GENETIC MAPPING OF XENOTROPIC MURINE LEUKEMIA VIRUS-INDUCING LOCI IN FIVE MOUSE STRAINS

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A number of lines of evidence indicate that the genetic determinants of the xenotropic mouse leukemia viruses (MuLV)[1] are inherited as chromosomal genes in mice. Sequences homologous to the complete viral genome have been identified in the cellular DNA of all laboratory mouse strains as well as in wild house mice (1). An MuLV gp70 found in serum of all mouse strains shows a tryptic digest pattern similar to that of the envelope gp70 of a xenotropic virus isolated from NZB mice (2). Furthermore, all mice express cell surface antigens on their lymphocytes (XenCSA) cross-reactive to the gp70 of these viruses (3).

Despite the ubiquity of xenotropic MuLV genomes in mice, the frequency of production of infectious virus differs sharply among mouse strains. High virus strains such as NZB continually produce virus in vivo or in cultured cells (4). Low virus strains such as BALB/c show a lower level of spontaneous expression of xenotropic virus in vivo, but cultured cells of these strains can be readily induced to produce virus (5). A third category consists of strains such as NIH Swiss from which virus has only rarely been obtained in vivo, and which are not inducible for virus in culture (6) (J. W. Hartley and W. P. Rowe. Unpublished data.).

Genetic crosses between strains which differ in their pattern of virus expression have shown classic mendelian segregation of the determinants of virus induction. The most complex genetic control of virus expression is seen in NZB mice, the prototype for high virus strains. Two independently segregating loci have been identified for production of xenotropic virus in this strain (7). These loci show distinct patterns of high or low virus expression, and the viruses induced are different by fingerprint analysis of the viral gp70 (8).

A single locus for inducibility has been identified in two low virus strains, C57BL/10 and BALB/c (5, 9); the tryptic digest patterns of the viral gp70 from these mice resemble that of one of the NZB viral isolates (8). Our previous genetic studies have shown that the single xenotropic virus-inducing loci carried in BALB/cN and C57BL/10 mice are both linked to the *Pep-3* (formerly *Dip-1*) locus on chromosome 1 (9). However, the data suggested that these loci might be nonallelic and separated by at

[1] *Abbreviations used in this paper:* AK-1, adenylate kinase-1; cM, centimorgans; FFU, focus-forming units; GLO-1, glyoxylase; GPI-1, glucose phosphate isomerase; GR-1, glutathione reductase; HAT, hypoxanthine, aminopterin, thymidine; HPRT, hypoxanthine phosphoribosyl transferase; ID-1, isocitrate dehydrogenase-1; IdU, 5-iododeoxyuridine; LPS, lipopolysaccharide; MOD-1, malic enzyme; MuLV, mouse leukemia virus(es); NP-1, purine nucleoside phosphorylase; PEP-1, peptidase 1; PEP-2, peptidase 2, PEP-3, peptidase 3; PGM-1, phosphoglucomutase 1; PGM-2, phosphoglucomutase 2; SOD-1, cytoplasmic superoxide dismutase; TPI, triose phosphate isomerase.

least 12 recombinational units. We therefore expanded these studies in an effort to define specific map positions for the genes in BALB/c and C57BL/10 and to examine the linkage of induction loci in other inbred strains to chromosome 1 markers. Our data demonstrate that five mouse strains carry a single genetic locus for xenotropic virus inducibility on chromosome 1. The position of this locus, designated *Bxv-1*, is *Id-1-Pep-3-[Bxv-1-Lp]*. Expression of virus from *Bxv-1* is induced either by treatment of fibroblasts with 5-iododeoxyuridine or of spleen cell suspensions with B cell mitogens. Finally, we report on studies using somatic cell hybrids to determine if there are any additional chromosomal requirements for induction of virus.

Materials and Methods

Mice. The parental strains used in genetic crosses and the relevant genetic markers are given in Table I. Hybrid mice were bred in our laboratory.

Virus Induction and Assay. Tissue cultures were prepared from tail biopsy tissue from 3- to 5-wk-old animals (10); cultures were maintained in McCoy's medium with 10% fetal calf serum and antibiotics. When the cultures were in subconfluent growth, 20 μg/ml of 5-iododeoxyuridine (IdU) was added for 48 h. The cultures were then washed and overlaid with cells of the mink lung line CCL64. The mixed cell cultures were fluid changed twice weekly with Dulbecco's medium containing 10% fetal calf serum. After 2 wk, the cells and culture fluid were harvested from each plate and frozen. The samples were subsequently thawed, clarified, and tested for the presence of xenotropic virus by the focus induction test in the mink S+L− cell line of Peebles (11). Virus titers of 75–800 focus-forming units (FFU)/0.2–0.4 ml were generally obtained for the virus-inducible strains and their F1 hybrids. This protocol gave consistently negative results with the four virus-negative strains listed in Table I.

