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Report

Origin and Diffusion of mtDNA Haplogroup X

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A maximum parsimony tree of 21 complete mitochondrial DNA (mtDNA) sequences belonging to haplogroup X and the survey of the haplogroup-associated polymorphisms in 13,589 mtDNAs from Eurasia and Africa revealed that haplogroup X is subdivided into two major branches, here defined as "X1" and "X2." The first is restricted to the populations of North and East Africa and the Near East, whereas X2 encompasses all X mtDNAs from Europe, western and Central Asia, Siberia, and the great majority of the Near East, as well as some North African samples. Subhaplogroup X1 diversity indicates an early coalescence time, whereas X2 has apparently undergone a more recent population expansion in Eurasia, most likely around or after the last glacial maximum. It is notable that X2 includes the two complete Native American X sequences that constitute the distinctive X2a clade, a clade that lacks close relatives in the entire Old World, including Siberia. The position of X2a in the phylogenetic tree suggests an early split from the other X2 clades, likely at the very beginning of their expansion and spread from the Near East.

mtDNA and the nonrecombining part of the Y chromosome are widely used in archaeogenetic studies (Renfrew 2000; Cavalli-Sforza and Feldman 2003) that aim to reveal the human past. The uniparental inheritance and complete linkage of mutations in these two loci allow an unambiguous determination of the phylogenetic relationships between individual lineages. However, the putative genetic histories of the lineages that are obtained do not fully reflect the complex dynamics of ancient populations; thus, the data must be interpreted carefully. Phylogenetic clustering of mtDNA haplogroups has been found to be congruent with geography—there are haplogroups specific to African (Chen et

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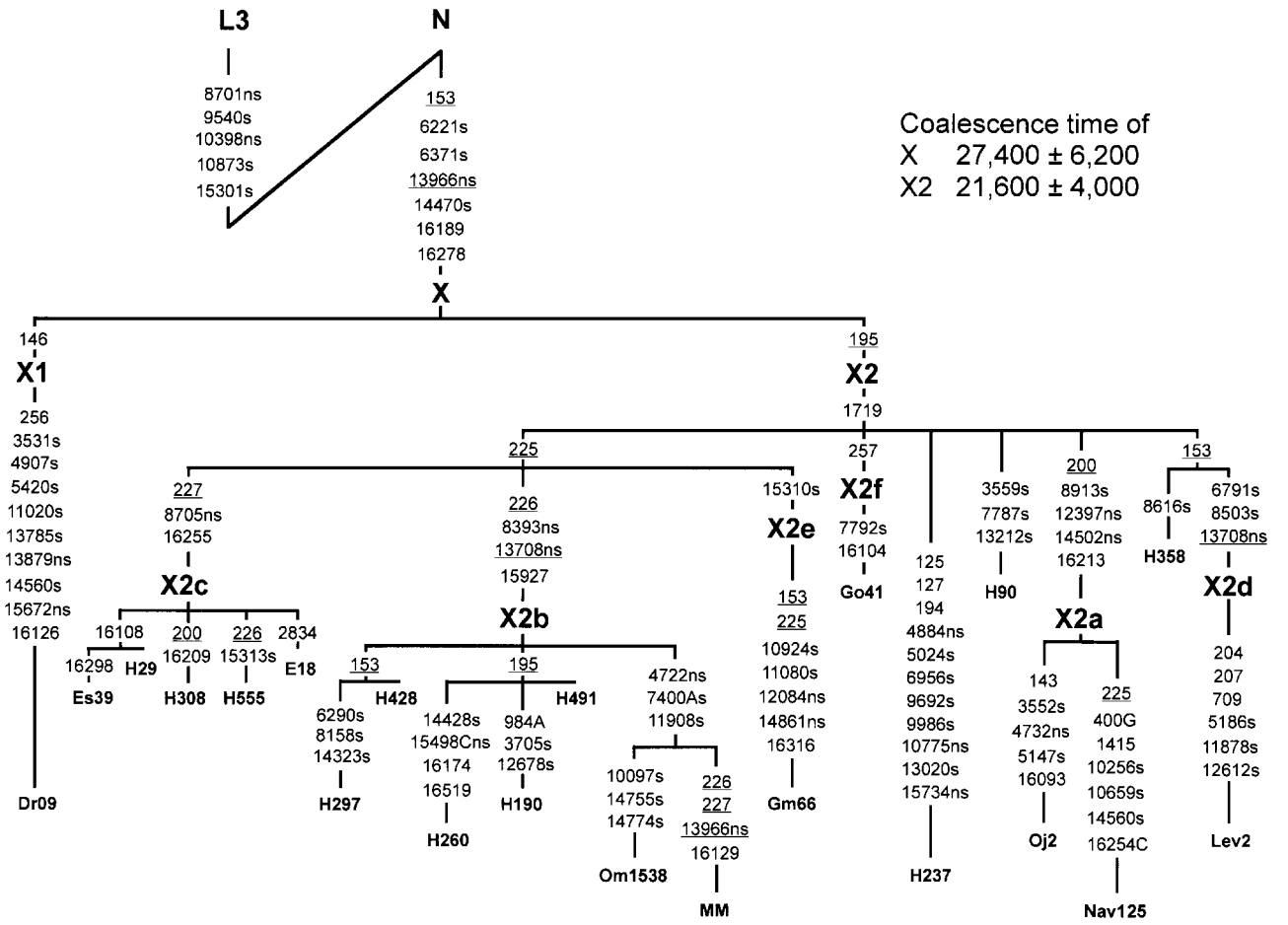
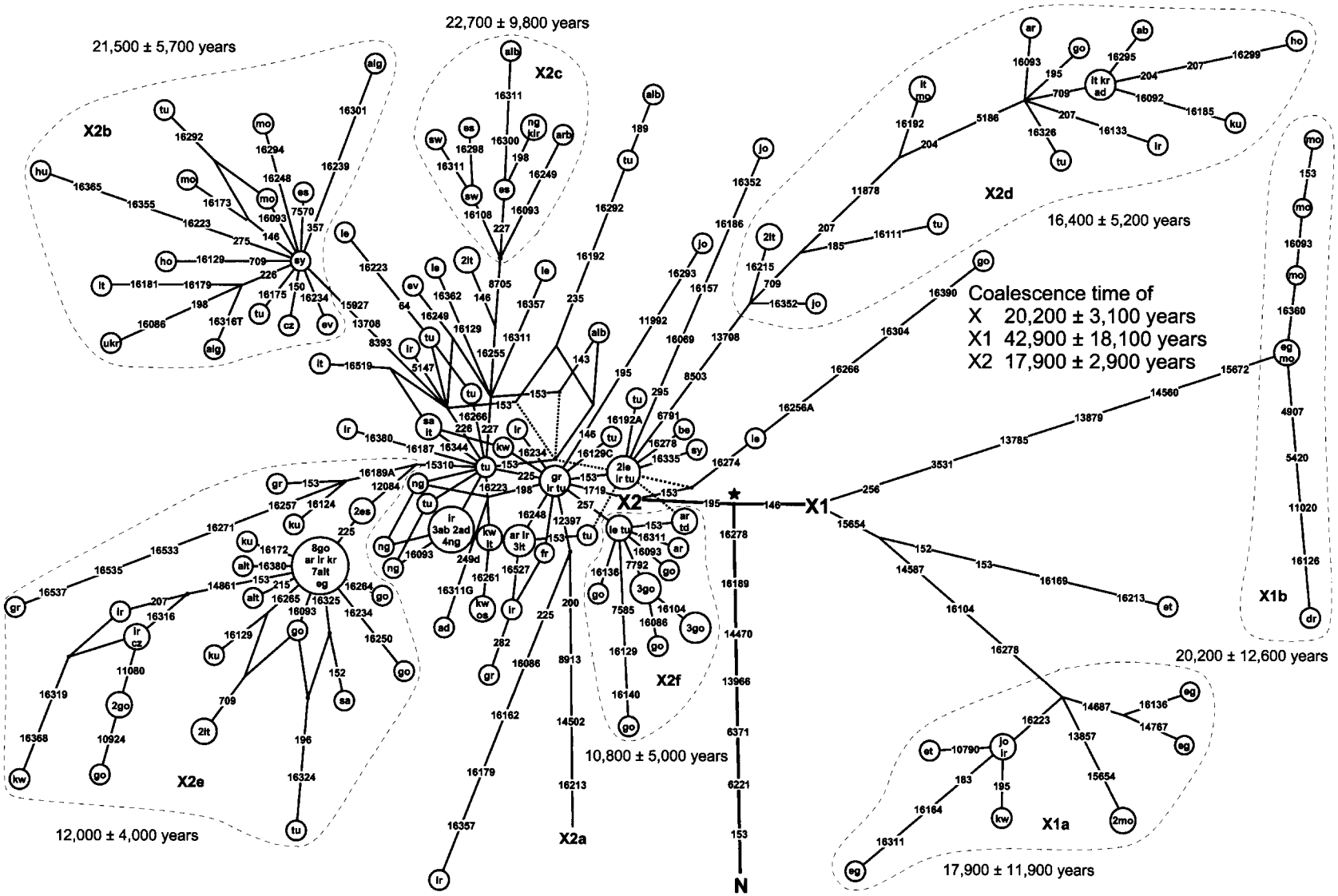


