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Mapping the mouse X chromosome: possible symmetry in the location of a family of sequences on the mouse X and Y chromosomes

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Summary

Major advances in our knowledge of the genetic organization of the mouse X chromosome have been obtained by the use of interspecific crosses involving *Mus spretus*-derived strains. This system has been used to study sequences detected by three probes 80Y/B, 302Y/B and 371Y/B isolated from a mouse Y-chromosome library which have been shown to recognize both male–female common and male–female differential sequences. These patterns are due to the presence of a family of cross-reacting sequences on the mouse X and Y chromosomes. Detailed genetic analysis of the localization of the X-chromosome-specific sequences using both a somatic cell hybrid panel and an interspecific mouse cross has revealed the presence of at least three discrete clusters of loci *(X–Y)A*, *(X–Y)B* and *(X–Y)C*. Two of these clusters, *(X–Y)B* and *(X–Y)C*, lie distally on the mouse X chromosome, the other cluster *(X–Y)A* being situated close to the centromere. *In situ* hybridization shows a striking symmetry in the localization of the major sequences on both the X and Y chromosomes detected by these probes, hybridization being preferentially localized to a subcentromeric and subtelomeric region on each chromosome.

This striking localization symmetry between the X and Y chromosome sequences is discussed in terms of the extensive pairing of the X–Y chromosomes noted during meiosis.

Key words: X chromosome, Y chromosome, *Mus spretus* mapping, *in situ* hybridization, X–Y sequences, mouse.

Introduction

Our knowledge of the detailed genetic organization of particular chromosomes in man and mouse has accelerated markedly over the last few years, the best characterized of all chromosomes at present being the human X chromosome (Goodfellow, Davies & Ropers, 1985). Progress has been linked to the increasing availability of molecular probes detecting restriction fragment length polymorphisms (RFLPs) for use in extended recombinational studies, and the development of techniques such as pulsed-field gel electrophoresis (Schwartz & Cantor, 1984) (Van Ommen *et al.* 1986) and chromosome-mediated gene transfer (Pritchard & Goodfellow, 1986), for analysis of particular chromosomal regions at or below the resolution of recombinational analysis. The establishment of accurate detailed genetic maps for the majority of human chromosomes has been aided by the identification of probes for hypervariable regions (Wong, Wilson, Jeffreys & Thein, 1986), the use of large overlapping family panels allowing the analysis of what amounts to a series of nested three-point crosses (Drayna & White, 1985) and multipoint and pedigree analysis of particularly favourable family/probe combinations (Camerino *et al.* 1986).

In the mouse, the most recent progress in this area has been linked to the increasing use of interspecific mouse crosses in which advantage has been taken of the establishment of inbred strains from wild mice belonging to one or other of the mouse subspecies or species.

Wild and laboratory mice: structure of the *Mus* genus

For simplicity sake, the *Mus* genus can be divided up into the complex species *Mus musculus* containing

the four major biochemical grouping *Mus musculus domesticus*, *Mus musculus musculus*, *Mus musculus castaneus* and *Mus musculus bactrianus* all of which can be treated as subspecies, and at least six other species including the mound-building mouse *Mus spicilegus*, the western *Mediterranean short-tailed mouse Mus spretus*, the eastern Mediterranean short-tailed mouse known provisionally as *Mus* 4A and a certain number of species of Asian and Indian origin including *Mus caroli*, *Mus cervicolor*, *Mus cooki*, *Mus booduga* and *Mus dunni* (for review see Bonhomme & Guénet, 1987).

None of the mice belonging to the different groups within the complex species *Mus musculus* ever produce hybrids in the wild with mice from the other species, even though to take an example, *Mus musculus domesticus* mice and *Mus spretus* mice are found living sympatrically (side by side) in both Spain and North Africa.

It is, however, possible to breed without too much difficulty under laboratory conditions *Mus musculus domesticus* or *Mus musculus musculus* mice with *Mus spretus*, *Mus spicilegus* or *Mus 4A mice* (Bonhomme *et al.* 1984). These findings have opened the way for exploiting the considerable polymorphism and genetic variation accumulated, on account of their natural genetic isolation, within each of these species for genetic studies. Such studies have been aided by the recent establishment in different laboratories of a whole series of inbred mouse strains derived from wild mice which are members either of the different subspecies of the *Mus musculus* complex species or of distinct species such as *Mus spretus* and *Mus spicilegus* (Bonhomme & Guénet, 1987).

Amongst those species allowing hybridization under laboratory conditions, it is *Mus spretus* which has proved to possess the greatest degree of variation and polymorphism compared to laboratory mice belonging to *Mus musculus musculus* or *Mus musculus domesticus*. Because of this, much of the work using interspecies crosses has used either the SPE/Pas inbred strain or analogous strains derived from *Mus spretus*.

