

The Western and Eastern Roots of the Saami—the Story of Genetic “Outliers” Told by Mitochondrial DNA and Y Chromosomes

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The Saami are regarded as extreme genetic outliers among European populations. In this study, a high-resolution phylogenetic analysis of Saami genetic heritage was undertaken in a comprehensive context, through use of maternally inherited mitochondrial DNA (mtDNA) and paternally inherited Y-chromosomal variation. DNA variants present in the Saami were compared with those found in Europe and Siberia, through use of both new and previously published data from 445 Saami and 17,096 western Eurasian and Siberian mtDNA samples, as well as 127 Saami and 2,840 western Eurasian and Siberian Y-chromosome samples. It was shown that the “Saami motif” variant of mtDNA haplogroup U5b is present in a large area outside Scandinavia. A detailed phylogeographic analysis of one of the predominant Saami mtDNA haplogroups, U5b1b, which also includes the lineages of the “Saami motif,” was undertaken in 31 populations. The results indicate that the origin of U5b1b, as for the other predominant Saami haplogroup, V, is most likely in western, rather than eastern, Europe. Furthermore, an additional haplogroup (H1) spread among the Saami was virtually absent in 781 Samoyed and Ob-Ugric Siberians but was present in western and central European populations. The Y-chromosomal variety in the Saami is also consistent with their European ancestry. It suggests that the large genetic separation of the Saami from other Europeans is best explained by assuming that the Saami are descendants of a narrow, distinctive subset of Europeans. In particular, no evidence of a significant directional gene flow from extant aboriginal Siberian populations into the haploid gene pools of the Saami was found.

Introduction

Although not homogeneous, the European genetic landscape has been characterized by relatively short genetic

distances between individual populations. Classic genetic markers have revealed a few clearly pronounced outliers, like the Sardinians, the Greeks, the Basques, the Finns and, in particular, the Saami (Cavalli-Sforza and Piazza 1993; Cavalli-Sforza et al. 1994). The Saami (Lapps) are aboriginal inhabitants of Fennoscandia. The Saami language belongs to the Finno-Ugric branch of the Uralic language family and can be divided into 10 dialects (Sammallahti 1998). The closest linguistic neighbors of the Saami are the Finns, the Karelians, and the

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Estonians. At present, ~60,000 Saami live in the northern regions of Norway, Sweden, and Finland, as well as in the Russian Kola Peninsula (Haetta 1996). Soon after the beginning of the retreat of the ice sheets covering the area, in the 8th–10th millennia before present (BP), populations of hunters and fishermen, the producers of the Mesolithic Komsa and Fosna-Hensbacka cultures, inhabited the coastal region of Scandinavia, extending well into Finland and to the Kola Peninsula (Kozłowski and Bandi 1984; Nygaard 1989; Sumkin 1990). The linguistic affiliation of these pioneer settlers of the north is largely unknown, but it has been suggested that they are the descendants of the Ahrensburgian population, which migrated toward the north from western Europe, along the Atlantic coast of Norway. It has been proposed that they might have been the ancestors of the present-day Saami (e.g., Sumkin 1990). Another presumably important component in the postglacial recolonization of northern Fennoscandia came from the east, via Karelia and Finland. It has been associated with the movement of Mesolithic populations, carriers of post-Swiderian cultures, to the north. Starting in the Neolithic period, the northern population came into contact with tribes of territories lying to the south (e.g., Sumkin 1990). Thus, according to archeological data, the present-day Saami population might have been shaped in different times both by the eastern and western influences.

Analyses of classic chromosomal marker variation have demonstrated that the genetic distances between the Saami and other European populations are significantly larger than between any other pair of European populations (Cavalli-Sforza et al. 1994). This distinctive pattern has suggested to some that the genetic composition of the Saami population arose from extensive admixture between Caucasoid and Mongoloid populations. Estimates of the relative contribution of each have varied from an equal input to ~80% Caucasoid and 20% Mongoloid genes (Guglielmino et al. 1990; Cavalli-Sforza et al. 1994, pp 272–273). However, not all classic genetic studies support an idea of an extensive Caucasoid-Mongoloid admixture in the Saami genetic background (e.g., Beckman et al. 1988, 1993).

Similarly, studies of mtDNA have identified large genetic distances between the Saami and other Europeans, including the Finns (Sajantila and Pääbo 1995; Sajantila et al. 1995). Likewise, Lahermo et al. (1996) found no overlap between Saami and the remaining European mtDNA patterns and concluded that the Saami and the Finns must have different genetic histories. One alternative hypothesis to explain the presence of genetic differences and language similarities in the Finns and the Saami involves a language shift by the Finns from Indo-European to Finno-Ugric (Sajantila and Pääbo 1995).

The combined sequence information from the first hypervariable segment (HVS-I) in the D-loop of mtDNA

and the variations in the mtDNA coding region of European populations have been exploited to generate a common phylogenetic nomenclature for mtDNA variants in Europe (Torroni et al. 1996; Macaulay et al. 1999). Classification of the Saami mtDNA lineages revealed that the absolute majority of these are clustered in a subset of the European mtDNA pool (Torroni et al. 1998; VILLEMS et al. 1998), where two haplogroups—V and U—cover ~80% of the variability of this subset (Torroni et al. 1998; Tambets et al. 2000).

In contrast to the predominance of European mtDNA haplogroups observed among the Saami, nearly half of their Y chromosomes share a TatC allele (haplogroup N3, according to the nomenclature of the Y Chromosome Consortium [YCC 2002]) with most Finno-Ugric and Siberian populations. This variant is found at high frequencies among Siberian populations, such as the Yakuts and the Buryats, but is virtually absent in western and Mediterranean Europe; even among the Norwegians and the Swedes, populations that have historically lived in close proximity to the Saami, it is found at frequencies of only 4%–8% (Zerjal et al. 2001; Passarino et al. 2002). High frequencies of the TatC allele have also been observed in Baltic (30%–40%) and Volga-Finnic-speaking populations (20%–50%) (Zerjal et al. 1997; Rootsi et al. 2000; Rosser et al. 2000; Semino et al. 2000; Laitinen et al. 2002). These findings have been interpreted according to the classic view that a substantial element of the Saami (and other European Finno-Ugric-speaking populations) genetic lineages originated in a recent migration from Asia (Zerjal et al. 1997, 2001).

Another half of the Saami paternal lineages have primarily mutations M170, SRY-1532, or M173 (Semino et al. 2000; Raitio et al. 2001; Wells et al. 2001). Accordingly, they are identified as haplogroups I, R1a, and R1b (YCC 2002). Y chromosomes possessing those mutations are widely spread in European populations (Rosser et al. 2000; Semino et al. 2000). Whereas SRY-1532 and M173 are present at moderate frequencies in some Siberian populations as well, M170 Y chromosomes are very rare there (Wells et al. 2001; Karafet et al. 2002).

Here, we first analyze mtDNA variation in the Swedish Saami and improve the resolution level of their Y-chromosomal haplotypes. Second, we examine the hypothetical descent of the Saami gene pool from Siberian ancestors. We exploit extensive data on mtDNA and Y-chromosome variation in Eurasia, in particular among Uralic-, Indo-European-, and Altaic-speaking populations in eastern Europe and western Siberia. Finally, we refine the phylogenetic topology of a frequent Saami mtDNA haplogroup, U5b, to identify the founder haplotypes. We draw conclusions about the possible origin of mtDNA and NRY haplotypes present in the Saami gene pool.

Subjects and Methods

Population Samples

We analyzed mtDNA sequences from 17,541 Eurasian individuals sampled from 65 different Eurasian populations (table 1). These data consist of previously published sequences ($n = 9,154$) and new sequences analyzed in this study ($n = 8,387$). Comparisons of different Saami subpopulations are presented separately in table 2. Y-chromosomal markers were also analyzed from 32 different populations. Data from 1,598 of a total of 2,967 individuals reported in table 3 were taken from published sources, whereas the remaining 1,369 DNA samples were extracted and analyzed in the present study. Further details about the populations other than the Saami will be published elsewhere. Blood samples were collected from healthy unrelated individuals after obtaining informed consent. DNA was extracted using the phenol-chloroform method, as used by Sambrook (1989).

mtDNA Analysis

HVS-I was sequenced between nucleotide positions (nps) 16024 and 16383 of the revised Cambridge Reference Sequence (Andrews et al. 1999) in 73 Swedish Saami and 8,314 other mtDNA samples. RFLP analysis of diagnostic mtDNA positions was performed, and mtDNA haplogroups were assigned to each sample by use of published criteria (Torroni et al. 1992, 1994, 1996; Richards et al. 1998; Macaulay et al. 1999; Schurr et al. 1999; Finnilä et al. 2000, 2001; Herrnstad et al. 2002; Kivisild et al. 2002). In addition, all U5b genomes ($n = 160$) from 31 populations were typed by sequencing for the np 5656 A→G mutation that differentiates between individuals belonging to haplogroups U5b* and U5b1. All identified U5b1 individuals (5656G) were further sequenced to assess the variation at nps 7385 (A or G) and 10927 (T or C). A summary of these data is given in table 4.

Y-Chromosome Analysis

Sixteen Y-chromosomal biallelic markers were assayed in 1,369 DNA samples. Nomenclature of haplogroups is as defined by the YCC (2002). Markers were analyzed as follows. The polymorphic SNPs underlying markers M52, M130 (RSP4Y), M170, M173, M178, M201 (Underhill et al. 2001), M269 (Cruciani et al. 2002), and M242 (Seielstad et al. 2003) were assayed after PCR amplification and sequencing. Markers M9, Tat, SRY-1532, 92R7, M89, and P43 were assayed through restriction digest analysis by use of published protocols (Mathias et al. 1994; Whitfield et al. 1995; Zerjal et al. 1997; Akey et al. 2001; Raitio et al. 2001;

Karafet et al. 2002). The YAP and 12f2 polymorphisms were identified following the procedures of Hammer and Horai (1995) and Casanova et al. (1985), respectively. Furthermore, 35 Swedish Saami DNA samples that have previously been analyzed for Y-chromosomal variation by Rosser et al. (2000) were also typed in the present study for the biallelic markers M89, M52, M130 (RSP4Y), M170, M173, M178, M201, and M269 (YCC 2002).

