Mitochondrial Eve

Mary Anne Clark (Max Chatnoir)
Texas Wesleyan University

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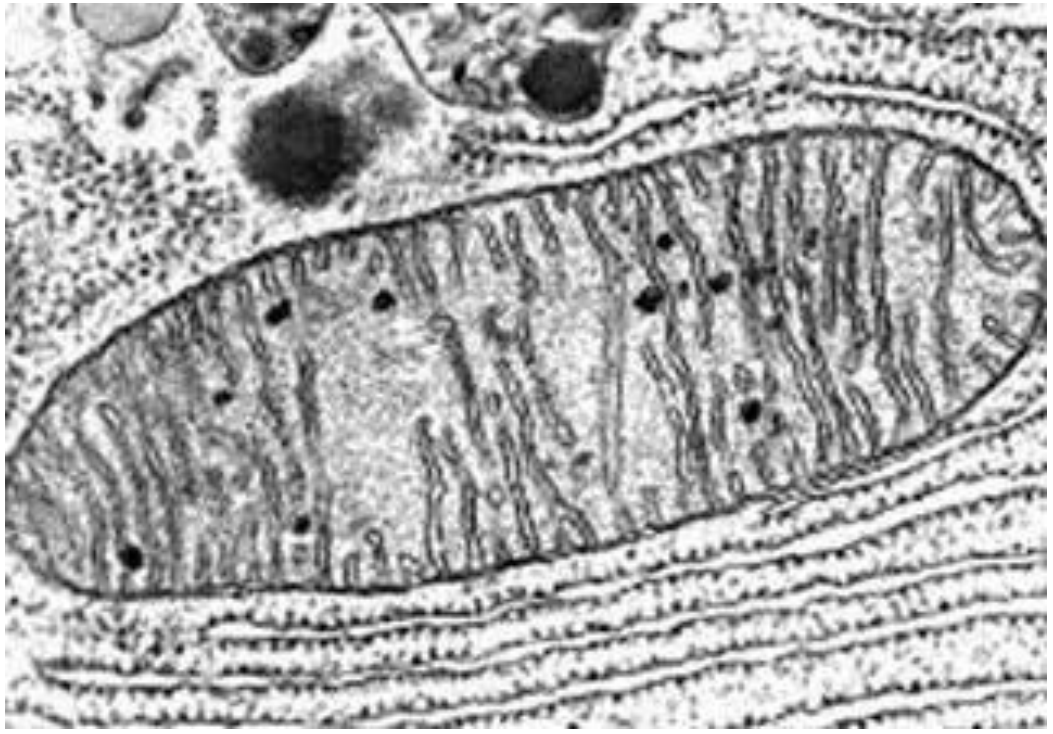
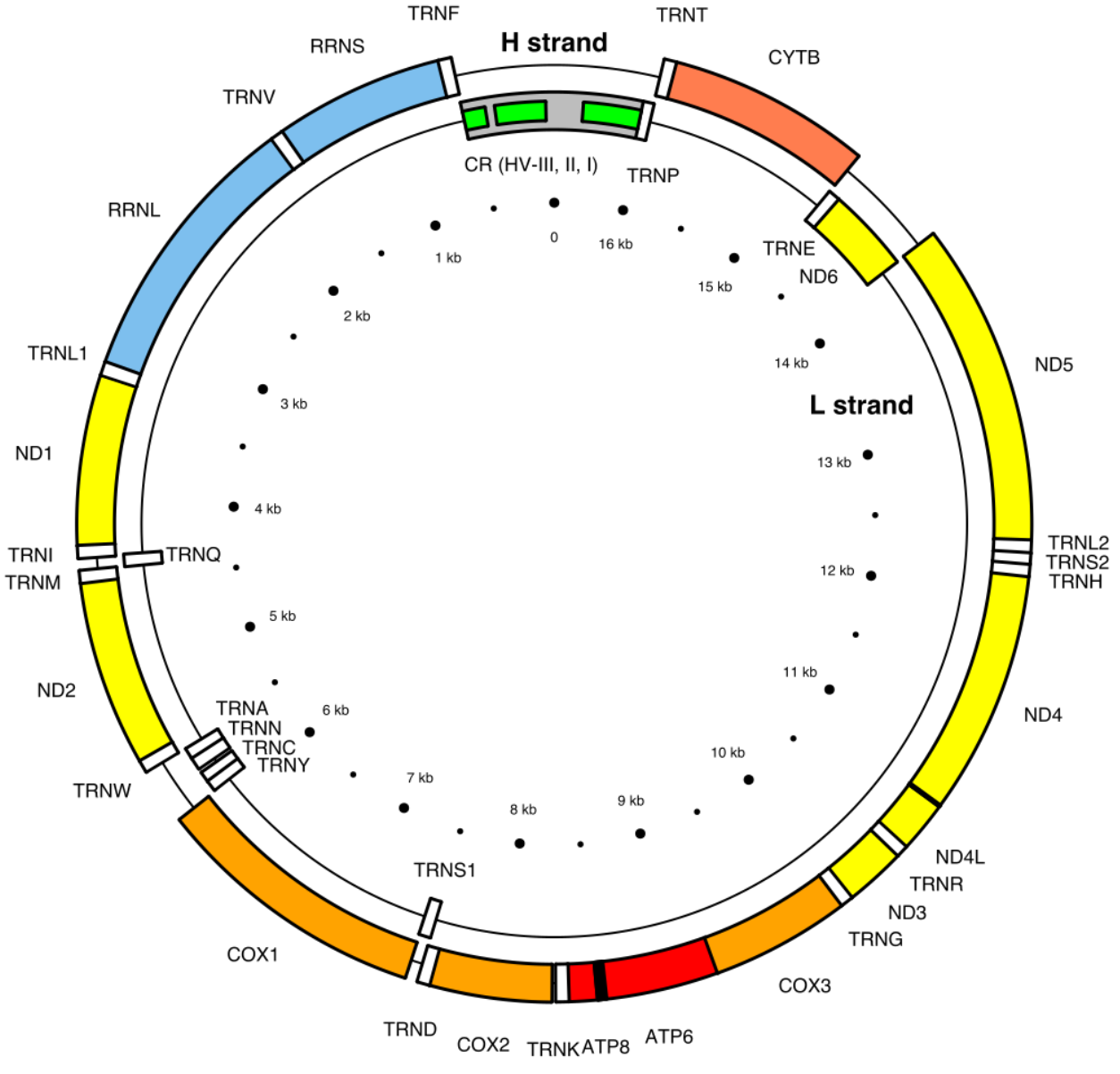
Mitochondria



Mitochondria are intracellular energy-producing organelles in eukaryotic cells.

Eukaryotes are cells with chromosomes contained within a membrane-bounded vesicle – the nucleus.

https://blog.library.gsu.edu/2010/12/01/generators-for-generations-online-databases-for-mtdna/mtdna/



The human mitochondrial genome

16565 nucleotides
Coding sequences on both strands

Coding sequences include
22 transfer RNAs
12S and 16S ribosomal RNAs
13 mitochondrial proteins:

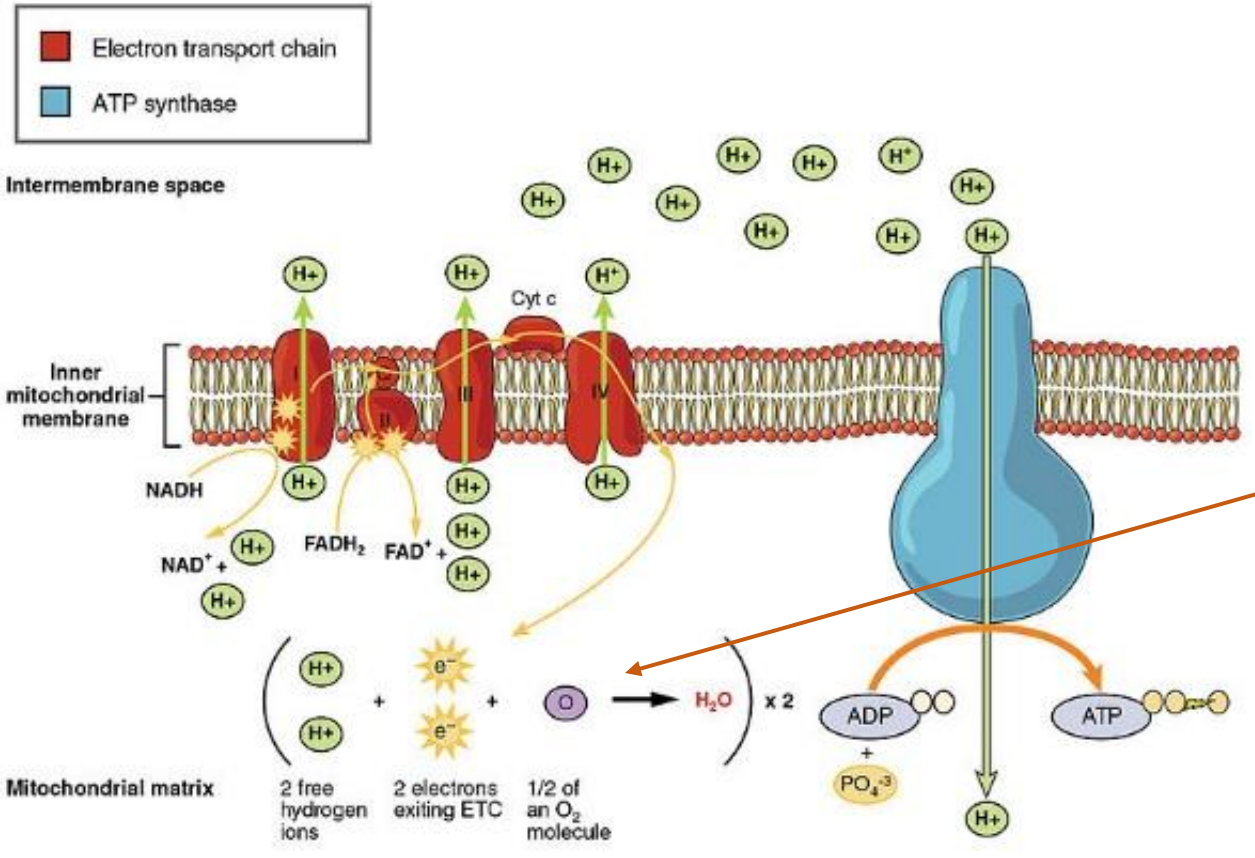
- NADH dehydrogenase
- Cytochrome B
- Cytochrome oxidase
- ATP synthetase

- Noncoding control region with

3 hypervariable DNA regions

https://commons.wikimedia.org/wiki/File%3AMap_of_the_human_mitochondrial_genome.svg

Mitochondrial Proteins



Mitochondria produce energy-storing ATP by using energy released during transport of high-energy electrons down an electron transport chain to oxygen.

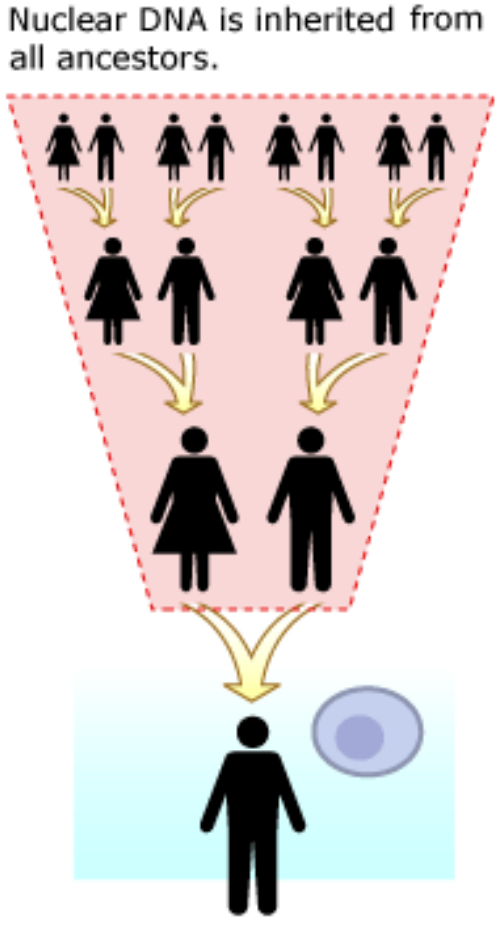
Most of the oxygen you inhale is used to power your mitochondria.

https://commons.wikimedia.org/wiki/File:2508_The_Electron_Transport_Chain.jpg

Why do mitochondria have genomes?

- Mitochondria have genomes because they are the descendants of ancient aerobic bacteria that established a symbiotic relationship with ancient nucleated cells.
- Vertebrate mitochondria are relatively small.
- Many of the original symbiont's genes were transferred to the nuclear genome after the endosymbiosis was established.
- Mitochondria replicate inside of their host cell and are therefore inherited.

Nuclear chromosome inheritance



Six generations ago, you had 64 great-great-great grandparents.

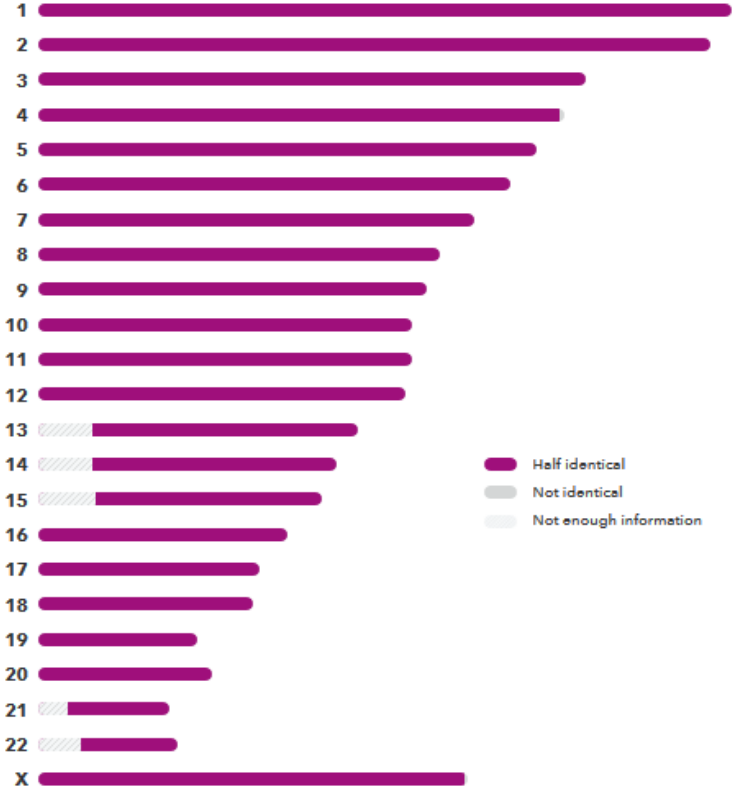
You only have 46 chromosomes.

Some of your nuclear heritage from any given individual is gone.

