Concerted Evolution of Light Satellite DNA in Genus *Mus* Implies Amplification and Homogenization of Large Blocks of Repeats

Barbara Dod, † Estelle Mottez, ‡ Erick Desmarais, † François Bonhomme, † and Gérard Roizès

*C.R.M., CNRS I.P 8402, INSERM U 249, and †Institut des Sciences de l'Évolution, CNRS UA 327, U.S.T.L.

Light satellite DNA components present in species belonging to the genus *Mus* and to related murids were studied using the Southern blot technique. The results show species variations in both the amount and periodic structure of the repeating units, which suggests that families of related higher-order repeats developed in a common ancestor and were then amplified and/or deleted to different extents during the subsequent evolutionary period. Although the patterns generated by a series of type B enzymes (restriction enzymes that possess sites in a limited number of segments making up the total satellite DNA) in the species closely related to the *M. musculus* complex were very similar, sequence analysis of cloned unit repeats in two of these species (*M. musculus domesticus* and *M. spreoides*) showed near fixation of species-diagnostic variant nucleotides. This suggests that the important amplification and homogenization events that occurred after the divergence of *M. spreoides* must have involved large blocks of satellite sequences.

Introduction

Satellite DNA consists of large tandem arrays of repeated sequences that are mainly found in the centromeric regions of eukaryotic chromosomes and can represent as much as 40% of the total DNA. Comparison of these DNAs in different *Drosophila* species (Strachan et al. 1982; Lohe and Brutlag 1987b), Primates (Musich et al. 1980), and various other taxa has shown that they are subject to frequent changes in copy number, the length of the repeating unit, and its nucleotide sequence. Another striking feature is that within a given species the individual nucleotide sequences that form a family or subfamily of repeats are generally very similar (Pages and Roizes 1984; Strachan et al. 1985; Willard and Waye 1987a). Amplification and homogenization events that often lead to the invasion and near fixation of new variants characterize the evolution of these sequences. This mode of evolution is a form of concerted evolution (Dover 1982).

The mechanisms underlying these processes in satellite DNA have been the subject of debate for the past 20 years. It has been proposed on the basis of theoretical considerations that the increase in copy number and the spread of new variants are the result of many unequal crossovers involving one or a few repeat units of satellite DNA.

1. Key words: satellite DNA, genus *Mus*, concerted evolution.
2. Present address: Institut Pasteur, U 277 INSERM Paris F-75724 Cédez.

Address for correspondence and reprints: Dr. G. Roizès, CNRS (LP 8402, INSERM U249), Institut de Biologie, Boulevard Henri IV, 34060 Montpellier Cédez, France.

© 1989 by The University of Chicago. All rights reserved.
0737-4038/89/0605-0004$02.00
Satellite DNA Evolution in the Genus Mus 479

(Tartof 1974; Smith 1976). An alternative model for the sequence homogeneity of tandem repeats is that arrays are formed by saltatory amplification events that expand a single sequence into a homogeneous array that is then free to diverge through mutation (Britten and Kohne 1968; Southern 1970; Sutton and McCallum 1972). Southern (1975b) provided data that suggest that both unequal crossing-over and rapid amplification events played a role in the evolution of the mouse light satellite DNA. Lohe and Brutlag (1987b) showed that the simple satellite sequences of sibling Drosophila species are highly conserved although their abundance varies considerably. This supports the idea that massive amplification of the same satellite sequence from copies present in an ancestral species is the cause of this sequence conservation. The role and the nature of the amplification and recombination mechanisms involved in the evolution of satellite DNA, however, require further clarification. Also, as pointed out by Dover (1982), one should consider the population mechanisms that can lead to the concerted spread of evolutionary novelties to all the individuals in the species.

