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Mouse DNA 'fingerprints': analysis of chromosome localization and germ-line stability of hypervariable loci in recombinant inbred strains

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ABSTRACT

Human minisatellite probes cross-hybridize to mouse DNA and detect multiple variable loci. The resulting DNA "fingerprints" vary substantially between inbred strains but relatively little within an inbred strain. By studying the segregation of variable DNA fragments in BXD recombinant inbred strains of mice, at least 13 hypervariable loci were defined, 8 of which could be regionally assigned to mouse chromosomes. The assigned loci are autosomal, dispersed and not preferentially associated with centromeres or telomeres. One of these minisatellites is complex, with alleles 90 kb or more long and with internal restriction endonuclease cleavage sites which produce a minisatellite "haplotype" of multiple cosegregating fragments. In addition, one locus shows extreme germ-line instability and should provide a useful system for studying more directly the rates and processes of allelic variation of minisatellites.

INTRODUCTION

Hypervariable tandem-repetitive regions of the human genome provide genetic markers ideal for linkage analysis [1-8]. The repeat units of some of these human minisatellites share a common "core" sequence which may act as a recombination signal involved in generating minisatellites and in promoting the unequal exchanges which are thought to maintain allelic variability in the number of repeats at these loci [9]. Hybridization probes comprised of tandem repeats of the core sequence detect many hypervariable minisatellites simultaneously in human DNA to provide an individual-specific DNA 'fingerprint' of general use in human genetics [9-14]. Pedigree analysis in man shows that these minisatellites are autosomal and dispersed [14]. The precise localization of these hypervariable loci is, however, unknown, and can only be determined by cloning and localizing individual minisatellites [15]. In view of the association of satellite DNA with centromeres and telomeres [see 16] and the prevalence of hypervariable DNA in the pseudoautosomal telomeric region of the human sex chromosomes [see 17], it remains possible that

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human minisatellites are preferentially associated with such tandem-repetitive regions. If so, this would diminish their usefulness as markers in human linkage analysis.

If the core sequence is a recombination signal, then it is likely to be conserved in evolution. As predicted, human polycore probes can detect multiple variable DNA fragments in a wide range of vertebrate DNAs with varying degrees of success depending on the species examined ([18], A.J. Jeffreys, J. Hillel and D. Morton, unpublished data). In particular, we now show that DNA fingerprints can be obtained from mouse DNA using human minisatellite probes, and that recombinant inbred strains of mice can be used both to localize mouse minisatellites and to assess the germ-line stability of these hypervariable regions of DNA.

MATERIALS AND METHODS

C57BL/6J and DBA/2J inbred mice and animals from the BXD recombinant inbred strains were received in Edinburgh directly from the Jackson Laboratory. Mice from strains A, AKR, C57BL/10, BALB/c, C3H/He and SWR were purchased from Bantin and Kingman Ltd., Hull, UK. They had originally all been obtained from Searle Ltd except A (NIMR) and BALB/c (ICI); their substrain designations are not known but their genetic authenticity has been validated [19]. *Mus musculus domesticus* mice were trapped in Ammoudia, Epirus, Greece [20].

Mouse (*Mus musculus*) liver DNA was prepared as described elsewhere [21]. 6 µg samples of DNA were digested with 15 units of *Hin*fI, *Alu*I or *Sau*3A under conditions recommended by the manufacturers, in the presence of 4 mM spermidine trichloride. Digests were recovered by phenol extraction and ethanol precipitation and electrophoresed through a 0.8% agarose gel until all DNA fragments less than 1.5 kb long had electrophoresed off the gel [14]. DNA was denatured, blotted onto nitrocellulose (Schleicher and Schuell BA85) and hybridized to ^{32}P-labelled human minisatellite probes 33.6 or 33.15 prepared by primer extension of single-stranded M13 templates as described elsewhere [9,10,14]. Hybridization and washing stringencies were at 1xSSC at 64°.

