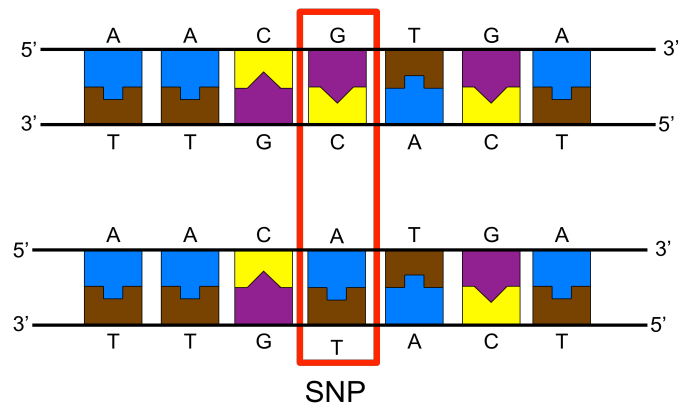


Day 1: Mitochondrial DNA and Ancestry

Genomic DNA is found in the cell nucleus and is passed down equally from both parents. Genomic DNA codes for all of your traits such as eye color, hair color, and just about anything that is inherited. Your cells also have another type of DNA called mitochondrial DNA. Mitochondrial DNA (mtDNA) is independent of nuclear DNA. While nuclear DNA is located in the nucleus of the cell, mitochondrial DNA is located in the mitochondria. Mitochondria is the organelle present in all cells which converts sugars into energy. Mitochondria is unusual in that it is the only organelles which has its own circular loop of DNA. Human mitochondrial DNA is much smaller than human nuclear DNA. Human nuclear DNA has around 3 billion base pairs or nucleotides, while human mitochondrial DNA only has 16,600 base pairs.

Mitochondrial DNA is inherited from the mother alone, rather than being inherited from the father and the mother. Additionally, recombination (or crossing over) does not occur in mitochondrial DNA (mtDNA). For both of these reasons, the sequence of mitochondrial DNA stays the same over generations, and thus is a useful tool for looking at maternal ancestry. Scientists have found that the mitochondrial genome mutates 5-10 times faster than nuclear DNA. One type of mutation, called a single nucleotide polymorphism (SNP), is a single base pair in a DNA sequence that has been swapped out for a different nucleotide. Below is an example of a SNP.

Single Nucleotide Polymorphism



Source: K. Minnehan thesis presentation.

In the above example, the fourth nucleotide from the left side is different. Person 1 has a guanine/cytosine (G/C), and person #2 has an adenine/thymine (A/T).

Scientists compare all DNA sequences to the DNA sequence of one individual from Cambridge England known as the Cambridge Reference Sequence or “rCRS”. This individual was chosen to serve as a comparison point for all other DNA sequences. This is similar to using a standard unit like a meter to measure the length of an object. The Cambridge Reference Sequence is the genome all scientists use as their standard for comparison; it is scientists’ “ruler” for comparing an individual’s DNA sequence to a standard.

Looking Back in Time

By looking at the patterns of SNPs in mitochondrial DNA, scientists can trace maternal ancestry back hundreds of thousands of years. Scientists do this by comparing the patterns in mitochondrial DNA between different groups of people. If two people have very similar patterns of SNPs in their DNA, they are most likely related in maternal lineage.

As our ancestors traveled throughout the world they settled in different communities. After a few generations of reproduction, people in similar settings evolved with similar patterns of mtDNA. Since the patterns are not

changed by recombination of the egg and the sperm or by crossing over, SNPs found in today's individuals can be used as a clue to who their ancient ancestors could be.

Human Migration Patterns

Scientists can gather clues about ancient human migration patterns by studying the patterns of SNPs in a modern day population. When a group of people share similar SNPs, they are part of the same "haplogroup". Scientists associate different haplogroups with different geographic locations on Earth such as "Africa", "Asia", "the Americas" and "Europe". By categorizing an individual into a haplogroup, it is possible to trace migration routes by observing the branching points in an ancestral map containing all known haplogroups.

Most scientists believe that all humans originated in Africa from a single female ancestor they named "mitochondrial Eve". This "Eve" was not the first female human, nor was she the only human alive at that time, but for some reason all of Eve's descendants survived to form the entire human species.

The climate of Earth changed, causing humans to migrate out of Africa in search of food. One possible map of different migration patterns of different haplogroups is depicted in Figure 1.2.

