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Short Communication

Mitochondrial DNA Sequences from Switzerland Reveal Striking Homogeneity of European Populations*

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Mitochondrial DNA sequences from 74 Swiss individuals were compared to sequences from British and Finnish populations. We found that the nucleotide sequence differences between these populations are almost as low as those within the populations. This is in contrast to three African populations, which display substantial differences between each other. The homogeneity of the mitochondrial gene pool in Europe suggests a recent common ancestry for European populations. This may reflect the arrival of anatomically modern humans about 40000–30000 years ago or, alternatively, the spread of agriculturalists about 10000–6000 years ago. Taking into account the estimated rate of evolution of the mitochondrial control region, the data favor the former explanation.

Key words: Mitochondrial DNA / Nucleotide sequence / Pairwise sequence differences / Genetic diversity / Population history.

The nucleotide sequence of the 360-bp-long hypervariable segment I of the human mitochondrial control region (Vigilant *et al.*, 1989) was determined from 74 unrelated native Swiss individuals. Forty-two positions displayed substitutions, defining 44 mitochondrial lineages. These sequences were compared to 100 British (Piercy *et al.*, 1993) and 50 Finnish sequences (this article and A. Sajantila, unpublished). Table 1 shows that the mean pairwise sequence difference within the analyzed Swiss is 3.63 whereas that of the British and the Finns is 4.37 and 3.90, respectively. Unexpectedly, the calculation of the pairwise sequence differences between the populations reveals that they are similar in magnitude to those within the populations, ranging from 3.80 to 4.17 (Table 1).

Nucleotide sequences from the same segment of the mitochondrial control region were also compared for three African populations, the !Kung, the Pygmies and the Yoruba (Vigilant *et al.*, 1991). Here, the mean pairwise sequence differences within populations are 3.68, 8.74, and 6.82, respectively. Thus, with the exception of the !Kung, the within-population diversity is greater in Africa than in Europe. Interestingly, when comparing the African populations with each other, the mean pairwise sequence differences range from 9.07 to 9.95. These between-population differences are more than twice as large as the differences within and between the European populations, and they are also substantially larger than the differences found within the African populations.

When the genetic distances between the populations are corrected for the within-population differences (Table 1) the pattern becomes even more striking in that the distances calculated between the African populations are two orders of magnitude larger than those between the European populations. This difference between the two continents is due to the fact that in Europe, the diversity between the populations is almost as low as that within the populations. Thus, the European populations seem to be part of one homogeneous mitochondrial gene pool whereas regional divergence of the gene pool exists in Africa.

In order to obtain a further perspective on the genetic diversity of populations in Europe, the distributions of pairwise sequence differences for the three populations were calculated. Figure 1 shows that the pairwise sequence dif-

Table 1 Mean Pairwise Sequence Differences and Genetic Distances in Three European and Three African Populations. Upper-right triangle including diagonal shows mean pairwise sequence differences within (bold) and between European and African populations. Lower-left triangle (italicized numbers) shows genetic distances[1] (× 100).

	British	Finnish	Swiss	!Kung	Pygmy	Yoruba
British	**4.37**	4.17	4.02	9.76	10.81	7.17
Finnish	*4*	**3.90**	3.80	9.44	10.57	6.78
Swiss	*2*	*4*	**3.63**	9.46	10.56	6.85
!Kung	*574*	*565*	*580*	**3.68**	9.07	9.43
Pygmy	*426*	*425*	*438*	*286*	**8.74**	9.95
Yoruba	*158*	*142*	*163*	*418*	*217*	**6.82**

[1] The genetic distances were calculated from mean pairwise sequence differences as followings: $D_S = D_{BET} - [(D_{W1} + D_{W2})/2]$, where D_{BET} denotes mean pairwise sequence difference between population 1 and 2, D_{W1} is the mean pairwise sequence difference within population 1 and D_{W2} denotes mean pairwise sequence difference within population 2.

