current issues in molecular biology

MDPI

Supplementary Materials

Table S1. Frequency distribution of the different haplogroups in diabetic and control cases.

Macrohaplogroup	ALL N=2366 (100%)	Controls N=1105 (46.7%)	T2D N=1261 (53.3%)
Haplogroups L			
L4	1 (0.08)	0 (0.00)	1 (0.08)
L3	2 (0.16)	0 (0.00)	2 (0.16)
Haplogroups M			
M (includes Q)	10 (0.86)	6 (0.54)	4 (0.32)
M7	48 (4.02)	19 (1.72)	29 (2.30)
M8 (includes C, Z)	9 (0.71)	0 (0.00)	9 (0.71)
M9 (includes E)	22 (1.80)	5 (0.45)	17 (1.35)
G	10 (0.84)	4 (0.36)	6 (0.48)
D	64 (5.32)	22 (1.99)	42 (3.33)
Haplogroups N			
N1 (includes I)	65 (5.52)	33 (2.99)	32 (2.54)
N2 (includes W)	33 (2.82)	18 (1.63)	15 (1.19)
N9 (includes Y)	16 (1.36)	8 (0.72)	8 (0.63)
A	13 (1.06)	3 (0.27)	10 (0.79)
X	31 (2.57)	10 (0.90)	21 (1.67)
Haplogroups R			
R (includes P)	7 (0.57)	1 (0.09)	6 (0.48)
R0 (includes HV, H, V)	1070 (90.36)	492 (44.52)	578 (45.84)
JT (includes J, T)	411 (34.96)	211 (19.10)	200 (15.86)
R9 (includes F)	43 (3.62)	19 (1.72)	24 (1.90)
B	49 (4.13)	22 (1.99)	27 (2.14)
U (includes K)	462 (39.23)	232 (21.00)	230 (18.24)

Table S2. Proportion test of mtDNA variants associated to type 2 diabetes.

Variant	X^2	95% IC	*p-Value*
m.1438A>G	53.326	0.5565098 0.5977890	2.826e-13*
m.14766C>T	53.326	0.5565098 0.5977890	2.826e-13*
m.16519T>C	180.18	0.3383346-0.3784139	<2.2e-16*

* Statistical difference with p value < 0.05; df = 1.

Table S3. Pearson's Chi-squared test with Yates' continuity correction of mtDNA variants associated to type 2 diabetes. Significant differences were identified between variants m.1438A>G and m.14766C>T as m.1438A>G and m.16519T>C. In the table are showed statistic as X^2(*p-value*).

Variants	m.1438A>G	m.14766C>T	m.16519T>C
m.1438A>G	-		
m.14766C>T	76.435 (<2.2e-16) *	-	
m.16519T>C	81.9 (<2.2e-16) *	1.8746 (0.171)	-

* Statistical difference with p value < 0.05; df = 1.

Table S4. Standardized residual test and Bonferroni adjustment of mtDNA variants associated to type 2 diabetes. * Statistical difference with p value < 0.05.

m.1438A>G

Variant	Type 2 diabetes	Control
Present	-3.1790157*	0.7386723
Absent	3.0827652	-0.7163076*

m.14776C>T

Variant	Type 2 diabetes	Control
Present	-5.310265*	6.205626
Absent	5.149487	-6.017740*

m.16519T>C

Variant	Type 2 diabetes	Control
Present	-1.552454*	1.159618
Absent	1.505451	-1.124508*

Table S5. Standardized residual test and Bonferroni adjustment between mtDNA. variants associated to type 2 diabetes. *Statistical difference with p value < 0.05.

m.1438A>G vs. m.14776C>T

Loci		**14776**	
		C	**T**
1438	**A**	5.598096	-6.541988*
	G	-1.300767*	1.520089

X^2= 76.435, df = 1, *p-value* = <2.2e-16.

m.1438A>G vs. m.16519T>C

Loci		**16519**	
		T	**C**
1438	**A**	7.139048	-5.332567*
	G	-1.658821*	1.239069

X^2= 76.453, df = 1, *p-value* = <2.2e-16.

m.14776C>T vs. m.16519T>C

Loci		**16519**	
		T	**C**
14776	**C**	0.7363876	-0.5500504*

T	-0.8605495*	0.6427941

X^2= 1.8746, df = 1, *p-value* = 0.171.