RESULTS AND DISCUSSION

Detection of multiple polymorphic mouse DNA fragments using human minisatellite probes

Human polycore probes 33.6 and 33.15 contain tandem repeats of different versions of the human core sequence and detect different sets of

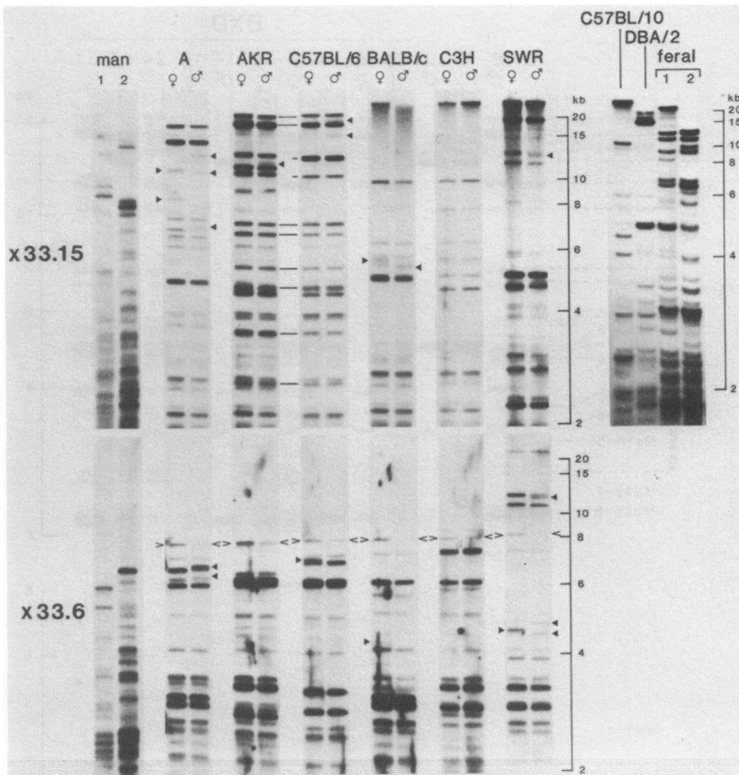

Figure 1. DNA fingerprints of inbred and feral mice (Mus musculus domesticus) detected by Southern blot hybridization of HinfI digests of mouse DNA with ^{32}P-labelled human minisatellite probes 33.15 and 33.6 [9,10]. Feral mice 1 and 2 were wild-caught in Greece. DNA samples from two humans were included for comparison. The 10 marked fragments in inbred strain C57BL/6 are linked and constitute a "haplotype" of hypervariable locus Ms15-1; 8 of these fragments are present in AKR mice. DNA fragments which vary between the two individuals sampled from each inbred strain are marked by filled arrows. The open arrows indicate an invariant 8.1 kb HinfI fragment which shows sex dosage and is presumably X-linked.

human minisatellites [10,14]. To determine whether mouse DNA also contains multiple minisatellites, these probes were hybridized to Southern blots of DNA from a selection of inbred strains of mice and from two feral Greek mice (Mus musculus domesticus); DNA was digested with HinfI to maximise the resolution of polymorphic minisatellites [9,10].

Mouse DNA fingerprints comprised of a large number of variable hybridizing DNA fragments were detected with each probe, with a complexity