We compared the light satellite components of species belonging to the genus Mus and of related murid rodents in order to explore the molecular processes of its evolution. So far, M. musculus has been the most widely studied species, and its major light satellite component has been well characterized (Southern 1975b; Hörz and Zachau 1977; Brown and Dover 1980a, 1980b; Hörz and Altenburger 1981; Manuelidis 1981). Related sequences have also been shown to be present in M. spretus (Brown and Dover 1980a, 1980b), M. caroli, M. cervicolor, and M. cooki (Sutton and McCallum 1972). As reasonable consensus phylogenies based on molecular and karyological data are available (Bonhomme 1986), we were able to establish the probable sequence of events underlying the evolution of the sequence arrays related to the musculus light satellite that are present in these genera.

Material and Methods

Animals

Figure 1 shows the consensus phylogenetic relationships among the species referred to in the present paper. They were obtained using protein loci (Bonhomme 1986). For convenience, and because in the case of Mus4A and Mus4B the Linnean nomenclature is far from clear, the biochemical notation (Bonhomme et al. 1984) is used as well as the Latin binomen. Except for Nannomys setulosus, N. minutoides, and Apodemus sylvaticus, which came directly from the wild, all the animals used belonged to laboratory lines established from animals of known geographical origin that are maintained in our breeding facilities.

DNA Samples

Total DNA was prepared from individual livers by the method of Jahn et al. (1980). The Mus musculus satellite DNA that was used as a hybridization probe was fractionated in three separate runs on Hoechst-33258 CsCl gradients according to a method described by Manuelidis (1977). Its purity was checked by analytical centrifugation and restriction analysis. The cloned satellite probe consisting of several long TaqI fragments of the major mouse light satellite DNA inserted in the Clal site of Z-pBR 322/TK HSV-M4 was provided by Dr. P. Schulz (Munich).

Southern Blotting

DNA restriction fragments were transferred to Hybond-N membranes (Amer- sham) from 1.4% agarose gels (Southern 1975a). The blot hybridization and washing
Cloning and Sequencing of Satellite Monomers

The satellite monomer bands from *Mus l* and *Mus 4A* DNA digested with the restriction enzyme *Bst*NI were excised from a 2% agarose gel, and the DNA was recovered by electro-elution. After filling in the overhanging ends by using the Klenow DNA polymerase, the blunt-ended fragments were cloned in the *SmaI* site of the vector mp10 and were sequenced using the Amersham M13 sequencing kit.

Results

Organization of Light Satellite DNA Components in Species Closely Related to the *Mus Musculus* Complex

Quantitative Aspects

The *Mus musculus* species complex—*M. m. domesticus* (*Mus l*), *M. m. musculus* (*Mus 2A*), *M. m. castaneus* (*Mus 2C*)—and the European species *M. spretus* (*Mus 3*), *M. spretoides* (*Mus 4A*), and *M. spicilegus* (*Mus 4B*) probably diverged from each other within the past 1-4 Myr (see fig. 1). Even so, it has been shown that, unlike *Mus l*, no light satellite DNA component can be detected in *Mus 3* DNA on neutral CsCl gradients, although it can be detected by the Southern blotting technique (Brown and Dover 1980a). This interesting result led us to compare the amounts of light satellite DNA present in the other species of this group.

They all have sedimentation profiles that show an easily detectable light satellite component (results not shown). These results were confirmed using the dot blot technique. In the conditions used, only 0.3%-0.5% of the DNA of *Mus 3* genome hybridized to a *Mus l* light satellite probe, while approximately 15 times more signal was obtained with *Mus l*, *Mus 2A*, *Mus 2C*, *Mus 4A*, and *Mus 4B* DNA (fig. 2). Neither technique, however, was sensitive enough to detect minor differences that might exist among the latter group of species.

Restriction-Enzyme Analysis

The following two categories of restriction enzymes were used to analyze the structure of the mouse satellite DNAs: (1) enzymes that possess a site in the majority of the repeats (type A) and (2) enzymes that are present in only a limited number of segments of the satellite DNA (type B). The type B segments defined by different enzymes have been shown to be small, essentially nonoverlapping, tandem arrays (Hörz and Zachau 1977; Brown and Dover 1980a).