Table S6. List of pre graduate students who collaborated in different stages of the process and analysis carried out in this project as part of the activities during the Pacific Scientific and Technological Research Summer Program 2019-2022 https://programadelfin.org.mx, in the research lines *Automation for Detection of Heteroplasmy in Mitochondrial Sequences, Mitochondrial Genomics associated with Chronic Degenerative Diseases* and *Applications of Data Science in Health*.

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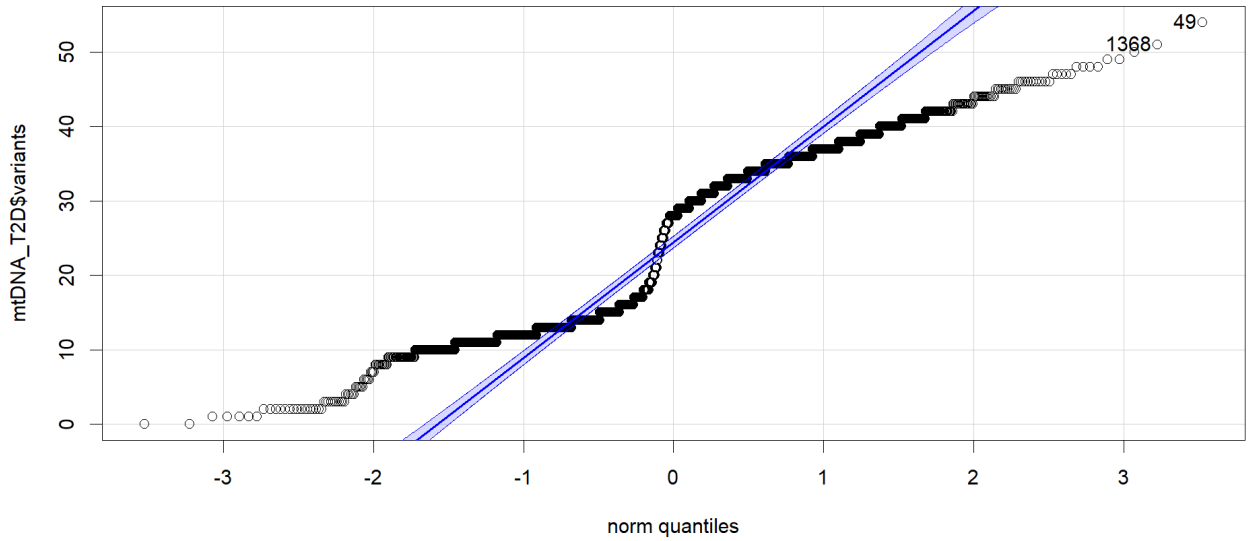
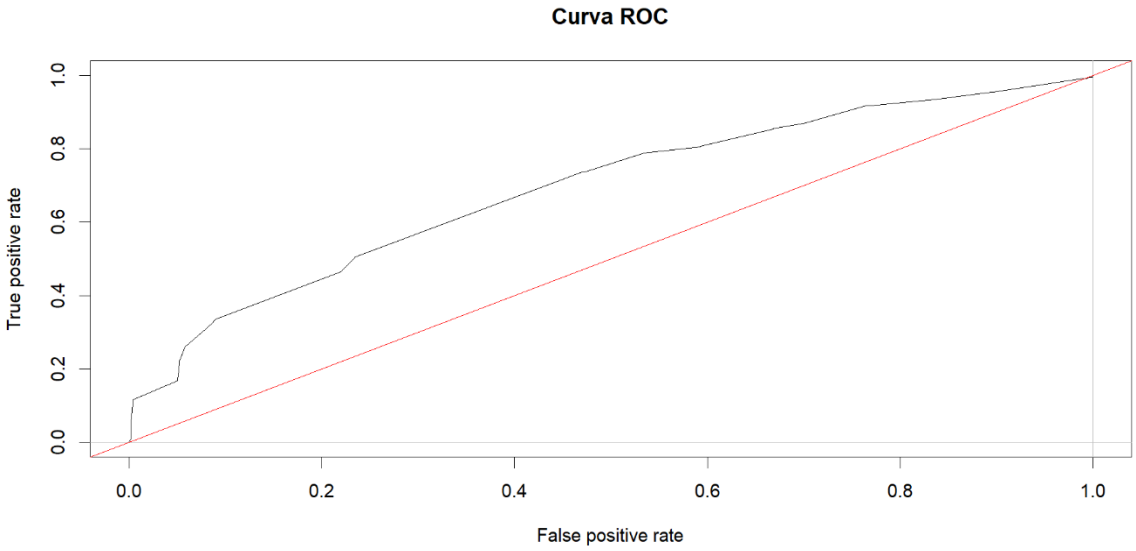