Figure 1 Maximum parsimony phylogenetic tree of complete mtDNA sequences belonging to haplogroup X. Five mtDNAs were selected for complete sequence analysis in the course of the present study (Dr09, Es39, Gm66, Go41, and Om1538), 11 coding region sequences were from the work of Herrnstadt et al. (2002), but their control region sequences have now been added, and 5 complete sequences (Lev2, MM, E18, Nav125, and Oj2) were taken from the literature (Levin et al.1999; Maca-Meyer et al.2001; Mishmar et al. 2003; Bandelt et al., in press). The diagnostic mutations relative to the revised reference sequence (Andrews et al. 1999) are indicated on the branches. Transversions are specified by suffixes, and underlined mutations appear more than once in the tree. For protein-coding genes, "ns" indicates nonsynonymous and "s" synonymous mutations. For coalescence-time estimates, a mutation rate of 1 mutation per 5,139 years in the coding region (nps 577–16023) was used (Mishmar et al. 2003). mtDNA sequence data are available at the Estonian Biocentre Web page.

al. 1995; Watson et al. 1997), Asian (Ballinger et al. 1992; Torroni et al. 1994; Kivisild et al. 2002), European/West Eurasian (Torroni et al. 1996; Macaulay et al. 1999), and Native American (Torroni et al. 1993) populations.

Haplogroup X is an exception to this pattern of limited geographical distribution. It is found, generally at low frequencies, in both West Eurasians (Richards et al. 2000) and some northern groups of Native Americans (Ward et al. 1991; Forster et al. 1996; Scozzari et al. 1997; Brown et al. 1998; Smith et al. 1999; Malhi et al. 2001), but, intriguingly, it is absent in modern north Siberian and East Asian populations (Brown et al. 1998; Starikovskaya et al. 1998; Schurr et al. 1999), which are genetically and geographically closest to those of Native Americans. Among Siberians, haplogroup X mtDNAs have only been detected in some Altaian populations of southwestern Siberia (Derenko et al. 2001).

When the sequence variation of the first hypervariable segment (HVS-I) of the control region is analyzed, haplogroup X mtDNAs from Europe and the Near East are found to yield similar coalescence times: 17,000–30,000 years before present (YBP) and 13,700–26,600 YBP, respectively (Richards et al. 2000). These estimates are consistent with a pre-Holocene origin and spread of this haplogroup into West Eurasia. For Native Americans, the relatively old presence of haplogroup X is confirmed by the analysis of ancient human remains (Stone and Stoneking 1999; Malhi and Smith 2002). Moreover, Native American haplogroup X mtDNAs form a clade dis-


21,500 ± 5,700 years
22,700 ± 9,800 years
16,400 ± 5,200 years
20,200 ± 12,600 years
10,800 ± 5,000 years
12,000 ± 4,000 years
17,900 ± 11,900 years
Coalescence time of
X 20,200 ± 3,100 years
X1 42,900 ± 18,100 years
X2 17,900 ± 2,900 years
X2b
X2c
X2d
X1b
X2
X1
X2f
X2e
X2a
X1a
N

tinct from that of West Eurasians and with coalescence time estimates varying widely depending on both the method of estimation and the number of assumed founders. Thus, the coalescence times ranged from 12,000–17,000 YBP to 23,000–36,000 YBP, times that are consistent with both a pre- and a postglacial population diffusion (Brown et al. 1998).

To obtain further information about the extent of haplogroup X diversity, 5 mtDNAs (from 1 Druze, 1 Estonian, 2 Georgians, and 1 Omani) were completely sequenced and were compared with 16 previously published X sequences (fig. 1). These latter sequences included the 11 haplogroup X coding sequences published by Herrnstadt et al. (2002) that have now been completed with the sequencing of the control region.

A maximum parsimony tree of the 21 haplogroup X sequences revealed that one nonsynonymous (13966) and three synonymous (6221, 6371, and 14470) substitutions in the coding region, as well as three transitions in the control region (153, 16189, and 16278), distinguish haplogroup X from the root of superhaplogroup N. Moreover, haplogroup X is subdivided into two major subhaplogroups, designated "X1" and "X2." Subhaplogroup X1, represented by a single Druze mtDNA in figure 1, differs from the root of haplogroup X by eight coding and three control region transitions and lacks the two transitions (195 and 1719) that characterize X2. These two nucleotides are rather mutable (Finnilä et al. 2001; Herrnstadt et al. 2002); thus, it cannot be completely ruled out that X1 is indeed a subset of X2 that reverted at both nucleotide positions. However, this possibility appears very unlikely, especially when one considers the time depth and the distinct geographic distribution of X1 (see below).

In contrast with X1, X2 is well represented in the tree, and it is further subdivided into at least six major clades (X2a–X2f), which include clades X1 and X2 as defined by Herrnstadt et al. (2002). All 20 X2 sequences, including the 2 Native American X2a sequences, share transitions at nucleotide positions (nps) 195 and 1719. A recurrence of the nonsynonymous substitution at 13708 was observed (clades X2b and X2d). In addition, the nonsynonymous transition 13966 was found to have reverted in the Moroccan X2b sequence. These were the only recurrent mutations found among the 67 variable positions in the coding region sequences. The ratio of nonsynonymous to synonymous substitutions was 0.40 (18/45). Six mutations were located in RNA genes.

