Geographic origin of the Y Chromosomes in "old" inbred strains of mice

Priscilla K. Tucker,[1,2] Barbara K. Lee,[1] Barbara L. Lundrigan,[2] and Eva M. Eicher[1]

[1]The Jackson Laboratory, Bar Harbor, Maine 04609, USA; [2]The Museum of Zoology and Department of Biology, University of Michigan, Ann Arbor, Michigan 48109, USA

Abstract. Six distinct Y Chromosomes (Chr) were identified among 39 standard inbred strains of mice with five probes that identified Y Chr-specific restriction fragments on Southern blots. Three Y Chr types, distributed among 31 strains, were of Asian *Mus musculus* origin. The remaining three Y Chr types, distributed among eight strains, were of *M. domesticus* origin. The Asian source of the *M. musculus* Y Chr was confirmed by determining the DNA sequence of 221 bp from an open reading frame within the *Sry* (sex determining region Y) gene (Gubbay et al., *Nature 346:* 245–250, 1990) in three inbred strains (C57BL/6J, AKR/J, and SWR/J) and comparing the sequence to the homologous sequences derived from wild caught European and Asian *M. musculus* males. These data indicate that a minimum of six male mice contributed to the formation of the old inbred strains.

Introduction

The "old" inbred strains of the laboratory mouse are known to be derived from the rodent species complex *Mus musculus* (Family Muridae, subfamily Murinae). This cosmopolitan species complex is composed of numerous geographically isolated populations displaying considerable genetic differentiation and identified as either distinct subspecies or species (reviewed in Bonhomme 1986; Moriwaki et al. 1986). Bonhomme and co-workers recognize four biochemically defined subspecies of *Mus musculus* (Bonhomme et al. 1986): *Mus musculus domesticus,* which is distributed throughout Western Europe, the Mediterranean basin, Africa, and the Middle East, and has been introduced by man to other continents; *M.m. bactrianus,* which ranges from Iran to Pakistan and India; *M.m. castaneus,* which

ranges from Ceylon to South East Asia; and *M.m. musculus,* which ranges from Eastern Europe, across northern Asia, to Japan. *M.m. molossinus* from Japan, an additional subspecies frequently mentioned in the literature, is actually a mixture of Asian *M.m. musculus, M.m. castaneus,* and *M.m. domesticus* genomes (Yonekawa et al. 1986, 1988; Bonhomme et al. 1989). (For convenience we refer to samples of *M. musculus* from Japan as *M.m. molossinus.*) The classification system of Bonhomme and co-workers is generally accepted except for *M.m. domesticus,* which is considered by some to be a separate species.

Species designation is justified because European populations of *M. domesticus* and *M.m. musculus* hybridize only restrictively in a narrow zone of overlap (Hunt and Selander 1973; Ferris et al. 1983b; Vanlerberghe et al. 1986, 1988a, 1988b; Sage et al. 1986a, 1986b; Tucker et al. 1992). For this reason we hereafter refer to *M.m. domesticus* as *M. domesticus.*

Although the genealogical history of many of the "old" inbred strains is documented (reviewed in Morse 1978; Atchley and Fitch 1991), information regarding the relationship of the founding individuals to their wild ancestors is not recorded. It is believed that mice from Japan contributed to the formation of the "old" inbred strains by way of the mouse fanciers' trade (Keeler 1931; Potter 1978; Festing and Lovell 1981). This is in accord with biochemical data suggesting that Japanese *M.m. musculus* (*M.m. molossinus*) and *M.m. castaneus* both contributed to the formation of inbred strains (Blank et al. 1986).

During the past decade, the origins of inbred mouse strains have been investigated by use of restriction fragment length polymorphism (RFLP) studies of two clonally inherited molecules, maternally inherited mitochondrial DNA (mtDNA) and paternally inherited Y Chr-specific DNA (Yonekawa et al. 1980, 1982; Ferris et al. 1982, 1983a; Bishop et al. 1985; Nishioka and Lamothe 1986; Nishioka 1987). The majority of the "old" inbred strains carry *M. domesticus* mtDNA and

an *M. musculus* Y Chr, while a smaller number carry *M. domesticus* mtDNA and an *M. domesticus* Y Chr. Because the Y-specific probes used in these studies could not distinguish between Asian- and European-derived *M. musculus* Y Chrs, it was unclear whether the *M. musculus* Y Chr of the inbred strains was of Asian or Eastern European origin.

