

Different Genetic Components in the Ethiopian Population, Identified by mtDNA and Y-Chromosome Polymorphisms

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Summary

Seventy-seven Ethiopians were investigated for mtDNA and Y chromosome-specific variations, in order to (1) define the different maternal and paternal components of the Ethiopian gene pool, (2) infer the origins of these maternal and paternal lineages and estimate their relative contributions, and (3) obtain information about ancient populations living in Ethiopia. The mtDNA was studied for the RFLPs relative to the six classical enzymes (*HpaI*, *BamHI*, *HaeII*, *MspI*, *AvaII*, and *HincII*) that identify the African haplogroup L and the Caucasoid haplogroups I and T. The sample was also examined at restriction sites that define the other Caucasoid haplogroups (H, U, V, W, X, J, and K) and for the simultaneous presence of the *DdeI*₁₀₃₉₄ and *AluI*₁₀₃₉₇ sites, which defines the Asian haplogroup M. Four polymorphic systems were examined on the Y chromosome: the *TaqI*/12f2 and the 49a,f RFLPs, the Y *Alu* polymorphic element (DYS287), and the sY81-A/G (DYS271) polymorphism. For comparison, the last two Y polymorphisms were also examined in 87 Senegalese previously classified for the two *TaqI* RFLPs. Results from these markers led to the hypothesis that the Ethiopian population (1) experienced Caucasoid gene flow mainly through males, (2) contains African components ascribable to Bantu migrations and to an in situ differentiation process from an ancestral African gene pool, and (3) exhibits some Y-chromosome affinities with the Tsumkwe San (a very ancient African group). Our finding of a high (20%) frequency of the "Asian" *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (++) mtDNA haplotype in Ethiopia is discussed in terms of the "out of Africa" model.

Introduction

The peopling of sub-Saharan Africa has been greatly affected by the Bantu expansions that originated near the confluence of the Niger and Benue rivers ~3,000 years ago (Cavalli-Sforza et al. 1994, p. 162). Both linguistic (Greenberg 1963) and genetic (Hiernaux 1975; Excoffier et al. 1987; Cavalli-Sforza et al. 1994, pp. 169–171) studies show that most sub-Saharan populations are related to each other, the most differentiated being Pygmy, Khoisan, and eastern African populations. Pygmies appear to be the most divergent, although some Pygmy groups show a certain degree of admixture with neighboring populations (Cavalli-Sforza 1986; Chen et al. 1995). Interestingly, Khoisan and Ethiopians display both great differences and important similarities with respect to each other. This has been clearly shown by the principal-components (PC) analysis (PCA) of African populations (Cavalli-Sforza et al. 1993; 1994, p. 191). Although the second PC places Ethiopians and Khoisan as the genetically most distant groups, the third PC indicates that they are closely related. Although these two groups are currently geographically separated by Bantu-speaking populations, archaeological findings suggest that Khoisan territory once extended to Ethiopia (Nurse et al. 1985, p. 105). In contrast to the situation for Bantu speakers, it has been proposed that both Khoisan and Ethiopians share some Caucasoid features, which were acquired at very different times (~20,000 or more years ago for Khoisan and beginning as recently as 3,000 years ago for Ethiopians) (for details, see Cavalli-Sforza et al. 1994, pp. 174–175). Linguistic data also attest to the separate evolution of these two populations. Khoisan speak unique languages that make use of click sounds (Cavalli-Sforza et al. 1994, p. 164), whereas most Ethiopians speak Afro-Asiatic (Cushitic, Omotic, and Semitic) languages.

Recently, genetic studies of African populations have been approached through the analysis of DNA markers (Wainscoat et al. 1986; Cann et al. 1987; Scozzari et al. 1988, 1994; Torroni et al. 1990; Soodyall and Jenkins 1992, 1993; Spurdle and Jenkins 1992; Graven et al.

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Table 1**Continent-Specific Haplogroup Mutations Tested in Ethiopians**

Haplogroup	Characterizing Mutation(s)
African ^a	
L	+ <i>Hpa</i> I ₃₅₉₂
Caucasoid: ^b	
H	- <i>Dde</i> I ₁₀₃₉₄ , - <i>Alu</i> I ₇₀₂₅
T	- <i>Dde</i> I ₁₀₃₉₄ , + <i>Bam</i> HI ₁₃₃₆₆ - <i>Ava</i> II ₁₃₃₆₇ , + <i>Alu</i> I ₁₅₆₀₆ , - <i>Msp</i> I ₁₅₉₂₅
U	- <i>Dde</i> I ₁₀₃₉₄ , A→G at 12308 ^c
V	- <i>Dde</i> I ₁₀₃₉₄ , - <i>Nla</i> III ₄₅₇₇
W	- <i>Dde</i> I ₁₀₃₉₄ , + <i>Ava</i> II ₈₂₄₉ , - <i>Hae</i> III ₈₉₉₄
X	- <i>Dde</i> I ₁₀₃₉₄ , - <i>Dde</i> I ₁₇₁₅
I	+ <i>Dde</i> I ₁₀₃₉₄ , - <i>Dde</i> I ₁₇₁₅ , - <i>Hae</i> II ₄₅₂₉ , + <i>Ava</i> II ₈₂₄₉ , + <i>Alu</i> I ₁₀₀₂₈ , + <i>Bam</i> HI ₁₆₃₈₉
K	+ <i>Dde</i> I ₁₀₃₉₄ , - <i>Hae</i> II ₉₀₅₂ , A→G at 12308 ^c
J	+ <i>Dde</i> I ₁₀₃₉₄ , - <i>Bst</i> NI ₁₃₇₀₄ , - <i>Hin</i> I ₁₆₀₆₅
Asian: ^d	
M	+ <i>Dde</i> I ₁₀₃₉₄ , + <i>Alu</i> I ₁₀₃₉₇

^a Source: Chen et al. (1995).

^b Source: Torroni et al. (1996).

^c Detected as *Hin*I polymorphism after a PCR amplification using a mismatched primer (see Torroni et al. [1996]).

^d Source: Ballinger et al. (1992) and Chen et al. (1995).

1995; Poloni et al. 1995; Armour et al. 1996; Soodyall et al. 1996; Tishkoff et al. 1996; Watson et al. 1996). The Ethiopian population, however, has not yet been the target of these studies, although it occupies a central geographic position with regard to the “out of Africa” model (Lewin 1987). In fact, it has been proposed that *Homo sapiens sapiens* left Africa both through Suez and by the Ethiopia–western India route (Cavalli-Sforza et al. 1993; Cavalli-Sforza et al. 1994, p. 195). In addition, the complexity of the ancient Ethiopians’ interactions with very different populations gave origin to the present “stunning heterogeneity of Ethiopia’s ethnic composition” (Levine 1974, p. 33).

In order to increase our knowledge of the genetic structure of Ethiopians and to better understand the relationships between Ethiopians and other African and non-African populations, we analyzed a sample of 77 Ethiopians, for a set of mtDNA and Y-chromosome polymorphisms. Because of their uniparental inheritance, these polymorphisms are particularly useful for tracing the separate ancestry of maternal and paternal lineages in human populations.

The Ethiopian mtDNAs were analyzed for the six core enzymes that can detect RFLPs specific to the major ethnic groups. In addition, we have searched for all those markers that define the Caucasoid haplogroups (table 1) not detectable with the six-core-enzyme analysis and for the simultaneous presence of *Dde*I₁₀₃₉₄ and *Alu*I₁₀₃₉₇ sites, which defines an eastern/southern Asian-specific haplotype, *Dde*I₁₀₃₉₄*Alu*I₁₀₃₉₇ (++) (Ballinger et al. 1992; Passarino et al. 1996c). Although virtually absent in the other examined sub-Saharan Africans (Chen et al. 1995;

Passarino et al. 1996a, 1996c), this haplotype was present (frequency 18%) in a smaller Ethiopian sample that we have studied previously (Passarino et al. 1996a, 1996c).