The data obtained from the analyses of complete mtDNA sequences belonging to haplogroup X were then used to survey 13,589 mtDNAs (21,682 when mtDNA data from the literature are included) from 66 populations of Eurasia and North Africa (table 1). A total of 175 mtDNAs were found to harbor the four coding region transitions—at 6221, 6371, 13966, and 14470—that define haplogroup X. The four markers were always found in association and, by combination of the control and coding variation, all 175 mtDNAs could be apportioned to subhaplogroups X1 and X2 (table 2). No other main branches occur, and the root haplotype was not present among the sequences. The adenine at np 153 appears relatively conserved in the phylogenetic context of 376 complete human mtDNA sequences taken worldwide, exhibiting a change to guanine only in haplogroups A and X (Ingman et al. 2000; Finnilä et al. 2001; Maca-Meyer et al. 2001; Derbeneva et al. 2002; Mishmar et al. 2003). In contrast, this position shows a high level of variation in the background of haplogroup X as both the 153A and 153G alleles are present in its different subclades. It is possible that the A→G transition at 153 arose only once in the haplogroup X ancestor and the recurrent reverse mutations in 11 branches in figure 2 bear witness to the process of favored fixation of the more stable A allele.

Subhaplogroup X1 was found to be largely restricted to the Afro-Asiatic–speaking populations of North Africa and neighboring areas, including Ethiopia, suggesting a possible geographic diffusion of X1 alongside the

Figure 2 Median-joining (MJ) network of 175 haplogroup X partial sequences. The MJ (Bandelt et al. 1999) algorithm was implemented within the Network 3111 program (A. Röhl; Shareware Phylogenetic Software Web site). Default settings were used for HVS-I (nps 16024–16383), HVS-II (nps 16518–310), and coding-region sequence variation as given in table 2. Highly variable (Hasegawa et al. 1993) positions of HVS-I (16093, 16126, 16129, 16187, 16189, 16223, 16234, 16278, 16292, 16293, 16311, 16325, 16355, and 16362) were assigned a weight of 1, other HVS-I and HVS-II sites were assigned a weight of 2, and coding-region sites were assigned a weight of 10. Areas of the circles are proportional to haplotype frequencies. Populations are indicated by the following abbreviations: ab = Abazin, ad = Adygei, alb = Albanian, alg = Algerian, alt = Altaian, ar = Armenian, arb = Arab from Uzbekistan, be = Bengali, cz = Czech, dr = Druze, eg = Egyptian, es = Estonian, et = Ethiopian, ev = Evenk, fr = French, go = Georgian, gr = Greek, ho = Croat, hu = Hungarian, ir = Iranian, it = Italian, jo = Jordanian, kir = Kyrgyz, kr = Karachay, ku = Kumyk, kw = Kuwaiti, le = Lebanese, mo = Moroccan, ng = Nogay, os = Ossetian, sa = Saudi Arabian, sw = Swede, sy = Syrian, td = Tadjik, tu = Turk, and ukr = Ukrainian. Variant bases are numbered (Anderson et al. 1981) and are shown along links between haplotypes. Nucleotide changes are specified by suffixes only for transversions, and a "d" indicates a deletion. The node marked with a large asterisk (★) matches the root type of haplogroup X. The coalescence times of the clades are shown near the clades. Coalescence times of HVS-I clusters were calculated by means of ρ, the average mutational distance to the founder haplotype of the cluster, by using a mutation rate of 1 transition per 20,180 years in the segment between nps 16090 and 16365 (Forster et al. 1996). Standard deviations for ρ were calculated as in the work of Saillard et al. (2000), a procedure which ignores the variance due to molecular clock calibration. mtDNA sequence data are available at the Estonian Biocentre Web page.

Table 1

Frequency and Diversity of Subhaplogroups X1 and X2 in Eurasian and African Populations

Region and Population[a]	Sample Size	Value for Subhaplogroup[b,c]			
		X1		X2	
		Mean Frequency [95% CR] (%)	Diversity	Mean Frequency [95% CR] (%)	Diversity
North and northeastern Africa:	1,606	.8 [.5–1.4]	.936	.9 [.5–1.5]	.978
Ethiopians[1]	270	.7 [.2–2.6]		0 [.0–1.1]	
Egyptians[1]	193	2.1 [.8–5.2]		.5 [.1–2.8]	
Libyans[1]	72	0 [.0–4.0]		0 [.0–4.0]	
Tunisians[1]	417	.2 [.1–1.3]		1.7 [.8–3.4]	.952
Algerians[1]	124	0 [.0–2.4]		1.6 [.5–5.7]	
Moroccans[1]	530	1.1 [.5–2.4]		.8 [.3–1.9]	
West and southern Africa:	537	0 [.0–.6]		0 [.0–.6]	
*Senegalese[27]	121	0 [.0–2.4]		0 [.0–2.4]	
*17 ethnic groups in Mozambique[24,32]	416	0 [.0–.7]		0 [.0–.7]	
Near East:	2,299	.5 [.3–.9]	.564	2.9 [2.3–3.6]	.887
Yemenis[1]	116	0 [.0–2.5]		.9 [.2–4.7]	
Omanis[1]	78	0 [.0–3.7]		1.3 [.3–6.9]	
Saudi-Arabians[1]	204	0 [.0–1.5]		1.5 [.5–4.2]	
Kuwaitis[1]	202	.5 [.1–2.7]		2.0 [.8–5.0]	
*Israeli Palestinians[9,29]	117	0 [.0–2.5]		3.4 [1.4–8.5]	
Israeli Druze[17]	45	15.6 [7.8–28.9]	0	11.1 [4.9–23.6]	
Jordanians[1]	202	.5 [.1–2.7]		1.5 [.5–4.3]	
Lebanese[1]	172	0 [.0–1.7]		5.8 [3.2–10.4]	.867
Syrians[1]	219	0 [.0–1.4]		1.8 [.7–4.6]	
*Iraqis[29]	116	.9 [.2–4.7]		.9 [.2–4.7]	
Turks[1]	388	0 [.0–.8]		4.4 [2.8–6.9]	.919
Iranians[1]	440	.2 [.1–1.3]		3.0 [1.7–5.0]	.833
Mediterranean Europe:	2,900	.0 [.0–.2]		2.5 [2.0–3.2]	.859
Cypriots[1]	179	0 [.0–1.7]		6.7 [3.9–11.4]	.864
Greeks from mainland and Crete[1]	273	0 [.0–1.1]		4.4 [2.5–7.5]	.455
Albanians[1]	199	0 [.0–1.5]		2.5 [1.1–5.7]	
Croats[1]	884	0 [.0–.3]		.9 [.5–1.8]	.786
Italians from mainland and Sicily[1,19,33]	859	0 [.0–.3]		2.9 [2.0–4.3]	.923
*Basques[3,4,29]	147	0 [.0–2.0]		1.4 [.4–4.8]	
Spaniards[5]	118	0 [.0–2.5]		4.2 [1.9–9.5]	
Portugese[23]	241	.4 [.1–2.3]		1.7 [.7–4.2]	
Northwestern Europe:	1,775	0 [.0–.2]		1.7 [1.2–2.5]	.665
French[1,30]	398	0 [.0–.7]		.8 [.3–2.2]	
*English[12,26,28]	334	0 [.0–.9]		.9 [.3–2.6]	
*Scots[12]	891	0 [.0–.3]		1.6 [.9–2.6]	.692
*Orkney inhabitants[12]	152	0 [.0–1.9]		7.2 [4.1–12.5]	.473
Scandinavia:	1,271	0 [.0–.2]		.9 [.5–1.5]	.491
Swedes[1]	318	0 [.0–.9]		.6 [.2–2.2]	
*Norwegians[12,20,29]	559	0 [.0–.5]		.4 [.1–1.3]	
Icelanders[11]	394	0 [.0–.8]		1.8 [.9–3.6]	0
Alps:	255	0 [.0–1.2]		.8 [.2–2.8]	
Swiss[8]	154	0 [.0–1.9]		.6 [.2–3.5]	
Austrians[22]	101	0 [.0–2.9]		1.0 [.2–5.3]	
North-Central Europe:	1,419	0 [.0–.2]		1.3 [.8–2.0]	.948
Poles[1,18]	547	0 [.0–.5]		1.6 [.9–3.1]	.972
*Germans[13,16,25,28]	532	0 [.0–.6]		1.1 [.5–2.4]	
Czechs[1]	94	0 [.0–3.1]		2.1 [.7–7.4]	
Slovaks[1]	130	0 [.0–2.3]		0 [.0–2.3]	
Hungarians[1]	116	0 [.0–2.5]		.9 [.2–4.7]	
Northeastern Europe:	1,611	0 [.0–.2]		1.1 [.7–1.8]	.902
Finns[10]	192	0 [.0–1.5]		2.1 [.8–5.2]	
Estonians[1]	401	0 [.0–.7]		1.2 [.5–2.9]	
Latvians[1]	192	0 [.0–1.5]		.5 [0.1–2.9]	
Russians[1,18,21]	826	0 [.0–.4]		1.0 [.5–1.9]	.964
Volga-Ural region:	1,037	0 [.0–.3]		0 [.0–.3]	
Komis[2]	136	0 [.0–2.2]		0 [.0–2.2]	
Udmurds[2]	101	0 [.0–2.9]		0 [.0–2.9]	
Maris[2]	136	0 [.0–2.2]		0 [.0–2.2]	
Mordvins[2]	102	0 [.0–2.9]		0 [.0–2.9]	
Nenets[31]	58	0 [.0–5.0]		0 [.0–5.0]	
Chuvashis[2]	55	0 [.0–5.2]		0 [.0–5.2]	
Tatars[2]	228	0 [.0–1.3]		0 [.0–1.3]	
Bashkirs[2]	221	0 [.0–1.3]		0 [.0–1.3]	

