

Supplemental Data

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**Comparing Phylogeny and the Predicted Pathogenicity
of Protein Variations Reveals Equal Purifying Selection
across the Global Human Mitochondrial DNA Diversity**

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Supplemental Figures

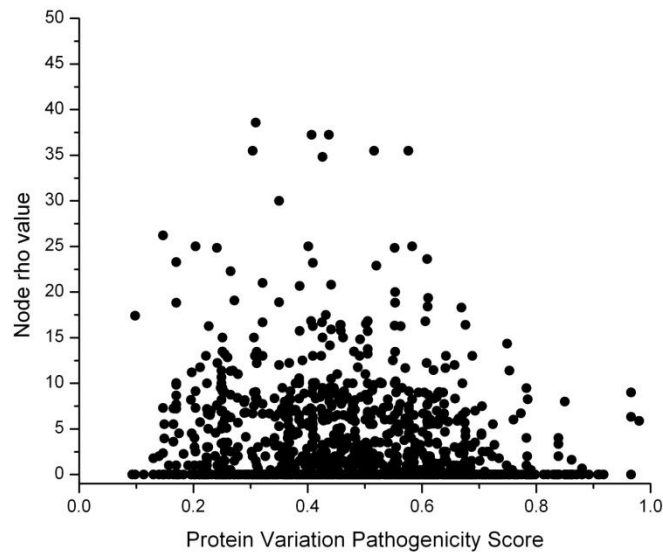


Figure S1. The pathogenicity scores for all non-synonymous amino acid variations occurring in the three human mtDNA subtrees as a function of the ρ value.

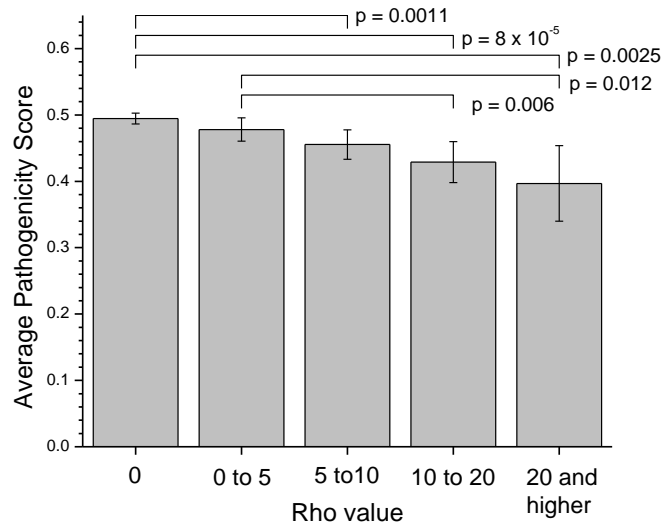


Figure S2. The average pathogenicity scores for all non-synonymous amino acid variations occurring in the three human mtDNA subtrees binned by the ρ value. There is a slight but steady and significant decrease in the average pathogenicity score as the rho value increased.

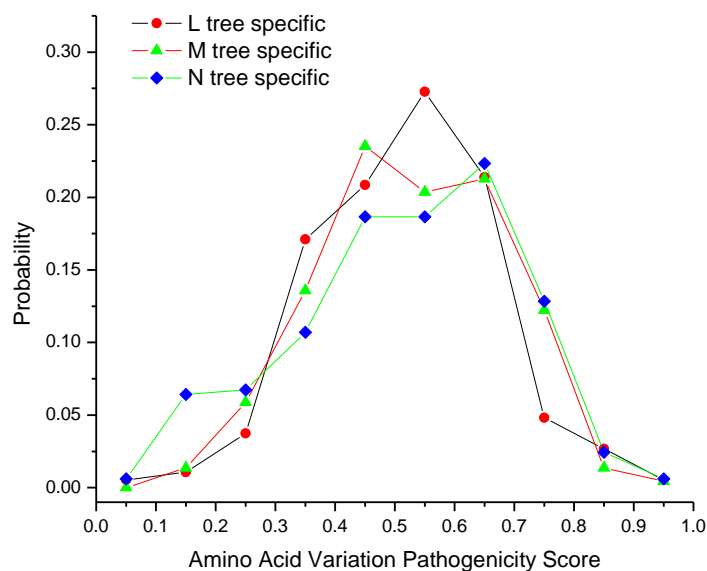


Figure S3. Distributions of pathogenicity scores in the three trees when analyzing only the set of amino acid variants which were unique to each tree. There are no statistically significant differences in these three data sets.

