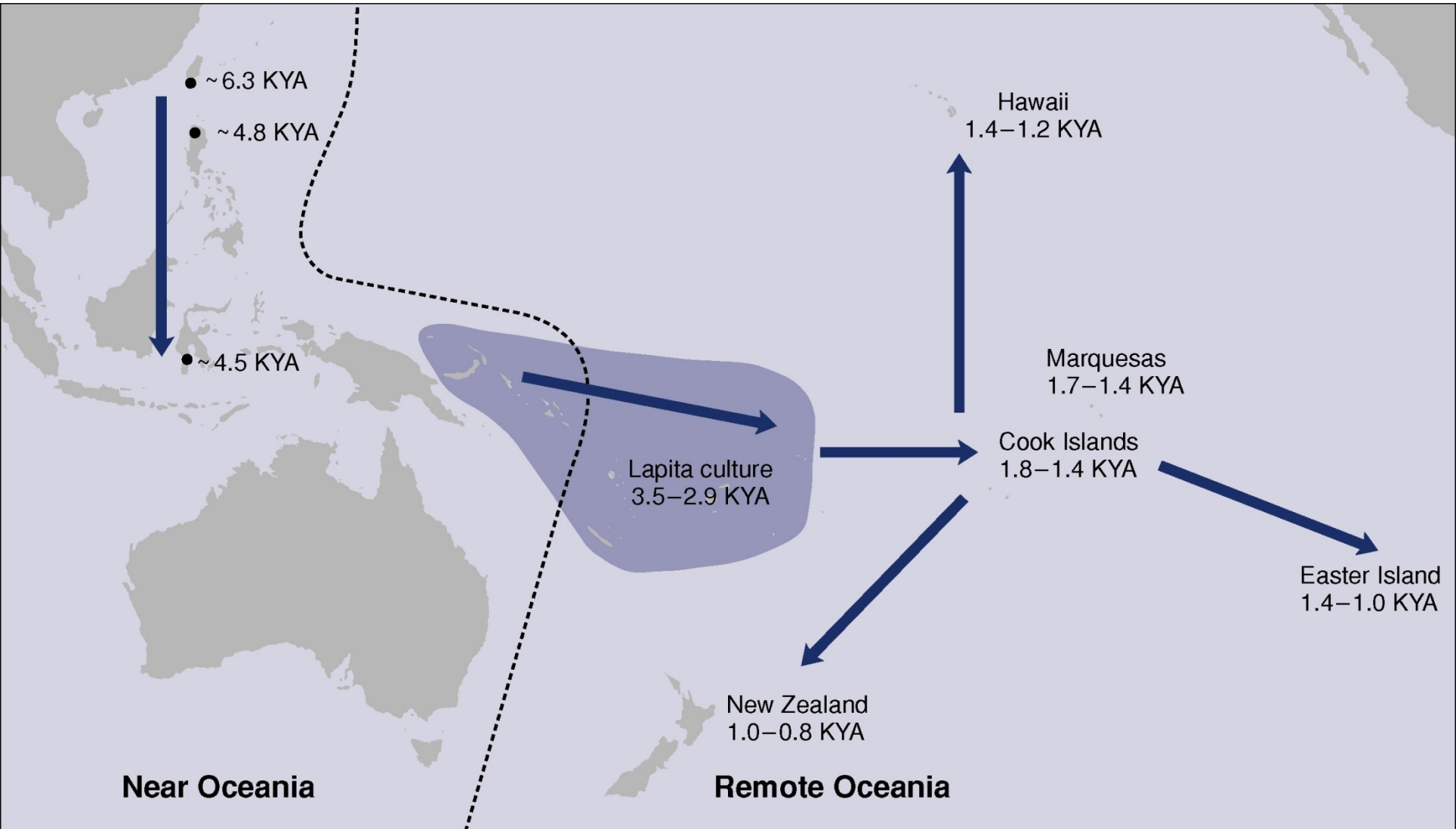




**Across the Bering Straits
into N. & S. America
11,000-15,000 YBP**

**Ocean Levels were lower
during Ice-Age**

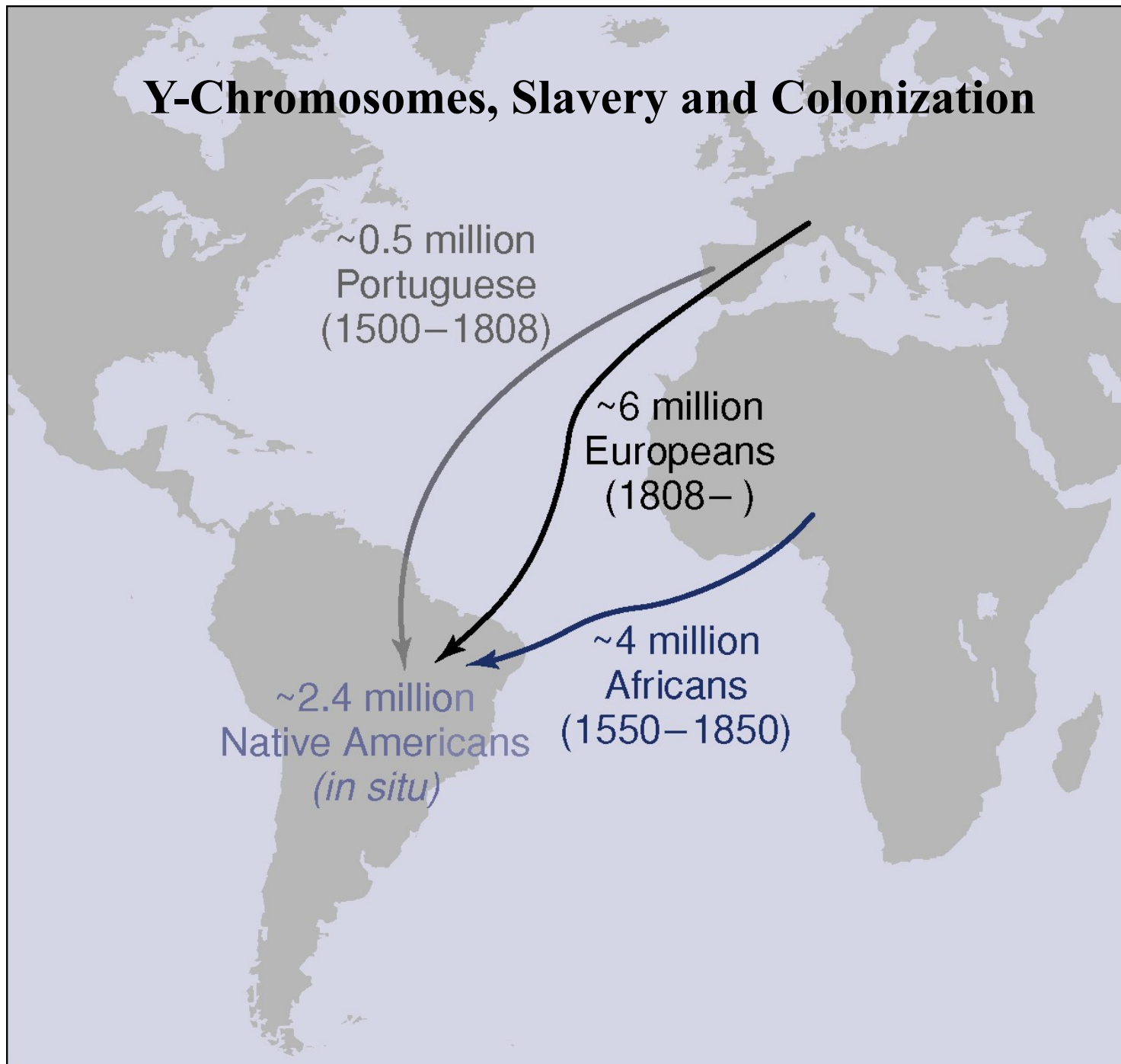
Migrations in the South Pacific Islands



SCANDINAVIANS HAVE SCOT AND IRISH mtDNA



Y-Chromosomes, Slavery and Colonization

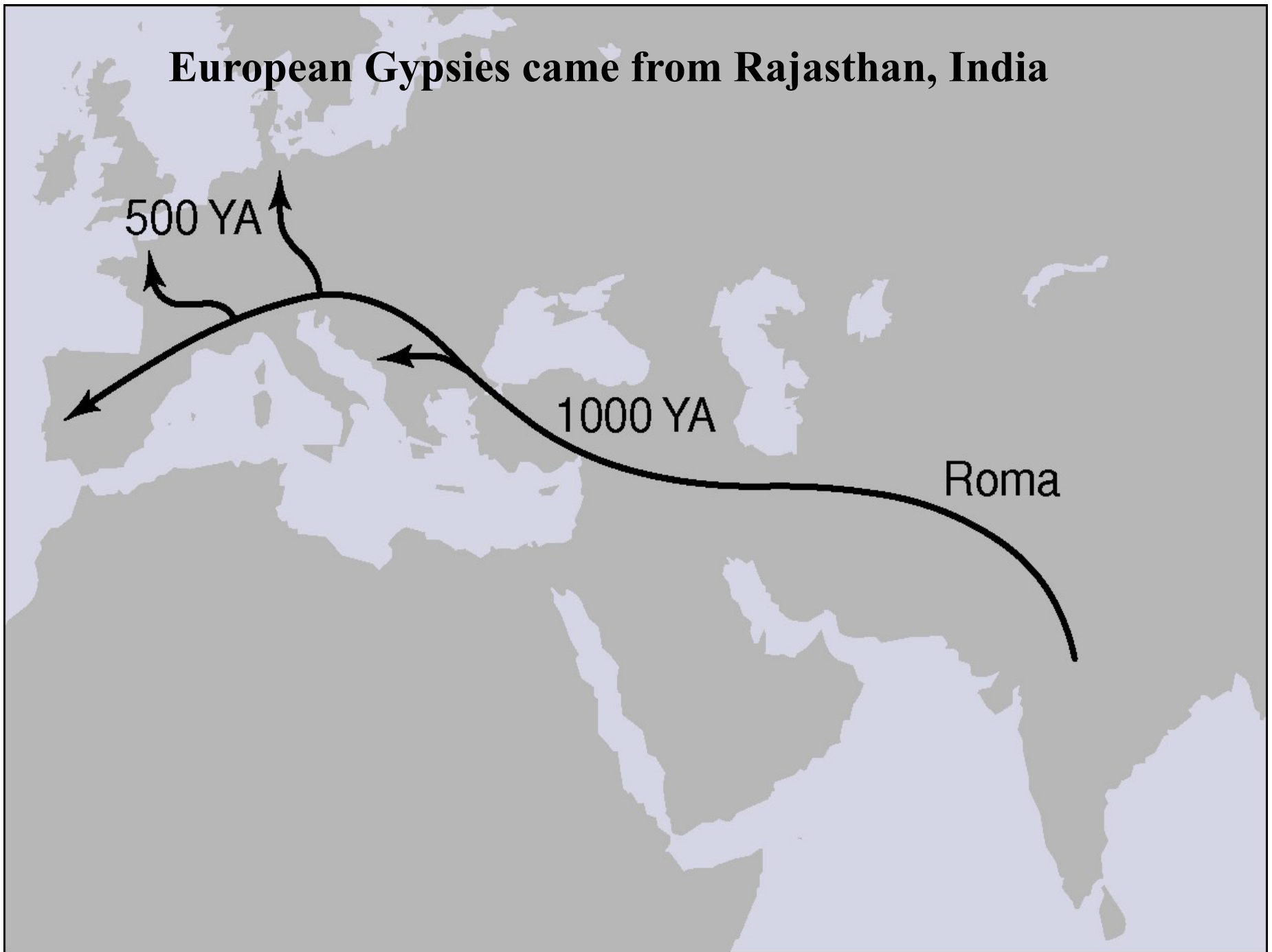


European Gypsies came from Rajasthan, India

500 YA

1000 YA

Roma



mtDNA and the Jewish Migrations out of Palestine



Where can I learn more?

- **Take a Genetics Class**
- **Popular Books:**
 - **Matt Ridley: 'Genome', 'The Red Queen', 'Nature via Nurture'**
 - **Richard Dawkins: 'The Ancestor's Tale', 'The God Delusion', 'The Selfish Gene', 'River out of Eden', 'The Blind Watchmaker'**
 - **Brian Sykes: 'The Seven Daughters of Eve', 'Adam's Curse'**
- **Text Books:**
 - **Hartl, Clark: 'Principals of Population Genetics'**
 - **J. Gillespie: 'Population Genetics, a concise guide'**
 - **Jobling et al: 'Evolutionary Pop. Genetics and Disease'**
 - **Ewens, 'Mathematical Population Genetics'**
 - [→](#)

How can I find my ancestral mtDNA and Y haplogroup?

How can I trace my ancestry?

- <https://genographic.nationalgeographic.com/genographic/index.html>
- http://www.dnaancestryproject.com/ydna_intro_howto.php
- <http://www.familytreedna.com/>

