SUPPLEMENTAL DATA

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Identification of the m.14692A>G mutation in the mitochondrial tRNA^{Glu} gene.

Supplemental Figure S2

Three Han Chinese pedigrees with diabetes and deafness.

Supplemental Figure S3

The analysis of the stability of tRNA^{Glu}.

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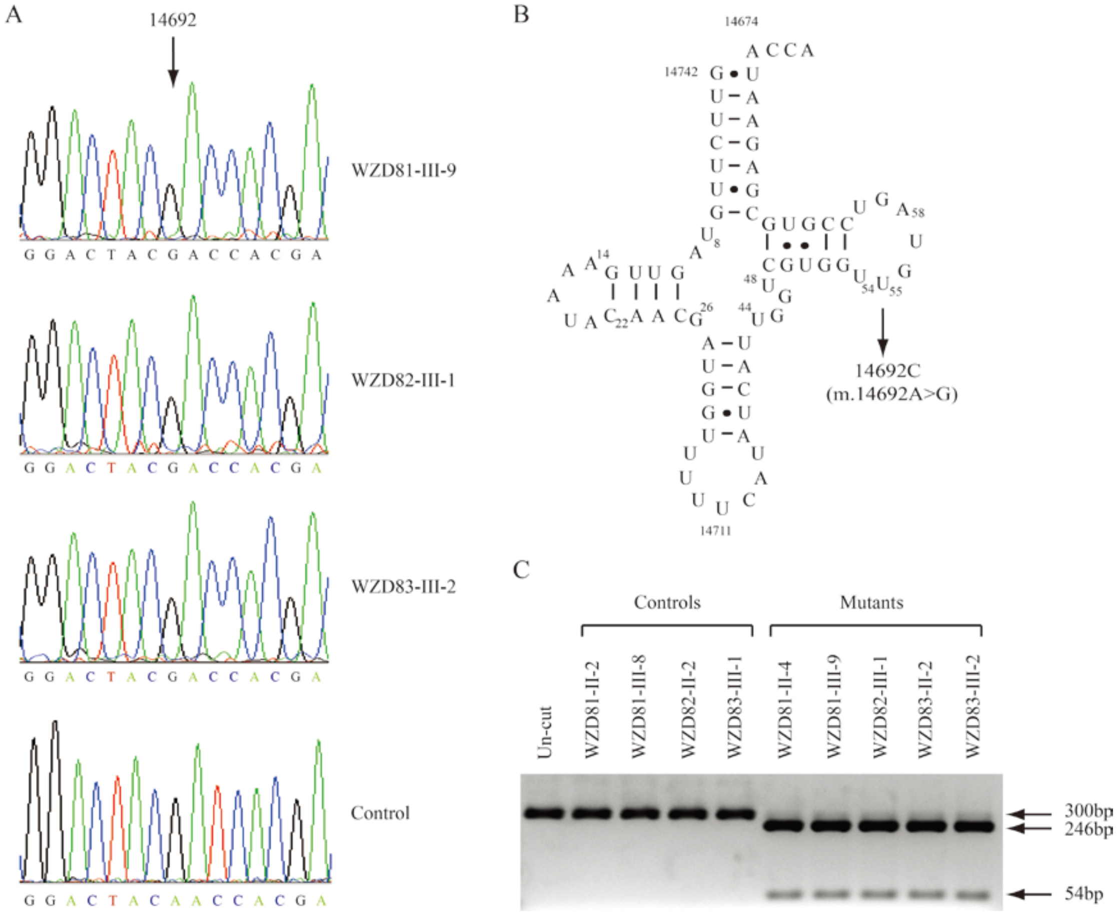
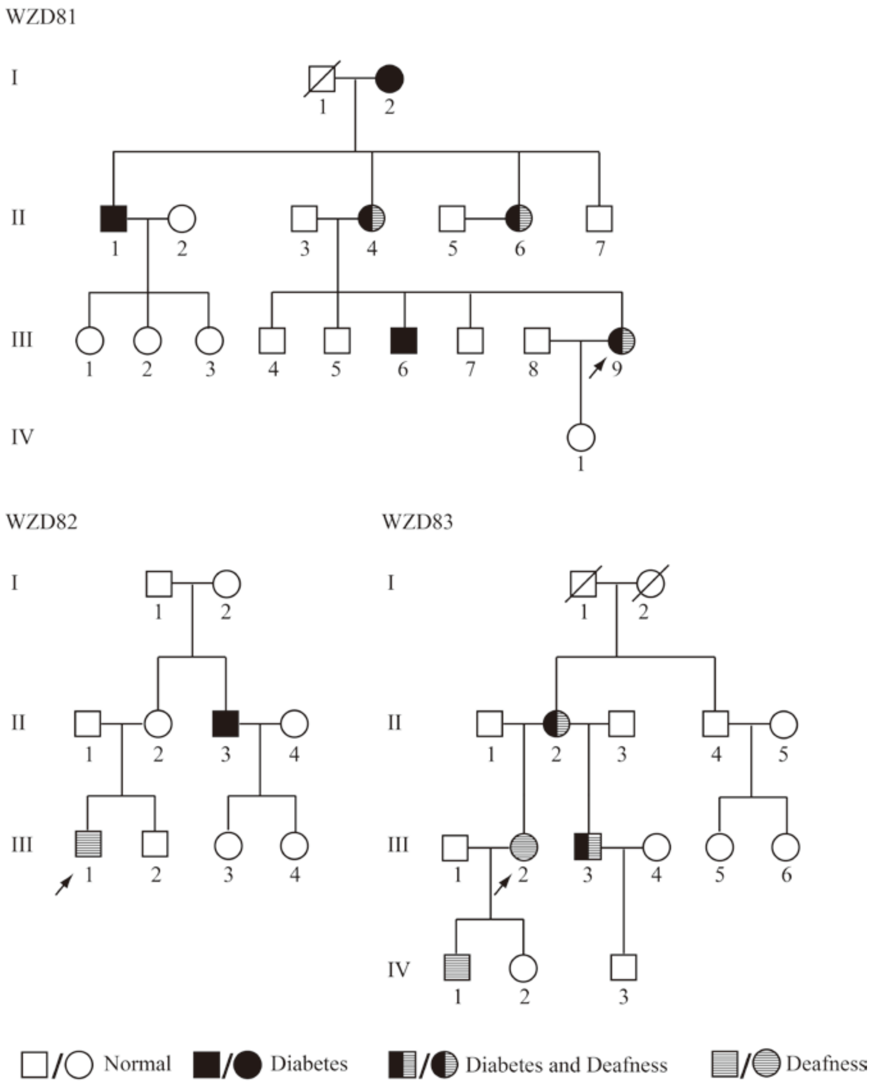
Summary of clinical and biochemical data of matrilineal relatives in three Chinese pedigrees with deafness and diabetes

