Reappraising the Relationship Between Mitochondrial DNA Variant m.16189T>C and Type 2 Diabetes Mellitus in East Asian Populations

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Abstract: The role of mitochondrial DNA (mtDNA) variant 16189T>C in type 2 diabetes mellitus (T2DM) remains hotly debated in the past decade. If mutation 16189T>C indeed posed a risk to T2DM, as echoed by some recent studies, correlation between this mutation and disease should be observed when carrying out a systematical study using data and samples collected in a large geographic region in China. To test this hypothesis, we first performed a linear regression analysis between the prevalence of T2DM and the allele frequency of 16189C variant in 10 East Asian populations, and further genotyped this variant in two case-control cohorts from west Han Chinese (Kunming and Xining). Linear regression analysis showed that no significant correlation was observed (r^2=0.211, P=0.181), and the genotyping results indicated that the m.16189T>C frequency difference between case and control was not significant in either populations (P=0.38 and 0.89 for Kunming and Xining, respectively). Matrilineal backgrounds constitution (in terms of haplogroups) analysis generated a similar haplogroup distribution in both populations (P>0.1). All results failed to substantiate that m.16189T>C may play an active role in the development of T2DM in East Asian populations.

Keywords: Haplogroup, mitochondrial DNA, type 2 diabetes mellitus, m.16189T>C.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a common metabolic disorder and has been recognized as a global health problem nowadays, which is supposed to affect more than 300 million individuals worldwide by 2025 [1]. However, the exact mechanisms underlying the development and progression of T2DM still remain unclear. Due to the facts that mitochondrial oxidative phosphorylation (OXPHOS) plays an important role in glucose simulated insulin secretion by beta cells [2], and that some T2DM patients present a maternal inherited pattern [3], it has then been speculated that some mutations on mitochondrial DNA (mtDNA) may contribute to the onset of T2DM. One example is mtDNA 3243 A>G mutation, which has been proven to impair the cellular metabolic pathways in beta cells [4].

One common variant in mtDNA control-region, m.16189T>C, which triggers the length variation of C-stretch in region 16184-16193, was suggested to be associated with T2DM in United Kingdom [5, 6] and East Asia [7-10]. However, the association could not be replicated by the subsequent studies on UK populations [11, 12], emphasizing the necessity of further studies to put deeper insights into this issue. If m.16189T>C does confer susceptibility to T2DM, it would be expected that the prevalence of this disease should in general be associated *positively* with the distribution frequency of 16189C across different populations in a region. However, the potential correlation between these two important indexes has never been investigated.

Human mtDNAs can be classified into various haplogroups based on some specific variants inherited from the most recent common (matrilineal) ancestor [13, 14], and the m.16189T>C serves as one of the specific mutations for some well-characterized haplogroups, such as X, T1, and U2e in West Eurasian and B and D5 in East Eurasian [13, 14]. If m.16189T>C does confer susceptibility to T2DM, some special

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mtDNA haplogroups, especially those characterized by this variant, should naturally be expected to present higher frequency in the samples with T2DM than that in healthy controls. In contrast, supposing that m.16189T>C is a neutral polymorphism, the observed haplogroup distribution in T2DM patients may actually mirror the specific haplogroup(s) background.

In present study, we first retrieved m.16189T>C frequencies and T2DM prevalence data in 10 East Asian populations from literatures and performed a linear regression analysis to test correlations between them. Moreover, we genotyped m.16189T>C in two west Chinese Han case-control populations and compared their frequencies and haplogroup constitution, with a special attempt to assess the matrilineal background effect on the onset of T2DM. No significant results were obtained, which suggested that m.16189T>C is likely a benign variant rather than a pathogenic one. Our study provided new insights into the role m.16189T>C in T2DM development and substantiated the importance of performing exhaustive analysis in the disease study.

MATERIALS AND METHODS

Frequency Data Mining and Analysis

The mtDNA control region re-sequencing data were collected for East Asian populations from Hangzhou [15], Xi'an [15, 16], Shanghai [15], Xi'ning [15], Dalian [15], Nanjing [15], Changsha [15, 16], Taiwan [17], Korea [18], and Japan [19], among which the distribution frequencies of m.16189T>C were counted respectively. The prevalence data of T2DM for each population were retrieved from literatures [20-28] with some published in Chinese [20-25].

Case-Control Populations

Two case-control cohorts from west Han Chinese were collected. Kunming cohort (Yunnan, southwest China) contained 593 unrelated patients with T2DM that were diagnosed according to the criteria recommended by the World Health Organization at the First Affiliated Hospital of Kunming Medical University and 277 age-matched healthy Han subjects from the same area. The 43 Han samples from Kunming, Yunnan Province published in Yao *et al*. [29] were also included in the analysis as controls. We also collected 228 T2DM patients and 191 healthy control subjects in Xining (Qinghai, northwest China) as a second cohort. This study was approved by the ethics committee of Yunnan University and informed consent was obtained from all donors.

DNA Extraction and Amplification

The genomic DNA was extracted from peripheral blood by standard phenol/chloroform method. Hypervariable segment I (HVS-I), which contained the m.16189T>C, was amplified in all samples by using the primer pair L15996 (5'-CTCCACCATTAGCACCCAA AGC-3')/H16201 (5'- GGTTGATTG CTGTACTTGCTT G -3'). PCR reaction was performed under the following condition: 94°C for 2 minutes, 35 cycles of 94°C for 40 seconds, 60°C for 1 minute and 72°C for 1 minute, then ended with incubation at 72°C for 5 minutes. Each fragment was digested by endonuclease *Mnl*1. Wild-type mtDNA would yield two fragments while mtDNA with mutation would generate only one, which could be distinguished on 3% agarose gel. All samples with m.16189T>C were further amplified with the primer pair L15996/H16498 [29], and re-sequenced by using the BigDye^{TM} Terminator Cycle Sequencing kit (Applied Biosystems, USA) on an ABI PRISM 3700 sequencer (Applied Biosystems).

Data Analysis

Sequences were edited and aligned by DNAStar software (DNAStar Inc., USA), and variants were recorded according to the revised Cambridge Reference Sequence [30]. All mtDNAs with 16189T>C were tentatively classified into respective haplogroups according to the updated East Asian mtDNA phylogenetic tree [14]. Their haplogroup classifications were further substantiated by detecting additional coding-region variation(s) as fully described in our previous studies [29].

Statistical Analysis

Statistical analyses were performed by using SPSS 13.0 (SPSS Inc., USA). Linear regression was used to evaluate the association between the prevalence of T2DM and m.16189T>C frequency. The frequencies of m.16189T>C in the case and control groups were compared by the χ^2 test (with Yates' correction for 2×2 contingency tables). Relative risk associated with the m.16189T>C was estimated by the odd ratio (OR). Statistical significance was accepted when $P<0.05$. The association between matrilineal background (*viz*. haplogroup) and T2DM was assessed by the χ^2 test or fisher's exact test and the minimum false discovery rate (FDR) for each test was estimated with QVALUE (http://faculty.washington.edu/~jstorey/qvalue/) [31]. An FDR < 0.05 was regarded as a significant result.