We previously reported that the Y-specific probe pYB10 could identify different Y Chrs among populations of *M. musculus* and *M. domesticus* mice and, in particular, could differentiate between *M. musculus* Y Chrs of Asian and Eastern European origin (Tucker et al. 1989). We have extended this study to determine the Y chromosomal origin of 39 inbred strains of mice.

Materials and methods

Mice

Pedigreed pairs of mice from the following inbred strains and sublines were obtained from either the Foundation or Research colonies of The Jackson Laboratory and are listed in Table 1. Wild mice used in this study were either field-caught or were obtained from established laboratory colonies. Original collecting localities for field-caught mice and wild mice obtained from laboratory colonies are given in Tucker and co-workers (1989). Thirty inbred strains were

Table 1. Summary table of the six types of Y Chrs among inbred strains identified using three distinct hybridization probes. In some cases more than one subline (identified by indentation) of an inbred strain was examined.

Asian *M. musculus*		*M. domesticus*
Type 1A	*Type 1B*	*Type 3*
A/HeJ[a,b]	HRS/J[a,c]	SJL/J[a,b]
AEJ/GnLe[a]	NZB/BlNJ[a,b,c]	SWR/J[a,b,c]
AU/SsJ[a]		BUB/BnJ[a,b]
BALB/c	*Type 2*	ST/bJ[a,b]
BALB/cBy[a,b,c]	CBA	
BALB/cWtEi[a]	CBA/J[a,b]	*Type 4*
BDP/J[a,b]	CBA/CaJ[a,b]	MA/MyJ[a,b]
C57BL/6	C3H	PL/J[a,b]
C57BL/6J[a,b,c]	C3H/HeJ[a,b,c]	
C57BL/6ByJ[a]	C3H/OuJ[a]	*Type 5*
C57BL/6KsJ[a]	DBA/1J[a,b]	AKR/J[a,b,c]
C57BL/10	DBA/2J[a,b]	RF/J[a,b]
C57BL/10J[a,b]		
C57BL/10GnDgWtKk[a]		
C57BL/10SnJ[a]		
C57BL/10ScSnJ[a]		
C57BR/cdJ[a,b]		
C57L/J[a,b]		
C58/J[a,b,c]		
CE/J[a,b]		
DA/HuSn[a]		
FS/Ei[a]		
I/LnJ[a]		
LG/J[a]		
LP/J[a,b]		
LT/SvEi[a,b]		
P/J[a,b]		
RIIIS/J[a,b]		
SEA/GnJ[a,b]		
SEC/1ReJ[a,b]		
SM/J[a,b,c]		
V/Le[a]		
YBR/Ei[a,b]		
129/J[a,b]		

[a] Inbred strains probed with pXenv and pMo-MCFenv.
[b] Inbred strains probed with pYB10.
[c] Inbred strains probed with $XENO_{112}$ and MCF_{100}.

used in the pYB10 analysis. An additional nine strains for a total of 39 strains were used in the pXenv and pMo-MCFenv analyses. Nine strains (of the 39 sampled) were used in the $XENO_{112}$ and MCF_{100} analysis (see footnote in Table 1).

Hybridization probes and radiolabeling

Five probes were used: (1) pYB10 (EMBL accession #X12900), a 305-bp *Eco*RI-*Pst*I anonymous sequence that detects multiple copy sequences on the Y Chr of C57BL/10 and on the Y Chr of five species in the genus *Mus* (Eicher et al. 1989); (2) pXenv, a 455-bp *Bgl*II-*Eco*RI *env*-specific sequence of NSF-Th-1 xenotropic MLV proviral DNA (Buckler et al. 1982); (3) pMo-MCFenv, a 622-bp *Bam*HI-*Eco*RI *env*-specific sequence of the Moloney-MCF virus (Bosselman et al. 1982); (4) $XENO_{112}$, a unique 112-bp xenotropic *env*-specific sequence isolated from the NZB-IU-6 virus; and (5) MCF_{100}, a 100-bp of unique (mink cell focus-forming) *env*-specific sequence (O'Neill et al. 1986). Probes were labeled to a specific activity of 0.5×10^9 cpm/µg (pYB10) or 1×10^9 cpm/µg (pXenv and pMo-MCFenv) with α-^{32}P-dCTP (Amersham) according to Maniatis and colleagues (1982) and with the T_4 polymerase kit supplied by BRL. The $XENO_{112}$ and MCF_{100} probes were labeled according to a modification of the M13 dideoxy sequencing method previously described (Eicher et al. 1989).