Sequencing

PCR-amplified products were purified using shrimp alkaline phosphatase and exonuclease treatment following Kaessmann (1999). These were sequenced using the DYEnamic ET terminator cycle sequencing kit (Amersham Pharmacia Biotech) on an ABI 377 DNA Sequencer. Sequences were aligned and analyzed using the Genetics Computer Group Wisconsin Package.

Data Analysis

Principal-component (PC) analysis was undertaken using the POPSTR program, kindly provided by H. Harpending (see details described by Richards et al. [2002]). Only those haplogroups that had a noticeable impact on the scatterplot were used for the analysis (the sum of the absolute values for both coordinates of each allele was >0.2 [M, V, U5, H, A, J, and U4 for mtDNA and Q, N2, I, R1b, R1a, and N3 for the Y chromosome]). Bayesian 95% credible regions (CRs) for haplogroup frequencies were calculated with the computer program SAMPLING, kindly provided by V. Macaulay. The diversity of mtDNA haplotypes was estimated as by Nei (1987).

Phylogenetic networks of mtDNA HVS-I haplotypes were constructed using the program Network 3.1.1.1 (Fluxus Engineering Web site). Different weights were assigned to substitutions, as in the study by Richards et al. (1998). Coalescence-age calculations and SDs were estimated following the formulae of Forster et al. (1996) and Saillard et al. (2000).

Results

Saami mtDNA Haplogroup Frequencies

The mtDNA haplogroup frequencies were estimated in Swedish Saami ($n = 73$) and in 8,314 samples from different European and Siberian populations, through use of HVS-I sequencing and RFLP analysis. The combined D-loop and coding region information also enabled us to infer the haplogroup affiliations from previously published data for the Finnish, Swedish, and Norwegian Saami (Sajantila et al. 1995; Dupuy and Olaisen 1996; Delghandi et al. 1998) that has been scored for the presence of the HVS-I polymorphisms (fig. 1; tables 1 and 2).

Table 1**Frequencies (%) of the Predominant mtDNA Haplogroups of the Saami among Other Eurasian Populations**

REGION AND POPULATION ^a	LANGUAGE FAMILY ^b	SAMPLE SIZE	FREQUENCY OF HAPLOGROUP (%)					REFERENCE(S)
			V	U5b1b1 ^c	H1 ^d	D5 ^e	Z	
Scandinavia:								
*Saami	U-FU	445	41.6	47.6	2.5	3.1	1.3	Sajantila et al. 1995, corrected by Bandelt et al. 2001; Dupuy and Olaisen 1996; Delghandi et al. 1998; present study
*Swedes	IE-G	503	3.2	.8	3.4	0	.4	Sajantila et al. 1996; present study
*Norwegians	IE-G	641	3.4	1.2	1.9	0	.6	Dupuy and Olaisen 1996; Opdal et al. 1998; Helgason et al. 2001; Passarino et al. 2002
Northern Europe:								
*Karelians	U-FU	83	6.0	6.0	6.0	1.2	0	Sajantila et al. 1995
*Finn	U-FU	581	6.4	6.7	3.6	.2	1.5	Pult et al. 1994; Sajantila et al. 1995; Lahermo et al. 1996; Kittles et al. 1999; Meinilä et al. 2001
*Estonians	U-FU	545	3.3	.7	4.8	.2	0	Sajantila et al. 1995, 1996; present study
Latvians	IE-B	299	3.0	0	1.0	0	0	Present study
Lithuanians	IE-B	45	2.2	2.2	2.2	0	0	Present study
North-Russians	IE-S	134	0	3.0	2.2	5.2	0	Present study
Eastern Europe:								
*Russians	IE-S	761	3.8	1.2	1.2	0	.3	Orekhov et al. 1999; Malyarchuk et al. 2001, 2002; present study
Ukrainians	IE-S	686	4.8	.6	1.5	0	.1	Malyarchuk et al. 2001; present study
*Poles	IE-S	583	4.5 ^g	.7	1.0	0	0	Richards et al. 2000; Malyarchuk et al. 2002; present study
*Northwestern Europe	IE-C/G	1,851 (1,547) ^f	2.8 ^g	0	1.6	0	0	Piercy et al. 1993; Richards et al. 1996, 2000; Helgason et al. 2000, 2001
Volga-Ural region:								
*Maris	U-FU	147	10.2	.7	.7	0	2.7	Sajantila et al. 1995; Bermisheva et al. 2002; present study
*Mordvin	U-FU	111	3.6	2.7	0	0	0	Sajantila et al. 1995; Bermisheva et al. 2002
Komis	U-FU	340	.6	1.8	2.1	1.8	1.8	Bermisheva et al. 2002; present study
Udmurts	U-FU	182	.5	0	8.2	0	7.1	Bermisheva et al. 2002; present study
Chuvashes	A-T	89	5.6	1.1	2.2	0	0	Richards et al. 2000; Bermisheva et al. 2002
Tatars	A-T	176	4.5	0	0	0	0	Bermisheva et al. 2002; present study
Bashkirs	A-T	209	3.3	2.4	0	0	1.0	Bermisheva et al. 2002
Southern Europe:								
*Italians	IE-R	397 (240) ^f	1.7 ^g	0	1.0	0	0	Francalacci et al. 1996; Richards et al. 2000; Mogentale-Profizi et al. 2001; Tagliabracci et al. 2001; present study
Sardinians	IE-R	115 (133) ^f	6.0 ^g	0	.9	0	0	Richards et al. 2000; Cali et al. 2001
*Sicilians	IE-R	732 (634) ^f	2.2 ^g	0	.8	0	0	Di Rienzo and Wilson 1991; Richards et al. 2000; Cali et al. 2001; Forster et al. 2002; present study
Cypriots	IE	188	0	0	1.6	0	0	Present study
Greeks (mainland and Crete)	IE	399 (414) ^f	.7 ^g	0	0	0	0	Richards et al. 2000; present study
Albanians	IE	199	.5	0	0	0	0	Present study

Croats	IE-S	440	2.7	.5	.5	0	0	Present study
Bosnians	IE-S	395	3.3	.8	.8	0	.3	Malyarchuk et al. 2003; present study
Western Europe:								
*French	IE-R	577	3.1	.3	2.3	0	0	Rousselet and Mangin 1998; Danan et al. 1999; Richards et al. 2000; Cali et al. 2001; present study
*Spaniards	IE-R	479 (293) ^f	2.0 ^g	0	.4	0	0	Corte-Real et al. 1996; Salas et al. 1998; Crespillo et al. 2000
*Portugese	IE-R	295 (54) ^f	3.7 ^g	0	1.4	0	0	Corte-Real et al. 1996; Pereira et al. 2000
*Basques	Isolate	106 (97) ^f	12.4 ^g	0	0	0	0	Bertranpetit et al. 1995; Corte-Real et al. 1996
*Central Europe:								
*Germans	IE-G	582	4.3 ^g	0	2.9	0	0	Richards et al. 1996; Hofmann et al. 1997; Baasner et al. 1998; Lutz et al. 1998; Pfeiffer et al. 1999
*Swiss	IE-G	230	3.9	0	.9	0	0	Pult et al. 1994; Dimo-Simonin et al. 2000
Austrians	IE-G	101	1.0	0	0	0	0	Parson et al. 1998
Hungarians	U-FU	116	2.6	.9	1.7	0	0	Present study
Czechs	IE-S	177	4.0	0	.6	0	0	Richards et al. 2000; present study
Slovaks	IE-S	129	2.3	0	4.7	0	0	Present study
Slovenes	IE-S	110	5.5	1.8	3.6	0	0	Present study
Caucasus	IE, CA-N/S; A-M/T	1,383	.5	.4	.5	0	.7	Richards et al. 2000; present study
Siberia:								
Khants	U-FU	255	0	0	0	0	0	Present study
Mansis	U-FU	138	.7	0	0	.7	0	Derbeneva et al. 2002b; present study
Nganasans	U-SA	131	0	0	.8	0	2.3	Derbeneva et al. 2002a; present study
Nenets	U-SA	137	0	0	0	0	0	Saillard et al. 2000; present study
Selkups	U-SA	120	0	0	0	0	0	Present study
Kets	Isolate	104	0	0	0	0	2.9	Derbeneva et al. 2002a; present study
Dolgans	A-T	130	0	0	.8	0	1.5	Present study
*Yakuts	A-T	395	0	.5	0	0	0	Fedorova et al. 2003; Pakendorf et al. 2003; Puzyrev et al. 2003
*Buryats	A-M	126	0	0	0	0	1.6	Pakendorf et al. 2003
Evenks	A-TN	105	0	0	0	0	1.0	Present study
Altaians	A-T	339	0	0	0	.3	5.0	Present study
Total		17,541						

^a Populations for which frequencies were deduced from published HVS-I sequences are indicated by an asterisk (*). Populations are divided into geographic regions; for northwestern Europe (consists of Scots [$n = 891$], English and Welsh [$n = 426$], Irish [$n = 101$], and Icelanders [$n = 433$]) and for the Caucasus region (consists of Nogays [$n = 183$], Adygeis [$n = 159$], Abazins [$n = 64$], Kabardins [$n = 66$], Karachays [$n = 106$], Kumyks [$n = 109$], Kalmyks [$n = 120$], Georgians [$n = 138$], Southern Ossetians [$n = 198$], Armenians [$n = 192$], and Azeris [$n = 48$]), only summary data are shown.

^b Language-family codes used for each population are as follows: U = Uralic (FU = Finno-Ugric; SA = Samoyedic); IE = Indo-European (B = Baltic; C = Celtic; G = Germanic; R = Romance; S = Slavic); A = Altaic (M = Mongolic; T = Turkic, TN = Tungusic); CA = Caucasian (N = North; S = South).

^c Only haplotypes with HVS-I motif 16144-16189-16270 and its derivatives have been taken into account.