Interspecific mouse crosses and genetic sequence localization

Interspecies crosses involving laboratory mouse strains and *Mus spretus*-derived inbred strains such as SPE/Pas have been used for both assigning genes to particular linkage groups (Robert *et al.* 1985) and for the high-resolution mapping of particular mouse chromosomes, including the X chromosome, using molecular probes (Avner *et al.* 1987*a*; Dautigny *et al.* 1986; Amar *et al.* 1985; Bucan *et al.* 1986). The backcross used for mapping X-chromosome sequences is shown in Fig. 1A. RFLPs corresponding to each probe are identified and their segregation followed and compared to that of alleles at the *Hprt*, *Tabby* (*Ta*) and *jimpy* (*jp*) loci which also segregated within the cross (Fig. 1B) (Amar *et al.* 1985). Both recombinational frequency and pedigree analysis (Dautigny *et al.* 1986; Avner *et al.* 1987*a*; and see later) can be used to orientate and localize the loci

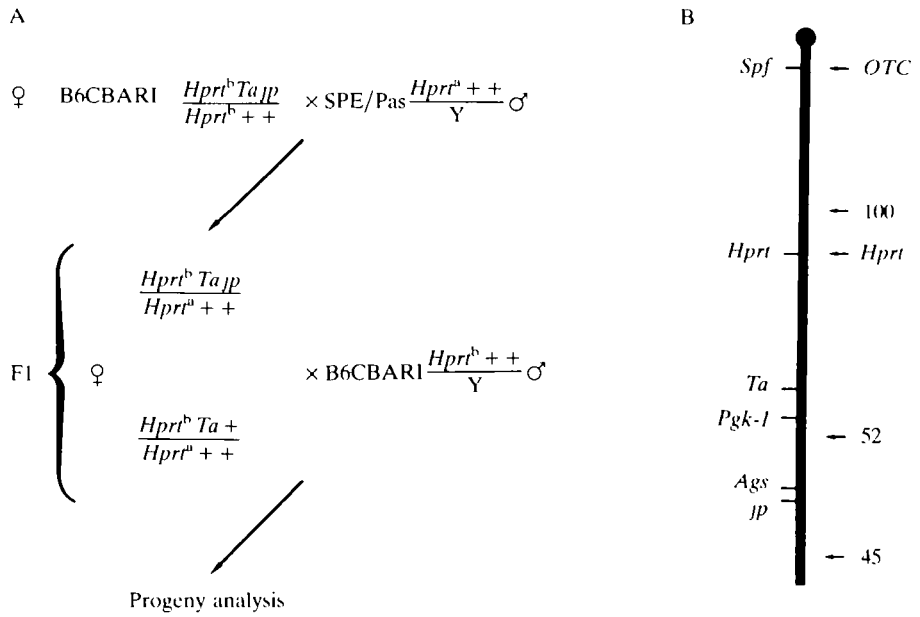

Fig. 1. (A) Configuration of the interspecies backcross used for probe localization. F_1 females *Ta jp*/++ and F_1 females *Ta* +/++ were used, their genotypes being characterized subsequently by progeny testing. (B) Position of five of the key markers used in this study on the mouse X chromosome. These were *otc* (synonymous with the Sparse fur locus *Spf*) *Hprt*, 100, 52 and 45 (corresponding to loci *DXPas5*, *DXPas2* and *DXPas1*).

defined by the various probes by comparison both with the original three fixed loci and each other.

Whilst the results obtained using X-chromosome-linked sequences cannot be necessarily extrapolated to autosomal sequences, it is interesting to note that out of the 30 or so X-chromosome-specific sequences tested in our laboratory up until now, over 90% detected RFLPs between SPE/Pas and the B6CBARI laboratory mouse using the *Taq*I restriction endonuclease alone.

This genetic system possesses marked advantages in terms of its ability to allow:

(1) generation of RFLPs for virtually any probes including those corresponding to coding sequences;

(2) the analysis of large numbers of progeny and

(3) the possibility of carrying out in parallel both pedigree analysis and recombination frequency analysis on such progeny.

It is this genetic system and its use along with other approaches to analyse and characterize a series of probes detecting sequences present simultaneously on both the mouse X and Y chromosomes that will be described in the rest of this article.

Isolation and characterization of X/Y-chromosome-specific probes

The isolation of chromosome-specific probes has up until now depended on either the availability of particular interspecific somatic cell hybrids carrying the chromosome of interest as sole chromosomal representative of one of the species, the use of microdissection or the finding of experimental situations in which flow sorting of the chromosome in question can be undertaken (Baron *et al.* 1984). Both flow sorting (Baron *et al.* 1986) and microdissection (A. Weith and C. E. Bishop, unpublished data) have been used successfully to isolate sequences specific for the mouse Y chromosome or for particular regions of this chromosome (See also Bishop *et al.* this volume).

In most mouse strains, the chromosomes show only small differences in size and are difficult to distinguish by flow sorting. In particular, the mouse Y chromosome cannot be resolved from chromosome 19. Use of the inbred Rb(9:19)163H mouse strain, which carries chromosome 19 as a Robertsonian translocation with chromosome 9, however, allows resolution of the Y chromosome due to the increased size and the biarmed chromosome 19 in this strain. Purified Y chromosomes were thus obtained by flow cytofluorometry of chromosomes obtained from 163H males and an *Eco*RI library constructed in the λ vector NM1149 (Baron *et al.* 1986; Bishop *et al.* 1985). Probes that were characterized as being present on both the X and Y chromosomes have been isolated along with Y-specific probes from this library. Three such probes 80Y/B, 302Y/B and 371Y/B have been analysed in some detail.

