Genesis Healthcare

GeneLife
Generations

White Paper 20-1

GeneLife Generations

"The Science Behind Maternal and Paternal Ancestral Lineage"

(mtDNA and Y-DNA haplogroup and possible migration routes)

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Introduction

Embarking on a journey of ancestry is truly nostalgic and customers will be introduced to many different concepts and terms that GeneLife Generations will bring to them. As many read through the report, they will discover what their DNA reveals about their maternal and paternal ancestors, fueling unique experiences about unveiling possible migration routes.

GeneLife Generations is a genetic composition analysis service that comprehensively predicts the shared genetic composition of ancestors from generations ago. Along with the genetic ancestral composition analysis, this report will identify origins and migration routes of both maternal and paternal lineages traced back to approximately 150,000 to 270,000 years ago.

Our Testing Method

Haplogroups are informative and useful for the understanding of genetic lineage and it also reveals undiscovered ancient migration routes from ancestors.

The GeneLife Generations report provides the result of an individual's paternal and maternal haplogroups and their possible migration routes based on their mtDNA and Y-DNA mutation analysis. Genesis Healthcare uses its specially designed chip for populations in Asia and across the globe, with support from the Micro-array technology platform. This platform is an industry standard and widely used for genotype calling. For the test, DNA is simply extracted from saliva samples and subjected to genotype calling according to our stringent protocols.

For analyzing maternal and paternal haplogroup, Genesis Healthcare has used HaploGrep (Weissensteiner H et al., 2016) and Snappy (Severson AL et al., 2018).

The Y and X Chromosomes

Y chromosome is one of the two sex chromosomes, genetically the determinant of the male gender and the SRY gene in this chromosome triggers the male development. The other is known as the X chromosome. Males have two sex chromosomes X and Y while females have two X chromosomes. Your gender, either male or female is determined depending on which chromosome you inherit from your father. If your father passes a copy of Y chromosome, you are genetically a male. If you are a female, you inherited a copy of x chromosome from both of your parents.

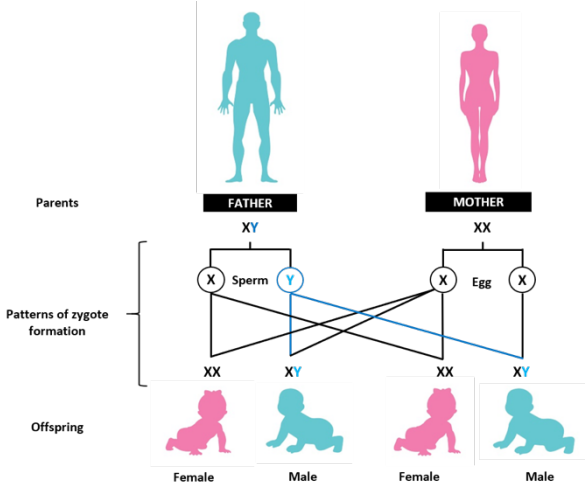

Figure 1: Graphical representation of gender determination by Y chromosome in human: The probability of being a male or female is 50%.

Mitochondrial DNA (mtDNA)

mtDNA is a small circular DNA chromosome that is found inside mitochondria in the cell. mtDNA is passed only from a mother to her offspring through the egg cell. mtDNA is a potential tool for tracing back to the single common maternal ancestor and for the understanding of the human evolution.

Maternal ancestors

Tracing maternal haplogroups, via the Mitochondrial DNA, allows to identify migrations from your matriline over centuries and sheds light about the history of your female ancestors. Maternal haplogroups are scientifically and internationally categorized. Any individuals belonging to a haplogroup, is assigned letters of the alphabet and the refinements consist of additional numbers (e.g. D4a1c). The alphabetical ordering does not have any meaning in terms of the actual genetic relationships.

Maternal haplogroups and related migrations can be traced for both females and males as they are passed down by women to their children from generations to generations.

As mutations occur across generations, analyzing the patterns of accumulated mutations allow the researcher to identify common ancestors from approximately 150,000 to 200,000 years ago. Through sequence analysis, comparison and identification of differences, scientists have constructed a mitochondrial phylogenetic tree, showing how maternal lineage are related to one another.

Updated comprehensive phylogenetic tree of worldwide human mitochondrial DNA variation with the defining mutation is provided here: https://www.phylotree.org/tree/index.htm

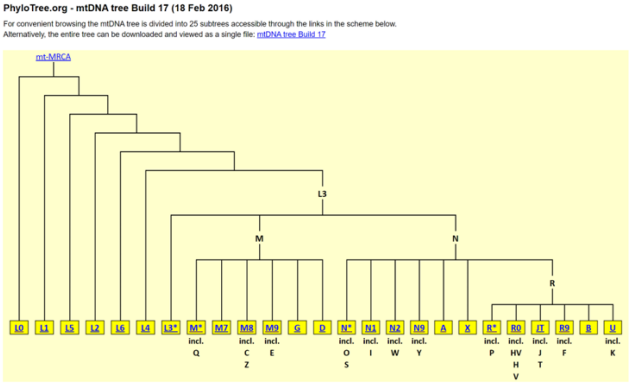

Figure 2: A representative image of phylogenetic tree of the worldwide human mitochondrial DNA variations. The full tree could be seen using the above link.

Paternal ancestors

Tracing paternal haplogroups allows for identification of migrations from your patriline over centuries and sheds light about the history of your male ancestors.