^d Only haplotypes with HVS-I motif 16162 and its derivatives have been taken into account.

^e Only haplotypes with HVS-I motif 16126-16136-16189-16223-16360-16362 and its derivatives have been taken into account.

^f In the estimation of haplogroup V proportions, data from Torroni et al. (2001) have been used, and the corresponding sample size is given in parentheses after the sample size analyzed for calculating other haplogroup frequencies (in case of German population, the pooled data of different German subpopulations from Torroni et al. [2001] have been used).

^g Frequencies of haplogroup V are from Torroni et al. (2001).

Table 2**Frequencies (%) of mtDNA and Y-Chromosomal Haplogroups in Different Saami Subpopulations**

HAPLOGROUP	FREQUENCY (95% CR) ^a (%)			
	Swedish Saami ^b (<i>n</i> = 98/35)	Finnish Saami ^c (<i>n</i> = 69/69)	Norwegian Saami ^d (<i>n</i> = 278/...)	Kola Saami ^e (<i>n</i> = .../23)
mtDNA:				
H:	3.1 (1.1–8.6)	2.9 (.9–9.9)	4.7 (2.8–7.8)	...
H1	.0 (.0–3.0)	.0 (.0–4.2)	4.0 (2.2–6.9)	...
W	1.0 (.2–5.5)	.0 (.0–4.2)	1.4 (.6–3.6)	...
T	.0 (.0–3.0)	.0 (.0–4.2)	.4 (.1–2.0)	...
U:	26.5 (18.8–36.1)	43.5 (32.4–55.3)	57.6 (51.7–63.2)	...
U5a	.0 (.0–3.0)	2.9 (.9–9.9)	.7 (.2–2.6)	...
U5b	26.5 (18.8–36.1)	40.6 (29.8–52.4)	56.8 (51.0–62.5)	...
V	68.4 (58.6–76.7)	37.7 (27.2–49.5)	33.1 (27.8–38.8)	...
M:	1.0 (.2–5.5)	15.9 (9.2–26.4)	2.9 (1.5–5.6)	...
D5	.0 (.0–3.0)	8.7 (4.1–17.7)	2.9 (1.5–5.6)	...
Z	1.0 (.2–5.5)	7.2 (3.2–15.9)	.0 (.0–1.1)	...
NRY:				
E	.0 (.0–8.0)	.0 (.0–4.2)	...	8.7 (2.7–27.0)
F*	5.7 (1.8–18.7)0 (.0–11.7)
I	31.4 (18.6–48.1)	40.6 (29.8–52.4) ^f	...	17.4 (7.1–37.4)
J	.0 (.0–.8)	4.3 (1.0–21.1)
N3	37.1 (23.1–53.8)	55.1 (43.3–66.3)	...	39.1 (22.1–59.4)
R1b	5.7 (1.8–18.7)	1.4 (.3–7.7)	...	8.7 (2.7–27.0)
R1a	20.0 (10.1–36.0)	2.9 (.9–9.9)	...	21.7 (9.8–42.2)

^a Sample size (*n*) is given separately for mtDNA/NRY data sets, respectively.^b mtDNA data are from this study and inferred from Sajantila et al. (1995); NRY data from Rosser et al. (2000) are further analyzed for markers M89, M52, M130 (RSP4Y), M170, M173, M178, M201, and M269 (YCC 2002) in the present study.^c mtDNA data are inferred from Sajantila et al. (1995); NRY data are inferred from Raitio et al. (2001).^d mtDNA data are inferred from Sajantila et al. (1995), Dupuy and Olaisen (1996), and Delghandi et al. (1998).^e NRY data are from Wells et al. (2001).^f Frequency is that of haplogroups F, I, and J combined.

The phylogenetic network in figure 1 relates all the HVS-I sequence haplotypes in the three geographic subpopulations of the Saami. It also indicates a limited number of highly frequent haplotypes, which are, in most cases, shared by all analyzed geographic subpopulations (see table 2). Thus, 98% of the Saami mtDNA pool is encompassed within haplogroups V, U5b, H, Z, and D5. The two largest subsets, V and U5b, account for a lion's share (89%) of the Saami mtDNA pool. The representative proportion of individual haplogroups varies substantially among different Saami subpopulations (table 2). Haplogroup V is by far the most frequent haplogroup in the Swedish Saami and is present at significantly lower frequencies ($P < .0001$) in Norwegian and Finnish subpopulations. We note that, in all three Saami subpopulations, U5b was virtually the only subclade of the otherwise frequent and divergent western Eurasian haplogroup U5 (Tambets et al. 2003). It is the most frequent haplogroup among Norwegian and Finnish subpopulations (table 2).

The frequencies of the most widely spread haplogroups among the Saami in other analyzed populations are shown in table 1. Both haplogroups V and U5b are spread at moderate frequencies across Europe, from Iberia to the Ural Mountains. In contrast, among 393 Ob-Ugric speakers (including 98 Mansi, published elsewhere by Derbeneva et al. [2002b]) and 388 Samoyeds (including 58 Nenets, published elsewhere by Saillard et al. [2000]), only one haplogroup V-carrying individual was found in the Mansi sample, whereas not a single Saami variant of U5b (U5b1b1) was identified there (table 1). These two variants of maternal lineages are virtually absent in the other 1,199 native Siberians analyzed in this study.

The third-most-frequent haplogroup among the Saami is H, which is present at a frequency of 4%, ~10-fold lower than that of other North European populations (Richards et al. 2000). The majority of the Saami haplogroup H lineages (61%) contain transitions at nps 73 and 16162. According to information obtained from

Table 3

Frequencies (%) of Selected Y-Chromosomal Haplogroups in the Saami and in Other Eurasian Populations

REGION AND POPULATION ^a	LANGUAGE FAMILY ^b	SAMPLE SIZE	FREQUENCY OF HAPLOGROUP (%)							REFERENCE(S)
			I ^c	R1b ^d	R1a	N3	N2	Q	C	
Scandinavia:										
*Saami ^e	U-FU	127 (58) ^f	25.9 ^f	3.9	11.0	47.2	0	0	0	Raitio et al. 2001; Wells et al. 2001; present study
Swedes	IE-G	141	48.2	22.0	18.4	2.8	0	0	0	Present study
Norwegians	IE-G	72	40.3	27.8	23.6	6.9	0	0	0	Passarino et al. 2002
Danes	IE-G	194	38.7	36.1	16.5	.5	0	0	0	Sanchez et al. 2003
Northern Europe:										
*Finns	U-FU	38	28.9	0	7.9	63.2	0	0	0	Zerjal et al. 2001
Estonians	U-FU	209	18.2	9.1	33.5	30.6	0	0	0	Present study
Latvians	IE-B	86	7.0	9.3	38.4	41.9	0	0	0	Present study
North Russians	IE-S	77	20.8	0	40.3	28.6	0	0	0	Wells et al. 2001
Eastern Europe:										
Russians	IE-S	61	13.1	21.3	42.6	8.2	8.2	0	0	Karafet et al. 2002 (supplementary data obtained by request from the author)
Ukrainians	IE-S	50	18.0	2.0	54.0	6.0	0	0	0	Semino et al. 2000
Poles ^e	IE-S	93	16.1	13.4	55.9	3.2	0	0	0	Present study
Volga-Ural region:										
Maris	U-FU	111	8.1	2.7	47.7	31.5	9.9	0	0	Semino et al. 2000; present study
Mordvin	U-FU	83	19.3	13.3	26.5	16.9	2.4	0	0	Present study
Komis	U-FU	94	5.3	16.0	33.0	22.3	12.8	0	0	Present study
Udmurts	U-FU	87	1.1	2.3	10.3	56.3	28.7	0	0	Present study
Chuvashes	A-T	79	11.4	3.8	31.6	17.7	10.1	0	1.3	Present study
Tatars	A-T	126	4.0	8.7	34.1	18.3	4.8	.8	1.6	Present study
Southern Europe:										
Croats	IE-S	109	37.6	15.6	33.9	0	0	0	0	Barac et al. 2003
Western Europe:										
French	IE-R	61	16.4	59.0	0	0	0	0	0	Semino et al. 2000; present study
Central Europe:										
Germans	IE-G	16	37.5	0	0	0	0	0	0	Semino et al. 2000
Hungarians	U-FU	113	28.3	20.4	20.4	.9	0	2.6	.9	Present study
Siberia:										
Khants	U-FU	47	0	19.1	4.3	38.3	38.3	0	0	Karafet et al. 2002 (supplementary data obtained by request from the author)
Nganasans	U-SA	38	0	0	0	92.1	0	5.3		Karafet et al. 2002 (supplementary data obtained by request from the author)
Nenets	U-SA	148	0	0	0	40.5	56.8	1.4	0	Karafet et al. 2002 (supplementary data obtained by request from the author)
Selkups	U-SA	131	0	6.1	19.1	0	6.9	66.4	1.5	Karafet et al. 2002 (supplementary data obtained by request from the author)
Kets	Isolate	48	0	0	0	0	93.7	6.2		Karafet et al. 2002 (supplementary data obtained by request from the author)
Dolgans	A-T	67	1.5	1.5	16.4	22.4	11.9	0	37.3	Karafet et al. 2002 (supplementary data obtained by request from the author)
Yakuts	A-T	155	1.3	1.9	1.9	88.4	0	0	3.2	Karafet et al. 2002 (supplementary data obtained by request from the author); present study
Buryats	A-M	81	0	1.2	1.2	28.4	2.5	0	60.5	Karafet et al. 2002 (supplementary data obtained by request from the author)
Evenks	A-TN	96	5.2	0	1.0	16.7	3.1	4.2	67.7	Karafet et al. 2002 (supplementary data obtained by request from the author)
Evens	A-TN	31	3.2	0	6.5	12.9	0	0	74.2	Karafet et al. 2002 (supplementary data obtained by request from the author)
Altaians	A-T	98	0	0	46.9	1.0	2.0	17.3	22.4	Karafet et al. 2002 (supplementary data obtained by request from the author)
Total		2,967								

^a Populations for which data are deduced from published sources are indicated with an asterisk.