(*continued*)

Table 1 (continued)

Region and Population[a]	Sample Size	Value for Subhaplogroup[b,c] X1 Mean Frequency [95% CR] (%)	X1 Diversity	X2 Mean Frequency [95% CR] (%)	X2 Diversity
Southeastern Europe:	357	0 [.0–.8]		2.0 [1.0–4.0]	.952
Ukrainians[1]	357	0 [.0–.8]		2.0 [1.0–4.0]	.952
Northern Caucasus:	838	0 [.0–.4]		2.7 [1.8–4.1]	.798
Nogays[1]	213	0 [.0–1.4]		4.2 [2.3–7.8]	.722
Adygeis[1]	159	0 [.0–1.9]		2.5 [1.0–6.3]	
Karachays[1]	106	0 [.0–2.8]		1.9 [.6–6.6]	
Abazins[1]	63	0 [.0–4.6]		6.3 [2.6–15.2]	
Kabardins[1]	66	0 [.0–4.4]		0 [.0–4.4]	
Kumyks[1]	111	0 [.0–2.6]		3.6 [1.5–8.9]	
Kalmyks[1]	120	0 [.0–2.4]		0 [.0–2.4]	
South Caucasus:	782	0 [.0–.4]		4.3 [3.1–6.0]	.797
Georgians[1]	340	0 [.0–.9]		7.6 [5.3–11.0]	.738
Southern Ossetians[1]	201	0 [.0–1.5]		.5 [.1–2.7]	
Armenians[1]	193	0 [.0–1.5]		2.6 [1.1–5.9]	
*Azeris[29]	48	0 [.0–5.9]		4.2 [1.3–14.0]	
Central Asia:	1,036	0 [.0–.3]		.8 [.4–1.5]	.929
Uighurs from Kazakhstan[1]	122	0 [.0–2.4]		.8 [.2–4.4]	
Kazakhs[1]	495	0 [.0–.6]		.6 [.2–1.8]	
Kyrgyz[1]	105	0 [.0–2.8]		1.0 [.2–5.1]	
Tadjik[1]	77	0 [.0–3.8]		1.3 [.3–6.9]	
Uzbeks[1]	160	0 [.0–1.8]		.6 [.2–3.4]	
Arabs from Uzbekistan[1]	77	0 [.0–3.8]		1.3 [.3–6.9]	
India:	1,010	0 [.0–.3]		.2 [.1–.7]	
Western Bengalis[1]	106	0 [.0–2.8]		.9 [.2–5.1]	
Gujaratis and Konkanastha Br.[1]	111	0 [.0–2.6]		0 [.0–2.6]	
Punjabis[1]	112	0 [.0–2.6]		0 [.0–2.6]	
Moors[1]	50	0 [.0–5.7]		0 [.0–5.7]	
Singhalese from Sri Lanka[1]	82	0 [.0–3.5]		0 [.0–3.5]	
Uttar Pradesh[14]	122	0 [.0–2.4]		.8 [.2–4.4]	
Telugus[14]	250	0 [.0–1.2]		0 [.0–1.2]	
Chenchu[15]	96	0 [.0–3.0]		0 [.0–3.0]	
Koya[15]	81	0 [.0–3.6]		0 [.0–3.6]	
Siberia:	2,949	0 [.0–.1]		.4 [.2–.7]	.455
Altaians[1,7]	481	0 [.0–.6]		1.9 [1.0–3.5]	0
Buryats[7]	105	0 [.0–2.8]		0 [.0–2.8]	
Tuvins[1,7]	314	0 [.0–.9]		0 [.0–.9]	
Koryaks[1,7]	105	0 [.0–2.8]		0 [.0–2.8]	
Evens[7]	65	0 [.0–4.4]		0 [.0–4.4]	
Evenks[1,7]	185	0 [.0–1.6]		1.1 [.3–3.8]	
Yakuts[1,7]	340	0 [.0–.9]		0 [.0–.9]	
Khakassians[7]	54	0 [.0–5.3]		0 [.0–5.3]	
Shors[1,7]	207	0 [.0–1.4]		0 [.0–1.4]	
Sojots[7]	34	0 [.0–8.2]		0 [.0–8.2]	
Kets[1]	66	0 [.0–4.4]		0 [.0–4.4]	
Selkups[1]	120	0 [.0–2.4]		0 [.0–2.4]	
Nenets[1]	79	0 [.0–3.7]		0 [.0–3.7]	
Dolgans[1]	130	0 [.0–2.3]		0 [.0–2.3]	
Nanais[1]	88	0 [.0–3.3]		0 [.0–3.3]	
Komis[1]	78	0 [.0–3.7]		0 [.0–3.7]	
Nganasans[1]	107	0 [.0–2.7]		0 [.0–2.7]	
Khants[1]	253	0 [.0–1.2]		.4 [.1–2.2]	
Mansis[1,6]	138	0 [.0–2.1]		0 [.0–2.1]	