Previous studies have shown that the *M. m. domesticus* satellite repeat has one type A site for *EcoR I* and possesses three other positions (position 58, 118, and 146 on the consensus sequence shown in fig. 5) in which single base changes could create type B sites for this enzyme. Either loss of the type A site or the spread of a type B site in the other species would change the periodic structure of the satellite DNA fragments generated by *EcoR I*. This has not occurred in *Mus 2A*, *Mus 2C*, *Mus 4A*, and *Mus 4B*, in which no change is detected, and they all give a ladder of fragments with a main periodic structure of 234 bp, as well as minor ones of \(~120\) bp and \(~60\) bp (fig. 3). As reported previously by Brown and Dover (1980a), the same pattern is obtained with *Mus 3* DNA but with a much lower signal intensity.

In the consensus repeat, there are 56 nucleotide positions where a single base change could create a type B site for the restriction enzymes *AluI*, *HaeIII*, *HinfI*,...
Satellite DNA Evolution in the Genus *Mus* 481

<table>
<thead>
<tr>
<th>Species</th>
<th>Periodicity</th>
<th>Copy Number</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mus musculus domesticus</em> (Mus 1)</td>
<td>234 bp</td>
<td>high</td>
</tr>
<tr>
<td><em>M. m. musculus</em> (Mus 2A)</td>
<td>234</td>
<td>high</td>
</tr>
<tr>
<td><em>M. m. castaneus</em> (Mus 2C)</td>
<td>234</td>
<td>high</td>
</tr>
<tr>
<td><em>M. spretoides</em> (Mus 4A)</td>
<td>234</td>
<td>high</td>
</tr>
<tr>
<td><em>M. spicilegus</em> (Mus 4B)</td>
<td>234</td>
<td>high</td>
</tr>
<tr>
<td><em>M. spretus</em> (Mus 3)</td>
<td>234</td>
<td>medium</td>
</tr>
<tr>
<td><em>M. cerveri</em></td>
<td>-60</td>
<td>medium</td>
</tr>
<tr>
<td><em>M. cervicolor cervicolor</em></td>
<td>-60</td>
<td>medium</td>
</tr>
<tr>
<td><em>M. c. popoeus</em></td>
<td>-260</td>
<td>medium</td>
</tr>
<tr>
<td><em>M. cooki</em></td>
<td>-60</td>
<td>medium</td>
</tr>
<tr>
<td><em>Nannomys setulosus</em></td>
<td>-260</td>
<td>low</td>
</tr>
<tr>
<td><em>N. minutoides</em></td>
<td>-260</td>
<td>low</td>
</tr>
<tr>
<td><em>Pyromys platythrix</em></td>
<td>-260</td>
<td>low</td>
</tr>
<tr>
<td><em>Rattus norvegicus</em></td>
<td>-260</td>
<td>low</td>
</tr>
<tr>
<td><em>Coelomys pahari</em></td>
<td>?</td>
<td>low</td>
</tr>
<tr>
<td><em>Mastomys sp.</em></td>
<td>?</td>
<td>low</td>
</tr>
<tr>
<td><em>Apodemus sylvaticus</em></td>
<td>?</td>
<td>low</td>
</tr>
</tbody>
</table>

**Fig. 1.**—Consensus phylogeny for seven murid genera analyzed by standard electrophoresis at 28–42 protein loci (Bonhomme 1986). The scale is arbitrary, and the notation, based on biochemical groups and proposed by Bonhomme et al. (1984), is given in brackets. A (●) indicates a point where alternative branching orders are possible. The periodic structure and the amount of satellite DNA related to the *musculus* light satellite present in these species is indicated in the right-hand columns.