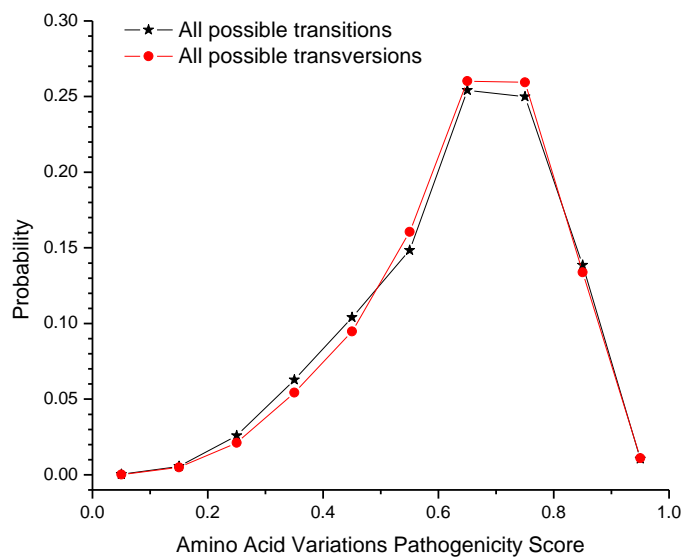


Figure S4. Distributions of pathogenicity scores for “all possible transitions” and “all possible transversions”. The list of the “all possible” variants was split into those arising from transitions and those arising from transversions. The mean pathogenicity score was 0.637 for transitions and 0.643 for transversions. Due to the large number of data values, this slight difference was statistically significant ($p = 0.004$). However, as these distributions are nearly identical, there is no strong difference in the pathogenicity scores for transitions compared to transversions.

Table S2. List of all pathogenic single amino acid variations in mtDNA encoded proteins listed in OMIM

OMIM ID	Gene	Variation	Amino Acid Change	Mutpred Score
*516000.0001	<i>MT-ND1</i>	m.3460A	Ala52Thr	0.857
*516000.0002	<i>MT-ND1</i>	m.4160C	Leu285Pro	0.853
*516000.0003	<i>MT-ND1</i>	m.4216C	Tyr304His	0.611
*516000.0004	<i>MT-ND1</i>	m.3394C	Tyr30His	0.783
*516000.0005	<i>MT-ND1</i>	m.3397G	Met31Val	0.723
*516000.0006	<i>MT-ND1</i>	m.4136G	Thr277Cys	0.374
*516000.0007	<i>MT-ND1</i>	m.3308C	Met1Thr	0.577
*516000.0010	<i>MT-ND1</i>	m.4171A	Leu289Met	0.591
*516000.0011	<i>MT-ND1</i>	m.3796G	Thr164Ala	0.54
*516000.0012	<i>MT-ND1</i>	m.3697A	Gly131Ser	0.854
*516000.0013	<i>MT-ND1</i>	m.3946A	Glu214Lys	0.778
*516000.0014	<i>MT-ND1</i>	m.3949C	Tyr215His	0.76
*516000.0015	<i>MT-ND1</i>	m.3733A	Glu143Lys	0.885
*516001.0001	<i>MT-ND2</i>	m.4917G	Asn150Asp	0.628
*516001.0002	<i>MT-ND2</i>	m.5244A	Gly259Ser	0.866
*516001.0003	<i>MT-ND2</i>	m.4640A	Ile57Met	0.604
*516001.0006	<i>MT-ND2</i>	m.4681C	Leu71Pro	0.8
*516002.0001	<i>MT-ND3</i>	m.10191C	Ser45Pro	0.394
*516002.0002	<i>MT-ND3</i>	m.10398G	Thr114Ala	0.17
*516002.0003	<i>MT-ND3</i>	m.10158C	Ser34Pro	0.394
*516002.0004	<i>MT-ND3</i>	m.10197A	Ala47Thr	0.594
*516003.0001	<i>MT-ND4</i>	m.11778A	Arg340His	0.852
*516003.0002	<i>MT-ND4</i>	m.11084G	Thr109Ala	0.482
*516003.0003	<i>MT-ND4</i>	m.11696G	Val313Ile	0.581
*516003.0004	<i>MT-ND4</i>	m.11777A	Arg340Ser	0.836
*516004.0001	<i>MT-ND4L</i>	m.10563C	Cys32Arg	0.766
*516004.0002	<i>MT-ND4L</i>	m.10663C	Val65Ala	0.479
*516005.0001	<i>MT-ND5</i>	m.13708A	Ala458Thr	0.409
*516005.0002	<i>MT-ND5</i>	m.13730A	Gly465Glu	0.825
*516005.0003	<i>MT-ND5</i>	m.12706C	Phe124Leu	0.704
*516005.0004	<i>MT-ND5</i>	m.12770G	Glu145Gly	0.763
*516005.0005	<i>MT-ND5</i>	m.13045C	Met237Leu	0.713
*516005.0006	<i>MT-ND5</i>	m.13084T	Ser250Cys	0.685
*516005.0007	<i>MT-ND5</i>	m.13513A	Asp393Asn	0.834
*516005.0008	<i>MT-ND5</i>	m.13042A	Ala236Thr	0.754
*516005.0009	<i>MT-ND5</i>	m.12848T	Ala171Val	0.738
*516005.0010	<i>MT-ND5</i>	m.12397G	Thr21Ala	0.426
*516006.0001	<i>MT-ND6</i>	m.14484C	Met64Val	0.627
*516006.0002	<i>MT-ND6</i>	m.14459A	Ala72Val	0.623