^b Language-family codes for each population are as follows: U = Uralic (FU = Finno-Ugric; SA = Samoyedic); IE = Indo-European (B = Baltic; G = Germanic; R = Romance; S = Slavic); A = Altaic (M = Mongolic; T = Turkic, TN = Tungusic).

^c Haplogroup I is, in the case of data deduced from literature, defined by the characteristic STR pattern of haplogroup 2 Y chromosomes (Barac et al. 2003; present study).

^d Haplogroup R1b is, in the case of data deduced from literature, defined here by M173(xSRY-1532) as studied western Europeans (except three Danes, who belong to R1* [Sanchez et al. 2003]) from this clade have been shown to share the additional mutation M269 (Cruciani et al. 2002; present study).

^e 35 Swedish Saami and 93 Poles from the study by Rosser et al. (2000) were further analyzed for markers M52, M89, M130, M170, M173, M178, M201, and M269.

^f In the estimation of haplogroup I proportions, only the data from the present study and from Wells et al. (2001) were used. The corresponding sample sizes are given in parentheses.

Table 4

Phylogeographic Distribution of Haplogroup U5b Subclades (Excluding U5b1b1)

HVS-I SEQUENCE ^a	U5b SUB HG ^b	NO. OF INDIVIDUALS IN POPULATION ^c																								BASE AT NP ^d									
		WSE						SC				EE				Other																			
		al	bo	br	cr	cz	fr	gr	hu	it	si	sk	sl	sw	ba	es	ko	la	mo	po	ru	ta	ud	uk	mc	ng	go	tu	sh	ku	td	<i>n</i> ^d	A	ND	ND
270	U5b*											1	2																			3	A	ND	ND
051-168-189-270-362	U5b*												1	1																		1	A	ND	ND
086-192-270-304	U5b*								1																							1	A	ND	ND
093-172-189-270-362	U5b*																							1								1	A	ND	ND
093-234-270-325	U5b*	1																														1	A	ND	ND
093-258-270-292-362	U5b*																							1								1	A	ND	ND
145-189-270	U5b*																					1										1	A	ND	ND
169-172-189-270	U5b*																								1							1	A	ND	ND
169CA-192-235-270-304	U5b*							1																								1	A	ND	ND
189-192-201-270-398	U5b*					1																										1	A	ND	ND
189-192-217-234-270-398	U5b*																						2									2	A	ND	ND
189-192-234-256-270-311-362-398	U5b*		1																													1	A	ND	ND
189-192-266-270-398	U5b*																															1	A	ND	ND
189-192-270	U5b*					1						1	1	1	1																	5	A	ND	ND
189-192-270-398	U5b*			1																			1									3	A	ND	ND
189-239CA-270	U5b*																		1													1	A	ND	ND
189-261-270	U5b*																															1	A	ND	ND
189-270	U5b*							1																3			2					6	A	ND	ND
189-270-288-292	U5b*																	1														1	A	ND	ND
189-270-311	U5b*	1													1						1											3	A	ND	ND
189-292-311	U5b*							1																								1	A	ND	ND
192-212-270	U5b*					1																										1	A	ND	ND
192-224-261	U5b*																							1								1	A	ND	ND
192-235-270-304	U5b*															1																1	A	ND	ND
192-257-270-304	U5b*							1																								1	A	ND	ND
192-270	U5b*											1	1																			3	A	ND	ND
192-270-278-304	U5b*							1																								1	A	ND	ND
192-270-304	U5b*					1		1																								2	A	ND	ND
192-311	U5b*					1	1						1		4		2															9	A	ND	ND
222-224-270-311	U5b*												1																			1	A	ND	ND
224-270-311	U5b*							1																1								2	A	ND	ND
234-270	U5b*																															1	A	ND	ND
258-270-292-362	U5b*																							1								1	A	ND	ND
261-270	U5b*		1																													3	A	ND	ND
261-270-390	U5b*									1							1															1	A	ND	ND
051-189-270	U5b1*							2																								2	G	A	T

086-189-192-270-311-336	U5b1*									3										3	G	A	T									
092-189-270-294	U5b1*																		1	1	G	A	T									
093-182-189-192-270	U5b1*		1																		1	G	A	T								
093-189-270	U5b1*										1										1	G	A	T								
093-189-270-362	U5b1*											2									2	G	A	T								
129-189-223-270	U5b1*		1																		1	G	A	T								
129-189-270	U5b1*		1																		1	G	A	T								
129-192-270	U5b1*										1										1	G	A	T								
147-189-270	U5b1*		1													3					1	G	A	T								
174-189-223-270	U5b1*										1										1	G	A	T								
174-189-270-311	U5b1*	1																		1	2	G	A	T								
182-189-192-270	U5b1*		1																		1	G	A	T								
186-189-270-293	U5b1*		1																		1	G	A	T								
189-192-218-270-320	U5b1*									1											1	G	A	T								
189-192-270	U5b1*												6							3	1	G	A	T								
189-192-270-292	U5b1*	1																			1	G	A	T								
189-192-270-311	U5b1*			1																	1	G	A	T								
189-221-223-270	U5b1*												1								1	G	A	T								
189-221-270	U5b1*											1									1	G	A	T								
189-223-270	U5b1*										1										1	G	A	T								
189-270	U5b1*			8	1		1		1		5	2	1		5						2	G	A	T								
189-270-311-336	U5b1*	1																			1	G	A	T								
192-224-261-270	U5b1*						1														1	G	A	T								
192-270	U5b1*	1	1					1				1									1	G	A	T								
192-270-296	U5b1*						1														1	G	A	T								
192-270-319	U5b1*			1																	1	G	A	T								
074-172-189-270	U5b1b							1													1	G	G	C								
074-189-270	U5b1b										1										1	G	G	C								
093-129-189-270	U5b1b											1									2	G	G	C								
093-189-270	U5b1b		1												1						2	G	G	C								
093-189-270-301	U5b1b		1																		1	G	G	C								
093-189-270-301-311	U5b1b																				1	G	G	C								
173-189-270-235	U5b1b						1														1	G	G	C								
189-192-270	U5b1b						1														1	G	G	C								
189-270	U5b1b			1				1							1						1	1	G	G	C							
189-270-325	U5b1b						1														1	G	G	C								
Total		3	5	1	20	4	13	3	2	1	9	1	1	9	4	14	11	6	5	1	16	5	1	13	3	1	2	2	1	1	2	160

NOTE.—mtDNAs belonging to subclade U5b1b1 were screened selectively for the presence of the mutations in nps 5656, 7385, and 10927. All of those (18 Saami, 5 individuals from eastern Europe, and 5 individuals from western and southern Europe) possessed aforementioned transitions.

^a Mutations in sequences are relative to the revised Cambridge Reference Sequence (Andrews et al. 1999). HVS-I sequences are given minus 16,000; only transversions are further indicated. ND = not determined.

^b SubHG = subhaplogroup.

^c Geographic subdivision codes are as follows: WSE = western and southern Europe; SC = Scandinavian Europe; EE = eastern Europe. Population codes are as follows: al = Albanians; bo = Bosnians; br = Bretons; cr = Croats; cz = Czechs; fr = French; gr = Greeks; hu = Hungarians; it = Italians; si = Sicilians; sk = Slovaks; sl = Slovenians; sw = Swedes; ba = Bashkirs; es = Estonians; ko = Komis; la = Latvians; mo = Mordvin; po = Poles; ru = Russians; ta = Tatars; ud = Udmurts; uk = Ukrainians; mc = Moroccans; ng = Nogays; go = Georgians; tu = Turks; sh = Shors; ku = Kumyks; td = Tadjik. In addition to population data from table 1, data of Bretons, Moroccans, Shors, Tadjiks, and Turks are shown (authors' unpublished data).

^d Number of subjects analyzed in haplotype.

