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Genetics

Flow of mitochondrial DNA across a species boundary

(European mouse populations/restriction enzymes/cleavage maps/protein electrophoresis/hybrid zone)

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ABSTRACT **Restriction analysis shows that wild Scandinavian mice belonging to the species *Mus musculus* contain the mitochondrial DNA of a neighboring species, *M. domesticus*. This demonstration results from comparisons of Scandinavian mice with authentic *M. domesticus* and *M. musculus* from other parts of Europe. Electrophoretic and immunological analysis of eight diagnostic proteins confirms that mice from north of the hybrid zone in Denmark are *M. musculus* in regard to their nuclear genes. In contrast, the mice tested from this region and a nearby part of Sweden have exclusively *M. domesticus* types of mitochondrial DNA. Phylogenetic analysis of the restriction maps suggests that the mitochondrial DNAs found in Scandinavian *M. musculus* could stem from a single *M. domesticus* female.**

The growing use of mtDNA as a tool for genetic research on animal populations (1, 2) makes it important to compare the ability of nuclear and mitochondrial genomes to move between populations. [mtDNA differs conspicuously from nuclear DNA not only by being outside the nucleus but also by existing in thousands of copies per cell, being inherited maternally, and evolving quickly (3, 4).] Such a comparison can be made by examining the distribution of genes across a hybrid zone—i.e., a geographic zone where two species meet and interbreed but where there is limited flow of nuclear genes (5).

Of all the hybrid zones examined by both organismal and molecular biologists, that between two species of mice in Denmark is the best known (6–8). The comprehensive study by Hunt and Selander (7) of proteins encoded by the nuclei of 2,696 mice caught at 44 Danish localities delineated the hybrid zone as regards nuclear genes. In addition, the protein evidence agrees with anatomical evidence as to the geographic location of this hybrid zone (6–8).

Further protein work has shown how these Danish mice are related to other commensal mice (9, 10). Commensal mice are those species that live in close association with buildings used by humans. They contrast with aboriginal mice (in Europe: *Mus spretus*, *M. hortulanus*, and *M. abbotti*), which live predominantly independent of human dwellings and, in nature, do not interbreed with commensal mice (10–12). According to a phylogenetic analysis of the protein data, there are two commensal mouse species in Europe. One, known as *M. domesticus*, lives in southern Denmark, in most of the rest of western Europe, and around the Mediterranean Sea (11, 12) (see Fig. 1). The second, *M. musculus*, lives in northern Denmark, the rest of Scandinavia, and eastern Europe (11, 12). The hybrid zone defined by Ursin (6) and Selander and co-workers (7, 8) is the meeting place of *M. domesticus* and *M. musculus* in Denmark (see Fig. 1). These two types of mice are sometimes considered as semispecies. Our decision to refer to them as separate species is based not only on extensive morphological and biochemical evidence (10–12) but also on the observation that there is a high incidence of sterility in the male offspring of crosses between *M. musculus* females and males from laboratory strains of *M. domesticus* (13).

Mice are also appropriate for comparing mitochondrial and nuclear gene flow because much is already known about their mtDNA. Bibb *et al.* (14) worked out the complete nucleotide sequence for mtDNA from a common laboratory strain of *M. domesticus*, and genetic variation in the mtDNA of mice from various localities in Europe, North Africa, and the Near East has been surveyed (1, 15, 16).

This paper reports the use of restriction enzymes to compare mtDNA from mice collected in the vicinity of the Danish hybrid zone with mtDNA from authentic *M. domesticus* and *musculus* populations collected elsewhere. We also made a parallel study of proteins encoded by the nuclei of these mice. The results of the two studies contrast sharply.

MATERIALS AND METHODS

Mice. Most of the mice examined were trapped in the wild or were descendants of wild individuals caught within the last 10 years at 13 localities, 11 of which are shown on the map (Fig. 1). An inbred strain of *M. domesticus* (DBA/2, from National Institutes of Health) was included for reference.

mtDNA Comparisons. mtDNA was purified to homogeneity from single animals and then digested with three restriction enzymes (*Xba* I, *Mbo* I, and *Hin*fI from New England BioLabs); fragments were labeled at the ends with ^{32}P, separated electrophoretically in 1.2% agarose or 3.5% polyacrylamide gels, and detected with x-ray film (1). The sizes of the fragments were estimated by comparison with the known sizes of the fragments of old inbred mtDNA, whose complete base sequence is established (14). By considering these fragment sizes in relation to those predicted by the known sequence, we constructed cleavage maps for about 70 cleavage sites in each of the *M. domesticus*-like mtDNAs and about 40 cleavage sites in each of the *M. musculus* mtDNAs.