The Ethiopian Y chromosomes were analyzed for the following Y chromosome-linked polymorphic systems: the *Taq*I/12f2 RFLP, which consists of two allelic Y chromosome-specific bands, of 8 and 10 kb (Casanova et al. 1985); the *Taq*I/49a,f RFLP, which is characterized by numerous polymorphic bands (Ngo et al. 1986) and identifies >140 haplotypes (for a review, see Poloni et al. 1997); the Y *Alu* polymorphism (YAP), which is due to an *Alu* insertion (Hammer 1994); and the sY81 sequence-tagged site (STS) polymorphism, which is due to an A→G transition (Seielstad et al. 1994).

In addition, we have completed the typing of two Senegalese samples (the Mandenkalu and the Wolof) that we formerly studied for the *Taq*I polymorphisms revealed by probes 49a,f (both samples: Torroni et al. 1990; Excoffier et al. 1996a, 1996b) and 12f2 (Wolof: Brega et al. 1987). These data were used to construct mtDNA and Y-chromosome haplotypes, and phylogenetic analyses were performed. The frequencies and phylogenetic relationships of these haplotypes served as the bases for our investigation into the evolutionary history of maternal and paternal lineages in the Ethiopians.

Peoples of Ethiopia

The first known inhabitants of Ethiopia were hunting peoples whose scattered descendants remained in southern Ethiopia. As early as the 8th millennium B.C., a Negroid element appeared, probably only in the southern part of the country, and mingled with people arriving later (Encyclopaedia Britannica 1964, vol. 8, p. 782).

By ~4,000–5,000 years B.C., Afro-Asiatic peoples (proto-Cushites, proto-Omotc speakers, and proto-Semites) were present in Ethiopia (Levine 1974). They probably derived from the Sahara (Levine 1974) or from Arabia (Encyclopaedia Britannica 1964, vol. 8, p. 782), although a local Ethiopian origin of Afro-Asiatic languages has also been hypothesized (Levine 1974). These early Ethiopians underwent a strong diversification, and, by 2,000 B.C., the following different clusters of peoples (Levine 1974) were present:

1. the Omotic speakers (divided into 50 small societies), who were agriculturists and who settled in the southwestern part of the country;
2. the Cushites, who were divided into (a) northern Cushites (Beja), who were nomadic pastoralists living in the northern lowlands, (b) the central Cushites (Agaw), who settled on the northwestern plateau highlands and who practiced agriculture (cereals); and (c) the eastern

Table 2

mtDNA Types Detected by RFLP Analysis with the Six Classical Enzymes, and Their Frequencies, in Ethiopians and Relevant Comparison Populations

TYPE ^a	ENZYME MORPHS ^b	FREQUENCY IN (%)				
		Ethiopians (N = 77)	Niger-Congo Speakers ^c (N = 321)	Khoisan ^d		Caucasoids ^e (N = 298)
				Sekele (N = 49)	Nama (N = 46)	
Previously published:						
1-2	(2.1.1.1.1.2)	51.9 ^f	24.3	2.0	6.5	62.1
1-7	(2.1.1.1.1.7)	2.6 ^f				.3
2-2	(3.1.1.1.3.2)	14.3	31.8			1.0
2-10	(3.1.1.1.3.10)		1.2			
3-2	(3.1.1.2.2.2)		.9	14.3	54.3	
4-2	(3.1.1.3.2.2)			40.8		
5-2	(3.1.1.2.5.2)		.3	2.0	6.5	
6-2	(2.1.2.1.1.2)	2.6				6.7
7-2	(3.1.1.1.1.2)	5.2	21.8	20.4	6.5	
8-1	(1.1.1.1.1.1)		1.9			
10-2	(3.1.1.1.2.2)		1.9	12.2	6.5	
11-2	(2.2.3.1.5.2)					2.3
18-2	(2.3.1.4.9.2)	1.3				7.7
21-2	(2.1.1.1.2.2)	2.6		4.1	13.0	4.0
22-2	(2.1.1.1.5.2)					1.7
24-2	(2.1.1.4.2.2)					1.0
27-2	(2.1.4.1.6.2)		.6			
28-2	(2.1.1.4.1.2)	1.3				1.0
34-2	(3.1.2.1.3.2)		.9			
38-2	(2.1.1.1.1.2)					.7
39-2	(2.1.4.1.1.2)	2.6	4.0			
52-2	(2.1.1.1.1.2)		.9			
47-2	(2.1.1.1.3.2)					2.0
56-2	(2.1.1.1.6.2)	3.9	.3			
57-2	(2.3.1.4.13.2)					3.0
63-2	(3.1.7.1.3.2)		.9			
64-2	(2.1.12.1.1.2)		.6			
68-2	(2.1.1.12.1.2)		.6			
72-2	(2.1.1.1.12.2)	1.3				
75-2	(2.1.1.4.9.2)					1.3
78-2	(2.4.3.1.28.2)					.7
79-2	(2.5.1.1.6.2)					.7
139-2	(7.1.6.13.1.2)				4.3	
154-2	(3.1.1.17.1.2)		.9			
New:						
209-2	(2.1.2.1.6.2)	1.3				
210-2	(3.1.1.20.1.2)	3.9				
211-2	(2.1.1.21.1.2)	1.3				
212-2	(3.1.1.22.1.2)	1.3				
213-2	(2.1.16.1.1.2)	1.3				
214-2	(2.1.2.1.38.2)	1.3				
Other ^g			5.9	4.0	2.2	3.3

^a The classification for this enzyme is used for subtyping, since *HincII* data were not always included in the previous studies.

^b Order: *HpaI*, *BamHI*, *HaeII*, *MspI*, *AvaII*, and *HincII*.

^c Includes 40 Bantu (Johnson et al. 1983), 186 Senegalese (Scozzari et al. 1988), and 95 Cameroonians (Scozzari et al. 1988, 1994); Bantu, who were not classified for the enzyme *HincII*, were here considered *HincII*-2.

^d Source: Soodyall and Jenkins (1992).

^e Includes 118 Greeks (Astrinidis and Kouvatzi 1994) and 180 southern continental Italians (reviewed in Brega et al. 1994).

^f Approximately 30% of these molecules displayed the Asian *DdeI*_{10,394}*AluI*₁₀₃₉₇ (++) haplotype.

^g Include types observed in only one subject of a single comparison group.

Table 3

Frequencies of Associations between mtDNA *DdeI*₁₀₃₉₄/*AluI*₁₀₃₉₇ Haplotypes (See Table 4), Continent-Specific Haplogroups (See Table 1), and the Classical Enzyme Types (See Table 2) in Ethiopians, with Evaluation of Contribution of Different Ethnic Components

TYPE	<i>DdeI</i> ₁₀₃₉₄ / <i>AluI</i> ₁₀₃₉₇ (++) (N = 15)	<i>DdeI</i> ₁₀₃₉₄ / <i>AluI</i> ₁₀₃₉₇ (+-) (N = 41)			<i>DdeI</i> ₁₀₃₉₄ / <i>AluI</i> ₁₀₃₉₇ (--) (N = 18)				TOTAL
	M	Other	L	K	T	W	U	Other	
1	12	13					6	9	40
2			11						11
6		1		1					2
7			4						4
18					1				1
21		1				1			2
28	1								1
39		2							2
56	2								2
72		1							1
209				1					1
210			3						3
211								1	1
212			1						1
213		1							1
214		1							1
Total	<u>15</u>	<u>20</u>	<u>19</u>	<u>2</u>	<u>1</u>	<u>1</u>	<u>6</u>	<u>10</u>	<u>74</u>
	Asian (20.3%)	African (52.7%)			Caucasoid (5.4%)		Caucasoid or African (8.1%)	Uncertain origin (13.5%)	

Cushites, who also were agriculturists and who were differentiated into >20 different groups (including the Oromo, or Galla) and who settled in the southern part of the Rift Valley;

3. the Semites, who separated into two main branches, one on the northern plateau and one in the central part of the country, and who gave rise to seven distinct clusters with various kinds of livelihood.