RESULTS

The correlation analysis between the prevalence of T2DM and the allele frequency of 16189C was shown in Fig. (**1**). The T2DM prevalence in the 10 East Asian populations ranged from 3.05% in Xi'an, China, to 10.1% in Japan. The average m.16189T>C frequency was 29.6%, with highest in Korean (33.9%) and lowest in Changsha, China (20.4%). When linear regression was performed, no significant association was observed (Pearson r^2=0.211, P=0.181), and thus failed to support the hypothesis. However, several cautions should be noted when discussing this result. For Taiwan Han Chinese, the prevalence of T2DM was estimated for Tainan city [26], while the mtDNAs data was not exactly for this city but came from the whole Taiwan region [17]. A similar situation also appeared in the Japanese sample: the prevalence of T2DM was estimated for rural Japanese [28], while the mtDNAs data was from the whole Japan [19]. After removing

these two populations, the negative result still persisted (Pearson r^2=0.182, *P*=0.292), despite of the fact that the correlation coefficient showed some association trend.

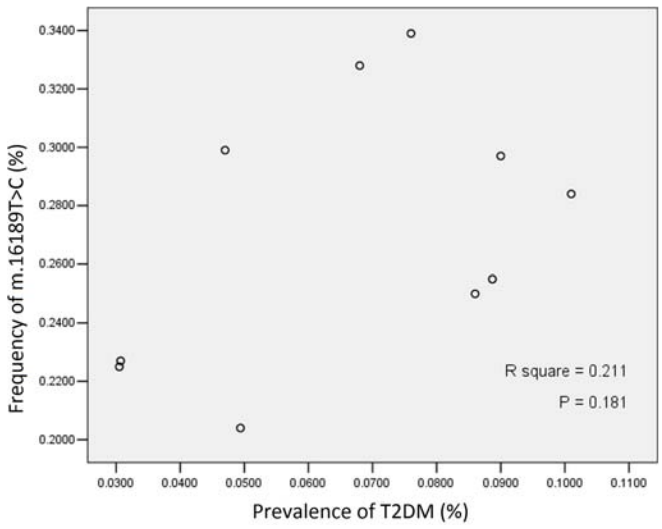

Fig. (1). Correlation between m.16189T>C frequency and T2DM prevalence in 10 East Asian populations. X-axis indicates the T2DM prevalence while Y-axis represents the percentage of m.16189T>C variant in corresponding region. Data were taken from literatures [15-28].

In order to further evaluate the contribution of m.16189T>C to T2DM, we compared m.16189T>C frequencies in two Chinese Han case-control populations (Kunming and Xining). The frequencies of m.16189T>C in T2DM patients and healthy controls in these two cohorts were shown in Table **1**. In Kunming Han population, the m.16189T>C frequency was a little higher in T2DM patients (185/593, 31.2%) than in normal controls (90/317, 28.4%), but the difference was not significant (OR 1.14, 95% CI 0.85-1.54, *P*=0.38). A similar pattern was observed in the Xining Han population (26.8% in case and 26.2% in control respectively; OR 1.03, 95% CI 0.67-1.59, *P*=0.89). The result was not changed when we combined the two populations for analysis (30.0% in case and 27.5% in control respectively; OR 1.12, 95% CI 0.88-1.44, *P*=0.35). All these result suggested that m.16189T>C was not likely to contribute to T2DM risk, despite of the fact that the sample size was a little bit small.

We further classified these mtDNAs with m.16189T>C into respective haplogroups and attempted to discern the potential contribution of matrilineal background to T2DM. Haplogroup distribution of samples harboring m.16189T>C was compared in case and control cohorts (Table **2**). Among the 386 mtDNAs with m.16189T>C that were distilled from 1,329 subjects, a total of 18 haplogroups were identified, in which the majority (70.0%; Tables **S1-S4**) are the haplogroups with diagnostic m.16189T>C (in combination with some other specific variants), such as B, D5, F1b, and M7b2. The occurrence of m.16189T>C in other haplogroups could be attributable to parallel mutation event --- an observation that was in accordance with the hypervariable character of the site [32]. No haplogroup showed significantly different frequency between T2DM and control (*P*>0.05) in both Kunming and Xining Han population, especially after a correction for multiple testing (FDR>0.90 and >0.85, respectively). In the combined set, haplogroup B showed slightly significant (*P*=0.03), but failed to pass multiple correction (FDR=0.63). These results suggested that matrilineal genetic background does not influence T2DM onset.

Table 1. Frequency of variant m.16189T>C in T2DM patients and controls.

	Individuals with 16189C (%)	Odds Ratio (95% CI)	*P* Value
Kunming, Yunnan			
Cases (n=593)	185 (31.2)	1.14 (0.85–1.54)	0.38
Controls (n=317)	90 (28.4)		
Xi'ning, Qinghai			
Cases (n=228)	61 (26.8)	1.03 (0.67–1.59)	0.89
Controls (n=191)	50 (26.2)		
Combined			
Cases (n=821)	246 (30.0)	1.12 (0.88–1.44)	0.35
Controls (n=508)	140 (27.5)		

DISCUSSION

T2DM is a complex metabolic disorder and its major etiology remains unknown. mtDNA is a suggested candidate factor of T2DM since mitochondria play an essential role in insulin secretion by pancreatic beta cells [33]. m.16189T>C in mtDNA control region was widely investigated for its association with T2DM, but no consistent conclusion has reached so far, even in the same (UK) populations [5, 11]. In the present study, we performed a systematical investigation using both epidemiologic and phylogenic approches, to evaluate the potential association between m.16189T>C and T2DM. All results, including association analysis between m.16189T>C frequency and T2DM prevalence, m.16189T>C frequency comparison in two case-control populations, and haplogroup distribution analysis, failed to support the association between the variant and T2DM susceptibility in East Asian populations.

Our results were different from those in previous studies on Asians [7-10]. Besides genetic heterogeneity, sample size, and statistic power, sampling bias might be reasonable to explain this inconsistence. Essentially, m.16189T>C frequency varies substantially in a broad geographical area across East Asian. To substantiate this, we extended our m.16189T>C frequency analysis to 2,197 mtDNAs across East Asian, including Korean, Japan and 20 provinces in China [15-19, 29, 34]. Our results suggested that in East Asian populations, the 16189C frequencies were significantly different depending on

Table 2. mtDNA haplogroup distribution in Han Chinese with variant m.16189T>C.