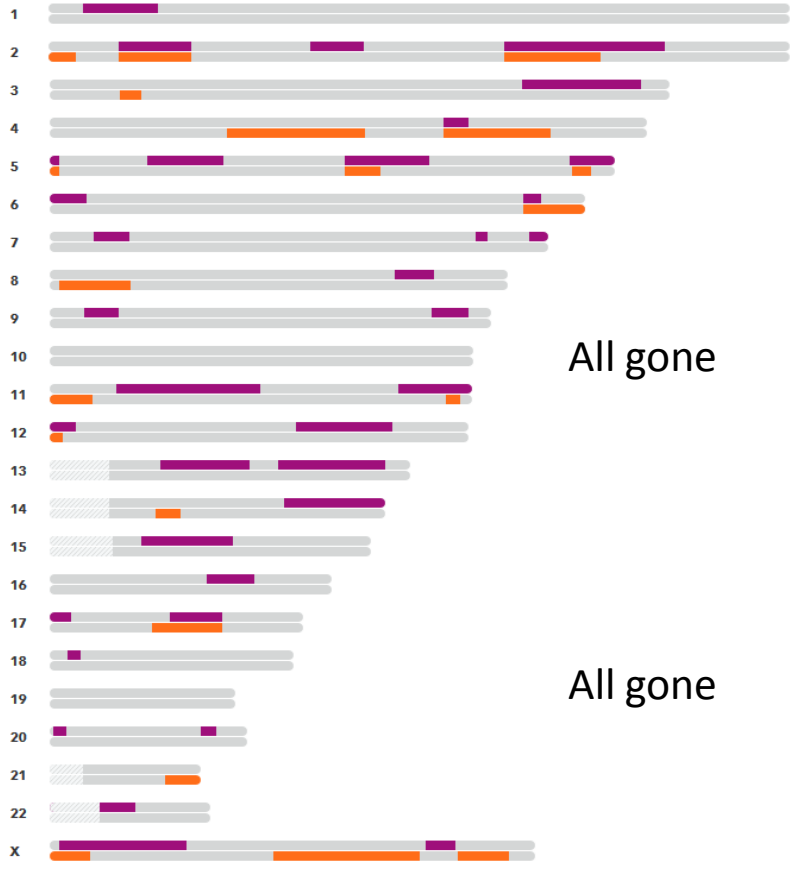
https://evolution.berkeley.edu/evolibrary/news/100501_xwoman

In addition, crossing over mixes chromosomes in the nuclear genome

Daughter



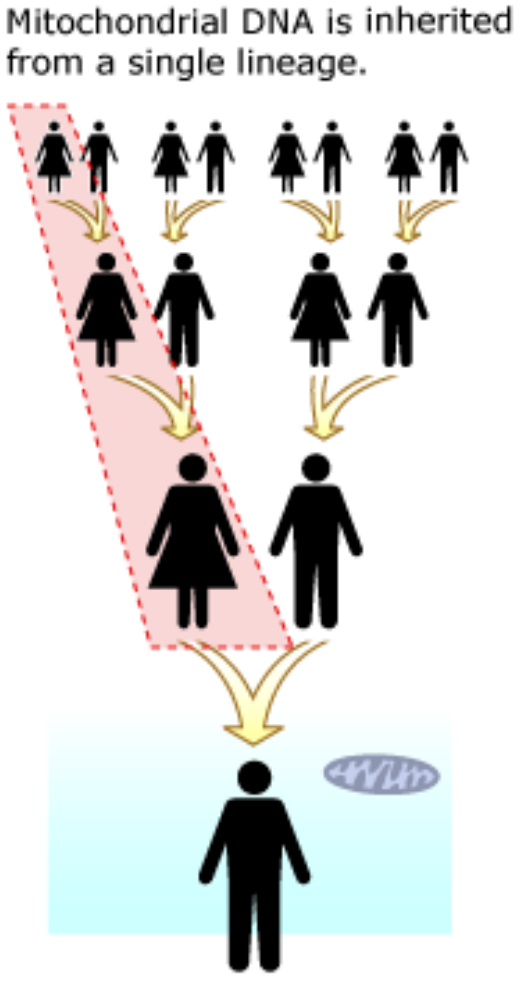
Maternal Cousins (first and second)



All gone

All gone

Mitochondrial chromosome inheritance



Mitochondrial DNA is maternally inherited.

Your mitochondrial heritage is intact.

But only a single female ancestor contributes to it.

Mitochondrial lineages are unmixed, and differ only by acquired mutations.

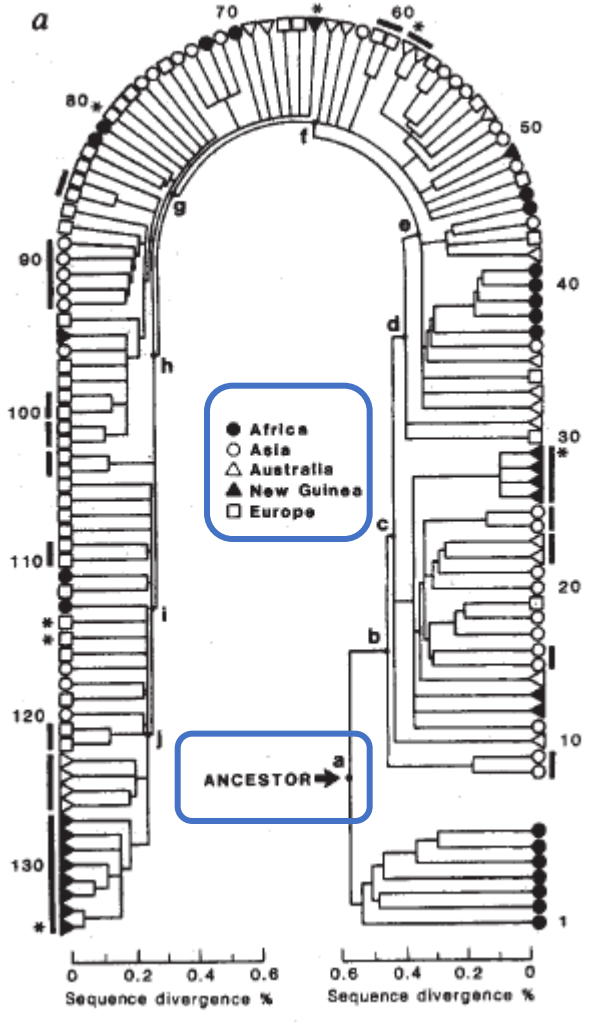
https://evolution.berkeley.edu/evolibrary/news/100501_xwoman

Who is Mitochondrial Eve?

- In January 1987, Rebecca Cann, Mark Stoneking and Allan Wilson published an article in Nature: Mitochondrial DNA and human evolution.
- They compared mitochondria from 147 women from five different geographic areas: Africa, Asia, Europe and the Middle East, Australia and New Guinea.
- The mitochondrial genomes were not fully sequenced, but they were examined for 467different restriction (enzyme recognition) sites.
- They identified 133 different mitochondrial types, each of which was found in only one of the geographic areas, although some types were found in several individuals.

Who is Mitochondrial Eve?

- Cann, Stoneking and Wilson constructed a phylogenetic tree showing the relationships among the 133 mitochondrial types.
- They identified two primary branches, one that was exclusively African and the other that was from all the other geographical locations (see shape codes).
- Variation within the African group was greater than within the groups from other locations (16 differences = 0.1%).
- They inferred that the mitochondrial gene pool originated in Africa.
- Assuming a constant mutation rate of 2-4%/MY, they suggested that the common ancestral lineage arose in Africa between 140,000 and 290,000 years ago.



