Chromosome Mapping in the Mouse

Fluorescence banding techniques permit assignment of most genetic linkage groups.

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The introduction of staining methods that produce differential banding of mitotic chromosomes (*1*) has revolutionized cytogenetic studies during the last 2 years. Most striking have been the advances this has made possible in the field of mouse cytogenetics.

The laboratory mouse, *Mus musculus*, has been a particularly useful mammal for genetic studies because of its small size, short generation time, and ease of breeding, even as highly inbred lines. Large amounts of genetic data have accumulated as a result of studies of the inheritance of a wide variety of traits, such as coat color, behavioral characteristics, antigenic differences, and enzyme variants. Mutant alleles at nearly 500 gene loci are known (*2*) and more than 220 of these loci have been shown to be genetically linked to one or more other loci (*3, 4*). Linked genes are on the same chromosome, but they may be separated by crossing-over between homologous chromosomes during meiosis. The frequency of recombination of linked genes provides an estimate of the genetic distance between them (usually expressed in crossover units, or centimorgans) because genes that are far apart are more likely to be separated than genes that are located near one another. With sufficient data a linkage map can be constructed in which each collection of linked genes, or linkage group, corresponds to one chromosome. Because the haploid number of chromosomes in the mouse is 20, there should be at least 20 linkage groups, one for each of the 19 autosomes and one for the X chromosome. Nineteen linkage groups have been identified, with from 2 to 24 loci already mapped within each one (*3, 4*). In view of the small size of some of these linkage groups, and the absence of information concerning the chromosome to which each one belongs, it is possible that two of these collections of linked genes may belong to the same linkage group. It is likely in any event that each chromosome carries many more genes than have yet been identified.

Sometimes, gene loci that are not normally linked do show linkage in a stock of mice, because of the presence of a translocation. This can occur as a result of breakage in two nonhomologous chromosomes in a cell of the germ line, nonhomologous broken chromosomes rejoining to produce a reciprocal exchange, or translocation. It is also possible for two nonhomologous chromosomes to become fused together in their centromeric region, producing a single biarmed chromosome. The two linkage groups involved in such a centric fusion (Robertsonian) type of translocation will segregate as a single unit—that is, they will be replaced by a single, larger, linkage group, while a reciprocal translocation leads to the formation of two new groupings of linked genes. Recognition of altered linkage relationships is one of several methods used to determine the linkage groups involved in translocations, especially the second one. The first linkage group is usually identified by standard linkage tests, the translocation being treated as a dominant gene that can be identified either cytologically or by the semisterility of the offspring (*5*).

Hundreds of translocations, most of them induced by radiation, have been observed in the mouse. Stocks of mice, each carrying a specific translocation, have been developed and genetic studies have been conducted on some of them to determine the linkage groups involved. Each translocation stock is given a unique designation (*6*); for example, *T163H* is the 163rd translocation in the Harwell series. If the linkage groups involved in the translocation are known, they are included in parentheses; for example, the designation *T(2;12)163H* indicates that linkage groups II and XII are involved in *T163H*.

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Chromosome Identification

The wealth of information derived from genetic analysis of the mouse was, until recently, in marked contrast to the paucity of information derived from studies of the mitotic chromosomes. All 20 pairs of chromosomes are telocentric, and in Giemsa-stained preparations only one pair of autosomes, number 19, can be recognized with certainty, because of its small size and the frequent presence of a secondary constriction. The remainder of the autosomes and the X chromosome are not individually identifiable in such preparations (*7*). The presence of a translocation can be demonstrated in these standard Giemsa-stained preparations only if a chromosome of abnormal length [either very long, as in *T190Ca* (*8*), or very short, as in *T6Ca* (*9*)] or a biarmed chromosome, as in *T163H* (*10*), is present. Usually, however, no abnormal chromosome can be detected cytologically in mitotic preparations.

The development of new methods for examining mitotic chromosomes has permitted a rapid development of mouse cytogenetics in the past year. Each chromosome can now be identified by the banding pattern produced with quinacrine fluorescence staining (*11, 12*) or with one of the modified Giemsa staining methods (*13, 14*). Brief descriptions of the patterns are presented by Dev *et al.* (*11*) and by Buckland *et al.* (*13*). The nature of the banding patterns is unknown (*15*) but the pattern of each chromosome is consistent from cell to cell and is the same within each strain that has been tested, although there are strain differences in the size of secondary constrictions (*11*). The chromosomes can be identified and homologs paired on the basis of the banding patterns. Chromosomes identified in this way have been measured and the chromosome pairs arranged in order of decreasing size. A standard system for numbering mouse chromosomes based