Haplogroups	Kunming, Yunnan			Xi'ning, Qinghai			Combined		
	Case (%)	Control (%)	*P* Value[a]	Case (%)	Control (%)	*P* Value[a]	Case (%)	Control (%)	*P* value[a]
A	5 (2.7)	1 (1.1)	0.68	1 (1.6)	2 (4.0)	0.59	6 (2.4)	3 (2.1)	1.00
B	78 (42.2)	49 (54.4)	0.06[b]	22 (36.1)	24 (48.0)	0.20[b]	100 (40.6)	73 (52.1)	0.03[c]
C	9 (4.9)	3 (3.3)	0.76	0 (0.0)	0 (0.0)	1.00	9 (3.6)	3 (2.1)	0.55
D	6 (3.2)	2 (2.2)	1.00	2 (3.3)	2 (4.0)	1.00	8 (3.3)	4 (2.9)	1.00
D5	25 (13.5)	10 (11.1)	0.58[b]	16 (26.2)	9 (18.0)	0.30[b]	41 (16.7)	19 (13.6)	0.47[b]
F	18 (9.7)	7 (7.8)	0.60[b]	5 (8.2)	4 (8.0)	1.00	23 (9.3)	11 (7.9)	0.71[b]
F1b	10 (5.4)	4 (4.4)	1.00	3 (4.9)	3 (6.0)	1.00	13 (5.3)	7 (5.0)	1.00[b]
G	2 (1.1)	1 (1.1)	1.00	2 (3.3)	0 (0.0)	0.50	4 (1.6)	1 (0.7)	0.66
M7	2 (1.1)	3 (3.3)	0.33	1 (1.6)	3 (6.0)	0.33	3 (1.2)	6 (4.3)	0.08
M7b2	5 (2.7)	4 (4.4)	0.48	0 (0.0)	1 (2.0)	0.45	5 (2.0)	5 (3.6)	0.51
M8	2 (1.1)	0 (0.0)	1.00	4 (6.6)	0 (0.0)	0.13	6 (2.4)	0 (0.0)	0.09
M9	2 (1.1)	0 (0.0)	1.00	0 (0.0)	0 (0.0)	1.00	2 (0.8)	0 (0.0)	0.54
M10	0 (0.0)	1 (1.1)	0.33	0 (0.0)	0 (0.0)	1.00	0 (0.0)	1 (0.7)	0.36
M12	3 (1.6)	0 (0.0)	0.55	0 (0.0)	0 (0.0)	1.00	3 (1.2)	0 (0.0)	0.56
M*	4 (2.2)	3 (3.3)	0.69	1 (1.6)	1 (2.0)	1.00	5 (2.0)	4 (2.9)	0.73
R11	6 (3.2)	1 (1.1)	0.43	1 (1.6)	1 (2.0)	1.00	7 (2.8)	2 (1.4)	0.50
N9	3 (1.6)	0 (0.0)	0.55	2 (3.3)	0 (0.0)	0.50	5 (2.0)	0 (0.0)	0.16
T	1 (0.5)	0 (0.0)	1.00	1 (1.6)	0 (0.0)	1.00	2 (0.8)	0 (0.0)	0.54
U	1 (0.5)	0 (0.0)	1.00	0 (0.0)	0 (0.0)	1.00	1 (0.4)	0 (0.0)	1.00
Z	1 (0.5)	0 (0.0)	1.00	0 (0.0)	0 (0.0)	1.00	1 (0.4)	0 (0.0)	1.00
N*	2 (1.1)	1 (1.1)	1.00	0 (0.0)	0 (0.0)	1.00	2 (0.8)	1 (0.7)	1.00
Total	185 (100.0)	90 (100.0)		61 (100.0)	50 (100.0)		246 (100.0)	140 (100.0)	

*Unassigned haplorgroups.
[a]*P* value estimated by fisher exact tests.
[b]*P* value estimated by the Chi square.
[c]*P* value estimated by the Chi square, after FDR test, it is no significant (FDR = 0.63).

the sampling regions, with highest value (52.2%) in Jiangxi Province, immediate value (29.9%) in Jiangsu Province, and lowest (6.7%) in Gansu Province. Moreover, haplogroup B, D5, F1b and M7b2 contributed mostly to m.16189T>C (>60%) in 17 different populations, and the total frequencies of these four haplogroups were also differently distributed across different populations, of which the lowest in Gansu Province (0.0%) and highest in Jiangxi Province (47.8%), following with the distribution of m.16189T>C in those populations (linear regression Pearson r^2=0.76, P<0.001, data not shown). All these observation suggested that the fluctuation of 16189C frequency in different populations might mirror the distribution of these specific halogroups in those populations. Therefore, it is certainly not surprising that m.16189T>C shows considerably different frequencies across a broad geographical area. Before the conclusion is reached, it is indispensable to properly estimate the potential effect of population substructure, which easily caused spurious positive results, especially in evaluating the role of mtDNA variants in developing T2DM.

Alternatively, the observed conflicting relationships between m.16189T>C and T2DM in different ethnic groups could be attributable to the influence of mtDNA background. To shed more light on the potential contribution of matrilineal background(s) to the distribution of m.16189T>C and to evaluate the relationship between the relevant matrilineal genetic background and T2DM, further efforts on the determination of haplogroup affiliation in the subjects with m.16189T>C were carried out and the frequency of each haplogroup between the two groups of case-control samples was compared in this study. Although the power to detect T2DM with major mithochondrial DNA haplogroup (etc. haplgroup B) was modest (data not shown) [35], our result failed to identify any specific haplogroups (*viz*. matrilineal background) showing preference in either patient or control samples in both Han regional populations, suggesting that there has no specific matrilineal background involved in the "penetrance" of m.16189T>C in the T2DM cohort.

In summary, our investigation of the potential role of m.16189T>C in T2DM failed to confirm the correlation between either m.16189T>C or matrilineal background and T2DM, suggesting that m.16189T>C or its matrilineal background may play a subtle role in development of T2DM in Chinese Han population, and further studies are mandatory in the future to clarify this issue.

ABBREVIATIONS

HVS-I = Hypervariable segment I

MtDNA = Mitochondrial DNA

OXPHOS = Oxidative phosphorylation

T2DM = Type 2 diabetes mellitus

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's web site along with the published article.

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SUPPLEMENTARY MATERIAL

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Table S1. mtDNA sequence variation in Yunnan T2DM patients harboring m.16189T>C (n = 185).

Subject	Haplogroup	HVS-I (+16000)[a]	HVS-II (73 and 263 in addition)[a]	9bp[b]	RFLP [c]
YDM134	A	189 196 223 290 311 319 362			+663*Hae*III
YDM19	A	183 189 223 274 290 319 362 (519)	195 315+C		
YDM23	A	183 189 223 274 290 319 362 (519)	195 315+C		
YDM734	A	189 223 290 319			+663*Hae*III
YDM96	A	183 189 223 274 290 319 362 (519)	195 315+C		
YDM748	B	183C 189 249		1	
YDM241	B	129 182C 183C 189 311		1	
YDM351	B	051 182C 183C 189 (519)	146 152 315+C 356+C	1	
YDM228	B	136 183C 189 (519)	207 315+C		+12406*Hinc*II
YDM320	B4	182C 183C 189 217 362	214 315+C 368	1	
YDM334	B4	182C 183C 189 217 362	214 315+C 368	1	
YDM400	B4	182C 183C 189 217 293C	214 309+CC 315+C	1	
YDM101	B4	182C 183C 189 217		1	
YDM123	B4	182C 183C 189 217		1	
YDM138	B4	150 183C 189 217 234 269		1	
YDM145	B4	183C 189 217 294		1	
YDM272	B4	129 182C 183C 189 217		1	
YDM479	B4	182C 183C 189 217 311 362		1	
YDM5	B4	182C 183C 189 217 223		1	
YDM681	B4	147 183C 184A 189 217 235		1	
YDM706	B4	147 183C 189 217 235		1	
YDM327	B4a	182C 183C 189 217 240 261	309+C 315+C	1	
YDM402	B4a	093 182C 183C 189 217 261	315+C	1	
YDM503	B4a	182C 183C 189 217 261	309+C 315+C	1	