https://www.nature.com/articles/325031a0

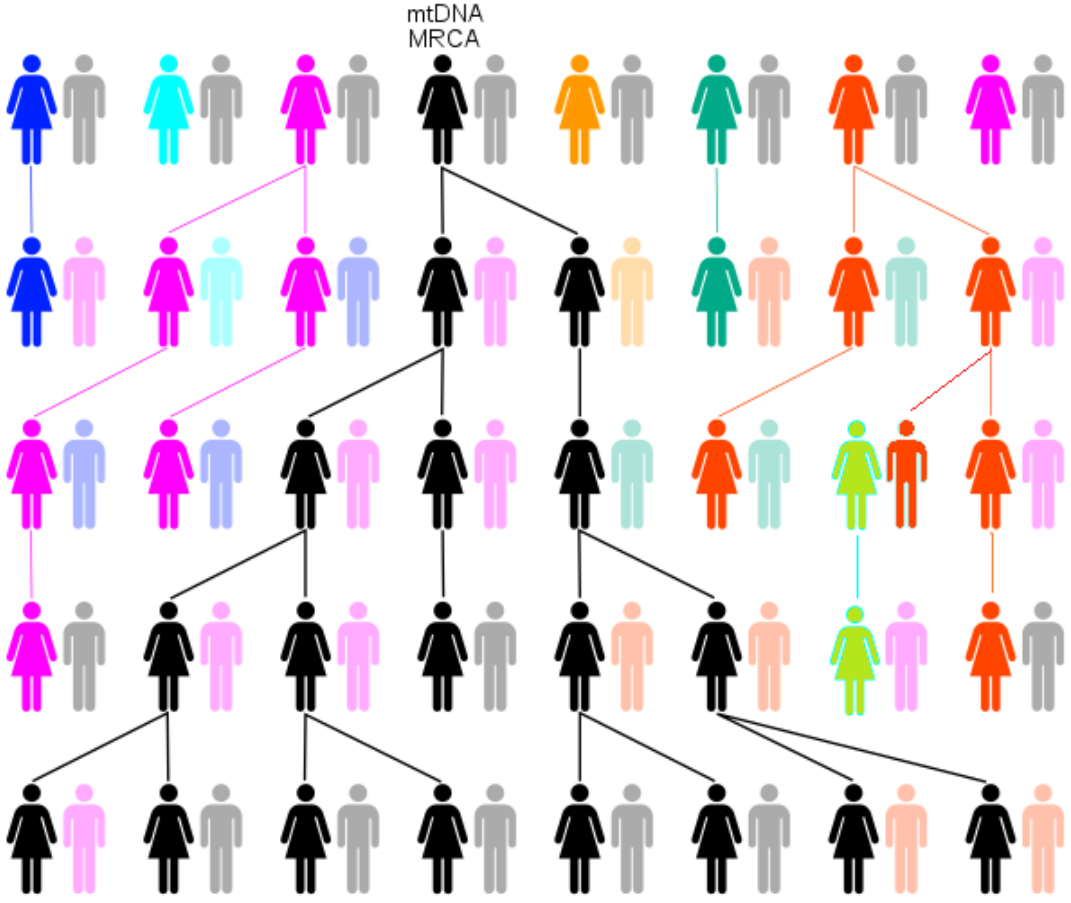
Who is Mitochondrial Eve?

- In October 1987, Roger Lewin reported the work in Science, using the reference term “Mitochondrial Eve.” However earlier news reports had associated the mitochondrial ancestor with the Biblical Eve.
- Lewin and others were quick to caution against taking the association too literally.
- All living humans are the descendants of a few thousand early modern humans: not a single human couple.
- Mitochondrial Eve represents a matriline. A matriline is an unbroken lineage of females that have transmitted their mitochondria to all females living today.

Who is Mitochondrial Eve?

- The founder or most persistent contributor of this lineage is sometimes called the matrilineal MRCA or most recent common maternal ancestor. The mitochondrial lineage was founded in Africa about 160 thousand years ago.
- Was “Mitochondrial Eve” necessarily an early modern human? Maybe.
- EMH arose in Africa about 200,000 years ago and spread into Asia and Europe about 100,000 years ago.
- Many genes in the human nuclear genome existed before modern humans, e.g. the rhodopins and the globins. Why should the mitochondrial genome not also have existed before we emerged as a species?

Not all mitochondrial lineages survive



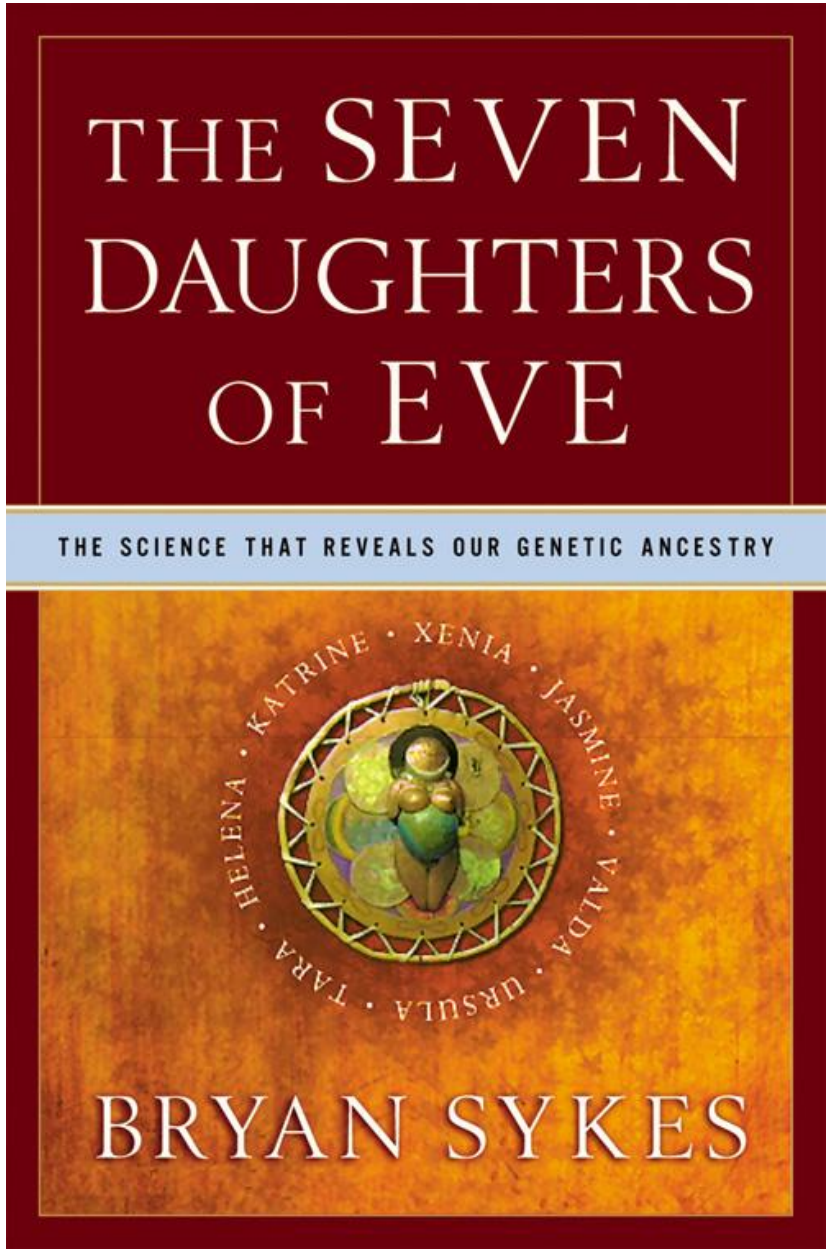
Black figures represent a persistent lineage.

Various colored figures are parts of lineages that did not persist into the final generation.

Some females do not reproduce.

Male children do not pass on their mitochondria.