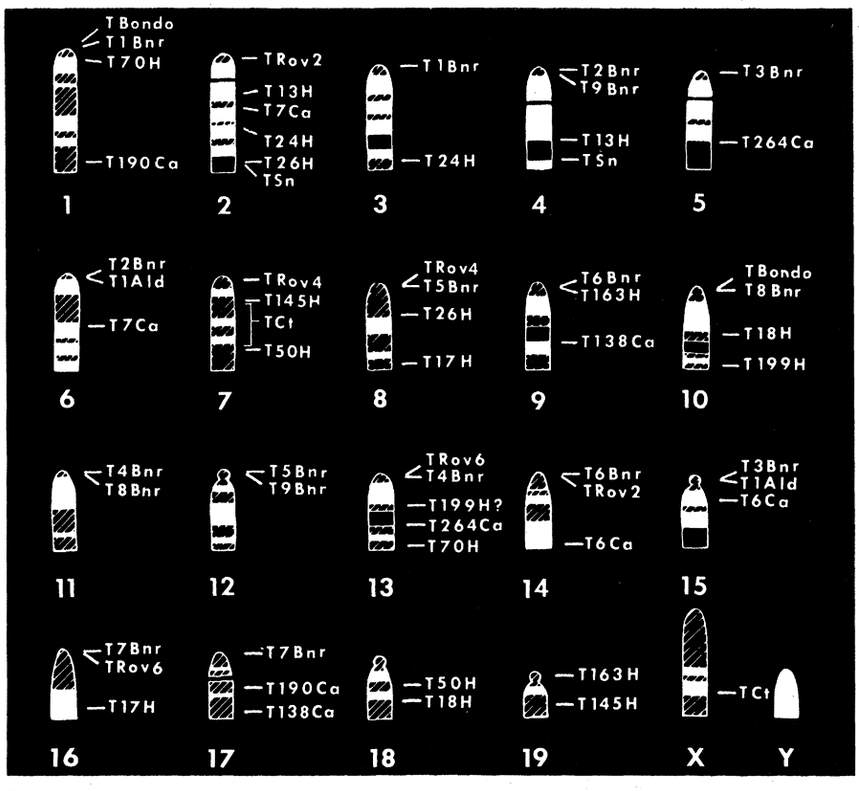

Fig. 1. Idiogram of the banding patterns of the chromosomes of *Mus musculus*. Cytologic breakpoints are shown for the translocations that have been analyzed by the fluorescent banding technique. References are listed in Tables 2 and 3.

on these results has been published by the Committee on Standardized Genetic Nomenclature for Mice (*16*) and will be used throughout this article. The Committee's report includes a list of the corresponding chromosome numbers used in earlier papers from each of four laboratories. An idiogram conforming to the standard system is shown in Fig. 1.

The banding pattern of each segment of a translocation chromosome is similar to the banding pattern of the same segment in the corresponding normal chromosome. It is, therefore, possible to identify the chromosomes involved in a translocation by direct cytological examination. In a reciprocal translocation it is usually easier to analyze the karyotype in heterozygous animals in which the normal homologous chromosomes are present within the same cell for comparison, but with sufficient knowledge of the normal karyotype even homozygous translocations can be analyzed cytologically. For example, it has been shown by the quinacrine fluorescent technique that the translocation in the *T(2;12)163H* stock was produced by centric fusion of chromosomes 9 and 19 (*17, 18*). In this case, conventional staining methods showed that chromosome 19 (the only identifiable autosome) was part of the biarmed chromosome (*10*), but the other chromosome could not be identified.

We and our colleagues, Allderdice, Dev, and Grewal at Columbia, and Hutton and Kouri at the Roche Institute of Molecular Biology, have used the quinacrine fluorescent technique to identify the chromosomes included in the translocations in 18 stocks of mice. These stocks were selected to represent as many linkage groups as possible (Table 1). Four of the translocations were analyzed independently by Nesbitt and Francke (*18–20*) with concordant chromosomal findings. The identification of the chromosomes involved in each translocation, and the approximate position of the breakpoints observed in each chromosome are shown in Fig. 1. Every chromosome except numbers 11, 12, and the Y is involved in one or more of these translocations. References for each of the cytologic breakpoints are listed in Table 2. All the translocations we studied are reciprocal except *T163H* and *T1Ald*, which are of the centric fusion type. Figure 1 includes a series of other naturally occurring centric fusion translocation chromosomes which are listed in Table 3.

