

genetic landscape of Europe has probably been further confounded by the major climatic changes that have occurred since the arrival of the first modern humans. In particular, the early Paleolithic populations of Northern and Central Europe either became extinct or retreated to the south during the Last Glacial Maximum (LGM) ~20 kya, and there was a gradual re peopling from southern refuge areas only when climatic conditions improved, from ~15 kya. This scenario is supported not only by recent work on archaeological dating (Housley et al. 1997; Richards 2003) but also by the phylogeographic evidence provided by mtDNA haplogroup V (Torroni et al. 1998; 2001a) and Y-chromosome haplogroups R1b and I1b2 (Semino et al. 2000; Cinnioglu et al. 2004; Rootsi et al. 2004).

Among the mtDNA haplogroups of Europe, haplogroup H displays two unique features: an extremely wide geographic distribution and a very high frequency in most of its range. Indeed, it is by far the most prevalent haplogroup in all European populations except the Saami, is very common in North Africa and the Middle East, and retains frequencies of 5%–10% even in northern India and Central Asia, at the edges of its distribution range (Richards et al. 2002).

Previous studies have proposed that haplogroup H (i) originated in the Middle East ~30–25 kya; (ii) expanded into Europe in association with a second Paleolithic wave, possibly contemporary with the diffusion of the Gravettian technology (25–20 kya); and (iii) was strongly involved in the late-glacial expansions from ice-age refugia after the LGM (Torroni et al. 1998; Richards et al. 2000). In addition, because of its high frequency and wide distribution, haplogroup H most likely participated in all subsequent episodes of putative gene flow in western Eurasia, such as the Neolithic diffusion of agriculture from the Near East, the expansion of the