EcoRI, TaqI, MboI, or MboII. All these enzymes produce type B patterns with *Mus1*, *Mus2A*, *Mus2C*, *Mus4A*, and *Mus4B* satellite DNA, which shows that none of these B sites have spread and taken over in any of these species. These results are illustrated in figure 4, which shows the patterns obtained with *Alu1*, *HinfI*, and *EcoRI*. With *Alu1* and *HinfI*, only very small species differences can be detected. Similar results (not shown) were obtained with *HaeIII*, *MboI*, *MboII*, and *TaqI*, although the sites for the last two enzymes are more frequent. Also, they each possess a large number of sites that are minus one base in the repeat (13 and 18, respectively) and that give an important background smear owing to the presence both of randomly distributed sites and of those giving the ladder of type B bands. As all these enzymes except *EcoRI* possess more than one potential type B site per repeat, these results do not necessarily mean that there are no interspecies differences in the organization of the type B segments. Bands resulting from tandem arrays of different type B sites for the same enzyme would comigrate and could mask differences in their distribution. With *EcoRI*, for which this problem does not arise, there is in fact detectable interspecies variation.
FIG. 2.—Dot blot of total DNA from Mus1, Mus2A, Mus3, Mus4A, Mus4B, and Mus2C hybridized to purified nick-translated Mus musculus satellite DNA. Two concentrations of DNA (4 µg and 2 µg) were denatured in 0.1 N NaOH and then were applied to a nitrocellulose filter. Hybridization was carried out overnight at 42°C in 50% formamide and 5 × SSC. The filter was washed three times at room temperature in 2 × SSC, 1% sodium dodecyl sulfate (SDS) and three times in 0.1% SDS.

In Mus1 the relative intensities of the bands corresponding to the 120-bp and 234-bp registers are nearly equal, whereas in the other species the normal periodic pattern is observed. Similar results were obtained for Mus1 by Hörz and Zachau (1977) using ethidium bromide staining. These results suggest that in Mus1 the minor periodic structures, which were presumably originally generated by random out-of-register crossovers (Southern 1975b), are at least occasionally amplified into small tandem arrays in the same way that the other type B segments are produced.

Sequence Analysis

The nucleotide positions involved in the formation of the type B restriction-enzyme sites discussed above cover only 25% of the 234-bp repeat. Major homogenization events that are not detectable by these enzymes may, however, be detected by sequence analysis of cloned satellite repeat DNA from the different species. Strachen et al. (1985) showed that the comparative analysis of sequence variation in individual repeats of multicopy DNA can provide information about the dynamics of the homogenization processes that occur in these families, information that would be obscured if only percentage differences based on consensus sequences are considered. We therefore compared the sequences of cloned satellite monomers isolated from the two closely related species Mus1 and Mus4A genomic DNA.

The results, given in figure 5, show that there are three nucleotide positions (118, 197, and 228) that, although they are not completely diagnostic individually, can discriminate between these two species in almost all cases when they are considered together. The characteristic Mus4A nucleotides, however, are present in four of the 12 Mus1 clones: both positions 118 and 197 in clone 1.4, positions 118 and 228 in clone 1.6, and only position 118 in clones 1.7 and 1.8. Of the 234 nucleotides that make up the monomer, 121 are unvaried in all the clones, and at 90 other positions only one variant was found. The average intraspecies nucleotide divergence, calculated
from pairwise comparisons between all the clones, was 4.2% and 5.5% for the *MusI* and *Mus4A*, respectively. These percentages are not significantly different from each other and are in good agreement with that calculated by Southern (1975b) on the basis of the extent of divergence in the EcoRII site that has to be assumed in order to account for the proportion of polymers produced on complete digestion of mouse satellite DNA with this enzyme. The interspecies divergence of 5.6% is not significantly different from the intraspecies divergence. Less than a fifth of the interspecific divergence is due to the three diagnostic positions, while most of it appears to be attributable to private mutations rather than to obvious species-specific subfamilies. It is not possible, however, to draw from these results any conclusions concerning minor variants, as the number of repeats analyzed is too small.