Cell suspensions were prepared from spleens of individual animals 1–8 mo of age. Cells were washed twice and suspended in RPMI-1640 medium (Grand Island Biological Co., Grand Island, N. Y.) with 10% fetal calf serum. Cultures were prepared with 1–2 × 10^6 cells/ml in RPMI-1640 medium with 10% serum and containing 20 μg/ml of IdU and 100 μg/ml of bacterial lipopolysaccharide (LPS), LPS W from *Escherichia coli* 0128:B12 (Difco Laboratories, Detroit, Mich.). IdU alone was found to be a less efficient inducer of xenotropic virus (0–100

TABLE I

Mouse Strains Used in Genetic Crosses

	Chromosome 1 markers			Virus inducibility	
	Pep-3	Id-1	Other	Tail	Spleen
AKR/J	b	b		+	+
BALB/cN	a	a		+	+
C57L/J	a	b		+	+
C57BL/10J	a	a		+	+
B10.BR/SgLi	a	a		+	+
C57BR/J	a	b		+	+
SEA/G/nJ	a	a		−	−
NFS/N	b	a		−	−
A/J	b	a		−	−
SWR/J	b	a		−	−
Lp/+	a	ND	*Lp*	+	+

Pep-3 and *Id-1* are loci for the isozymes of peptidase-3 and isocitrate dehydrogenase-1.

The *Lp* (loop-tail) gene is expressed in heterozygotes as a curly tail, imperforate vagina in females, and/or tossing of the head. Penetrance is not complete. The gene is an embryonic lethal in homozygotes.

ND, not done.

FFU/0.2 ml) than LPS (50–800 FFU/0.2 ml). However, addition of IdU during LPS mitogenesis increased viral titers fivefold or more.

After 48 h, the induced spleen cells were washed, and 5–10 × 10^6 cells were plated on mink lung cells in medium containing polybrene (16 μg/ml; Abbott Laboratories, North Chicago, Ill.). The polybrene was removed 24 h later, and cultures were maintained for 2 wk with frequent fluid changes. Cultures were then harvested and assayed for xenotropic virus as described above.

Hybrid Cells. Peritoneal macrophages or spleen cells of BALB/cN mice were fused with cells of the Chinese hamster line, E36, using β-propiolactone-inactivated Sendai virus (12). Hybrid clones were isolated in Dulbecco's medium containing 10% fetal calf serum with hypoxanthine, aminopterin, thymidine (HAT) selection (13). 35 independent primary hybrid clones were isolated in two separate fusion experiments and maintained in nonselective medium. 67 secondary subclones were isolated from 9 primary clones by plating single hybrid cells in the wells of microtiter dishes, in some cases following backselection in medium containing 8-azaguanine. Hybrid clones were expanded immediately after isolation for virus induction, isozyme assays, and karyotypic analysis.

Karyotypic Analysis. 15–25 metaphase spreads of selected primary and secondary hybrid clones were analyzed by staining with the fluorochrome Hoechst 33258 (Hoechst-Rousell Pharmaceuticals Inc., Somerville, N. J.) (14). The number of mouse chromosomes in each metaphase spread was determined by the bright centromeric fluorescence, and individual chromosomes were identified by their characteristic fluorescent banding patterns after Nesbitt and Francke (15).

Isozyme Assays. Extracts prepared from somatic cell hybrids were assayed in starch gels for the expression of the following 13 isozyme markers mapped on 13 mouse chromosomes: phosphoglucomutases 1 and 2 (PGM-1 and PGM-2, EC 2.7.5.1); peptidases 3, 1, and 2 (PEP-3, PEP-1, PEP-2, formerly DIP-1, DIP-2 and TRIP-1, EC 3.4.—); purine nucleoside phosphorylase (NP-1, EC 2.4.2.1); glucose phosphate isomerase (GPI-1, EC 4.3.1.9); malic enzyme (MOD-1, EC 1.1.1.40); glutathione reductase (GR-1, EC 1.6.4.2); cytoplasmic superoxide dismutase (SOD-1, EC 1.15.1.1); adenylate kinase-1 (AK-1, EC 2.7.4.3); triose phosphate isomerase (TPI, EC 5.31.1.); glyoxylase (GLO-1, EC 4.4.1.5).

