# A Mitochondrial Genome Scan for Thrifty Genes in Maori

**Miles Benton**[1,2], Donia Macartney Coxson[2], David Eccles[1,2], Lyn Griffiths[3], Geoff Chambers[1], and Rod Lea[1,2]

[1] School of Biological Science, Victoria University of Wellington, New Zealand. [2] Kenepuru Science Centre, Institute of Environmental Science and Research, New Zealand.
[3] Genomics Research Centre, School of Medical Science, Griffith University, Australia. **Contact r.lea@griffith.edu.au**

## Background

- The high risk of Type II diabetes (T2D) in Maori may be partly explained by elevated prevalence of genes involved in energy metabolism.

- The genetics of Maori populations has been shaped by island hoping migration events which have possibly favoured “thrifty” genes via positive selection (see Figure 1).

- The aim of this study was to scan the mitochondrial (MT) genome in a Maori population to identify potential thrifty genes.

- Identification of thrifty genes should justify formal studies of T2D risk with the view of developing more effective DNA-based treatment for Maori.

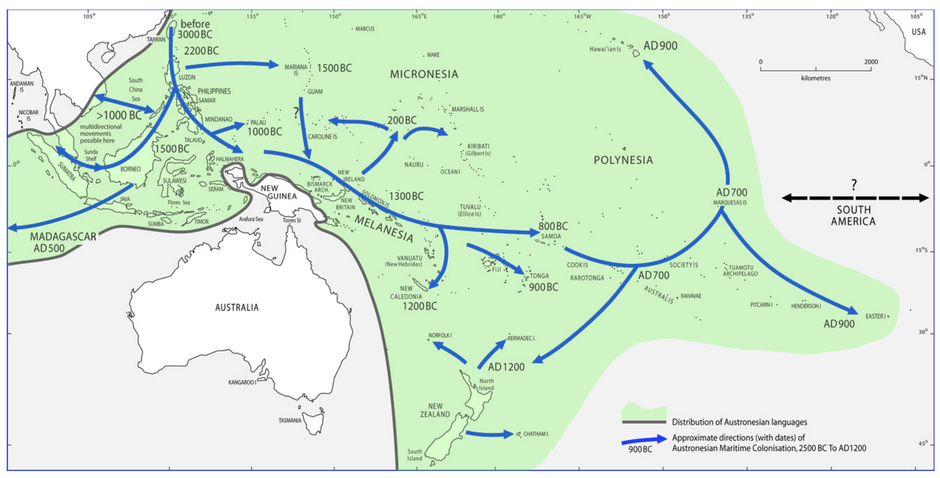