All three probes were isolated after preliminary screening had removed clones containing moderately and highly repetitive sequences and were shown to be Y-chromosome limited in so far as Southern blot analysis with them revealed male–female common bands in addition to several male-specific Y-encoded bands (Fig. 3). Cognate bands identified using these probes on *Eco*RI restricted DNA's of C57BL/6 mice were identified only in male animals confirming that the cognate sequences are Y-chromosome encoded. Whilst all the male–female common sequences have been shown to be X-linked by analysis of a somatic cell hybrid panel (Fig. 4), careful analysis of the male–female DNA profiles obtained suggests that the sequences present on the X chromosome are of two types: those present only on the X chromosome and therefore showing dosage dependence between male and female mice and those that give stronger signals on male than on females and therefore probably

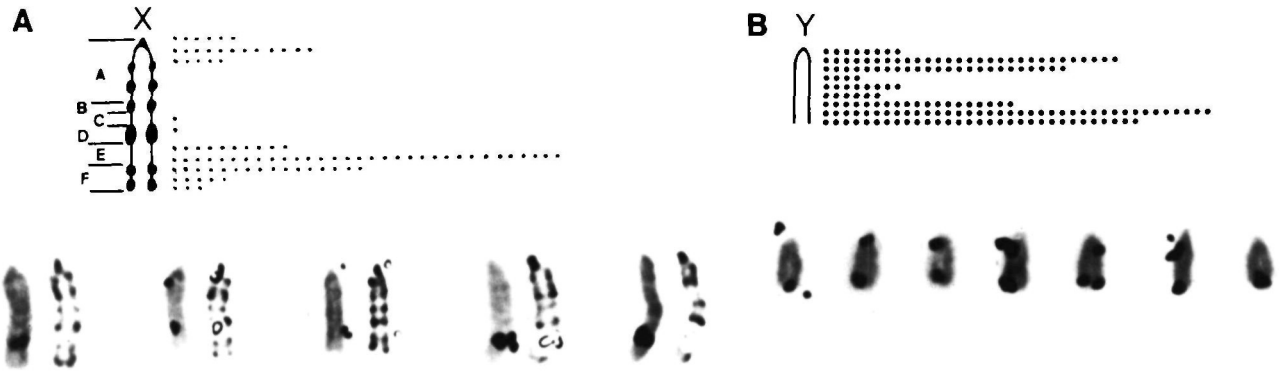

Fig. 2. *In situ* hybridization using probe 302Y/B. Grain distributions on A the X chromosome and B the Y chromosome. Below the total grain distributions are shown adjacent examples as individual autoradiographic X chromosome spreads and G-banded preparations (A) and autoradiographic Y chromosome spreads (B).

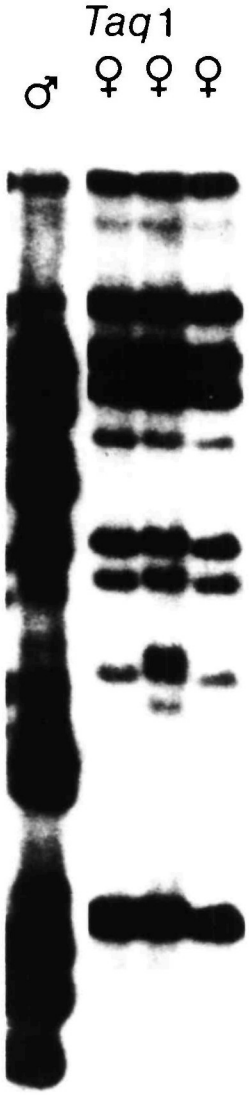

Fig. 3. Hybridization of probe 80Y/B on *Taq*I restricted male and female from the *spretus* backcross.

represent sequences which are present simultaneously on both the X and Y chromosomes and are amplified on the Y chromosome. No cross reaction of these probes with human or Chinese hamster DNAs has been observed even under conditions of reduced stringency.

In situ localization on the X and Y chromosomes

In the same way that the use of mouse strains carrying Robertsonian translocations facilitates flow sorting of particular mouse chromosomes by introducing a size differential into the standard karyotype, so they can be helpful for *in situ* hybridization. The female WMP mouse, for instance, carries all its chromosomes other than the X and 19 in the form of biarmed Robertsonian translocations. Since the chromosome 19 is much smaller than the X chromosome, use of this strain allows rapid identification of the X chromosome thus facilitating the *in situ* analysis of X-specific sequences (Dautigny *et al.* 1986).

Of the three probes discussed here, 371Y/B and 302Y/B have both been tested by *in situ* hybridization. Essentially similar patterns were obtained with both probes. When low probe concentrations and short exposure times were used, the X chromosome was only slightly labelled whilst the Y chromosome was heavily labelled, the label localizing essentially to the YA (40% of the grains counted) and YD/YE regions (60% of the grains counted (Fig. 2B)).

Use of longer exposure times and increasing probe concentration revealed hybridization to two regions of the X chromosome. A minor peak, equivalent to 25% of the X-specific grains was observed on the proximal part of the X, centred over XA1, XA2, as well as a major peak centred over the XE/XF1 band which corresponded to 75% of the X-specific grains (Fig. 2A). The easier detection of the Y sequences compared to those of X chromosome is linked to the amplification of the Y-specific sequences also observed by Southern blot analysis. Two other salient facts are obvious from this analysis.

(1) The family of sequences recognized on the X and Y are not uniformly distributed over the chromosome but are preferentially restricted to several separable regions on both the X and Y chromosomes.

(2) The arrangement of the sequences on the X and Y chromosomes as revealed by *in situ* hybridization suggests some symmetry in their distribution with subcentromeric and subtelomeric zones being clearly identified on both chromosomes.