Linkage Assignments

It thus became possible to assign most of the mouse linkage groups to specific chromosomes by correlating the linkage groups included in translocations with the chromosomes involved. The method requires the use of two translocation stocks that have one linkage group in common. For example, the *T(2;12)163H* (*10*) and the *T(2;9)138Ca* (*5*) translocation chromosomes each involve linkage group II. Karyotype analysis shows that the translocation in *T163H* involves chromosomes 9 and 19 while that in *T138Ca* involves chromosomes 9 and 17 (*17*) (Fig. 2). The only chromosome in common in the two translocations is chromosome 9, which must therefore carry the only linkage group in common, linkage group II (Table 4). The remaining chromosome in each translocation must carry the remaining linkage group: chromosome 19 must carry linkage group XII and chromosome 17, linkage group IX. The assignment of linkage group IX to chromosome 17 has been confirmed by studying another translocation which, like *T138Ca*, involves this linkage group: *T(9;13)190Ca* (*5*). Karyotype analysis has shown that *T190Ca* involves chromosomes 1 and 17 (*17*) (Fig. 2). The only chromosome which the *T138Ca* and the *T190Ca* translocations have in common, chromosome 17, must carry the common linkage group, IX (Table 4).

Linkage group XII has been assigned to chromosome 19, which can be recognized without the use of a banding technique, by Eicher (*21*) and by Lyon and Glenister (*22*). By the same reasoning as that described above, Eicher showed that because chromosome 19 is involved in both the *T(2;12)163H* and the *T(1;12)145H* translocations, this chromosome must carry the common linkage group, XII (*21*). Lyon and Glenister (*22*) showed that a normal number 19 chromosome was present in double heterozygotes carrying the *T(2;12)163H* and the *T(2;9)138Ca* translocations; this indicated that chromosome 19 was involved in only one of these translocations. Because chromosome 19 was known to be involved in the *T163H* translocation it could not be involved in *T138Ca*. Chromosome 19 therefore carried linkage group XII, which was present in the *T163H* but not the *T138Ca* translocation.

Using the method illustrated in

Table 4, we have been able to assign most of the linkage groups to specific chromosomes (Table 2). Although the method is most effective when applied to translocations for which the linkage groups are known from genetic studies, cytologic analysis may provide sufficient information to permit the assignment of linkage groups that have not been established in this way. *T(3;?)6Ca* (*5*) presented a problem because one of the linkage groups has not been established and the other linkage group, III, is not known to be carried by any other translocation in *M. musculus*. Karyotype analysis shows that this translocation involves chromosomes 14 and 15 (*17, 20*), one of which must carry linkage group III. Two separate studies suggest that linkage group III is carried by chromosome 14. Eicher and Green (*23*) have found evidence that the *hr* (hairless) and *s* (piebald) loci of linkage group III are between the centromere and the *T6* breakpoint, and are not on the tiny T6 marker chromosome which has the centromere of chromosome 15 (*17, 20*). Therefore linkage group III cannot be on chromosome 15, but must be on chromosome 14. Lyon *et al.* (*24*) found evidence suggesting that linkage group III is not involved in the *T(11;?)Ald* translocation, which was produced by centric fusion of chromosomes 6 and 15 (*16*). This, too, indicates that linkage group III cannot then be on chromosome 15, which is present in both *T6Ca* and *T1Ald*, but must be on number 14, which is involved only in *T6Ca*.

Confirmation by Meiotic Studies

The *T(13;?)70H* translocation provides another example of the problem raised when only one of the linkage groups in a translocation is known, and how it can be resolved cytologically. Karotype analysis has shown that the unknown linkage group in *T70H* must be on either number 9 or number 13 (*25*), chromosomes which are difficult to distinguish on the basis of their banding patterns. Chromosome 9, which carries linkage group II, is involved in *T163H* (*17*). Chromosome 13, which carries linkage group XIV or XVII, is involved in *T264Ca* (*26*). In order to find out whether the chromosome in *T70H* is the same as that in *T163H* or that in *T264Ca*, meiotic studies were conducted on animals heterozygous for two of the translocations. During meiosis homologous chromosomes pair to form bivalents. In an animal heterozygous for a translocation, the translocation chromosomes (or chromosome) pair with the normal homologous chromosomes to form a quadrivalent (or, in the case of a centric fusion chromosome, a trivalent) in place of two bivalents. During meiosis in an animal heterozygous for two translocations involving different chromosomes for each translocation a quadrivalent or trivalent replaces two bivalents, so that first meiotic division figures contain 16 bivalents and 2 multivalents. However, in an animal heterozygous for two translocations which have one chromosome in common, no normal copy of that chromosome will be present. During meiosis the two translocations will be part of the same pairing configuration and there will be 17 bivalents and 1 multivalent. Slizynski (*27*) first used this method in the mouse. We have been able to show by observing the meiotic configurations that *T70H* and *T163H* involve different chromosomes, whereas *T70H* and *T264Ca* involve a common chromosome (*28*). Therefore, *T70H*, like the

Table 1. Mouse translocations studied by quinacrine fluorescence with linkage groups indicated.