Figure S1. Qqplot to explore normality in number of variants per sequence in 2366. mtDNA chromosomes obtained of type diabetes cases and controls. Kolgomorov Smirnov with Lilliefors correction obtain a *D* statistic equal to 0.17113 with a *p-value* < 2.2e-16, demonstrating that the data have a non-parametric distribution outside normality. Since the data are discrete, a Pearson normality test was also performed corroborating the maximum result.



Call: glm(formula = Dx ~ m.73A>G + m.1189T>C + m.1193T>C + m.1420T>C + m.1438A.>G + m.1811A>G + m.2667T>C + m.3027T>C + m.10398A>G + m.14766C>T + m.16126T>C + m.16519T>C, family = binomial, data = data_base)

Deviance Residuals: Min -2.2363 , 1Q -1.1391, Median 0.5615, 3Q 1.1718, Max 2.1528.

Coefficients: (2 not defined because of singularities)

Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	0.96212	0.21050	4.571	4.86e-06 ***
m.73A.G	1.43941	0.16153	8.911	< 2e-16 ***
m.1189T.C	-0.45868	0.30003	-1.529	0.126323

m.1193T.C	10.92498	324.74374	0.034	0.973163
m.1420T.C	NA	NA	NA	NA
m.1438A.G2	-0.76045	0.22262	-3.416	0.000636 ***
m.1811A.G	-0.25097	0.20613	-1.218	0.223395
m.2667T.C	NA	NA	NA	NA
m.3027T.C	0.46311	0.52232	0.887	0.375265
m.10398A.G	0.49912	0.13907	3.589	0.000332 ***
m.14766C.T2	-2.04259	0.15259	-13.386	< 2e-16 ***
m.16126T.C	-0.37249	0.13756	-2.708	0.006773 **
m.16519T.C2	-0.18837	0.09758	-1.931	0.053544

Signif. codes: 0 *** 0.001** 0.01* 0.05

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 3110.1 on 2244 degrees of freedom.

Residual deviance: 2838.9 on 2234 degrees of freedom, AIC: 2860.9

Figure S2. Generalized linear model and risk prediction evaluation with receiver operating characteristic (ROC) curve between mtDNA variants associated to type 2 diabetes. True positive rate (sensitivity) against the false positive rate (1-specificity) for the different possible cut points of presence of variants m.73A>G, m.1189T>C, m.1193T>C, m.1420T>C, m.1438A>G, m.1811A>G, m.2667T>C, m.3027T>C, m.10398A>G, m.14766C>T, m.16126T>C and m.16519T>C. The estimated area under the curve (AUC) was 0.6911773.