Subject	Haplogroup	HVS-I (+16000)[a]	HVS-II (73 and 263 in addition)[a]	9bp[b]	RFLP [c]
YDM104	B4a	129 182C 183C 189 261		1	
YDM183	B4a	182C 183C 189 217 261		1	
YDM207	B4a	182C 183C 189 217 261 294		1	
YDM210	B4a	150 182C 183C 189 217 261		1	
YDM211	B4a	182C 183C 189 194C 195 217 261 294		1	
YDM238	B4a	181C 182C 183C 189 213 217 261 292		1	
YDM243	B4a	129 182C 183C 189 261		1	
YDM252	B4a	181C 182C 183C 189 213 217 261 292		1	
YDM265	B4a	129C 181C 182C 183C 189 217 261 (519)		1	
YDM282	B4a	093 145 182C 183C 189 217 261 (519)	146 309+CC 315+C	1	
YDM310	B4a	093 182C 183C 189 217 261		1	
YDM39	B4a	182C 183C 189 217 221 240 261		1	
YDM468	B4a	182C 183C 189 217 240 261		1	
YDM506	B4a	182C 183C 189 217 261 360		1	
YDM528	B4a	182C 183C 189 217 240 261		1	
YDM532	B4a	182C 183C 189 217 243 261 278		1	
YDM550	B4a	150 182C 183C 189 217 261		1	
YDM625	B4a	092 182C 183C 189 217 261 399		1	
YDM727	B4a	182C 183C 189 217 261 360		1	
YDM747	B4a	182C 183C 189 217 240 261		1	
YDM761	B4a	182C 183C 189 217 240 261		1	
YDM92	B4a	093 182C 183C 189 217 261		1	
YDM93	B4a	084 182C 183C 189 217 261 362 399		1	
YDM94	B4a	181C 182C 183C 189 213 217 261 292		1	
YDM257	B4b	136 183C 189 217 284		1	
YDM47	B4b	069 136 183C 189 217 218		1	
YDM537	B4b	093 136 183C 189 217		1	
YDM199	B4c	140 183C 189 217 274		1	
YDM438	B4c	129 138 140 166 183C 189 217 274 335		1	
YDM646	B4c	129 140 166 172 183C 189 217 274 293 335		1	
YDM541	B5a	129 140 183C 189 223 249 266A (519)	210 309+CCC 315+C	1	+5176*Alu*I, -4831*Hha*I
YDM309	B5a	140 183C 189 266A (519)	93 210 315+C	1	
YDM341	B5a	140 183C 189 266A (519)	152 210 309+C 315+C	1	
YDM384	B5a	140 183C 189 266A (519)	210 315+C	1	
YDM386	B5a	092 129 140 182C 183C 189 239 266A (519)	210 309+C 315+C	1	
YDM410	B5a	140 182C 183C 189 261 266A (519)	152 210 309+CC 315+C	1	
YDM618	B5a	140 183C 189 266A (519)	146 210 309+CC 315+C	1	
YDM200	B5a	140 183C 189 266A		1	
YDM203	B5a	140 182C 183C 189 266A		1	
YDM246	B5a	140 182C 183C 189 266A		1	
YDM249	B5a	140 183C 189 266A 304		1	
YDM288	B5a	183C 189 266A		1	

Subject	Haplogroup	HVS-I (+16000)[a]	HVS-II (73 and 263 in addition)[a]	9bp[b]	RFLP [c]
YDM31	B5a	140 183C 189 262 266A 325		1	
YDM422	B5a	140 182C 183C 189 266A		1	
YDM452	B5a	066 183C 189 266A		1	
YDM593	B5a	140 183C 189 266A		1	
YDM619	B5a	140 182C 183C 189 266A 354		1	
YDM632	B5a	140 182C 183C 189 250 261 266A		1	
YDM504	B5b	111 140 182C 183C 189 234 243 463 (519)	103 131 309+CC 315+C	1	
YDM115	B5b	140 183C 189 243		1	
YDM248	B5b	093 124 179 182C 183C 189 243		1	
YDM350	B5b	093 179 182C 183C 189 243		1	
YDM439	B5b	140 183C 189 243		1	
YDM443	B5b	140 182C 183C 189 243		1	
YDM525	B5b	066 183C 189 223 243		1	
YDM590	B5b	111 140 183C 189 234 243 463		1	
YDM613	B5b	140 182C 183C 189 243		1	
YDM675	B5b	140 183C 189 243		1	
YDM71	B5b	136 140 183C 189 243 311		1	
YDM328	C	093 189 223 298 327 (519)	199 249d 309+C 315+C		-13259*Hinc*II
YDM170	C	189 223 298 327			
YDM230	C	183C 189 223 298 327			
YDM255	C	183C 189 223 298 311 327			
YDM260	C	183C 189 223 298 327			
YDM275	C	183C 189 223 298 311 327			
YDM312	C	189 223 298 327 357			-13259*Hinc*II
YDM49	C	189 223 261 298 327			
YDM737	C	092 129 189 223 298 327 355			
YDM767	D	189 223	195 309+CC 315+C	2	-5176*Alu*I
YDM720	D	176 189 223 311 362	152 185 309+C 315+C		-5176*Alu*I
YDM387	D4	189 192 223	195 309+C 315+C		-5176*Alu*I, -4831*Hha*I
YDM12	D4	184 189 223 311 362			-5176*Alu*I
YDM197	D4a	129 189 223 362 (519)	152 309+C 315+C		-5176*Alu*I
YDM24	D4a	129 189 223 362 (519)	152 309+C 315+C		-5176*Alu*I
YDM297	D5	184 189 223 311 362 468	200 309+C 315+C		-5176*Alu*I
YDM167	D5	183C 189 223 362 (519)	150 315+C		-5176*Alu*I
YDM20	D5	179G 183C 189 223 274 362 (519)	195 298 310 316		-5176*Alu*I
YDM262	D5	189 223 362	94 309+C 315+C		-5176*Alu*I
YDM600	D5	164 182C 183C 189 223 362			-5176*Alu*I
YDM601	D5	183C 189 223 362			-5176*Alu*I
YDM626	D5	183C 189 223 357 362			-5176*Alu*I
YDM677	D5	189 223 274 362			-5176*Alu*I
YDM690	D5	176 189 223 311 362	152 185 309+C 315+C		-5176*Alu*I
YDM7	D5	184 189 223 311 362	200 309+C 315+C		-5176*Alu*I