mtDNA Report

HVS1 Sequence

Haplogroup: M*

16111T, 16223T, 16311C, 16519C

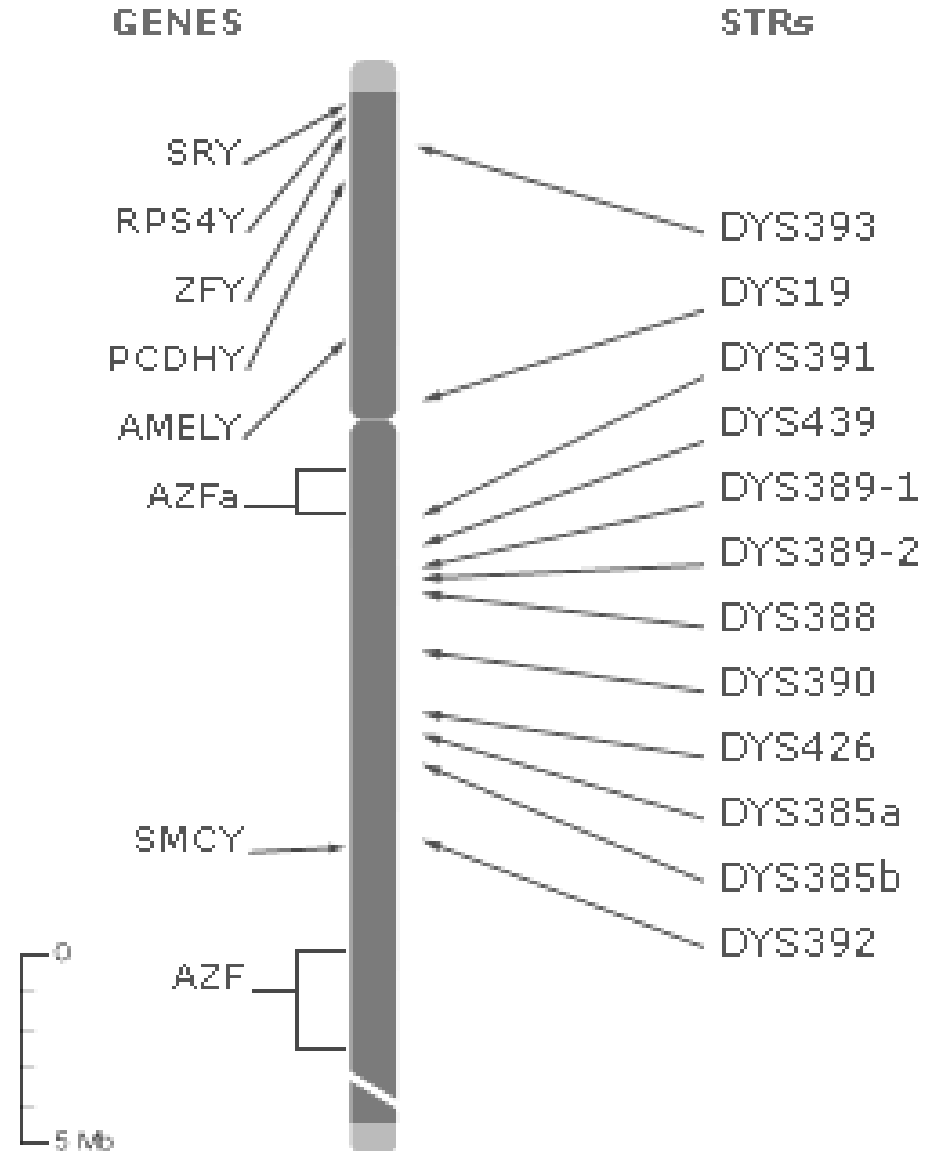
```
ATTCTAATTTAAACTATTCTCTGTTCTTTCATGGGGAAGCAGATTTGGGTA  
CCACCCAAGTATTGACTCACCCATCAACAACCGCTATGTATTTTCGTACATT  
ACTGCCAGTCACCATGAATATTGTACGGTACCATAAATACTTGACCACCTG  
TAGTACATAAAAACCCAATCCACATCAAACCCCCTCCCCATGCTTACAAG  
CAAGTACAGCAATCAACCTTCAACTATCACACATCAACTGCAACTCCAAAG  
CCACCCCTCACCCACTAGGATACCAACAAACCTACCCACCCTTAACAGTAC  
ATAGCACATAAAGCCATTTACCGTACATAGCACATTACAGTCAAATCCCTT  
CTCGTCCCCATGGATGACCCCCCTCAGATAGGGGTCCCTTGACCACCATCC  
TCCGTGAAATCAATATCCCGCACAAGAGTGCTACTCTCCTCGCTCCGGGCC  
CATAACACTTGGGGGTAGCTAAAGTGAAGTGTATCCGACATCTGGTTCCTA  
CTTCAGGGCCATAAAGCCTAAATAGCCCACACGTTCCCCTTAAATAAGACA  
TCACGATG
```

Y-Chromosome Report

Haplogroup: R (M173)

STRs:

DYS393: 13, DYS439: 12
DYS388: 12, DYS385a: 12
DYS19: 15 DYS389-1: 14
DYS390: 23 DYS385b: 13
DYS391: 10 DYS389-2: 16
DYS426: 12 DYS392: 10