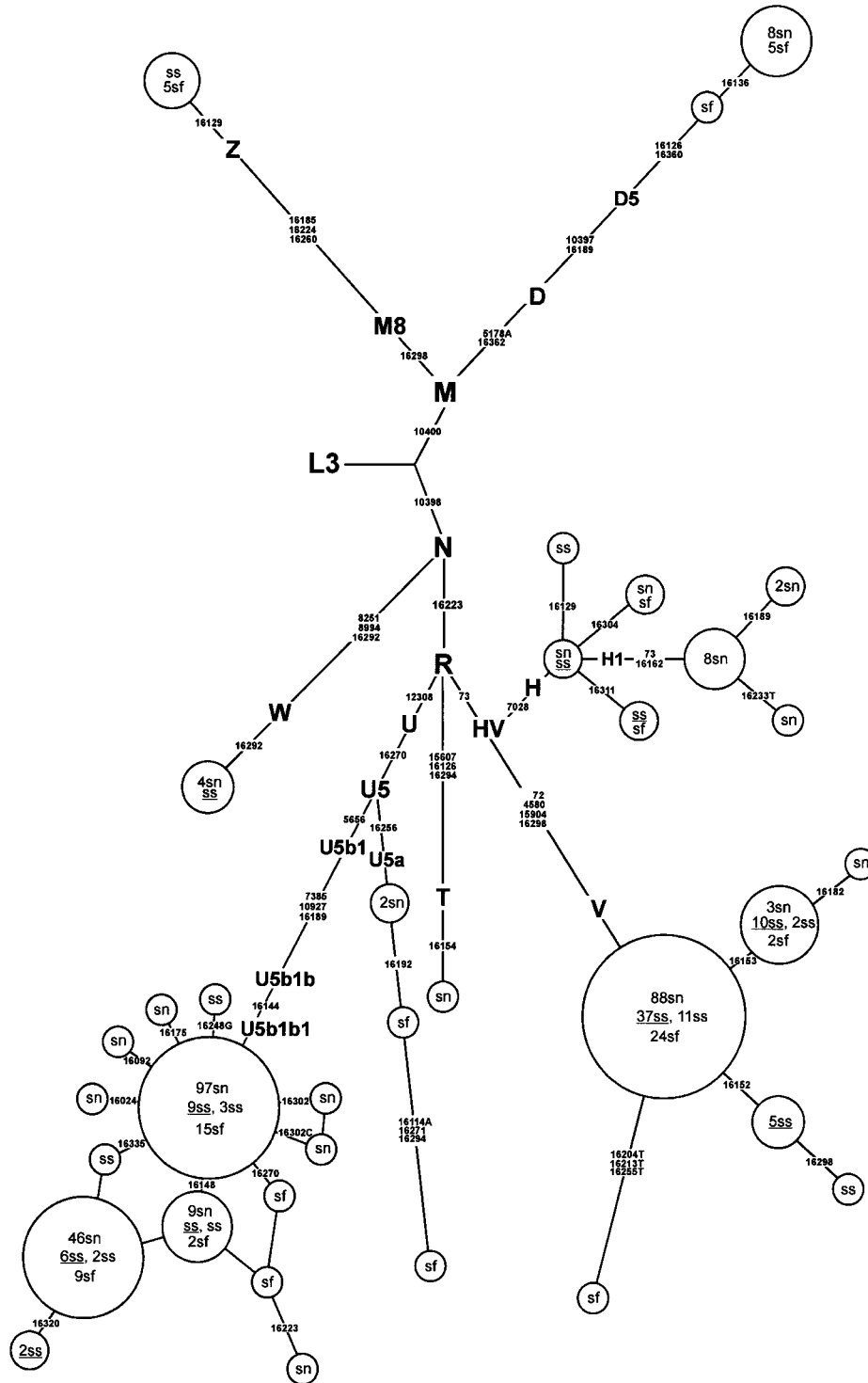


Figure 1 Phylogenetic network of 445 Saami mtDNA HVS-I sequences. Only those coding-region markers that have been analyzed in this study are shown (for finer resolution of haplogroup U subbranches, see fig. 3). Observed mutations are numbered according to the revised Cambridge Reference Sequence (Anderson et al. 1981; Andrews et al. 1999). The tree is rooted in haplogroup L3. Variable nps are shown on the links; nucleotide change is specified by suffixes only for transversions. Nodes indicate different haplotypes and have sizes that are proportional to their frequencies. HVS-I sequences are from Sajantila et al. (1995), using the corrections given by Bandelt et al. (2001) ($n = 114$); from Dupuy and Olaisen (1996) ($n = 197$); from Delghandi et al. (1998) ($n = 61$); and from the present study ($n = 73$, *underlined samples*). The analysis of coding region variation has been performed for only the 73 samples analyzed in the present study; haplogroup affiliations for data published elsewhere are inferred from HVS-I sequences. sf = Saami from Finland, sn = Saami from Norway, ss = Saami from Sweden. Note that the presence of three transversions reported in a single haplotype (sf) from haplogroup V (Sajantila et al. 1995) has not been reconfirmed by an independent study.

complete sequences, these lineages belong to subhaplogroup H1, defined by the coding region transition at np 3010 (Finnilä et al. 2001). We notice here that HVS-I haplotypes with a transition at np 16162 in the Volga-Ural area people (Bermisheva et al. 2002) and other European populations studied by us belong exclusively to this branch of subhaplogroup H1 (authors' unpublished data). This variant of mtDNA can be found both in western and eastern Europe, being as frequent in Germanic-speaking Scandinavians and the Germans as among the Norwegian Saami but absent in the Finnish and Swedish Saami (table 2). Though present in several Volga-Finnic populations, H1 haplotypes with mutation 16162 are extremely rare or absent in almost 2,000 Siberian Ugric-, Samoyedic-, and Altaic-speaking people (table 1) as well as in central Asians (Comas et al. 1998; Metspalu et al. 1999)—that is to say that this clade has an overwhelmingly European phylogeographic pattern. Its presence only in the Norwegian Saami sample may have been generated by admixture with the Norwegian population. This inference is supported by the presence of one H1 haplotype, with HVS-I motif 16162–16189, found among the Saami, in the Norwegian sample (Helgason et al. 2001). This haplotype has not been found in any other population analyzed in the present study.

Only a minor portion of the Saami maternal lineages (average ~5%) that exhibit restricted diversity belong to haplogroups that are characteristic of Asian populations—that is, D5 and Z (table 1). These eastern Eurasian haplogroups are significantly more frequent ($P < .05$) among the Finnish Saami compared with Norwegian and Swedish Saami samples (table 2). Such fluctuations in haplogroup frequencies could be due to genetic drift or just due to stochastic variation in relatively small samples. At the same time, the similar pattern of mtDNA haplogroup distribution found in different subpopulations of the Saami provides evidence of their common genetic background.

Saami Y-Chromosomal Haplogroup Pattern and Frequencies

The Y-chromosomal variation of 35 Swedish Saami, published by Rosser et al. (2000), was further analyzed to improve the resolution of paternal lineage clusters according to the YCC (2002). For comparison, data from different European and Siberian populations were used (table 3). To include the data published before the high-resolution nomenclature of biallelic markers (YCC 2002) was available, a combination of the results of the analysis of biallelic markers and polymorphisms of STRs was used, when possible (Zerjal et al. 2001), to infer the haplogroup frequencies presented in table 3. In some cases (haplogroups N3 and R1a), the updating of the data was simple and unambiguous. In the case of haplogroups R1b and

I, the classification of the samples was more problematic. However, the STR pattern of those haplogroups in combination with the typed biallelic markers is, in most cases, haplogroup-specific enough to make the misclassification of the samples highly unlikely. The probability of misclassification is higher in the data set from Raitio et al. (2001), in which only some informative biallelic markers and no STRs were scored. Therefore, these samples are left at a lower resolution level in table 2. Detailed criteria used in the process of deduction are given in the footnotes of table 3.

Three major haplogroups—N3, I, and R1a—comprise >80% of the Saami Y-chromosomal gene pool (table 2) and appear, likewise, as the major haplogroups in northeastern Europe (table 3). The nearly equal distribution of the Y-chromosomal variants among different Saami populations strongly supports their common paternal history. The comparison of the Y-chromosomal haplogroup frequencies in different subpopulations shows that, similar to mitochondrial haplogroup frequencies, some Y-chromosomal haplogroups (J and R1a) exhibit notable variation between geographic subpopulations of the Saami (table 2).

Haplogroup N3, the most frequent haplogroup in the Saami population, is distributed in eastern European and northern Asian populations but it is rare or absent in western Europe (table 3). All analyzed Swedish Saami N3 lineages fall into subcluster N3a, defined by M178 (YCC 2002). Although N3a is widespread in Siberia, other haplogroups, characteristic of Samoyedic-speaking and other Siberian populations (such as C and Q), are either almost absent in Baltic-Finnic populations, including the Saami, or are only sporadic, as for haplogroup N2, which is found only among Volga region Finnic speakers (table 3).

The second largest haplogroup, I, corresponds to roughly one-third of the Saami Y-chromosomal lineages. It is widespread in Europe but virtually absent in Asian populations (table 3). The defining mutation of haplogroup I, M170, most likely arose in Europe (Semino et al. 2000). It is well dispersed over the continent, as well as among Volga River basin Finnic and Turkic speakers (table 3). At the current level of resolution, the phylogenetic reconstructions do not identify the geographic origin of haplogroup I in Europe. Nevertheless, its virtual absence among Samoyeds as well as among Ugric-speaking Mansis and Khants suggests that these populations have not shared a recent ancestry with the Saami. Indeed, the high frequencies of haplogroup I in the Norwegians, Swedes, Finns, and the Saami (table 3) suggest that haplogroup I represents the heritage from the very first settlers of Fennoscandia. Analyses of microsatellite variation of the Saami haplogroup I Y chromosomes reveals that 9 of 10 Saami M170 chromosomes share the same modal microsatellite haplotype (6/9) or its de-

rivatives with other Nordic haplogroup I chromosomes (authors' unpublished data). The latter corresponds to haplogroup 2 chromosomes with alleles 14-23-10-11-13, defined by DYS19-390-391-392-393, respectively, in the studies by Helgason et al. (2000), Zerjal et al. (2001), Weale et al. (2002), and Capelli et al. (2003). These haplotypes form a subclade of haplogroup I that is different from the variety of equally abundant M170 chromosomes found in the Adriatic coastal region, where the Dinaric Modal Haplotype (16-24-11-11-13) is common (Barac et al. 2003).

Haplogroup R1a, encompassing 11% of the Saami Y-chromosomal gene pool, is a frequent Y-chromosomal variety in eastern Europe, but it is also found in Siberia, the Altai Mountains (table 3), and India (Kivisild et al. 2003). Like haplogroup I, it is absent among Nenets, the largest Samoyed population, living partly in north-east Europe. Haplogroup R1a is present in the Swedish and Kola Saami at frequencies that are comparable to those observed among other Scandinavian and north-eastern European populations, but it is relatively rare in Finland, both in the Saami and non-Saami populations (table 3).

Haplogroup R1b is present in the Saami population at a level of 4%. It is the most frequent haplogroup in western Europe, especially among the French, and it is relatively frequent in Scandinavian Germanic-speaking populations, but it has not been found among the Finns. In the Volga-Ural region populations, R1b is present at frequencies similar to those of the Saami (table 3).

Haplogroups J and E, found solely among Kola Saami (table 2), may have arisen as a recent contribution from the neighboring northern Russian population, since these Y-chromosomal variants are present there (Wells et al. 2001).

PC Analysis

The results of the PC analysis based on mtDNA haplogroup frequencies (fig. 2A) illustrate why the Saami are identified as mitochondrial genetic "outliers" in Europe. Here, it is the relative haplogroup proportions and not the phylogeographic affiliations that are distinctive. The first PC (fig. 2A) reflects predominantly the differences between frequencies of haplogroups characteristic of the eastern and western parts of Eurasia (H, J, V, and U5 vs. A and M). All Saami subpopulations cluster together as a distinct group, but the distance between the Saami and native Siberians is much greater than between the Saami and other Europeans. Different distributions of the populations along the axis of the second PC arise primarily from the different proportions of haplogroups H, U5, and V in the populations. In addition, the lack of haplogroups J, U4, and A among the Saami plays a relatively important role here.