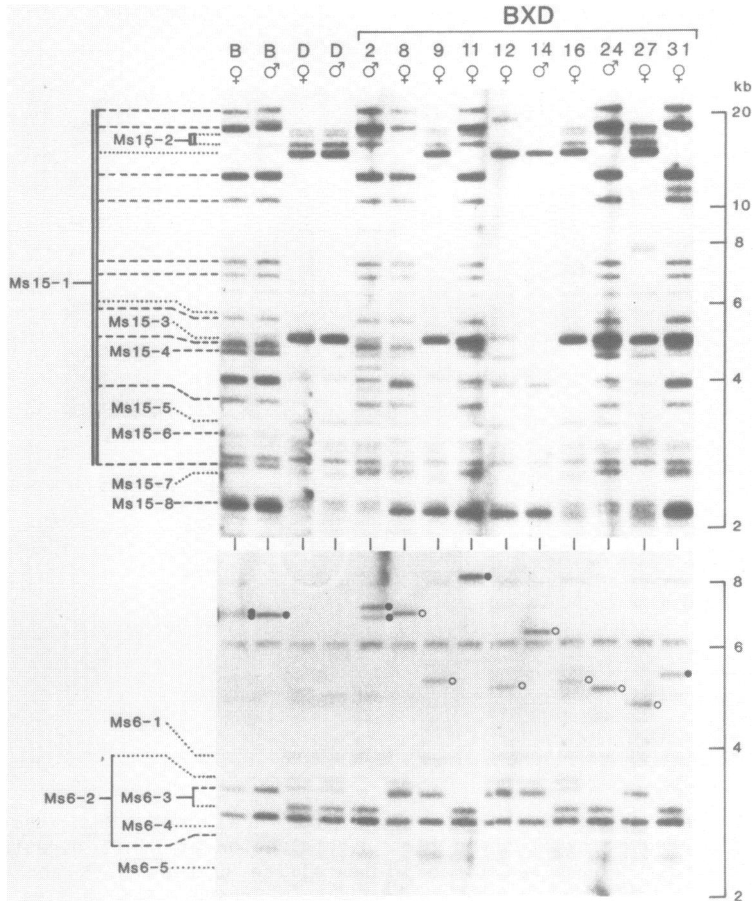

Figure 2. Segregation analysis of variable DNA fingerprint fragments in BXD recombinant inbred strains. HinfI digests of the progenitors C57BL/6J (B) and DBA/2J (D) and of ten different BXD strains were hybridized with probe 33.15 (upper panel) and 33.6 (lower panel). Strain distribution patterns (Table 1) were determined for the 27 different progenitor fragments indicated; ----, fragment present in B strain DNA; ....., fragment present in D. Additional fragments were either poorly resolved, shared by B and D strains or absent from most or all BXD strains, and were not scored. The 27 scored fragments define 13 different loci termed Ms15-1 to Ms15-8 and Ms6-1 to Ms6-5. Allelic B and D fragments are joined by a single vertical line, and linked B or D fragments by a double vertical line. Thus locus Ms15-1 is defined by ten cosegregating B fragments allelic to two cosegregating D fragments. Fragments marked ● are derived from a single hypervariable locus Ms6hm (see Fig. 3); additional fragments marked O are also probably derived from this locus.

and autoradiographic intensity comparable to those obtained from human DNA (Fig. 1). As with human DNA, probe 33.6 and 33.15 produced different DNA fingerprints. The overall patterns are specific to each inbred strain, though minor variations exist within all strains examined. This variation is not solely due to additional male-specific DNA fragments, and cannot therefore be attributed entirely to Y chromosome-specific minisatellites. The feral mouse DNA fingerprints are noticeably more complex, presumably reflecting heterozygosity at these variable loci.

Evidence for an invariant X-linked DNA fragment

One fragment detected by probe 33.6 is shared by all inbred strains examined and furthermore consistently shows an approximately two-fold reduced hybridization signal in males compared with females (Fig. 1). This sex-dependent hybridization intensity is also seen in recombinant inbred strains (data not shown), and strongly suggests that this monomorphic 8.1 kb *Hin*fI fragment is derived from the X chromosome.

DNA fingerprints of BXD recombinant inbred strains of mice

Strains C57BL/6J (B6) and DBA/2J (D2), the progenitors of BXD recombinant inbred strains of mice [22], show markedly different DNA fingerprints with both human minisatellite probes (Fig. 2). The segregation of strain-specific markers has therefore been followed in different BXD strains to detect instances of allelism between B6 and D2 DNA fragments, to test for linkage between progenitor DNA fragments, and to estimate germ-line stability of these polymorphic loci. Representative examples of BXD strain DNA fingerprints are shown in Fig. 2.

