

Outline

Mitochondrial DNA

mitochondria

inheritance

evolution

recent history

Human evolution

Neanderthal evolution

The use of mtDNA to study history

Between 1976 and 1983, the military of Argentina kidnapped, jailed, and killed 10,000-30,000 dissidents. Along with their parents, many infants and toddlers disappeared.

In 1977, the grandmothers of these children began to hold vigils

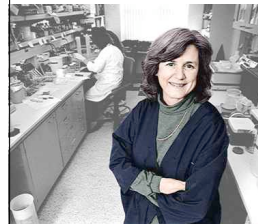
in the main square of Buenos Aires to inform others that about the disappearance of their children and grandchildren. This group became known as the "Grandmothers of the Plaza de Mayo." They contacted many organizations for help, including the American Association for the Advancement of Science (AAAS).



First, different alleles of the HLA locus were used.

In 1983, the easiest way to confirm or exclude the familial relationship between two people was to compare the human lymphocyte antigens (HLAs) on white blood cells. Even if a child's parents were missing or dead, the child should still have one allele shared by one of the paternal grandparents and the other shared by one of the maternal grandparents.

The AAAS put the grandmothers in contact with Mary Claire King, then a geneticist at Cal. Professor King taught Argentine medical workers to analyze HLA markers on white blood cells, and the workers typed HLAs from family members of the missing children. The grandmothers set up a bank of the HLA information. The probability that a tested child belonged to the family claiming him or her on the basis of eye-witness accounts of abduction varied from 75-99%.



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Then, mtDNA analysis was used.

By the mid-1980s, the simpler cases had been solved and limitations of the HLA approach became apparent. Professor King turned to her former mentor and colleague Allan Wilson, a molecular biologist at Cal who was studying mtDNA. PCR amplification and sequencing of the highly variable region of mtDNA made it possible to match a child with his or her maternal grandmother.

The probability that two unrelated individuals would be identical for this 131 bp region extremely small. In addition, the high copy number of the mtDNA aided in the identification of the remains of individuals killed by the military regime.

The Grandmothers' organization is still active



Analysis of human mtDNA led to the Mitochondrial Eve Hypothesis

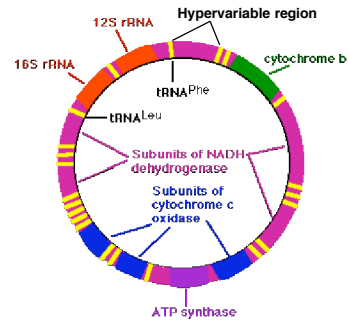
In the 1980s, Allan Wilson pioneered the use of mtDNA to study human evolution.



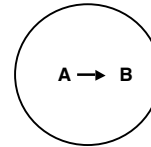
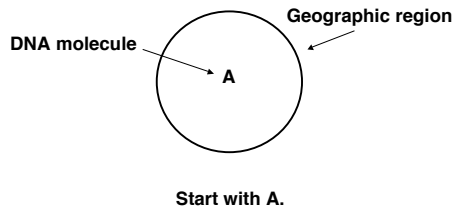
In two papers published in 1987 and 1991, he and his colleagues at Cal proposed that we all come from a population of humans that lived in Africa approximately 200,000 years ago.



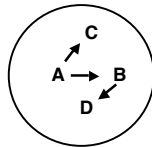
Wilson used the mtDNA hypervariable region



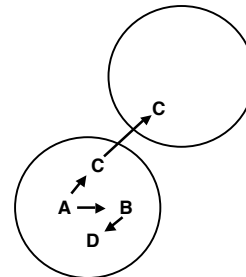
Here's the logic behind the hypothesis.



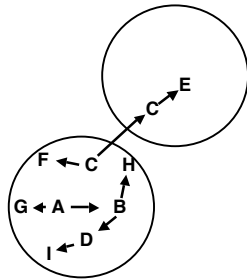
Mutation generates B from A; now have individuals with both A and B DNAs in population.