To estimate the percentage divergence between base sequences of pairs of mtDNAs, we used two approaches. The first, based on map comparisons, uses equation 16 of Nei and Li (17), which assumes that there is heterogeneity among cleavage sites with respect to the probability of base substitution. This assumption has been validated by recent sequence studies (18). The second approach, based on the fraction of shared fragments, uses equation 20 of Nei and Li (17), which assumes homogeneity among cleavage sites with respect to the probability

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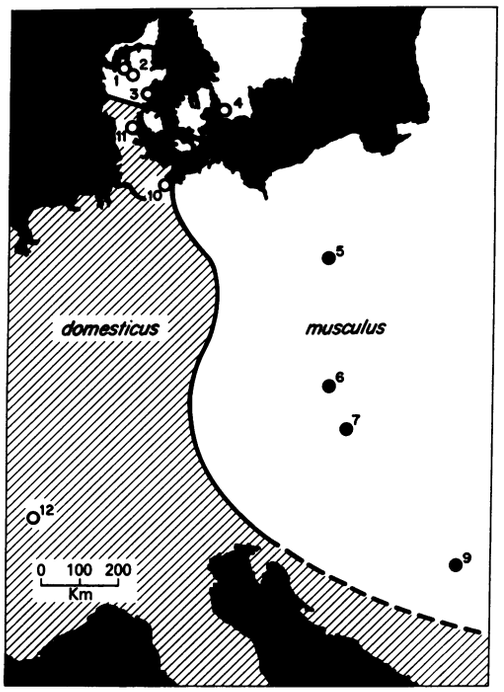

FIG. 1. Map of a part of Europe showing the distribution of the two commensal species of house mice, *M. domesticus* and *M. musculus*, and their mtDNAs. The two species meet and hybridize in a narrow zone, indicated by the thick line, extending from Denmark through Central Europe to the Black Sea (7, 9). The numbers refer to localities where mice were collected for this study. On the *M. musculus* side of the hybrid zone are Skive (*1*), Viborg (*2*), and Hov (*3*), northern Denmark; Malmö (*4*), Sweden; Turew (*5*), Poland; Brno (*6*) and Bratislava (*7*), Czechoslovakia; Halbturn (*8*), Austria (not shown because these mice were analyzed for proteins encoded by the nucleus but not for mtDNA); and Belgrade (*9*), Yugoslavia. On the *M. domesticus* side of the hybrid zone are Lübeck (*10*), Federal Republic of Germany; Haderslev (*11*), southern Denmark; Nyon (*12*), Switzerland; and Giza (*13*), Egypt (not shown). The empty and solid circles mark sites of occurrence of *M. domesticus*-like and *musculus* mtDNA, respectively.

of base substitution and takes no account of back mutations. Because both approaches ignore the fact that transitions occur more often than transversions (18), they can underestimate the extent of point mutational divergence. However, the degree of underestimation is slight for sequences that differ by <5%. For closely related mtDNAs, sequence determination and restriction analysis generally produce very similar estimates of sequence divergence, provided that at least 40 restriction sites are examined per mtDNA (18).

Protein Comparisons. From an electrophoretic study of 56 protein-encoding loci in mouse populations (10), we selected seven loci for their power to discriminate between the *M. domesticus* and *musculus* species. The preparation of tissue extracts and the electrophoretic methods of separating and detecting enzymes were described by Sage (19). Genetic variants of immunoglobulins were surveyed by testing mouse sera in solid-phase radioimmunoassays for reactivity with 18 monoclonal antibodies, which were directed against products of three immunoglobulin loci (*Igh-1*, *Igh-3*, and *Igh-4*) (20). *Igh-3* was chosen for its superior ability to discriminate between *M. domesticus* and *musculus*.