Supplemental Table S3

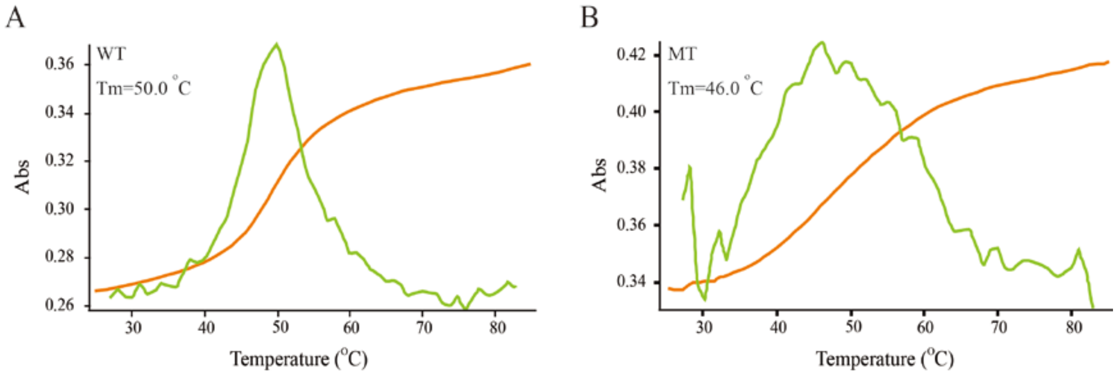
Relationship between the decrease level of mitochondrial proteins and the number or proportion of glutamic acid codons.



SupplementalFigure S1. Identification of the m.14692A>G mutation in the mitochondrial tRNA^{Glu} gene.(A) Partial sequence of the tRNA^{Glu} gene from three affected individuals (WZD81-III-9, WZD82-III-1, WZD83-III-2) and a control subjects, respectively. The arrow indicates the location of the base change at position 14692.(B) The location of the m.14692A>G mutation in human mitochondrial tRNA^{Glu}.Cloverleaf structure of human mitochondrial tRNA^{Glu} was derived from Florentz et al. (28). (C) Quantification of the m.14692A>G mutation infive hearing-impaired individuals and control subjects. PCR products amplified from whole bloods were digested with *Mbo*I and analyzed by electrophoresis in a 3% agarose gelstained with ethidium bromide.



SupplementalFigure S2. Three Han Chinese pedigrees with diabetes and deafness. Affected individuals are indicated by filled symbols.



Supplemental Figure S3. The analysis of the stability of tRNA^{Glu}. Melting profiles of transcripts of (A) wild type tRNA^{Glu} and (B) A14692G mutant measured at 260 nm with a heating rate of 1°/min from 25 to 85° (orange curves). First derivative (dA/dT) against temperature curves are shown to highlight the Tm value transitions (green curves).