Most DNA fragments detected in BXD strains by human probe 33.15 can be traced back to one or other progenitor strain. The shorter DNA fragments in particular tend to be shared by B6 and D2 strains, and their segregation in BXD strains cannot therefore be followed. Almost all of the DNA fragments specific to contemporary B6 or D2 mice are each present in about half of the BXD strains (Table 1), suggesting that these B6 and D2 fragments are stably inherited and are representative of the ancestral B6 and D2 mice used to generate the BXD strains 50-80 generations ago [22]. In contrast, there are several instances of fragments present in BXD strains which are absent from B6 and D2 DNA fingerprints. Most of these unascribable fragments are present in no more than one BXD strain, and therefore presumably represent new length ("mutant") alleles of minisatellites generated during the ~60 rounds of brother-sister mating

Table 1. Strain distribution patterns of minisatellite loci in BXD recombinant inbred strains.

		BXD																								
Locus	**scored in**	1	2	5	6	8	9	11	12	13	14	15	16	18	19	20	21	22	24	25	27	28	29	30	31	32
Ms6-1	D	B	D	B	D	B	D	B	D	D	D	B	D	?	B	D	D	B	D	D	D	D	B	D	D	D
Ms6-2	BD	D	*	D	B	D	B	B	D	D	D	B	D	D	B	B	D	B	B	B	B	D	B	D	B	D
Ms6-3	BD	B	D	B	D	B	B	D	B	B	B	B	D	D	D	D	D	B	D	D	B	D	B	B	D	D
Ms6-4	D	D	(D)	D	D	D	B	D	B	D	B	B	B	B	D	B	D	D	D	D	D	B	B	B	B	B
Ms6-5	D	B	D	(B)	D	D	D	D	D	(B)	D	B	D	D	D	(D)	(B)	B	B	B	B	B	D	B	D	D
Ms15-1	BD	D	B	D	B	B	D	B	D	B	D	D	D	D	D	B	D	D	B	D	D	D	D	D	B	D
Ms15-2	D	B	D	D	B	B	D	D	B	D	B	D	D	B	B	(D)	B	D	D	B	D	D	B	B	B	D
Ms15-3	D	D	B	D	D	B	D	D	B	B	B	B	D	D	B	B	D	D	D	D	D	D	B	D	D	D
Ms15-4	B	B	B	B	B	B	D	B	B	B	D	D	D	D	D	B	B	(D)	B	B	B	B	D	B	B	D
Ms15-5	D	(D)	D	D	(B)	D	B	D	D	B	B	B	D	(D)	(B)	(B)	D	D	D	B	B	B	D	D	B	D
Ms15-6	B	B	D	D	B	B	D	B	D	B	D	B	D	B	D	(B)	B	D	D	B	B	D	D	D	D	(D)
Ms15-7	D	B	D	B	D	D	D	(D)	B	B	D	D	D	D	D	(B)	B	D	B	B	B	B	D	B	D	D
Ms15-8	B	B	D	B	D	B	B	B	B	B	B	B	D	D	B	B	D	B	D	D	D	D	B	B	B	D
		1	2	5	6	8	9	11	12	13	14	15	16	18	19	20	21	22	24	25	27	28	29	30	31	32

Hybridizing variable DNA fragments which define each locus are shown in Fig. 2. Allelic B6- and D2-specific fragments could be detected only for Ms6-2, Ms6-3 and Ms15-1; each other locus had a resolvable allele in only one of the two progenitor strains indicated. ?, not typed; ( ), phenotype provisional; *, neither B6 nor D2 fragment present, either BXD 2 is a new mutant at this locus, or the b and d "alleles" of Ms6-2 are derived from two closely-linked minisatellites.

used to produce each BXD strain [21]. In addition there is a low level of variability detectable within individual BXD strains, comparable to that seen within other inbred strains of mice (Fig.1, data not shown).