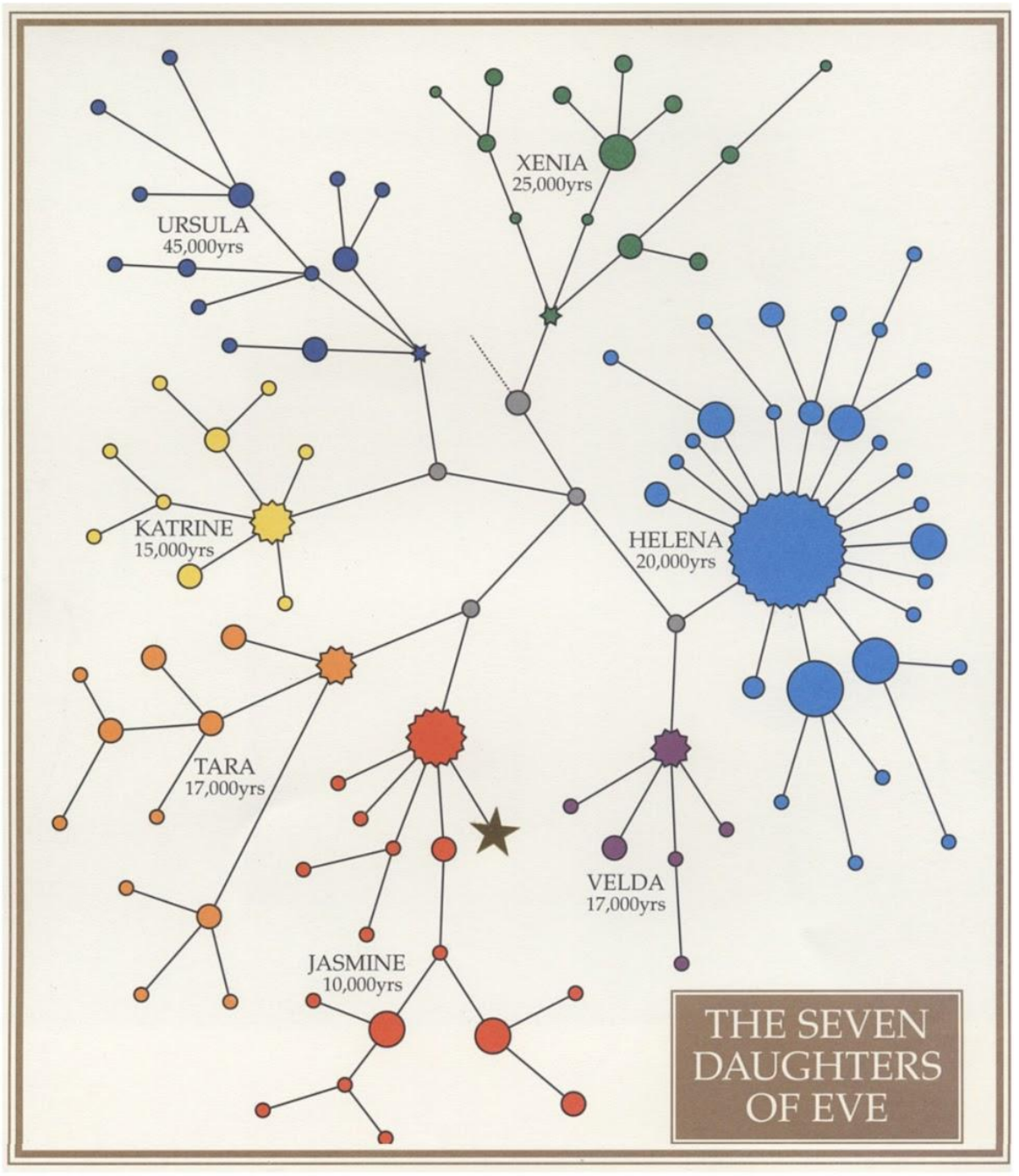
Modified from https://en.wikipedia.org/wiki/Mitochondrial_Eve#/media/File:MtDNA-MRCA-generations-Evolution.svg



Seven Daughters of Eve

- The idea of Mitochondrial Eve caught the public imagination and in 2001 Bryan Sykes published *The Seven Daughters of Eve*.
- In this book major European and Middle Eastern lineages were represented by an imaginary woman named for one of the mitochondrial variants or haplogroups.
- Haplogroup: a group of people sharing a common set of mitochondrial mutations.
- The book told a plausible story about the life of each of these haplogroup founders.

https://www.amazon.com/Seven-Daughters-Eve-Science-Ancestry/dp/0393323145/ref=pd_sbs_14_1?



Seven Daughters of Eve

- Haplogroup H = Helena
- Haplogroup X = Xenia
- Haplogroup U = Ursula
- Haplogroup K = Katrine
- Haplogroup T = Tara
- Haplogroup J = Jasmine
- Haplogroup V = Velda

The Iceman

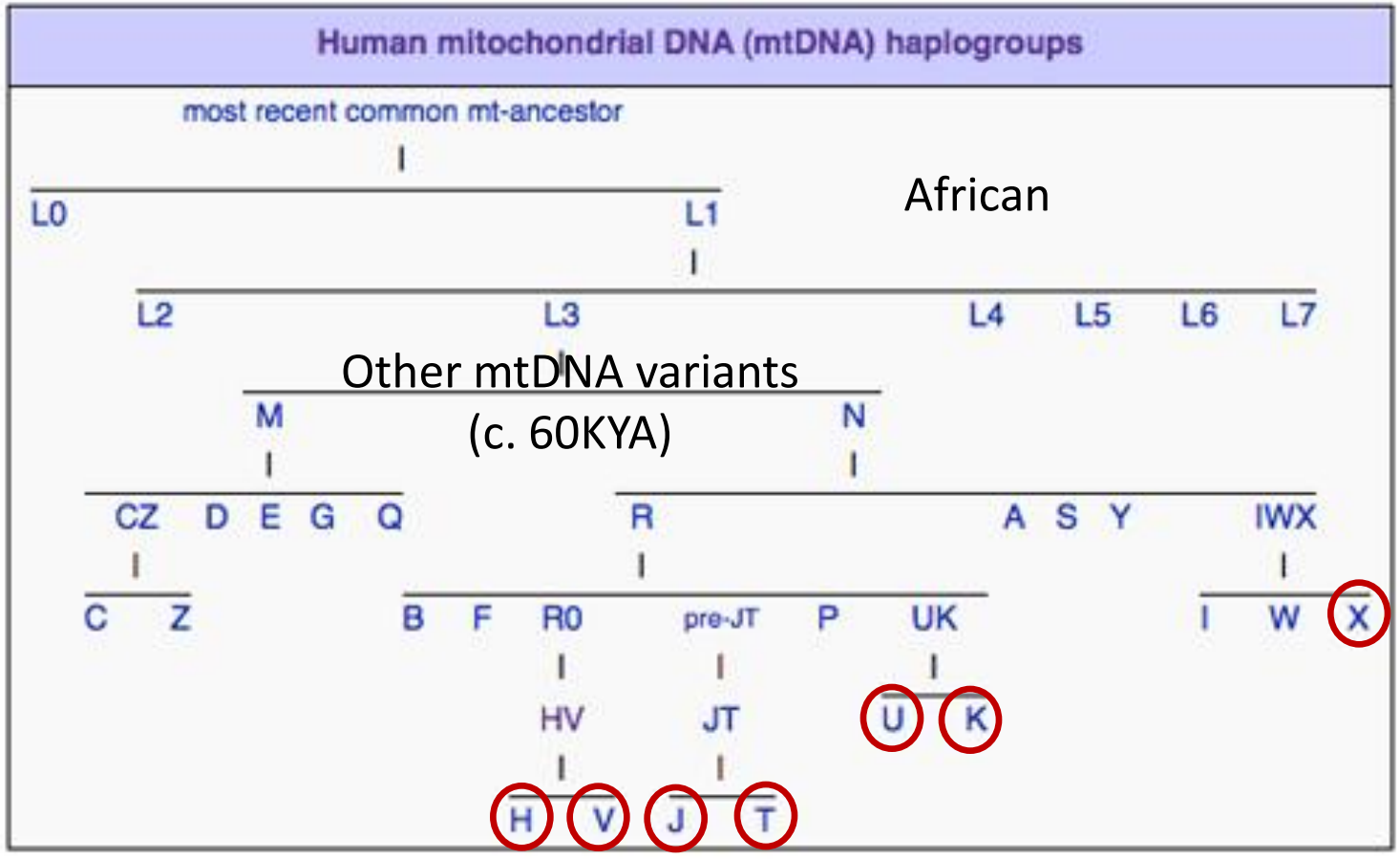
Seven Daughters also told how mtDNA was used to identify the ancestry of the Otzi, the Iceman, a frozen neolithic human body found in the Italian Alps.

Sykes's description of the discovery of Otzi:

On Thursday 19 September 1991 Erika and Helmut Simon, two experienced climbers from Nuremberg in Germany, were nearing the end of their walking holiday in the Italian Alps. The previous night they had made an unscheduled stop in a mountain hut, planning to walk down to their car the next morning. But it was such a brilliantly sunny day that they decided instead to spend the morning climbing the 3,516 metre Finailspitze. On their way back down to the hut to pick up their rucksacks they strayed from the marked path into a gully partly filled with melting ice. Sticking out of the ice was the naked body of a man.

