The History of Human Migration: A Genomic Approach

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Approximately 1.8 to 0.5 million years ago (Baab 2012), a hominins species left Africa for Eurasia in an expansion known as 'Out of Africa I' ("Recent" 2019). Human migration out of Africa occurred later, sometime during the Pleistocene era (Bons et al 2018). Migration out of Africa occurred in waves of large groups of people who left Africa together (Bons et al 2018); additionally, it is probable that smaller waves of migration leaving Africa also accompanied these larger waves (Bons et al 2018, Mascarelli 2016). Beginning in Africa, migration spread to the parts of the European and Asian continent closest to Africa, before traveling further into Europe, Asia, North America, Australia, South America, and Antarctica (Science Insider). This migration had a major impact on human evolution.

Humans (*Homo sapiens*) evolved from common ancestors *Homo heidelbergensis* and *Homo erectus* (O'Neil 2013). The earliest fossils of modern *Homo sapiens*, found at Omo Kibish, in Ethiopia, date back 200,000 years ("Map of Human Migration," 2019). The first human left Africa between 60,000 and 70,000 years ago; some reached Australia 50,000 years ago, while, at the same time, a second group crossed the Red Sea. Humans entered Europe through the Southeast and another group went to Middle East and Central Asia 35,000 years ago ("Map of Human Migration" 2019). 15,000 years ago, humans reached America (Hodges, 2015).

There are many theories which attempt to explain why humans migrated out of Africa (Bons et al 2018). For example, it is thought that climatic conditions became more favorable at this time, which led to humans migrating out of Africa in periodic waves (Mascarelli 2016). Some theories suggest that migration was driven by climate swings on the continent starting approximately 100,000 years ago (ibid). It appears that major fluctuations within the climate created certain areas where travel was not as arduous of a task. Additionally, the land bridge theory regarding the arrival of early humans in the Americas theorizes that a change in the environment, for instance a drought or a disappearing food source, may have motivated humans to migrate to new regions. It is possible that a steady supply of food was not as readily available and competition for the available resources may have made matters worse ("Homo Sapiens And Early Human Migration"). In addition to scarcity being a factor in migration, there would usually be waves of humans migrating towards a particular region, since most hominids (especially humans) lived primarily in groups. Furthermore, it is also possible, though not definitive, that some very basic technologies assisted human migration out of Africa (Frischkorn 2016).

Early humans were hunter gatherers. When it comes to sustaining this hunter gatherer lifestyle, these groups of humans had to be somewhat nomadic to follow

where their resources may be. Thus, migratory patterns of early humans may have been similar to that of the fauna they hunted.

Humans and Other Hominins

Homo neanderthalensis (Neanderthal) and modern humans might have shared the common ancestor *Homo heidelbergensis*. After migrating out of Africa, anatomically modern humans bred with other hominin species, including Neanderthals and Denisovans (Alex 2016). Neanderthal's bodies were stockier and their limbs slightly shorter and more robust than modern human counterparts. Additionally, Neanderthals had barrel chests along with stocky statures. The average height and weight for the Neanderthals were approximately 1.50m-1.75m and 64 kg to 82kg (Hendry 2018). One of the major differences between Neanderthals and modern humans is the shape of the skull. The average brain size for humans is about 1,349 cm^3, smaller than the average brain size for Neanderthals, about 1,410 cm^3 (Alex, 2018). It is interesting to note that modern humans also have smaller stomachs compared to Neanderthals. About 500,000 years ago, humans and Neanderthals went separate ways: Neanderthals moved north and westward, to the Middle East and Europe, while humans stayed in Africa ("Ancient DNA And Neanderthals").

Neanderthal mtDNA genomes and the human genome differ from each other by an average of 20.4 base pairs. The mtDNA genome is only 1/3 as diverse as that of modern humans, which might be due to a small population size of Neanderthals ("Ancient DNA And Neanderthals," 2019). There are 78 non-synonymous nucleotide substitutions in modern humans that differ from the Neanderthal genome. Fragments of DNA sequences from the mDNA genome indicate the presence of a mutation in the MCPH1 gene, which causes Neanderthals to have red hair and pale skin (Ahmed & Liang 2013). Neanderthals and modern humans share the ABO blood groups, as well as the TAS2R38 allele (taste receptor gene) for tasting bitterness. Additionally, modern humans and Neanderthals share the same FOX2 gene, linked to language ability (Ahmed & Liang, 2013). There are DNA sequences in the Neanderthal genome associated with diabetes, lupus and Crohn's disease in the human genome (Hendry 2018).

Denisovans are relatives of both modern humans and Neanderthals, and likely diverged from these lineages around 300,000 to 400,000 years ago ("Ancient DNA And Neanderthals," 2019). The Denisovans received their name from the fact that they lived and interbred with Neanderthals within the Denisova environs. In 2018, paleoanthropologists found a 40,000-year-old adult tooth and a pinky bone inside a cave in Siberia that belonged to a young Denisovan girl who was between five and seven years old when she died. The DNA sequencing showed that the young girl had brown hair, eyes and skin ("Why am I Denisovan?" 2019). The mtDNA from the finger bone differs from that of modern humans by 385 bases out of approximately 16,500 base pairs.