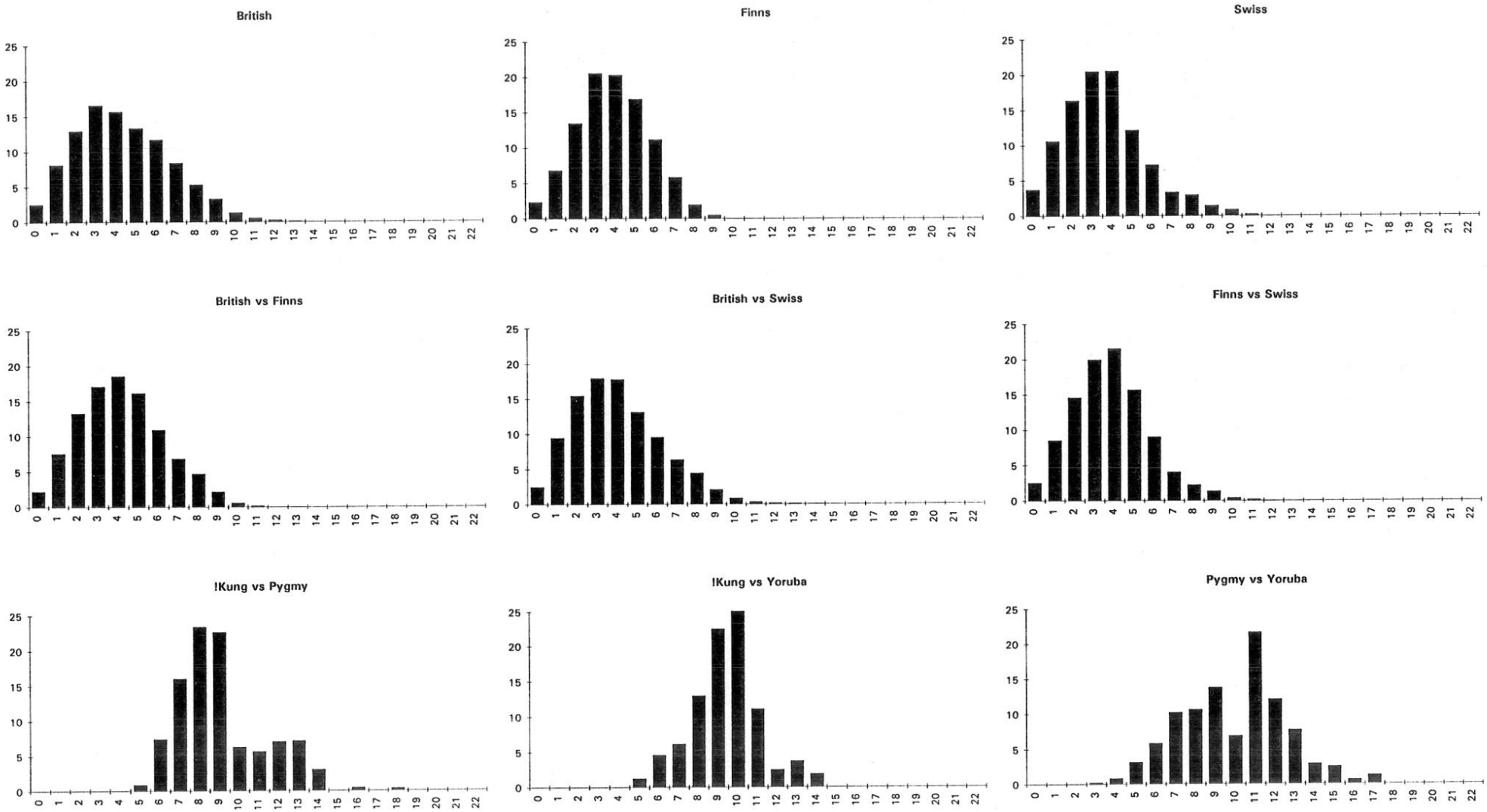

Fig. 1 Pairwise Sequence Difference Distributions Within and Between Three European Populations and Between Three African Populations.
The sample sizes were 100, 50 and 74 individuals in the British, Finnish and Swiss populations, respectively, and 25, 37 and 13 in !Kung, Pygmy and Yoruba, respectively. In each diagram, the abscissa shows the number of substitutions and the ordinate the percentage of comparisons.
Methods: The nucleotide sequences were obtained for 360 bp of the hypervariable segment I in the control region of the mitochondrial DNA corresponding to nucleotides 16024–16383 in the human reference sequence (Anderson *et al.*, 1981) using previously described methods (Ward *et al.*, 1991). The difference distributions of pairwise differences between the individuals were calculated using unpublished software by A. von Haeseler, Munich. The Swiss sequences have been deposited in the EMBL Data Library under accession numbers X 83128 – X 83201.