Figure 2B shows a similar analysis undertaken on the Y-chromosomal haplogroup frequencies. Here, the first PC is determined, on the one hand, by the western Eurasian-specific haplogroups I, R1a, and R1b and, on the other hand, by Asian-specific haplogroup C and by the largely Siberian-specific N2, which both separate all Samoyeds and Ob-Ugric-speaking populations (except Selkups) from the Saami. In contrast to that of other Samoyedic-speaking populations, the Selkup Y-chromosomal pool is dominated by eastern Eurasian haplogroup Q, which explains their solitary location on the second dimension of the PC graph. Two Saami subpopulations map close together and are placed in the immediate vicinity of the Finns, Volga-Finnic, and Volga-Turkic populations, as well as the Russians. The latter two are characterized by haplogroup N3 at moderate frequencies (table 3). Furthermore, at this resolution, Germanic-speaking populations (including Scandinavian Norwegians and Swedes) and the French form an additional cluster that is close to other European populations included in the analysis.

Phylogeography of Haplogroup U5b1b and the "Saami-Specific" Motif (U5b1b1)

Haplogroup U5b is found at low frequencies all over Europe (Richards et al. 1998). A distinct phylogenetic subbranch of U5b carries the "Saami-specific" HVS-I motif defined by 16144-16189-16270 in the study by Sajantila et al. (1995) and has been named "U5b1" by Richards et al. (1998). All U5b sequences share two diagnostic synonymous substitutions at nps 7768 and 14182 (see fig. 3A). The major U5b subset found among the Finns contains a derived G allele at noncoding np 5656 and a synonymous substitution at np 12618 (Finnilä et al. 2001). Through use of complete mitochondrial sequence data, it has previously been demonstrated that the Finnish sequences containing the "Saami-specific" HVS-I motif share an additional synonymous mutation at np 10927, which is often associated with another transition at np 7385 (Finnilä et al. 2001).

To study the phylogeography of the "Saami-specific" branch of U5b, an analysis of np 5656 variation among the relevant genomes was performed. The results reveal (see table 4) that 95 of 160 samples carried the derived 5656G allele and belong, thus, to a subhaplogroup referred to as "U5b1." We note that this subhaplogroup is different from the U5b1 branch defined by Richards et al. (1998) using HVS-I data alone. Here, "U5b1" refers to a deeper phylogenetic node of U5b (see fig. 3A). The transition at np 7385 was always found to be associated with a transition at np 10927 and is referred to as "U5b1b." This cluster also includes the "Saami-specific" subclade, which we name here as "U5b1b1" (fig. 3). Notice that the sequence motif 16189-16192-

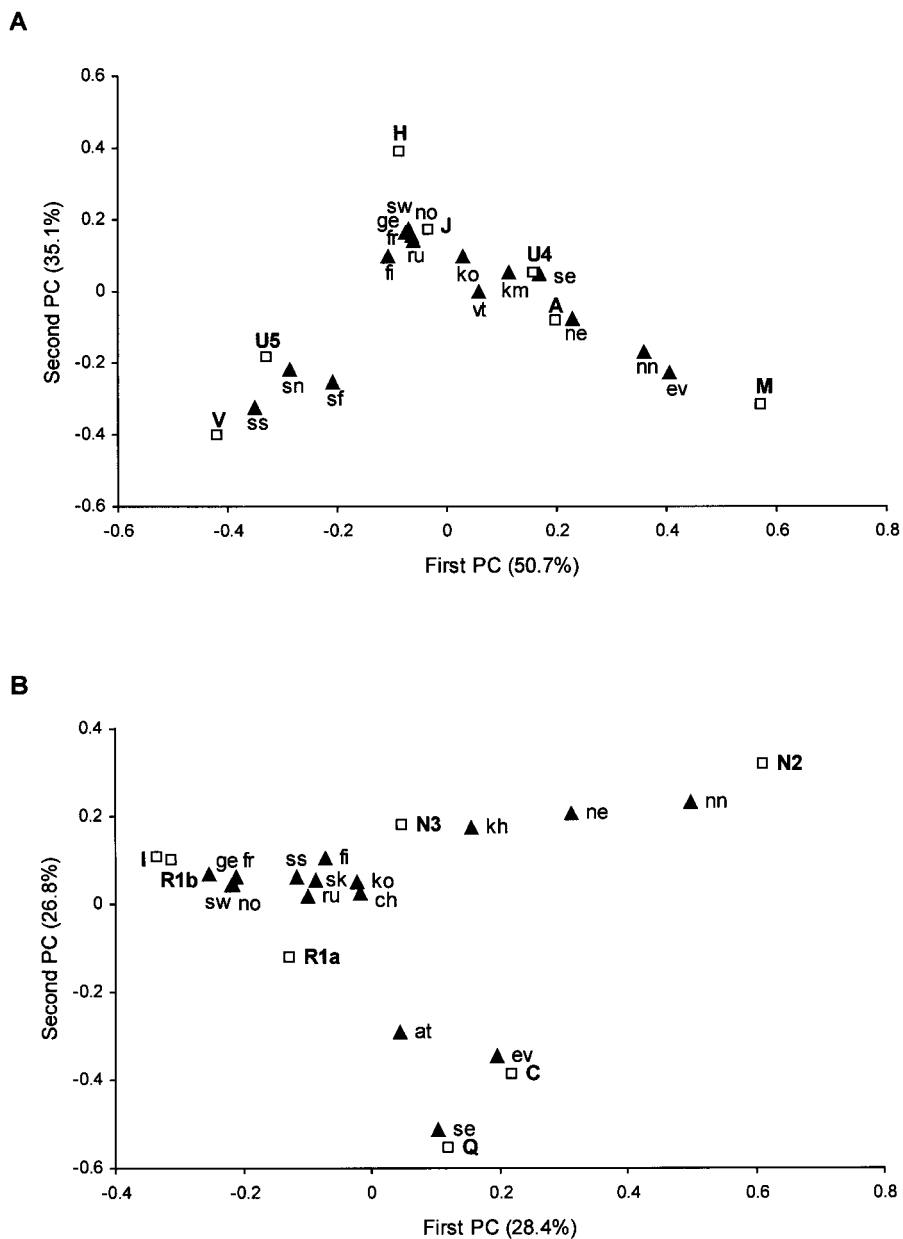


Figure 2 PC analysis based on mtDNA (A) and Y-chromosomal (B) haplogroup frequencies in some European and Siberian populations. Only the seven haplogroups (squares) having the main impact on the scatter plot have been used (see the “Subjects and Methods” section). Numbers in parenthesis indicate the proportion of the total genetic information retained by a given PC. The Saami population is subdivided according to the present location of the subpopulations. Population data (triangles) are the same as in tables 1 and 3 and are listed here in alphabetical order as follows: at = Altaians, ch = Chuvashes, ev = Evenks, fi = Finns, fr = French, ge = Germans, kh = Khants, km = Khants and Mansis, ko = Komis, ne = Nenets, nn = Nganasans, no = Norwegians, sf = Saami from Finland, sk = Saami from Kola Peninsula, Russia, sn = Saami from Norway, ss = Saami from Sweden, se = Selkups, sw = Swedes, vt = Volga-Uralic Turkic-speakers (Bashkirs and Chuvashes). Inclusion of all populations listed in tables 1 and 3 did not change the overall outcome (data not shown).

16270 in U5b1 appears to be associated with at least three independent subhaplogroups of U5b: U5b* (5656A), U5b1*/U5b1a (5656G, 7385A, and 10927T), and U5b1b (5656G, 7385G, and 10927C) (fig. 3; table 4). Therefore, reliance on published HVSI sequences alone, without regard to the relevant coding region information, makes

the exploration of the phylogeography of haplogroup U5b1b ambiguous, and these sequences were not included in the analysis.

The 5656G allele, including all major subsets of U5b1, is broadly distributed both in western and eastern Europe (fig. 3A; table 4). The U5b1b subclade is found all