Restriction endonuclease digestions and Southern blot analyses

Five restriction enzymes, including one four-base cutter (*Taq*I) and four six-base cutters (*Bgl*II, *Eco*RI, *Pvu*II, *Pst*I), were used in the analysis of pYB10. One restriction enzyme (*Bgl*II) was used in the analysis of pXenv, pMo-MCFenv, $XENO_{112}$, and MCF_{100}. Restriction endonuclease digestions, Southern blot preparations, hybridization conditions, and autoradiography were performed as described by Tucker and co-workers (1989).

Analysis of autoradiographs and phylogenetic analysis

The approximate size of each YB10 restriction fragment was ascertained. Fragments of indistinguishable size generated by the same restriction enzyme were assumed to be identical between taxa, and each taxon was scored for presence or absence of each restriction fragment identified. The restriction fragments were used as characters in a phylogenetic analysis by use of parsimony (PAUP, version 2.4; Swofford 1985). Variation in copy number among equal-sized restriction fragments was not scored as a separate character. The use of a multiple copy DNA sequence for phylogenetic analyses presents a methodological problem because restriction fragments of a repeated sequence cannot be mapped to specific sites, and thus it is impossible to determine whether the presence or absence of each restriction fragment represents an independent evolutionary event. Despite this problem, previous analyses have demonstrated that the YB10 repeat is phylogenetically informative (Tucker et al. 1989). Sizes of Y-specific restriction fragments also were determined for each of the nonecotropic viral probes, but were not included in the phylogenetic analysis.

PCR amplification and sequencing of an Sry open reading frame

Two oligonucleotide primers (5' AGATCTTGATTTTTAGTGTTC 3' and 5' GAGTACAGGTGTGCAGCTCTA 3') were used to enzymatically amplify a 471-bp fragment from the *Sry* locus (Gubbay et al. 1990) following Saiki and colleagues (1985) and the protocol of Perkin-Elmer Cetus, except that only one-half of the recommended concentration of each 10-µM primer was used. Controls consisted of primers, dNTPs, buffer, and *Taq* polymerase, but no template DNA. Double-stranded products were separated on a 3% Nusieve

gel, stained with ethidium bromide, and visualized under UV light. To verify that amplified sequences were Y specific, preliminary amplification experiments included both male and female genomic DNA from each inbred strain and subspecies under investigation. Amplification of the target size sequence (the 471 bp open reading frame) in males only was taken as evidence that the sequence was Y-specific.

Double-stranded products were purified by centrifugation dialysis as described by Allard and co-workers (1991). Purified double-stranded products were dried under vacuum and resuspended in 15 μl of 1 × TE. Single-stranded DNA was amplified from 2 μl of the double-stranded product by use of the reaction conditions for the double-stranded amplification, except that only the 5' primer was included. Single-stranded sequences were visualized and purified by the procedure described for double-stranded products. Purified single-stranded products were dried under vacuum and resuspended in 15 μl of 1 × TE buffer. Half of the purified single-stranded product was sequenced by the Sanger dideoxy sequencing technique (Sanger et al. 1977) and the Sequenase Version 2.0 sequencing kit (United States Biochemical) according to the manufacturer's recommendations.

Sry sequence analysis

Sequences were aligned (Altschul and Ericson 1986) with the published sequence from the 129 inbred strain (Gubbay et al. 1990). Aligned sequences were inspected for nucleotide substitutions.

Results

RFLP analysis with pYB10

Five distinct YB10 hybridization patterns identifying Y Chr types 1 through 5 (Table 1) were detected on Southern blots containing male genomic DNA from 30 inbred mouse strains (Table 2, Fig. 1). Representatives of these five patterns were included in a phylogenetic analysis (PAUP, version 2.4; Swofford 1985) along with 25 samples from geographically distinct populations of *M. musculus* and *M. domesticus,* and one sample of *M. spicilegus.* (*M. spicilegus* is considered a sister taxa to *M. domesticus* and *M. musculus* and thus served as the outgroup). In total, 123 restriction fragments generated from single digests were used as characters, and 25 most parsimonious trees were found in a heuristic search. In all 25 trees the relationship of inbred strains to wild-caught *M. domesticus, M.m. molossinus,* European *M.m. musculus,* and *M.m. castaneus* were identical (Fig. 2). The two types of inbred strains represented by C57BL/6J (type 1) and CBA/J (type 2) were most closely related to *M. m. molossinus,* and the three classes of inbred strains represented by SWR/J (type 3), AKR/J (type 5), and MA/MyJ (type 4) were most closely related to *M. domesticus.* The inbred strains represented by SWR/J were most closely related to *M. domesticus* collected in Germany; the inbred strains represented by AKR/J and MA/MyJ were most closely related to *M. domesticus* collected in Maryland.

