

Y-chromosomal DNA polymorphism in mouse inbred strains

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Summary

Mice are the most widely used experimental mammals, and many inbred strains are available. However, except for the relatively recent strains derived from known wild populations, the relationships between wild and laboratory mice are not well understood. Based on the Y-chromosomal restriction fragment-length polymorphism, seventeen inbred strains were classified into two groups: strains with the *Mus musculus musculus* type Y chromosome and those with the *M. m. domesticus* type Y chromosome. We extended the survey to an additional twenty-two inbred strains. The *M. m. musculus* type Y chromosome was found in AEJ/GnLe, AAU/SsJ, BDP/J, BXSb/MpJ, DA/HuSn, HTG/GoSfSn, I/LnJ, LP/J, NZW/LacJ, RIIS/J, SB/Le, SEA/GnJ, SF/CamEi, SK/CamEi, SM/J, WB/ReJ, WC/ReJ and YBR/Ei, while the *M. m. domesticus* type Y chromosome was present in BUB/BnJ, MA/MyJ, PL/J and ST/bJ.

1. Introduction

The availability of many inbred strains is a major reason for the extensive use of mice (*Mus musculus*) in mammalian genetical research. However, except for the strains recently established from wild populations, the origins of most inbred strains cannot be traced back to particular wild populations because of mixing of mice at the early stage of their maintenance in laboratories (Keeler, 1931; Festing & Lovell, 1981; Potter, 1978). Two subspecies of house mice exist in Europe, *M. m. musculus* and *M. m. domesticus*, and a narrow hybrid zone has been identified (Ferris *et al.* 1983; Hunt & Selander, 1973; Selander, Hunt & Yang, 1969). Analyses of nuclear and mitochondrial DNA suggested that the genetic background of classical inbred strains is mostly that of *M. m. domesticus* (Ferris *et al.* 1983; Morse, 1978; Yonekawa *et al.* 1980, 1982). However, recent studies with Y chromosomal DNA fragments showed that many classical strains have the *M. m. musculus* type Y chromosome (Bishop *et al.* 1985; Nishioka & Lamothe, 1986).

It is well documented that Japanese mice (*M. m. molossinus*) were imported into Europe during the last century and that they were also used in many American laboratories in the early part of this century (Festing & Lovell, 1981; Keeler, 1931; Potter, 1978). Thus it is likely that the *M. m. musculus* type Y chromosome in classical inbred strains was derived from *M. m. molossinus*, whose Y chromosome is as yet indistinguishable from that of *M. m. musculus* (Nishioka & Lamothe, 1986). Detailed molecular analysis may cast light on the dubious origins of classical inbred strains.

Based on the Y-chromosomal DNA polymorphism, seventeen inbred strains have already been classified into two categories, those with the *M. m. musculus* type Y chromosome and those with the *M. m. domesticus* type Y chromosome (Bishop *et al.* 1985; Nishioka & Lamothe, 1986). Here we describe an extended survey of another twenty-two additional inbred strains.

2. Materials and methods

Mice

All inbred strains used in this study were purchased from the Jackson Laboratory (Bar Harbor, Maine). Wild house mice were caught in a barn at Macdonald College, McGill University, Ste Anne de Bellevue, Quebec. Authentic *M. m. musculus* and *M. m. domesticus* were obtained from Dr M. Potter of the National Cancer Institute (Bethesda, Maryland).

Filter hybridization

High-molecular-weight DNAs isolated from liver were digested with EcoRI (Gibco/BRL, Burlington, Ontario) and electrophoresed on 0.8% agarose gel in a buffer consisting of 40 mM Tris (pH 8.0), 80 mM sodium acetate and 1 mM EDTA. DNA fragments were transferred to membrane filters (Gene Screen, New England Nuclear Canada, Lachine, Quebec) by the method of Southern (1975). Filters were then air-dried and hybridized to ³²P-labelled fragment 1 of

AC 11 (Nishioka & Lamothe, 1986) in a solution containing $5 \times \text{SSC}$ ($1 \times \text{SSC}$ is 0.15 N sodium chloride and 0.015 N sodium citrate), 50% formamide, $1 \times$ Denhardt's solution (Denhardt, 1966), 0.1% SDS and $100 \mu\text{g/ml}$ of denatured herring sperm DNA for 16 h at 40°C . Filters were washed in 500 ml of $0.1 \times \text{SSC}$ at 50°C and exposed to Kodak XAR-5 film for 16–24 h.