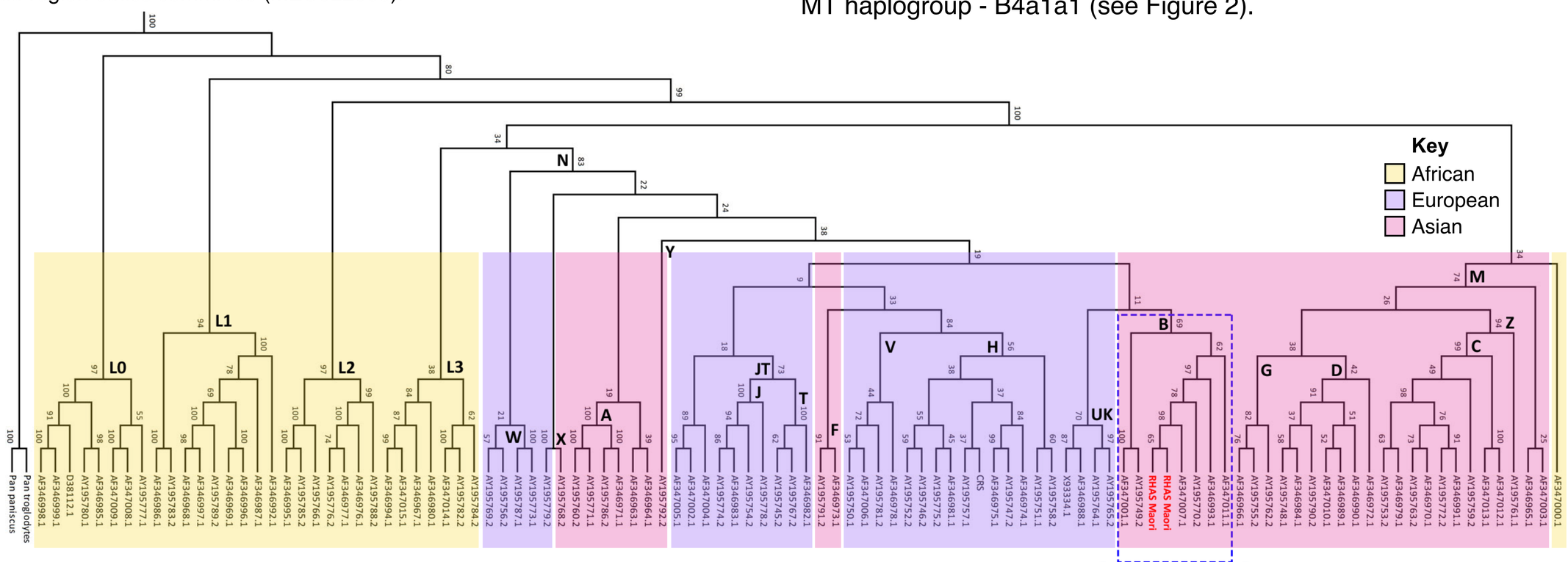

**Figure 1.** Map outlining migratory paths of Austronesian speaking populations. Adapted from Bellwood et al., (unpublished).

## Methods

We sequenced the complete MT genomes of 20 non-admixed Maori subjects using Mitochip™ technology. The DNA sequence data were analysed in-silico using standard population genetic methods. Ethical approval for this research was granted by the Maori Iwi and the Multi-region ethics committee (MEC022005).

## Phylogenetics

Sequence alignment showed the Maori group to have reduced MT genome diversity, which is consistent with historical bottleneck and founder effects. Global phylogenetic analysis posited these Maori subjects specifically within MT haplogroup - B4a1a1 (see Figure 2).




## A unique Maori mtDNA signature

Compared to ancestral populations we observed marked increases in the frequency of most coding gene variants in the Maori group (see Figure 3), which is a pre-requisite for the thrifty gene notion. However, subsequent neutrality testing did not support the hypothesis of selection effects acting on these genes.