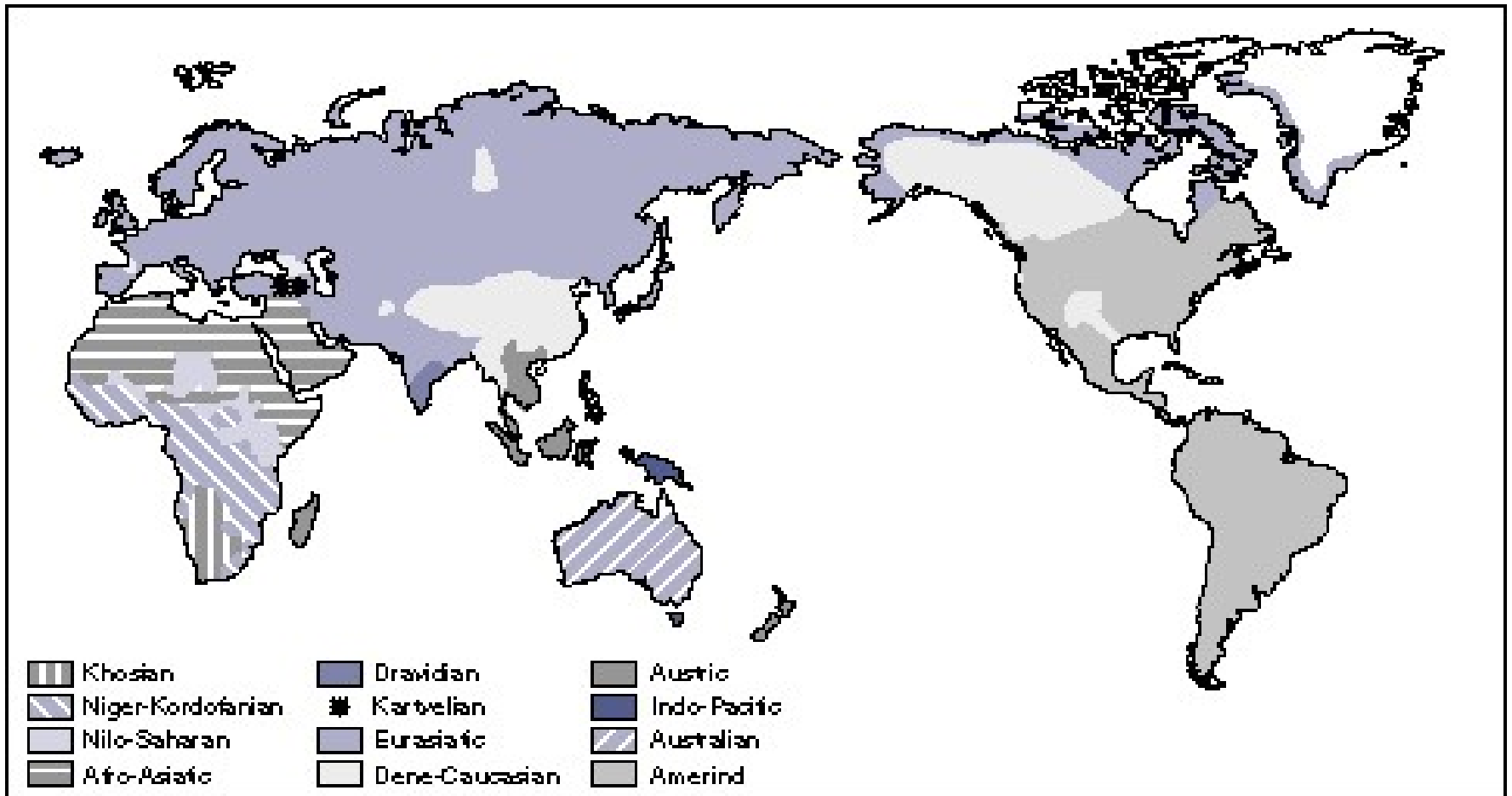


Typical Reports

- Maternal Lineage based on 10 SNPs plus HVS1 sequence
- Paternal Lineage based on Y chromosome STRs + SNPs
- [mtDNA report 1](#), [mtDNA report 2](#)
- [Y-Chromosome report](#)

Open Questions

12 Major Language Groups (Greenberg) into which the 6000 languages in the world can be classified



Questions from fossils and archaeology

~800 KYA

heidelbergensis (antecessor)