[a] An asterisk (*) denotes frequencies deduced from published HVS-I sequences. Populations are divided into regions basically as in (Richards et al. 2000), with some changes: North African and South Caucasian populations were considered separately from populations of the Near East, and all European populations of the Mediterranean area were aggregated into a single Mediterranean European region. Sources are denoted as follows: [1]present study, [2]Bermisheva et al. (2002), [3]Bertranpetit et al. (1995), [4]Corte-Real et al. (1996), [5]Crespillo et al. (2000), [6]Derbeneva et al. (2002), [7]Derenko et al. (2001), [8]Dimo-Simonin et al. (2000), [9]Di Rienzo and Wilson (1991), [10]Finnilä et al. (2001), [11]Helgason et al. (2000), [12]Helgason et al. (2001), [13]Hofmann et al. (1997), [14]Kivisild et al. (1999), [15]Kivisild et al. (2003), [16]Lutz et al. (1998), [17]Macaulay et al. (1999), [18]Malyarchuk et al. (2002), [19]Mogentale-Profizi et al. (2001), [20]Opdal et al. (1998), [21]Orekhov et al. (1999), [22]Parson et al. (1998), [23]Pereira et al. (2000), [24]Pereira et al. (2001), [25]Pfeiffer et al. (1999), [26]Piercy et al. (1993), [27]Rando et al. (1998), [28]Richards et al. (1996), [29]Richards et al. (2000), [30]Rousselet and Mangin (1998), [31]Saillard et al. (2000), [32]Salas et al. (2002), [33]Tagliabracci et al. (2001).

[b] The 95% credible regions (CR), calculated using software kindly provided by Vincent Macaulay, are shown in brackets.

[c] Haplotype diversities were calculated as in the work of Nei (1987), only for regions where more than six haplogroup X mtDNAs were available considering the sequence variation observed between nps 16090 and 16365.

Table 2

Control-Region and Coding-Region Variation of Haplogroup X mtDNAs

Sequence[c]	Haplogroup	Control Region Sequence[a] HVS-I[d]	HVS-II[e]	Coding Region Sequence and RFLP Variation[b]
				1111111111111111111111111111
				1122333445556666777888889000111122233333344444445555
				7475855679114233755735579827900890360377889455567836 69
				0113335230482268978990701359228798903608576606886615 72
				9357111427760193105213253040400724781645796520777104 25
				lckg w k we e e j u ygmt s i
CRS[f]				G++--G+A-TGATT-+AAAC+T+TAC+TCAT+TCA++-+CATA-TGAATGTTT+
et 216	X1*	169 189 213 223 278	146 152	G + T TC T A + + GAAT CT
eg 96	X1a	104 136 189 223	146 153	G + G T ATC+ A T T A + +CATG+ GGGT CT
eg 818	X1a	104 164 189 311	146 153 183	G + G T T T A +CATG+ GGAT CT
et 146	X1a	104 189	146 153	G + T T + A T C A + + + G+ GGAT CT
ir 143	X1a	104 189	146 153	G + G T T T A +CATG+ GGAT CT
jo 924	X1a	104 189	146 153	G + G T T T A +CATG+ GGAT CT
kw 103	X1a	104 189	146 153 195	G + G T ATC+ A T T A + +CATG+ GGAT CT
eg 971	X1a	104 189 223	146 153	G + G T T T A +CATG+ GGGC CT
mo 90E	X1a	104 189 223	146 153	G + G T T T A +CGTG+ GGAT TT
mo E99	X1a	104 189 223	146 153	G + GTG+ GG TT
dr 09	X1b	126 189 223 278	146 153 256	G++--A+A-CGACC++AAAC+T+TAC+TCGT+TCA++-+TACG+TAAATGTTC+
eg 443	X1b	189 223 278	146 153 256	G + A T ATC+ A T T A + +TACG+ AAAT TC
mo C49	X1b	189 223 278	146 153 256	+ T T C +
mo A79	X1b	189 223 278 360	146 153 256	G + A T T A TACG+ AA TC
mo A17	X1b	93 189 223 278 360	146 153 256	G + T T A TACG+ TC
mo B64	X1b	93 189 223 278 360	146 256	+ T T C +
le 938	X2*	129 189 223 278 362	153 195 225 227	G - - G + +T T
tu 47	X2*	129C 189 223 278	153 195	G+- + - A + A T + + A+ + G+ T
ir 71	X2*	187 189 223 278 380	153 195 225	G - + - G A A + +T T
alb 53	X2*	189 192 223 278 292	143 189 195 225 226 235	G - + - GA C+ A A C T+ A+ + +T T +
tu 208	X2*	189 192 223 278 292	143 195 225 226 235	G - + - GA + A T A C T+ A+ -+ G+T T +
tu 296	X2*	189 192A 223 278	195	G -- + - GA + A T A + CA+ + G+T GT
be 50	X2*	189 223	195	G - A + A T + C + + G+ T
ir 161	X2*	189 223 234 278	195 225	G - + - G A CA + +T T
ir 282	X2*	189 223 248 278	153 195	G - + - G A A + +T T
it 173	X2*	189 223 248 278	153 195	G - + C + + T
it 74	X2*	189 223 248 278	153 195	G - - G + T A C + +T T
it 33	X2*	189 223 248 278	153 195	G - + A T + C + + G+ T
ar 175	X2*	189 223 248 278	153 195	G+- - G + T A + + + + G+T T
ng 227	X2*	189 223 248 278	153 195 198 225	- - + + T
ir 224	X2*	189 223 248 278	153 195 225	G - + - G TA A + +T T
ng 167	X2*	189 223 248 278	153 195 225	G - - G + +T T
ab 17	X2*	189 223 248 278	153 195 225	G - + - G A CA + +T T
ab 31	X2*	189 223 248 278	153 195 225	- + - G A A + +T T
ab 44	X2*	189 223 248 278	153 195 225	G - + + T
ad 67	X2*	189 223 248 278	153 195 225	G - - G A + +T T
ad 79	X2*	189 223 248 278	153 195 225	- - G A + +T T
ng 2	X2*	189 223 248 278	153 195 225	- + A + + T
ng 264	X2*	189 223 248 278	153 195 225	G - + + T
ng 6	X2*	189 223 248 278	153 195 225	G - + A A + + T
ir 240	X2*	189 223 248 278	16527 153 195	G - + - G A CA + +T T
gr 34	X2*	189 223 248 278	16527 153 195 282	G - + + +
tu 196	X2*	189 223 248 278	195	G+-- + - GA + A T A + + C + + G+T T
ev 4076	X2*	189 223 249 278	153 195 225 226 227	G - - G A + +T T
it 4202	X2*	189 223 255 278	146 153 195 225 227	G - - A + A T T + C ++ + G+ T
it 204	X2*	189 223 255 278	146 153 195 225 227	G - - - G + A T TA + ++ + G+T T
gm 30	X2*	189 223 256A 266 274 278 304 (390)	195	G +- ATC+ T C T+ C + G+ GT
tu 83	X2*	189 223 266 278	153 195 225	G+- - + - G + A T A + + A++ + G+T T
tu 131	X2*	189 223 266 278	153 195 225 226	G - - + - GA + A T TA + CA++ + G+T T +
le 376	X2*	189 223 274 278	195	G + TC+ A + + G+ G
gr 70	X2*	189 223 278	153 195	G+- + - G + AC T A + + A+ + G+T T
alb 128	X2*	189 223 278	143 195 225 227	G+--- - GA C+ A A + + ++-+ +T T +
ir 241	X2*	189 223 278	153 195	G - + - G A C + +T T
tu 265	X2*	189 223 278	153 195	G+- + - GA + A AC A + A + +T T
ng 144	X2*	189 223 278	153 195 198 225	G - - - A + + T
tu 212	X2*	189 223 278	153 195 225	G+- - + - GA + A T TA + + A++ + G+T T +
ir 267	X2*	189 223 278	153 195 225 226	G - + - A TAC + +T T
fr 53	X2*	189 223 278	16527 153 195	G+- + GA + A + A + +T T
ir 254	X2*	189 223 278	195	G - + - G T A A CA + G+T T
le 547	X2*	189 223 278	195	G - - G A C + G+T T
le 550	X2*	189 223 278	195	G - A C + + T
tu 264	X2*	189 223 278	195	G -- + - GA + A T A C T+ C + G+T GT
jo 992	X2*	189 223 278 293	146 153	G - G -TG T A A T A CC +CATG+TGAAT TTT
le 936	X2*	189 223 278 311 357	153 195 225 227	G - - G + +T T
ad 40	X2*	189 223 278 311G	153 195 198 249d	- - G A + +T T
sy 289	X2*	189 223 278 335	195	G -- + - + A T C T+ CA + + GT
kw 148	X2*	189 223 278 344	153 195	G+- + - + A + + A + + T
sa 844	X2*	189 223 278 344	153 195 225	G - + - T A + G+ T
it 154	X2*	189 223 278 344	153 195 225	G+- - + - G + A TA + CA + + +T T

