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Genetic Transmission of Endogenous N- and B-Tropic Murine Leukemia Viruses in Low-Leukemic Strain C57BL/6

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Spontaneous expression of endogenous N- and B-tropic murine leukemia viruses was studied in mice in relation to the *Fv-1* genotype. Mice used were from C57BL/6 (*Fv-1*^{bb}), DDD (*Fv-1*^{nn}), DDD-*Fv*^{r} (*Fv-1*^{nn}), (DDD or DDD-*Fv*^{r} × C57BL/6)F1, and 16 partially inbred lines with either the *Fv-1*^{nn} or *Fv-1*^{bb} genotype, which had been established from hybrids between C57BL/6 and DDD-*Fv*^{r}. When tested at middle age, virus-positive mice were found in C57BL/6, F1 hybrids, and 9 out of 16 partially inbred lines. N-tropic viruses were isolated from *Fv-1*^{nn}, *Fv-1*^{nb}, and *Fv-1*^{bb} mice, whereas B-tropic viruses, except for one isolate, were from *Fv-1*^{bb} mice only. C57BL/6 mice were positive for both N- and B-tropic viruses, whereas DDD-*Fv*^{r} mice were negative. With respect to the *Fv-1* genotype and the presence of endogenous murine leukemia viruses, the partially inbred lines were grouped into five types: (i) *Fv-1*^{bb}, both N- and B-tropic virus positive, like C57BL/6; (ii) *Fv-1*^{nn}, virus negative, like DDD-*Fv*^{r}; (iii) *Fv-1*^{bb}, virus negative; (iv) *Fv-1*^{nn}, only N-tropic virus positive; and (v) less convincingly, *Fv-1*^{bb}, only B-tropic virus positive. These findings indicate that the transmission of N- and B-tropic viruses in C57BL/6 is genetically controlled and that the expression of B-tropic virus, but not of N-tropic virus, is closely associated with the *Fv-1* genotype.

Endogenous C-type RNA viruses are present in cells of various species, and emerging evidence indicates host gene control of their expression. High-leukemic mouse strains, such as AKR and C58, carry a few genes that induce murine leukemia virus (MuLV) early in life or in embryo cells treated with halogenated pyrimidines in culture (10–13, 16). MuLV also occurs naturally in mice of low-leukemic strains, but later in life, less regularly, and less in quantity than in the high-leukemic strains (2, 7, 10, 12). In these strains, genetic studies have been carried out only on embryo cells treated with the drugs in culture. The induced viruses are, however, less infectious to mouse cells than those occurring naturally in old mice of the same strain (1, 15).

N- and B-tropic viruses are major forms of naturally occurring MuLV. N-tropic virus grows better in cells with *Fv-1*^{nn} than in those with the *Fv-1*^{bb} genotype, whereas B-tropic virus shows the reciprocal pattern (3, 8, 9). As far as inbred strains were studied, N-tropic virus has been isolated from both *Fv-1*^{nn} and *Fv-1*^{bb} strains, whereas B-tropic virus has been isolated from *Fv-1*^{bb} strains only (10, 12). This distribution pattern has not yet been explained in genetical terms.

In the present study, expression of endogenous N- and B-tropic viruses was studied in mice derived from the cross between virus-positive strain C57BL/6 (*Fv-1*^{bb}) and virus-negative strain DDD-*Fv*^{r} (*Fv-1*^{nn}) or DDD (*Fv-1*^{nn}). The results show that even in a low-leukemic strain the spontaneous expression of endogenous MuLV is controlled by host genes.

MATERIALS AND METHODS

Mice. AKR, BALB/c, C57BL/6, C57BL/6-*Fv*^{a} (4), DDD, DDD-*Fv*^{r} (5), (DDD × AKR)F1, (DDD-*Fv*^{r} × AKR)F1, (DDD × C57BL/6)F1, (DDD-*Fv*^{r} × C57BL/6)F1, and partially inbred lines were used. Details of the establishment of the partially inbred lines were reported previously (6). In brief, a female DDD-*Fv*^{r} was crossed with a male C57BL/6. This one pair gave rise to all of 16 lines. A female F1 mouse was backcrossed with a male DDD-*Fv*^{r}, and a male F1 was backcrossed with a female C57BL/6. At the first backcross generation, *Fv-1*^{nb} heterozygotes were selected and intercrossed. From the progeny thus produced, *Fv-1*^{nn} or *Fv-1*^{bb} homozygotes were selected and intercrossed. The progeny were maintained thereafter by brother-sister mating. Since the mice used in the present study were from generations that had passed three to seven brother-sister matings, they might be still heterozygous at gene loci other than *Fv-1*.