Subject	Haplogroup	HVS-I (+16000)[a]	HVS-II (73 and 263 in addition)[a]	9bp[b]	RFLP [c]
YDM704	D5	111 172 183C 189 223 311 362 (519)	185 189 195 234 315+C		-5176*Alu*I, -4831*Hha*I
YDM72	D5	167 189 223 271 362 (519)	150 309+C 315+C		
YDM84	D5	179G 183C 189 223 274 362 (519)	195 298 310 316		
YDM345	D5a	164 172 182C 183C 189 223 266 362	150 315+C		-5176*Alu*I
YDM405	D5a	092 164 172 182C 183C 189 223 243 266 362	150 315+C		-5176*Alu*I
YDM102	D5a	164 172 182C 183C 189 223 266 362			-5176*Alu*I
YDM26	D5a	164 172 182C 183C 189 223 266 362	146 150 315+C		-5176*Alu*I
YDM337	D5a	164 172 182C 183C 189 223 266 362			-5176*Alu*I
YDM395	D5a	066 075 092 172 182C 183C 189 223 266 362			-5176*Alu*I
YDM45	D5a	164 172 182C 183C 189 223 266 362	150 309+CC 315+C		
YDM52	D5a	164 172 182C 183C 189 223 266 362			-5176*Alu*I
YDM521	D5a	092 164 172 182C 183C 189 223 266 362	150 315+C		-5176*Alu*I
YDM615	D5a	092 154 164 167 172 182C 183C 189 223 266 362			-5176*Alu*I
YDM63	D5a	164 172 182C 183C 189 223 266 362	146 150 315+C		-5176*Alu*I
YDM655	D5a	092 164 172 182C 183C 189 223 266 362			-5176*Alu*I
YDM126	F1	183C 189 243 304			
YDM135	F1	183C 189 243 304			-12406*Hinc*II
YDM15	F1	189 304 422			-12406*Hinc*II
YDM186	F1	093 183C 189 304 357			-12406*Hinc*II
YDM3	F1	189 304 422			-12406*Hinc*II
YDM444	F1	183C 189 304			-12406*Hinc*II
YDM51	F1	183C 189 304			-12406*Hinc*II
YDM574	F1	183C 189 304			-12406*Hinc*II
YDM589	F1	172 189 304			
YDM598	F1	172 189 304			-12406*Hinc*II
YDM651	F1	189 304			-12406*Hinc*II
YDM763	F1	183C 189 304			-12406*Hinc*II
YDM76	F1	183C 189 261 291 304			-12406*Hinc*II
YDM77	F1	183C 189 304			-12406*Hinc*II
YDM88	F1	189 304			-12406*Hinc*II
YDM90	F1	183C 189 304 311			-12406*Hinc*II
YDM322	F1b	093 182C 183C 189 232A 304 (519)	152 249d 309+CC 311 315+C		-12406*Hinc*II
YDM377	F1b	183C 189 232A 249 304 311 (519)	90 204 249d 309+C 315+C		-12406*Hinc*II
YDM389	F1b	129 183C 189 232A 249 304 311	203 204 249d 309d 315+C		-12406*Hinc*II
YDM147	F1b	183C 189 232A 249 304 311			-12406*Hinc*II
YDM148	F1b	183C 189 227 232A 249 304 311			-12406*Hinc*II
YDM165	F1b	182C 183C 189 232A 249 304 311 (519)	249d 315+C		-12406*Hinc*II
YDM28	F1b	093 182C 183C 189 232A 304 (519)	152 249d 309+C 315+C		-12406*Hinc*II
YDM509	F1b	168 183C 189 232A 242 249 304 311			-12406*Hinc*II
YDM629	F1b	183C 189 232A 249 304 311			-12406*Hinc*II
YDM630	F1b	183C 189 232A 249 304 311			-12406*Hinc*II
YDM103	F3	117 183C 189 298 355 356 362			

Subject	Haplogroup	HVS-I (+16000)[a]	HVS-II (73 and 263 in addition)[a]	9bp[b]	RFLP [c]
YDM189	F3	117 183C 189 298 355 356 362			
YDM716	G	129 189 223 274 309 362	143 315+C		+5176*Alu*I
YDM448	G2a3	189 223 261 278 362			+5176*Alu*I, +4831*Hha*I
YDM175	M*	111 172 183C 189 223 311 362 (519)	185 189 195 234 315+C		+5176*Alu*I, -4831*Hha*I
YDM213	M*	172 183C 189 223 362	185 189 285 309+CC 315+C		+5176*Alu*I, -4831*Hha*I
YDM245	M*	111 172 183C 189 223 311 362 (519)	185 189 195 234 309+CC 315+C		+5176*Alu*I
YDM61	M*	172 189 223 234 260 290 (519)	125 127 128 146 195 315+C		+5176*Alu*I, -4831*Hha*I
YDM40	M7b1	189 192 223 297	150 199 204 207 315+C		
YDM516	M7b2	129 189 223 297	150 199 204 309+C 315+C		+9820*Hinf*I
YDM132	M7b2	129 189 223 248 297			+9820*Hinf*I
YDM250	M7b2	129 172A 189 223 297			+9820*Hinf*I
YDM390	M7b2	129 189 223 248 294 297			+9820*Hinf*I
YDM644	M7b2	129 189 223 248 297			+9820*Hinf*I
YDM409	M7c	111 184 189 223 274 295	315+C		-9820*Hinf*I
YDM263	M8a	184 189 223 298 319 470 471 473			
YDM271	M8a	184 189 223 298 319			
YDM66	M9	158 189 223 234 261 362 (519)	150 152 153 315+C		
YDM347	M9a	189 223 234 291 316 362 465	150 153 309+C 315+C		+3391*Hae*III
YDM519	M12	148 172 189 223 234 290 (519)	125 127 128 146 195 315+C		+5176*Alu*I, -4831*Hha*I
YDM744	M12	148 172 189 223 234 290 (519)	125 127 128 146 195 315+C		+5176*Alu*I, -4831*Hha*I
YDM78	M12	172 189 223 234 260 290	125 127 128 146 195 315+C		
YDM284	N*	145 183C 189 223 355 (519)	195 240 315+C		+5176*Alu*I, -4831*Hha*I
YDM295	N*	145 183C 189 223 355 (519)	195 240 315+C		
YDM168	N9a	129 182C 183C 189 223 257A 261 320			
YDM179	N9a	129 182C 183C 189 223 257A 261 320			
YDM198	N9a	179 182C 183C 189 223 257A 261 325			
YDM244	R11	182C 189 311 390 399			
YDM251	R11	182C 183C 189 311 390 399			
YDM62	R11	182C 183C 189 295 311 463			
YDM34	R11	182C 183C 189 295 311 463			
YDM304	R11	182C 183C 189 249A 311 (519)	185 189 235 309+CC 315+C		
YDM376	R11	092 182C 183C 189 311 390 399 (519)	185 189 309+C 315+C		
YDM505	T1	093 126 163 186 189 294 (519)	152 195 204 309+C 315+C		
YDM299	U1a	182C 183C 189 249	285 309+C 315+C		
YDM266	Z	185 189 223 260 298			

HVS I & II = Hyper Variable Segment I & II;
RFLP = Restriction Fragment Length Polymorphism;
T2DM = type 2 diabetes; mtDNA: mitochondrial DNA;
YDM = Yunnan Diabetes Mellitus subjects.
Sites are numbered according to the revised Cambridge reference sequence [rCRS; (Andrews *et al., Nat Genet* 1999)]. All individuals have been read for regions 16000-16497, and 30-407, and mutations located outside the region are listed in parentheses.
When the sequence information is not available, the items have been left blank.
a Suffixes A, C, T, and G indicate transversion, "d" indicates deletions, and "+" indicates insertions.
b "1"denotes the presence of the 9-bp (CCCCCTCTA) deletion in the COII/tRNALys intergenic region, "2"denotes non-deletion.
c "–" and "+" denote the absence and presence of the restriction site respectively.
* unassigned haplorgroups

Table S2. mtDNA sequence variation in Yunnan controls harboring m.16189T>C (n = 90).

