Does background genetic variation in mitochondrial DNA affect the expression of mutations?

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1) Introduction

Mitochondria are called the powerhouse as they generate energy in the form of ATP for the cell to function. It contains genetic materials known as mitochondrial DNA (mtDNA).

Mutations refer to the mistakes that occur within this genetic material, which may or may not cause diseases. When a mutation causes diseases, it is referred to as "pathogenic" while the term "polymorphic" means that it is not disease-causing. Genetic materials vary among different populations, influencing whether or not a certain mutation is shown or expressed.

2) Aims

- To investigate whether background genetic variation affects expression of mtDNA mutations
- To explore whether or not a pathogenic mutation in one population can be polymorphic in another population

3) Methods

Classification of mutations based on databases

- Including mamit-tRNA[1], Yarham's score[2], Mitotip[3] and Genbank[4]

Literature search

- To investigate if a pathogenic mutation has been reported as polymorphic and vice versa

Assessment of gathered data

- To draw conclusions

Figure 1: Project overview.

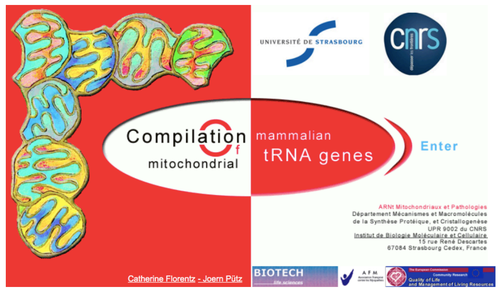

Figure 2: Database known as mamit-tRNA[1]

4) Results

- Throughout the project, we encountered some mutations which could be both polymorphic and pathogenic in different populations
- Mutation can be easily understood if you thought of it as a spelling mistake. For instance, m.593T>C refer to a mistake that happens at position 593 where a T is mistakenly replaced by a C in the mitochondria
- m.593T>C has previously been classified as polymorphism or non disease-causing according to mamit-tRNA and Yarham's score[1,2]. Both these resources focus mainly on the European population
- In a recent paper published in China, this mutation was identified in a family with hearing loss. Along with some other tests performed, this paper provided strong evidence to show that this mutation can result in diseases[5]

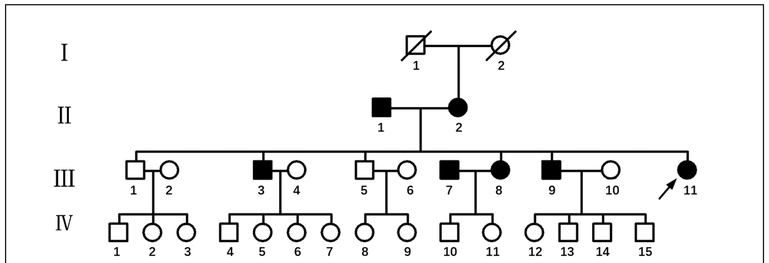

Figure 3: Chinese family where m.593T>C was identified. Affected individuals are indicated as black symbols[5].

- m.593T>C has therefore shown us that a mutation can give different results in different populations. If you are an Asian with this mutation, you are likely to experience some problems but if you are an European with the same mutation, you are likely to be completely healthy

5) Discussion

- Mitochondrial diseases that result from mitochondrial DNA mutations, despite being serious and fatal, has not been fully understood
- The lack of knowledge in this field therefore pose challenges for medical team to properly diagnose and deal with patients of suspected mitochondrial diseases. This condition is worse in certain populations such as Black African and Asian as compared to European. We therefore address this problem by linking different populations and bringing data together in this study
- The main limitation in this study is the lack of studies in populations other than European. The database focuses mainly on European and we believe that mitochondrial diseases are under-diagnosed in other populations
- More studies regarding mitochondrial diseases are needed and more case reports should be published as there are mutations that give different results in different populations as seen in our study

6) Conclusion

- The expression of mitochondrial DNA mutations is greatly affected by one's genetic background in different populations
- A mutation that is pathogenic in one population can be polymorphic in another

7) Acknowledgement

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8) References

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