SupplementalTable S1. mtDNA variants in the 3 Chinese pedigrees carrying the m.14692A>G mutation

Gene	Position	Replacement	[a]Conservation (H/B/M/X)	[b]CRS	WZD81	WZD82	WZD83	C3	C4	[c]Previously reported
D-loop	73	A to G		A	G	G	G	G	G	Yes
	146	T to C		T	C	C	C			Yes
	150	C to T		C	T				T	Yes
	210	A to G		A				G		Yes
	227	A to T		A				T		Yes
	263	A to G		A	G	G	G	G	G	Yes
	310	T to TC		T	TC	TC	TC	CTC	TC	Yes
	489	T to C		T	C	C	C			Yes
	16136	T to C		T					C	Yes
	16140	T to C		T	C			C	C	Yes
	16182:16183	AA to CC		AA	CC				AC	Yes
	16189	T to C		T	C			C	C	Yes
	16193	C to CC		C					CC	Yes
	16217	T to C		T					C	Yes
	16223	C to T		C		T	T			Yes
	16224	T to C		T		C	C			Yes
	16245	C to T		C		T	T			Yes
	16249	T to C		T					C	Yes
	16266	C to G		C				G		Yes
	16274	G to A		G					A	Yes
	16291	C to T		C					T	Yes
	16292	C to T		C		T	T			Yes
	16362	T to C		T			C			Yes
	16365	C to T		C		T				Yes
	16519	T to C		T		C	C	C	C	Yes
12S rRNA	709	G to A	G/A/A/-	G	A			A	A	Yes
	750	A to G	A/A/A/-	A	G	G	G	G	G	Yes

	856	A to G	A/A/A/A	A		G	G			Yes
	1119	T to C	T/T/T/-	T	C				C	Yes
	1438	A to G	A/A/A/G	A	G	G	G	G	G	Yes
16S rRNA	2483	T to C	T/C/C/C	T					C	Yes
	2706	A to G	A/G/A/A	A	G	G	G	G	G	Yes
	2766	C to T	C/T/T/T	C		T	T			Yes
	3010	G to A	G/G/A/A	G		A	A			Yes
	3107	N to del	N/T/T/T	N				del		Yes
ND1	3398	T to C (Met-Thr)	M/M/M/M	T		C				Yes
	3435	C to T (syn)	Y/Y/Y/T	C					T	Yes
	3497	C to T (Ala-Val)	A/A/L/S	C	T				T	Yes
	3537	A to G (syn)	L/M/L/M	A				G		Yes
	3571	C to T (Leu-Phe)	L/L/L/L	C					T	Yes
ND2	4625	C to T (syn)	S/A/S/A	C	T					Yes
	4704	A to C (Met-Leu)	M/M/K/W	A	C					Yes
	4769	A to G (syn)	M/M/M/I	A	G	G	G		G	Yes
	4883	C to T (syn)	P/P/P/P	C		T	T			Yes
	5178	C to A (Leu-Met)	L/T/T/T	C		A	A			Yes
	5178	C to G (Leu-Val)	L/T/T/T					G		No
CO1	6663	A to G (Ile-Val)	I/I/I/I	A				G		Yes
	7028	C to T (syn)	A/A/A/A	C	T	T	T	T	T	Yes
Non-coding	8281-8289	9bp-del		CCCCCTCTA				del	del	Yes
ATP8	8414	C to T (Leu-Phe)	L/F/M/W	C		T	T			Yes
ATP6	8584	G to A (Ala-Thr)	A/V/V/I	G				A		Yes
	8701	A to G (Thr-Ala)	T/S/L/Q	A		G	G			Yes
	8860	A to G (Thr-Ala)	T/A/A/T	A	G	G	G	G	G	Yes
	8902	G to A (Ala-Thr)	A/A/A/G	G				A		Yes
	9100	A to G (Ile-Val)	I/T/T/T	A				G		Yes
	9128	T to C (Ile-Thr)	I/I/I/L	T					C	Yes
CO3	9540	T to C (syn)	L/L/L/L	T		C	C			Yes