T(11;?)1Ald	*T(1;X)Ct*	*T(1;?)50H*
T(3;?)6Ca	*T(5;8)13H*	*T(13;?)70H*
T(5;11)7Ca	*T(18;?)17H*	*T(1;12)145H*
T(2;9)138Ca	*T(10;?)18H*	*T(2;12)163H*
T(9;13)190Ca	*T(5;?)24H*	*T(10;?)199H*
T(14;17)264Ca	*T(5;18)26H*	*T(5;8)Sn*

Table 2. Sources of information on the translocation stocks used for chromosome mapping.

Chromosome	Linkage group	Translocation	References			
			Breakpoint		Centromeric end of linkage group	
			Cytologic	Genetic	Cytologic	Genetic
1	XIII	*T70H*	(*25*)	(*39*)	(*25, 26*)	(*39*)
		T190Ca	(*17*)	(*5*)		
2	V	*T7Ca*	(*26*)	(*5*)	(*26*)	(*39*)
		T13H	(*25*)	(*37*)		
		T24H	(*25*)			
		T26H	(*26*)	(*39*)		
		TSn	(*46*)	(*47*)		
3	?	*T24H*	(*25*)			
4	VIII	*T13H*	(*25*)	(*37*)	(*46*)	(*48*)
		TSn	(*46*)	(*47*)		
5	XVII	*T264Ca*	(*20, 26*)	(*5*)		
6	XI	*T1Ald*	(*17*)	(*49*)		(*50*)
		T7Ca	(*26*)	(*5*)		
7	I	*T50H*	(*25*)	(*51*)	(*25*)	(*51*)
		T145H	(*25*)	(*22*)		
		TCt	(*19, 52*)	(*53*)		
8	XVIII	*T17H*	(*25*)	(*37*)	(*25, 26*)	(*54*)
		T26H	(*26*)	(*54*)		
9	II	*T138Ca*	(*17*)	(*55*)		(*38*)
		T163H	(*17, 18*)	(*10*)		
10	X	*T18H*	(*25*)	(*56*)		(*56*)
		T199H	(*25*)	(*57*)		
11	?					
12	?					
13	XIV	*T70H*	(*25, 27*)			(*39*)
		T199H	(*25*)			
		T264Ca	(*20, 26*)	(*29*)		
14	III	*T6Ca*	(*17, 20*)	(*23*)		(*23*)
15	?	*T1Ald*	(*17*)	(*49*)		
		T6Ca	(*17, 20*)			
16	?	*T17H*	(*25*)			
17	IX	*T138Ca*	(*17*)	(*35*)	(*26*)	(*38*)
		T190Ca	(*17*)	(*5*)		
18	?	*T18H*	(*25*)			
		T50H	(*25*)			
19	XII	*T145H*	(*25*)	(*22*)		
		T163H	(*17, 18*)	(*58*)		
X	XX	*TCt*	(*19, 52*)	(*59*)	(*26*)	(*51*)
Y						

Table 3. Different naturally occurring biarmed mouse chromosomes. References for chromosome identification are shown in parentheses.

Designation	Chromosomes	References
T1Bnr	3/1	(*32*)
T2Bnr	6/4	(*32*)
T3Bnr	15/5	(*32*)
T4Bnr	13/11	(*28, 32*)
T5Bnr	12/8	(*32*)
T6Bnr	14/9	(*32*)
T7Bnr	17/16	(*32*)
T8Bnr	11/10	(*33*)
T9Bnr	12/4	(*33*)
TBondo	10/1	(*33*)
TRov2	14/2	(*33*)
TRov4	8/7	(*33*)
TRov6	16/13	(*33*)
T1Ald	15/6	(*17*)
T163H	19/9	(*17, 18*)

T264Ca translocation, must involve chromosome 13, which carries linkage group XIV or XVII. *T(10;?)199H* also involves an unknown linkage group carried by either chromosome 9 or 13, number 13 being more probable on the basis of the mitotic chromosome banding pattern (*25*). Meiotic studies with double heterozygotes would show conclusively whether chromosome 9 or 13 is involved in the *T199H* translocation.