(*continued*)

Table 2 (continued)

Sequence[c]	Haplogroup	Control Region Sequence[a] HVS-I[d]	HVS-II[e]	Coding Region Sequence and RFLP Variation[b] lckg w k we e e j u ygmt s i
it 4327	X2*	189 223 278 344	16519 153 195 225 226	G − + − G + A T TAC + A+ + G+T T +
os 107	X2*	189 261 278	153 195 225	G − − G + A T TA + + + +T T
kw 172	X2*	189 261 278	153 195 225	G − − + − GA + A A + A + + +T T
le 1056	X2*	189 266 278	64 153 195 225 226	G − − G + +T T
kw 237	X2*	189 278	153 195 225	G+− − + − G + A T TA + + A + + +T T
it 8	X2*	189 278	153 195 225	G+− − + − G + TA + C + + + T
jo 761	X2*	69 157 186 189 223 278 352	195 295	G − − G C + +T T
ir 404	X2*	86 162 179 189 223 278 357	153 195 225	G+− − + − G + A T TA + + G + + +T T
ng 68	X2*	93 189 223 248 278	153 195 225	G − − G A + +T T
tu 145	X2*	93 189 223 278	153 195 225	G+− − + − G + A T TA + + A++ + G+T T
ho 78	X2b	129 189 223 278	153 195 225 226	A − +AA + + − +
mo E26	X2b	173 189 223 278	146 153 195 225 226	− − − +
tu 42	X2b	175 189 223 278	153 195 225 226	G − A ++AA −T+T C + − + −
it 13	X2b	179 181 189 223 278	153 195 225	G − − A ++ A − +T C + ++ − + −
ev 4107	X2b	189 223 234 278	153 195 225 226	G − − +
alg R34	X2b	189 223 239 278 301	153 195 225 226 (357)	− − − +
mo B45	X2b	189 223 248 278 294	153 195 225 226	− − − +
cz 63	X2b	189 223 278	150 153 195 225 226	G − A A ++AA −T+T C + + − G+ −
es 15	X2b	189 223 278	153 195 225 226	G − ++AG −T+ + + − G+ −
sy 184	X2b	189 223 278	153 195 225 226	G − A ++AA −T+T C + − + −
alg R47	X2b	189 223 278 316T	153 195 225	− − − +
hu 16	X2b	189 278 355 365	153 195 225 226 275	G − A ++ A − +T C − + −
ukr	X2b	86 189 223 278	153 195 198 225	G − − G+
mo D17	X2b	93 189 223 278	153 195 225 226	− − − +
tu 77	X2b	93 189 223 278 292	146 153 195 225 226	G − A ++AA −T+T C + + − G+ −
sw 44	X2c	108 189 223 255 278	153 195 225 227	G − C + +
es 39	X2c	108 189 223 255 278 298	153 195 225 227	G+−−−G+A−TGATC++AAAC+T+CAC+TCAT+TCA++−+CATG+TGAATGTTT+
sw 18	X2c	108 189 223 255 278 311	153 195 225 227	G − C G+
kir 16m	X2c	189 223 255 278	153 195 198 225	G − C + +
ng 250	X2c	189 223 255 278	153 195 198 225	G − C + +
es 314	X2c	189 223 255 278	153 195 225	G+− − + A T C + + ++ + G+
alb 124	X2c	189 223 255 278 300 311	153 195 225	G − − C+ A C + ++ + +
arb 60	X2c	93 189 223 249 255 278	153 195 225 227	G − C + +
tu 144	X2d	111 189 223 278	185 195	A − A + G C + + − G+ G
ir 347	X2d	133 189 223 278	195 204	A − G + G + + − − +
mo C16	X2d	189 192 223 278	195 207	A − − − +
it 350	X2d	189 192 223 278	195 207	A − A + G +C+ − − − +
it 80	X2d	189 215 223 278	195	G − A + G C + − +
it 82	X2d	189 215 223 278	195	G − A + C + − +
it 101	X2d	189 223 278	195 204 207	G − G C+ G +C+ − + − +
ad 37	X2d	189 223 278	195 204 207	G − G − − +
kr 71	X2d	189 223 278	195 204 207	G − G − − +
go 57	X2d	189 223 278	204 207	A − G + G +C+ − − +
ab 21	X2d	189 223 278 295	195 204 207	G − G − − +
ho 83	X2d	189 223 278 299	195	G − G + G C − + − G+
tu 162	X2d	189 223 278 326	195 204 207	A − G + G +C+ − + − G+
jo 958	X2d	189 223 278 352	195	G − G C + C − + T
ku 31	X2d	92 185 189 223 278	195 204 207	G − G − − +
ar 31	X2d	93 189 223 278	195 204 207	A − G C+ G +C+ − + − G+
ku 26	X2e	124 189A 223 278	153 195 225	G − C + + GC
ku 14	X2e	129 189 223 265 278	153 195	G − T + + GC
ku 39	X2e	172 189 223 278	153 195	G − T + + GC
go 3	X2e	189 223 234 250 278	153 195	G+− A C+ T + + T + + G+ GC
go 78	X2e	189 223 264 278	153 195	G+− A C+ A C T + + T + + + GC
go 28	X2e	189 223 278	153 195	G − + A C T + + GC
eg 596	X2e	189 223 278	153 195	G − A T + + GC
kr 18	X2e	189 223 278	153 195	G − T + + GC
ir 184	X2e	189 223 278	153 195	G − T + + GC
ar 118	X2e	189 223 278	153 195	G − A C+ AC T + + C
alt 81	X2e	189 223 278	153 195	G − C T T + GC
alt 161	X2e	189 223 278	153 195	G − C T T + GC
alt 171	X2e	189 223 278	153 195	G − C T T + G
alt 188	X2e	189 223 278	153 195	− C T T + GC
alt 208	X2e	189 223 278	153 195	G − C T T +
gm 168	X2e	189 223 278	153 195	G+− A C+ C T + + T + + G+ GC
gm 42	X2e	189 223 278	153 195	G − + T + + GC
gm 6	X2e	189 223 278	153 195	G −− C+ AC C T T + + GC
go 111	X2e	189 223 278	153 195	G − + A C T T + + GC
go 60	X2e	189 223 278	153 195	G − C+ C T + + GC
alt 17	X2e	189 223 278	153 195	G − T + + GC