~250 – 28 KYA

neanderthalensis

~40 KYA

Modern humans

~20 KYA

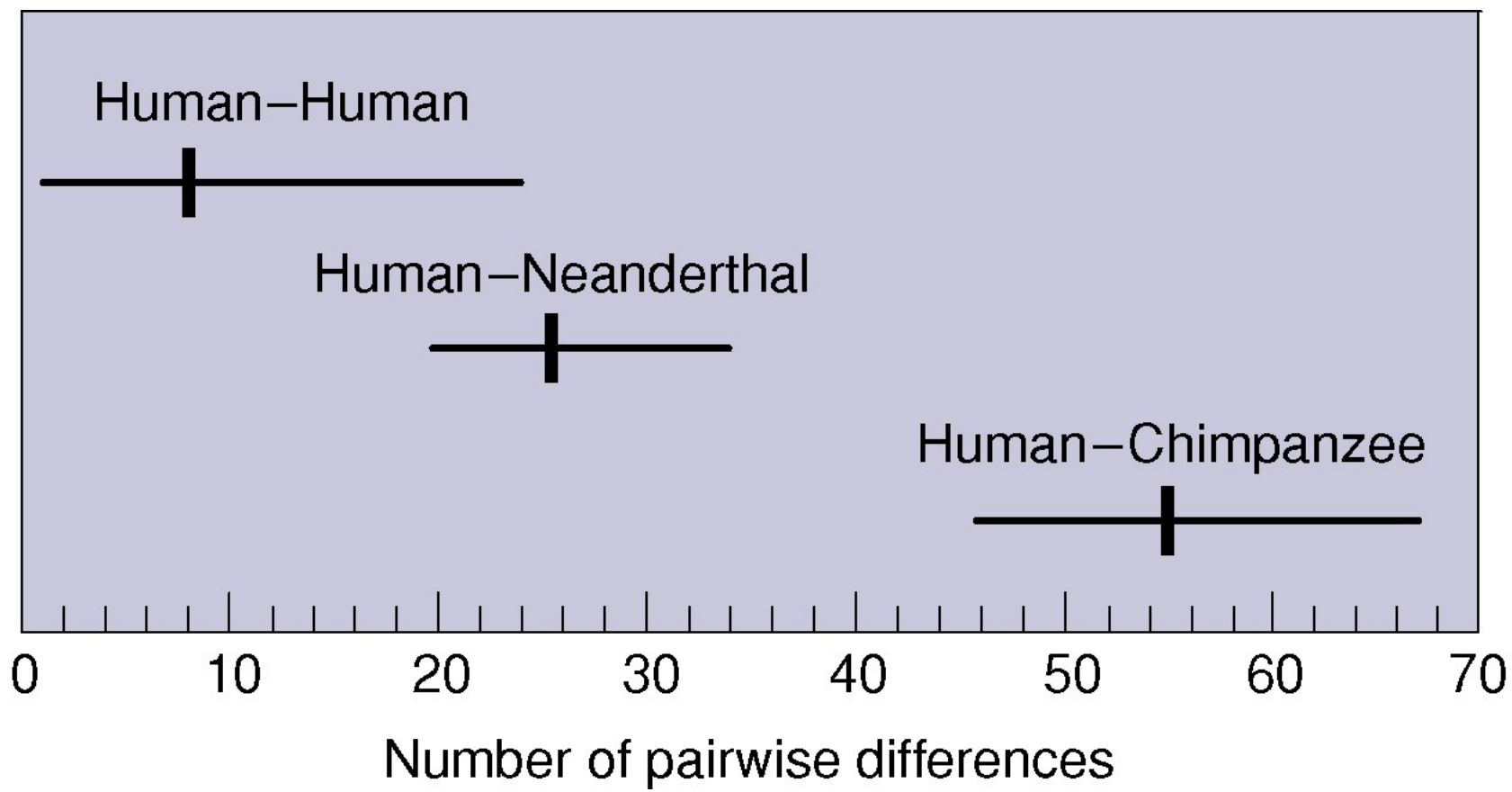
Glacial maximum

~10 KYA

▼ Beginning of Neolithic transition

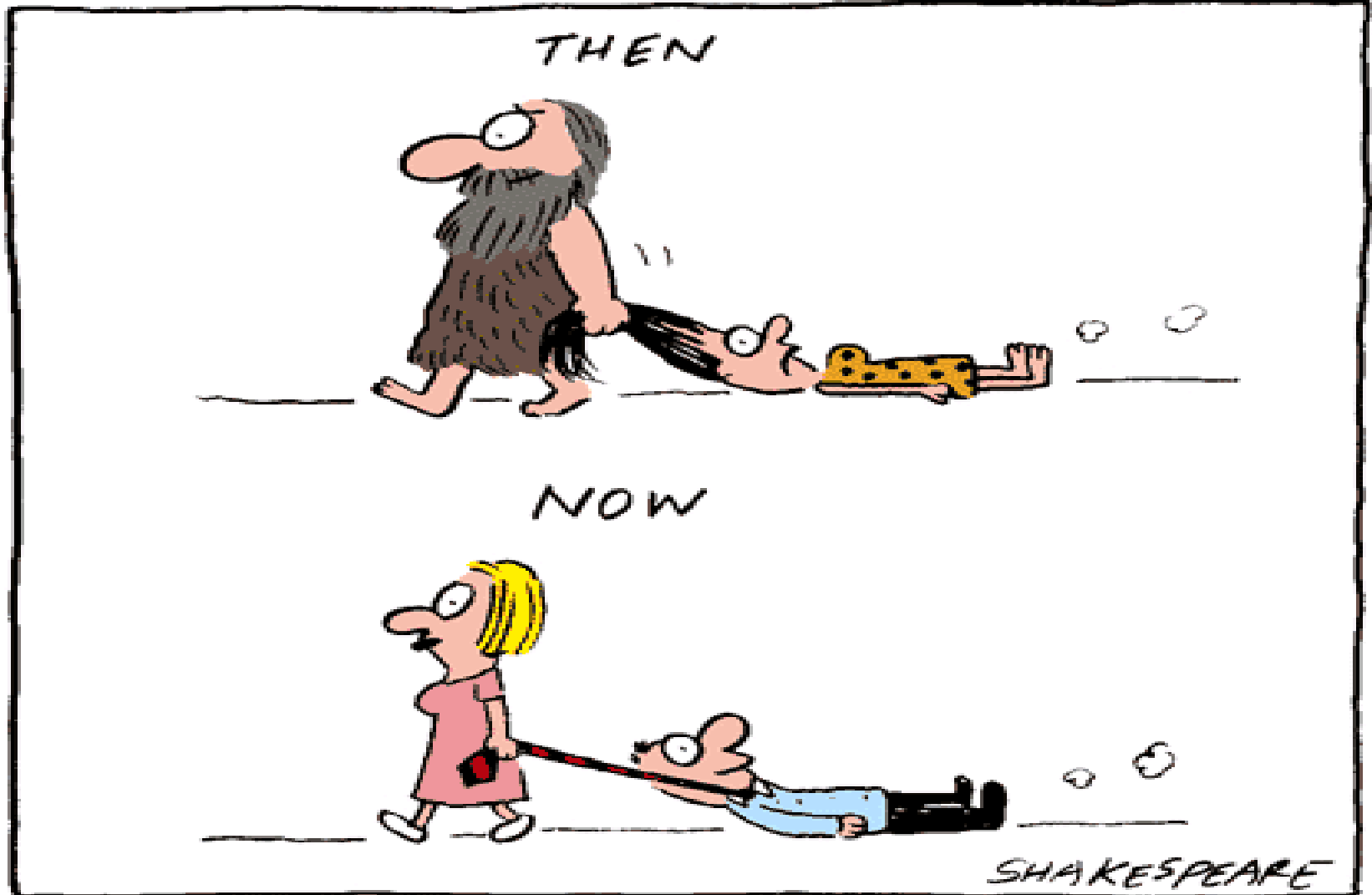
- Did early hominids (*H. heidelbergensis*, *H. neanderthalensis*) contribute to the modern gene pool?
- What were the relative contributions of Paleolithic and Neolithic settlers?

Were Neanderthals a Different Species or do we still carry their DNA?