Components Homologous to the *musculus* Light Satellite DNA in More Distantly Related Species

The Asian mice *M. caroli*, *M. cervicolor*, and *M. cooki*, which diverged before the *Mus* species discussed above (see fig. 1), were shown by Sutton and McCallum
Fig. 4.—Type B restriction patterns with Hinf I, AluI, and EcoRI. Four micrograms total DNA from MusI, Mus2A, Mus3, Mus4A, Mus4B, and Mus2C hydrolyzed with the relevant restriction enzyme were run on 1.4% agarose gels, transferred to Hybond-N membranes, and hybridized overnight at 42°C in 5 × SSC, 50% formamide to the cloned Mus musculus satellite probe. The blots were washed at 42°C three times in 2 × SSC, 0.1% SDS and two times in 0.1 × SSC, 0.1% SDS. The apparent differences in the amount of B segments in Mus2A seen with Hinf I and AluI are due to the reduced amount of DNA for this species that was loaded on the gels. Arrows indicate an ascending series of multimers based on a monomer length of 234 bp.

(1972) to contain small amounts of satellite DNA that cross-hybridize with the MusI light satellite. Under the conditions they used, no appreciable cross-hybridization with Rattus norvegicus or Apodemus sylvaticus DNA could be detected.

In the present study we investigated the periodic structure of satellite-DNA components hybridizing to the main musculus satellite in these species and to that in the other more distantly related murid rodents shown in figure 1. To increase the chances of detecting small amounts of diverged satellite sequences, hybridization to a high-specific-activity MusI satellite probe was carried out in 10% formamide, 6 × SSC (1 × SSC = 0.15 M NaCl, 0.015 sodium citrate pH 7) for 48 h at 42°C.

Figure 6 shows that, at low stringency, the type A restriction enzyme BstNI (iso-schizomer of EcoRII) generates satellite fragments with a primary periodic structure of ~60 pb in M. caroli, M. cervicolor cervicolor, and M. cooki DNA. However, the major periodic structure of the M. c. popaeus satellite component is ~240 pb, which is rather surprising when one considers that analysis of biochemical markers show
that this subspecies is very close to *M. c. cervicolor*. These differences in the distribution of the *EcoRII* sites on the satellite DNA of two very closely related subspecies show that satellite DNA can turn over very rapidly. This could occur either by amplification and deletion of related satellite families with different size repeats or by the spread of a variant in which the disposition of the *EcoRII* sites is altered.

Under the conditions used, the amount of probe hybridizing to *M. c. cervicolor*, *M. c. popaeus*, and *M. cooki* DNA is similar to that hybridizing to *Mus3* DNA. The signal obtained with *M. caroli* DNA is both less intense and less regular. If the washing stringency is increased (0.1 × SSC at 50°C), a slight superimposition of a 120-bp periodic structure is revealed in *M. c. cervicolor* and *M. cooki* (results not shown). Ellis (1979) obtained similar results for *M. caroli* and *M. cooki*. Our results are also in good agreement with the results of Sutton and McCallum (1972), who detected both two minor satellite components in both *M. cervicolor* and *M. cooki* and there different ones in *M. caroli*.

Figure 6 also shows that *Nannomys setulosus*, *N. minutoides*, *Pyromys platythrix*, and *R. norvegicus* possess small amounts of satellite DNA with a main periodic structure of ~240 bp. As one does not know the extent of the similarity existing between these components and the *Mus1* repeat, it is difficult to estimate their copy number, but it would appear to be relatively small—perhaps on the order of a hundred to a few thousand copies. With *Coclomys pahari*, *A. sylvaticus*, and *Mastomys* species, no obvious periodic pattern can be detected with *EcoRII*, and only a smeared signal is obtained.