(*continued*)

Table 2 (continued)

		Control Region Sequence[a]		Coding Region Sequence and RFLP Variation[b]
				11111111111111111111111111111
				11223334455566667778888890001111222333333344444445555
				74758556791142337557355798279008903603778894555678366 9
				01133352304822689789907013592287989036085766068866157 2
				93571114277601931052132530404007247816457965207771042 5
Sequence[c]	Haplogroup	HVS-I[d]	HVS-II[e]	lckg w k we e e j u ygmt s i
go 6	X2e	189 223 278	153 195	G – C+ A C T + T + + G+ GC
gm 120	X2e	189 223 278	153 195	G – C+ C T + + GC
alt 43	X2e	189 223 278	153 195	– C T T + GC
alt 16	X2e	189 223 278	153 195 215	– C T T + GC
es 167	X2e	189 223 278	153 195 225	G – + T C T + + GC
es 297	X2e	189 223 278	153 195 225	G+- – A ++ A + +T + T + + + GC +
ir 304	X2e	189 223 278	195 207	G – A T + G+ AC
cz 55	X2e	189 223 278 316	195	G –– A + A T C T+ T + + G+ AC
gm 164	X2e	189 223 278 316	195	G – C+ A T C C+ T + + G+ AC
gm 66	X2e	189 223 278 316	195	G+---G+A-TGATC++AAAC+T+TAC+TTAC+TTA++-+CATG+TGAATACTT+
gm 96	X2e	189 223 278 316	195	G – + T C C+ T + + AC
ir 81	X2e	189 223 278 316	195	G – A T + + AC
kw 225	X2e	189 223 278 316 319 368	195 207	G – A + A C T+ T + + AC
sa 1159	X2e	189 223 278 325	152 153 195	G – T + + C
alt 61	X2e	189 223 278 380	153 195	G – T + G+ GC
gr 5	X2e	189A 223 257 271 278	16533 16535 16537 153 195 225	G+- – A + T T + + C ++ + G+ GC
gr 95	X2e	189A 223 278	195 225	G+--- A + + C T+ C ++-+ G+ GC
it 56	X2e	93 189 223 265 278	153 195	A – + A T + T + + G+ C
it 57	X2e	93 189 223 265 278	153 195	A – + T + + GC
gm 156	X2e	93 189 223 278	153 195	G+- A C+ A C T + + T + + G+ GC
tu 114	X2e	93 189 223 278 324 325	153 195 196	G – A + A + T + + GC
go 105	X2f	104 189 223 278	153 195 257	G – C+ T + +
go 110	X2f	104 189 223 278	153 195 257	G – A C+ A AT T + + + G+
go 41	X2f	104 189 223 278	153 195 257	G+---G+A-TGATC++AAAT+T+TAC+TCAT+TCA++-+CATG+TGAATGTTT+
go 17	X2f	129 140 189 223 278	153 195 257	G – C+ A GC T + + + G+
gm 172	X2f	136 189 223 278	153 195 257	G – A + AC T + + + G+
gm 140	X2f	189 223 278	153 195 257	G – + T + +
le 208	X2f	189 223 278	153 195 257	G – + A AC T + + +
go 133	X2f	189 223 278	153 195 257	G – + AT + +
go 24	X2f	189 223 278	153 195 257	G – + A T + +
tu 344	X2f	189 223 278	153 195 257	G – A + A AC + + +
td 41m	X2f	189 223 278	195 257	G – C T C + + T
ar 101	X2f	189 223 278	195 257	G –– C+ A AC T + C + + G+ T
ar 140	X2f	189 223 278 311	153 195 257	G – + +
gm 143	X2f	86 189 223 278	153 195 257	G – C+ A AT T + + + G+
go 39	X2f	93 189 223 278	153 195 257	G – A C+ A AC T + + + G+

[a] Two hypervariable segments of the control region were sequenced: HVS-I (16024-16383) and HVS-II (16518-310). Nucleotide change is specified for transversions; d = deletion. Length variation in the C stretch (16184-16193) is not shown. Mutations that were sequenced outside the specified range are shown in parentheses. Sequence analyses were performed using the Sanger dideoxy chain-termination method with the Amersham DYEnamic ET Terminator Cycle Sequencing Kit (Amersham Pharmacia Biotech) on an ABI PRISM 377 DNA Sequencer. Sequences were alignedand analyzed with the Wisconsin Package (GCG).

[b] Restriction-endonuclease sites are indicated as follows: c = *Dde*I, e = *Hae*III, g = *Hin*fI, i = *Msp*I, j = *Mbo*I, k = *Rsa*I, l = *Taq*I, m = *Bam*HI, s = *Acc*I,t = *Bst*OI, u = *Mse*I, w = *Mbo*II, y = *Bfm*I. Haplogroup assignments are according to figure 2.

[c] Populations are indicated by the following letter code: ab = Abazin, ad = Adygei, alb = Albanian, alg = Algerian, alt = Altaian, ar = Armenian, arb = Arab from Uzbekistan, be = Bengali, cz = Czech, dr = Druze, eg = Egyptian, es = Estonian, et = Ethiopian, ev = Evenk, fr = French, gm and go = Georgian, gr = Greek, ho = Croat, hu = Hungarian, ir = Iranian, it = Italian, jo = Jordanian, kir = Kyrgyz, kr = Karachay, ku = Kumyk, kw = Kuwaiti, le = Lebanese, mo = Moroccan, ng = Nogay, os = Ossetian, sa = Saudi Arabian, sw = Swede, sy = Syrian, td = Tadjik, tu = Turk, ukr = Ukrainian.

[d] HVS-I nucleotide positions are −16000.

[e] All listed HVS-II sequences also harbored the transitions 16519, 73, and 263.

[f] Revised Cambridge reference sequence (Andrews et al. 1999).

Mediterranean Sea and the Red Sea (table 1). This subhaplogroup is subdivided into the two clades X1a and X1b, which are defined by two and five coding region mutations, respectively (fig. 2). Both clades share a recurrent transition at 146 in HVS-II. The coalescence time of the entire X1 subhaplogroup using HVS-I variation is 42,900 ± 18,100 YBP, whereas the coalescence time of the X1a clade is 17,900 ± 11,900 YBP.