Assay methods for the first eight of these enzymes have been described by Nichols and Ruddle (16). Procedures for the remaining assays were obtained as follows: GR (17), TPI (18), GLO-1 (19), AK-1 (20). Hamster and mouse SOD-1 activities were separated in starch gels using a Tris-citrate, pH 7.0 buffer system (P. A. Lalley. Personal communication.). Hybrid cell growth in selective media containing HAT or 8-azaguanine was used as an indirect indication of mouse hypoxanthine phosphoribosyl transferase activity, (HPRT, EC 2.4.2.8).

In the breeding studies, two isozyme markers, PEP-3 and isocitrate dehydrogenase-1 (ID-1, EC 1.1.1.42) (16) were used to monitor recombination on chromosome 1, using kidney extracts prepared from animals of the first backcross generation.

Results

Single Gene Control of Virus Inducibility. Five induction positive mouse strains were crossed and backcrossed with induction negative strains, and the progeny examined for xenotropic virus inducibility in tail and/or spleen cell cultures. In all cases, virus inducibility segregated with single gene ratios (Table II).

Backcross animals showed the same virus induction phenotype whether tested by IdU treatment of cultured tail cells or mitogenesis of spleen cells. 56 backcross animals arbitrarily selected from crosses involving 3 induction positive strains (C57L, AKR, and BALB) were tested by both procedures. All were concordantly inducible or noninducible for virus (32 positive, 24 negative) in both tail and spleen cell inductions.

These data indicate that in these strains a single locus governs induction of a xenotropic virus detectable by focus formation on mink S+L− cells and that expres-

TABLE II

Xenotropic Virus Production in Backcross Animals Tested as Tail Cell Cultures Induced by IdU or Spleen Cell Suspensions Induced by LPS and IdU

	Number positive/number tested (percent positive)	
	Tail	Spleen
NFS × (SWR × BALB)	36/66 (54)	29/54 (54)
NFS × (C57L × NFS)		27/63 (43)
NFS × (SEA × AKR)	24/42 (57)	30/54 (56)
NFS × (NFS × C57BR)	5/12 (42)	17/29 (59)
$\left\{\begin{matrix}A\\or\\NFS\end{matrix}\right\} \times \left[\left\{\begin{matrix}A\\or\\NFS\end{matrix}\right\} \times \left\{\begin{matrix}C57BL/10\\or\\B10.BR\end{matrix}\right\}\right]$	101/219 (46)	

TABLE III

Recombination between Virus Inducibility and Pep-3 and Id-1 in Three Crosses: NFS × (C57L × NFS), NFS × (NFS × C57BR), NFS × (SEA × AKR)

	Inheritance of the allele of the induction-positive strain			Number of animals in backcross from:		
	Virus induction	Pep-3	Id-1	C57L	C57BR	AKR
Nonrecombinant	+	+	+	18*	15	18
	−	−	−	18*	8	21
Single recombinant	+	+	−	5	7	8
	−	−	+	9	5	3
	+	−	−	4	2	8
	−	+	+	6	4	2
Double recombinant	+	−	+	0	2	0
	−	+	−	3	1	1
	Percentage recombinant: + SE.					
	Inducibility-*Pep-3*			13/63 = 21 ± 5	9/41 = 22 ± 6	11/61 = 18 ± 5
	Inducibility-*Id-1*			24/53 = 45 ± 7	15/41 = 36 ± 8	21/61 = 34 ± 6
	Pep-3-Id-1			17/53 = 32 ± 6	12/41 = 29 ± 7	11/61 = 18 ± 5

* Five mice in each of these two categories were not typed for *Id-1*.

sion of this locus can be effected by two different methods of induction in different cell types.

Linkage of Virus Inducibility to Chromosome 1 Markers. Our previous studies showed that the gene for xenotropic virus inducibility in both BALB/cN and C57BL/10 mice is linked to the *Pep-3* locus on chromosome 1; we designated the C57BL/10 locus *Bxv-1* (9). Other induction positive strains have now been examined for the presence of such loci on chromosome 1. Genetic crosses were also designed to establish a specific position for *Bxv-1* on chromosome 1. The order of the three loci used in these crosses and their estimated distances is: *Id-1*-27-*Pep-3*-24-*Lp*.