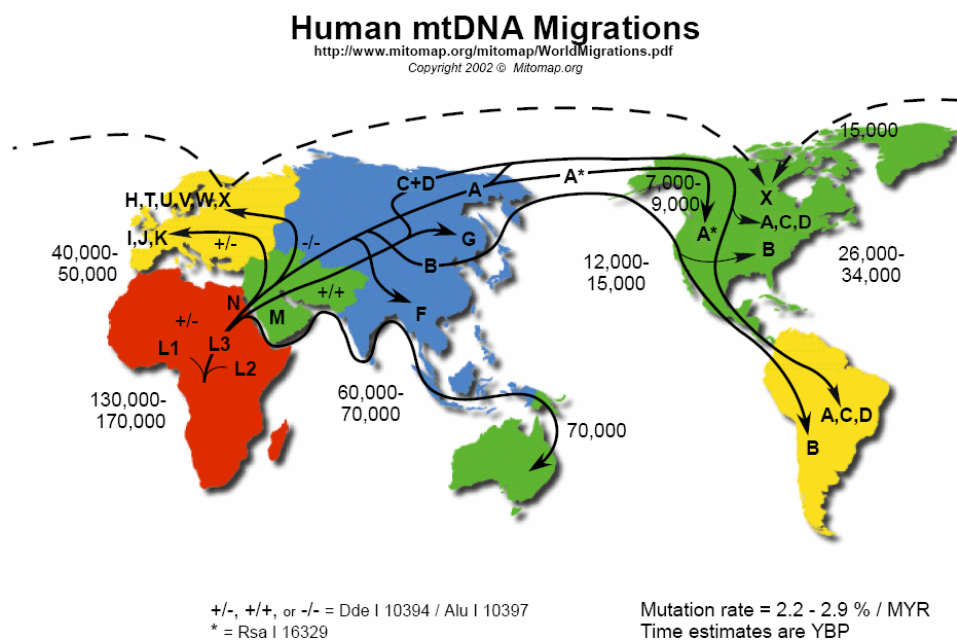


Figure 1.1. Migration routes of human beings dating back to 170,000 years ago. All humans originated in Africa and migrated out, branching into the two main out of Africa haplogroups, M and N. Individuals in haplogroup M headed west to Asia and later to the Americas, while haplogroup N moved into Europe.

Mitochondrial DNA in humans of African origin show the most diversity in the world. This supports the concept that ancient humans first existed in Africa, and stayed in Africa for thousands of years. The humans who left Africa took two major routes, to Asia (haplogroup M) and to Europe (haplogroup N). Later, evidence shows that some people turned away from Europe and headed east towards northern Asia (haplogroup A). These are three of the haplogroups we will be testing for in this experiment.

It's important to note that scientists use many different types of evidence (fossils, artifacts) in addition to mitochondrial DNA to determine these patterns. Mitochondrial DNA allows scientists to confirm other data they have collected.

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Questions:

1. What are two reasons why mitochondrial DNA is useful for determining maternal ancestry?
2. Explain why scientists use the Cambridge Reference Sequence.
3. You find that you are in the same haplogroup as your best friend. What does this mean?
4. In your own words, explain what a single nucleotide polymorphism is. Why do you think they are difficult to detect? What are they useful for?

What are some of YOUR Questions?

Glossary

Anneal – The pairing of complementary DNA or RNA sequences, via hydrogen bonding, to form a double-stranded molecule. Most often used to describe the binding of a short primer or probe.

Base pair – two nucleotides in a double strand of DNA, for example adenine and thymine (A and T) or cytosine and guanine (C and G) are the two base pairs that are repeated in DNA

Dehybridization – to break the hydrogen bonds connecting double stranded DNA so that two single strands remain. This is done by increasing the temperature of the sample.

dNTP – a generic way to say “nucleotide” that means any of the four DNA bases: adenine, guanine, cytosine, thymine

Genome – all of the genetic material (DNA) in a person or animal.

Haplogroup – a group of humans who share common maternal ancestors

Ligation – Joining linear DNA fragments together with covalent bonds is called ligation. The actual linking of DNA fragments is done with an enzyme called T4 DNA ligase.

Maternal ancestry – relatives of your mother who lived many thousands of years ago

Mitochondrial DNA (mtDNA) – a circular ring of DNA found in the mitochondria of cells, and passed down only from the maternal side

Nuclear DNA – found in the cell nucleus and comprised of DNA from both the mother and the father, this is the information code for all of an individual’s genetic traits.

Nucleotide – one of the four bases that link two strands of DNA together: adenine, guanine, cytosine, and thymine

Primers – A strand of nucleic acids that serve as a starting point for DNA synthesis. DNA polymerases can only add to existing strands of DNA, so primers help to start the process. Often, primers are used in the polymerase chain reaction (PCR). A PCR reaction typically contains two primers, one binding in the "forward" orientation to the 5' end of the target DNA sequence, and the other binding in the "reverse" orientation to the 3' end of the target.

Polymerase Chain Reaction (PCR) – a technique where a strand of DNA is copied many times by adding extra nucleotides to the solution, raising the temperature of the solution to break the double stranded DNA into single strands, and cooling the sample to allow the nucleotides to bind to the single strands.

Recombination – the creation of new DNA molecules from an original DNA molecule

Single Nucleotide Polymorphism (SNP) – a change in one base pair in a strand of DNA that can be useful for determining ancestry and other things such as risk for disease

Trait – a notable quality in a person which can be inherited genetically. Eye color and height, instinctual behaviors like migration of birds, and predisposition to diseases like cancer are all examples of different traits.