Most mice were from our laboratory, but some were provided by the Animal Production Section of our Institute. Older mice were mostly breeders. At autopsy, 10 mice were found to have enlarged mammary or lymphoid organs, but the others were macroscopically free from tumors.

Virus assay. The spleens of the mice to be tested were dissected individually with forceps in 5 ml of cold phosphate-buffered saline. The suspensions were pipetted, filtered through stainless-steel mesh, and used immediately for virus assay by the UV-XC procedure (14). The culture medium was Eagle minimal essential medium (Nissui Co. Ltd., Chiba, Japan) supplemented with heat-inactivated calf serum (10%). Occasionally, tryptose phosphate broth was added to 10%. Cultures were maintained at 37 C in a CO_2 incubator and fed at least every 2 days.

Embryo cells obtained from the above-mentioned mice (other than AKR) and confirmed to produce no spontaneous plaques on culture were used. Cells of secondary culture were seeded at 16×10^4 cells in 52-mm plastic plates, and 1 day later were inoculated with 0.2 ml of the spleen cell suspension. For each specimen, duplicate plates of *Fv-1*^{nn} and *Fv-1*^{bb} cells were used. Five or 6 days after inoculation, one *Fv-1*^{nn} and one *Fv-1*^{bb} plate for each specimen were irradiated with UV and overlaid with 10^6 XC cells. The remaining plates were each divided into two sets, subcultured for four to five days, and then subjected to the UV-XC procedure. Plaques were counted 2 or 3 days after the addition of XC cells. N/B ratios were calculated by dividing the number of plaques produced on *Fv-1*^{nn} cells by that on *Fv-1*^{bb} cells.

RESULTS

Isolation of infectious virus. By the UV-XC procedure, mice were tested for infectious virus in the spleen (Table 1). Mice whose spleen cells produced plaques on first culture or subculture of *Fv-1*^{nn} and/or *Fv-1*^{bb} cells were scored as virus positive. Those that produced no plaques on cells of both types after subculture were considered negative for virus.

As reported previously (7, 13), AKR mice consistently showed a high level of infection irrespective of age, and BALB/c mice were virus

TABLE 1. *MuLV in the spleens of mice of inbred strains, their F1 hybrids, and the partially inbred lines*[a]

Mice	*Fv-1* genotype	Group	No. positive/no. tested				
			1-2[b]	3-4	5-7	8-10	11-12
AKR	*nn*		6/6	5/5	4/4		
BALB/c	*bb*					7/11	
C57BL/6	*bb*		0/10	0/3	7/18	0/5	6/13
DDD	*nn*				0/11		
DDD-*Fv*^{r}	*nn*				0/20		0/13
(DDD × AKR)F1	*nn*		8/8				
(DDD-*Fv*^{r} × AKR)F1	*nn*		8/8				
(DDD × C57BL/6)F1	*nb*				0/2	5/5	
(C57BL/6 × DDD)F1	*nb*		1/3	1/2	3/6	2/2	
(DDD-*Fv*^{r} × C57BL/6)F1	*nb*			3/3	3/8		
(C57BL/6 × DDD-*Fv*^{r})F1	*nb*			0/5	2/3	2/5	
2B12S-1	*nn*	B			6/6		
2B12S-2	*nn*	B			11/12		
5B8S	*nn*	B	2/9		13/16	4/4	
2B13R-1	*bb*	B			9/10		
2B13R-2	*bb*	B	1/7		9/12		
5B9R-1	*bb*	B			2/7		
5B9R-2	*bb*	B		1/1	2/13		
3D8S-1	*nn*	D			7/8		
3D8S-2	*nn*	D			0/8		
5D10S	*nn*	D			0/12		
3D14R-1	*bb*	D			0/11		
3D14R-2	*bb*	D			2/4	1/3	
5D12AR-1	*bb*	D			0/7		
5D12AR-2	*bb*	D			0/11		
5D12BR-1	*bb*	D			0/11		
5D12BR-2	*bb*	D			0/9	0/2	

[a] In designations of F1, mother strains are written first. Mouse lines from 2B12S-1 through 5D12BR-2 are derived from hybrids between C57BL/6 and DDD-*Fv*^{r}. B group is from C57BL/6 × (DDD-*Fv*^{r} × C57BL/6)F1, whereas D group is from (DDD-*Fv*^{r} × C57BL/6)F1 × DDD-*Fv*^{r}.