**Discussion**

**Evolutionary Origin of the Mouse Light Satellite Components**

The imperfect internal repetitions in the prototype sequence of the 234-bp *Mus musculus* satellite monomer (Hörz and Altenburger 1981; Manuelidis 1981) provide strong support for the structural aspects of the evolutionary scheme proposed by Southern (1975b) on the basis of restriction-enzyme and reassociation data. This scheme involves a series of steps in which repeats with periodic structures of ~60, ~120, and ~240 bp were generated successively from a small 9–18-bp sequence. Our results show that satellite segments with a main periodic structure of ~240 bp were formed at a relatively early stage in the evolution of murid rodents, well before the radiation of the genus *Mus*. The interspecific copy-number variance detected in the species we studied, which diverged within the past 10 Myr, shows that forces leading to important changes in array size have acted over relatively short lapses of time within this evolutionary period. The 60-bp periodic structures detected with *EcoRII* in *M. cervicolor*, *M. cooki*, and *M. caroli* could correspond to amplified tandem arrays of one of the internal repetitions found in the 234-bp repeat. However, one cannot exclude the possibility that they are due to the spread of subfamilies of variants with more than one *EcoRII* site per repeat.

**Phylogenetic Implications**

So far it has not been possible to determine the precise order in which *M. musculus* (represented here by *Mus1*, *Mus2A*, and *Mus2C*), *Mus3*, and the two closely related species *Mus4A* and *Mus4B* diverged from each other, as the various sets of available biochemical data give conflicting phylogenies (Bonhomme 1986). The fact that *Mus1*, *Mus2A*, *Mus2C*, *Mus4A*, and *Mus4B* possess far more light satellite DNA than do all the other *Mus* species we studied suggests, however, that *Mus3* diverged first, as oth-
FIG. 5.—Nucleotide sequences of cloned monomers of Mus1 and Mus4A satellite DNA. The sequences are aligned under the Mus musculus consensus sequence (Hötz and Altenburger 1981; Manuelidis 1981). The beginning and the end of the sequence are delimited by the restriction site BstNI. Clones 1-1 to 1-11 and clones 4-1 to 4-11 were isolated from Mus1 and Mus4A, respectively. The sequence psat is a cloned satellite repeat sequenced by Butner and Lo (1986). d = Deletion; i = insertion; asterisk (*) = sequence not done.

erwise one has to postulate both an amplification event in an ancestral species and a large-scale deletion of satellite DNA in Mus3 once it had diverged. Similar parsimony considerations lead one to suppose that the amplification process originated only once and at least began in an ancestor common to the other species before they in turn diverged. The extensive spread of the corresponding diagnostic nucleotide variants in Mus1 and Mus4A must therefore be due to large-scale homogenization in one or both branches after their divergence.

Mechanisms Underlying the Converted Evolution of Mouse Satellite DNA

There are two aspects of the concerted evolution of satellite DNAs that should be considered separately. One deals with the balance between (a) the divergence of individual copies of the repeated sequence as the result of point mutation and (b) the forces that tend to spread new variants and homogenize the whole family. The other concerns the amplification mechanisms that can lead to important variations in the amount of satellite DNA present in closely related species.