These groups, the distribution of which has remained fairly constant ever since, experienced exogenous influences from Sudanese, Arabian, and Mediterranean peoples. The first external influence on Ethiopians came from Sudanese Nilotic speakers, who, in two waves, at 3,000 B.C. and 1,000 B.C., settled in the southwestern part of the country and partially intermixed with Omotic and eastern Cushitic speakers.

Migrations from the Arabian peninsula into Ethiopia, from the 1st millennium B.C. onward, were continuous. One of the most important occurred in the second half of the 1st millennium B.C., when southern Arabians brought Sabean culture into Ethiopia and originated the proto-Geeze-speaking group, from which Amhara, Tigrinya, and Gurage derived. Further Semitic migrations took place: Jews (in the first centuries A.D.), Syrian Christians (4th–6th century A.D.), and Arabian Muslims (11th–12th centuries A.D.); these influenced the Ethiopian groups and cultures. Finally, Mediterranean cultures (mainly from Egypt and Byzantium) penetrated Ethiopia, but they did not affect its ethnic composition (Levine 1974).

Subjects and Methods

Subjects

The Ethiopian sample was collected in the Black Lion Hospital of Addis Ababa and consisted of 77 unrelated males coming from different parts of Ethiopia; 55 were individuals hospitalized for trauma, and the remaining 22 were healthy hospital personnel. These subjects have been classified according to their language and the place of origin of their four grandparents; 19 were Oromo (Cushitic speakers), and 58 were from the northern part of the country and spoke languages derived from the Semitic Geeze (Amhara, Tigrinya, and Gurage). Since the analyses of the two groups did not show important differences, the data from both the Ethiopian groups have been pooled. The Senegalese sample, comprising 31 Wolof and 68 Mandenka DNAs, has already been described elsewhere (Scozzari et al. 1988; Graven et al. 1995).

DNA Extraction

Ethiopian blood samples were collected in EDTA, kept at 4°C, and transported to Pavia in ≤48 h. DNA was extracted from buffy coats, according to standard methods.

mtDNA Analyses

Restriction analysis, Southern blotting, and mapping were performed as reported by Johnson et al. (1983).

Table 4**Frequencies of mtDNA *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ Haplotypes in Ethiopians and Relevant Comparison Populations**

POPULATION (N)	FREQUENCY ± SE OF HAPLOTYPE (%)			REFERENCE(S)
	++	+-	--	
Ethiopian (74) ^a	20.3 ± 4.7	55.4 ± 5.8	24.3 ± 5.0	Present study
Sub-Saharan African (197)	1.5 ± .8	88.8 ± 2.2	9.6 ± 2.1	Chen et al. (1995), Passarino et al. (1996a)
Caucasoid:				
Middle Eastern (68) ^b	1.5	26.5 ± 5.3	72.1 ± 5.4	Passarino et al. (1996a)
Mixed (315)	1.0 ± .5	20.3 ± 2.3	78.7 ± 2.3	Torrioni et al. (1994b), Passarino et al. (1996a)
Indian (211) ^c	47.4 ± 3.4	6.2 ± 1.7	46.4 ± 3.4	Passarino et al. (1996a), (1996c)
Oriental (619)	53.8 ± 2.0	8.4 ± 1.1	37.8 ± 1.9	Ballinger et al. (1992), Torrioni et al. (1993b), (1994c)

^a Includes smaller sample reported elsewhere (Passarino et al. 1996c).

^b Includes 15 Jews, 20 Lebanese, and 33 Turks.

^c Indians are clearly differentiated from the other Caucasoids. The frequencies of haplotypes *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (++) and *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) in the Indian group are mean values of two-frequency north-south gradients with opposite direction (increasing for the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ [++] and decreasing for the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ [+]). These gradients were interpreted as being due to a different Indo-European contribution to the preexisting Indian gene pool (see Passarino et al. 1996c).

Restriction enzymes *HpaI*, *BamHI*, *HaeII*, *MspI*, and *HincII* (Promega) and *AvaII* (Boehringer Mannheim) were used according to the suppliers' directions. The probe was prepared as described by Passarino et al. (1993). The new or rare morphs that were produced by site acquisition were all further defined through appropriate analyses. The Caucasoid-specific restriction polymorphisms, untested by Southern blotting analysis, were examined by amplification of the relevant fragments, which were then digested with the appropriate enzymes (see table 1). The presence of *DdeI*₁₀₃₉₄ and *AluI*₁₀₃₉₇ sites was detected according to the method of Passarino et al. (1993).

Y-Chromosome Analyses

RFLP analyses involving the *TaqI*/12f2 (DYS11) and 49a,f (DYS1) polymorphisms were performed as described by Torrioni et al. (1990). Filters were hybridized first with the 49a,f probes and then, after being stripped, with the 12f2 probe. The probes and their origin have been described by Ngo et al. (1986) and Casanova et al. (1985), respectively. The presence of the YAP element (DYS287) was determined according to the method of Hammer and Horai (1995). The A→G transition at the sY81 STS (DYS271) was revealed by means of the procedure of Seielstad et al. (1994).

Phylogenetic Analyses

The evolutionary relationships among the Ethiopian mtDNA types and those reported for other African populations (Johnson et al. 1983; Scozzari et al. 1988, 1994; Soodyall and Jenkins 1992, 1993) were inferred by parsimony analysis (PAUP 3.0; Swofford 1992). The dendrograms were generated by midpoint rooting, using the Tree Bisection and Reconnection (TBR) algorithm. We terminated our search after 3,000 maximum-parsimony

(MP) trees were found, saving ≤10 trees for each replication.

Y-chromosome superhaplotypes were constructed by combining, for each individual, the phenotypes observed with each Y chromosome-linked polymorphic system. The evolutionary relationships among these superhaplotypes were determined by means of PAUP 3.0 (Swofford 1992). In these analyses, the gain and the loss of one of the 49a,f bands was considered as a single mutational event. The mutations 12f2-10 kb to 12f2-8 kb, YAP⁻ to YAP⁺, and sY81-A to sY81-G were assumed to have occurred only once and were weighted twice, relative to the possibly homoplastic 49a,f variations. The dendrograms were generated by midpoint rooting, using the TBR algorithm. After 1,000 replications 49 MP trees were obtained.

We have also performed the mtDNA and Y-chromosome PCAs, according to the method of Guglielmino et al. (1996). With this analysis, for each population it is possible to condense a large fraction of the information obtained, for all the genes tested, into a few metric values (for details, see Cavalli-Sforza et al. 1994, p. 28). In our case, the first two principal components account for the most important features of the multidimensional original sets. For the mtDNA analysis, the data of various populations pooled in table 2 were used separately. Additional control populations were also included (for details, see the legend to fig. 4A). For the Y-chromosome analysis, we used, for comparison, the populations analyzed for the compound haplotype YAP/12f2/49a,f (see the legend to fig. 4B).

Results

mtDNA Polymorphisms

Table 2 shows the mtDNA types detected by RFLP analyses using the six classical enzymes in the Ethiopian

Table 5

Frequencies of 49a,f /TaqI Y Chromosome-Specific Haplotypes in Ethiopians, Other Sub-Saharan Africans, and Middle Eastern Caucasoids