	9575	G to A (syn)	P/P/P/P	G					A	Yes
	9950	T to C (syn)	V/V/V/V	T				C		Yes
ND3	10398	A to G (Thr-Ala)	T/T/T/A	A		G	G	G		Yes
	10400	C to T (syn)	T/T/T/A	C		T	T			Yes
ND4L	10493	T to C (syn)	I/I/L/F	T					C	Yes
ND4	10873	T to C (syn)	P/S/S/S	T		C	C			Yes
	11440	G to A (syn)	G/G/G/G	G					A	Yes
	11719	G to A (syn)	G/G/G/G	G	A	A	A	A	A	Yes
ND5	12705	C to T (syn)	I/L/L/T	C		T	T			Yes
	12853	C to T (syn)	L/L/L/I	C	T					Yes
	13437	T to C (syn)	P/P/P/P	T	C					Yes
ND6	14668	C to T (syn)	M/L/N/I	C		T	T			Yes
tRNA^{Glu}	14692	A to G	A/A/A/A	A	G	G	G			Yes
CytB	14766	C to T (Thr-Ile)	T/S/T/S	C	T	T	T	T	T	Yes
	14783	T to C (syn)	L/I/I/I	T		C	C			Yes
	15043	G to A (syn)	G/G/G/G	G		A	A			Yes
	15077	G to A (Glu-Lys)	E/E/E/E	G				A		Yes
	15235	A to G (syn)	W/W/W/W	A				G		Yes
	15263	C to T (Pro-Ser)	P/A/A/A	C				T		Yes
	15301	G to A (syn)	L/L/L/L	G		A	A			Yes
	15326	A to G (Thr-Ala)	T/M/I/I	A	G	G	G	G	G	Yes
	15346	G to A (syn)	L/L/L/L	G					A	Yes
	15777	G to A (Ser-Asn)	S/E/E/E	G				A		Yes

[a] Conservation of amino acid for polypeptides in human (H), bovine (B), mouse (M), and *Xenopus* (X).

[b] CRS: Cambridge reference sequence.

[c] See the online mitochondrial genome database MITOMAP.

Supplemental Table S2. Summary of clinical and biochemical data of matrilineal relatives in three Chinese pedigrees with deafness and diabetes

Subjects	Gender	Age at test/onset (yrs) diabetes	Fasting glucose (mmol/L)	Oral glucose tolerance (mmol/dL or mg/dL)	HbAlc (%)	Age at test/onset (yrs) deafness	PTA (dB) right/left ear	Level of hearing impairment
WZD81-I-2	F	78/72	10.0	1.42 (278)	6.9	72/-	23/28	Normal
WZD81-II-1	M	72/68	16.1	1.78 (300)	7.6	72/-	24/25	Normal
WZD81-II-4	F	74/72	15.8	1.73 (298)	7.4	74/28	80/85	Severe
WZD81-II-6	F	68/67	15.2	1.68 (288)	7.3	68/26	95/90	Profound
WZD81-II-7	M	66/-	5.5	0.82 (149)	5.4	66/-	20/25	Normal
WZD81-III-4	M	58/-	6.8	0.94 (169)	6.2	58/-	21/26	Normal
WZD81-III-5	M	56/-	4.8	0.73 (128)	5.4	56/-	29/22	Normal
WZD81-III-6	M	45/44	14.5	1.43 (246)	7.2	45/-	14/24	Normal
WZD81-III-7	M	44/-	5.6	0.88 (162)	5.9	44/-	23/20	Normal
WZD81-III-9	F	44/42	7.8	1.36 (268)	6.8	44/20	77/79	Normal
WZD81-IV-1	F	20/-	5.6	0.77 (139)	5.0	20/-	23/16	Normal
WZD82-I-2	F	72/-	6.4	0.94 (182)	5.6	72/-	24/26	Normal
WZD82-II-2	F	52/-	5.8	0.81 (145)	5.5	52/-	22/25	Normal
WZD82-II-3	M	50/50	7.2	1.14 (210)	6.6	50/-	23/27	Normal
WZD82-III-1	M	26/-	5.3	0.76 (136)	5.7	26/26	75/78	Severe
WZD82-III-2	M	24/-	5.6	0.77 (138)	5.3	24/-	28/17	Normal
WZD83-II-2	F	64/60	11.4	1.43 (250)	7.3	64/22	82/88	Severe
WZD83-II-4	M	60/-	6.5	0.94 (178)	6.1	60/-	21/26	Normal
WZD83-III-2	F	40/-	5.8	0.90 (170)	6.0	40/16	70/86	Severe
WZD83-III-3	M	40/40	7.1	1.18 (220)	6.8	40/20	65/70	Moderate
WZD83-IV-1	M	18/-	5.5	0.77 (140)	5.5	18/18	56/67	Moderate
WZD83-IV-2	F	16/-	5.3	0.72 (139)	5.0	16/-	20/23	Normal

Glycated hemoglobin: HbAlc; pure-tone audiometry: PTA; Decibel: dB.

Supplemental Table S3. Relationship between the decrease level of mitochondrial proteins and the number or proportion of glutamic acid codons

	Number of amino acids	Number of glutamic acid codons	Proportion of glutamic acid codons (%)	Decrease level of mitochondrial proteins (%)
ATP6	227	3	1.3	20.4
CO2	225	11	4.8	66.2
ND4	459	9	2	20.1
ND1	318	11	3.5	51.7
ND5	604	9	1.5	30.0
ND6	175	10	5.7	33.9
CYTB	380	4	1.1	-21.1