Linkage groups XIV and XVII were known to be present in *T264Ca* (*5, 29*) but until a second translocation was found involving either of these linkage groups it was not possible to specify the chromosome, 5 or 13, carrying each of the linkage groups. This problem has recently been solved by using an animal carrying a biarmed chromosome from *M. poschiavinus*. The tobacco mouse, *M. poschiavinus*, is a naturally occurring animal that has seven pairs of biarmed chromosomes and six pairs of telocentric chromosomes (*30*). The seven biarmed chromosomes, which have been designated *T1Bnr*, *T2Bnr*, . . . *T7Bnr* (*31, 32*), are assumed to have arisen by centric fusion of normal mouse chromosomes since the tobacco mouse can be bred with *M. musculus*. Zech *et al.* (*32*) have recently shown that the banding patterns of the *M. poschiavinus* chromosome are indeed the same as those of *M. musculus* and have identified the chromosomes present in each of the biarmed chromosomes (Table 3 and Fig. 1). Gropp and his associates (*33*) have extended these studies to feral mice in rather isolated Swiss valleys and have found six additional biarmed chromosomes whose banding patterns are consistent with their origin by centric fusion of normal mouse chromosomes. Each autosome except number 18 is involved in one or more of these naturally occurring biarmed chromosomes (Table 3 and Fig. 1).

Cattanach and associates (*34*) used meiotic studies to determine the linkage groups in each of the *M. poschiavinus* biarmed chromosomes. In each case their findings agreed with the mitotic findings. In addition, they found that one arm of the *T4Bnr* chromosome is a chromosome which is present in *T264Ca* and that this carries linkage group XIV. Since both *T4Bnr* and *T264Ca* involve chromosome 13 (*26, 28*), this chromosome must carry linkage group XIV. The other linkage group involved in *T264Ca*, linkage group XVII, can therefore be assigned to chromosome 5.

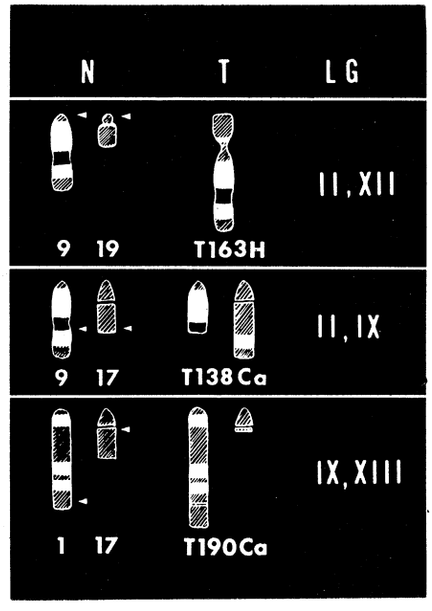

Fig. 2. The quinacrine fluorescent idiogram of the translocation chromosomes (*T*) and their normal homologs (*N*) in three mouse translocations. The position of the breakpoint in each normal chromosome is shown by an arrow. The linkage groups (*LG*) involved are indicated for each translocation. In *T163H* a biarmed chromosome has been formed by centric fusion of chromosomes 9 and 19. In *T138Ca* a reciprocal exchange between chromsomes 9 and 17 has produced two translocation chromosomes, neither of which can be detected in mitotic preparations without the use of a banding technique. In *T190Ca* a reciprocal exchange between a very long chromosome, number 1, and a short chromosome, 17, has produced two translocation chromosomes of abnormal length. Although both of these can be detected in mitotic preparations without the use of a banding technique, the chromosomes from which they were produced cannot be identified in this way.

Table 4. Method used to assign linkage groups to chromosomes.

Linkage groups		Translocation	Chromosome numbers	
II	XII	*T163H*	9	19
II	IX	*T138Ca*	9	17
XIII	IX	*T190Ca*	1	17
XIII	?	*T70H*	1	13
XVII	XIV	*T264Ca*	5	13

We can also conclude that because the *T70H* translocation involves chromosome 13, it involves linkage group XIV (Table 4). That is, the linkage group involved in this, and many other, translocations can be specified without further genetic analysis, simply by cytological identification of the chromosomes involved.

Standard Nomenclature

The Committee on Standardized Genetic Nomenclature for Mice (*16*) has proposed that in the future the designation of translocation stocks should include the chromosomes involved in the translocation rather than the linkage groups. For example, the *T(2;12)163H* is to be designated *T(9;19)163H*, with the chromosome numbers printed in boldface italics. The revised designations, indicating the chromosomes included in each of the 18 translocations that have been studied by analysis of their chromosome banding patterns are presented in Table 5.