*516006.0004	<i>MT-ND6</i>	m.14495G	Leu60Ser	0.634
*516006.0005	<i>MT-ND6</i>	m.14453A	Ala74Val	0.657
*516006.0006	<i>MT-ND6</i>	m.14482A	Met64Ile	0.585
*516006.0007	<i>MT-ND6</i>	m.14487C	Met63Val	0.644
*516006.0008	<i>MT-ND6</i>	m.14319C	Asn119Asp	0.446
516060.0001	<i>MT-ATP6</i>	m.8993G	Leu156Arg	0.824
516060.0002	<i>MT-ATP6</i>	m.8993C	Leu156Pro	0.846
516060.0003	<i>MT-ATP6</i>	m.9101C	Ile192Thr	0.571
516060.0005	<i>MT-ATP6</i>	m.9176C	Leu217Pro	0.719
516060.0006	<i>MT-ATP6</i>	m.8851C	Trp109Arg	0.78
516060.0008	<i>MT-ATP6</i>	m.9185C	Leu220Pro	0.751
516060.0010	<i>MT-ATP6</i>	m.8528C	Met1Trp	0.907
516070.0001	<i>MT-ATP8</i>	m.8393T	Pro10Ser	0.569
516070.0003	<i>MT-ATP8</i>	m.8528C	Trp55Arg	0.77
*516030.0002	<i>MT-CO1</i>	m.6742C	Ile280Thr	0.69
*516030.0003	<i>MT-CO1</i>	m.6721C	Met273Thr	0.681
*516030.0004	<i>MT-CO1</i>	m.6480A	Val193Ile	0.664
*516030.0008	<i>MT-CO1</i>	m.6489A	Leu196Ile	0.641
*516030.0009	<i>MT-CO1</i>	m.6328T	Ser142Phe	0.831
*516030.0010	<i>MT-CO1</i>	m.6277G	Gly125Asp	0.938
*516040.0001	<i>MT-CO2</i>	m.7587C	Met1Thr	0.648
*516040.0002	<i>MT-CO2</i>	m.8009A	Val142Met	0.581
*516040.0003	<i>MT-CO2</i>	m.7671A	Met29Lys	0.689
*516050.0001	<i>MT-CO3</i>	m.9438A	Gly78Ser	0.839
*516050.0002	<i>MT-CO3</i>	m.9804A	Ala200Thr	0.708
*516020.0001	<i>MT-CYB</i>	m.15257A	Asp171Asn	0.785
*516020.0002	<i>MT-CYB</i>	m.15812A	Val356Met	0.518
*516020.0003	<i>MT-CYB</i>	m.14985A	Arg80His	0.833
*516020.0004	<i>MT-CYB</i>	m.15572C	Phe276Leu	0.69
*516020.0005	<i>MT-CYB</i>	m.15615A	Gly290Asp	0.727
*516020.0006	<i>MT-CYB</i>	m.14846A	Gly34Ser	0.846
*516020.0009	<i>MT-CYB</i>	m.15197C	Ser151Pro	0.715
*516020.0010	<i>MT-CYB</i>	m.15579G	Tyr278Cys	0.729
*516020.0011	<i>MT-CYB</i>	m.15498A	Gly251Asp	0.502
*516020.0012	<i>MT-CYB</i>	m.14849C	Ser35Pro	0.733
*516020.0014	<i>MT-CYB</i>	m.15497A	Gly251Ser	0.477