RFLP analysis with nonecotropic virus probes

Four distinct male-specific hybridization patterns were observed when *Bgl*II-digested DNA from males and females of 39 inbred strains was hybridized with the nonecotropic virus probes pXenv and pMo-MCFenv. The eight inbred strains identified as having a *M. domesticus* Y Chr with pYB10 (types 3, 4, and 5, Table 1) contained no *Bgl*II male-specific proviral fragments. The remaining 31 strains, including the 22 inbred strains identified as having an *M. musculus* Y Chr with pYB10, were divided into three types (Table 1): type 1A contained a 7.8, 6.0, and 4.6 kb *Bgl*II male-specific fragment; type 1B contained the 7.8 and 4.6 kb *Bgl*II male-specific fragments; and type 2 contained only the 4.6 kb *Bgl*II male-specific fragment. Because pXenv and pMo-MCFenv do not distinguish xenotropic from MCF proviral sequences, further analysis was performed with $pXENO_{112}$, a xeno-specific probe, and $pMCF_{100}$, an MCF-specific sequence on DNA from females and males of nine inbred strains (see Table 1), representing each of the previously identified types. Male-specific patterns of hybridization identical to those observed with the pXenv and pMo-MCFenv were observed only with $pXENO_{112}$; no male-specific *Bgl*II fragments were identified with $pMCF_{100}$, indicating that the proviral sequences located on these *M.m. musculus* Y Chrs are xenotropic in origin.

Sequence analysis of the Sry open reading frame

The nucleotide sequence of 221 bp (positions 162–383) of the 471 bp open reading frame from *Sry* was determined for three inbred strains (SWR/J, AKR/J, and C57BL/6J), two *M.m. musculus* males from Europe (Skive, Denmark; and Sladeckovce, Czechoslovakia), one *M.m. molossinus* male from Asia (Kyushu, Japan), one *M.m. castaneus* male from Asia (Chonburi, Thailand), and three *M. domesticus* males (Poschiavo, Switzerland; Tirano, Italy; and Erfoud, Morocco). Only a single base pair substitution was found among these 10 samples; the samples of *M.m. molossinus* and C57BL/6J contain a thymine in place of cytosine at nucleotide position 285, resulting in a non-conservative amino acid change (threonine to isoleucine) in the putative open reading frame.

Discussion

We identified six types of Y Chrs among the 39 inbred mouse strains examined, based on the combined results of RFLP analyses with pYB10 and three nonecotropic virus probes (Table 1). These six types include three Y Chrs of Asian *M. musculus* origin and three of *M. domesticus* origin. Our data both corroborate and augment earlier findings in which two types of Y Chrs were identified in inbred mice (Lamar and Palmer 1984; Bishop et al. 1985; Nishioka and Lamothe 1986; Nishioka 1987).

The Asian origin of the *M. musculus* Y Chr found in most "old" inbred mouse strains is supported by the RFLP analysis with *YB10* and the analysis with the male sex-determining gene *Sry.* The 221-bp sequence of *Sry* from Asian *M. musculus* (*M.m. molossinus*) is

Table 2. Presence and absence of YB10 restriction fragments in inbred strains of mice and representative samples from *Mus musculus* and *M. domesticus*. The presence of a specific size restriction fragment is given by an "X," and the absence of a restriction fragment is given by a "−."