Subject	Haplogroup	HVS-I (+16000)	HVS-II (73 and 263 in Addition)	9bp	RFLP
YC154	A	093 189 223 290 319 362	151 152 200 235 315+C		+663*Hae*III
YC126	B	183C 189 362 (519)	315+C 316	1	
YC172[a]	B	093 179 182C 183C 189	150 185 309+CC 315+C	1	
YC154[a]	B4	140 183C 189 217 274	150 152 309+C 315+C	1	
YC169[a]	B4	182C 183C 189 217 234	309+C 315+C	1	
YC233	B4	108 182C 183C 189 217 362G (519)	309+CC 315+C	1	
YC246	B4	108 182C 183C 189 217 362 (519)	309+C 315+C	1	
YC247	B4	147 183C 184A 189 217 (519)	309+C 315+C	1	
YC273	B4	108 182C 183C 189 217 354A 362G (519)	309+CC 315+C	1	
YC49	B4	182C 183C 189 217 218A (519)	309+C 315+C	1	
YC64	B4	183C 189 217 (519)	152 309+CC 315+C 316	1	
YC77	B4	182C 183C 189 217 218A	309+C 315+C	1	
YC1	B4a	182C 183C 189 217 219 261 286 (519)	309+CC 315+C	1	
YC11	B4a	182C 183C 189 217 240 261 (519)	309+CC 315+C	1	
YC113	B4a	182C 183C 189 217 240 261	309+CC 315+C	1	
YC116	B4a	168 182C 183C 189 217 261 311 (519)	182 185 309+C 315+C	1	
YC144	B4a	129 82C 183C 189 217 261 311		1	
YC155[a]	B4a	182C 183C 189 217 261 299 355 390	35 36 152 309+CC 315+C	1	
YC158[a]	B4a	092 182C 183C 189 217 261 299	193 309+C 315+C	1	
YC159	B4a	182C 183C 189 217 218 239 261 (519)	89 315+C	1	
YC174[a]	B4a	129 182C 183C 189 217 261	146 195 257 309+C 315+C	1	
YC186	B4a	129C 181C 182C 183C 189 213 217 261 292 (519)	309dC 315+C	1	
YC200	B4a	182C 183C 189 217 261 287	200 309+CC 315+C	1	
YC24	B4a	182C 183C 189 217 261 286 (519)	309+CC 315+C	1	
YC270	B4a	182C 183C 189 217 261 293 (519)	315+C	1	
YC5	B4a	093 182C 183C 189 217 261 327 (519)	146 309+CC 315+C	1	
YC54	B4a	129 182C 183C 189 217 261	309+C 315+C	1	
YC57	B4a	181C 182C 183C 189 213 217 261 292		1	
YC61	B4a	182C 183C 189 217 261 299 (519)	309+CC 315+C	1	
YC80	B4a	182C 183C 189 240 261		1	
YC189	B4b1	136 182C 183C 189 217 309 354 (519)	207 309+CC 315+C	1	
YC281	B4b1	136 182C 183C 189 217 309 354	207 315+C	1	
YC10	B4c1	140 182C 183C 189 217 274 316 335 (519)	146 150 309+CC 315+C	1	
YC259	B4c1	140 182C 183C 189 217 274 335		1	
YC271	B4c1	140 182C 183C 189 217 274 335 (519)	146 150 189 195 309+CC 315+C	1	
YC31	B4c1	140 182C 183C 189 217 274 316 335 (519)	146 150 309+CC 315+C	1	
YC135	B5a	140 187 189 256 266G 342 (519)	93 210 315+C	1	
YC150[a]	B5a	140 145 183C 189 217 266A	93 146 315+C	1	
YC168[a]	B5a	140 145 183C 189 266A	210 309+C 315+C	1	

Subject	Haplogroup	HVS-I (+16000)	HVS-II (73 and 263 in Addition)	9bp	RFLP
YC214	B5a	140 183C 189 262 266A (519)	64 210 309+CC 315+C	1	
YC222	B5a	140 183C 189 266A (519)	210 309+CC 315+C	1	
YC238	B5a	140 183C 189 261 266A (519)	210 309+C 315+C	1	
YC251	B5a	140 183C 189 266A (519)	210 309+C 315+C	1	
YC4	B5a	140 182C 183C 189 266A (519)	189 210 315+C	1	
YC40	B5a	111 140 182C 183C 189 266A (519)	210 309+CC 315+C	1	
YC133	B5b	140 183C 189 243 311 319 (519)	103 204 207 309+C 315+C	1	
YC216	B5b	140 183C 189 243 (519)	204 309+CC 315+C	1	
YC284[a]	B5b	111 129 140 182C 183C 189 234 243 249 250 463	131 199 204 292 315+C	1	
YC39	B5b	140 183C 189 243 342 355 (519)	103 309+C 315+C	1	
YC256	B6	093 179 182C 183C 189 342		1	
YC142	C	189 223 298 327 355 (519)	249d 309+C 315+C		-13259*Hinc*II
YC177[a]	C	092 183C 189 223 298 327 355	249d 309+C 315+C	2	
YC18	C	183C 189 223 298 327 (519)	207 249d 315+C		-13259*Hinc*II
YC204	D	183C 189 223 278 362	94 315+C		-5176*Alu*I, -4831*Hha*I
YC171[a]	D4b	184d 186 189 223 319 362	185 189 315+C	2	-5176*Alu*I
YC257	D5	079 086 145 189 223 362	151 309+C 315+C		-5176*Alu*I
YC289[a]	D5	189 223 362	150 315+C	2	-5176*Alu*I
YC112	D5a	086 092 164 182d 183C 186 189 223 266 362	150 315+C		-5176*Alu*I
YC117	D5a	164 172 182C 183C 189 223 239 266 362	150 309+C 315+C		-5176*Alu*I
YC167[a]	D5a	172 182C 183C 189 223 266 299 319 362	150 309+C 315+C	2	-5176*Alu*I
YC231	D5a	092 164 172 182C 183C 189 223 266 362	150 315+C		-5176*Alu*I
YC27	D5a	093 164 172 182C 183C 189 223 266 311 362	16T 146 150 195 309+C 315+C		-5176*Alu*I
YC283	D5a	164 172 182C 183C 189 223 266 269 354 362	150 309+CC 315+C		-5176*Alu*I
YC50	D5a	092 164 182C 183C 189 223 266 362 399 (519)	150 309+C 315+C		-5176*Alu*I
YC78	D5a	092 129 164 172 182C 183C 189 223 266 362	150 315+C		-5176*Alu*I
YC153	F1	093 189 335 357	152 249d 309+C 315+C	2	-12406*Hinc*II
YC156	F1	126 183C 189 304 390 (519)	61A 63 64 195 249d 309+C 315+C		-12406*Hinc*II
YC22	F1	182C 183C 189 304 (519)	249d 309+C 315+C		-12406*Hinc*II
YC248	F1	189 304 (519)	146 249d 309+C 315+C		-12406*Hinc*II
YC3	F1	183C 189 304 (519)	249d 309+C 315+C		-12406*Hinc*II
YC56	F1	183C 189 304 (519)	249d 309+C 315+C		-12406*Hinc*II
YC83	F1	183C 189 304 (519)	249d 309+C 315+C		-12406*Hinc*II
YC166[a]	F1b	183C 189 232A 249 304 311	146 204 207 249d 309+C 315+C	2	
YC23	F1b	129 183C 189 232A 249 304 (519)	152 249d 309+CC 315+C		-12406*Hinc*II
YC290[a]	F1b	129 145 182C 183C 189 232A 249 304 311 344	152 249d 315+C	2	
YC45	F1b	182C 183C 189 232A 249 304 (519)	152 249d 309+CC 315+C		-12406*Hinc*II
YC151	G2	189 223 261 278 362	204 207 309+C 315+C		+5176*Alu*I, +4831*Hha*I
YC130	M*	068 183C 189 223 311 (519)	146 150 152 310dT		+5176*Alu*I