3. Results and discussion

In America there were no aboriginal house mice and the predominant commensal species found today is *M. m. domesticus* (Sage, 1981). Previously we reported the presence of the *M. m. domesticus* type Y chromosome in eight wild American specimens from eight localities (Nishioka & Lamothe, 1986). In the summer of 1986 we trapped fourteen mice in a Quebec barn, including six males. As expected, Southern blot analysis showed the *M. m. domesticus* type Y chromosome in all of them (Nishioka, unpublished data). Furthermore, the *M. m. domesticus* type Y chromosome was present in *M. m. poschiavinus*, *M. m. brevirostris* and *M. m. praetextus*, all of which probably represent local varieties within *M. m. domesticus* (Nishioka & Lamothe, 1986. For a review on mouse systematics see Thaler, Bonhomme & Britton-Davidian, 1981).

In Asia the *M. m. musculus* type Y chromosome appears to be predominant. AC 11 identified the *M. m. musculus* type Y chromosome in two *M. m. molossinus* specimens as well as in four *M. m. musculus* specimens (Nishioka & Lamothe, 1986). Recently we examined six Asian specimens from six localities (Japan, China and Taiwan) and found the *M. m. musculus* type Y chromosome in all of them (Nishioka, unpublished data).

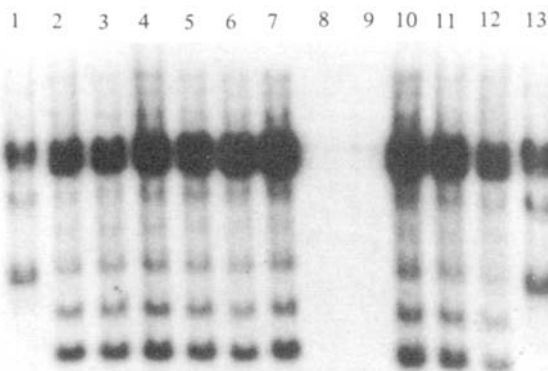


Fig. 1. Genomic Southern blots of DNAs isolated from inbred strains. 1, *M. m. domesticus*; 2, *M. m. musculus*; 3, AEJ/GnLe; 4, AU/SaJ; 5, BDP/J; 6, BXSb/MpJ; 7, DA/HuSn; 8, female (*M. m. domesticus*); 9, female (*M. m. musculus*); 10, HTG/GoSfSn; 11, I/LnJ; 12, LP/J; 13, AKR/J.

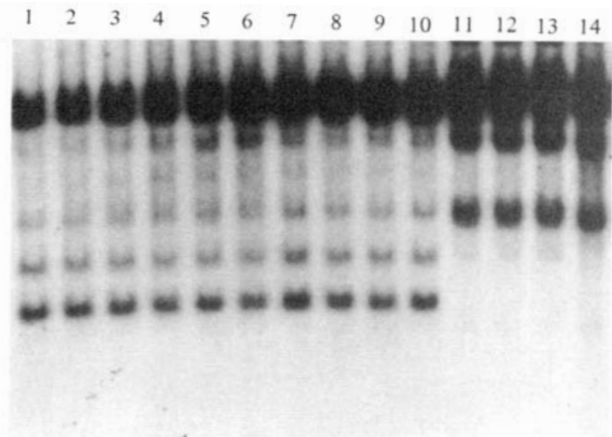


Fig. 2. Genomic Southern blot of DNAs isolated from inbred strains. 1, NZW/LacJ; 2, RIIS/J; 3, SB/Le; 4, SEA/GnJ; 5, SF/CamEi; 6, SK/CamEi; 7, SM/J; 8, WB/ReJ; 9, WC/ReJ; 10, YBR/Ei; 11, BUB/BnJ; 12, MA/MyJ; 13, PL/J; 14, ST/bJ.

Thus no discrepancy exists in the classification of wild mouse Y chromosomes with AC 11, and we have extended the survey to an additional twenty-two inbred strains obtained from the Jackson Laboratory. The *M. m. musculus* type Y chromosome was present in AEJ/GnLe, AU/SsJ, BDP/J, BXSb/MpJ, DA/HuSn, HTG/GoSfSn, I/LnJ, LP/J, NZW/LacJ, RIIS/J, SB/Le, SEA/GnJ, SF/CamEi, SK/CamEi, SM/J, WB/ReJ, WC/ReJ and YBR/Ei, whereas the *M. m. domesticus* type Y chromosome was found in BUB/BnJ, MA/MyJ, PL/J and ST/bJ (Figs 1 and 2). The results are summarized in Table 1.