HAPLOTYPE ^a	POLYMORPHIC FRAGMENT ^b					MISSING FRAGMENT(S) ^c	FREQUENCY IN (%)				
	A	C	D	F	I		Ethiopians (N = 69)	Niger-Congo Speakers ^d (N = 175)	Khoisan ^e		Caucasoids: Jews ^f (N = 166)
								Nama+Omega San (N = 72)	Tsumkwe San (N = 23)		
Previously published:											
2	0	0	1	1	1		2.9				
3	1	0	0	1	0				4.3		
4	1	0	0	1	1			3.4			
5	2	0	0	1	1		27.5	68.6	33.3		
7	2	0	1	1	0			5.1		10.2	
8	2	0	1	1	1		27.5		1.4	19.3	
10	3	0	0	1	0			2.9	1.4	23.5	
11	3	0	0	1	1		24.6	4.0	12.5	1.8	
12	3	0	1	1	0				4.3	12.7	
13	3	0	1	1	1		2.9			4.8	
15	3	1	2	1	1					1.2	
18	4	0	1	1	1					3.0	
24	2	1	1	1	1					5.4	
25	0	0	0	0	1			1.7		1.2	
26	2	0	0	0	1		7.2	.6	9.7	30.4	
27	1	0	0	0	1			6.3		.6	
28	1	0	0	1	0	G		2.9			
30	2	0	0	1	0			1.1		1.8	
35	3	1	0	1	1					3.5	
50	3	0	0	0	0				4.2	26.1	
51	2/3	0	0	1	1				16.7	21.7	
53	3	0	0	0	1				5.5	.6	
55	4	0	0	1	1		2.9	.6			
57	2/3	0	0	1	0	B, H				8.7	
58	0	0	0	0	0				1.4	4.3	
68	2	0	1	1	0	B				3.6	
71	4	0	0	0	1				2.8		
73	3	1	0	0	1					1.2	
80	3/4	1	0	1	1					1.8	
New:											
116	2	0	0	1	0	G	1.4				
117	2/3	0	0	0	1		1.4				
128	3	0	0	1	0	G	1.4	1.6			
Other ^g								3.2	4.2		2.4

^a With the exception of the first eight haplotypes, all the others have been renamed according to the revised nomenclature of Poloni et al. (1997).

^b “0” and “1” denote presence and absence, respectively, of the band, except for the “A” fragment; for the latter, the numbers indicate which band of the “allelic” set is present, and; two numbers separated by a slash indicate presence of two “allelic” bands in the same haplotype, in which case a locus duplication was supposed (Torrioni et al. 1990; Spurdle and Jenkins 1992; Santachiara-Benerecetti et al. 1993).

^c All other fragments were always present.

^d Includes 64 Mandenkalu (Excoffier et al. 1996b), 80 other Senegalese, and 31 Cameroonians (Torrioni et al. 1990).

^e Source: Spurdle and Jenkins (1992).

^f Source: Santachiara-Benerecetti et al. (1993).

^g Includes haplotypes found in only one subject of a single comparison group.

sample. Similar data sets from relevant African and Caucasoid samples are also shown, for comparison. Six new types were observed: one is a new association of previously described morphs (type 209-2), whereas the others are due to five new morphs (types 210-2–214-2). These five new morphs include three for *MspI* (morphs 20–22) and one each for *HaeII* (morph 16) and *AvaII* (morph 38). The *MspI* new morphs 20 and 21 derive

from *MspI* morph 1 and are due to site gains in the 2,213-bp band. The *MspI* morph 22 derives from morph 6 for a site acquisition in the 2,396-bp band. The *MspI* digestions of the relevant amplified fragments allowed the new sites to be located at nt 14157 (C →G at nt 14159), for *MspI* morph 20; at either nt 14557 (C→G at nt 14559) or nt 14558 (A→G at nt 14561), for *MspI* morph 21; and at nt 9808 (A→C at nt 9809), for *MspI*

Table 6
Frequencies of *TaqI*/12f2-8 kb Allele in Ethiopians, Mandenkalu, and Relevant Comparison Populations

Population (N)	Frequency \pm SE of 8-kb Allele (%)	Reference
Ethiopian (59)	25.4 \pm 5.7	Present study
Jewish (160)	40.6 \pm 3.9	Santachiara Benerecetti et al. (1993)
Lebanese (87)	43.7 \pm 5.3	Santachiara Benerecetti et al. (1993)
Czechoslovak (100)	6.0 \pm 2.4	Santachiara Benerecetti et al. (1993)
Turkish (194)	33.0 \pm 3.4	Semino et al. (1996)
Northern Italian (69)	17.4 \pm 4.6	Brega et al. (1987)
Southern Italian (74)	32.4 \pm 5.4	Brega et al. (1987)
Northern African (183)	31.1 \pm 3.4	Semino et al. (1996)
Senegalese:		
Mandenka (68)	0	Present study
Wolof and Peul (65)	0	Brega et al. (1987)
African black (15)	0	Casanova et al. (1985)
Southern African Bantu (182)	0	Spurdle and Jenkins (1996)
Khoisan (90)	0	Spurdle and Jenkins (1996)

morph 22. *HaeII* morph 16 is a morph-1 derivative for a site gain in the 4.5-kb fragment. By *PstI/HaeII* double digestion, the site has been located as being at either nt 6165 (T→C at nt 6167) or nt 6179 (T→C at nt 6183); the first location is more likely, because it does not change the amino acid sequence. *AvaII* morph 38 is very similar to morph 2. *PstI/AvaII* double digestion, however, placed the new site at approximately nt 7000—not at nt 8249, as in morph 2. *AvaII* digestion of the relevant amplified fragment located the site at nt 7118 (A→G at nt 7118). In contrast to all of the other African populations surveyed so far (for a review, see Scozzari et al. 1994), type 1 is the most frequent mtDNA type (frequency 54.5%) in the Ethiopian sample. This is the mtDNA type that is the most common in Caucasoids and in eastern Asian populations.

Haplotypes with the *HpaI* site gain at nt 3592 (*HpaI* morph 3 and its derivative morphs 7 and 8), which defines the African haplogroup L, account for 24.7% of Ethiopian mtDNAs, whereas they represent 100% of Pygmy (Chen et al. 1995), 93.9% of Sekele and 80.4% of Nama (the San and KhoiKhoi populations of Namibia, respectively: Soodyall and Jenkins 1992), 70% of southern African Bantu (Johnson et al. 1983), 66.1% of

Senegalese (Scozzari et al. 1988), and 60.0% of Cameroon Bantu (Scozzari et al. 1994) mtDNAs.

Type 6-2 (with its derivatives 209-2 and 214-2), which is considered Caucasoid if associated with other specific mutations, and the Caucasoid type 18-2 have been found in Ethiopia. Type 18-2 is characterized by the G→A transition at nt 13368 (*BamHI* morph 3 and *AvaII* morph 9) and by the *MspI* site loss at nt 15925 (*MspI* morph 4) and belongs to haplogroup T (tables 1 and 3). Type 6-2 is characterized by the *HaeII* site loss at nt 9052 (*HaeII* morph 2), which, in association with the *DdeI* site gain at nt 10394 and the A→G transition at nt 12308, defines Caucasoid haplogroup K (tables 1 and 3). However, of the four mtDNAs with the *HaeII* site loss at nt 9052, only two showed the nt 12308 A→G transition that is associated with Caucasoid haplogroup K. With regard to the other Ethiopian mtDNAs, except for one subject (type 21-2) belonging to haplogroup W and six subjects (type 1-2) belonging to the uninformative haplogroup U (table 3), which is shared between European (10%–16%) and Senegalese (5%) populations (Torroni et al. 1996), none exhibited the markers that identify the remaining Caucasoid haplogroups (table 1).

The distribution of the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ haplotypes

Table 7
Frequencies of YAP⁺ Allele and of Its sY81 Subtyping, in Ethiopians, Mandenkalu, and Wolof from Senegal and in Relevant Comparison Populations

POPULATION (N)	FREQUENCY \pm SE ^a (%)		REFERENCE(S)
	YAP ⁺	sY81-G/ YAP ⁺	
Ethiopian (64)	50.0 \pm 6.2	0	Present study
Senegalese:			
Mandenka (56)	98.2 \pm 1.8	94.5	Present study
Wolof (31)	100	71.0	Present study
Mixed African (44)	59.1 \pm 7.4	69.2	Seielstad et al. (1994)
Bantu (442)	78.0 \pm 2.0	NT	Hammer (1994), Spurdle et al. (1994)
Khoisan:			
Nama+Sekele San (68)	46 \pm 6	NT	Spurdle et al. (1994)
Tsumkwe San (38)	11 \pm 5	NT	Spurdle et al. (1994)
Egyptian (64)	53.1 \pm 6.2	NT	Persichetti et al. (1992), Hammer (1994)
Saudi Arabian (21)	10.0 \pm 6.4	NT	Hammer (1994)
European (192)	7.0 \pm 1.8	NT	Persichetti et al. (1992), Hammer (1994), Spurdle et al. (1994)

^a NT = not tested.