AKR/J, C57L/J, C57BR/J. These three induction-positive strains were bred with virus-negative strains having allelic differences at the *Pep-3* and *Id-1* loci. In all three cases, inducibility in backcross mice showed linkage to *Pep-3* but not to *Id-1* (Table III). These data show that the xenotropic virus inducibility locus of all three strains is on chromosome 1, 20 cM (centimorgans) distal to the *Pep-3* locus.

LP/+. Tail cultures of Lp/+ mice and (Lp/+ × NFS)F1 mice consistently

produced xenotropic virus following induction with IdU. Virus inducibility in the first six litters of NFS × (NFS × Lp/+) mice showed single gene segregation (23 virus positive, 23 virus negative) and linkage to *Lp* (r = 7/46 = 15 ± 5%). However, these data did not provide an accurate estimate of recombination between *Lp* and the virus locus because of the incomplete penetrance of the *Lp* gene, particularly, in our experience, in crosses with NFS mice. In accord with this, six of the seven presumptive recombinants had normal tails and were induction positive. Therefore, in subsequent litters we assayed only loop-tailed segregants for virus induction. Of a total of 59 loop-tailed progeny tested, 55 were inducible for virus. Therefore, the xenotropic virus-inducing locus carried by the Lp/+ stock is on chromosome 1 closely linked to the *Lp* gene (r = 4/59 = 7 ± 3%) although the order of the viral locus and *Lp* on the chromosome could not be determined. The map position of this locus is thus consistent with that of the loci carried in the strains described above.

BALB/cN. Our previous studies with NFS × (SWR × BALB) mice showed linkage of virus inducibility and *Pep-3* (9). A total of 101 animals in this cross have now been tested for recombination between these loci, and 14 recombinants were observed (r = 14 ± 4%).

Because *Id-1* does not segregate in this cross, *Lp* was used to localize the inducibility gene on chromsome 1. BALB/cN mice were crossed with the virus-negative, loop-tailed segregants obtained in the matings between Lp/+ and NFS, and loop-tailed progeny were mated to NFS mice. Three recombinants between virus inducibility and *Lp* were identified among 57 progeny (r = 5 ± 3). However, closer linkage is suggested by the fact that all three recombinants were virus-positive and had normal tails.

Allelism of Inducibility Loci in BALB/c and C57BL/10. Although all strains tested here carry xenotropic inducibility loci on chromosome 1, and four of the loci have been mapped to the distal region of the chromosome, the different linkage estimates obtained in backcross studies suggested that these genes may not map at an identical site. The viral locus of BALB/cN mice showed closest linkage to *Pep-3* (r = 14), whereas that of C57 BL/10 mapped at a position 23 cM from *Pep-3*, with gene order not determined (11). These linkage estimates indicated that the virus-inducing loci in BALB and C57BL/10 mice may be separated by 9 cM (or 37 cM if the C57BL/10 locus was the opposite side of the *Pep-3* locus). Because nonallelic sites for endogenous ecotropic virus-inducing loci have been identified in different mouse strains, we did an additional cross to determine if these xenotropic virus-inducing loci on chromosome 1 might also map at nonallelic sites.

(BALB × C57BL/10)F_1 mice were crossed to the induction-negative strain NFS. If the virus-inducing loci are at the same site on chromosome 1, all progeny would be virus positive. If however, the loci are nonallelic, recombination would produce virus-negative animals in 4.5% of the progeny if the loci were separated by 9 cM, or in 18.5% if separated by 37 cM. The results of testing 99 progeny of this cross showed that no recombinants were identified; all animals showed the virus-inducible phenotype. Thus, the two virus-inducing loci are clearly on the same side of the *Pep-3* locus, and in the absence of any evidence for recombination between these two inducibility loci, we infer that they are allelic. We can further infer that the loci in all five strains studied are at the same site. We shall therefore use *Bxv-1* to designate this site in all these strains.

Xenotropic Virus Induction in Somatic Cell Hybrids. The *Bxv-1* locus defined in genetic crosses may represent either an integrated viral genome activated by induction, or it may be a regulatory locus which in turn activates endogenous viral genes elsewhere in the mouse genome. In an attempt to differentiate between these possibilities, we analyzed Chinese hamster × mouse somatic cell hybrids which retain different chromosome complements of the BALB/cN mouse.