A hypermutable mouse minisatellite

BXD DNA fingerprints detected by probe 33.6 show similar properties to those produced by probe 33.15, with the notable exception of a prominent 7 kb HinfI fragment specific to B6 DNA (indicated in Fig. 2), which is not present in any of the 25 different BXD strains tested. Furthermore, many of the BXD strains contain a DNA fragment of corresponding intensity varying in length from strain to strain from 5-13 kb. At least some of these novel fragments represent different length alleles of the 7 kb HinfI fragment in B6 DNA (see below). Most of these BXD fragments are not present in the DNA fingerprints of the B6 or D2 progenitors, and furthermore are each found in no more than one BXD strain. This suggests that this locus, termed Ms6hm (minisatellite

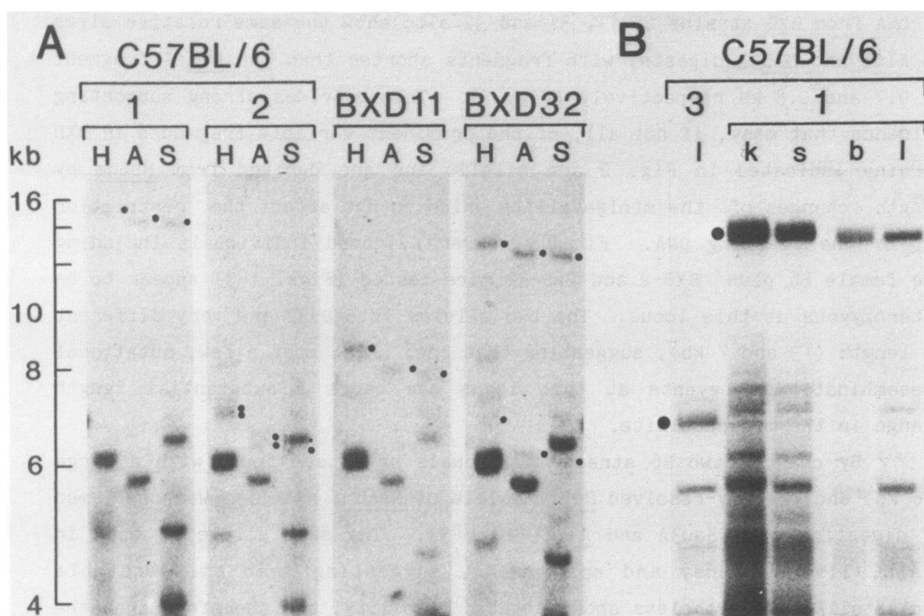

Figure 3. Identification of a highly unstable minisatellite in mouse DNA. A, characteristic patterns of alleles derived from Ms6hm in inbred mouse DNA digested with HinfI, AluI or Sau3A and detected by probe 33.6. Alleles of this locus are indicated by dots. C57BL/6 individual 2 is the same female as shown in Figs. 1 and 2. This mouse and the BXD 32 individual each carry two detectable Ms6hm fragments and are presumably heterozygous at this locus. C57BL/6 individual 1 has a large (16 kb) allele. B, somatic stability of this large locus. Liver (l), kidney (k), spleen (s) and brain (b) DNA from C57BL/6 individual 1 were digested with Sau3A and Southern blot hybridized with probe 33.6.

detected by probe 33.6, hypermutable), is so unstable that new mutant alleles have arisen in most or all of these strains, including possibly the contemporary B6 strain individual during its descent from the ancestral B6 individual used to construct the BXD lines about 60 generations ago [21].

A DNA fragment corresponding to the 7.0 kb B6 strain HinfI fragment is also seen in mouse DNA digested with AluI (6.3 kb) and with Sau3A (6.2 kb) (Fig. 3). This suggests that this HinfI DNA fragment contains a restriction site-deficient minisatellite flanked by normal mouse DNA containing multiple 4 bp restriction endonuclease cleavage sites, rather than being derived from a longer satellite DNA containing internal HinfI cleavage sites. Furthermore, the variable DNA fragments in HinfI digests

of DNA from BXD strains 2, 11, 31 and 32 also show the same relative sizes in AluI and Sau3A digests, with fragments shorter than the HinfI fragment by 0.7 and 0.8 kb respectively (Fig. 3). This provides strong supporting evidence that many, if not all, of the prominent variable fragments in BXD strains indicated in Fig. 2 are allelic and are derived from Ms6hm by length changes of the minisatellite which do not affect the restriction map of the flanking DNA. Finally, several inbred individuals including the female B6 plus BXD-2 and BXD-32 mice tested (Figs. 1-3) appear to be heterozygous at this locus. The two alleles in BXD-32 are very different in length (13 and 7 kb), suggesting that one, or at most a few, mutational (recombinational) events at this locus can cause a substantial length change in the minisatellite.