Table 8

Y-Chromosome Superhaplotypes Obtained by Combining the Different "Alleles" Observed, in Each Individual, for the 12f2, YAP, sY81-A/G, and 49a,f Polymorphisms, and Their Frequencies in Ethiopians and Senegalese

SUPERHAPLOTYPE	49a,f										SUPERHAPLOTYPE FREQUENCY IN (%)	
	12f2	YAP	sY81	Haplotype	Polymorphic Fragment ^b					Missing Fragment ^c	Ethiopians (N = 54)	Senegalese ^a (N = 87)
					A	C	D	F	I			
S1	10	+	G	3	1	0	0	1	0			3.4
S2	10	+	G	4	1	0	0	1	1			68.9
S3	10	+	G	25	0	0	0	0	1			2.3
S4	10	+	G	27	1	0	0	0	1			5.7
S5	10	+	G	28	1	0	0	1	0	G		4.6
S6	10	+	A	5	2	0	0	1	1		24.1	4.6
S7	10	+	A	10	3	0	0	1	0			2.3
S8	10	+	A	11	3	0	0	1	1		22.2	4.6
S9	10	+	A	26	2	0	0	0	1		1.9	
S10	10	+	A	30	2	0	0	1	0			1.1
S11	10	+	A	55	4	0	0	1	1		1.9	
S12	10	+	A	116	2	0	0	1	0	G	1.9	
S13	10	+	A	126	6	0	0	1	1			1.1
S14	10	-	A	2	0	0	1	1	1		3.7	
S15	10	-	A	5	2	0	0	1	1		1.9	
S16	10	-	A	11	3	0	0	1	1		1.9	
S17	10	-	A	13	3	0	1	1	1		3.7	
S18	10	-	A	26	2	0	0	0	1		7.4	
S19	10	-	A	30	2	0	0	1	0			1.1
S20	10	-	A	117	2/3	0	0	0	1		1.9	
S21	8	-	A	8	2	0	1	1	1		27.8	

^a Mandenkalu and Wolof have been pooled.

^b "0" and "1" denote presence and absence, respectively, of the band, except for the "A" fragment; for the latter, the numbers indicate which band of the "allelic" set is present, and; two numbers separated by a slash indicate presence of two "allelic" bands in the same haplotype, in which case a locus duplication was supposed (Torroni et al. 1990; Spurdle and Jenkins 1992; Santachiara-Benerecetti et al. 1993).

^c All other fragments were always present.

in Ethiopia is shown in table 4. The 20% frequency of the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (++) haplotype, is very similar to the 18% previously reported for a smaller sample (Passarino et al. 1996c). The frequency of the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) haplotype in Ethiopia (55.4%) falls between the value reported in sub-Saharan Africans (88.8%) and the value reported in Caucasoids (20%–26% [Indians were excluded; see footnote c to table 4]). The frequency of the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (--) haplotype (24.2%) also is intermediate relative to that in sub-Saharan Africans (9.6%) and that in Caucasoids (77.5%). In table 3, the associations between the mtDNA *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ haplotypes, the "continent specific" haplogroups, and the types obtained with the six classical enzymes are reported, together with an evaluation of the contribution of the different ethnic components. The 15 molecules with the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (++) haplotype, which defines the Asian M haplogroup, are mainly (80%) type 1. With regard to the 41 mtDNAs (+-), 2 are recognizable as Caucasoid and belong to haplogroup K, and 19 are clearly of African origin, since they correspond to types 2, 7, 210, and 212, all of which

share the *HpaI* morph 3, which defines African haplogroup L and is in absolute linkage disequilibrium with the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) haplotype. The remaining 20 *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) mtDNAs are very likely of African origin, because this haplotype has very high frequencies in sub-Saharan Africans, low frequencies in Orientals (see table 4), and, apart from haplogroups I–K (table 1), has not been found so far in Caucasoid populations (Torroni et al. 1994b, 1996; A. Torroni, personal communication). Of 18 *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (--) mtDNAs, 2 are Caucasoid specific and belong to haplogroups T and W, 6 are in the uninformative haplogroup U, and 10 are not classifiable as being in any of the previously defined haplogroups.

Y-Chromosome Analyses

Ten 49a,f haplotypes were observed in the Ethiopian sample, three of which are new haplotypes—haplotype 116 (A₂C₀D₀F₁I₀-G), haplotype 117 (A_{2/3}C₀D₀F₀I₁), and haplotype 128 (A₃C₀D₀F₁I₀-G). Their frequencies are reported in table 5, where data from Niger-Congo speakers

(Torrioni et al. 1990), Khoisan (Spurdle and Jenkins 1992), and Caucasoid populations (Santachiara-Benerecetti et al. 1993) are also given, for comparison.

The most frequent 49a,f/*TaqI* RFLP haplotypes found in Ethiopia are haplotypes 5 ($A_2C_0D_0F_1I_1$), 8 ($A_2C_0D_1F_1I_1$), and 11 ($A_3C_0D_0F_1I_1$), each accounting for ~25% of the sample. Haplotype 5 is widespread in Africa, with particularly high frequencies in northern Africa, and in other populations of the eastern Mediterranean basin (Persichetti et al. 1992; Semino et al. 1992; Spurdle and Jenkins 1992). Haplotype 11 is also a widespread marker, with high frequencies in some north-eastern European (Santachiara-Benerecetti et al. 1993; Passarino et al. 1996b) and Indian populations (Spurdle and Jenkins 1992; A. S. Santachiara-Benerecetti, unpublished data). Moreover, haplotypes 5 and 11 have probably arisen more than once, because they have been seen in association with both YAP⁺ and YAP⁻ alleles in Ethiopian and other examined populations. Therefore, it is not easy to advance a simple hypothesis for their derivation. Although haplotype 8 is virtually lacking in the surveyed sub-Saharan African populations (Torrioni et al. 1990; Spurdle and Jenkins 1992), it reaches one of the highest observed frequencies in Ethiopia—frequencies similar to those found in the Middle East (Santachiara-Benerecetti et al. 1992, 1993; Ritte et al. 1993a; Lucotte et al. 1996) and in some populations that have been particularly affected by migrations starting from that area (e.g., northern Africans, Indians, and southeastern Europeans: Persichetti et al. 1992; Spurdle and Jenkins 1992; A. S. Santachiara-Benerecetti, unpublished data).

On the other hand, the $A_1C_0D_0$ combination is not found in the Ethiopian sample, even though it is commonly found in most sub-Saharan African populations. As is shown in table 5, this combination, almost completely represented by haplotype 4 ($A_1C_0D_0F_1I_1$), accounts for ~80% of Niger-Congo speakers and for 35% of Nama+Omega San Y chromosomes. It is, however, quite uncommon in the Tsumkwe San, in which only one individual was typed as haplotype 3 ($A_1C_0D_0F_1I_0$).

Also of interest is haplotype 26 ($A_2C_0D_0F_0I_1$) (corresponding to haplotype 41 of Torrioni et al. [1990] and to haplotype 33 of Spurdle and Jenkins [1992]), which is present in 7.2%, 9.7%, and 30.4% of the examined Y chromosomes in the Ethiopian, Nama+Omega San, and Tsumkwe San populations, respectively. This haplotype, which was found in only one individual from Cameroon, among the Niger-Congo speakers (table 5), was not observed in 480 Bantu of southern Africa (Spurdle and Jenkins 1992). It is worth noticing that this haplotype, which is also rare in other populations, represents >50% of a small sample of Ethiopian Jews (Ritte et al. 1993a).