RESULTS

mtDNA Comparisons. Table 1 lists the fragment sizes (in base pairs) observed electrophoretically after digesting mtDNA from 36 mice with three restriction enzymes. Twenty-three

Table 1. Sizes of fragments produced by digestion of mouse mtDNA with three restriction enzymes

M. domesticus-like					*M. musculus*			*M. spretus*
A		B			C	D		E
7576		7576			5066	5066		9361
5066		5066			3994	3994		5066
1923		2378			3241	3582		934*
934		934			1254	1254		
455		341			934	934		
341					669	669		
					455	455		
					341*	341		
A	D	F	I	K	L	M	N	P
2009	2009	2009	2009	2009	2009	2009	2009	1400
1608	1819	1724	1608	1608	1608	1608	1608	1310
1372	1344	1372	1564	1564	1530	1530	1372	1200
1344	885	936	1344	1344	1372	1452	1350	1020
845	845	845	845	845	1080	1080	1080	1000
772	772	772	772	772	845	845	845	655
705	705	705	705	705	772	772	772	635
598	598	598	598	598	705	705	685	630
581	581	581	581	581	598	598	598	620
533	533	533	529	529	533	533	581	610
529	529	529	488	488	520	520	533	598
488	488	488	468	468	488	488	488	591
468	487	468	461	461	478	478	478	529
461	468	461	444	444	468	468	468	478
439	461	439	439	369	450	450	450	468
369	439	408	369	343	369	369	369	461
343	369	369	343	320	297	327	297	435
340	343	343	320	301	269	297	269	410
301	340	340	301	297	259	269	259	389
297	301	301	297	279	255	259	255	337
259	297	297	259	259	222	255	222	335
222	259	259	222	222	211	211	211	295
211	222	222	213	213	147	147	192	255
192	192	192	211	211	120	120	147	219
155	155	155	155	160	112	112	120	214
147	147	147	147	155	105	95	112	192
120	120	120	120	147	95	88	105	182
105	105	105	105	120	88	67	95	147
104	104	104	95	105	80	63	88	145
95	95	95*	88	95	67	55†	67	112
88	88	88	67	88	63	34†	63	104
67	67	67	63†	67	55†	31†	55†	88
63	63†	63†	34†	63†	34†		34†	85
34	34†	34†	31†	34†	31†		31†	67
31	31†	31†		31†				63†
								34†
								31†
A	E	I	L	O	P	Q	R	S
1993	1993	1734	1993	1734	2248	2248	2248	1993
1734	1734	1631	1734	1631	1993	1653	1993	1140
1329	1026	1329	1459	1459	1370	1370	1370	1026
1026	946	1326	1329	1329	1026	1026	1026	980
946	920	1026	1242	1026	880	880	950	935
920	879	946	1030	946	855	650	855	920
879	713	920	946	879	638	638	638	905
638	638	638	879	638	539	539	539	765
539	539	539	732	533	505	505	505	732
533	533	533	638	497	493	493	493	638
497	497	497	485	489	489	489	489	630
489	489	489	480	485	485	485	485	575
485	485	485	447	480	480	480	480	533
480	480	455	417	447	450	450	450	485
447	447	417	405	417	447	447	447	463
417	417†	405	399	399	383	383	383	460
399	416†	399	368	368	368	368	368	447
368	405	368	367	367	360	360	360	417
367	399	367	318	362	355	355	355	383
318	368	362	212	318	318	340	318	368
263	367	318	195	263	243	318	243	333
243	318	243	144	243	216	243	216	225
216	243	216	67†	216	212	216	212	216
212	216	212	9†	212	203	212	203	212
195	212	195		195	190	205	190	190
144	200	144		144	98	203	98	180
94	195	67†		94	90	190	90	95†
67	144	25†		67	73	185	73	9†
48†	67†	9†		48†	70	90	67	
9†	9†			9†	67	73	52†	
					52†	70	9†	
					9†	67		
						52†		
						9†		

Sizes of fragments produced by *Xba* I (*Top*), *Mbo* I (*Middle*), and *Hin*fI (*Bottom*) are shown in base pairs.

*Two fragments of this size are predicted from the band intensity and comparison with the nucleotide sequence of old inbred mtDNA (14).