Enzyme	Fragment[b] (kb)	C57BL/6J[c]	CBA/J[d]	AKR/J[e]	MA/MyJ[f]	SWR/J[g]	M. domesticus[a]	M. musculus[a] molossinus	musculus	castaneus
*Taq*I	6.6	−	−	X	X	X	X	−	−	−
	5.8	X	X	X	X	X	X	X	X	X
	5.5	X	X	−	−	−	−	X	−	X
	4.6	−	−	X	X	−	−	−	−	−
	2.8	X	X	−	−	−	−	X	X	X
	2.5	−	−	−	−	X	X	−	−	−
	2.3	X	X	−	−	X	−	−	−	−
	2.1	X	X	X	X	X	X	X	X	X
	1.6	−	X	−	−	−	−	X	X	X
	1.5	−	X	X	X	X	X	X	X	X
	1.3	X	X	X	X	X	X	X	X	X
*Bgl*II	9.6	X	X	X	X	X	X	X	X	X
	8.2	X	X	−	−	−	−	X	−	−
	7.8	−	−	X	X	−	−	−	−	−
	7.1	−	−	−	−	−	−	X	−	X
	6.8	−	−	X	X	−	−	−	−	−
	6.0	−	−	X	X	X	X	−	−	−
	5.8	−	−	−	−	−	−	−	X	−
	5.6	−	−	X	X	X	X	−	−	−
	5.0	X	X	X	X	X	X	X	X	X
	4.5	−	−	X	X	X	X	−	−	−
	4.1	−	−	−	−	X	X	−	−	−
	3.5	−	−	−	−	−	−	−	X	−
	3.3	−	−	X	X	X	X	−	−	−
	3.0	X	X	−	−	−	−	X	X	X
	2.9	X	X	−	−	X	−	X	−	X
	2.8	−	−	−	−	−	−	−	X	−
	2.5	−	−	−	−	X	X	−	−	−
*Eco*RI	12.5	X	X	−	−	−	−	X	X	X
	10.0	X	X	X	X	X	X	X	X	X
	8.8	−	X	−	−	−	−	X	X	X
	7.4	X	X	X	X	X	X	X	X	X
	5.4	−	−	−	−	−	−	−	X	−
	4.6	X	X	−	−	−	−	X	−	−
	4.5	−	−	−	−	−	−	X	X	−
	4.3	X	X	−	−	−	−	−	−	−
	4.0	−	−	−	−	X	−	−	−	−
	3.7	X	X	X	X	X	X	X	X	X
	3.3	−	−	X	X	−	−	−	−	−
	3.0	X	X	−	−	−	−	X	−	−
	2.9	−	X	X	X	X	X	X	X	X
	2.7	−	−	X	X	−	−	−	−	−
	2.6	X	X	−	−	−	−	−	−	−
	2.5	−	−	X	X	−	−	−	−	−
	2.3	−	−	X	X	−	−	−	−	−
*Pvu*II	19.0	−	−	−	−	−	−	−	−	X
	14.0	X	X	−	−	−	−	X	−	−
	8.9	X	X	X	X	X	X	X	X	X
	8.4	X	X	X	X	X	X	X	X	X
	7.7	−	−	X	X	X	X	−	−	−
	6.9	X	X	X	X	X	X	X	−	X
	6.5	−	−	X	X	X	X	−	−	−
	6.0	X	−	−	−	−	−	X	−	−
	5.8	−	X	−	−	−	−	−	−	−
	5.5	−	−	−	−	X	X	−	−	−
	5.0	−	−	−	−	−	−	−	X	−
	4.7	−	−	X	X	−	−	−	−	−
	4.5	−	−	X	X	−	−	−	−	−
	4.4	−	−	−	−	X	−	−	−	−
	3.7	−	−	−	X	X	−	−	−	−
	3.1	−	−	−	−	−	−	−	X	−
	2.8	−	−	X	X	X	X	−	−	−
	2.7	−	−	X	X	X	X	−	−	−
*Pst*I	5.8	−	−	X	X	X	X	−	−	−
	4.5	−	−	X	X	−	−	−	−	−
	4.2	−	−	X	X	−	X	−	−	−
	3.5	−	−	X	X	X	X	−	−	−
	3.0	−	−	X	X	X	X	−	−	X
	2.7	−	−	X	X	X	X	−	−	−
	2.6	X	X	X	X	X	X	X	X	X
	2.2	X	X	X	X	X	X	X	X	X
	2.0	X	X	X	X	X	X	X	X	X
	1.8	−	−	X	X	−	−	−	−	−

[a] Hybridization patterns for *M. domesticus* and *M. musculus* are given for individual samples. Thus, some fragments are characteristic of the species or subspecies, and others are specific to the individual sampled.
[b] Presumed variation in copy number based on slight differences in the intensity of hybridization were observed among a few equal-sized fragments. Thus, this table represents minimal variation in YB10 sequences across taxa.
[c] Identical patterns of hybridization were observed in A/HeJ, BALB/cBy, BDP/J, CE/J, C57BL/10J, C57BR/cdJ, C57L/J, C58/J, LP/J, LT/Sv, NZB/BlNJ, P/J, RIIIS/J, SEA/GnJ, SEC/1ReJ, YBR/Ei, and 129/J.