Subject	Haplogroup	HVS-I (+16000)	HVS-II (73 and 263 in Addition)	9bp	RFLP
YC149[a]	M*	183C 189 293C 325 362	146 234 315+C	2	-3391*Hae*III, -4831*Hha*I, +5176*Alu*I, -9820*Hin*fI
YC258	M*	068 126 182C 183C 189 223 325 (519)	146 150 152 195 309+CC 315+C	2	+5176*Alu*I
YC262	M7b	129 189 214 223 297 399 (519)	150 199 309+C 315+C		+9820*Hin*fI
YC266	M7b	093 129 189 223 248 297	150 199 204 207 315+C		+9820*Hin*fI
YC2	M7b2	129 189 223 297 357 399 (519)	150 199 309+C 315+C		+9820*Hin*fI
YC208	M7b2	129 189 223 297	150 199 309+C 315+C		+9820*Hin*fI
YC218	M7b2	129 189 223 297	150 199 309+C 315+C		+9820*Hin*fI
YC221	M7b2	129 189 223 297	150 199 309+C 315+C		+9820*Hin*fI
YC205	M7c	145 150 182C 183C 189 223 (519)	146 199 207 315+C		-9820*Hin*fI
YC86	M10	182C 183C 189 217 223 311 320			+5176*Alu*I
YC95	N*	145 189 223 355 (519)	195 240 315+C		+5176*Alu*I, -9820*Hin*fI
YC8	R11a	182C 183C 189 311 390 399	185 189 215 309+CC 315+C		

YC: Yunnan Control subjects.
a These 16 samples have been reported in Yao *et al*. (Yao *et al*., *Am J Hum Genet* 2002).

Table S3. mtDNA sequence variation in Qinghai T2DM patients harboring m.16189T>C (n = 61).

Subject	Haplogroup	HVS-I (+16000)	HVS-II (73 and 263 in Addition)	9bp	RFLP
QDM1792	A	093 189 223 278 290 319 362	146 152 235 309+CC 315+C		+663*Hae*III
QDM1689	B4	182C 183C 189 217 299 (519)	152 199 309+CC 315+C	1	
QDM1788	B4	183C 189 217 (519)	152 309+CC 315+C 319	1	
QDM54	B4	147 168 172 189 217 249 325 390		1	
QDM63	B4	150 189 217 234		1	
QDM26	B4	189 217 218 223		1	
QDM1772	B4a	092 182C 183C 189 217 261 299 (519)	193 309+TC 315+C	1	
QDM1777	B4a	092 182C 183C 189 217 261 299 (519)	193 309+TC 315+C	1	
QDM36	B4a	129 189 261		1	
QDM11	B4a	092 167 189 217 261 317AT		1	
QDM42	B4b	086 136 189 217		1	
QDM71	B4b	136 189 217 284 343		1	
QDM1790	B4b1	136 183C 189 217 270 298 (519)	150 152 309+CC 315+C	1	
QDM1809	B4b1	136 182C 183C 189 217 298 362 (519)	152 309+CCC 315+C	1	
QDM1644	B4c	140 169+C 182C 183C 189 217 242A 274 335 (519)	146 150 315+C	1	
QDM1707	B4c	140 183C 189 217 274 335 (519)	150 204 315+C	1	
QDM1752	B4c	182C 183C 189 217 274	214 309+CC 315+C	1	
QDM1762	B4c	136 140 183C 189 217 249 274 280 291 335 (519)	150 315+C	1	
QDM1701	B5a	140 183C 189 245 266G (519)	93 210 309+C 315+C	1	
QDM66	B5a	140 189 266CA		1	
QDM12	B5b	111 140 189 234 243 304 463		1	