†Fragments too small to be observed routinely with the present method (or fragments of nearly identical size that give overlapping bands) but predicted from the cleavage maps (Fig. 3).

Table 2. Quantitative comparison of fragment patterns for mouse mtDNA

Population	No. of mice	Fragment patterns	Difference matrix: Scandinavian 1	2	3	4	*M. musculus* 5	6	7	9	*M. domesticus* 10	11	12	13	14
Scandinavian															
Skive (1)	1	BIL	—	0	3	3	67	68	71	68	6	28	40	32	28
Viborg (2)*	1	BIL	0	—	3	3	67	68	71	68	6	28	40	32	28
Hov (3)	22	AIL	0.2	0.2	—	0	66	67	70	67	3	25	37	29	25
Malmö (4)	1	AIL	0.2	0.2	0	—	66	67	70	67	3	25	37	29	25
M. musculus															
Poland (5)	1	DNP	5.7	5.7	5.5	5.5	—	11	16	15	67	60	67	63	56
Czechoslovakia (6)	1	CLP	5.7	5.7	5.6	5.6	0.6	—	11	12	68	64	70	66	60
Czechoslovakia (7)	1	DLQ	6.0	6.0	5.9	5.9	1.0	0.6	—	17	71	65	71	69	63
Yugoslavia (9)	2	DMR	6.0	6.0	5.9	5.9	0.9	0.7	1.1	—	68	66	72	66	62
M. domesticus															
W. Germany (10)	1	AKL	0.3	0.3	0.2	0.2	5.6	5.7	6.0	5.9	—	28	40	32	28
S. Denmark (11)	1	AAO	1.9	1.9	1.7	1.7	4.5	4.9	4.9	5.3	2.0	—	20	20	6
Switzerland (12)	1	AFI	3.0	3.0	2.8	2.8	5.3	5.7	5.7	6.1	3.0	1.3	—	22	20
Egypt (13)	1	ADE	2.3	2.3	2.1	2.1	4.8	5.0	5.4	5.3	2.3	1.3	1.5	—	14
Inbred (14)	1	AAA	1.9	1.9	1.7	1.7	4.1	4.4	4.7	4.8	2.0	0.4	1.3	0.9	—

The mouse mtDNAs examined come from populations 1–13 (Fig. 1) and the inbred mouse (14). The single letters identify, from left to right, the fragment patterns listed in Table 1 for the enzymes *Xba* I, *Mbo* I, and *Hin*fI. The upper right half of the matrix gives the number of fragment differences. Estimates of the percentage difference in nucleotide sequence shown in the lower left half were made with equation 20 of Nei and Li (17). Similar values were obtained by comparing the mtDNA maps with equation 16 of Nei and Li (17).
*The patterns reported earlier (1) for Viborg mtDNA were in error.

fragment patterns were observed, each being designated by a capital letter. In each case, the summed sizes of the fragments produced by a given enzyme equals about 16.3 kilobases, which corresponds to one mitochondrial genome (14). The total number of fragments observed in the three digests, and hence the average number of restriction sites examined, is ≈70 for a typical mtDNA.

Table 2 gives the correspondence between mice and fragment patterns; there are 11 types of mtDNA in the commensal mice examined. The upper right part of Table 2 shows the number of fragments that were different for each pair of mtDNAs. The five types of mtDNA from authentic *M. domesticus* mice differed from each other by the presence or absence of 6–40 fragments. [This extent of variation among *M. domesticus* mice is representative of the results obtained from a study of a much larger sample ($N > 100$). Some of the results of this larger study appear in ref. 1; all will be reported in a comprehensive paper on the genealogical relationships among wild and laboratory strains of *M. domesticus*.] Likewise, the authentic *M. musculus* mtDNAs differed by 11–17 fragments from one another. In contrast, there are 56–72 fragment differences between the mtDNAs of authentic *M. domesticus* and *musculus*.

mtDNAs from Scandinavian localities on the *musculus* side of the hybrid zone are extremely similar to one another. Only two types, differing from each other by three fragments, were