Detailed genetic localization on the X chromosome

A series of *Taq*I and *Msp*I RFLPs between the B6CBARI strain belonging to *Mus musculus domesticus* and the inbred SPE/Pas strain are detected by probes 80Y/B, 371Y/B and 302Y/B. This has allowed an interspecies backcross of the type already described in this article between B6CBARI and SPE/Pas to be used for recombinational mapping studies (Fig. 1A). The complex patterns on genomic blots (Fig. 3) shown by these X–Y probes introduces certain constraints into their analysis which do not apply when single copy or non X–Y limited probes are used. The first limitation is that the reciprocal allelic form corresponding to a given band is either not normally identifiable or not available for analysis. Since we are dealing with congenic mice, this does not however cause a major problem since absence of the C57BL/6 allelic form of a given band for instance, automatically implies the presence of the *Mus spretus* form even if this cannot be identified. Second, certain

X bands can only be analysed in female progeny since the Y-chromosome pattern in males overlaps and obscures some of the X-chromosome sequences. Similarly maternally derived B6 bands cannot be identified in female backcross progeny, their presence in such progeny being covered up by the obligatorily inherited paternal B6 allelic form. B6 alleles can be identified in such progeny only on the difficult and unsure basis of a 2:1 gene-dosage effect between different female animals.

The RFLPs detected with these probes on female DNAs have been verified as being X linked through (1) the use of a panel of somatic cell hybrids either having or lacking the murine X chromosome. All the B6 bands detected with all three probes was confirmed by this method to be X-chromosome encoded (Fig. 4). (2) Comparison of the hybridization patterns of *Mus spretus*-derived RFLPs on female B6CBARI mice and male (B6CBARI×SPE/Pas) F_1 mice. Bands present in female SPE/Pas DNA but absent from the male F_1 DNA must be X-chromosome linked. The latter approach to identifying *Mus spretus*-derived RFLPs was taken as no somatic cell hybrid containing the *Mus spretus* X chromosome was available.

All the *Mus spretus* bands which could be analysed (see above) with all three probes were confirmed by this method to be X-chromosome encoded. A typical hybridization profile of *Taq*I restricted backcross progeny DNA's from the interspecies cross is shown in Fig. 5. The sequences thus identified polymorphism were localized genetically on the X chromosome using two approaches. The first involved inspection of the pedigrees of the various BX animals and correlation of the crossover events which had occurred on the X chromosome of each animal with the allele exhibited for the marker in question. This is illustrated in simplified form in Table 1 for the localization of two of the sequences detected by probe 80Y/B, 80TI and 80TII (see also Fig. 5). Sequence 80TI is clearly localized by BX animals 37 and 67 distal to the loci defined by probe 52 (*DXPas2*) and by BX animals 33 and 44, as proximal to the *jp(PLP)* locus. It must therefore lie within the 12 centimorgans (cM) span delineated by these two loci. Similarly sequence 80TII is shown by BX animals 38 and 66 to be distal to the *jp(PLP)* locus and by BX animal 45 to be proximal to locus *DXPas1* defined by probe 45. This places it within a span estimated to cover some 13 cM. From similar analysis carried out on sequences 371T1, 371T2, 371T3 and 302M4 it is clear that all of these sequences fall within the *DXPas2* (probe 52) – *jp(PLP)* interval defined by 80TI.

We have been unable to localize by such RFLP analysis the subcentromeric band detected by *in situ* hybridization. This band has however been localized by deletion mapping using a panel of Chinese hamster × mouse somatic cell hybrids carrying partially deleted X chromosomes. Two of the hybrid clones obtained from fusions involving T13RI and T7RI X:autosome translocation-bearing mice (Avner *et al.* 1987*b*) carry X chromosomes deleted proximally to the *Hprt* locus, whilst three other hybrids derived from T16H, T14RI and T6RI mice, are deleted at different points in the distal half of the chromosome. Southern blot profiles after *Taq*I or *Eco*RI restriction of the B48c(T16H) hybrid (Fig. 6A) shows clearly that all but one of the bands detected by probe 80 must lie on that part of the X chromosome distal to the T16 breakpoint close to the Tabby (*Ta*) locus, in

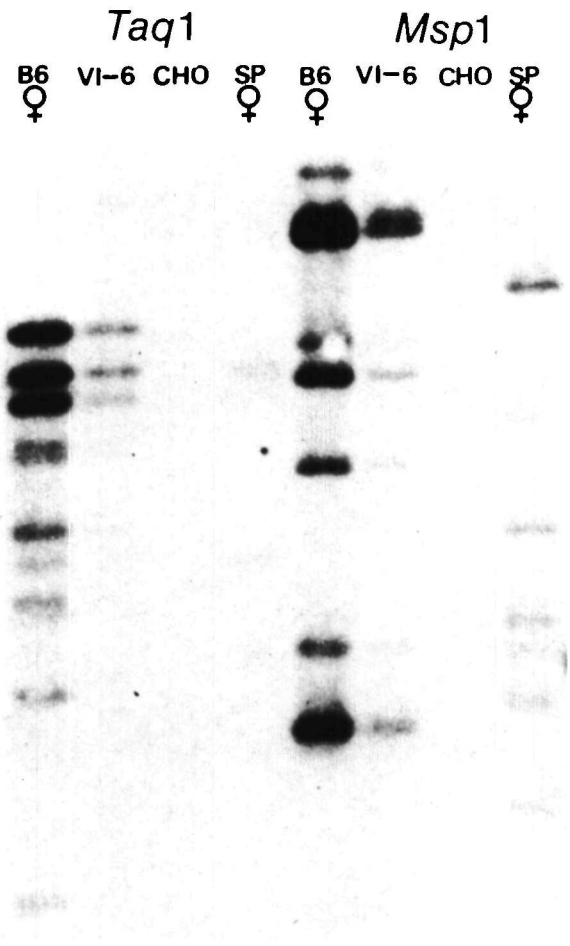

Fig. 4. Hybridization of probe 302Y/B *Taq*I and *Msp*I restricted female C57BL/6 DNA (B6 female), Chinese hamster DNA(CHO), female *Mus spretus* DNA (Sp female), and the VI-6 (mouse × Chinese hamster) hybrid cell line containing mouse chromosomes X and 16. Wash conditions 0·4 SSC at 65°C.