[b] Age (months).

positive. In strain C57BL/6, the virus was detected in mice older than 5 to 7 months. The frequency of positive mice was less than 50%, and it had not increased by the time the mice were 1 year old. Except for one mouse with 4,250 PFU/spleen, C57BL/6 mice contained less than 250 PFU/spleen, and plaques sufficient in number to calculate N/B ratios were usually detected on subculture. In contrast, specimens obtained from DDD and DDD-Fv^r mice never produced plaques on $Fv\text{-}1^{nn}$ and $Fv\text{-}1^{bb}$ cells. Thirteen DDD-Fv^r at the age of 1 year were also negative. F1 hybrids between virus-positive (AKR, C57BL/6) and virus-negative strains (DDD, DDD-Fv^r) gave results similar to those of the virus-positive parental strains. The direction of cross had no effect on the frequency of positive mice.

Sixteen partially inbred lines consisted of two groups. Lines of B group were derived from the C57BL/6 × F1 backcross, whereas D group lines were from the F1 × DDD-Fv^r backcross. Positive mice were found in all of seven lines of B group, whereas only two out of nine lines of D group provided positive mice (Table 1). Among the lines tested, virus was most easily detectable in 5B8S. Most specimens produced many plaques on first culture. Out of 13 positive mice, 7 had more than 2,500 PFU/spleen, including one mouse of 1 month old.

Tropism of isolated viruses. N-tropic virus produces XC plaques more efficiently on $Fv\text{-}1^{nn}$ than on $Fv\text{-}1^{bb}$ cells (N/B ratio should be more than 1), whereas B-tropic virus shows the reciprocal pattern (N/B ratio less than 1) (3). Therefore, each specimen was assayed simultaneously on both $Fv\text{-}1^{nn}$ and $Fv\text{-}1^{bb}$ embryo cells, and N/B ratios were calculated. Figure 1 shows the N/B ratios of the specimens that were positive in Table 1. The ratios were from first culture if specimens showed more than five plaques per plate on either or both types of cells; otherwise, the ratios were from the subculture.

Specimens of AKR mice produced innumerable numbers of plaques on $Fv\text{-}1^{nn}$ and less on $Fv\text{-}1^{bb}$ cells. Therefore, accurate N/B ratios could not be obtained, but the ratios were consistently more than 1. This is compatible with the known N-tropism of AKR virus (10). In contrast, N/B ratios of BALB/c and C57BL/6 were variable. This pattern of C57BL/6 did not differ essentially from between age groups of 5 to 7 and 11 to 12 months, indicating that both N- and B-tropic viruses are already present when this strain is 5 to 7 months old. Unexpectedly, the N/B ratio pattern obtained from