The frequencies of the 12f2–8 kb allele in Ethiopians

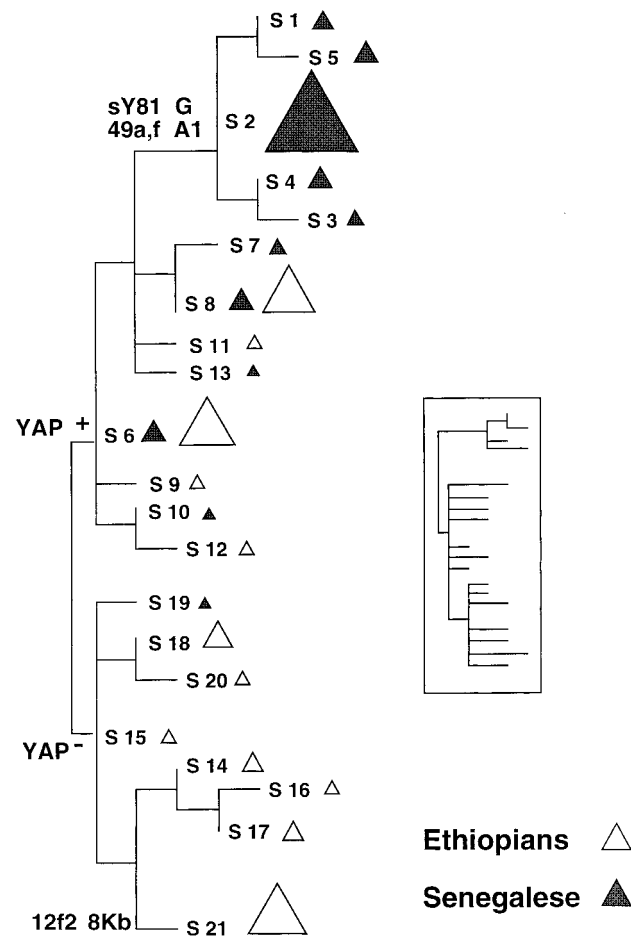


Figure 1 One of 49 MP trees obtained by PAUP analysis after 1,000 replications. This tree includes 21 Y-chromosome superhaplotypes (S1–S21; table 8). It is 23 steps in length and has consistency and retention indexes (CI and RI) of .522 and .711, respectively. Markers (YAP⁺, YAP⁻, sY81-G, 49a,f-A₁, and 12f2 8-kb) characterizing the most important lineages are indicated. The lengths of the horizontal branches are proportional to the number of mutational events, and triangular areas are proportional to superhaplotype frequencies. The strict consensus tree of the 49 MP trees is illustrated in the inset: it is 35 steps in length and has a CI of .343 and a RI of .395. Haplotypes are in the same order as in the main figure.

and Mandenkalu are reported in table 6, together with those of some other populations of interest. The Mandenkalu, similar to other examined Senegalese and sub-Saharan Africans, have only the 12f2–10 kb allele, whereas ~25% of the Ethiopians display the Caucasoid 12f2–8 kb allele. This allele has always been observed in association with 49a,f haplotype 8.

Similar to the reported frequencies in Egyptian (53.1%) and Khoisan (46%) samples (Persichetti et al. 1992; Hammer 1994; Spurdle et al. 1994), 50% of the Ethiopians carry YAP⁺ chromosomes (table 7). This incidence is much lower than either that in the Senegalese

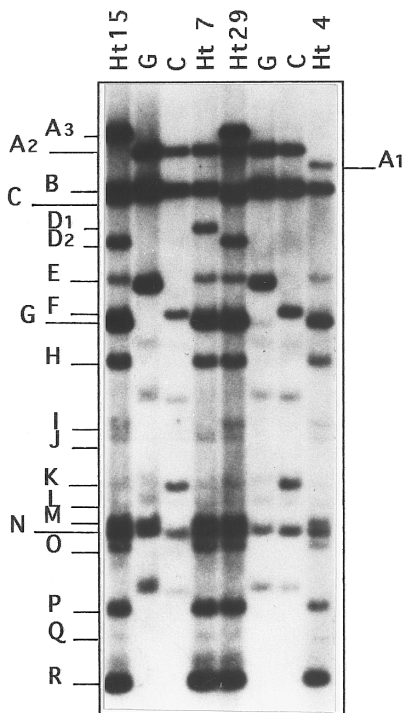


Figure 2 *TaqI* electrophoretic patterns detected by 49a,f probes in one gorilla (G) and one chimpanzee (C), compared with human haplotypes 15 (A₃C₁D₂F₁I₁), 7 (A₂C₀D₁F₁I₀), 29 (A_{2/3}C₁D₂F₁I₁), and 4 (A₁C₀D₀F₁I₁)

in the present study (98.8%) or that in the Bantu speakers examined by Spurdle et al. (1994) (78.0%).

The distribution of the sY81-G allele is given, in table 7, as a percentage of YAP⁺ chromosomes, because of its complete linkage disequilibrium with this marker. None of the Ethiopian YAP⁺ chromosomes carried the sY81-G allele, which accounts for 94.5% and 71.0% of the Mandenka and Wolof YAP⁺ chromosomes, respectively.

Table 8 shows the superhaplotypes obtained by combining the “alleles” observed in each individual, for the polymorphisms examined. The evolutionary relationships among these superhaplotypes were inferred by an MP analysis. Figure 1 shows one of the 49 MP trees that were obtained after 1,000 replications. These 49 trees could be divided into four groups, with either 49a,f haplotype 5 (A₂C₀D₀F₁I₁), haplotype 11 (A₃C₀D₀F₁I₁), haplotype 26 (A₂C₀D₀F₀I₁), or haplotype 30 (A₂C₀D₀F₁I₀) as the ancestral haplotype. It can be seen that haplotypes 5, 26, and 30 have the A₂C₀D₀ combination that we observed in two nonhuman primates (one chimpanzee and one gorilla; fig. 2). However, haplotype 5 is the best candidate for the ancestral haplotype, because it is the only one that is widely distributed in African, European, and some western Asian populations. Apart from these

considerations, all the MP trees shared the following basic features (see fig. 1):

1. a YAP⁺ branch including both Senegalese and Ethiopian superhaplotypes;
2. a YAP⁺ subgroup characterized by the sY81-G allele, which consists only of Y chromosomes from Senegal. The sY81-G allele is strictly associated (72 of 74 sY81-G Y chromosomes) with the Niger-Congo 49a,f A₁C₀D₀ combination, which is mostly represented by the 49a,f haplotype 4, A₁C₀D₀F₁I₁ (S2), but also by haplotypes 3, 27, and 28—A₁C₀D₀F₁I₀ (S1), A₁C₀D₀F₀I₁ (S4),

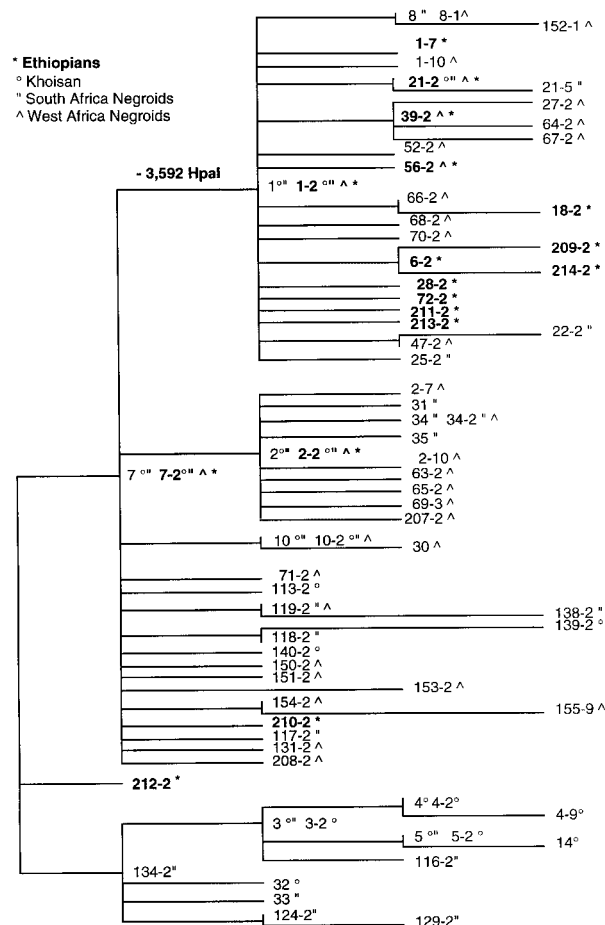


Figure 3 Parsimony tree correlating mtDNA types, obtained by means of the six classical enzymes, that have been found in Ethiopians (present study), Khoisan (Soodyall and Jenkins 1992), Niger-Congo speakers of southern Africa (Johnson et al. 1983; Soodyall and Jenkins 1993), and western Africans (Scozzari et al. 1988, 1994; Graven et al. 1995). This is one of the 3,000 parsimony trees generated by the TBR algorithm (Swofford 1992). It is 72 steps long, with CI and RI indexes of .583 and .746, respectively. The lengths of the horizontal branches are proportional to the number of mutational events. mtDNA types found in Ethiopia are in boldface. The *HpaI* site at nt 3592 defines most of the African types. Only one of the branches is defined by the absence of this site.

