Genetic Marker Patterns and Endogenous Mammary Tumor Virus Genes in Inbred Mouse Strains of Japan

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(Received 8 October 1985/Accepted 31 January 1986)

In order to establish the genetic relatedness of the inbred mouse strains kept in Nara, genetic marker patterns were determined in conjunction with a study on endogenous mammary tumor viral genes in these strains. Isoenzyme patterns combined with patterns of other genetic markers, show that the unrelatedness between various inbred strains of the dd stock is as high or even higher as between strains of known different origin and genealogy. Based on endogenous viral gene patterns the dd stock derived mice can be subdivided into three groups, (1) DDD, DDN, DDO, (2) KF and (3) DD/Tbr. The DD/Tbr and its foster-nursed substrain (DD/Tbrf) have the lowest number of endogenous viral genes, i. e. two, while the other strains carry 4–6 such genes. The SLN and SHN strains, derived from a Swiss stock, have a similar pattern of viral genes different from that of all other strains studied, also strains of Swiss origin from other sources, such as the NFS and the GR.

Inbred mouse strains are important “tools” to understand the genetic basis for diseases, notably the origin of neoplasms. Their usefulness depends very much on knowledge of their genetic background and characteristics. In order to compare for example tumor incidences in inbred strains between various laboratories, it is inconceivable to date that the genetic marker patterns of the strains would not be known.

Some of the largest inbred mouse colonies in the world, such as those in the Jackson Labs in the USA and the Netherlands Cancer Institute in Amsterdam, have very well defined and genetically characterized inbred strains of diverse origin for genetically oriented research

[24]. The isoenzyme and other genetic marker patterns of these strains are now well known [23, 24, 55]. Some important conclusions of such work is that many mouse strains were separated too early during inbreeding and that residual heterozygosity is an important problem [1], that mutations can occur after decades of separation [1, 23] and that endogenous retroviral genes can segregate and get amplified [7].

Since endogenous viral genes, e. g. of the mammary tumor virus, are known to influence spontaneous mammary cancer incidence very dramatically (for review, see [2, 22]). It is self evident that the number and quality of such genes should be determined, if one wants

to study the mechanisms of mammary tumorigenesis.

In this study we have compared the genetic marker patterns of some widely used inbred strains in Japan, notable of the dd stock, with that of the patterns of endogenous mammary tumor virus. We conclude that differences between the inbred dd strains are much higher than expected. Although these strains represent a quite unique series of useful sublines, they differ widely among each other.

Materials and Methods

Origin of Mouse Strains (see Figs. 1 and 2) [56]. In 1910, non-inbred albino mice were brought from Germany to Japan by S. Hata, and were raised in the Kitazato Institute, Tokyo. They were transferred to Dairen in 1935 and brought back to the Institute of Infections Diseases (Denken in Japanese abbreviation) in Japan in 1943. The mice

were designated as dd : one d stands for German (Deutsch) origin and the other d stands for Denken (Present designation : Institute for Medical Science).

The DD/Tbr strain has been inbred by Y. Tsubura from this "dd" stock mice. some dd mice were transferred to Osaka University, from where some of them were obtained and inbreeding has been carried out at Nara Medical College (Japan) by Tsubura in order to raise the mammary cancer incidence. This DD/Tbr strain is a high mammary cancer strain and reached the 77th inbred generation. The DD/Tbrf strain was foster-nursed on C57BL/6J mice to eliminate it's milk-factor and was designated as DDf.

In 1952, some dd mice were transferred to the Central Institute for Experimental Animals (CIEA) in Tokyo, where they were designated as ddN, N standing for the name of the director (Nomura). Some ddN mice were transferred to Osaka University, where

Fig. 1. Family tree of German Mouse Group

Fig. 2. Family tree of Swiss Mouse Group

Fig. 1. Detection of MTV DNA sequences in liver DNA of DDD, DD/Tbr, NFS, SLN, SHN, DDN, DDf, GR, DDO, KF and BALB/c mice.

they were raised by J. Kawamata, and were designated as ddO (O stands for Osaka).

ddN mice were transferred from CIEA to the National Institute of Health (Yoken in Japanese abbreviation) in 1953, where the mice were designated as ddY (Y stands for Yoken). In 1963, some ddY mice were transferred to Shizuoka Agriculture Cooperative Association for Laboratory Animals, from which mice were purchased in 1979.

Some ddN mice in the CIEA were transferred to Gumma University, where the inbreeding was carried out and they were obtained from S. Mitsuhashi in 1979.

One dd stock was inbred by B. Kitasato to develop a strain susceptible to *Salmonella* infection. While maintaining the strain at the CIEA, occasional testicular tumors were observed. Some of them were brought to Nara Medical College in 1963. The strain was designated as KF. Occasional mammary

tumors and leukemias were observed but no testicular tumors developed. Inbreeding has reached the 40th inbred generation in Nara.

The DDD strain has been inbred from "dd" stock mice since 1962 at the Institute of Medical Science in Tokyo by K. Suzuki and A. Matsuzawa. Mice of early inbred generations showed a moderately high mammary cancer incidence, though mammary cancer incidence declined in later inbred generations.