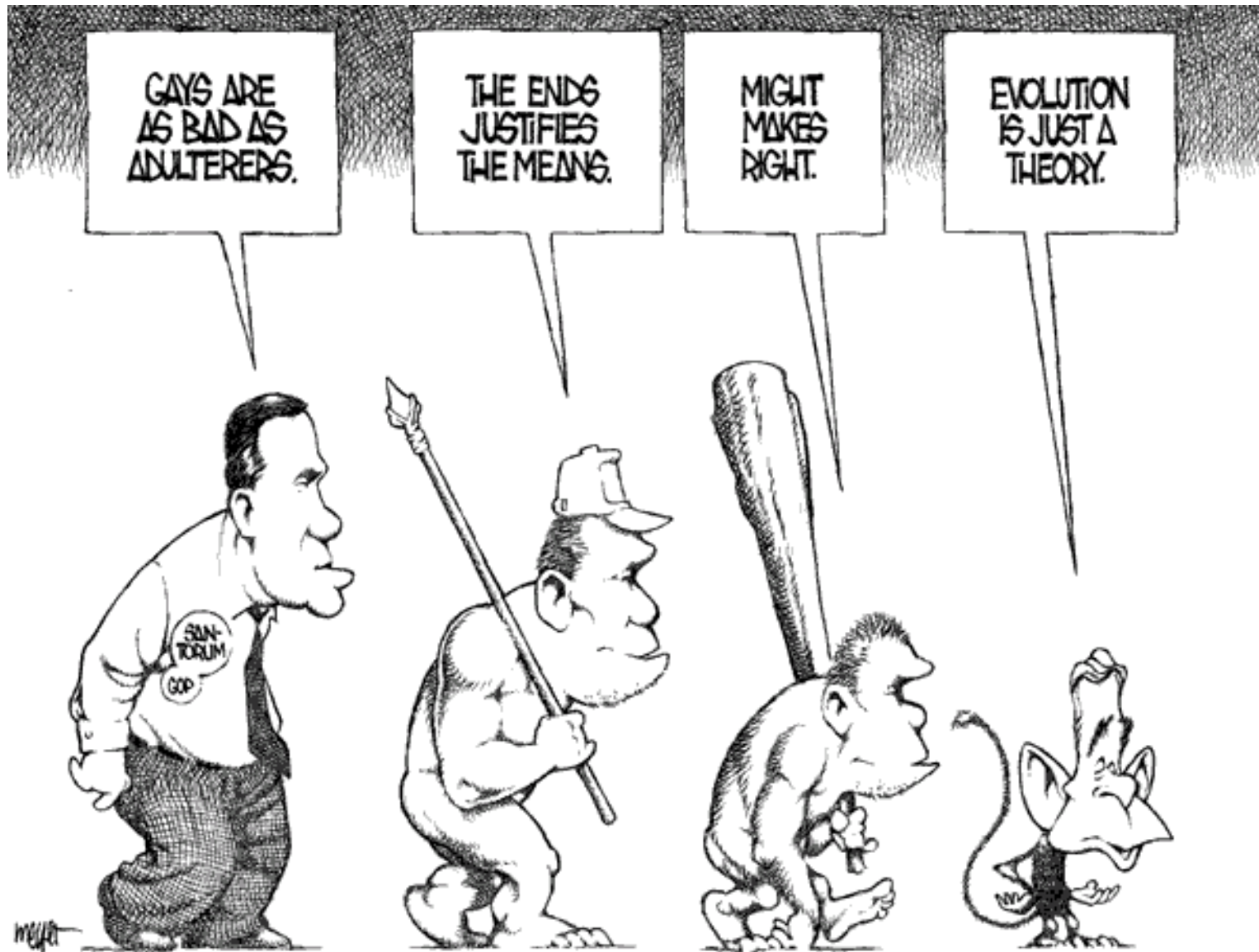


How 50% of humanity views EVOLUTION!

www.johnshakespeare.com.au



And then there are the doubters



The Real Promise of Genetics

- **Individualized therapy: markers for disease risk, prognosis and treatment efficacy.**
- **Understanding and treating complex diseases: Cancer, Diabetes, Heart disease, Parkinson's Disease, Alzheimers, Obesity, Hypercholesterolemia**
- **Understanding Complex Traits: Longevity, Athleticism, Height, Musical Ability**
- **Making effective Vaccines: HPV, FLU, HIV/AIDS, Hepatitis**

Physics is what physicists do at night.

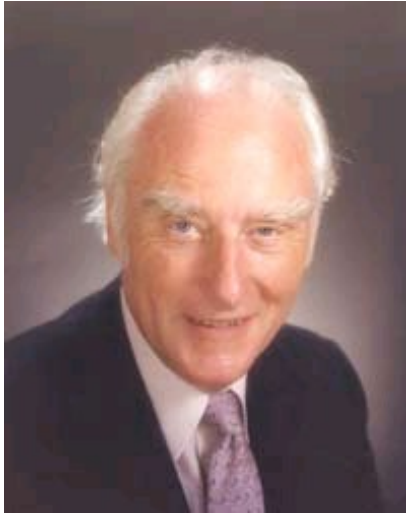
R. Feynman



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Biology ~~Physics~~ is what ^{some} physicists do at night.

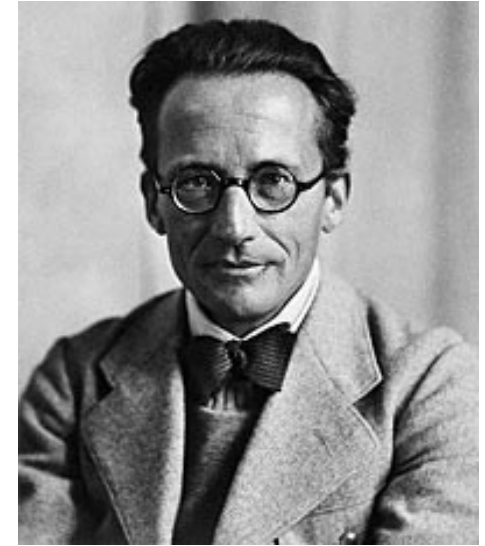
Crick



Pauling



Schrödinger



Delbrück



Who is this physicist?

Venki →
Ramakrishnan
2009 Nobel
Prize for
Chemistry



Szilard



TIME TO LEARN A NEW GAME





Gabriela Alexe



**Tony Hui
Michael Seiler
Tamanna Bhanot
(Rutgers University)**



**Daniel Platt
(IBM Research)**



**Arnold Levine
(IAS)**



Masashi Tanaka (TMIG)



Ravi Vijaya Satya (UCF)