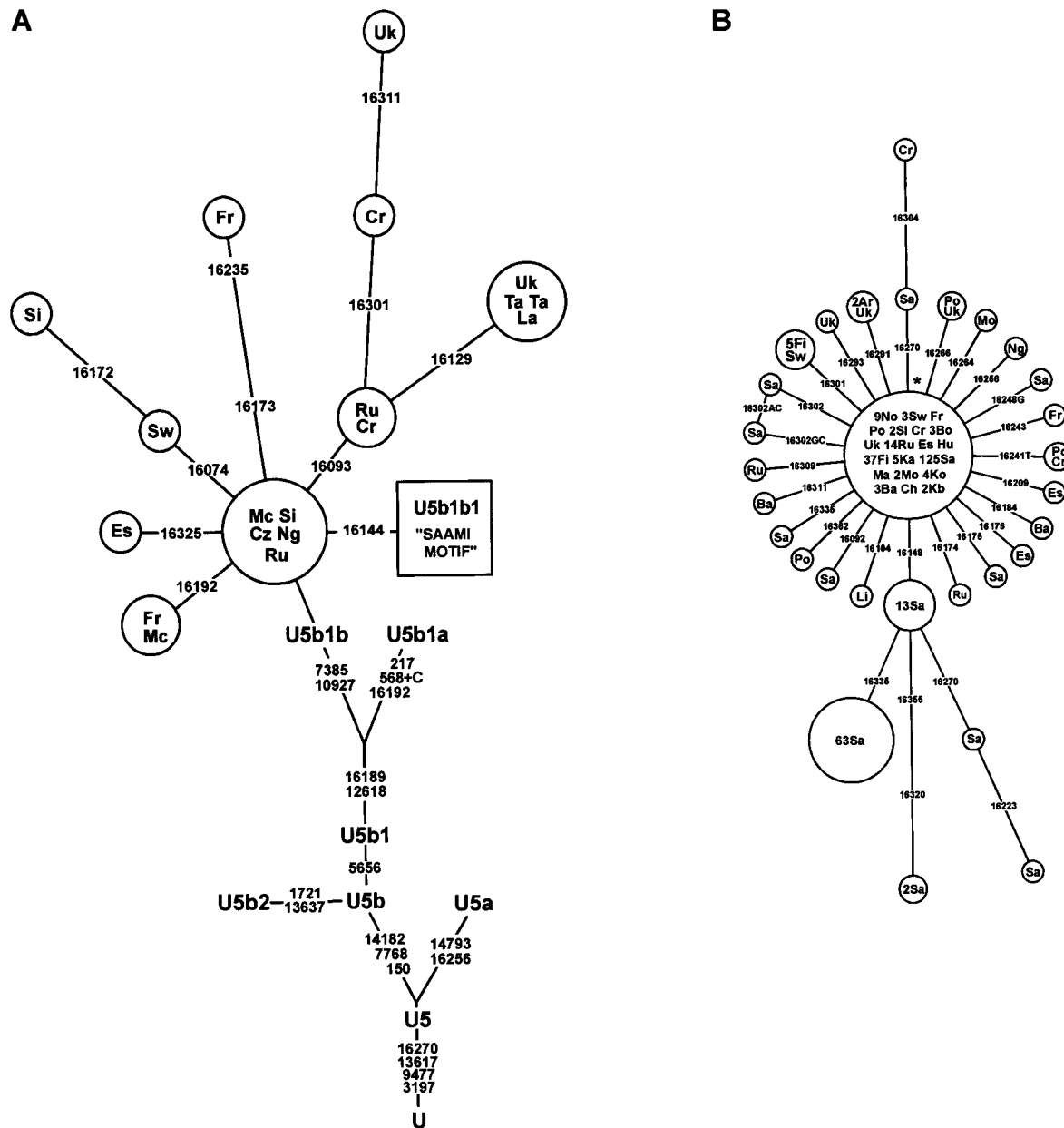


Figure 3 A, Phylogenetic network of U5b1b lineages based on HVS-I sequences and its position in the phylogeny of haplogroup U. Sequence information from Herrnstadt et al. (2002) and Finnilä et al. (2001) has been used for the coding region and HVS-II (see also table 4). The nucleotide positions relative to the revised Cambridge Reference Sequence (Anderson et al. 1981; Andrews et al. 1999), at which two nodes differ, are listed along links. Nucleotide changes are specified by suffixes only for transversions; “+” indicates an insertion. Note that we have redefined subclade U5a of Finnilä et al. (2001) and Herrnstadt et al. (2002) as “U5b2,” on the basis of its position in the phylogenetic tree. U5b1b1 haplotypes are shown as the square labeled as “Saami motif” and are further refined in panel B. B, Phylogenetic network of 330 U5b1b1 lineages based on HVS-I sequences. The star indicates the basal node (transitions in nps 16144, 16189, and 16270). Population sizes and U5b1b1 frequencies are shown in table 1. Ar = Armenians, Ba = Bashkirs, Bo = Bosnians, Ch = Chuvashes, Cr = Croats, Cz = Czechs, Es = Estonians, Fi = Finns, Fr = French, Hu = Hungarians, Ka = Karelians, Ko = Komis, La = Latvians, Li = Lithuanians, Ma = Maris, Mc = Moroccans, Mo = Mordvin, Ng = Nogays, No = Norwegians, Po = Poles, Sa = Saami, Sl = Slovaks, Ru = Russians, Si = Sicilians, Sw = Swedes, Ta = Tatars, Uk = Ukrainians. For further information, see the legend to figure 1.

Table 5
Coalescence Ages for Different Subsets of Subhaplogroup U5b1b1

Set of Sequences Considered ^a	<i>n</i>	ρ^b	<i>T</i> ^c (years)	ΔT^d (years)
U5b1b1 (without Sa)	118	25/118 = .212	4,300	1,400
U5b1b1 in Scandinavia (without Sa)	55	6/55 = .109	2,200	2,200
U5b1b1 in Scandinavia (with Sa, without subfounder 16148)	187	11/187 = .059	1,200	700
U5b1b1 in eastern Europe (Es/Li/ Ma/Mo/Ko/Ru/Uk/Po/Ba/Ch)	47	13/47 = .277	5,600	1,700
U5b1b1 in southern and western Europe (Bo/Cr/Sl/Hu/Fr)	11	3/11 = .273	5,500	3,200

^a Population codes are the same as those used in figure 3.

^b Average mutational distance to the founder haplotype of the cluster.

^c Coalescence time, calculated by means of ρ with a mutation rate of 1 transition per 20,180 years in the HVS-I segment between nps 16090 and 16365 (Forster et al. 1996).

^d SD for ρ , calculated as in the study by Saillard et al. (2000).

over Europe, but it occurs in western and central Europe with notable sequence variation. The haplotype diversity (excluding subclade U5b1b1) is 0.96. We note that U5b1b was also identified in a northwestern African population, among the Moroccans (fig. 3A). In contrast, its diversity in eastern Europe is much lower. There, the haplotype diversity (excluding subclade U5b1b1) is 0.79, whereas most of the U5b1b sequences in eastern Europe belong to the U5b1b1 branch (fig. 3A and 3B). In the Eurasian cohort, U5b1b (other than U5b1b1) is absent from native Siberians and is notably absent from the Ob-Ugric populations and the Samoyeds.

Most importantly, the data indicate that U5b1b1, the only subcluster of U5b in the Saami population, is present outside the Scandinavian-Baltic and the Volga-Uralic regions—namely, in the French, Croatian, Bosnian, Slovenian, Czech, Russian, Ukrainian, Polish, and Hungarian mtDNA pools—and, further, is present even in the Caucasus, among the Nogay, Kabardinian, and Armenian mtDNAs (fig. 3B). Thus, this subhaplogroup is much more widely distributed than was believed previously (Sajantila et al. 1995). Two principal haplotypes, differing by one mutational step, define the Saami U5b1b1 (fig. 3B). One, with transitions at nps 16144, 16189, and 16270, can be identified as the founder haplotype because of its presence in many other populations. The second, containing an additional transition at np 16148, is so far exclusive to the Saami population. This subfounder comprises 38% of their U5b1b1 mtDNAs and is present in all studied subpopulations of the Saami. Furthermore, no other derivatives of the U5b1b1 founder node present in the Saami sample was identified in other Scandinavians, including the Finns, irrespective of the previous observation that the northern-central Finnish population is relatively rich in U5b1b1 (Meinilä et al. 2001). Thus, the “leakage” of the Saami U5b1b1 to neighboring populations seems to be rather limited. The coalescence time of

all non-Saami U5b1b1 lineages in Europe (see fig. 3B) is $4,300 \pm 1,400$ years BP (table 5). This is approximately the same as that for the eastern or western-southern European subsets but is older than that observed for Scandinavians.

Discussion

Samoyed/Siberian Heritage of the Saami Population?

Uralic-speaking Samoyeds, Khants, Mansis, and Altaic-speaking Siberians virtually lack the European mtDNA haplogroups V and U5b1b1 that predominate in the Saami mtDNA pool (fig. 1; table 1). Eastern Eurasian mtDNA variants in the Saami are represented by a restricted set of lineages that belong to superhaplogroup M. In this respect, the Saami do not differ markedly from Finnic-speaking Karelians, Maris, Komis, Udmurts, or northern Russians, all of whom possess haplogroups of eastern Eurasian origin at similar frequencies (table 1). This minor part of the Saami mtDNA pool consists of two branches of the eastern Eurasian mtDNA tree—D5 and Z1. According to published data, the frequency of haplogroup D5 is relatively high in China (Yao et al. 2002). D5 is also present among Mongols and Siberians (Kolman et al. 1996; Derbeneva et al. 2002b). However, the Saami haplogroup D5 lineages, with the HVS-I motif 16126-16136-16360 and its derivatives (defined as “D5b” by Derenko et al. 2003), have been identified only in some northern and eastern European populations (among Karelians, Finns, Estonians, North-Russians, and Komis) and in some Siberian populations but not in Samoyeds (table 1). This suggests, again, the lack of gene flow from Samoyeds to eastern Europe.

Haplogroup Z, a subcluster of the M8 clade within the haplogroup M family of mtDNA (Kivisild et al. 2002), is found at highest frequencies in the northeastern

Asians: the Itelmens and Koryaks (Schurr et al. 1999). It is also present in several Siberian populations, including the Altaic people (table 1). Though not identified in a large data set of the Yakuts (Fedorova et al. 2003; Pakendorf et al. 2003), haplogroup Z has been observed among several Finnic- and Turkic-speaking populations of the Volga-Ural region (Bermisheva et al. 2002). It is curious that it is more frequent there in Finnic- than in Turkic-speaking populations. The absence of haplogroup Z from most of the Siberian Uralic-speaking populations (Samoyedic-speaking Nenets and Selkups, as well as Siberian Ob-Ugric-speaking Khants and Mansis) (table 1) is therefore striking. We note that all haplogroup Z lineages that are found in eastern Europe belong to a subhaplogroup Z1, characterized by transitions at nps 151, 10325, and 16129 within the Z phylogeny (Kong et al. 2003a, 2003b). A matching HVSI founder haplotype has been observed in the Koryak and the Itelmen populations (Schurr et al. 1999). The limited diversity of haplogroup Z in Europe suggests its relatively recent spread west of the Urals.

The sister clade of Z—haplogroup C—is far more diverse and frequent than haplogroup Z in eastern Eurasians (Derenko et al. 2003), as well as in the populations of the Volga-Ural region (Bermisheva et al. 2002), but it is absent among the Saami. Here, again, the lack of haplogroup C in the Saami is specifically indicative of the absence of possible genetic links between the Saami and the Samoyeds. Indeed, the only Samoyedic-speaking population that also inhabits northeastern Europe and is thus geographically close to the Saami, the Nenets, has haplogroup C as the most frequent (~30% frequency) variant of mtDNA.