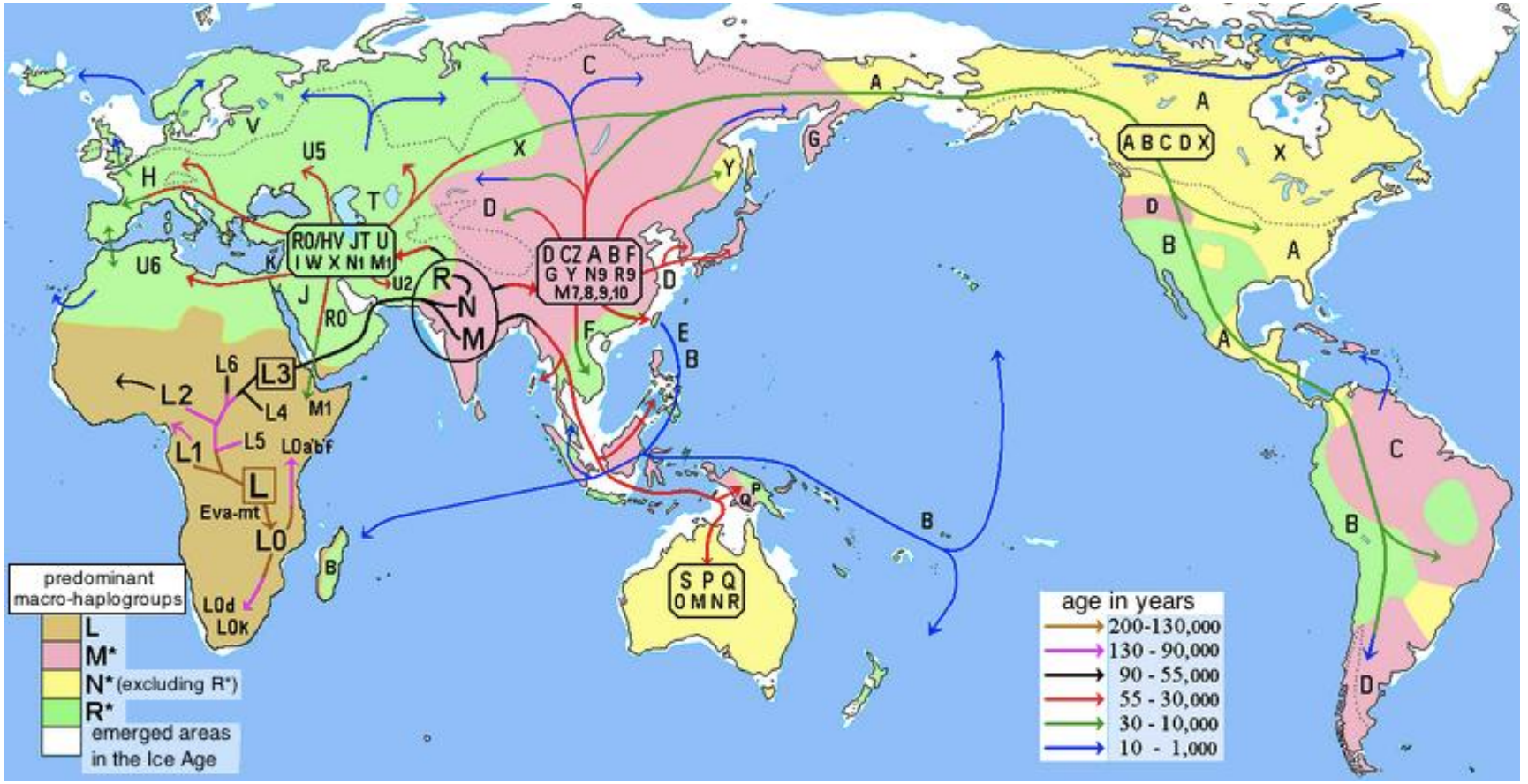
More on Otzi later….

More than seven daughters



https://en.wikipedia.org/wiki/Human_mitochondrial_DNA_haplogroup

Mitochondrial migration Map



https://en.wikipedia.org/wiki/Human_mitochondrial_DNA_haplogroup

My haplogroup is I2

- The I haplogroup is descended from the N subgroup of L3 African emigrants
- Haplogroup I2 diverged from the I group about 6500 years ago.
- I2 originated around Iran and migrated from the middle east through Anatolia into Europe.
- Eventually my female ancestor wound up in Ireland.

The Cambridge Reference Sequence

- The Cann, Stoneking and Wilson studies were based on restriction markers.
- In 1981, S. Anderson and 12 other scientists in the Sanger lab at Cambridge reported the full sequence of the human mitochondrial genome. This sequence, from a European woman, became known as the Cambridge Reference Sequence (CRS)
- Several reported inconsistencies in the CRS led to its revision in 1999 by Richard Anderson and his colleagues. This rCRS is now used as the reference sequence for defining mitochondrial variants.

Mitochondrial Control Region: rCRS

```
    1 gatcacaggt ctatcaccct attaaccact cacgggagct ctccatgcat ttggtatttt     HV2
   61 cgtctggggg gtatgcacgc gatagcattg cgagacgctg gagccggagc accctatgtc
  121 gcagtatctg tctttgattc ctgcctcatc ctattattta tcgcacctac gttcaatatt
  181 acaggcgaac atacttacta aagtgtgtta attaattaat gcttgtagga cataataata
  241 acaattgaat gtctgcacag ccactttcca cacagacatc ataacaaaaa atttccacca
  301 aacccccccct cccccgcttc tggccacagc acttaaacac atctctgcca aaccccaaaa
  361 acaaagaacc ctaacaccag cctaaccaga tttcaaattt tatcttttgg cggtatgcac
  421 ttttaacagt caccccccaa ctaacacatt attttccccct cccactccca tactactaat     HV3
  481 ctcatcaata caacccccgc ccatcctacc cagcacacac acaccgctgc taaccccata
  541 ccccgaacca accaaacccc aaagacaccc cccaca

16021 ...ttctttc atggggaagc agatttgggt accacccaag tattgactca cccatcaaca     HV1
16081 accgctatgt atttcgtaca ttactgccag ccaccatgaa tattgtacGg taccataaat
16141 acttgaccac ctgtagtaca taaaaaccca atccacatca aaacccccctc cccatgctta
16201 caagcaagta cagcaatcaa ccctcaacta tcacacatca actgcaactc caaagccacc
16261 cctcacccac taggatacca acaaacctac ccacccttaa cagtacatag tacataaagc
16321 catttaccgt acatagcaca ttacagtcaa atcccttctc gtcccatgg atgacccccc
16381 tcagataggg gtcccttgac caccatcctc cgtgaaatca atatcccgca caagagtgct
16441 actctcctcg ctccgggccc ataacacttg ggggtagcta aagtgaactg tatccgacat
16501 ctggttccta cttcagggtc ataaagccta aatagcccac acgttccccct taaataagac
16561 atcacgatg
```