Table 1. *Pedigree analysis of individual progeny from the* Mus spretus *backcross*

	BX animals N°						
Loci	33	37	44	67	38	66	45
OTC	×	+	×	×	+	×	+
DXPas5 (100)	×	+	×	×	+	+	+
Hprt	×	+	×	×	+	+	×
DXPas2 (52)	×	+	×	×	×	+	×
80TI	×	×	×	+	NT	+	NT
jp (PLP)	+	×	+	+	×	+	×
80TII	+	×	+	+	+	×	×
DXPas1 (45)	+	×	+	+	+	×	+

The haplotypes illustrated for female progeny correspond to that of the X chromosome of maternal region
+, B6CBARI-derived allele.
×, *Spretus*-derived allele
NT, Untested.
The numbers identify the different backcross progeny animals

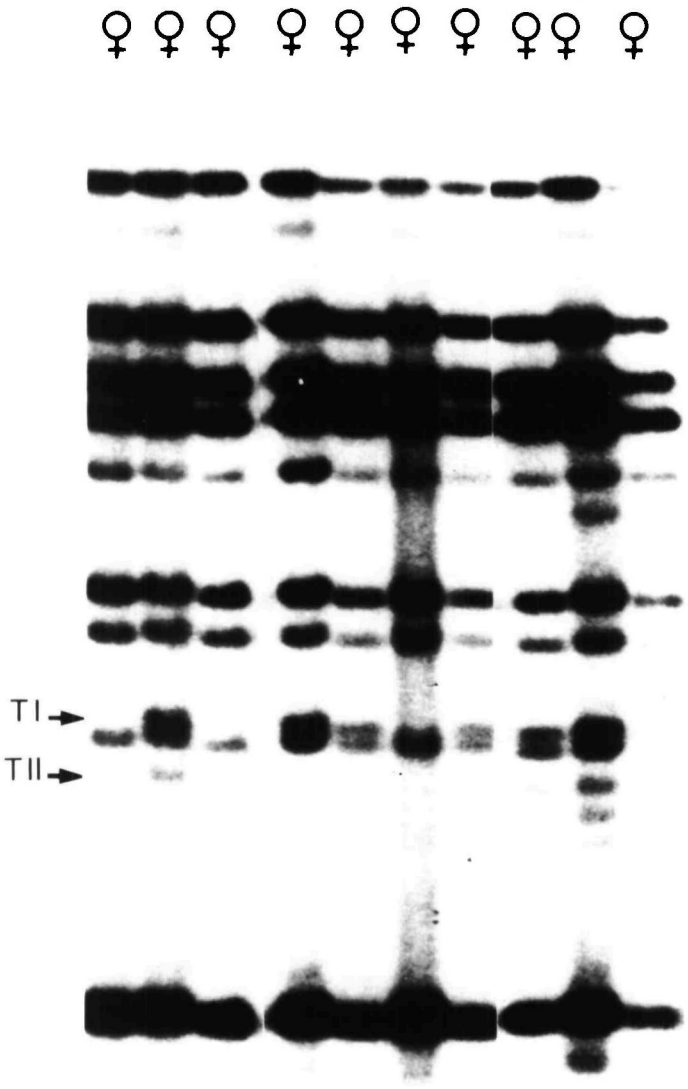

Fig. 5. Hybridization of probe 80Y/B to female progeny of the *spretus* backcross. TI and TII refer to the particular *spretus* RFLP revealed by probe 80Y/B and referred to in the text.

agreement with the RFLP and *in situ* hybridization analysis. The retained band in the B series hybrids, on the other hand, lies proximal to the T16 breakpoint and must correspond to the sequence identified by *in situ* hybridization close to the centromere of the X chromosome.

A single band is absent from hybridization profiles of probe 80Y/B on the I series subclones I5d2 and I5d3 (T13RI) which is present on blots of the subclones of the G hybrid series (T7RI) carrying an X chromosome which is broken more proximally (Fig. 6B). This locates the centromeric sequence between the T13RI and T7RI X:autosome translocation breakpoints in a region lying some 12–16 cm from the centromere (Avner *et al.* 1987*b*). Deletion mapping of the seven other sequences detected on *Taq*I restricted female DNAs by probe 80Y/B shows five to be localized in the region lying between the T16H and T14RI translocation breakpoints (data not shown) (Fig. 7).

This region corresponds genetically to a 19 cm span distal to locus *DXPas2 (52)*. Two other sequences must lie distal to the T14RI breakpoint and the T6RI breakpoint (Fig. 7), known from marker studies to be distal to the *jp* locus (Avner *et al.* 1987*b*). Both the recombination and deletion mapping studies indicate therefore the presence of at least three groups of sequences detected by these probes.

Sequence variability and polymorphism

Sequence polymorphism has been looked for in mouse strains other than *Mus spretus* and B6CBARI in order to obtain some idea of the variability of the

sequences detected by these probes. We have used males of different wild mouse strains belonging to the *Mus musculus domesticus* or *Mus musculus musculus* subspecies. After restriction with *Hin*dIII, no difference was observed either within the subgroup of *Mus musculus domesticus* animals (WLA, 22CD, DGD, C57BL/6) or within the subgroup of *Mus musculus musculus* animals (Mai, MBK, PWK) after probing with p302Y/B or 80Y/B (data not shown). Clear multiple differences were observed, however, between the two subgroups, suggesting that the p302Y/B and 80Y/B probes like the p353Y/B probe previously reported (Bishop *et al.* 1985) is capable of distinguishing the Y chromosome of these two subgroups.