The 35 primary and 67 secondary somatic cell hybrids were induced for xenotropic virus using IdU as described for the tail biopsy cultures. 27 primary clones and 34 secondary clones produced virus after induction. A comparison of virus induction and the activity of 13 isozymes and HPRT expression showed that only *Pep-3* (chromosome 1) was concordant with the viral phenotype (Table IV). 33 of the 35 primary clones concordantly showed presence or absence of virus and *Pep-3* activity, as did 65 of the 67 secondary clones. The two primary clones that produced xenotropic virus in the absence of *Pep-3* expression may have been false discrepancies because virus titers

TABLE IV

Correlation of Xenotropic Virus Inducibility with 13 Mouse Isozyme Phenotypes in Somatic Cell Hybrids

Isozyme	Chromosome	Number of clones* (Virus induction/isozyme)				Percent discordant
		+/+	−/−	+/−	−/+	
PEP-3	1	25	8	2	0	3
		34	31	0	2	3
AK-1	2	5	2	4	0	36
		10	5	10	2	44
PGM-2	4	16	6	10	2	35
		19	16	14	2	51
PGM-1	5	13	7	11	1	38
		2	12	27	1	67
TPI	6	23	3	1	4	16
		20	6	11	11	45
GPI-1	7	23	3	3	6	26
		30	7	2	11	26
GR-1	8	13	5	12	3	45
		15	16	17	2	50
MOD-1	9	17	6	7	3	33
		9	4	4	5	22
PEP-2	10	18	2	3	5	28
		7	6	18	1	59
NP-1	14	13	5	11	2	31
		11	9	6	4	33
SOD-1	16	10	8	5	6	29
		9	6	12	2	29
GLO-1	17	9	4	0	3	16
		17	3	6	6	38
PEP-1	18	18	6	6	3	33
		9	13	17	1	45
HPRT	X	22	0	0	10	31
		4	5	12	7	28

* For each enzyme, data are given for primary clones on the first line, and secondary clones on the second.

were lower than obtained with other induction positive clones (70 vs. 250–800 FFU/0.2 ml). This suggests that the proportion of cells with chromosome 1 in these hybrids might have been too low for detectable *Pep-3* activity. Similarly, the two discordant secondary clones showed only faint bands of mouse *Pep-3* activity in the absence of virus induction.

Karyotype analysis was done on 12 hybrids, 6 of which lacked chromosome 1 and were not virus inducible, and 6 of which retained chromosome 1 and were induction sensitive (Table V). No other chromosomes were found to cosegregate with virus inducibility.

The concordance between the virus phenotype and *Pep-3* expression in 98 of 102 hybrids and the discordance between this phenotype and the other 19 mouse chromosomes confirm and extend the mendelian studies by suggesting that mouse chromosome 1 alone is sufficient for virus induction. Whereas these data do not definitively characterize the locus on chromosome 1 as an integrated virus genome, they argue against the possibility that the genome activated by *Bxv-1* is on another chromosome of the mouse.

Discussion

Ecotropic virus-inducing loci are found at many different sites in the mouse genome. Using classical mendelian techniques it has been shown that various mouse strains may have up to four unlinked virus-inducing loci (21, 22), and that between strains

TABLE V

Correlation between Xenotropic Virus Inducibility and Mouse Chromosomes in Hybrid Clones as Determined by Karyotypic Analysis of 12 Primary Clones

Chromosome	Number of clones (Chromosome/virus induction)				Percent discordant
	Concordant		Discordant		
	+/+	−/−	+/−	−/+	
1	6	6	0	0	0
2	4	4	2	2	33
3	1	4	2	5	58
4	3	4	2	3	42
5	2	5	1	4	42
6	4	2	5	1	50
7	5	2	4	1	42
8	3	6	0	3	25
9	3	4	3	2	42
10	4	6	0	2	17
11	0	6	0	6	50
12	3	1	5	3	67
13	4	3	3	2	42
14	4	3	3	2	42
15	5	2	4	1	42
16	5	4	2	1	25
17	6	3	3	0	25
18	4	5	1	2	25
19	4	1	5	2	58
X	4	3	3	2	42

the loci do not appear to be at allelic sites (23, 24) (C. A. Kozak and W. P. Rowe. Unpublished data.). Only in closely related strains have allelic loci been found (25).