By chance, two B6 strain individuals have been found with a large (16 kb) and clearly-resolved HinfI allele of Ms6hm; allelism was confirmed by digestion with Sau3A and AluI (Fig. 3). The same allele is seen in brain, liver, kidney and spleen DNA, suggesting that this unstable minisatellite nevertheless shows somatic stability, and therefore that the BXD strain variability at this mutable locus results from germ-line alteration in the length of this minisatellite. This conclusion is supported by the observation that pairs of mice from the same BXD strain tend to carry the same length Ms6hm allele (4 different strains tested, data not shown).

Segregation analysis of DNA fingerprint fragments in BXD strains

Using both human minisatellite probes, the segregation of 15 resolved B6 strain-specific fragments and 13 D2-specific fragments could be followed in the 25 different BXD strains examined (Fig. 2). The deduced strain distribution patterns (SDPs) are given in Table 1. None of the DNA fragments detected by one probe showed the same SDP as any of the fragments detected by the second probe; thus, as in humans [10,14], probes 33.6 and 33.15 detect completely different sets of minisatellites in mouse DNA.

Ten of the B6 strain fragments detected by probe 33.15 showed complete linkage, and were either all present or all absent in each BXD strain. These fragments are presumably derived from a single large minisatellite locus, termed Ms15-1, which contains internal HinfI cleavage sites. This locus is represented in the D2 strain by two cosegregating DNA fragments (Fig. 2) which are present only in those BXD strains which do not contain the $Ms15\text{-}1^{b}$ allele.

Two further instances of allelism between B6 and D2 fragments could be found in the DNA fingerprints produced by probe 33.6 (Fig. 2); the loci so defined are termed Ms6-2 and Ms6-3. All remaining fragments detected by probes 33.6 and 33.15 are derived from different loci and show distinct SDPs (Table 1). For these remaining fragments, it is most unlikely that any pair of B6 and D2 fragments are allelic and derived from the same locus, but have suffered new mutations to give apparently different SDPs. Thus, every pairwise comparison of B6 and D2 fragments revealed at least several BXD strains containing both the B6 and the D2 fragment (Table 1). This formally excludes the possibility that such B6 and D2 fragments are allelic.

In summary, the 15 B6-specific fragments and 13 D2 fragments shown in Fig. 2 are derived from 13 distinct mouse loci termed Ms6-1 to Ms6-5 and Ms15-1 to Ms15-8, depending on whether fragments were detected by probes 33.6 or 33.15 respectively. Only 3 of these loci have both b and d alleles, from the prototype B6 and D2 strains respectively, resolvable in a DNA fingerprint. Each of the remaining loci was represented as a resolved fragment in only one of the progenitor strains. The apparent SDP of such loci (Table 1) was therefore deduced by determining whether the progenitor fragment was present or absent in each BXD strain.

Linkage analysis of minisatellites

In an attempt to localise the 13 minisatellites in the mouse linkage map, the SDP of each minisatellite was compared with the SDPs of other characterised mouse genetic markers in a search for linkage [22]. This approach should be reliable for loci Ms15-1, Ms6-2 and Ms6-3, for which complementary SDPs of allelic B6 and D2 fragments have been established (Table 1). For the remaining 10 loci sampled in only one of the two progenitor strains, it is possible that the SDPs may be inaccurate; in particular, BXD strains lacking the progenitor fragment may in fact contain the fragment in an unidentified new mutant form. Despite these uncertainties, significant linkage was found between conventional mouse loci and 8 of the 13 minisatellites, and the provisional linkage map locations deduced for these loci are detailed in Table 2. These 8 loci are dispersed over 5 autosomes. Chromosomes 4, 5, and 14 each bear two minisatellite loci; chromosome 6 and 17 bear single loci. Of the three syntenic pairs of minisatellites, only Ms15-7 and Ms6-5 on chromosome 14 show significant linkage to each other. The estimated distance between this pair is approximately 5 centimorgans. The regional localization of