https://www.ncbi.nlm.nih.gov/nuccore/NC_012920.1

Mitochondrial Haplogroups

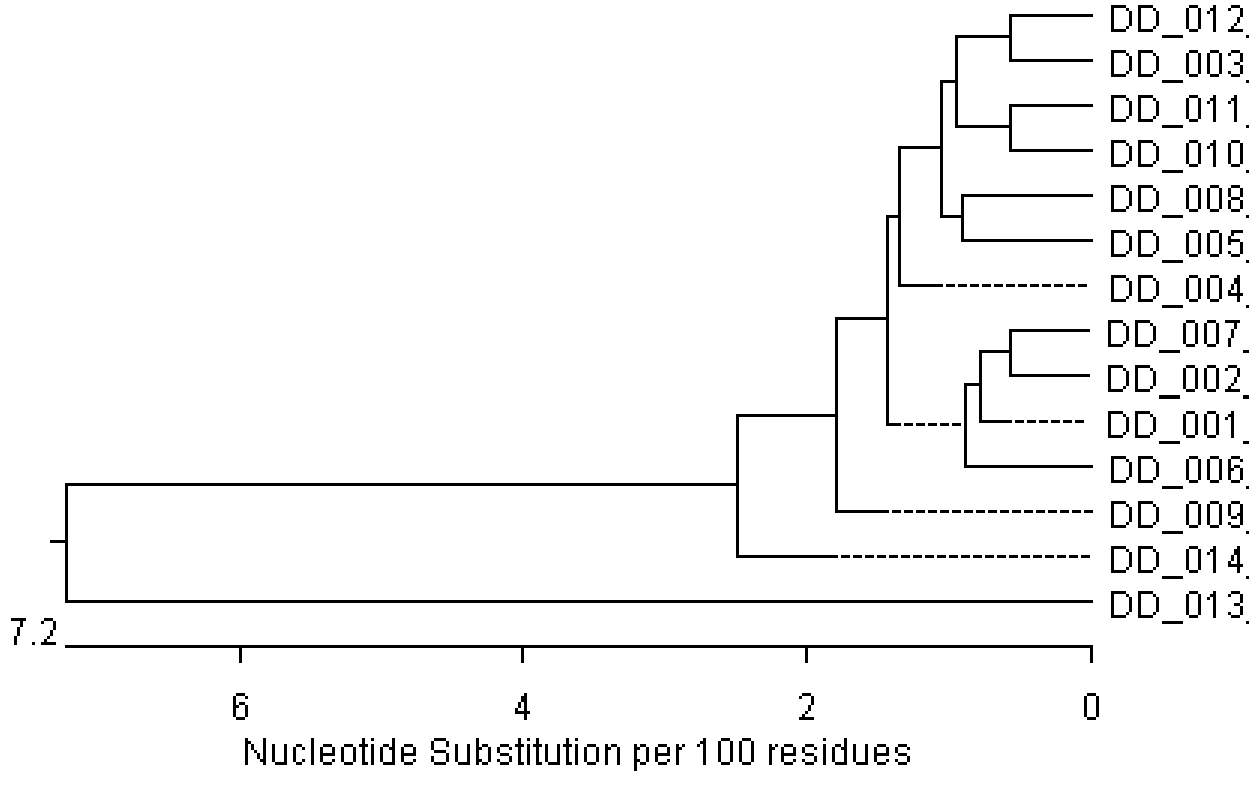
- The control region of mtDNA contains two major hypervariable regions.
- These regions don't encode proteins, so mutations can accumulate in the hypervariable regions without much danger of killing the mitochondria and their host. Since there is little or no recombination in mitochondrial DNA, lineages can be easily tracked.
- The mitochondrial haplogroups are defined with respect to the rCRS by specific mutations, some in the hypervariable regions, and others scattered through the coding regions.

Defining mutations of some haplogroups

L0	G263A, C1048T, C3516a, T5442C, T6185C, C9042T, A9347G, G10589A, G12007A, A12720G
L3	A769G, A1018G, C16311T
M	T489C, C10400T, T14783C, G15043A
N	G8701A, C9540T, G10398A, C10873T, A15301G!
R	T12705C, T16223C
H	G2706A, T7028C
I	T10034C, G16129A!
I2	A15758G

The first letter is from the rCRS, the number is the position, and the second letter is the altered base.
The ! mark represents substitutions that are a return to the ancestral base (from the previous branch) at that position.

Student Tree: HV1



What was the sequence for Mitochondrial Eve?

- The revised Cambridge Reference Sequence is a subgroup of haplogroup H2a2a1.
- Haplogroup H2 is a common European haplogroup.
- In 2012, a “Copernican” reassessment of the reference mitochondrial genome was done to shift the reference sequence from its Eurocentric position to “a phylogenetically valid reference point,” called the RSRS or Reconstructed Sapiens Reference Sequence.
- They compared 18,843 complete modern mtDNA genome sequences and 6 Neanderthal sequences.
- The resultant sequence falls between haplogroups L0 and L1, which differ from each other by 14 coding and 4 control region substitutions.
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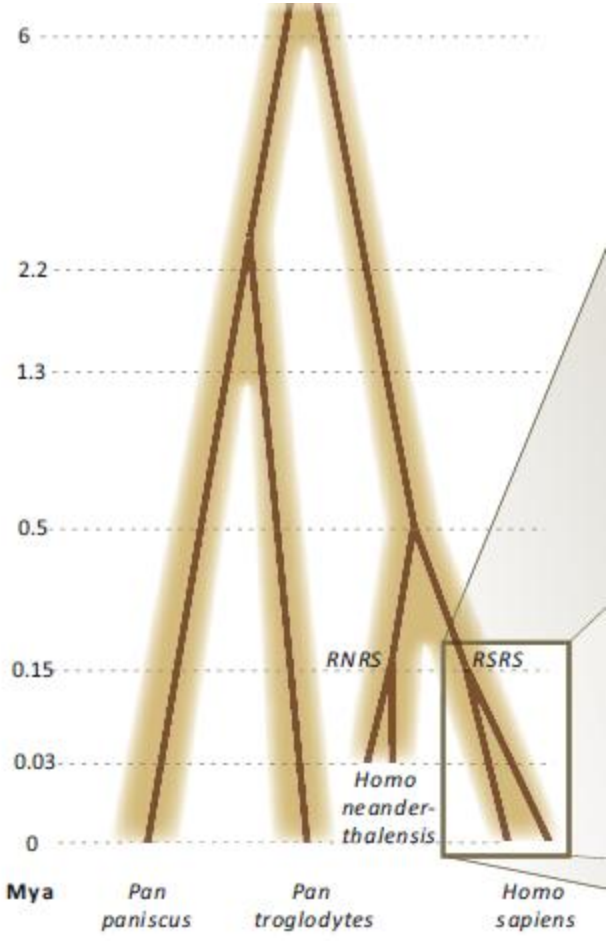


https://www.sciencedirect.com/science/article/pii/S0002929712001462?via%3Dihub

Control Region of the RSRS

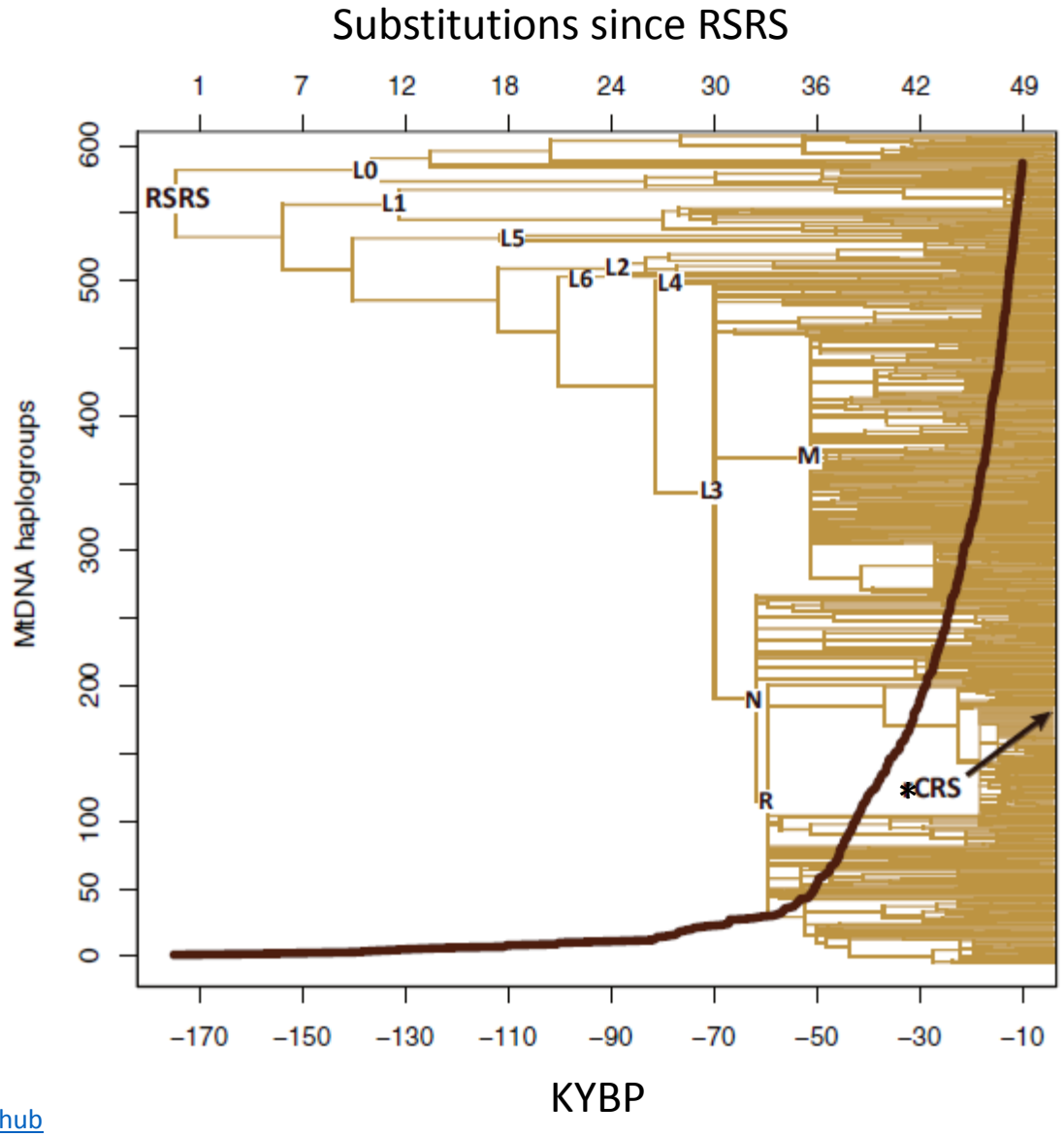
```
    1 gatcacaggt ctatcaccct attaaccact cacgggagct ctccatgcat ttggtatttt
   61 cgtctggggg gtgtgcacgc gatagcattg cgagacgctg gagccggagc accctatgtc
  121 gcagtatctg tctttgattc ctgccCcatc ccattattta tcgcacctac gttcaatatt
  181 acaggcgaac ataccCtacta aagtgtgtta attaatTaat gcttgtagga cataataata
  241 acaattAaat gtctgcacag ccgctttcca cacagacatc ataacaaaaa atttccacca
  301 aacccccccT cccccgcttc tggccacagc acttaaacaC atctctgcca aaccccaaaa
  361 acaaagaacc ctaacaccag cctaaccaga tttcaaattt tatcttttgg cggtatgcac
  421 ttttaacagt caccccccaa ctaacacatt attttccccT cccactccca tactactaat
  481 ctcatcaata caacccccgc ccatcctacc cagcacacac ac--cgctgc taaccccata
  541 ccccgaacca accaaacccc aaagacaccc cccaca

16021 nnnttctttc atggggaagc agatttgggt Accacccaag tattgactca cccatcaaca
16081 accgctatgt atTtcgtaca ttactgccag ccaccatgaa tattgtacAg taccataaat
16141 acttgaccac ctgtagtaca taaaaaccca atccacatca aAAcccTccc cccatgctta
16201 caagcaagta cagcaatcaa ccTtcaactG tcacacatca actgcaactc caaagCcAcc
16261 cctcacccac taggataTca acaaacctac ccacccttaa cagtacatag Cacataaagc
16321 catttaccgt acatagcaca ttacagtcaa atcccttctc gTccccatgg atgacccccc
16381 tcagataggg gtcccttgac caccatcctc cgtgaaatca atatcccgca caagagtgct
16441 actctcctcg ctccgggccc ataacacttg ggggtagcta aagtgaactg tatccgacat
16501 ctggttccta cttcagggCc ataaagccta aatagcccac acgttccccT taaataagac
16561 atcacgatg
```