The data presented in this paper show that the endogenous xenotropic virus-inducing loci have a more limited chromosomal distribution. We have identified an inducibility locus for xenotropic virus, *Bxv-1*, which is present at the same site, on chromosome 1, in five mouse strains, (C57L, C57BL/10, BALB/c, AKR, and C57BR). (The Lp/+ stock also carries *Bxv-1*, but it was probably acquired through the C57BL/6 matings in its ancestry [P. Lane, The Jackson Laboratory, Bar Harbor, Maine. Personal communication.]). This map position has also been described in C57BL by H. Meier and H. G. Bedigian (Personal communication.). The presence of this locus in all strains examined suggests that *Bxv-1* was widely distributed in mouse colonies before the establishment of inbred strains. The six mouse strains used in this study represent three clearly independent breeding lines. AKR, BALB/c, and the C57 related mice (C57L, C57BR, and C57BL) were derived from animals originally provided from separate mouse colonies. These three distinct lines of descent show great genotypic diversity at polymorphic loci (26) and also carry different ecotropic virus-inducing loci (24, 27) (C. A. Kozak and W. P. Rowe. Unpublished data.). Therefore, the ubiquity of *Bxv-1* suggests that this locus was present in the mouse germ line before the separation of these three breeding lines.

The identification of only one inducibility locus which is shared by diverse strains is not surprising because the restricted host range of these viruses precludes the generation of new loci by reinfection and reinsertion. However, *Bxv-1* does not represent the only xenotropic virus-inducing locus in the mouse. In the NZB mouse, two distinct xenotropic MuLV have been identified on the basis of their biological properties and gp70 fingerprints (8); mendelian studies show that there are two unlinked loci for xenotropic virus expression (7) (J. W. Hartley, H. C. Morse, and T. M. Chused. Unpublished data.). Our studies with congenic mice carrying one of the NZB loci for virus inducibility show that expression of this locus is not governed by *Bxv-1* (C. A. Kozak and W. P. Rowe. Unpublished data.). The second NZB locus has not yet been examined for chromosome 1 linkage.

Various lines of evidence also suggest that xenotropic viral loci other than *Bxv-1* exist in the mouse strains examined in this study, but were not detected using the induction protocols and assay procedures employed. Nucleic acid hybridization studies have shown that multiple copies of xenotropic viral genes are present in all mice, including strains defined here as IdU induction negative (1). Infectious xenotropic virus has, on several occasions, been isolated from tissues of the induction-negative NFS (and NIH Swiss) mice (6) (J. W. Hartley. Personal communication.) and from SEA/GnJ mice (C. A. Kozak and W. P. Rowe. Unpublished data.). Expression of the NFS virus is clearly not subject to activation by the same induction protocols which were used to define *Bxv-1*. Furthermore, mice carry a number of genetic loci which produce gp70 molecules (2) or cell surface antigens related to xenotropic virus envelope components (3). These loci, which may represent noninducible or partial xenotropic viral genomes, may eventually be detected and mapped using techniques other than induction of infectious virus.

The identification of *Bxv-1* as chromosomally integrated viral DNA, such as by molecular hybridization techniques, has not yet been accomplished. However, several factors suggest that this locus does represent viral sequences rather than a regulatory

locus. First, virus expression segregates with *Bxv-1* whether induction is achieved by IdU stimulation of fibroblast cultures or by mitogenesis of spleen cell suspensions. A regulatory locus might be expected to show differentiation specific sensitivity to these various inducers. Second, the analysis of somatic cell hybrids suggests that chromosome 1 carries the genetic information for xenotropic virus. Previous studies showed that IdU induction of ecotropic virus from these BALB/cN × Chinese hamster hybrid lines is controlled by a gene on chromosome 5 (24). However, only chromosome 1 cosegregates with xenotropic virus inducibility, and the uniform response of karyotypically different inducible hybrids to IdU suggests that no additional chromosomes carry loci which affect virus expression.

Summary

A single mendelian gene was identified for induction of the endogenous xenotropic murine leukemia virus in five mouse strains (C57BL/10, C57L, C57BR, AKR, and BALB/c). This locus, designated *Bxv-1*, mapped to the same site on chromosome 1 in all strains: *Id-1-Pep-3-*[*Bxv-1-Lp*]. Thus, inducibility loci for xenotropic virus are more limited in number and chromosomal distribution than ecotropic inducibility loci. Virus expression in mice with *Bxv-1* was induced by treatment of fibroblasts with 5-iododeoxyuridine or by exposure of spleen cells to a B cell mitogen, bacterial lipopolysaccharide. An analysis of the hamster × mouse somatic cell hybrids indicated that chromosome 1, alone, was sufficient for virus induction.

We thank J. Toliver and J. Williams for technical assistance and S. Grove for help in preparing the manuscript.

Received for publication 10 March 1980.

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