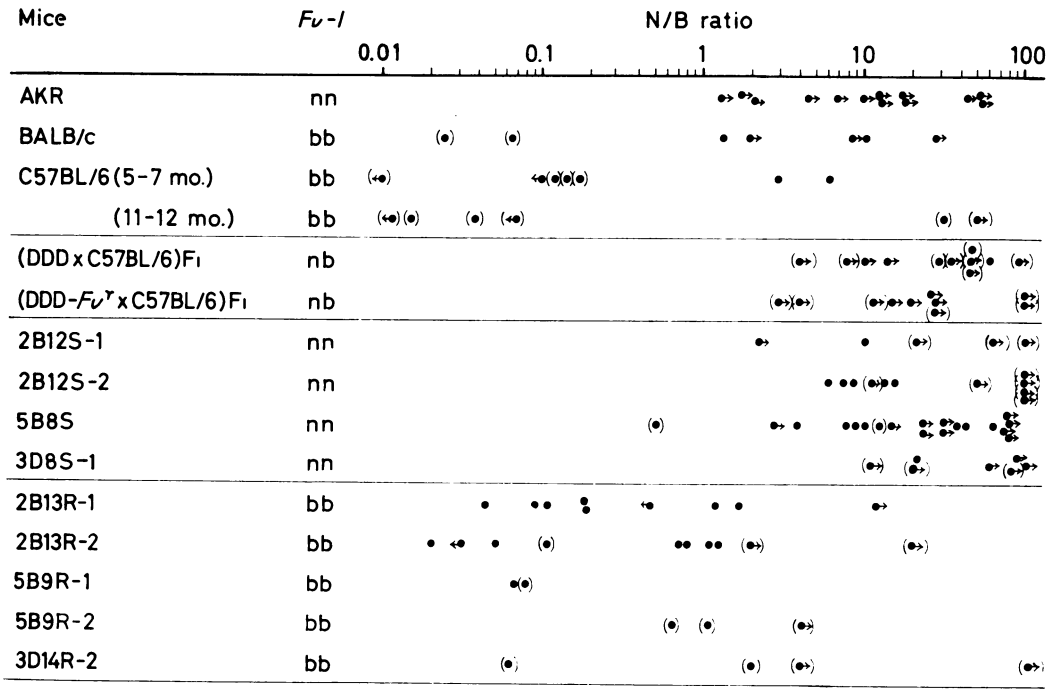

FIG. 1. *Tropism of isolated viruses. N/B ratios were obtained by dividing numbers of plaques on $Fv\text{-}1^{nn}$ cells by those on $Fv\text{-}1^{bb}$ cells on first culture or subculture (in parentheses). Innumerable plaques and absence of plaques are considered to be 300 and 0.5, respectively, and the ratios thus obtained are shown with arrows.*

(DDD × C57BL/6)F1 and (DDD-Fv^r × C57BL/6)F1 hybrids differed from that of C57BL/6, rather resembling that of AKR. The ratios could be determined for 21 specimens and were exclusively more than 3. If the partially inbred lines were grouped according to *Fv-1* genotype, a distinct tendency was observed in the N/B ratio. Except for one, all the isolates from four *Fv-1*^{nn} lines, 2B12S-1, 2B12S-2, 5B8S, and 3D8S-1, showed N/B ratios of more than 2, whereas N/B ratios from five *Fv-1*^{bb} lines, 2B13R-1, 2B13R-2, 5B9R-1, 5B9R-2, and 3D14R-2, varied from less than 0.1 to more than 10.

Some specimens from *Fv-1*^{nn} mice showed N/B ratios of 2 to 10. According to Rowe and Hartley (12), ratios expected for N-tropic virus are more than 10. However, our method differed from theirs. They examined cell extracts instead of intact cells. Use of intact cells as inoculum might facilitate transfer of N-tropic virus from the original spleen cells to *Fv-1*^{bb} test cells, thus lowering N/B ratios obtained. On the other hand, N/B ratios near 1 were obtained from some specimens of *Fv-1*^{bb} mice. These ratios might be due to either the mixture of N- and B-tropic viruses or, although less likely, to NB-tropic virus, which can grow equally well on *Fv-1*^{nn}, *Fv-1*^{nb}, and *Fv-1*^{bb} cells, but has never been isolated from normal mice (3). To determine the tropism of viruses contained in these specimens, the following experiments were carried out (Table 2).

Two specimens were selected. One (no. 412) was from strain 5B8S (*Fv-1*^{nn}) and the other (no. 176) was from strain 2B13R-1 (*Fv-1*^{bb}). On first culture, no. 412 produced 90 and 24 plaques, respectively, on *Fv-1*^{nn} and *Fv-1*^{bb} cells, the N/B ratio of 3.8 being low for isolates from *Fv-1*^{nn} mice. No. 176 produced 328 plaques on *Fv-1*^{nn} cells and 206 on *Fv-1*^{bb}; the ratio was 1.6. At the end of subculture, the culture fluids were harvested, stored at −80 C, and later assayed on *Fv-1*^{nn}, *Fv-1*^{nb}, and *Fv-1*^{bb} cells. If NB-tropic virus predominates in these specimens, cells of these three types would be expected to develop plaques of comparable numbers. As in routine tests, one plate of each type was developed by the UV-XC procedure after cultivation for 6 days, and the remaining one was divided into two parts and subjected to the UV-XC procedure after subculture for 4 days.