As each chromosome is identified with a specific linkage group it is desirable to rearrange the linkage group map to conform to the chromosome numbers. A modified (and partial) linkage map which includes the location of the breakpoint of the translocations we studied, as determined by genetic studies, is shown in Fig. 3. References for the breakpoints of each translocation are listed in Table 2. Although the breakpoints shown in Figs. 1 and 3 were estimated by independent methods they are generally in good agreement. This correspondence is more apparent that real because of the nature of the mapping process. On the one hand the cytologic breakpoint is only approximate since the visible bands are relatively wide. On the other hand, the linkage groups are only partially mapped. For example, the dis-

tance from the centromere to the proximal marker has been established only for chromosomes 6, 9, and 17 (Fig. 3) and no distal marker has been located definitively. The availability of stocks of mice carrying one of the *M. poschiavinus* centric fusion chromosomes should facilitate determination of the distance from the centromere to the proximal marker in other chromosomes and it is possible that the use of translocations with breakpoints close to the distal end of the chromosome will facilitate mapping of these regions (*35*). However, the genetical distance between two loci may not be closely correlated with the cytological distance even when the entire linkage group has been mapped because the genetic distance is based on crossover frequencies which are enhanced or suppressed by a variety of factors other than the physical distance separating them (*36*).

Six chromosomes, 3, 11, 12, 15, 16, and 18, have not yet been assigned a linkage group, although each has been found to be part of one or more translocations (Figs. 1 and 3). The six linkage groups which remain to be assigned are IV, VI, VII, XV, XVI, and XIX. It is anticipated that the remaining assignments will be made in the near future, and some clues already exist. Chromosome 16 probably carries linkage group XV, XVI, or XIX since it is part of the *T17H* (*25*) translocation for which genetic studies have excluded linkage groups IV, VI, and VII (*37*). Genetic studies have indicated that chromosome 11, which carries the unknown linkage group in *T4Bnr*, probably does not carry linkage group VI or XVI (*34*) and chromosome 18, which is involved in *T18H*, probably does not carry linkage group VI (*37*). Linkage group VI could then be located on chromosome 3, 12, or 15. It seems probable that one of the longer linkage groups, such as IV and VII, will be carried by chromosome 3.

Position of the Centromere

A linkage map represents the linear order of the genes along the chromosome, but should also include the position of the centromere. Several genetic methods have been used recently to determine the centromeric end of specific mouse linkage groups; for example, the frequency of recombination between genetic markers and a centromeric marker, that is, a biarmed chromosome (*38*), and the frequency of aberrant segregation in offspring of translocation heterozygotes (*39*). Study of the translocation chromosomes has provided a simple two-breakpoint cytogenetic method for determining the centromeric end of a linkage group. If a chromosome is involved in two or more translocations, the linear order of the breakpoints with respect to the centromere can often be established cytologically. This order: centromere–breakpoint in translocation 1–break-