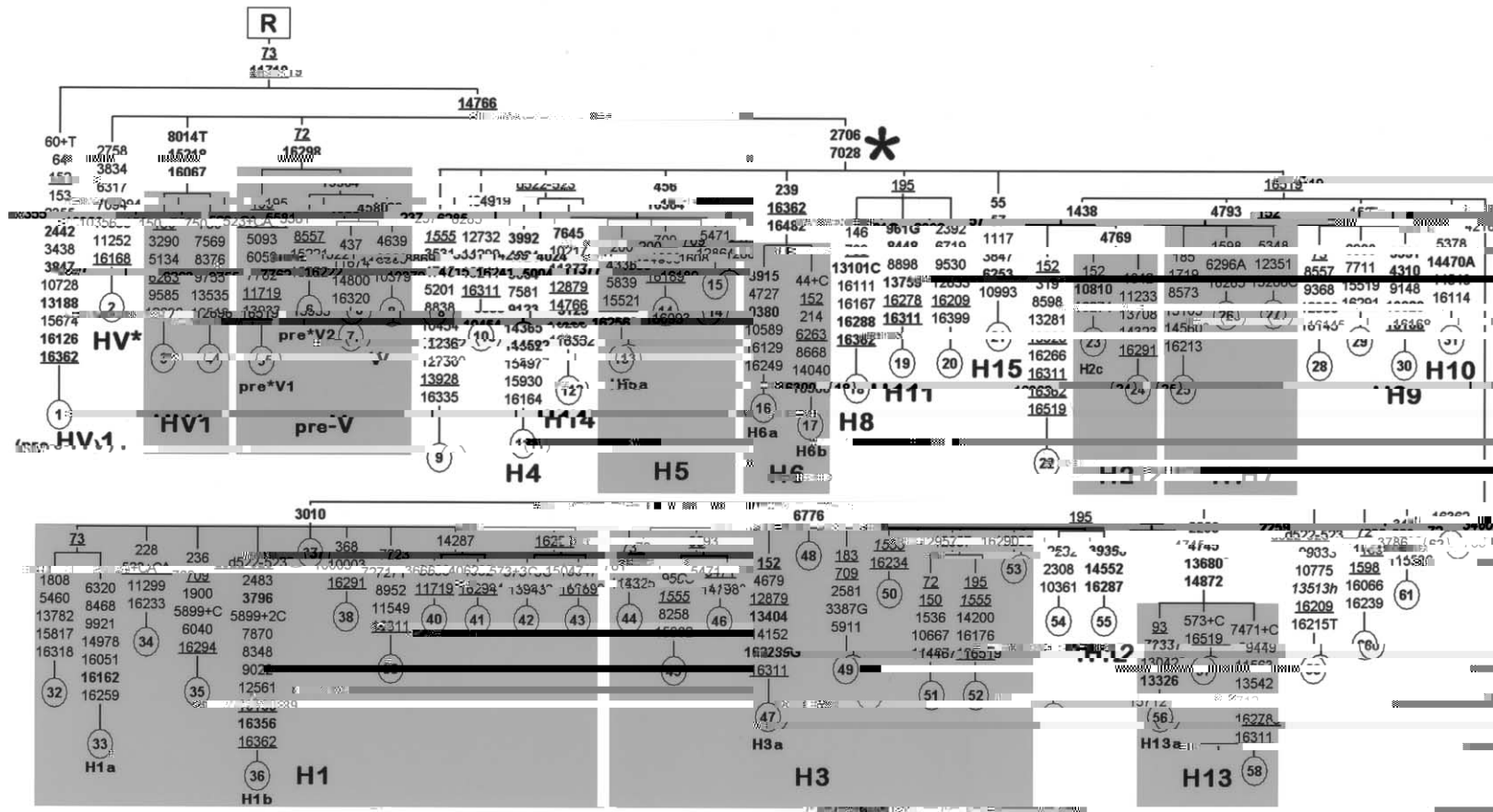


Figure 1 Most-parsimonious tree of complete (pre-HV)1, HV*, HV1, pre-V, and H mtDNA sequences. The tree, rooted in haplogroup R, includes 62 mtDNAs (1–62) sequenced in this study and illustrates subhaplogroup affiliations. Phylogeny construction was performed by hand, following a parsimony approach, and was confirmed by use of the program Network 4.0. We have applied the reduced median algorithm ($r = 2$) (Bandelt et al. 1995), followed by the median-joining algorithm ($\epsilon = 0$) (Bandelt et al. 1999) and the MP (maximum parsimony) calculation option, as explained at the Fluxus Engineering Web site. For the phylogeny construction, half weight was assigned to the control-region positions, and the pathological mutations 1555, 3460, and 13513 (shown in italics) were excluded. Mutations are shown on the branches; they are transitions, unless the base change is explicitly indicated. Deletions are indicated by a “d” preceding the deleted nucleotides. Insertions are indicated by a “+” preceding the inserted nucleotide(s). Heteroplasmy is indicated by an “h” following the nucleotide position. Underlining indicates recurrent mutations, whereas mutations in boldface are diagnostic of the haplogroup/subhaplogroup. The asterisk (*) indicates the most recent common ancestor of the H mtDNAs.

Table 1

Population Distribution and Frequencies of Haplogroup H, H1, and H3 mtDNAs

REGION, ID NUMBER, AND POPULATION	NO. OF SUBJECTS	H FREQUENCY (%)	SUBHAPLOGROUP FREQUENCY (%)
			H1080 0 0996s6-92.3183 32.3759 010.94



Figure 2 Geographical locations of populations surveyed for haplogroup H (*top*) and its spatial frequency distribution (*bottom*). Frequency values for populations 1–43 are from table 1, whereas those for populations 44–63 are from the literature, as follows: 44–46 from Helgason et al. 2001; 47–49 and 53 from Richards et al. 2000; 50

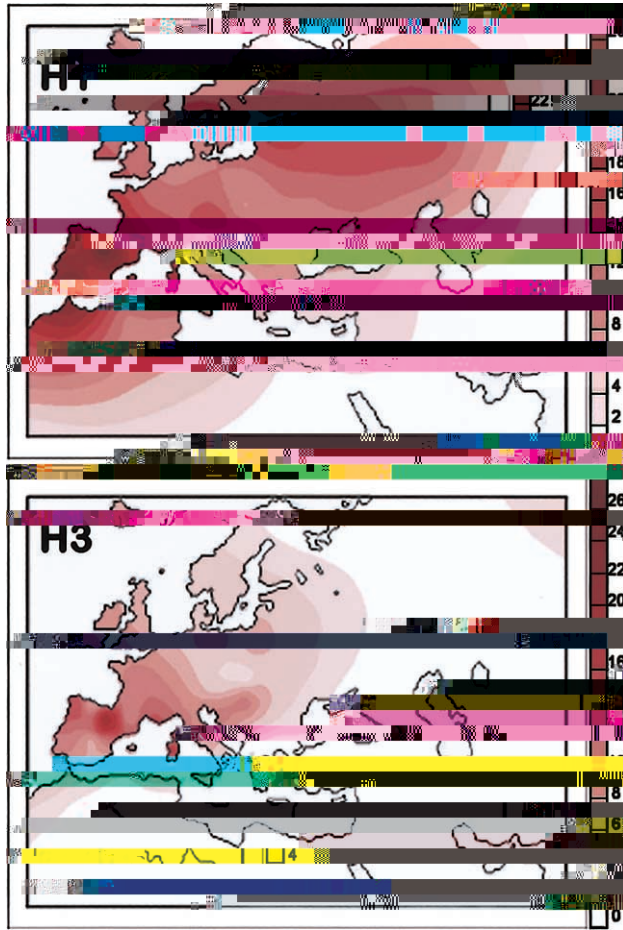


Figure 3 Spatial frequency distributions of subhaplogroups H1 and H3. Frequency values are from table 1. Maps were obtained as in figure 2.

Table 3

Frequency of H, H1, and H3 among Spanish Subjects Harboring the Deafness mtDNA Mutation A1555G

POPULATION	NO. OF SUBJECTS	HAPLOGROUP FREQUENCY (%)
		H

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