The culture fluids harvested from both *Fv-1*^{nn} and *Fv-1*^{bb} cells that had been inoculated with no. 412 produced plaques only on *Fv-1*^{nn} cells. However, no. 176 gave different results. The culture fluid harvested from *Fv-1*^{nn} cells contained virus that propagated more efficiently in *Fv-1*^{nn} than in *Fv-1*^{nb} and *Fv-1*^{bb} cells, whereas the fluid from *Fv-1*^{bb} cells contained the virus that preferentially propagated in *Fv-1*^{bb} cells. This finding indicated that no. 412 contained N-tropic virus only and no. 176 contained both N- and B-tropic viruses. Similar results were also obtained from one specimen from 5B8S, with an N/B ratio of 7.8, and one from 2B13R-1, with an N/B ratio of 0.44 or less.

TABLE 2. *Determination of tropism of viruses by passage of culture fluids*[a]

Mouse no.	Spleen cells		Culture fluid		
	Fv-1 genotype	First culture (PFU)	*Fv-1* genotype of cells	First culture (PFU)	Subculture (PFU)
412	*nn*	90	*nn*	30	>300
			nb	0	1
			bb	0	0
	bb	24	*nn*	4	43
			nb	0	0
			bb	0	0
176	*nn*	328	*nn*	198	>300
			nb	2	41
			bb	4	43
	bb	206	*nn*	1	6
			nb	0	2
			bb	13	267

[a] Spleen cell suspensions of no. 412 mouse of strain 5B8S (*Fv-1*^{nn}) and of no. 176 of strain 2B13R-1 (*Fv-1*^{bb}) were inoculated into *Fv-1*^{nn} and *Fv-1*^{bb} cell cultures. After the first culture, plaques developed by UV-XC procedure were counted. At the end of subculture, culture fluids were harvested and assayed on *Fv-1*^{nn}, *Fv-1*^{nb}, and *Fv-1*^{bb} cells.

DISCUSSION

Naturally occurring N- and B-tropic MuLV were examined in the partially inbred lines that had been derived from the hybrids between C57BL/6 and DDD-Fv^r. Both N- and B-tropic viruses occur in C57BL/6, but not in DDD-Fv^r (Table 1, Fig. 1). The DDD-Fv^r has been established from the cross of a male DDD with a female C57BL/6 by introducing Fv^r gene from C57BL/6 into the genetic background of DDD (5). Hoshino et al. in our laboratory examined old DDD mice and their spontaneous leukemias for N- and B-tropic viruses, but have found neither (unpublished data). A preliminary study on chemically induced leukemias of DDD-Fv^r indicates that leukemic cells contain neither N- nor B-tropic viruses (Odaka, unpublished data). In this respect, DDD and DDD-Fv^r

resemble NIH Swiss mice (2). The fact that DDD-*Fv*^{r} is free from N- and B-tropic viruses indicates that the chromosomal segment of C57BL/6 carrying the *Fv*^{r} gene has nothing to do with endogenous N- and B-tropic viruses.

A factor that must be considered is whether virus testing in mice 5 to 7 months old is adequate for detecting naturally occurring MuLV. Studies on AKR, BALB/c, and B10.D2 (old) mice indicate that the age when N- and B-tropic viruses attain the detectable level is dependent on the mouse strain (7, 12, 13). In C57BL/6 studied here, the incidence of MuLV and the ratio of B- to N-tropic isolates did not significantly differ between mice 5 to 7 and 11 to 12 months old (Table 1, Fig. 1). Therefore, virus testing of mice 5 to 7 months old seems to be reasonable to characterize the partially inbred lines.