The SHN and SLN mice were derived from Swiss albino mice transferred to Japan in 1963 from the City of Hope Medical Center in the U. S. A. The stock was maintained first at the Hokkaido University in Sapporo, and subsequently the National Institute of Genetics in Mishima where it was maintained by pen-matings. Inbreeding was started in 1964 by H. Nagasawa at the National Cancer Research Institute in Tokyo. The SHN and SLN strains were created by inbreeding Swiss mice with continuous selection for high and low mammary cancer incidence. Both strains were obtained from H. Nagasawa in 1978 in the F28 (SHN) and F27 (SLN) generations.

The GR/A (GR) strain has been obtained from S. Morii of Kansai Medical University in 1977. The strain originated in Switzerland and was inbred by Mühlbock in Amsterdam.

BALB/cHe (BALB/c) mice were transferred from Simonson's laboratory in 1920's and some mice were maintained in Taisho Pharmaceutical Co.. They were obtained in 1968 in Nara Medical College.

C57BL/6J (C57BL) mice have been inbred since 1980 by A. Matsuzawa at the Institute of Medical Science in Tokyo.

NFS mice are from a subline of the maintained in the National Institute of Health in the U. S. A. and were obtained in 1980 from A. Ishimoto at the Institute for Virus Research, Kyoto University.

Homogenate preparation—Tissue homogenate from freshly killed mice (10 males and 10 females) were prepared as previously described [28].

Cellulose acetate electrophoresis and staining—Homogenate supernatants were subjected to some electrophoresis on Titan III cellulose acetate plates (Helena Labs, TX) as described

previously [28].

Esterase assay—Polyacrylamide disc electrophoresis was performed on 7.5% slab gels using a Tris-glycine buffer system as described [43].

DNA Extraction—Liver was removed from the animals, and stored at -70°C . Tissues were dispersed in 0.02M Tris-HCl, pH 8.3, 0.01M EDTA, 0.1M NaCl, 0.1% NP40, using a motor-driven teflon-grass dounce homogenizer. Nuclei were pelleted by centrifugation for 5 min at $3000\times g$. The nuclear pellet was washed three times with 15ml of homogenization buffer and resuspended in 20 ml of TNE. Self-digested pronase and SDS were added to 0.2 mg/ml and 1% respectively. After incubation for 12 hr at 37°C the DNA was extracted with phenol-chloroform and precipitated by the addition of 2 vol of ethanol. The DNA was collected by centrifugation, resuspended in $2 \times \text{SSC}$ ($1 \times \text{SSC}$ is 0.15M NaCl, 0.015M Na-citrate) and treated with $50\mu\text{g/ml}$ ribonuclease A for 2 hr at 37°C . The DNA was then again extracted with phenol-chloroform and after precipitation with alcohol resuspended in 1mM EDTA and stored at 4°C .

Digestion of DNA with restriction endonucleases, gel electrophoresis, DNA transfer, and hybridization—Restriction enzyme EcoRI was purchased from Boehringer Mannheim Corp. Twenty micrograms of DNA was digested to completion with an excess of enzyme in the appropriate buffer for 12 hr at 37°C . The extraction of the DNA, gel electrophoresis conditions, DNA transfer, and hybridization with ^{32}P -labeled MuMTVcDNA were performed as described previously [39].

Results

Patterns of markers and details for each of the strains were as follows: Adh-1=Alcohol dehydrogenase-1 [26, 27, 30, 32, 33]. No variation was observed.

Adh-2=Alcohol dehydrogenase-2 [30]. No variation was observed.

Adh-3=Alcohol dehydrogenase-3 [30, 33]. The uncommon *b* alleles are present in the DDD and C57BL strain.

Adh-3t=Alcohol dehydrogenase temporal [33]. The uncommon *b* alleles are found in KF, DDD, DDN and C57BL strain. Linkage disequilibrium was observed between Adh-3 and Adh-3t in KF and DDN strain only.

Ahd-1=Aldehyde dehydrogenase-1 [26]. Both alleles are common.

Ahd-2=Aldehyde dehydrogenase-2 [62]. Only the *a* allele is observed in all strains.

Ahd-4=Aldehyde dehydrogenase-4 (stomach) [Mather, P. et al., private communication]. All carried *a* allele.

Ahd-5=Aldehyde dehydrogenase AHD-5 [Mather, P. et al., private communication]. All carried *a* allele.

Ahr-1=Aldehyde reductase-1 [16]. The *b* allele is present only in DDD strain.

Alr-1=Liver aldose reductase [Mather, P. et al., private communication]. All carried *a* allele.

Alr-2=Liver aldose reductase-2 [Mather, P. et al., private communication]. All carried *a* allele.

Akp-1=Alkaline phosphatase [24]. The *a* alleles are present in SHN, SLN and C57BL strain.

Aox-1=Aldehyde oxidase-1 [27, 31, 33, 34]. All strains carried *a* allele.