Sequence methylation in the X and Y chromosomes

The presence of this family of sequences distributed along the length of the X and Y chromosomes led us to examine their methylation states by the use of the paired restriction enzyme isoschizomers *Hpa*II and *Msp*I. *Hpa*II is unable to restrict DNA when the internal cytosine residue in its recognition sequence is methylated whilst *Msp*I, which has the same recognition sequence, is insensitive to methylation of this cytosine residue. It is clear from an analysis of male DNA restricted with these two enzymes that the Y-chromosome-located sequences are heavily methylated (Fig. 8). Equally the pattern revealed on female DNAs suggests that all the X-linked sequences are

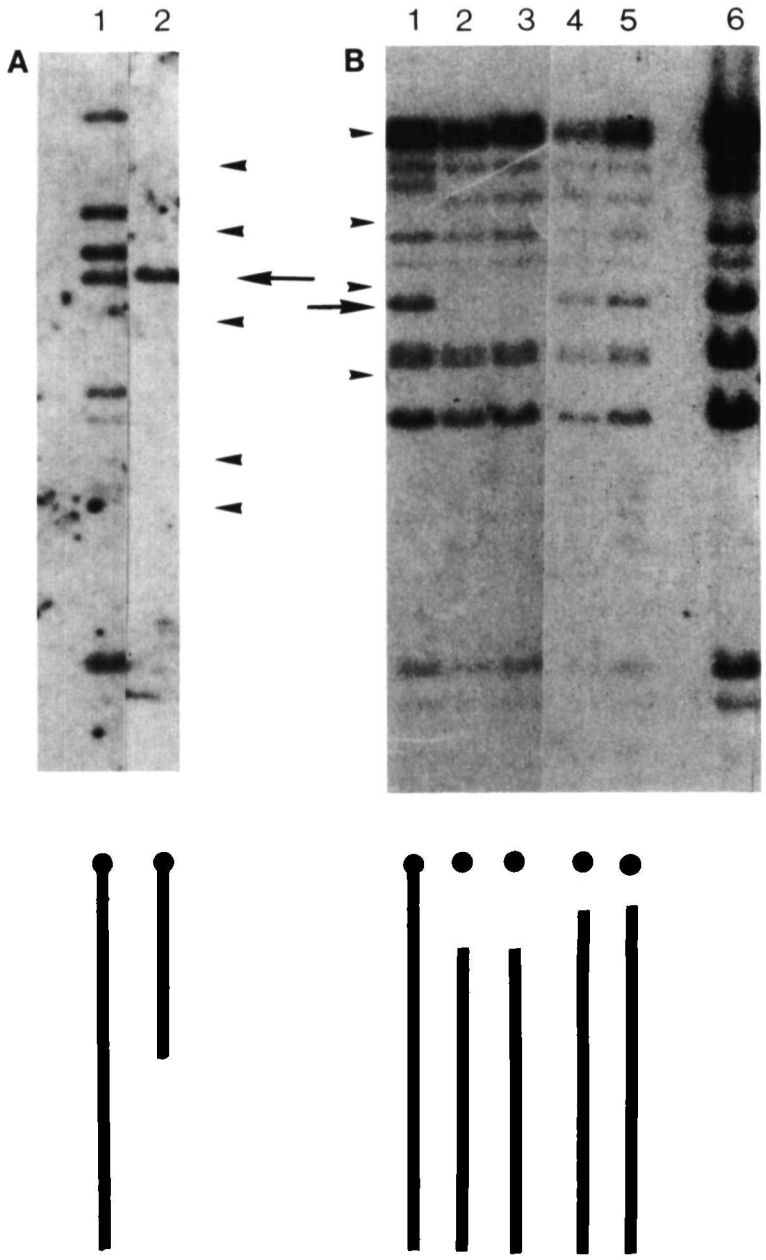

Fig. 6. Hybridization of probe 80Y/B to a mouse × Chinese hamster somatic cell panel carrying deleted mouse X chromosomes. (A) *Taq*I restricted DNAs lane 1: C57BL/6 female control lane 2; B48c (T16 deletion hybrid). (B) *Eco*RI restricted DNAs lane 1: VI-6 (16+ X control undeleted hybrid) lanes 2 and 3; I5d2 and I5d3 (T13RI deletion hybrids) lanes 4 and 5; G13n26 and G13n28 (T7RI deletion hybrids) lane 6 female C57BL/6 DNA (control). Wash conditions 0·4 SSC at 65°C.

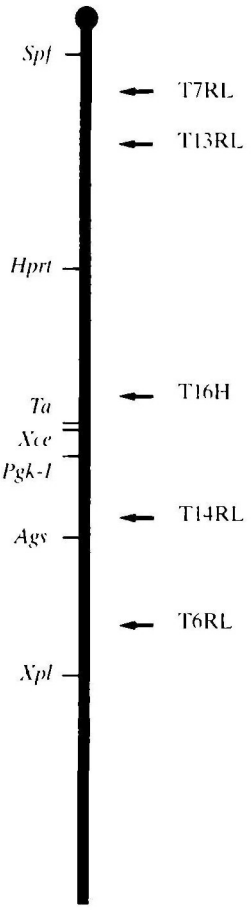

Fig. 7. Map of the X chromosome breakage points of the various X:autosome translocations concerned in the somatic cell hybrid panel.