While migrating to other parts of the world, humans encountered other hominins and bred with them. Neanderthal genome is more similar to non-African genome than to African genome. Modern non-African humans have 1-4% Neanderthal ancestry. Inhabitants of Pacific islands have up to 5% Denisovan ancestry (Ahmed & Liang 2013). The Denisovan genome also contributed to the Tibetans and Sherpas an allele of a specific gene, EPAS1, which regulates blood

hemoglobin and allows adaptation to areas of low oxygen. This allows Tibetans and Sherpas to live without difficulty in oxygen-thin environments above 13,000 feet (Gibbons 2014). There aren't a lot of fossils discovered from Denisovans, so as of today, researchers are still investigating how the Denisovan genome is compared to human genomes.

Genomic Analysis

Ancient DNA (aDNA) samples are retrieved from museum specimens, archeological finds and fossil remains. The samples have deteriorated due to long-term preservation, and extraction usually results in fragments as small as 100 bp. Samples are also prone to contamination from human, microbial and fungal sources. Ancient DNA was first successfully extracted in 1983 from an ancestor of the zebra. The extraction method was applied to Egyptian mummies in 1985, and Neanderthals in 1997 (Nesheva 2014).

Polymerase chain reaction (PCR), while amplifying the sample, also amplifies contaminants, making authentication difficult. In shotgun sequencing, researchers tried adding templates to repair the ends of the aDNA fragments before copying random fragments. However, specimens tend to be colonized by microbes, and the process cloned more microbial DNA than DNA from the intended specimen (Llamas et al., 2017). High-throughput sequencing (HTS) is achieved through the Roche 454 system, which adds adapters to the ends of aDNA fragments before amplification, making many copies simultaneously. Unfortunately, contamination was still an issue (Llamas et al., 2017).

After successfully extracting aDNA, researchers began attempting to sequence the whole mitochondrial genomes of different specimens. Illumina HTS, a different sequencing platform from Roche, was successfully used to sequence a genome of a 4,000-year-old Palaeo-Eskimo in 2010. (Illumina HTS reads shorter fragments than Roche, but has a lower error rate.) In the Neanderthal Genome Project, started in 2006, scientists at the Max Planck Institute sequenced the complete mitochondrial genome of a 38,000-year-old Neanderthal, using a combination of Sanger sequencing and 454 sequencing ("Neanderthal Mitochondrial And Nuclear DNA"). Although the sequencing was successful, contamination persisted. In addition, there are a limited number of available Neanderthal specimens in the world, so this type of research cannot continue indefinitely (Llamas et al, 2017).

Researchers use mitochondrial DNA (mtDNA) for several reasons. The genome size is smaller than the nuclear genome, making it easier to sequence. There are many copies of the mitochondrial genome in the body, since each cell contains multiple mitochondria. This type of DNA does not recombine, so any variations in the sequences are due to mutations. In addition, the mutation rate is higher than in nuclear DNA, which is useful for population studies, because it results in geographically restricted haplogroups. This reveals the linked inheritance of different mutations (Nesheva 2014). The original haplogroups originating in Africa were L1, L2 and L3. Haplogroup L3 gave rise to haplogroups M and N in Europe in Asia. Haplogroup N later gave rise to haplogroups H, I, J, N1b, T, U, V, W and X, which are still found in Europe today. Haplogroup M gave rise to haplogroups A, B, C, D, F and G in Asia. Haplogroups A, B, C and D are also found in Native Americans. MtDNA sequences are usually aligned using the revised Cambridge

reference sequence, which is the first completely sequenced mtDNA genome and is derived from the European haplogroup H (Nesheva 2014).

Machine learning has also been used to analyze human evolution. In this process, computers are given a set of algorithms that simulate the evolution of human DNA to analyze human genomes and predict human demographics. Eight different models were employed, based on existing theories of human evolution. The machines concluded that there is an ancestor that has not yet been identified (Handwerk 2019).

Conclusions and Questions

In conclusion, one of the questions still yet to be answered is whether we can discover a more definitive time frame from which humans began to evolve, rather than the general figure of around 200,000 years ago (Stoneking 1991). Additionally, because Neanderthals were quite similar to humans but went extinct, another question is whether certain factors caused the Neanderthal extinction, such as their being less prepared for climate change, or less adaptable (Daley 2018). Furthermore, it would be interesting to research whether or not sequencing Y-chromosomes would provide greater insights into evolutionary processes throughout our genetic development, such as the degeneration of certain genes, the accumulation of certain genes, and the transposition of a major segment of the X chromosome (Charlesworth 2003). Finally, an interesting recent study, "African evolutionary history inferred from whole genome sequence data of 44 indigenous African populations," indicates that geography and language had a major impact on the resulting genetic structure of modern humans (Fan et al 2019).

Future directions for this work would include research into these still-unanswered questions regarding human evolution and migration. A more thorough understanding of evolution will potentially allow for new and innovative treatment approaches to many currently untreatable and incurable diseases.

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