As mutations occur across generations, analyzing the patterns of accumulated mutations allows for researchers to identify common ancestors from approximately 275,000 years ago. Through sequence analysis, comparison and identification of differences, scientists have constructed a paternal lineage tree (also referred as Y-DNA haplogroup tree). The branches on this lineage tree comes from common male ancestors who share certain sets of Single Nucleotide Polymorphisms (SNPs) and shows how paternal lineages are related to one another. Any individuals belonging to a haplogroup is assigned letters of the alphabet and refinements consist of additional numbers (e.g. I2a1b). The alphabetical ordering does not have any meaning in terms of actual genetic relationships.

Paternal haplogroups and related migrations can be traced only for males. Since females do not have the Y chromosome, their paternal haplogroups and related migration patterns cannot be traced. However, if a female customer is interested to learn more about their paternal ancestors, it is recommended to connect with a first degree male relative, i.e. father or full brother to take the GeneLife Generations test and share their paternal haplogroup report.
To see the scientific details of a paternal lineage tree, visit this link: https://www.yfull.com/tree/.

The International Society of Genetic Genealogy (ISOGG) maintains the most up-to-date version of the Y-SNP tree for reference. If interested, please visit the site:
https://isogg.org/tree/2017/index17.html.

Y-DNA and mtDNA Haplogroups

Understanding the evolutionary path of the male and female lineages has helped population geneticists trace the patrilineal and matrilineal inheritance of modern humans back to human origins in Africa and their subsequent spreading across the globe.

As the SRY, gender regions on Y-chromosome and mtDNA are carried in a haploid state and cannot recombine, dispersive genetic forces act relatively quickly to change their sequences (mutations / SNPs) as populations diverge from one another. These variations collect in patterns that uniquely mark individual paternal lineages.
The distribution and migration of these variations across the world (geographic expansion) occurs in a different manner than the autosomal chromosomes since there is a natural difference in ratio between males and females due to biological and behavioral differences.

Y-DNA and mtDNA haplogroups allow genealogists to gain more insights into patrilineal and matrilineal ancestral origins of those who lived thousands of years ago and their possible migration routes since closely related haplogroups who share common mutations tend to also share common geographic routes.

Research and Partnership

Genesis Institute of Genetic Research has been actively involved in genetic research and development across multiple domains and has conducted an extensive research on human genetics and population migrations over the years and across the world. Multiple sources of research and information have been reviewed and compiled in developing the content featured in this report. In the domain of ancestry composition and population migrations, Genesis Healthcare has been collaborating in joint research with the National Institute Genetics in Japan for more than three years. For additional information, please visit https://www.nig.ac.jp/nig/.

Technical Limitations and Updates

The ancestry test results are interpreted in the context of current research knowledge, analysis technologies and other laboratory data including the internal quality check criteria. Based on the differences or in the limitation in analysis technology, criteria, and the data quality, certain SNPs may not be covered where variants cannot be confidently detected.

Due to the advances in research, analysis technologies, reference background genetics, and improvement of science, the results might be reflected differently due to the refreshment of data and updated comprehensive phylogenetic tree of worldwide human mitochondrial DNA variation, and ISOGG (International Society of Genetic Genealogy) Y-DNA Haplogroup Tree.

However, it does not necessarily mean that the customer's DNA has been changed, rather it should remain the same for the whole life.

Due to an enormous research advancement on Y-chromosome that occurred recently and the haplogroup tree underwent frequent updates, for some Y-DNA haplogroups, the migration information is less concordant compared to mtDNA haplogroup and its migration routes.
The prediction on place of origin, period and distribution of the reported haplogroups are based on the resources and current research and may vary based on sources and advancement of research. In addition, siblings who are supposed to belong to the same Y-DNA and mtDNA haplogroups might have a slight difference in their reports due to data quality of certain SNPs data where variants cannot be confidently detected due to sample or DNA quality, technical limitations, or due to some unknown reasons.

Glossary

- **Genetic variation:** Genetic variation is a term used in genetics to explain the differences in the DNA sequences between individuals to differences between larger populations.

- **SNP:** Single Nucleotide Polymorphism (SNP) is a genetic variation among a population. It is a substitution of a single base called nucleotide that occurs at a specific position in the genome, the DNA of the body cells. On average, SNPs occurs once in every 1,000 nucleotides in the human genome. Researchers have found these SNPs present in mtDNA and Y-DNA useful for tracing haplogroups, informative and useful to understand genetic lineage and reveals undiscovered ancient migration routes.

- **Allele:** Each single variation in the DNA results in two or more alternative forms found at the same place in a gene and these are called alleles.

- **Haplogroup:** A human haplogroup is defined as a genetic population group sharing a common ancestor on the patriline or/and matriline. Any individuals belonging to a haplogroup, is assigned letters of the alphabet and the refinements consist of additional numbers.

- **Maternal haplogroup:** Maternal haplogroup is a family of mitochondrial DNA, built based on the differences in mitochondrial DNA inherited from the mother where a single or group of alleles are inherited that traces back to single common ancestor.

- **Paternal Haplogroup:** A haplogroup defined by a set of mutations in the Y-chromosome DNA inherited from the father is called paternal haplogroup. People belong to a haplogroup share common mutations known as SNPs.

- **Ancestry:** The term ancestry is used to explain the origin or background history of one's family or line of ethnic descent. The more closely related two individuals, families, or populations are, the more patterns of variation they typically share.

For additional information, please visit the FAQs on our website. Users who have undertaken the test are able to access more detailed references for maternal and paternal migrations as well as related haplogroups in the GeneLife mobile application.

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