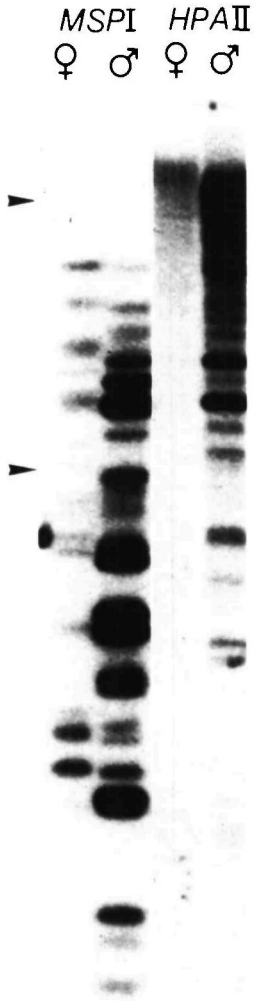

Fig. 8. Hybridization of probe 80Y/B to *Hpa*II and *Msp*I restricted C57BL/6 female and male DNAs. Wash conditions 0·4 SSC at 65°C.

heavily methylated. Since the bands detected on *Msp*I restricted female DNAs are completely absent on *Hpa*II restricted female DNAs rather than disappearing partially with the appearance of new bands, the methylation of X-chromosome sequences appears to be independent of whether the sequences are carried on the inactive or active X chromosomes. This conclusion is reinforced by the findings that the hybridization patterns of DNA from XO and XX adult females are essentially similar after restriction with *Msp*I and *Hpa*II (data not shown). The Y sequence methylation although extensive, does not necessarily affect all Y sequences. The complexity of the hybridization patterns does not however allow precise identification of the bands which may remain unmethylated.

Discussion and conclusion

Members of the complex families of sequences recognized by the three probes described here are apparently carried by both the X and Y chromosomes but are absent from the autosomes, at least in C57BL/6 and BALB/c mice for which hybrid cell lines exist.

A striking homology in the principal localization of the sequences on the X and Y chromosomes is apparent from the *in situ* hybridization studies carried out, using the 302Y/B and 371Y/B probes; two principal zones, one subcentromeric and one subtelomeric are labelled on both the X and Y chromosomes. The zones preferentially labelled on the Y chromosome are the A1 band and the interface region between the D and E bands. On the X chromosome the label is centred centromerically over the A1/A2 band interface and distally over the XE/XF1 band. Whilst it is currently impossible to localize genetically the Y sequence, it has proved possible to genetically map some of those on the X chromosome. For instance, the centromerically localized X chromosome band has been identified by

the use of three somatic cell hybrids partially deleted for either the proximal or distal parts of the X chromosome and has been mapped genetically to a region lying some 12–16 cM from the centromere and flanked by the *DXPas7(M2C)* and *DXPas3(66)* loci. A further series of noncontiguous loci defined by these three probes has been localized, using *Taq*I and *Msp*I-generated RFLP, to the distal part of the X chromosome. Taking together the pedigree and recombinational analysis and hybrid deletion mapping studies, there must be **at least** three distinct clusters of loci identified by these probes: those belonging to the (X–Y)B cluster, lying between the *DXPas2(52)* and *jp* loci, those belonging to the (X–Y)C cluster, lying between the *jp* and *DXPas1(45)* loci and the (X–Y)A cluster, lying in the subcentromeric region.

It has not always proved possible to distinguish between different members of a single cluster, in some cases because no recombination has so far been seen between them, in others for operational reasons already hinted at. Certain loci can for example only be analysed in female progeny, others in males, meaning that recombination studies are difficult until additional X-linked markers are mapped to these regions. Since the *jp* locus corresponding to the *PIP* structural gene (Dautigny *et al.* 1986) has been shown to map to XF1, both the (X–Y)B and (X–Y)C probably contribute to the *in situ* hybridization signal localizing to this subtelomeric band.

The sequences on the X and Y chromosomes share in common not only their apparently homologous position on their respective chromosome but also the fact that they are highly methylated. The methylation revealed by the use of the *Hpa*II/*Msp*I isoschizomers although extensive on the Y chromosome cannot be complete because some sites are still cleaved by *Hpa*II. The X-chromosome sequences, on the other hand, appear totally methylated and the methylation is independent of the inactivation status of the X chromosome.

In man, X–Y homologies have been found not only in the pseudoautosomal region (see Weissenbach, this volume) but also outside it (Cooke, Brown & Rappold, 1984; Page, Harper, Love & Botstein, 1984). The sequences outside of the pseudoautosomal region in man have not so far been found to occupy similar locations on both the X and Y chromosomes. The interest of the sequences reported here resides both in their distribution along the X chromosome into at least three discrete clusters and their symmetrical localization on the X and Y chromosomes.

If DNA sequence homology is necessary for X–Y chromosome synapse formation then the finding that up to 35 % of the mouse X chromosome can synapse with the Y (Tress, 1977; Ashley, 1984) could imply that regions of homology outside of the pseudoautosomal region exist, and in this respect the sequences reported here are potentially interesting. The high homology between these X and Y sequences, their similar localization on both chromosomes and the absence of related sequences in both man and the Chinese hamster all imply moreover that X–Y sequence transpositions and/or recombination may well have played a role in their establishment.

References

Amar, L. C., Arnaud, D., Cambrou, J., Guénet, J. L. & Avner, P. R. (1985). Mapping of the mouse X chromosome using random genomic probes and an interspecific mouse cross. *EMBO J.* **4**, 3695–3700.