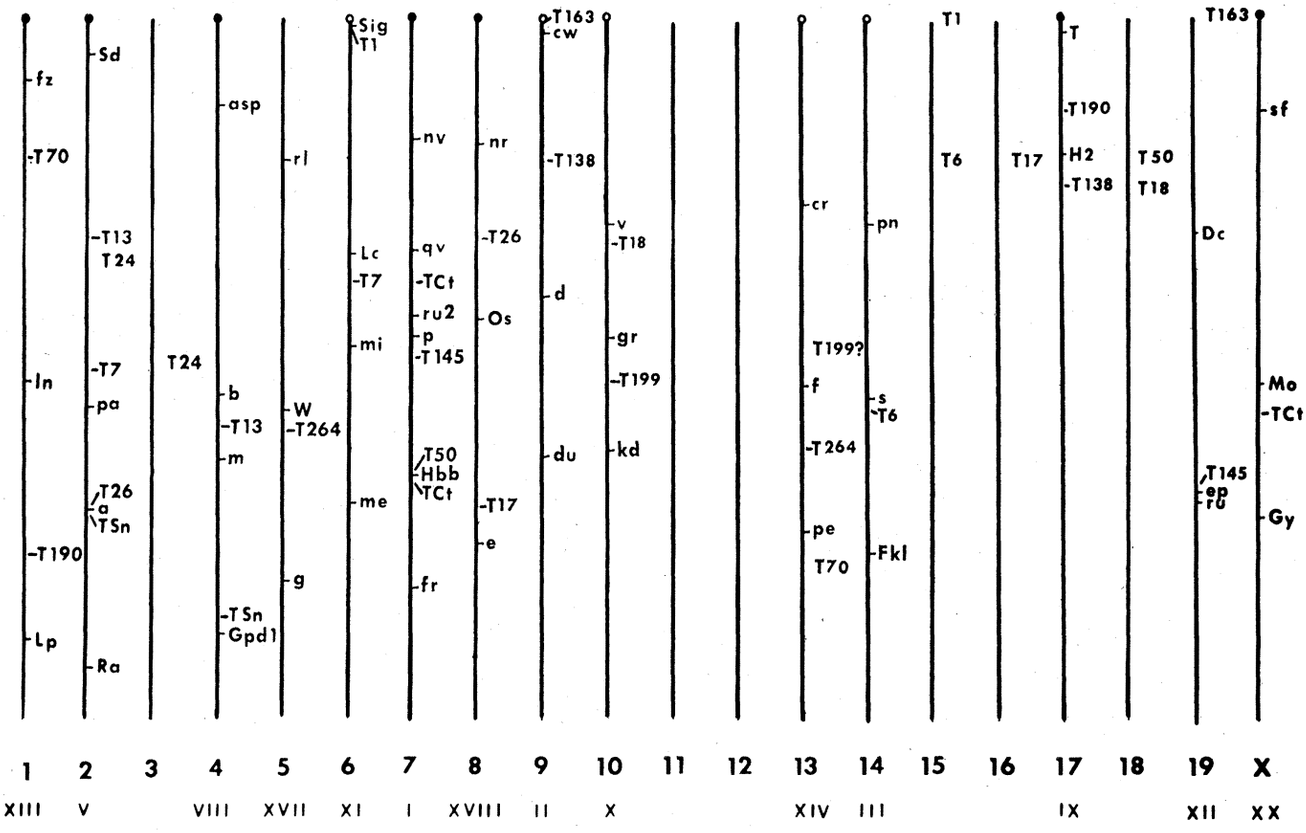

Fig. 3. Linkage map modified from Green (*4*) to show the approximate genetic breakpoints of each translocation listed in Table 1. Chromosomes are identified by Arabic numerals and linkage groups (if known) by Roman numerals. The position of selected genetic markers, including the known distal markers, are indicated by letter abbreviations (*2*). The position of the translocation breakpoints determined by genetic analysis are indicated *—T*; translocations that have been shown cytologically to be on a particular chromosome but have not been mapped genetically are indicated without a crossline, for example, *T24* on chromosome 3. Most of the centric fusion translocations listed in Table 3 have been omitted, but they are shown in Fig. 1. The centromeric end of chromosomes 6, 9, 10, 13, and 14 (open circles) were determined by previous genetic methods; the centromeric ends of chromosomes 1, 2, 4, 7, 8, 17, and the X (closed circles) were determined by the same methods and confirmed by fluorescent identification of the translocation chromosomes.

Table 5. Revised designations for translocations with chromosome numbers indicated in parentheses. The Committee on Standardized Nomenclature for Mice recommends that the chromosome numbers be boldface type, where possible.

T(6;15)1Ald	*T(7;X)Ct*	*T(7;18)50H*
T(14;15)6Ca	*T(2;4)13H*	*T(1;13)70H*
T(2;6)7Ca	*T(8;16)17H*	*T(7;19)145H*
T(9;17)138Ca	*T(10;18)18H*	*T(9;19)163H*
T(1;17)190Ca	*T(2;3)24H*	*T(10;13)199H*
T(5;13)264Ca	*T(2;8)26H*	*T(2;4)Sn*

point in translocation 2, will be the same in the chromosome and in the linkage group. Therefore, provided there is genetic information concerning the position of both translocation breakpoints in the linkage groups, the position of the centromeric end of the linkage group can be determined. For example, cytologic study of two translocations involving chromosome 1 showed the order: centromere–breakpoint *T70H*–breakpoint *T190Ca* (*17*, *25*) (Fig. 1). Genetic evidence placed the *T70H* breakpoint between *fz* (fuzzy) and *ln* (leaden) (*39*) and the *T190Ca* breakpoint on the side of *ln* away from *fz* (*5*). Therefore the centromeric end of the linkage group must be at the *fz* end (Fig. 3). This method was used to identify the centromeric end of linkage groups XIII, V, VIII, I, XVIII, and IX (*25*, *26*) (Fig. 3 and Table 2). In each case the results obtained by using the cytologic breakpoints agreed with those established by other methods (Table 2).

In selected cases it is possible to assign the centromeric end of a linkage group by means of a single translocation, provided the breakpoint is very near one end of the chromosome and provided the linkage group has been mapped over a sufficient length to assure that the polarity of the linkage groups corresponds to that of the chromosome. This is the same method used by Ford (*40*) in the *TSn* translocation in which the breakpoint is located near the distal end of chromosome 2 (Fig. 1). We used this one-breakpoint method to locate the centromere at the *sf* (scurfy) end of linkage group XX (the X chromosome) (*26*) (Fig. 3).