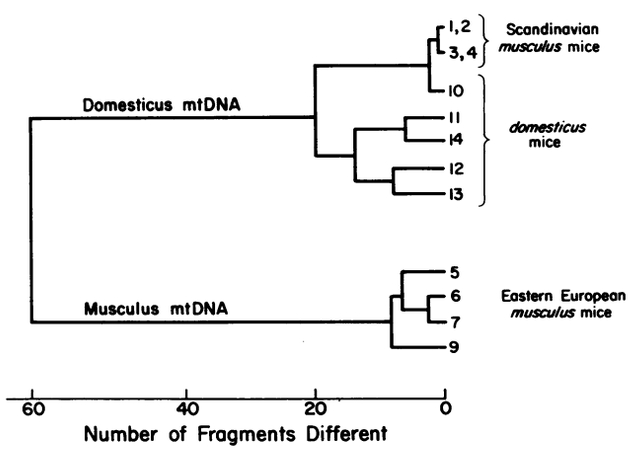

FIG. 2. Tree showing the close genealogical relationship of mtDNA from Danish mice to mtDNA from authentic *M. domesticus*. The tree was built with the parsimony method (21), by considering the fragment sizes in Table 1 as characters. This tree-building method, it should be emphasized, does not assume that the rate of mtDNA evolution is constant. To obtain a root for the tree, we used the mtDNA of *M. spretus*. The most parsimonious tree (shown here) requires 115 changes in character state. By contrast, an alternative tree which derives the Scandinavian mtDNAs from the *M. musculus* mtDNA lineage requires 27 more changes.

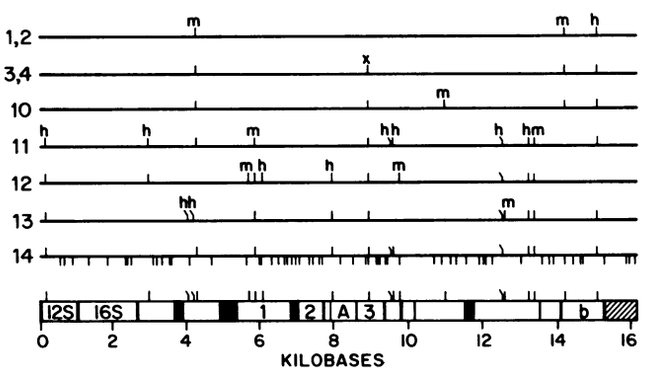

FIG. 3. Genetic maps for variable and constant cleavage sites in *M. domesticus* mtDNAs. The sites were mapped by the method of Cann *et al.* (2) and with reference to the published sequence for a laboratory mouse (14). The numbers 1–13 on the left indicate localities at which the mice were collected (see Fig. 1). Map 14 is for the laboratory mouse (patterns A in Table 1), and it shows below the line the 60 cleavage sites conserved in all the *M. domesticus*-like mtDNAs examined. The marks above each horizontal line indicate variable sites: *m*, *Mbo* I; *h*, *Hin*fI; *x*, *Xba* I. The maps are oriented with the origin of replication at 0. The bar shows the locations of the mitochondrial genes of known function: black areas indicate tRNA genes or spacers; 1, 2, and 3 are cytochrome oxidase genes; A is the ATPase gene; and b is the cytochrome *b* gene. The marks on the top of the bar show the 20 variable cleavage sites at which the seven maps differ.

found among the 25 mice examined (Table 2). Moreover, they differ only slightly from an authentic *M. domesticus* type of mtDNA (from locality 10). More recent results show that one of the Scandinavian mtDNA types (from localities 3 and 4) occurs also in a *M. domesticus* mouse from Cittaducale in central Italy. For these reasons, we consider the known Scandinavian types of mtDNA to belong in the *domesticus* category.

Tree analysis confirms the idea of a genealogical relationship between the mtDNAs of all Scandinavian mice tested and those of authentic *M. domesticus*. Fig. 2 shows the most probable order of branching of the lineages leading from a common ancestor to the 11 types of mtDNA. Alternative trees that ally the mtDNAs of northern Scandinavian mice (from localities 1–4) with authentic *M. musculus* mtDNAs require at least 27 more fragment changes than does the tree shown. The mtDNA tree indicates that the two northern Scandinavian lineages are highly related to each other and to the *M. domesticus* lineage from locality 10 and implies that the two northern Scandinavian types of mtDNA could be each other's closest relatives.