Another factor to be considered is the way of determining the N- or B-tropism. N/B ratios were used for this purpose. However, because of the relative resistance exerted by the *Fv-1* locus, the ratios do not give any information as to whether the isolated virus population is pure or mixed. The tropism of isolated viruses was determined only on four specimens by passage of culture fluids (Table 2). The results showed that the N/B ratio of 3.8 obtained from an *Fv-1*^{nn} mouse was due to N-tropic virus, not mixed with B-tropic virus, whereas the simultaneous presence of N- and B-tropic viruses in an *Fv-1*^{bb} mouse gave the N/B ratio of 1.6. This finding suggested that virus isolates from *Fv-1*^{nn} and *Fv-1*^{nb} mice were, except for one, all N-tropic, and B-tropic virus was confined to *Fv-1*^{bb} mice. The exception was 5B8S, which showed an N/B ratio of 0.52 on subculture. Whether this ratio was due to the presence of B-tropic virus or to other factors was not determined. In the following discussion, the terms N- and B-tropic viruses will be used in a loose sense, as described above, and the exceptional case will be set aside.

The genetic basis of transmission of endogenous MuLV in low-leukemic strains can not be studied by orthodox cross experiments, because even in inbred strains individual mice do not reveal completely their virus-producing potential. However, each strain has its stable pattern in the expression of endogenous MuLV. This fact may be ascribed to the presence of host genes with incomplete penetrance. In the present study, seven of seven lines of B group and two of nine lines of D group were found to be virus positive. This suggests the involvement of a few genes. A gene locus for N-tropic virus (tentatively named *N* locus) is neither linked with the *Fv-1* locus nor probably related with *Akv-1* locus (10), because N-tropic virus ap-

TABLE 3. *Model for the expression of endogenous MuLV in the partially inbred lines*[a]

Genotype	Virus isolated	Partially inbred line	Inbred strain
Fv-1^b, *N*, *B*	N- and B-tropic	2B13R-1 2B13R-2 5B9R-2 3D14R-2	BALB/c C57BL/10
Fv-1^b, *N*, —	N-tropic	None	None
Fv-1^b, —, *B*	B-tropic	5B9R-1	B10.D2 (old)
Fv-1^b, —, —	None	3D14R-1 5D12AR-1 5D12AR-2 5D12BR-1 5D12BR-2	None
Fv-1^n, *N*, *B* or *Fv-1*^{n}, *N*, —	N-tropic	2B12S-1 2B12S-2 5B8S 3D8S-1	C57BR DBA/2
Fv-1^n, —, *B* or *Fv-1*^{n}, —, —	None	3D8S-2 5D10S	C57L (NIH Swiss)

[a] This model is made on the following assumptions. N and B are genes for N- and B-tropic viruses, respectively, and — represents the recessive allele. C57BL/6 has the *Fv-1*^{b}, *N*, *B* genotype, whereas DDD-*Fv*^{r} has the *Fv-1*^{n}, —, —. The expression of B-tropic virus is inhibited by the *Fv-1*^{n} allele or by a gene linked with it. Data on inbred strains and NIH Swiss are from references 10 and 12.

pears in mice irrespective of *Fv-1* genotype and coat color. In contrast, the genetic control of B-tropic virus must be considered in a different way from that for N-tropic virus, because B-tropic virus is confined to *Fv-1*^{bb} mice. A locus termed *B* controls B-tropic virus, but its expression is suppressed by the *Fv-1*^{n} allele or by a gene linked with the *Fv-1*^{n}. This consideration is supported by the following observations. All 21 isolates from (DDD or DDD-*Fv*^{r} × C57BL/6) F1 hybrids and viruses isolated by Hoshino (unpublished data) from spontaneous leukemias of three (DDD × BALB/c)F1 mice were N-tropic. No *Fv-1*^{nn} lines yielded B-tropic virus. Rowe and Hartley (10, 12) observed that virus-positive *Fv-1*^{nn} inbred strains carry N-tropic virus only, and virus isolates from (AKR × *Fv-1*^{bb})F1 hybrids were almost exclusively N-tropic.

