Supplementary Data

Table S1. Baseline characteristics of healthy controls and diabetic patients

Variable	Healthy controls (HC) (*n*=39)	Diabetic patients (DM) (*n*=128)
Type of Diabetes (T1D:T2D)	NR	58:70
Age (years)	52 ± 25	57±15
Gender (female:male)	20:19	65:63
Diabetes duration (years)	NR	22 ± 10
BMI (kg/m^2)	23 ± 4	27 ± 4***
HbA$_{1c}$ (%)	ND	10 ± 9
ACR (mg/mmol)	ND	12 ± 41
eGFR (ml min^{-1} 1.73 m^{-2})	ND	78 ± 35
Systolic BP (mmHg)	ND	129 ± 16
Diastolic BP (mmHg)	ND	72 ± 9
Cholesterol (mmol/l)	ND	4 ± 0.08
MtDNA content (Mean ± SD)	34 ± 9	51 ±62
MtDNA (Median)	32 (35)	32(475)

Foot note: [a] NR: not required, [b] ND; not detected, [c] BMI: body mass index, BP: blood pressure, HbA1c: Haemoglobin A1c, ACR: albumin/creatinine ratio, GFR: glomerular filtration rate. [d] Data are means ±SD. [e] ***P<0.001 compared with healthy controls

Table S2: **Baseline characteristics of patients and healthy controls used in Seahorse subset showing a similar trend to the whole study group as in Table 1**

Variable	**Healthy controls** (**HC, n=13**)	**Diabetic controls** (**DC, *n*=14**)	**Diabetic Nephropathy** (**DN, *n*=16**)
Type of Diabetes (T1D:T2D)	NR	11:3	6:10
Age (years)	33±10	46.4±6.9	55.8±15.2
Gender (female:male)	8:5	9:6	7:8
Diabetes duration (years)	NR	24.8 ± 3.5	22 ± 10
BMI (kg/m^2)	23.2±2.9	24.7 ± 12	28.3 ± 4.8
HbA$_{1c}$ (%)	ND	8.8 ± 1.9	8.7 ± 1.5
ACR (mg/mmol)	ND	1.3 ± 2	23± 36*
eGFR (ml min^{-1} 1.73 m^{-2})	ND	120 ± 20	64 ± 34**
Systolic BP (mmHg)	ND	116 ±19.6	131 ±23
Diastolic BP (mmHg)	ND	74.4±15	76±10
Cholesterol (mmol/l)	ND	4.5 ±1.0	4.2 ± 1.2
MtDNA content (Mean± D)	33.5±8.1	40.2±20.5	24.8±10.0$^{**\#}$
BHI	3.2±0.5	4.0 ±1.3	3±0.4*

Foot note: [a] BMI: body mass index, BP: blood pressure, HbA1c: Haemoglobin A1c, ACR: albumin/creatinine ratio, GFR: glomerular filtration rate. [b] Data are means ±SD. [c] *P<0.05, **P<0.01 compared with diabetic controls, [d] # P <0.05, compared with healthy controls