Virtually all (97.2%) haplogroup X mtDNAs from the Near East, the South Caucasus, and Europe were found to belong to subhaplogroup X2, as did all (100%) of those from Siberia and Central Asia and some (36.8%) of those from North Africa (table 2). Thus, subhaplogroup X2 is characterized by a very wide geographic range but also by an infrequent occurrence. Indeed, it generally comprises <5% of the mtDNAs in West Eurasian and North African populations (table 1). Three exceptions include the Druze, the Georgians, and the Orkney Islanders, among whom the frequency of X2 reaches 11%, 8%, and 7%, respectively. The high frequencies of X2 in the Druze and the Orkney Islanders are combined with a low haplotype diversity (0.400 and 0.473, respectively), and the relatively high frequency in these populations is most likely due to genetic drift and

founder events. Overall, it appears that the populations of the Near East, the Caucasus, and Mediterranean Europe harbor subhaplogroup X2 at higher frequencies than those of northern and northeastern Europe ($P < .05$) and that X2 is rare in Eastern European as well as Central Asian, Siberian, and Indian populations and is virtually absent in the Finno-Ugric and Turkic-speaking people of the Volga-Ural region. Coalescence time estimates based on HVS-I and coding region variation—17,900 ± 2,900 YBP and 21,600 ± 4,000 YBP, respectively (figs. 1 and 2)—are consistent with the range expansion of X2 around or after the last glacial maximum (LGM). It is intriguing that the estimated coalescence time for X2 alone is very close to that obtained from HVS-I data for the entire haplogroup X (20,200 ± 3,100 YBP) (fig. 2). However, the latter is probably an underestimate due to both the higher proportion (>90%) of X2 mtDNAs included in the calculations and the fact that the HVS-I consensus sequence of X2 is completely identical to that of the overall haplogroup X.

Two-thirds of the subhaplogroup X2 sequences fall into the five clades X2b–X2f (fig. 2). Two sequences—one from Lebanon and one from Georgia—lacked the transition at np 1719, suggesting either the presence of an early X2 branch or a reversion at that nucleotide position. The sister groups X2b and X2c (X1 and X2, respectively, in the work of Herrnstadt et al. 2002) encompass one-third of the European sequences (excluding the samples from the North Caucasus). It is of interest that some North African sequences (from Morocco and Algeria) belong to X2b as well. Subhaplogroup X2b shows a diversity that is consistent with a postglacial population expansion in both West Eurasia and North Africa. Clades X2e and X2f encompass the majority (87.1%) of the sequences from the South Caucasus area and show coalescence times (12,000 ± 4,000 YBP and 10,800 ± 5,000 YBP, respectively) consistent with a Late Upper Paleolithic (LUP) origin and a subsequent spread in the region. We found significant differences between the haplogroup distribution between the North and the South Caucasian samples, a result that indicates a major geographical barrier between the two regions. The South Caucasian sample is enriched in mtDNAs belonging to clades X2e and X2f ($P < .01$), whereas the North Caucasian sample shows a higher proportion of sequences derived at nps 225 and 16248 ($P < .01$).

Clade X2e, defined by the synonymous substitution at 15310, encompasses all haplogroup X sequences in the Altaians (fig. 2). Among the nine Altaian X sequences, eight harbor the founder HVS-I motif of X2e, and seven of these eight also carry the HVS-II founder motif. As a result, a very low haplotype diversity of haplogroup X (0) in the Altaian region was obtained, making it significantly different from the haplotype diversities for haplogroups C and D (0.835 and 0.943, respectively) in the same region. Moreover, the nine Altaian mtDNAs do not harbor any nucleotide difference between nps 16090 and 16365. Therefore, under the assumption that these sequences are a random sample of the Altaian haplogroup X, an estimated ρ value <0.33 ($P < .05$) was obtained. This value corresponds to a time depth of <6,700 years (Forster et al. 1996), and it would suggest that Altaians have acquired haplogroup X2 only relatively recently. This scenario is supported by the concomitant presence in the Altaians of a wide range of other West Eurasian haplogroups (H, J, I, T, U1, U4, and U5) that comprise ~27% of their mtDNAs. Indeed, any recent migration (for example, from the [southern] Caucasus region) that might have carried X2e mtDNA sequences to the Altai region would also explain the presence of the other West Eurasian mtDNA haplogroups in modern Altaians.

Further northeast of the Altai area, haplogroup X sequences were detected in the Tungusic-speaking Evenks, of the Podkamennaya Tunguska basin (Central Siberia). In contrast to the Altaians, the Evenks did not harbor any West Eurasian mtDNA haplogroups other than X. However, neither of the two Evenk X haplotypes showed mutations characteristic of the Native American clade X2a. Instead, one sequence was a member of X2b and the other of X2* (fig. 2). Thus, one possible scenario is that several X haplotypes arrived in Siberia from western Asia during the Palaeolithic, but only X2a crossed Beringia and survived in modern Native Americans. Alternatively, the presence of two phylogenetically different haplogroup X mtDNA sequences in this particular subpopulation of Evenks might be due to recent gene flow.

The Native American–specific clade X2a appears to be defined by five mutations, three in the coding region (8913, 12397, and 14502) and two in the control region (200 and 16213) (fig. 1). The transition at np 200 was seen in virtually all previously analyzed Native American haplogroup X mtDNAs, whereas the transition at np 16213 was absent in some of the Ojibwa described by Brown et al. (1998). We surveyed our Old World haplogroup X mtDNAs for the five diagnostic X2a mutations (table 2) and found a match only for the transition at np 12397 in a single X2* sequence from Iran. In a parsimony tree, this Iranian mtDNA would share a common ancestor with the Native American clade (fig. 2). Yet, the nonsynonymous substitution at np 12397 converting threonine to alanine cannot be regarded a conservative marker, as it has also been observed in two different phylogenetic contexts—in haplogroups J1 and L3e—among 794 complete mtDNA sequences (Finnilä et al. 2001; Maca-Meyer et al. 2001; Herrnstadt et al. 2002). Therefore, the scenario that the threonine to alanine change in the haplogroup X background is indeed due to recurrence appears most plausible.

These findings leave unanswered the question of the geographic source of Native American X2a in the Old World, although our analysis provides new clues about the time of the arrival of haplogroup X in the Americas. Indeed, if we assume that the two complete Native American X sequences (from one Navajo and one Ojibwa) began to diverge while their common ancestor was already in the Americas, we obtain a coalescence time of 18,000 ± 6,800 YBP, implying an arrival time not later than 11,000 YBP.

The results of this study point to the following conclusions. First, haplogroup X variation is completely captured by two ancient clades that display distinctive phylogeographic patterns—X1 is largely restricted to North and East Africa, whereas X2 is spread widely throughout West Eurasia. Second, it is apparent that the Native American haplogroup X mtDNAs derive from X2 by a unique combination of five mutations. Third, the few Altaian (Derenko et al. 2001) and Siberian haplogroup X lineages are not related to the Native American cluster, and they are more likely explained by recent gene flow from Europe or from West Asia. Fourth, the split between "African" X1 and "Eurasian" X2 subhaplogroups of X is phylogenetically as deep as that within the branches of haplogroup U that also differ profoundly in their phylogeography. Thus, subhaplogroup U6 is largely restricted to North Africa (as X1), whereas subhaplogroup U5 is widespread in West Eurasia (as X2). The phylogeographic patterns and the coalescence times that we obtained here suggest that the basic phylogenetic structures of the mtDNA haplogroups in West Eurasia and North Africa are as ancient as the beginning of the spread of anatomically modern humans in this region. Finally, phylogeography of the subclades of haplogroup X suggests that the Near East is the likely geographical source for the spread of subhaplogroup X2, and the associated population dispersal occurred around, or after, the LGM when the climate ameliorated. The presence of a daughter clade in northern Native Americans testifies to the range of this population expansion.

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Electronic-Database Information

Accession numbers and URLs for data presented herein are as follows:

Estonian Biocentre, http://www.ebc.ee/EVOLUTSIOON/mtDNA-X/ (for mtDNA sequence data)
Shareware Phylogenetic Network Software, http://www.fluxus-engineering.com/sharenet.htm (for Network 3111)

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