Table 2. Linkage between Ms loci and other genetic markers typed in BXD RI strains

Ms locus	Chromosome	Linked marker[a] [references]	Recombinants[b] Total	Estimated map distance, cM[c] (95% confidence limits)	
Ms15-1	4	Mtv-13 [26,27]	0/25	0.0	(0.0-4.3)
Ms6-2	4	Ahd-1 [28]	2/24	2.4	(0.2-11.3)
Ms15-6	5	Pgm-1 [29]	3/23	4.1	(0.7-17.0)
Ms15-5	5	Ric [29]	2/19	3.1	(0.3-16.5)
Ms6-4	6	Lvp-1 [30]	0/24	0.0	(0.0-4.5)
Ms15-7	14	Mtv-11 [26,31]	3/23	4.1	(0.7-17.0)
Ms6-5	14	Tcra [32]	1/21	1.3	(0.03-7.3)
Ms15-3	17	H-2 [33]	1/25	1.1	(0.03-7.3)

[a] The identities of the genetic markers to which minisatellites show linkage are as follows: Mtv-13, mammary tumour provirus-13; Ahd-1, aldehyde dehydrogenase-1; Pgm-1, phosphoglucomutase-1; Ric, resistance to Rickettsia tsutsugamushi; Lvp-1, liver protein-1; Mtv-11 (formerly Mtv-12), mammary tumour provirus-11; Tcra, T cell receptor alpha chain; and H-2, major histocompatibility locus.

[b] Provisional strain typings were excluded from calculations of map distances.

[c] The estimated map distance between linked loci was calculated according to the standard method for determining map distances from recombinant inbred strain data [22]. The 95% confidence intervals were taken from a published table [34].

Ms15-1 is unknown since the position of the chromosome 4 marker to which it is linked, Mtv-13, has not been precisely defined. The most parsimonius ordering of genes on chromosome 5 is centromere - Pgm-1 - Ms15-6 - Ric - Ms15-5. The ordering of loci on chromosome 14 appears to be centromere - (Mtv-11, Ms15-7) - (Tcra, Ms6-5), where the ordering of loci within parentheses is uncertain.

DISCUSSION

Human minisatellite probes produce highly informative DNA fingerprints from mouse DNA. The patterns produced with both polycore probes are largely strain-specific and should prove useful in mouse strain identification. By studying the segregation of individual variable DNA fragments in BXD recombinant inbred strains, we have shown that these fragments are derived from multiple dispersed loci. Eight of these loci showed SDPs which correlated significantly with SDPs of other mapped mouse markers, to give the provisional linkage map locations shown in Table 2. The remaining loci did not fall within any known linkage group; such loci are either located in marker-deficient regions of the mouse genome, or alternatively, their SDPs are incorrect as a result of new mutation during the breeding of the BXD strains. All mapped loci are autosomal and dispersed, and are not preferentially located at centromeres or telomeres [23]. Previous pedigree analyses of human DNA fingerprints have also shown that human hypervariable fragments are derived from multiple unlinked autosomal loci [14]. The mouse localizations suggest that human hypervariable loci are also likely to be randomly dispersed over the human linkage map, and will therefore provide very useful markers for genetic analysis in man. However, the precise locations of minisatellites in the human and mouse genome are unlikely to be homologous, in view of the rapid rate of generation and evolution of long hypervariable minisatellites ([9], Z. Wong and A.J. Jeffreys, unpublished data).

Of the 13 mouse minisatellite loci examined in BXD strains, 10 (77%) had alleles detectable in only one of the two progenitor strains. A very similar situation holds for human DNA fingerprints, in which 84% of scorable heterozygous minisatellite loci in a given individual are represented by one, not both, alleles [14]. The inability to resolve both alleles of most loci is due to large differences in the lengths of minisatellite alleles, with short alleles being either unresolvable or electrophoresed off the gel [14,15].