QDM24	B5b	051 111 140 189 234 243 298 463		1	
QDM1810	B6	093 179 182C 183C 189 352	150 309+C 315+C	1	
QDM1760	D	093 176 189 223 362	94 194 309+C 315+C		-5176*Alu*I, -4831*Hha*I
QDM1823	D	126 189 223 239 362	309+CC 315+C		-5176*Alu*I, -4831*Hha*I
QDM1651	D5	111 189 223 287 291A 362 (519)	309+C 315+C		-5176*Alu*I, -4831*Hha*I
QDM1653	D5	189 223 362	146 150 315+C		-5176*Alu*I
QDM1673	D5	136 182C 183C 189 223 311 360 362	93 150 204 207 307 309+CCC 315+C		-5176*Alu*I
QDM1676	D5	051 136 189 362 390	146 150 151 152 309+C 315+C		-5176*Alu*I
QDM1739	D5	183C 189 223 362	150 309+C 315+C		-5176*Alu*I
QDM1675	D5	183C 189 223 311 362	146 309+C 315+C		-5176*Alu*I
QDM35	D5	189 223 362		2	-5176*Alu*I
QDM80	D5	189 223 362		2	-5176*Alu*I
QDM1681	D5a	092 172 182C 183C 189 223 266 362	150 309+CC 315+C		-5176*Alu*I
QDM1721	D5a	164 172 182C 183C 189 223 243 266 362	150 315+C		-5176*Alu*I
QDM1766	D5a	164 182C 183C 189 223 266 280 362 (519)	150 315+C		-5176*Alu*I
QDM1780	D5a	164 172 182C 183C 189 223 264 266 319 362	150 246 315+C		-5176*Alu*I
QDM1808	D5a	164 172 182C 183C 189 223 243 266 362	150 315+C		-5176*Alu*I
QDM1742	D5a	164 172 182C 183C 189 223 266 362	150 309+C 315+C		-5176*Alu*I, -4831*Hha*I
QDM03	D5a	172 189 223 266 362		2	-5176*Alu*I
QDM34	D5a	164 172 189 223 266 362		2	-5176*Alu*I
QDM1746	F1	183C 189 304 (519)	249d 309+CC 315+C		-12406*Hinc*II
QDM1783	F1	183C 189 300 304 357 (519)	131 150 195 204 249d 309+CC 315+C		-12406*Hinc*II
QDM09	F1	158 189 304		2	
QDM44	F1	093 189 304 311		2	
QDM1674	F1b	183C 189 232A 249 304 311 (519)	249d 315+C		-12406*Hinc*II
QDM1802	F1b	148 182C 183C 189 232A 249 304 311 (519)	199 204 249d 315+C		-12406*Hinc*II
QDM1806	F1b	183C 189 232A 249 304 311 (519)	249d 315+C		-12406*Hinc*II
QDM1817	F2a2	092A 183C 189 291 304	185 249d 315+C		+12406*Hinc*II
QDM1648	G2a	189 223 227 234 278 362	195 309+C 315+C		+4831*Hha*I,
QDM73	G2a	189 223 227 278 362		2	+4831*Hha*I,
QDM60	M*	068 124 189 223 311		2	+5176*Alu*I ,-4831*Hha*I
QDM65	M7b1	129 189 192 223 297		2	
QDM1665	M8a	093 184 189 223 294 298 319 355 362 (519)	309+C 315+C		
QDM1685	M8a	093 184 189 223 294 298 319 355 362 (519)	309+C 315+C		
QDM22	M8a	184 189 223 298 319 470 471 473		2	
QDM69	M8a	184 189 223 298 319 443 470 471 473 476AC		2	
QDM74	N9a	189 223 257CA 261		2	
QDM1767	N9b	092 148 183C 189 223 (519)	150 152 185 315+C		
QDM40	R11	189 311			
QDM16	T	126 163 186 189 294		2	+5176*Alu*I

QDM: Qinghai Diabetes Mellitus patients.

Table S4. mtDNA sequence variation in Qinghai controls harboring m.16189T>C (n = 50).

Subject	Haplogroup	HVS-I (+16000)	HVS-II (73 and 263 in Addition)	9bp	RFLP
QC9350	A	126 189 223 230 290 319 362	146 152 235 309+C 315+C		+663*Hae*III
QC9670	A	189 223 290 319 362			+663*Hae*III
QC9333	B4	150 183C 189 217 234 (519)	309+CC 315+C	1	
QC9353	B4	182C 183C 189 215T 217 (519)	55 56 207 309+CC 315+C	1	
QC9672	B4	182C 183C 189 217		1	
QC9486	B4	183C 189 217 234		1	
QC9498	B4	183C 189 217		1	
QC9365	B4a	129 182C 183C 189 261	309+CC 315+C	1	
QC9677	B4a	129 182C 183C 189 261		1	
QC9711	B4a	182C 183C 189 217 261		1	
QC9497	B4a	182C 183C 189 217 234 261		1	
QC9513	B4a	182C 183C 189 217 240 261		1	
QC9669	B4b1	136 183C 189 217 293C 298 311		1	
QC9362	B4c	129 140 182C 183C 189 217 274 335 (519)	146 150 315+C	1	
QC9693	B4c	183C 189 217 311		1	
QC9517	B4c	140 183C 189 217 274 325 355		1	
QC9323	B5a	140 183C 189 234 266A (519)	204 210 309+C 315+C	1	
QC9380	B5a	140 182C 183C 189 266A (519)	210 292 307-308d 315+C 392	1	
QC9383	B5a	140 183C 189 266A (519)	93 207 210 315+C	1	
QC9476	B5a	140 182C 183C 189 266A		1	
QC9660	B5a1	140 182C 183C 189 261 266A		1	
QC9348	B5b	140 183C 189 243 (519)	103 189 203 204 309+CC 315+C	1	
QC9491	B5b	140 172 182C 183C 189 243		1	
QC9688	B5b1	108 111 140 183C 189 234 243 399 463		1	
QC9710	B5b1	111 140 153 183C 189 234 243 319 463		1	
QC9668	B6	093 179 182C 183C 189 342		1	
QC9400	D4	185 189 223 232A 319 362	315+C		-5176*Alu*I, -4831*Hha*I
QC9702	D4	093 129 189 223 249 362			-5176*Alu*I, -3008*Taq*I, +10397*Alu*I
QC9303	D5	189 223 362 (519)	150 152 195 309+C 315+C		-5176*Alu*I
QC9312	D5	092 164 183C 189 223 362	150 315+C		-5176*Alu*I
QC9376	D5	092 164 182C 183C 189 223 362	150 315+C		-5176*Alu*I
QC9389	D5	093 183C 189 223 362	146 150 309+C 315+C		-5176*Alu*I
QC9367	D5a	092 164 167 172 182C 183C 189 223 266 362	150 315+C		-5176*Alu*I
QC9373	D5a	164 172 182C 183C 189 223 266 362	150 315+C		-5176*Alu*I
QC9665	D5a1	092 164 182d 183C 186 189 223 266 362			-5176*Alu*I, -10397*Alu*I
QC9671	D5a1	051 092 145 164 182C 183C 189 223 266 362			-5176*Alu*I, -10397*Alu*I
QC9681	D5c	188+C 189 193+C 298 362 390			-5176*Alu*I, -10397*Alu*I

Subject	Haplogroup	HVS-I (+16000)	HVS-II (73 and 263 in Addition)	9bp	RFLP
QC9402	F1	183C 189 300 304 311 (519)	150 152 189 195 249d 315+C		-12406*Hinc*II
QC9499	F1	182C 183C 189 304			-12406*Hinc*II
QC9503	F1	048 182C 183C 189 304 309			-12406*Hinc*II
QC9518	F1a	129 162 172 189 304			-12406*Hinc*II
QC9343	F1b	183C 189 232A 249 304 311 (519)	249d 315+C		-12406*Hinc*II
QC9701	F1b	183C 189 232A 249 304 311			-12406*Hinc*II
QC9515	F1b	183C 189 232A 249 304 311			-12406*Hinc*II
QC9480	M*	068 126 182C 183C 189 223 325			+5176*Alu*I, -9820*Hinf*I, -4831*Hha*I, +12406*Hinc*II
QC9345	M7b	129 189 223 297	150 199 204 207 309+C 315+C		+9820*Hinf*I
QC9484	M7b1	129 189 223 297			+9820*Hinf*I
QC9509	M7b1	129 189 192 223 297			+9820*Hinf*I
QC9379	M7b2	129 189 223 242 297 298	150 199 309+CC 315+C		+9820*Hinf*I
QC9704	R11	182C 183C 189 311		2	-663*Hae*III

QC: Qinghai Control subjects.