It has been proposed that unequal crossing-over is the main force involved in the evolution of tandemly repeated DNA, and there is considerable indirect evidence,
such as the presence of degenerate internal repetitions within many satellite sequences and the nonrandom distribution of the type B sites, that unequal exchange based on small numbers of repeats plays an important role in the homogenization process. However, as far as it is a symmetrical, unbiased phenomenon, unequal crossing-over alone is not a force driving toward overall amplification, although as the result of random drift it can lead to important fluctuations in copy number within a population. Several authors have derived models to evaluate the relative influence that inter- and intrachromatid crossover rates, selective pressure, and various other parameters may have on the stability of highly repeated DNAs (Ohta and Kimura 1981; Ohta 1983; Charlesworth et al. 1986; Stephan 1986, 1987; Walsh 1987). These, however, cannot be applied meaningfully to our data, as we have no idea, a priori, of either the rate of recombination occurring in the pericentromeric regions of the chromosomes, the average bite size of the unequal crossovers, the population sizes, or the intensity of the selective forces acting on the process. Still, it is reasonable to assume that increasing the copy number from \( \sim 5 \times 10^4 \) to \( \sim 10^6 \) copies in the very short evolutionary period (0–10\(^5\) generations) that has elapsed between the separation of \( M. \) spretus and the common ancestor of the other European species of the genus \( M. \) musculus could not have
occurred by unbiased unequal crossing-over unless the size of each increment was considerably larger than a single repeat. The more unbiased the phenomenon, the bigger the bites would have had to have been for the actual array size to have been reached by drift alone. Amplification by unequal crossing-over of large blocks leads, within a population, to a situation that, conceptually, is not very different from those that would occur as the result of other types of amplification forces. The precise amplification mechanism is not known, and multiplicative processes involving rolling-circle intermediates (Hourcade et al. 1973) or other types of replication aberrations (Varshavsky 1981; Schimke et al. 1986; Lohe and Brutlag 1987a) could also have been responsible for the large-scale change in copy number.

As the fixation time for a variant depends on the copy number, the segregation of the variant diagnostic nucleotides in \textit{MusAA} and \textit{MusI} satellite DNA, a segregation that followed the amplification event, must also have involved large blocks of sequences. This homogenization process gives rise to a considerable amount of interchromosomal exchange, as it is very unlikely that all the \textit{MusI} and \textit{MusAA} clones that we sequenced were derived from the same chromosome. Ohta and Dover (1983) showed, on theoretical grounds, that, even when the ratio of the exchange rates between nonhomologous chromosomes is quite low, homogenization throughout the whole genome can still occur, provided the number of repeats is large compared with the number of nonhomologous chromosomes. In the mouse, all the chromosomes are normally acrocentric, and, in humans, the acrocentric chromosomes 13, 14, 21, and 22 share very similar alpha-satellite variants (Jorgensen et al. 1986; Choo et al. 1988), while the chromosome-specific subfamilies of this satellite are associated with the metacentric chromosomes (Willard and Waye 1987b). This suggests that nonhomologous exchange occurs more readily between acrocentric than between metacentric chromosomes. Brown and Dover (1980b) showed that even the \textit{MusI} X chromosome is included in this phenomenon.

This evolutionary scheme for mouse satellite DNA, a scheme based on the amplification and differential homogenization of large blocks of satellite sequences, suggests that, if this process is still in action, one should be able to detect a polymorphism related to these large satellite segments in mouse populations. Although so far there are few data concerning satellite DNA polymorphism, the results of Butner and Lo (1986), who studied the integration of exogenous DNA in the centromeric region of the chromosomes in transformed mouse cell lines, indicate that rearrangements of mouse satellite DNA occur relatively frequently. Duplication either by unequal crossing-over of large blocks or by sequence amplification could also explain \((a)\) the important differences in the amount of deca-satellite DNA found in the genomes of individual African green monkeys (Maresca et al. 1984) and \((b)\) the variation in the amount of DNA present in a single satellite block bordered by the same flanking sequences found on individual human Y chromosomes (Tyler-Smith and Brown 1987). The study of satellite-DNA polymorphism in mouse populations by using techniques such as pulsed-field gel electrophoresis should provide more information about the nature of the observed amplification and homogenization events.

\textbf{Acknowledgments}

We would like to thank Dr. G. Dover for his helpful comments. This work was supported by grants from the CNRS, INSERM, the Association pour la Recherche contre le Cancer (to G.R. and F.B.), and the Fondation pour la Recherche Médicale.
(to F.B.). E.D. was supported by a stipend from the Ministère de la Recherche et de la Technologie.

LITERATURE CITED


WALTER M. FITCH, reviewing editor

Received February 1, 1989; final revision received May 3, 1989

Accepted May 4, 1989