The predominant Saami Y-chromosomal haplogroup N3 has a nearly uniform circumpolar distribution in Eurasia (table 3). The closely related N2 lineages are frequent in Siberian and Volga-Uralic populations. Thus, it is likely that haplogroup N variation represents a prehistoric link between the Siberian and eastern European/proto-Finnic populations via their paternal heritage. The improved resolution of the Y-chromosomal phylogenetic tree (Jobling and Tyler-Smith 2003) reveals an ancestral node shared by haplogroups N and O, with the latter restricted largely to eastern Asia. This connection is intriguing, but it is still unclear when and where this common ancestor first appeared. Nevertheless, one does not need to postulate a recent Siberian flow of Y chromosomes into the Saami gene pool to explain their high N3 frequency. First, such a flow from Samoyedic-speaking aboriginal Siberians to the Saami Y-chromosomal pool would predict the presence there of haplogroup N2 and/or haplogroup Q, widely spread in Samoyeds (Karafet et al. 2002). Second, the much higher diversity of N3 in eastern Europe than in Siberia (Villemis et al. 1998; Rootsi et al. 2000) suggests that eastern Europe, rather

than Siberia, is a possible origin of the earliest expansion of this haplogroup in northern Eurasia. Third, the lack of Y-chromosomal haplogroup C in Saami contrasts with its high frequency among Tungusic-speaking native Siberians (such as the Evenks and the Evens) as well as among Mongolic-speaking Mongols, the Buryats, the Kalmyks, and the Turkic-speaking Kazakhs and Uzbeks (Wells et al. 2001; Karafet et al. 2002; authors' unpublished data). Therefore, without introducing specific additional ad hoc scenarios, these observations make it unlikely that there was recent Y-chromosomal flow from these Siberian populations into the gene pool of the Saami.

Origins of the Saami mtDNA and Y Chromosomes

Scenarios involving extremes of genetic drift, such as that due to repeated bottlenecks, could explain how the Saami mtDNA pool evolved as a narrow subset of that found in other European populations. Indeed, there are good reasons to believe that even a much larger Finnish population went through several “bottlenecks” in its demographic history (Nevanlinna 1972; de la Chapelle and Wright 1998; Kittles et al. 1999; Peltonen et al. 2000). Likewise, it is possible that, when the proto-Saami gene pool was *in statu nascendi*, it was restricted to only a few basic mtDNA haplotypes that were carried by the founding settlers—a plausible scenario during the “Paleolithic isolation.”

Torrioni et al. (1998, 2001) have suggested that the spread of haplogroup V in Scandinavia and in eastern Europe is due to its late Pleistocene/early Holocene expansion from a Franco-Cantabrian glacial refugium. Haplogroup V shows high diversity and the presence of pre-V lineages in Iberia and the islands of Croatia (Tolk et al. 2000; Torrioni et al. 2001). However, the new data on Volga River basin and Slavic-speaking populations (Bermisheva et al. 2002; Malyarchuk et al. 2002; present study) show that haplogroup V is also well present in eastern Europeans. Furthermore, haplogroup V lineages with HVSI transitions 16153 and 16298 (fig. 1) that are frequent in the Saami population are much more widespread in eastern than in western Europe (Torrioni et al. 2001; Bermisheva et al. 2002; authors' unpublished data). This indicates that haplogroup V might have reached Fennoscandia via central/eastern Europe (see fig. 4A). Such a scenario is indirectly supported by the absence, among the Saami, of the pre-V mtDNAs that are characteristic of southwestern Europeans and northwestern Africans and that are also present in Germans (Torrioni et al. 2001).

The phylogeography and the ancestry of the other components of the Saami mitochondrial profile have so far not been well understood. Here, we showed that mtDNA haplogroup U5b1b1—the set of lineages with

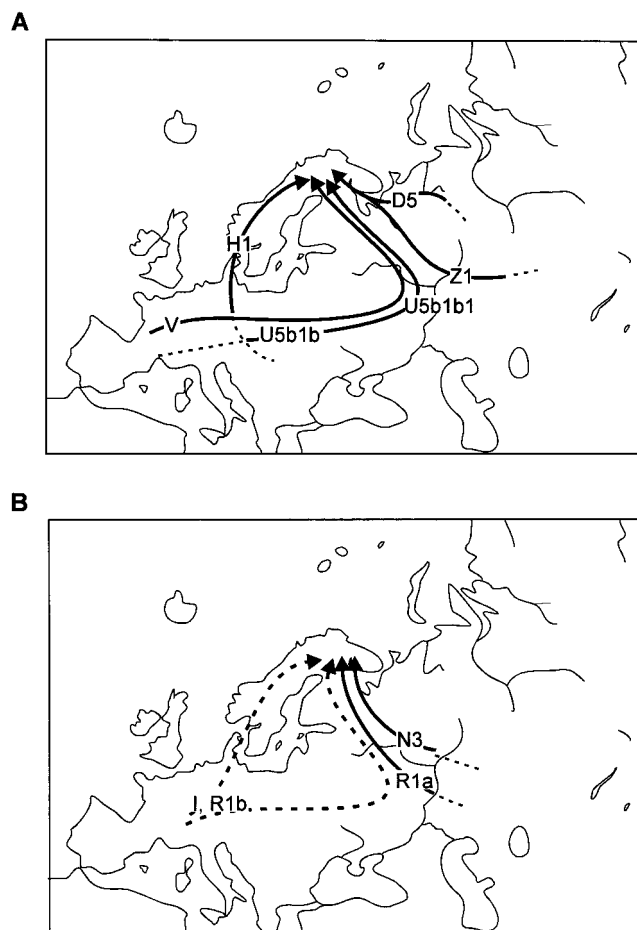


Figure 4 Schematic reconstruction of possible entry routes of the predominant Saami maternal (A) and paternal (B) lineages to Fennoscandia. Broken lines indicate that the exact place of origin/route of spread of the haplogroup is unsolved/not indicated.

the so-called “Saami-specific” motif—is spread, besides among the Saami, mostly in eastern Europe (fig. 3B). This might suggest that haplogroup U5b1b1 may have spread/arisen from eastern Europe. On the other hand, the considerable diversity of the U5b1b cluster in western and southern Europe suggests that these regions, rather than eastern Europe, were the likely place of origin of U5b1b. Thus, the distribution of U5b1b is similar to that suggested above for haplogroup V. Notice that this cluster, like haplogroup V, is also found in northwestern Africa (table 4). Hence, we envision an initial diversification of U5b1b in western Europe, followed by the spread of a particular subhaplogroup in eastern Europe, finally reaching Fennoscandia (but not the Samoyeds or any other aboriginal Siberians) via an eastern route (fig. 4A). Indeed, U5b1b1 is absent from a large sample set of Germans from Lower Saxony (Pfeiffer et al. 2001), and it is detected only in trace frequencies in

other western European populations. That makes it less likely that U5b1b1 entered the Saami mtDNA pool (or that the proto-Saami tribes carried it) directly from the west. The wide geographic distribution of both U5b1b1 and U5b1b in western Eurasian populations and the apparent absence of U5b1b “twigs” (except of U5b1b1) in Finno-Ugric speakers suggests that the latter may have originated before the differentiation of the European Finnic-speaking people.

Haplogroup H1 lineages most probably spread to Fennoscandia via a western route (fig. 4A). The diversity of H1 is relatively higher in Norwegian (0.76), Swedish (0.78), German (0.78), and Polish (0.80) populations than in Finnish (0.09), Estonian (0.35), Latvian (0.50), Karelian (0.0), and Volga-Uralic populations (highest among Komis: 0.40). Furthermore, as was mentioned above, the Saami may have obtained their H1 lineages from recent admixture with the Norwegians.

The two eastern Eurasian mtDNA variants, haplogroup Z1 and the particular subbranch of D5, have probably reached northeastern Europe not via the Arctic but via a more southern route across the southern Urals and, passing the Volga River basin (fig. 4A), left their “traces” among the gene pools of the Volga-Ural peoples, although not, as we have already stressed above, among Ob-Ugric and Nenets populations (table 1). Here, history and archeology provide several possible scenarios: not only events of historic times, like migrations of Huns, Avars, and Mongols, but also a likely influx of Asian tribes to eastern Europe during the early Holocene and contributing to the Kama culture of the upper Volga and Petchora basins (Kozłowski and Bandi 1984), could have been behind movements that brought a few selected and specific eastern Asian mtDNA variants to Fennoscandia. Note that northern Fennoscandia became accessible to humans at the very end of the Pleistocene/early Holocene, both from the west and the east (Donner 1995).

The Y-chromosomal haplogroups N3 and R1a, which make up ~60% of the Saami Y-chromosomal variants, have likely reached Fennoscandia from eastern Europe (fig. 4B), where these haplogroups can be found in high frequencies, as among the Saami. Haplogroups I and R1b, which together make up a third of Saami Y chromosomes, seem to have arisen in western Europe (fig. 4B). For R1b, this scenario is most plausible because it is a characteristically frequent Y-chromosomal variant in western Europe (table 3). In the case of haplogroup I, a specific pattern of STR variation in the Saami is close to that observed among other Scandinavians and western Europeans and is dissimilar to that observed in southern Europe.

We conclude that the phylogeography of mtDNA and Y-chromosome variants that correspond to the maternal and paternal gene pools of the Saami does not provide any evidence for the Saami population arising among

the northernmost Uralic-speaking populations—Siberian Ugric and Samoyedic speakers—or among any other aboriginal Siberians. The Samoyeds are the least genetically close to the Saami among the people of the Uralic language family, whereas nearly all of the mtDNA and Y-chromosomal heritage of the Saami can be adequately explained within the European pools of the two haploid genetic systems. This genetics-based reconstruction (fig. 4) is in agreement with the reconstruction of the spread of Ahrensburgian and Swiderian Mesolithic technologies in northern Europe, linking it with population expansion that can be likely traced back to the post–Last Glacial Maximum recolonization of the European north (Torroni et al. 2001; Tambets et al. 2003). The results also stress that the grouping of populations according to language families should be used exclusively only in a linguistic context.

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Electronic-Database Information

The URL for data presented herein is as follows:

Fluxus Engineering, <http://www.fluxus-engineering.com/> (for Network 3.1.1.1)

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