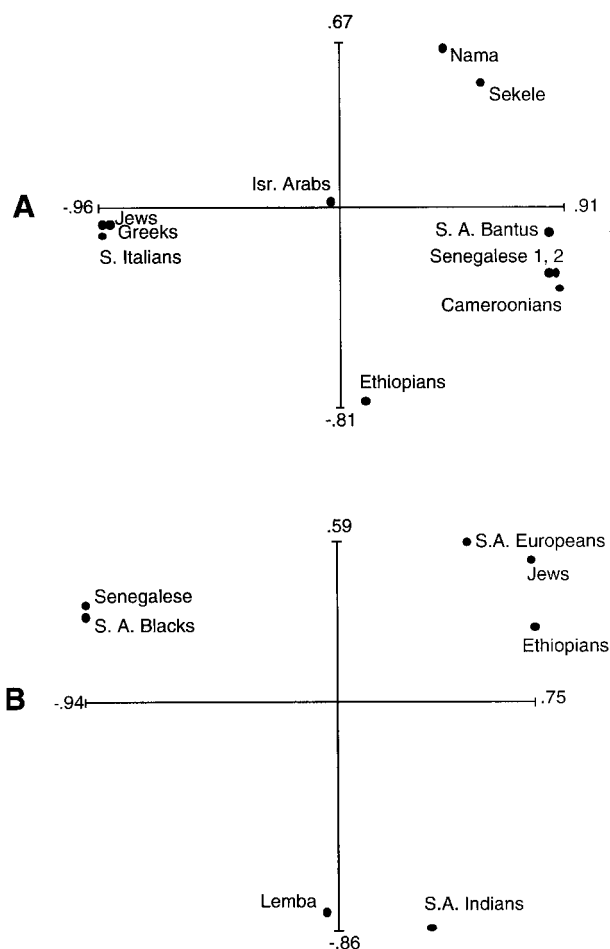


Figure 4 A, PCA of 11 populations tested for *HpaI*, *BamHI*, *HaeIII*, *MspI*, and *AvaII* mtDNA RFLPs. The first axis represents 64.1% of the total variance, and the second axis represents 16.7% of the total variance. Populations represented are Ethiopians (present study), Nama and Sekele (Soodyall and Jenkins 1992), Bantu (Johnson et al. 1983), Senegalese 1 (Mandekalu: Graven et al. 1995), Senegalese 2 (Wolof and Peul: Scozzari et al. 1988), Cameroonians (Scozzari et al. 1994), Jews (from Iraq, Yemen, and Turkey), and Israeli Arabs (Ritte et al. 1993b). Since the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ classification revealed ethnic heterogeneity within the Ethiopian mtDNA type 1, the frequency of this type (54.6%) has been subdivided as follows: 15.6% mtDNA type 1 *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (++) , which is Asian and is absent in all the comparison populations; 17.0% mtDNA type 1 *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) , which is African and was compared with 88.8% (see table 4) of the mtDNA type 1 frequencies of the African control populations; and 22.0% mtDNA type 1 *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (--) , which was compared with 12% of the mtDNA type 1 frequencies of the African populations and with the entire frequency of the Caucasoid control sample. B, PCA of seven populations classified for the Y-chromosome YAP/12f2/49a,f compound haplotypes. The first axis represents 45.4% of the total variance, and the second axis represents 33.1% of the total variance. Populations represented are Ethiopians and Senegalese (present study); southern African blacks, Indians, Lemba, and Europeans (Spurdle and Jenkins 1996); and Jews (25 from Spurdle and Jenkins [1996] and 65 from A. S. Santachiara-Benerecetti [unpublished data]).

and $A_1C_0D_0F_1I_0-G$ (S5), respectively. The fifth haplotype in association with the sY81-G allele is haplotype 25, $A_0C_0D_0F_0I_1$ (S3), which, because of the loss of the A_1 band, can be considered as a derivative of haplotype 27;

3. a YAP⁻ branch that, except for a single Senegalese with superhaplotype S19, is composed entirely of Ethiopian Y chromosomes. This branch includes the superhaplotype S21, which is characterized by the 12f2-8 kb/49a,f haplotype 8 association and accounts for 27.8% of the Ethiopian sample.

Discussion

On the basis of historical, linguistic, and genetic data, it has been suggested that the Ethiopian population has been strongly affected by Caucasoid migrations since Neolithic times (Cavalli-Sforza et al. 1994, p. 174). On the basis of autosomal polymorphic loci, it has been estimated that 60% of the Ethiopian gene pool has an African origin, whereas ~40% is of Caucasoid derivation (Guglielmino et al. 1987; Cavalli-Sforza et al. 1994, p. 174). Moreover, similarities between Ethiopian and Khoisan populations have been suggested by the PCA (Cavalli-Sforza et al. 1994, p. 191), although they are weakly supported by the F_{ST} genetic-distance method (Cavalli-Sforza et al. 1994, p. 78).

To better define the different components of the Ethiopian gene pool, we have studied the mtDNA and Y-chromosome polymorphisms in samples from Ethiopia and Senegal. Haplotypes based on these polymorphisms are easily constructed, because of the lack of recombination in these genomic regions, and permit inferences about the history of populations through female and male lineages separately.

A phylogenetic tree of the mtDNA types defined by the six classical restriction enzymes' RFLPs (table 2) is shown in figure 3. Unlike all the previously surveyed African populations, most of the Ethiopian mtDNA types cluster on the lineage lacking the *HpaI* site at nt 3592. The presence of this site, which is a specific African feature, accounts for ~25% of the Ethiopian mtDNAs and is represented on the mtDNA tree by the common types 2-2 and 7-2, as well as by types 210-2 and 212-2. None of the specific Khoisan types (types 3-5) were found in the Ethiopian sample. This study represents the first survey of mtDNA polymorphisms in an eastern African population and can help clarify the evolutionary relationships among African mtDNA types. Type 2, which is very frequent (40%) in Niger-Congo speakers (Johnson et al. 1983; Scozzari et al. 1988, 1994; Soodyall and Jenkins 1993), is virtually absent in Khoisan speakers (Soodyall and Jenkins 1992). Type 7, although less frequent, is present in all the surveyed sub-Saharan

African populations, with the exception of the Herero, a particular Bantu-speaking group from Namibia (Soodyall and Jenkins 1993). Because it is unlikely that a gene flow from Niger-Congo speakers to Khoisan has always resulted in the transfer of type 7, rather than in the transfer of the most frequent, type 2, we suggest that type 7 could have been present in the ancestral African population. In this scenario, type 2 would be considered a marker of Niger-Congo-speaking populations, and the presence (frequency 14.7%) of type 2 in Ethiopians would be indicative of a Niger-Congo maternal gene flow. Type 3 has a high frequency in Khoisan populations; however, unlike types 4 and 5, which are virtually absent in Niger-Congo speakers, it is present, at a low incidence, in southern African Bantu populations (Johnson et al. 1983; Soodyall and Jenkins 1992, 1993). However, type 3 has not been found in western African peoples (Scozzari et al. 1988, 1994; Graven et al. 1995). Two hypotheses have been advanced to explain the distribution of type 3 mtDNAs (Soodyall and Jenkins 1992): (1) it was present in the ancestral African population, or (2) it arose in the Khoisan and was acquired, through gene flow, by southern African Bantu speakers. The absence of type 3 in the Ethiopian sample lends support to the second hypothesis.