[d] Identical patterns of hybridization were observed in CBA/CaJ, C3H/HeJ, DBA/1J, and DBA/2J.
[e] Identical patterns of hybridization were observed in RF/J.
[f] Identical patterns of hybridization were observed in PL/J.
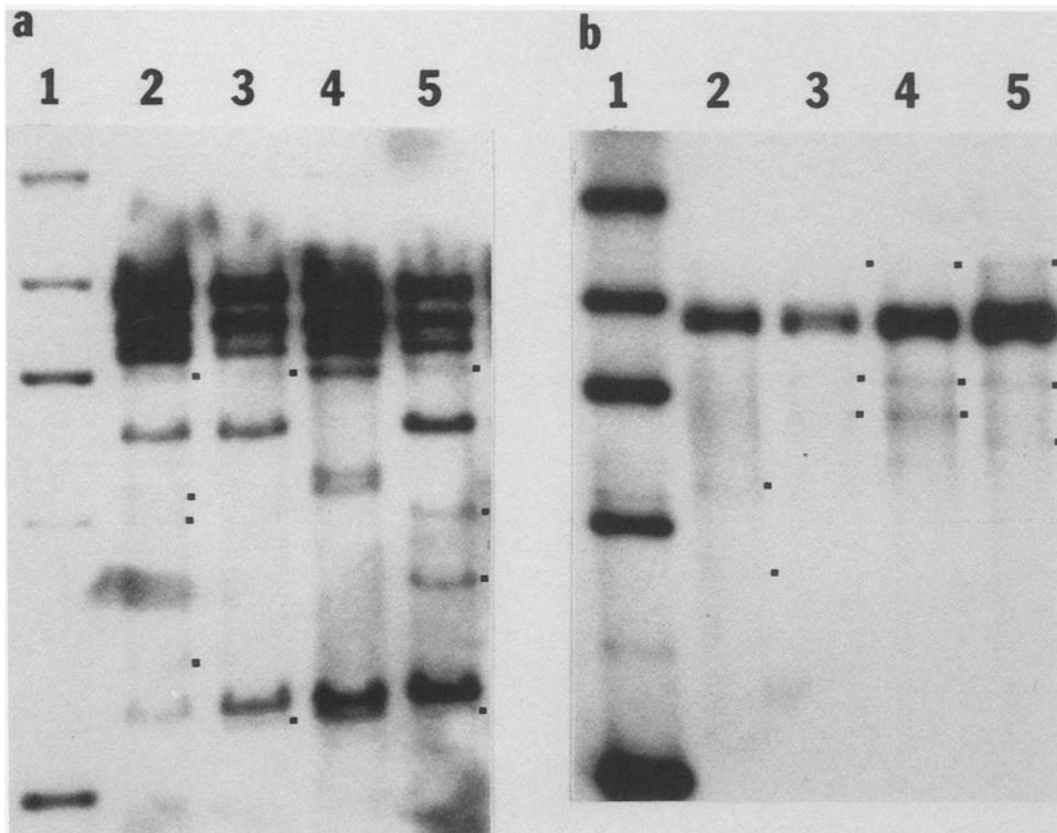[g] Identical patterns of hybridization were observed in SJL/J, BUB/BnJ, and ST/bJ.

Fig. 1. Two autoradiographs of male genomic DNA cut with *Pvu*II and probed with pYB10. (a) Lane 1, λ *Hind*III size standard; lane 2, *M. domesticus* from Heidelberg, Germany; lane 3, *M. domesticus* from Tübingen, Germany; lane 4, RF/J; and lane 5, ST/bJ. (b) Lane 1, λ *Hind*III size standard; lane 2, *M.m. musculus* from Vejrumbro, Germany; lane 3, *M.m. molossinus* from Japan; lane 4, LT/Sv; and lane 5, DBA/2J. Low copy number fragments are identified by **closed circles**.

identical to that of C57BL/6J and 129, the latter published by Gubbay et al. (1990), but differs from homologous sequences in other subspecies of *M. musculus* and *M. domesticus* by a single base pair change at position 285. Because both YB10 and *Sry* are from the region of the Y Chr that does not recombine with the X Chr, we hypothesize that all inbred strains with a C57BL/6J and 129 YB10 hybridization pattern also will carry an *Sry* sequence of Asian origin.