Table S3. Human Oligonucleotide primers used in this study

Gene	Accession number	Primers (5’->3’)	Amplicon Length (bp)
TFAM	NM_003201.2	F: GAACAACTACCCATATTTAAAGCTCA	95
		R: GAATCAGGAAGTTCCCTCCA	
PGC1a	NM_013261.3	F: ACTGCAGGCCTAACTCCACCCA	190
		R: ACTCGGATTGCTCCGGCCCT	
NFkB p65	NM_021975.3	F: CCTGGAGCAGGCTATCAGTC	213
		R: ATCTTGAGCTCGGCAGTGTT	
MYD88	NM_001172567.1	F: TTTGCACTCAGCCTCTCTCC	121
		GGTTGGTGTAGTCGCAGACA	
MFN1	NM_033540.2	F: GAGAAAATACAAAACAATTCAAAGCTC	96
		R:GCTTGAAGGTAGAAACTGCTTAGTAAA	
MFN2	NM_014874.3	F: AGCCACCAAGTCCAGCAG	117
		R: AACCTCAATTTTCTTGTTCATGG	
OPA1	NM_015560.2	F: GAGCCAGGTTACACCAAAACA	120
		R: GTTCCTGAATTCATGGTCTGC	
Pink1	NM_032409.2	F: CTTACAGAAAATCCAAGAGAGG	199
		R: CAGGGATAGTTCTTCATAACG	
Park2	NM_004562.2	F: GAGGATTTAACCCAGGAGAG	113
		R: ACAAACACTATCATGGTCAC	
Drp1	NM_012063.3	F: TCACGAGACAAGTTAATTCAGGA	344
		R: GCCTTTGGCACACTGTCTTG	
ND1[a]	NC_012920.1	F: GAGCAGTAGCCCAAACAATCTC	140
		R: GGGTCATGATGGCAGGAGTAAT	
ND6[a]	NC_012920.1	F: TGGGGTTAGCGATGGAGGTAGG	140
		R: AATAGGATCCTCCCGAATCAAC	
COX3[a]	NC_012920.1	F: TCCTCACTATCTGCTTCATCCG	140
		R: CCCTCATCAATAGATGGAGACA	
β-actin	NM_001101.3	F: GACGACATGGAGAAAATCTG	131
		R: ATGATCTGGGTCATCTTCTC	
hMito	NC_012920.1	F: CACTTTCCACACAGACATCA	127
		R: TGGTTAGGCTGGTGTTAGGG	
hB2M	NC_000015.10	F: TGTTCCTGCTGGGTAGCTCT	187
		R: CCTCCATGATGCTGCTTACA	
Mito primer[b] (damage)	J01415	F: TCTAAGCCTCCTTATTCGAGCCGA	8 900
		R: TTTCATCATGCGGAGATGTTGGATGG	
Mito amplicon A (damage) [c]	NC_013993.1	F:GATCACAGGTCTATCACCCTA	2027
		R: TTGGACAACCAGCTATCACCA	

Footnote: [a] Nagao et al., 2008, [b] Furda, A., et al., 2006,[c] Bannwarth et al., 2006

Table S4: Raw values of data for calculation of BHI

Group	Reserve Capacity	ATP-linked	Non-Mitochondrial	Proton leak	BHI (Untransformed	BHI
HC1	95	31	12	3	719	2.9
HC2	116	28	14	6	1360	3.1
HC3	75	39	21	2	242	2.4
HC4	180	37	16	10	4137	3.6
HC5	84	24	7	11	3228	3.5
HC6	144	23	4	10	8229	3.9
HC7	101	33	10	9	3161	3.5
HC8	64	26	12	8	1109	3.0
Mean	107	30	12	7	2773	3.2

Group	Reserve Capacity	ATP-linked	Non-Mitochondrial	Proton leak	BHI (Untransformed	BHI
DC1	185	4	20	44	1795	3.3
DC2	218	55	26	13	5731	3.8
DC3	147	33	14	6	1989	3.3
DC4	140	14	20	26	2634	3.4
DC5	104	30	12	11	2701	3.4
Mean	159	27	18	20	2970	3.4

Group	Reserve Capacity	ATP-linked	Non-Mitochondrial	Proton leak	BHI (Untransformed)	BHI
DN1	131	45	27	0	101	2.0
DN2	58	27	15	9	861	2.9
DN3	70	41	14	4	791	2.9
DN4	33	17	4	7	965	3.0
DN5	135	38	22	3	690	2.8
DN6	69	23	11	6	790	2.9
DN7	106	31	18	29	5305	3.7
DN8	60	33	17	10	1143	3.1
DN9	68	42	22	11	1489	3.2
DN10	67	38	19	13	1716	3.2
DN11	130	45	21	8	2372	3.4
DN12	61	27	9	5	910	3.0
Mean	82	34	17	9	1428	3.0

Table S5: MtDNA content of patients by sub-dividing as type 1 and type 2 diabetes

	Healthy Control (HC)	Diabetic Control (DC)	Diabetic Nephropathy (DN)
MtDNA content (Type 1 + Type 2 Diabetes)	N=39 34 ± 9	N=45 64 ± 75$^{\#\#}$	N=83 43 ± 52***
Type 1 diabetes MtDNA content		N=27 64 ± 87$^{\#}$	N=31 33 ± 37**
Type 2 diabetes MtDNA content		N=18 65 ± 54	N=52 49 ± 58

Foot note: [a] Non-parametric analysis was done by Kruskal –Wallis test and groups were compared with Mann-Whitney with Bonferroni correction. Data are means ±SD, [b] $^{**}p<0.01$ and $^{***}p<0.001$ compared with diabetic controls, [c] $^{\#}p<0.05$ and $^{\#\#}p<0.01$ compared with healthy controls