Table 3 shows possible combinations of *Fv-1*, *N*, and *B* loci and a classification of the partially inbred lines. For comparison, the inbred strains reported previously in literature (10, 12) are also included in the table. This model is tentative because the number of mice used is small and negative results are not conclusive. However, it may explain the observed differences in the expression of MuLV among the partially inbred lines. If C57BL/6 and DDD-*Fv*^{r} have, respectively, the genotypes of *Fv-1*^{b}, *N*, *B* and *Fv-1*^{n}, —, — (where — represents a recessive allele), combinations of these three loci provide eight different genotypes; however, due to the suppression of B-tropic virus in *Fv-1*^{nn} mice, only six phenotypes are distinguishable. It is noteworthy that one pair of C57BL/6 and DDD-*Fv*^{r} has given rise to five of six possible phenotypes; two are identical with, and the remaining three are different from, the parental phenotypes. These observed five phenotypes include the four of previously reported inbred strains, suggesting that similar assortment of these three gene loci has occurred during the establishment of inbred strains. Crucial questions are whether 5B9R-1 yields B-tropic virus only on further testing and whether the absence of *Fv-1*^{bb} lines with N-tropic virus is due to chance.

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LITERATURE CITED

1. Aaronson, S. A., and J. R. Stephenson. 1973. Independent segregation of loci for activation of biologically distinguishable RNA C-type viruses in mouse cells. Proc. Nat. Acad. Sci. U.S.A. **70**:2055–2058.
2. Hartley, J. W., W. P. Rowe, W. I. Capps, and R. J. Huebner. 1969. Isolation of naturally occurring viruses of the murine leukemia virus group in tissue culture. J. Virol. **3**:126–132.
3. Hartley, J. W., W. P. Rowe, and R. J. Huebner. 1970. Host-range restrictions of murine leukemia viruses in mouse embryo cell culture. J. Virol. **5**:221–225.
4. Odaka, T. 1969. Inheritance of susceptibility to Friend mouse leukemia virus. V. Introduction of a gene responsible for susceptibility in the genetic complement of resistant mice. J. Virol. **3**:543–548.
5. Odaka, T. 1970. Inheritance of susceptibility to Friend mouse leukemia virus. VII. Establishment of a resistant strain. Int. J. Cancer **6**:18–23.
6. Odaka, T. 1974. Inheritance of susceptibility to Friend mouse leukemia virus. XII. Effect of the *Fv-1* locus. Int. J. Cancer **14**:252–258.
7. Peters, R. L., J. W. Hartley, G. J. Spahn, L. Rabstein, C. E. Whitemire, H. C. Turner, and R. J. Huebner. 1972. Prevalence of the group-specific (gs) antigen and infectious virus expressions of the murine C-type RNA viruses during the life span of BALB/cCr mice. Int. J. Cancer **10**:283–289.
8. Pincus, T., J. W. Hartley, and W. P. Rowe. 1971. A major genetic locus affecting resistance to infection with murine leukemia viruses. I. Tissue culture studies of naturally occurring viruses. J. Exp. Med. **133**:1219–1233.
9. Pincus, T., W. P. Rowe, and F. Lilly. 1971. A major genetic locus affecting resistance to infection with murine leukemia viruses. II. Apparent identity to a major locus described for resistance to Friend murine leukemia virus. J. Exp. Med. **133**:1234–1241.
10. Rowe, W. P. 1972. Studies of genetic transmission of murine leukemia virus by AKR mice. I. Crosses with *Fv-1*^{n} strains of mice. J. Exp. Med. **136**:1272–1285.
11. Rowe, W. P. 1973. Genetic factors in the natural history of murine leukemia virus infection. Cancer Res. **33**:3061–3068.
12. Rowe, W. P., and J. W. Hartley. 1972. Studies of genetic transmission of murine leukemia virus by AKR mice. II. Crosses with *Fv-1*^{b} strains of mice. J. Exp. Med. **136**:1286–1301.
13. Rowe, W. P., and T. Pincus. 1972. Quantitative studies of naturally occurring murine leukemia virus infection of AKR mice. J. Exp. Med. **135**:429–436.
14. Rowe, W. P., W. E. Pugh, and J. W. Hartley. 1970. Plaque assay techniques for murine leukemia viruses. Virology **42**:1136–1139.
15. Stephenson, J. R., and S. A. Aaronson. 1972. Genetic factors influencing C-type RNA virus induction. J. Exp. Med. **136**:175–184.
16. Stephenson, J. R., and S. A. Aaronson. 1973. Segregation of loci for C-type virus induction in strains of mice with high and low incidence of leukemia. Science **180**:865–866.