Our data support the view that mice from Japan contributed to the formation of the "old" inbred strains by way of the mouse fanciers' trade (Keeler 1931; Potter 1978; Festing and Lovell 1981). The presence of *M.m. castaneus* as well as *M.m. molossinus* alleles in inbred mouse strains (Blank et al. 1986) can be explained if the founding males of most of the inbred strains were derived from Japanese *M.m. molossinus*, which is actually a mixture of Asian *M.m. musculus, M.m. castaneus,* and *M. domesticus* genomes (Yonekawa et al. 1986, 1988; Bonhomme et al. 1989).

Our data also are in accord with historical records documenting the establishment of many of the inbred strains (reviewed in Morse 1981). For example, one type of Asian *M. musculus* Y Chr is shared by four inbred strains that are known to be related through paternal ancestry. These include CBA, C3H, DBA/1J,

and DBA/2J (Table 1). Strong (1942) mated a male from "stock D", the progenitor strain of DBA/1 and DBA/2, to a female from "stock A" to produce "stocks" that ultimately gave rise to CBA and C3H inbred strains. A second type of Asian *M. musculus* Y Chr is shared by 20 of the inbred strains examined, including C57BL/6, C57BL/10, C57BR, C57L, and C58. The progenitor stocks to C57BL, C57BR, C57L, and C58 are known to be related through paternal ancestry, because a single male (mouse #52) was mated to two different females (#57 and #58) to produce the C57 and C58 lineages, respectively (Little and Bagg 1924). The observation that a large number of inbred strains carry the C57BL-type Y Chr may reflect the fact that these strains are related through paternal ancestry, because the progenitors of many inbred strains, including C57BL, can be traced back to A.E.C. Lathrop, a mouse fancier from Granby, Massachusetts (Morse 1981).

Our data should help to clarify the origin of inbred strains for which there are no historical records. For example, SWR/J and SJL/J, which share one type of *M. domesticus* Y Chr, are derived from the so-called "Swiss" mice developed at the Rockefeller Institute by C. Lynch and descended from a Pasteur Institute stock (Lynch 1969). The Y Chrs of SWR/J and SJL/J, as well as BUB/BnJ and ST/bJ, are most closely re-
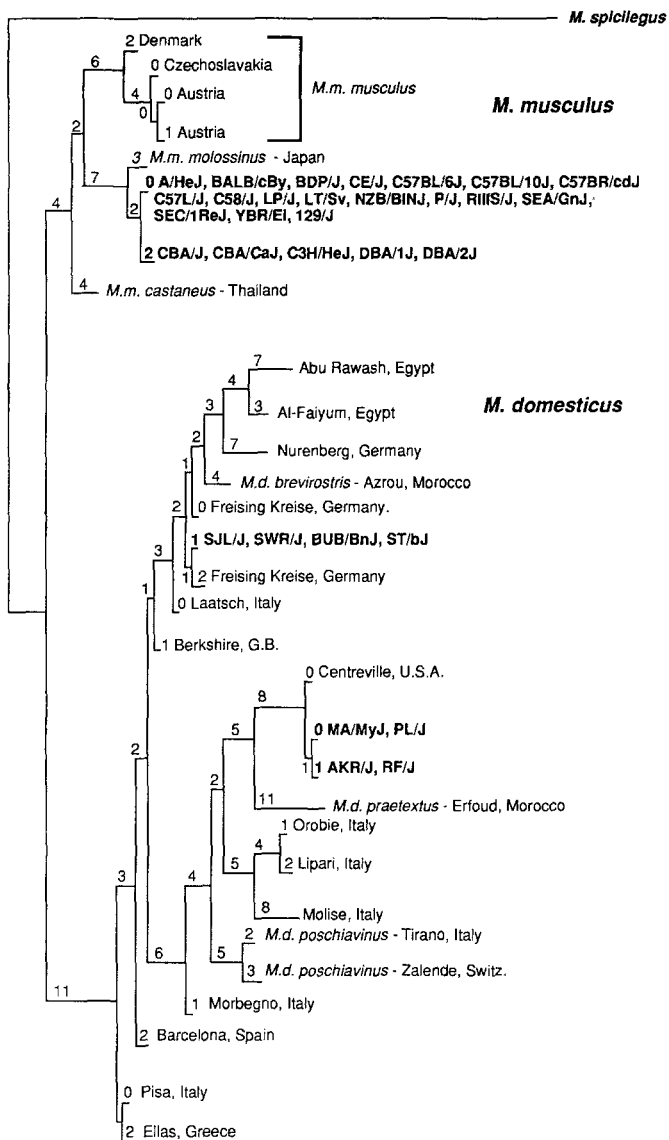
Fig. 2. An evolutionary tree constructed by a phylogenetic analysis by use of parsimony. This tree is one of 25 most parsimonious trees found in a heuristic search. The outgroup is *M. spicilegus* (also referred to as *M. hortulanus*). The length of the tree is 196 steps. The consistency index, a measure of the amount of homoplasy in the data, is 0.612. The number of characters (restriction fragments) that determine the length of each horizontal branch is given. Exact collecting localities for all samples are given in Tucker and co-workers (1989). Samples given subspecies designations are indicated.