Further Applications

Karyotypic analysis of mouse translocations by means of the new banding techniques can be used to solve a number of outstanding problems. It should greatly simplify the problem of finding out which linkage groups are involved in other mouse translocations. It has already proved useful, for example, in showing that *T70H* involves linkage group XIV and that *T24H* does not involve linkage group XIII (*25*), as had been suggested. It has provided a more rational basis for determination of the unknown linkage group in *T199H*, because only two linkage groups, II and XIV, need be examined seriously (*25*). It indicated that the genetic breakpoint in chromosome 10 in *T199H*, which initially was located only with respect to *v* (waltzer) (*41*), must in fact be on the side of *v* away from the centromere because the cytologic breakpoint is distal to that of *T18H*, which is close to *v* (*25*). It has provided a method for confirming the centromeric end of linkage group XIV as soon as the genetic breakpoint of *T70H* is established, because the breakpoint of *T70H* has been shown cytologically to be distal to that of *T264Ca*.

Our ability to recognize each mouse chromosome also permits new approaches to genetic problems. Dev *et al.* (*11*) showed that there are strain differences in the size of secondary constrictions on chromosomes 12, 15, 16, 18, and 19, thus providing a source of normal marker chromosomes for future genetic studies. By means of the banding techniques it is possible to analyze all the chromosomes in heteroploid mouse cell lines and to investigate the kinds of chromosomal changes associated with malignancy (*42*). In addition, since it is possible to distinguish mouse and human chromosomes in man/mouse hybrid cells (*43*, *44*), a system is available for correlating the presence of a chromosome with the presence of an enzyme product. This approach has been used to assign the thymidine kinase locus to human chromosome 17 (*44*, *45*) and the lactic dehydrogenase-A locus to number 11 (*44*), as well as to recognize a translocation between a mouse chromosome and a human chromosome (*44*).

Summary

Chromosome banding techniques have permitted the identification of every normal chromosome in the mouse, *Mus musculus*, and the demonstration of strain differences. By identifying the chromosomes involved in a series of translocations, it has been possible to assign 14 of the 19 known linkage groups to 14 different chromosomes. These powerful cytological methods promise to revolutionize cytogenetic studies in higher organisms.

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University-Industry Interaction Patterns

Past models are analyzed, some recent experiments described, and recommendations for the future given.

Rustum Roy

The research enterprise in the United States has been developing a pronounced lacuna in the areas of "applied science" or "applied research" (*1*). It has been my contention—since long before the shutdowns at U.S. Steel, RCA, Ford, Zenith, and others—that U.S. industry is increasingly withdrawing from fundamental research, even from research applied to its own problems, the support it had been giving for two decades. This gap must now be filled by universities, since no other performers are in sight. However, in order to do so, there must be a higher *general* level of effectiveness in the interaction between universities and industry in this country than has ever existed before. In this article, I examine briefly the situation in university-industry interaction, or coupling, in the recent past and describe viable models for the greatly enhanced interaction that is, in my opinion, essential to the well-being of national research and development (R & D).

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Standard Patterns of University-Industry Interaction

The taxonomy of the methods of university-industry scientific and technical interaction is not very complicated. The practices involved are standard; innovators are few and far between, since the person who can survive in a hostile environment from both camps is extremely rare. For several decades there have been only two or three universally acceptable mechanisms through which an entire university or a particular department could interact with industry. These mechanisms, summarized schematically in Fig. 1, are easily recognizable. The use of university faculty as consultants in industry is a time-honored and extremely effective way by which (given normal luck) the results of research and new ideas may be transmitted in one direction. There are innumerable examples of faculty consultants playing important roles in industrial developments. In the other direction, toward the university, flows (in addition to a fee) the most important benefit: a feel for the significance of problems on the scale of "value" to industry, relevance to the public's needs, and so on. It is my contention that in consulting, at least for large companies, the consultant gains as much as he gives. Such personal contacts occasionally, but not frequently enough, lead to interchange of samples and sharing of facilities, to the benefit of both industry and the university. Very often the latest results of government-supported research in the consultant's laboratory lead to new ideas that prove valuable to the company employing the consultant. The only problem with this method is its neglect: it is remarkable not how many, but how few, of the engineering and science faculty consult at all. While we have all read about abuses of the consultation privilege, an informal survey of science and engineering faculty all over the country would suggest that fewer than 10 percent of them spend 1 day a month in consulting. (Excessive consultation is a bogeyman, since every department head or dean has complete control of the matter.)

A second standard method of university-industry interaction is the research project funded by industry within a university laboratory or department. This is a highly desirable method of interaction. A high degree of monitoring and interaction is demanded,