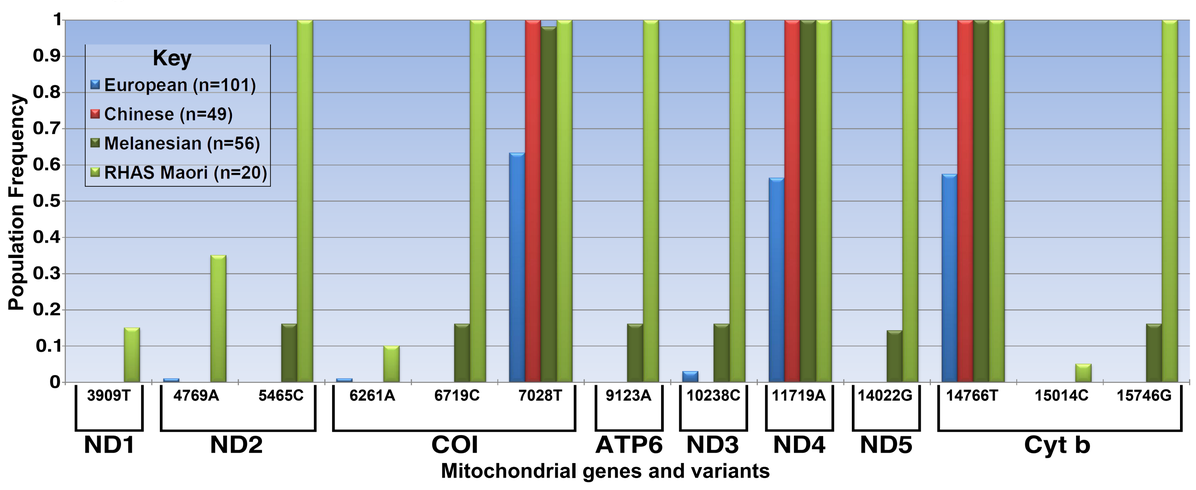



**Figure 3.** Frequency of novel MT signature variants in NZ Maori and 3 other geographic populations.

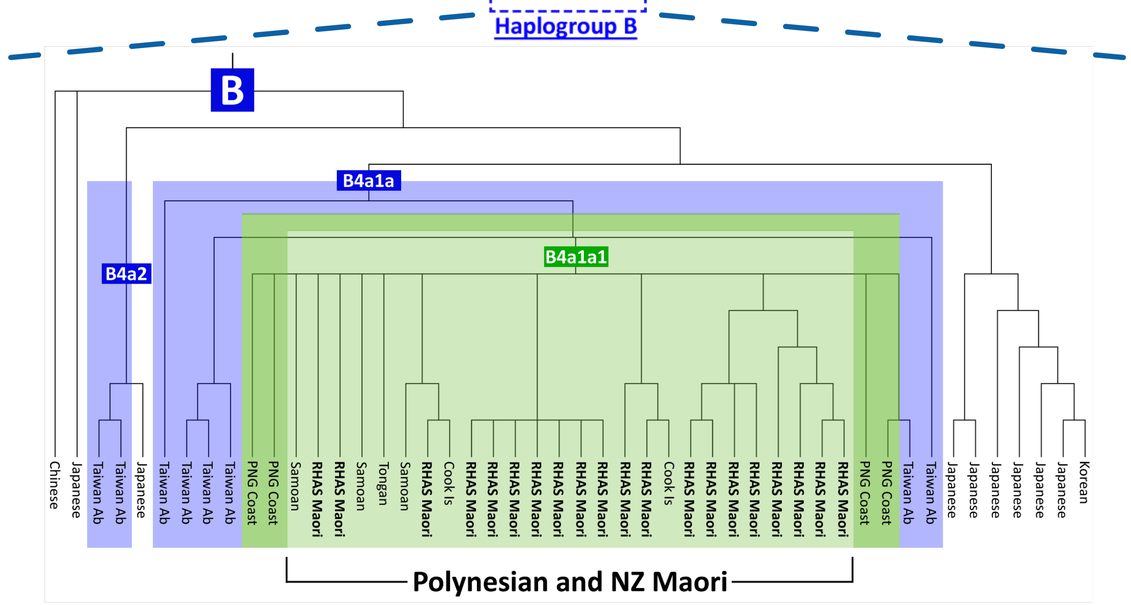



**Figure 2.** Phylogenetic reconstruction detailing a global tree of complete MT genome sequences, major haplogroups are represented by letters and bootstrap values are shown. Haplogroup B (includes NZ Maori) is shown in detail.

Interestingly, the MT genome scan identified numerous novel variants, several of which collectively form a unique MT motif in the Maori sequences (see table below).

## Novel mtDNA variants

| Gene | Nucleotide Change | Protein Change | No. Individuals | Percentage |
|---|---|---|---|---|
| 16SrRNA | m.1806T→C | NA | 1 (20) | 5 |
| ND1 | m.3909C→T | syn | 3 (20) | 15 |
| COXI | m.6782T→C | syn | 1 (20) | 5 |
| COXIII | m.9255C→T | p.MT-COXIII:Pro17Ser | 1 (20) | 5 |
| COXIII | m.9722T→C | syn | 1 (20) | 5 |
| Cyt b | m.15014T→C | p.MT-Cyt b:Phe90Leu | 1 (20) | 5 |
| HVRI[†] | m.16295C insA | NA | 1 (20) | 5 |

[†]control region (non-coding)

## Discussion

- This study reports the first complete MT genome sequence data for a Maori population.

- These new data enhance the global mtDNA tree and reveal a potential MT motif specific to Maori.

- Selection testing of coding genes in this sample did not support the thrifty gene hypothesis.

- The increased frequency observed for these MT variants is probably explained by genetic drift that occurred during migration and subsequent population expansion.

## Conclusion

The increased frequency of these MT metabolic genes makes them excellent candidates for future studies aimed at DNA-based assessment of T2D risk in Maori populations.

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