lated to the Y Chrs of *M. domesticus* from western Europe, suggesting that the paternal ancestors for these inbred strains were *M. domesticus* from western Europe. The two other types of *M. domesticus* Y Chrs found among four inbred strains, one in MA/MyJ and PL/J and the second in AKR/J and RF/J, are very similar to each other and are most closely related to a Y Chr found in *M. domesticus* mice collected in Maryland, suggesting that the paternal ancestors for these strains were *M. domesticus* whose ancestors "migrated" to the eastern United States. Although RF has been traced to a "Rockefeller Institute" stock (Morse 1981), Lynch (1969) states that RF was not derived

from the "Swiss" mice, but rather from another "Rockefeller Institute" stock developed in the United States. Our Y Chr data support her contention. It is interesting that AKR/J and RF/J, which have identical YB10 hybridization patterns, were both developed by Jacob Furth (Morse 1981). The close relationship of AKR and RF has recently been supported in phylogenetic analyses of other nuclear genes (Atchley and Fitch 1991).

Many of the inbred strains examined in this study contain *M. domesticus*-derived mtDNA (Yonekawa et al. 1980, 1982; Ferris et al. 1982, 1983a), but none of the old inbred strains examined to date carry Asian *M. musculus*-derived mtDNA. This is a surprising finding in light of the preponderance of Asian *M. musculus* Y Chrs among the inbred strains examined. It is conceivable that early in the development of European and English fancy mice, crosses were made between Japanese fancy mice of *M.m. molossinus* origin and *M. domesticus* mice of western European origin. Possibly, only crosses between female *M. domesticus* and male *M.m. molossinus* produced fertile offspring. As a consequence, European and English fancy mice acquired *M. domesticus* mtDNA and an *M.m. molossinus* Y Chr. Presumably, these mice became part of the American mouse fanciers' trade and contributed to the formation of the "old" inbred strains. Indeed, records indicate that Lathrop imported fancy mice from both England and western Europe (Lathrop and Loeb 1915). In some cases, fancy mice of pure *M.m. molossinus* origin may have been imported from Europe and subsequently crossed with wild *M. domesticus* from North America.

Finally, the presence of *M. domesticus* mtDNA and Asian *M. musculus* Y Chrs in most of the inbred strains examined is evidence that many inbred strains of the laboratory mouse are composed of a mixture of two, or possibly three (including *M.m. castaneus*), distinct genomes. As a consequence, inbred mouse strains should not be considered to be of *M. domesticus* or of *M. musculus* origin. Recently, Artzt and co-workers (1991) have suggested that all inbred mice be regarded by the scientific name *Mus laboratorius*. This is not appropriate from the standpoint of zoological classification because inbred mice do not constitute a single species characterized by a distinct set of shared derived traits. Rather, inbred mouse strains should be identified by their strain names and simply considered to be of a hybrid *M. musculus* × *domesticus* origin or possibly of a hybrid *M. musculus* × *domesticus* × *castaneus* origin. Furthermore, the use of *laboratorius* violates the standards set forth in Article 11 of the International Code of Zoological Nomenclature adopted by the General Assembly of the International Union of Biological Sciences (1985).

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