Cleavage maps were constructed for the *M. domesticus*-like mtDNAs (Fig. 3) by relating the fragment patterns to the known sequence of the old inbred type of mouse mtDNA (14). All of the differences in fragment patterns could be accounted for by base substitutions at a total of 20 cleavage sites, with no evidence for any large deletions or additions of DNA (i.e., >20 base pairs). The 20 variable sites are scattered widely in the genome, as has been observed in comparisons of mtDNAs from other closely related mammals (2). We also located numerous cleavage sites in *M. musculus* mtDNAs, obtaining complete maps for *Xba* I and partial maps for *Mbo* I and *Hin*fI, which establish that *M. musculus* mtDNAs have about the same overall length (16.3 ± 0.1 kilobases) as *M. domesticus* mtDNA. Therefore, the mtDNA differences within and between the two species likely arose by the usual process of point mutational divergence.

Table 3. Genetic variation at eight protein loci in mice

Protein-encoding locus	Allele	Allele frequency, % Danish 1–3	*M. musculus* 6–9	*M. domesticus* 12–14
Adh	1	7	5	100
	2	89	95	0
	3	4	0	0
Est-1	1	100	100	4
	2,3	0	0	96
Est-2	1	7	5	100
	2	4	90	0
	3	89	5	0
Est-D	1	4	25	82
	2	0	0	18
	3	96	75	0
Idh-s	1	100	100	22
	2	0	0	78
*Igh-3**	16	29	25	100
	23,24	71	75	0
Mpi	1	100	100	0
	2	0	0	100
Pnp	1,2	0	0	100
	3,4	86	0	0
	5	11	65	0
	6	3	0	0
	7	0	35	0

The Danish mice were from three localities (1–3) on the northern side of the hybrid zone; the other mice were from localities (6–14) far from the boundary between *M. domesticus* and *musculus* (see Fig. 1), or from the inbred strain DBA/2 (1). The proteins examined (and the loci that encode them) were alcohol dehydrogenase (*Adh*), esterases 1, 2, and D (*Est*-1, -2, and -D), isocitrate dehydrogenase (*Idh-s*), immunoglobulin 3 (*Igh-3*), mannose phosphate isomerase (*Mpi*), and purine nucleotide phosphorylase (*Pnp*). A preliminary analysis of the locus encoding esterase-1 shows the *M. domesticus* from localities 10 and 11 to have allele *2*, which predominates in other *M. domesticus*, and the *M. musculus* from locality 4 to have allele *1*, as in other *M. musculus*. Sample sizes for the 10 tabulated populations are 1, 1, 12, 1, 1, 1, 7, 9, 15, and 1.

* For immunoglobulin, phenotypic rather than allelic frequencies are reported. Sample sizes for the tabulated populations are 1, 1, 12, 4, 1, 0, 3, 1, 8, and 1 (population 8 was not examined).

The lower left part of Table 2 gives estimates of the percentage divergence in nucleotide sequence among all these mitochondrial genomes. Besides emphasizing the *domesticus*-like character of the Scandinavian mtDNAs, these estimates draw attention to the large sequence divergence between authentic *M. musculus* and *domesticus* mtDNAs, ≈5%. This value of 5% agrees with our expectation, which is based on the degree of nuclear DNA difference between the *domesticus* and *musculus* species and on the assumption that mtDNA consistently evolves faster than nuclear DNA. A comparison of humans and chimpanzees has shown that in them, as in other primates, mtDNA evolves 5 to 10 times faster than does nuclear DNA (18). The genetic distance between *M. domesticus* and *musculus* proteins (encoded by nuclear DNA) is about half as big as that between humans and chimpanzees (7, 10, 22). Likewise, the extent of mtDNA divergence for these two mouse species is about half of that between humans and chimpanzees (18). It follows that, for mice, mtDNA divergence has probably been 5 to 10 times faster than nuclear DNA divergence.