Some inbred strains can be traced back to local populations. The ancestors of SF and SK were trapped in a coal mine in California and on Skokholm island, off Pembrokeshire, respectively (Staats, 1980) and the presence of the *M. m. domesticus* type Y chromosome was inferred. Unexpectedly, we found the *M. m. musculus* type Y chromosome in SF/CamEi and SK/CamEi. It is tempting to speculate that the *M. m. musculus* type Y chromosome in SF/CamEi originated from an Asian mouse brought to California. The presence of the *M. m. musculus* type Y chromosome in SK/CamEi is more difficult to explain, but contamination in the laboratory remains a possibility. Indeed, from the analysis of mitochondrial DNA, Ferris, Sage & Wilson (1982) suggested that SK/CamEi has been mixed with SF/Cam.

Among the thirty-nine inbred strains listed in Table 1, only nine have the *M. m. domesticus* type Y chromosome, of which AKR and PL were established from mice obtained from U.S. dealers and ST originated from Danish white mice (Staats, 1980). From their anatomy, it is clear that the Swiss mice are *M. m. domesticus* (Marshall, 1981) and the surveys by us and others confirmed the presence of the *M. m. domesticus* type Y chromosome in strains RF, SJL, SWR and SWV, all of which belong to the Swiss mice (Morse, 1978, Rice & O'Brien, 1980). Note however

Table 1. Classification of inbred strains by Y chromosomal polymorphism*

<i>M. m. musculus</i> type		<i>M. m. domesticus</i> type	
Strain	Reference	Strain	Reference
A/J	1, 3, 4	AKR/J	1, 4
AEJ/GnLe	2	BUB/BnJ	2
AU/SsJ	2	MA/MyJ	2
BALB/cJ	1, 3, 4	PL/J	2
BDP/J	2	RF/J	1
BXSB/MpJ	2	SJL/J	3, 4
CBA/J	1, 3	ST/bJ	2
CE/J	1	SWR/J	1
C3H/HeJ	1, 3, 4	SWV	1
C57BL/6J	1, 3, 4		
DA/HuSn	2	1, Nishioka & Lamothe (1986)	
DBA/2J	1, 3, 4	2, Nishioka (this study)	
HRS/J	1	3, Bishop <i>et al.</i> (1985)	
HTG/GoSfSn	2	4, Lamar & Palmer (1984)	
I/LnJ	2		
LP/J	2		
NZB/BINJ	1, 4		
NZW/LacJ	2		
P/J	1		
RIIIS/J	2		
SB/Le	2		
SEA/GnJ	2		
SEC/1ReJ	1		
SF/CamEi	2		
SK/CamEi	2		
SM/J	2		
WB/ReJ	2		
WC/ReJ	2		
YBR/Ei	2, 4		
129/J	1, 3		

* Lamar & Palmer (1984) were the first to recognize the presence of two types of Y chromosome in inbred strains. Subsequently, Bishop *et al.* (1985) found that these two types corresponded to the *M. m. musculus* and *M. m. domesticus* type Y chromosomes. We extended the survey to a total of thirty-nine inbred strains (Nishioka & Lamothe, 1986 and this study). The results of Lamar & Palmer (1984) are adopted here, because it is now obvious which type of the Y chromosome occurs in the strains they examined.

that the history of RF is somewhat questionable (Staats, 1980). The only exception is DA, which is believed to have originated from outbred Swiss mice (Morse, 1978; Staats, 1980), but has the *M. m. musculus* type Y chromosome. Less information is available on the origins of MA and BUB (Staats, 1980).

The information provided in Table 1 would also be useful to infer the type of Y chromosome in strains established from crosses between known inbred strains. For example, BXSB and SEA are from C57BL × SB and BALB/cxP, respectively (Staats, 1980) and consequently they have the *M. m. musculus* type Y chromosome (Table 1).

Finally, it is generally accepted that Japanese mice (*M. m. molossinus*) contributed to the establishment of classical inbred strains (Keeler, 1931; Festing & Lovell, 1981; Potter, 1978). Recently, Yonekawa *et al.* (1986) presented evidence that *M. m. molossinus* is a

subspecific hybrid between *M. m. musculus* and *M. m. castaneus*, both of which have as yet indistinguishable Y chromosomes (Y. Nishioka, unpublished data). DNA probes that differentiate between these two subspecies would be powerful molecular tools to understand the origins of classical inbred strains.

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