ferences within the populations all display a single mode at three or four substitutions. When looking at differences between European populations essentially the same pattern is observed, namely unimodal distributions with modes at four or five substitutions. In addition, the relative amounts of identical sequences are similar for the comparisons within and between these populations. Thus, there is hardly any substructure discernable in the mitochondrial gene pool in Europe.

The analysis of the three African populations reveals a different picture. Here, the comparisons between the populations have several modes at 8 to 13 substitutions. Moreover, identical lineages are not found in the comparisons between the African populations – in fact, no lineages that are closer than 3 substitutions are shared (Figure 1). Again, African populations, unlike the European ones, display substantial divergence from each other. This is supported by a statistical test for detecting genetic differentiation of subpopulations (Hudson *et al.*, 1992). In this test, the probability (P) of obtaining either the observed value for K_{ST} or a higher one in random permutations of the matrix of observed sequences is calculated. (K_{ST} is a measure of the weighted amount of sequence differences within two subpopulations relative to sequence differences in the total population). For comparisons between the European populations, the P of K_{ST} values vary from 0.032 to 0.112, whereas in all comparisons between the African populations the values are zero (data not shown). This further supports the notion that the three European populations are genetically more homogeneous than the three African populations.

Several limitations of this analysis should be mentioned. Firstly, the sample sizes of the African populations are small. However, it is very unlikely that a larger sample would reduce the observed diversity; rather, by analyzing larger numbers of individuals, more diversity may be expected. This is supported by the observation that, as mentioned above, no pair of identical sequences was found between different African populations (Figure 1). Secondly, only three populations were analyzed on each continent. This reflects the paucity of sequence data available. In the future, it will be important to investigate if any European populations fall outside the homogeneous mitochondrial gene pool analyzed so far. In Africa, other population groups may turn out to be more closely related to each other than the ones examined to date. Thirdly, the mitochondrial gene pool represents only one locus and exclusively female descent and migration. Thus, in order to get a more complete picture of human genetic history, nuclear loci with a high resolving power will have to be characterized and subjected to comparative studies.

In spite of these caveats, the data support the notion that the history of African and European populations is considerably different. African populations are characterized by a higher intrapopulation diversity than European populations and by an even more pronounced diversity between populations. In contrast, the European mitochondrial gene pool analyzed so far is characterized by little, if any geographical substructure (see also DiRienzo and Wilson, 1991; Piazza, 1993; Handt *et al.*, 1994; Torroni *et al.*, 1994). This homogeneity could have at least two causes, which are not necessarily mutually exclusive. Firstly, extensive migration within Europe could have homogenized the gene pool subsequent to colonization of the continent. In view of the linguistic and geographical diversity in Europe, we feel that such high levels of migration over the entire continent are unlikely to be solely responsible for the homogeneity of the gene pool, in spite of some historically well known movements of populations, *e.g.* at the end of the Roman era. Alternatively, European populations may share a recent common ancestry that may be linked to the arrival of anatomically modern humans in the area some 40000 to 30000 years ago, or to the spread of agriculturalists from the Near East between 10000 and 6000 years ago (Cavalli-Sforza *et al.*, 1994). In any case, the unimodal peak in the distribution of pairwise sequence differences in Europe is characteristic for expanding populations (Slatkin and Hudson, 1991; Harpending *et al.*, 1993; but also Marjoram and Donelly, 1994). Using an evolutionary rate for the hypervariable segment of the mitochondrial control region of 0.118×10^{-6} along a mitochondrial lineage (Stoneking *et al.*, 1992), a date of around 50000 years is calculated for the mode of four substitutions (Figure 1, see also Harpending *et al.*, 1993). Thus, the putative expansion of European populations fits the arrival of modern humans in Europe. This hypothesis is compatible with the notion that modern humans replaced archaic forms (Neanderthals) in Europe without admixture.

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