Protein Comparisons. The results of our protein comparisons contrast sharply with the mtDNA findings. For several populations of mice, we examined the allele frequencies for eight protein-encoding loci which can easily distinguish between *M. domesticus* and *musculus*. In confirmation and extension of previous studies (7, 10), we found that at every one of these loci, the Scandinavian mice (from localities 1–3) resemble *M. musculus* more closely than *M. domesticus* (Table 3). Tree analysis also emphasizes the close relationship of the proteins of northern Scandinavian mice to those of authentic *M. musculus* (Fig. 4). Furthermore, each of the 14 mice sampled at localities 1–3 appears to be fully *M. musculus* as regards alleles at the eight

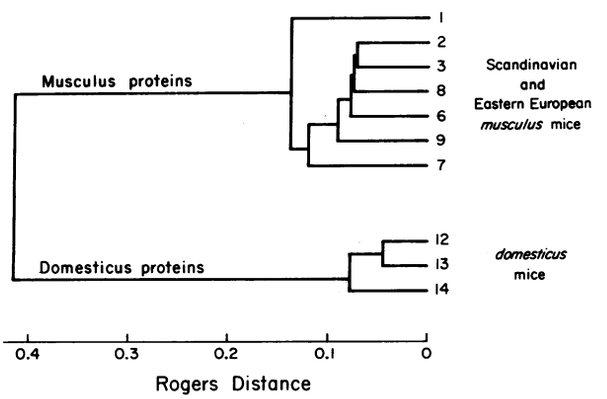

FIG. 4. Tree showing the close relationship of protein loci from Danish mice to those of authentic *M. musculus*. The tree was built by the distance Wagner method (23) from a matrix of Rogers distances (24) based on allele frequencies examined in 10 populations for seven of the eight diagnostic proteins (Table 3); because the immunoglobulin results are phenotypic frequencies, they were omitted. The length of this tree is 1.538. An alternative tree having the topology shown in Fig. 2 (and lacking sample 8) is of length 1.733 and, therefore, is less parsimonious.

diagnostic loci. The results support the conclusion that at none of the diagnostic loci has there been extensive introgression of *M. domesticus* nuclear genes into the *M. musculus* populations sampled in northern Denmark. We recognize that our present sample sizes are too small to allow detection of a low level of nuclear gene flow across the hybrid zone.

DISCUSSION

The ability of mtDNA from one species to invade another species and displace the resident mtDNA is not without precedent. A laboratory strain of mice, KL/oci, which belongs to the species *M. molossinus* with regard to its nuclear genes, has lost *M. molossinus* mtDNA and gained the old inbred type of mtDNA from *M. domesticus* during the past 15 years (1). The present study shows that interspecific transfer of mtDNA can take place in the wild as well. Yonekawa *et al.* (16) independently discovered that mtDNA from northern Danish mice is more related to that of *M. domesticus* than to that of eastern European *M. musculus*, but they did not point out the significance of this finding.

If the flow of organelle DNA between populations that exchange scarcely any nuclear DNA turns out to be common, it will have consequences for the definition of biological species. Traditionally, the biological species is defined as a group of individuals whose common gene pool is protected against the inflow of alien genes (25). While in no way suggesting that this biological species concept will have to be abandoned, we do foresee the possible need for defining species in terms of their nuclear genes.

Our limited survey has revealed only two closely related types of *M. domesticus* mtDNA in the *M. musculus* mice of Scandinavia. These two types could be the result of one colonization event, involving a single *M. domesticus* individual that entered *M. musculus* territory long enough ago to allow two of the descendant lineages to have diverged slightly in nucleotide sequence. A fuller survey will reveal how far *M. domesticus* mtDNA extends into *M. musculus* territory and whether, indeed, we are dealing with a single colonization event. It also should be possible to estimate from the magnitude of the nucleotide sequence diversity when the colonization event or events occurred. Assuming a divergence rate of 2–4% per 1×10^6 years for mtDNA (18), we already can estimate from the restriction data that the *M. domesticus* types of mtDNA in *M. musculus* territory had a common ancestor within the past 100,000 years, a time which is far more recent than that estimated for the divergence of *M. domesticus* and *musculus* mtDNAs (i.e., at least 1×10^6 years). Nucleotide sequence data will permit more accurate estimates of these times.

Experiments aimed at identifying the factors responsible for the replacement of *M. musculus* mtDNA by *M. domesticus* mtDNA in the Scandinavian mice should look for a possible selective or replicative advantage of *M. domesticus* mtDNA, as well as at the reproductive behavior and success of the two species of mice when they come into contact.

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