Whilst most mouse minisatellites are represented by a single allelic fragment in one or both progenitors, locus Ms15-1 linked to Mtv-13 on chromosome 4 is more complex. The b allele is comprised of 10 resolved DNA fragments which together constitute a minisatellite "haplotype" (Fig. 1). Summing the sizes of these fragments gives a minimum estimate of the length of the $Ms15\text{-}1^{b}$ minisatellite allele of 90 kb. The corresponding minimum length of the $Ms15\text{-}1^{d}$ allele, represented by two cosegregating fragments, is 19 kb. Inbred strains BALB/c, C3H and SWR possess large (>30 kb) hybridizing fragment(s) detected by probe 33.15 which might correspond to long alleles of this locus which are devoid of HinfI restriction sites (Fig. 1). Interestingly, inbred strains AKR and C57BL/6J (B6) have similar DNA fingerprints with probe 33.15 (Fig. 1), even though these strains have been derived independently [24,25]. The similarity between AKR and C57BL/6J is primarily due to the presence in AKR of 8 of the 10 $Ms15\text{-}1^{b}$ haplotype fragments. This implies that the $Ms15\text{-}1^{b}$ haplotype is not necessarily rare, and furthermore that it must show substantial germ-line stability; this stability is also evident in the BXD strains, with no evidence for new mutation (band loss) in this pattern in 8 different strains carrying the $Ms15\text{-}1^{b}$ allele.

In contrast to the germ-line stability of most of the mouse minisatellites, including Ms15-1, there does seem to be a subset of loci which are relatively mutable, creating heterozygosities in inbred strains and producing new length alleles in BXD strains. The most notable of these is locus Ms6hm represented by a prominent 7 kb HinfI fragment in the B6 strain. This locus appears to have produced new length alleles in many of the BXD strains and a large (16 kb) allele in a subset of B6 strain individuals. The SDP for this locus cannot be established, and thus its map location is unknown. In the absence of a specific probe for this locus, it is not possible to determine how many different alleles are present in the panel of BXD strains examined, nor what proportion of BXD strains are segregating at this locus. These data could be used to estimate the rate of generation of new alleles at this locus during the breeding of the BXD strains. However, in the 10 different BXD strains and the B6 progenitors shown in Fig. 2, only two appear to share a common Ms6hm allele (BXD 2 and the larger allele in the heterozygous B6 female). All other provisionally-identified alleles of this locus are strain-specific. If the shared allele is assumed to be a progenitor allele, then 9 out of 10 BXD strains carry a new mutant allele. Assuming

selective neutrality, this gives a new mutation rate during the ~60 rounds of brother-sister mating of >0.01 per gamete at this locus (p>0.95), or $>15\times10^{-4}$ per kb minisatellite per gamete. In contrast, the estimate of the rate of allelic length change for human minisatellites is $\sim10^{-4}$ per kb per gamete ([9] and unpublished data) and for the stable mouse *Ms15-1^b^* haplotype $<0.5\times10^{-4}$ per kb per gamete. Thus there is at least a 30-fold variation in the level of germ-line instability betweeen different mouse minisatellites. It remains to be seen whether this differential instability is an intrinsic property of the minisatellite sequence, or whether it is determined by chromosome position effects.

The hypermutable mouse minisatellite *Ms6hm* should provide a useful locus to study processes of allelic change at hypervariable loci. We are currently attempting to clone this locus to investigate more directly the rates and mechanisms of minisatellite length change, and to determine whether unequal exchange, particularly by meiotic recombination, is the predominant process as predicted by the hypothesis that the minisatellite core sequence serves as a recombination signal [9].

POSTSCRIPT

Elliott has recently reported a new tandem-repeat sequence capable of detecting multiple variable DNA fragments in the mouse genome [35]. The SDPs of eight of these fragments have been determined in BXD recombinant inbred strains, and all differ from the minisatellite SDPs reported in this paper. This new tandem-repeat probe is therefore detecting a set of variable loci in mouse DNA which is substantially different from those detected by human minisatellite probes.

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