Differences from the rCRS

Retains numbering of the rCRS

Some Ancestral Nodes

- RSRS: 176689.4 years (SD 11340)
- L0: 136289.1 years (SD 11754))
- L1: 128520.9 years (SD 10513)
- L3: 67262.0 years (SD 4434)
- M: 49590.1 years (SD 1824)
- N: 58859.9 years (SD 2352)
- H2:* 11905.3 years (SD 1364)
- I2: 6386.9 years (SD 2448)



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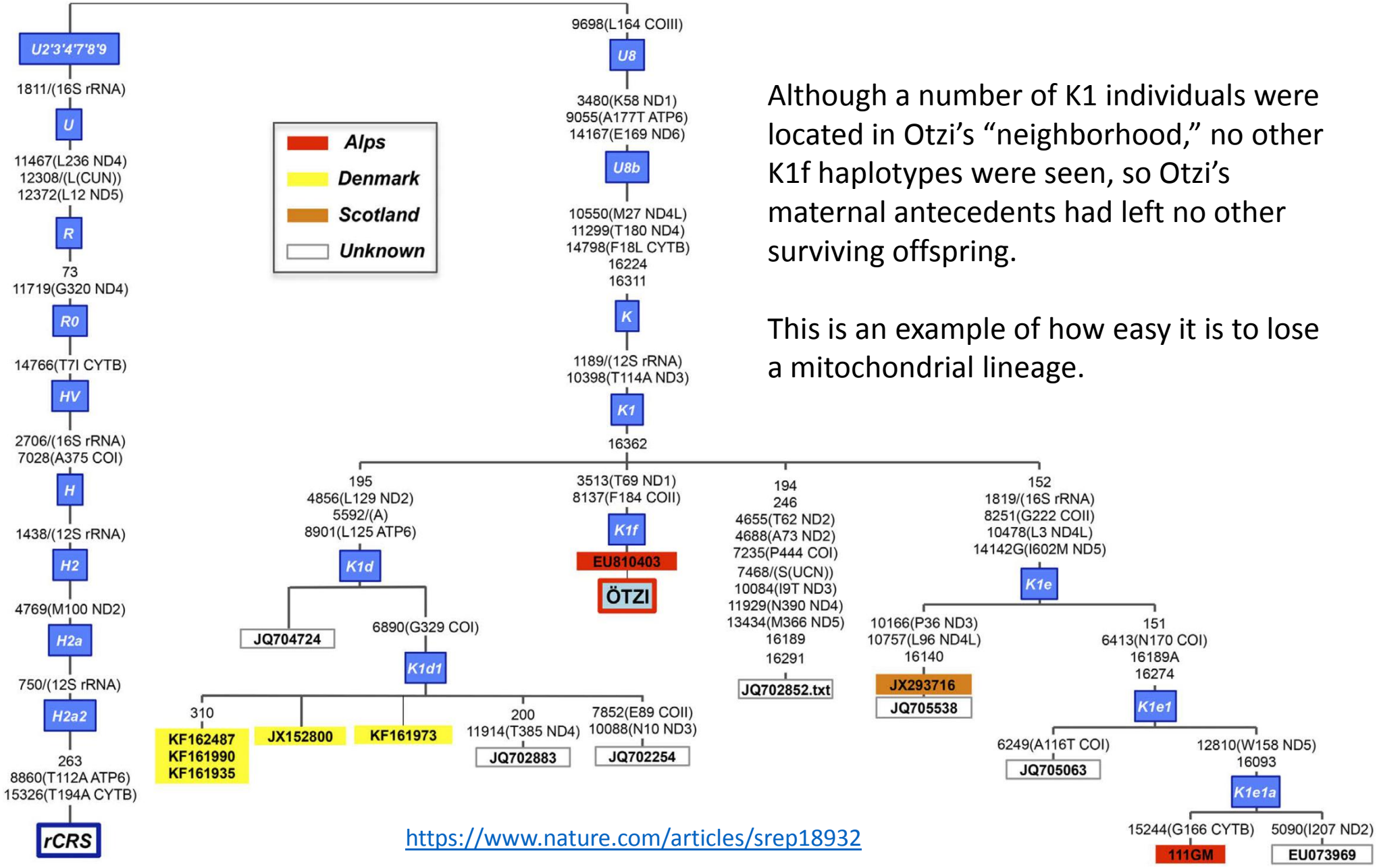
What about Otzi?

https://en.wikipedia.org/wiki/%C3%96tzi

- Otzi was freeze-dried, not a fossil, and provided massive amounts of both nuclear and mitochondrial DNA.
- Tools found with him dated the body to about 4000 years ago.
- He was blood type O, lactose intolerant, and might have had heart trouble had he not been killed by an arrow.
- His mitochondrial haplogroup was K1f, a subgroup of K1 with no known living relatives.
- mtDNA from 42 haplogroup K1 individuals from the Italian Alps were sequenced
- Otzi's genetic structure was compared with 42 haplogroup K1 samples from his region.



Although a number of K1 individuals were located in Otzi's "neighborhood," no other K1f haplotypes were seen, so Otzi's maternal antecedents had left no other surviving offspring.

This is an example of how easy it is to lose a mitochondrial lineage.

https://www.nature.com/articles/srep18932

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