Ashley, T. (1984). Reexamination of the case for homology between the X and Y chromosomes of mouse and man. *Human Genetics* **67**, 372–377.

Avner, P., Amar, L., Arnaud, D., Hanauer, A. & Cambrou, J. (1987*a*). Detailed ordering of markers localising to the Xq26-Xqter region of the human X chromosomes by the use of an interspecific Mus spretus mouse cross. *Proc. natn. Acad. Sci. U.S.A.* **84**, 1628–1633.

Avner, P., Arnaud, D., Amar, L., Cambrou, J., Winkling, H. & Russell, L. B. (1987*b*). Characterisation of a panel of somatic cell hybrids for the regional mapping of the mouse X chromosome. *Proc. natn. Acad. Sci. U.S.A.* **84**, 5330–5334.

Baron, B., Metezeau, P., Kelly, F., Bernheim, A., Berger, R., Guenet, J.-L. & Goldberg, M. E. (1984). Flow cytometry isolation and improved visualization of sorted mouse chromosomes. Purification of chromosomes X and ISO-1 from cell lines with Robertsonian translocations. *Expl Cell Res.* **152**, 220–230.

Baron, B., Metezeau, P., Hatat, D., Roberts, C., Goldberg, M. & Bishop, C. E. (1986). Cloning of DNA libraries from mouse Y chromosomes purified by flow cytometry. *Somatic Cell Mol. Genet.* **12**, 289–295.

Bishop, C. E., Boursot, R., Baron, B., Bonhomme, F. & Hatat, D. (1985). Most classical *Mus musculus domesticus* laboratory mouse strains carry a *Mus musculus musculus* Y chromosome. *Nature, Lond.* **315**, 70–72.

Bonhomme, F. & Guénet, J. L. (1987). The wild mouse and its relations. In *Genetic Variants and Strains of the Laboratory House Mouse* (ed. M. F. Lyon & A. G. Searle). Oxford University Press (in press).

Bonhomme, F., Catalan, J., Britton-Davidson, J., Chapman, V. M., Moriwaki, K., Nevo, E. & Thaler, L. (1984). Biochemical diversity and evolution in the genus *Mus*. *Biochem. Genet.* **22**, 275–303.

Bucan, M., Yang-Feng, T., Colberg-Poley, A., Wolgemuth, D. J., Guénet, J. L., Francke, U. & Lehrach, H. (1986). Genetic and cytogenetic localization of the homeo box containing genes on mouse chromosome 6 and human chromosome 7. *EMBO J.* **5**, 2899–2905.

Camerino, G., Oberlé, I., Wrogemann, K., Arveiler, B., Hanauer, A., Raimondi, E. & Mandel, J. L. (1986). Multipoint genetic mapping of the Xq26–Xq28 region in families with fragile X mental retardation. *Nucleic Acids Res.* (in press).

Cooke, H. J., Brown, W. A. R., Rappold, G. A. (1984). Closely related sequences in human X and Y chromosomes outside the pairing region. *Nature, Lond.* **311**, 259–261

Drayna, D. & White, R. (1985). The genetic map of the human X chromosome. *Science* **230**, 753–758.

Dautigny, A., Mattei, M. G., Morello, D., Alliel, P. M., Pham Dinh, D., Amar, L., Arnaud, D., Simon, D., Mattei, J. F., Guénet, J. L., Jollès, P. & Avner, P. (1986). The structural gene coding for myelin associated proteolipid protein is mutated in jimpy mice. *Nature, Lond.* **321**, 867–869

Goodfellow, P. N., Davies, K. E. & Ropers, H. H. (1985). Report of the committee on the genetic constitution of the X and Y chromosomes. Human Gene Mapping 8. *Cytogenetics Cell Genetics* **40**, 296–352.

Page, D. C., Harper, M. E., Love, J. & Botstein, D. (1984). Occurrence of a transposition from the X-chromosome long arm to the Y chromosome short arm during human evolution. *Nature, Lond.* **311**, 119–123.

Pritchard, C. & Goodfellow, P. N. (1986). Development of new methods in human gene mapping: selection for fragments of the human Y chromosome after chromosome mediated gene transfer *EMBO J.* **5**, 979–985.

Robert, B., Barton, P., Minty, A., Daubas, P., Weyder, A., Bonhomme, F., Catalan, J., Chazottes, D., Guénet, J. L. & Buckingham, M. (1985). Investigation of genetic linkage between myosin and actin genes using an interspecific mouse back-cross. *Nature, Lond.* **314**, 181–183.

Schwartz, D. A. & Cantor, C. R. (1984). Separation of yeast chromosome size DNAs by pulsed field gradient gel electrophoresis. *Cell* **37**, 67–75.

Tress, L. (1977). Extensive pairing of the X–Y bivalent in mouse spermatocytes as visualized by whole mount E.M. *J. Cell Sci.* **25**, 1–15.

Van Ommen, G. J. B., Verkerk, J. M. H., Hofker, M. H., Monaco, A. P., Kunkel, L. M., Ray, P., Worton, R., Wieringa, B., Bakker, E & Pearson, P. L. (1986). A physical map of 4 million bp around the Duchenne muscular dystrophy gene on the human X-chromosome. *Cell* **47**, 499–504.

Wong, Z., Wilson, V., Jeffreys, A. J. & Thein, S L. (1986). Cloning a selected fragment from a human DNA fingerpoint: isolation of an extremely polymorphic minisatellite. *Nucleic Acid Res.* **14**, 4605–4616.