Additional mutations generate diversity; now have individuals with both A, B, C and D DNAs.



C migrates to form separate population.



Additional mutations diversify DNAs in populations: original population more diverse (A, B, C, D, F, G, H, I) than newer population (C, E).

Evidence for Mitochondrial Eve hypothesis

Compared sequences from the highly variable region of mtDNA.

Greater sequence differences among native Africans than any other group, which included Europeans, American Indians, Papua New Guineans, Asians, aboriginal Australians and individuals of Middle Eastern origin.

The diversity of Africans is equivalent to the diversity of all groups combined.

These observations led Wilson to propose that the African population has had the longest time to evolve variation and thus humans originated in Africa.

But when did Mitochondrial Eve live?

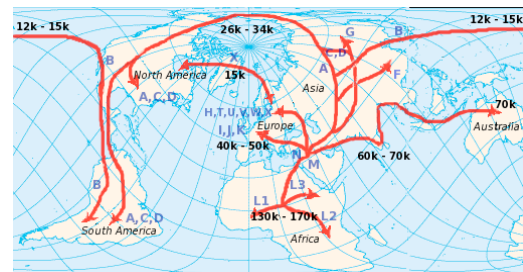
2.8% of the mitochondrial base pairs differed in the population of sub-Saharan Africans studied.

Chimpanzees and humans diverged about 5 million years ago, and human and chimpanzee mtDNAs differed at 15% of the base pairs of the mtDNA.

Adjusting the data to account for multiple substitutions at the same base pair, they calculated that mtDNA has been diverging at a rate of 13.8% per million years.

Assuming that this "molecular clock" is ticking at a constant rate, they determined that a "Mitochondrial Eve" from whom we are all derived lived 2.8/13.8 or 0.20 million years ago. Although there has been much argument about the assumptions and statistical methods used, most evolutionary geneticists accept that the women carrying our ancestral mtDNA lived in sub-Saharan Africa approximately 200,000 years ago.

Human migrations can be studied using Y chromosome and mtDNAs



Many mtDNAs /cell

2 for nuclear DNAs; 100s-1000s for mtDNAs

After death DNA slowly degrades

Can often amplify mtDNA but not nuclear DNA from preserved tissues and skeletons.

In 1883, the last existing Quagga died in an Amsterdam zoo.



More than 100 years later, analysis of mtDNA from museum Quagga tissue revealed that Quaggas were closely related to the extant plains zebra.

Neanderthals



Did Neanderthals interbreed with modern humans?

Two hypotheses account for interactions between modern humans and archaic Homo species.

The replacement hypothesis: As early *Homo sapiens* migrated out of Africa, they entered regions occupied by archaic Homo species and competed with them for resources. *H. sapiens* won the competition, leading to the extinction of archaic species.

The regional continuity hypothesis: *H. sapiens* interbred with the other species to generate modern humans.

Neanderthals were one of these archaic species, coexisting with modern humans for over 70,000 years until their extinction 30,000 years ago.



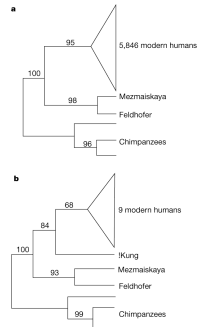
In 1997 and then again in 2000 scientists were able to amplify by PCR nucleotides from the highly variable region of mtDNA sequences from two Neanderthals, one from western Germany and one from the Caucasus.

mtDNA analysis favors the Replacement Theory

3x as many differences between human and Neanderthal sequences than between pairs of humans.

The types and positions of the differences were distinct in the two groups.

The line that gave rise to Neanderthals and modern humans diverged between 365,000 and 853,000 years ago. The two Neanderthal sequences were much more closely related, and the scientists estimated that the ancestor to the two Neanderthals existed 150,000 to 350,000 years ago. The investigators argued that these differences support the replacement theory.



Two trees showing relationships of mtDNAs from humans, Neanderthals (Mezmaiskaya & Feldhofer), and chimps. a and b are different statistical approaches using different human data sets.