Unlike other sub-Sahara African populations, Ethiopians display a high frequency of type 1, which is by far the most frequent type in Caucasoids and Asians. However, such a high frequency does not appear to be due to an explicit Caucasoid influence. In fact, as shown in table 3, of the 40 type 1 Ethiopian subjects, 12 displayed the Asian *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (++) haplotype, which is virtually absent among Caucasoids (see table 4); 13 are associated with the *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) haplotype, and none of these molecules belong to haplogroups I-K, which are the only *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (+-) Caucasoid-specific haplogroups (Torroni et al. 1994b, 1996; A. Torroni, personal communication); and, of the remaining 15 type 1 molecules, all of which are *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇ (--), 6 belong to haplogroup U (which is shared by Caucasoids and Africans), and 9 do not have any known Caucasoid-specific marker. Therefore, our mtDNA data do not support the hypothesis that a significant portion of the Ethiopian gene pool has a maternal Caucasoid origin.

As far as the Y chromosome-specific polymorphisms are concerned, Ethiopians completely lack the 49a,f haplotype 4 (A₁C₀D₀F₁I₁), which reaches frequencies of ~70% in Niger-Congo speakers (table 5 and Spurdle and Jenkins 1992). Our Ethiopian sample also lacks the sY81-G allele, which was associated with 86% and 69% of Senegalese and mixed-African YAP⁺ chromosomes, respectively (table 7). This suggests that male-mediated gene flow from Niger-Congo speakers to the Ethiopian population was probably very limited. As shown in fig-

ure 1, none of the superhaplotypes in the YAP⁺/sY81-G clade were found in the Ethiopians. This clade includes all of the 49a,f haplotypes with the A₁C₀D₀ combination and accounts for 85% of the analyzed Niger-Congo speakers. Therefore, it is reasonable to propose that most of the Y chromosomes that were spread by Bantu expansions were YAP⁺/sY81-G/49a,f (A₁C₀D₀). In contrast, the YAP⁻ branch is composed only of haplotypes found in Ethiopia (with the exception of superhaplotype S19, which was observed in one Senegalese) and accounts for 48.1% of Ethiopian Y chromosomes in this survey. More than half of these YAP⁻ Y chromosomes belong to superhaplotype S21, which is characterized by the Caucasoid 12f2-8 kb allele. This allele exhibits its highest (>40%) frequencies in the Middle East and can be considered a valuable indicator of Middle Eastern population expansions (Semino et al. 1996).

The only two superhaplotypes shared between the Senegalese and Ethiopian samples (S8—YAP⁺/sY81-A/12f2-10 kb/49a,f haplotype 11 and S6—YAP⁺/sY81-A/12f2-10 kb/49a,f haplotype 5) were associated with the YAP⁺/sY81-A branch of the Y-chromosome superhaplotype tree (fig. 1). We suggest that these haplotypes, which show a much higher frequency in the Ethiopian sample than in Senegalese, are representative of pre-Bantoid African Y chromosomes.

The association between YAP⁻/49a,f haplotype 26 (S18) is interesting in several respects. First, four of the five Ethiopians in this survey who had the 49a,f haplotype 26 were also YAP⁻. Although 49a,f haplotype-26 Y chromosomes were observed to be common in the Ethiopian Jews (Ritte et al. 1993a), the YAP element was not examined in this group. Second, with the exception of Ethiopians and Khoisan, this haplotype is very rare in nearly all surveyed populations. Finally, the Tsumkwe San, which show a high frequency of haplotype 26, were also analyzed for the YAP element (Spurdle et al. 1994), but the association YAP/haplotype 26 was not reported. However, the frequencies of the two markers (30% haplotype 26 and 11% YAP⁺) make it possible to deduce that at least two-thirds of the 49a,f haplotype 26 of this group should be YAP⁻. We speculate that the YAP⁻/49a,f haplotype 26 combination represents an African characteristic preceding the Bantu expansion and indicates reciprocal affinity between Ethiopians and Khoisan. If one excludes this possible specific element of affinity, these two groups seem to share only a generic dissimilarity with Niger-Congo populations, with regard to Y-chromosome haplotypes.

Considering both paternal and maternal lineages, only 5.4% of the mtDNAs can be classified as Caucasoid (table 3), whereas 25.4% of the Ethiopian Y chromosomes have a clear Caucasoid origin (12f2-8 kb; table 6). If one also includes as Caucasoid mtDNA types the ambiguous haplogroup U and the 10 *DdeI*₁₀₃₉₄*AluI*₁₀₃₉₇

(–) haplotypes that did not show any tested non-Caucasoid feature, there could be a maximum of 27.0% of “Caucasoid-like” mtDNAs in the Ethiopian population. On the other hand, considering that the 12f2–8 kb allele can account for as much as 44% of the Caucasoid Y chromosomes (the highest observed incidence of this allele), a male genetic admixture of 57.7% between Caucasoids and Africans is obtained in Ethiopia. Interestingly, the average level of admixture estimated from our mtDNA and Y-chromosome data (42.3%) is very similar to estimates based on autosomal studies (40%) (Guglielmino et al. 1987; Cavalli-Sforza et al. 1994, p. 174). However, our data suggest that Caucasoid gene flow into the Ethiopian gene pool occurred predominantly through males. Conversely, the Niger-Congo contribution to the Ethiopian population occurred mainly through females. This difference is well illustrated in figure 4, where data from the mtDNA and Y-chromosome PCAs are shown. The results of this study are another good example of how Y-chromosome and mtDNA polymorphisms can give distinct but complementary information reflecting the different male/female behavior in the history and social habits of a population (Torroni et al. 1990, 1994a; Zoosmann-Diskin et al. 1991; Excoffier et al. 1996b; Salem et al. 1996; Spurdle and Jenkins 1996; Huoponen et al. 1997; Zerjal et al. 1997).

Indeed, Ethiopians do not seem to result only from a simple combination of proto-Niger-Congo and Middle Eastern genes. Their African component cannot be completely explained by that of present-day Niger-Congo speakers, and it is quite different from that of the Khoisan. Thus, a portion of the current Ethiopian gene pool may be the product of in situ differentiation from an ancestral gene pool.

The frequency of the *DdeI*₁₀₃₉₄-*AluI*₁₀₃₉₇ (++) haplotype is of interest in this regard. As shown in table 4, this haplotype is virtually absent in Caucasoid populations (Indians excepted) and other sub-Saharan Africans. It has been found in India (Passarino et al. 1996c), in eastern Asia, and in peoples who migrated very early from eastern Asia (i.e., Australians, Papua New Guineans, and Amerindians: Ballinger et al. 1992; Torroni et al. 1992, 1993a, 1993b, 1994a, 1994c, 1994d). On the basis of its distribution and antiquity (estimated at 40,250–80,500 years ago [Chen et al. 1995] and 30,250–60,500 years ago [Passarino et al. 1996a]), we have suggested elsewhere that it preceded the split between proto-Indians and proto-eastern Asians (Passarino et al. 1996a, 1996c).

This haplotype reaches a frequency of ~20% in Ethiopia and has never been observed in mtDNA molecules of the other African or Caucasoid lineages (Torroni et al. 1994b, 1996; Chen et al. 1995; Passarino et al. 1996c; present study). Thus, it is likely that the Ethio-

pian and Asian *DdeI*₁₀₃₉₄-*AluI*₁₀₃₉₇ (++) haplotypes have a common origin. If so, then this marker either (1) has been acquired by Ethiopians through interchanges with Asians (indicating an Asiatic component in the Ethiopian genetic structure) or (2) was present in the ancient Ethiopian population and was carried by groups who migrated out of Africa. In the case of the second hypothesis, the very low (1%–2%) frequency of this marker in the Middle East (table 4; and A. S. Santachiara Benerecetti, unpublished data) would support the hypothesis of an early exit of *Homo sapiens sapiens* from Africa via the eastern Africa–western India route (Cavalli-Sforza et al. 1993; Cavalli-Sforza et al. 1994, p. 195).

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