Aox-2=Aldehyde oxidase-2 [27, 31, 33, 34]. The *b* allele are found in SHN and SLN strains only.

Bcd-1=Butyryl CoA dehydrogenase-1 [58]. Most of the strains carried *a* allele except for DDD strain.

Car-2=Carbonic anhydrase-2 [17]. The *a* and *b* alleles are almost equally divided among the strains except for ddY strain, which showed heterogeneity for *a* and *b* alleles.

Dao-1=D-amino acid oxidase [25]. The DD/Tbr and DDf strains carried *b* allele, while most of the other strains carried *a* allele.

Es-1=Serum albuminesterase-1 [52, 54]. The rare allele *a* is present in the C57BL strain only.

Es-2=Serum prealbuminesterase [48, 55]. carried *b* allele.

Es-3=Eserine-sensitive erythrocyte esterase, Chr 11 [55]. The *a* allele was found in BALB/c, C57BL, and NFS. Strain GR

carried the *b* allele whereas the other strains showed the *c* allele.

Es-5=Slowly migrating serum esterase, Chr 8, cluster 2 [49]. The null allele *a* was found in DDD and in DDN only.

Es-6=Ubiquitous carboxylesterase, first discovered in kidney. Chr 8, cluster 1 [40, 50]. No variation was found.

Es-7=Erythrocyte membrane carboxylesterase, Chr 8, cluster 2 [5, 43]. No variation was found.

Es-9=Sex dependent kidney carboxylesterase, Chr 8, cluster 1 [57]. No variation was found.

Es-10=Dimeric erythrocyte esterase, Chr 14 [46, 63]. The *a* and *b* alleles were almost equally distributed.

Es-11=Liver carboxyl esterase, Chr 8, cluster 2 [47]. The strains DDD and DDN carried the *b* allele. The other strains showed the more common *a* allele.

Es-13=A modifying locus, probably originating from mice of Switzerland, Chr 9 [64]. The unusual *b* allele was found in four strains: DD/Tbr, DDf, SHN, and NFS.

Es-14=Tetrameric erythrocyte esterase, Chr 9 [3, 4] All strains carried the allele *r* common in the European subspecies *M. m. domesticus*.

Es-16=Particle bound kidney arylesterase, Chr 3 [9]. All strains carried the common allele *a*.

Es-17=Acetylerase, Chr 9 [45]. All strains carried the common allele *a*.

Es-18=The structural locus of that esterase which is modified by *Es-13* [8]. No variation was found.

Es-22=Liver carboxylesterase, Chr 8, cluster 1 [18]. All strains carried the common *a* allele.

Es-23=Kidney carboxylesterase, Chr 8, cluster 2 [12]. All strains carried the *c* allele.

Es-24=Phenotype designation. Es-24 is a highly polymorphic, polymeric lung carboxylesterase, probably heteromeric. No separate gene locus was proposed until now. Chr 8, cluster 1 [10]. Strain KF showed the 24F phenotype.

Es-25=Water soluble kidney arylesterase, gene locus unknown [11]. Three strains, DDD,

DDN, and BALB/c carried the *a* allele.

Es-26=Liver cholinesterase, Chr 3 [13]. Three strains, DD/Tbr, DDf and DDO carried the *b* allele. The other strains showed the *a* allele.

Gpd-1=Glucose phosphate dehydrogenase-1 [56]. The *b* allele is found in the SLN, NFS and C57BL strains, while most of other strains carried *a* allele.

Gpi-1=Glucose phosphate isomerase-1 [14]. The *b* allele is found in the SLN, NFS and C57BL strains, while most of other strains carried *a* allele.

Hao-1=Alpha-hydroxyacid oxidase-1 [15, 35]. No variation was found.

Hbb=Hemoglobin beta-chain [51]. Both *d* and *s* allele are present.

Hc=Hemolytic complement. Strain with 1 allele have the C5 complement protein, while strain with the 0 allele lack the protein [6].

H-2=Histocompatibility-2 [38].

Idh-1=Isocitrate dehydrogenase-1 [20]. Both *a* allele are present.

Ldr-1=Lactate dehydrogenase regulator-1 [59]. The rare *o* allele is found in the NFS strain only.

Mod-1=Malic enzyme, supernatant [21]. The *a* and *b* alleles are almost equally divided among the various strains.

Mpi-1=Mannose phosphate isomerase-1 [41]. All strains carried *b* allele.

Mup-1=Major urinary protein [19]. Most of the strains carried *a* allele except for C57 BL strains.

Pep-3=Peptidase-3 (formerly Dip-1) [42]. The rare *c* allele is found in the DD/Tbr, DDf and DDO strain. The *a* allele is present in the BALB/c and C57BL strains.

Pgm-1=Phosphoglucomutase-1 [60]. Both *a* and *b* allele are present.

Sdh-1=Sorbitol dehydrogenase-1 [14, 28]. All strains have *a* allele.

Thy-1=Thymus cell antigen-1 (theta) [23]. All strains carried *b* allele.

Trf=Transferrin [61]. All strains carried *b* allele.

The inbred strains kept in Nara can be divided in four groups according to their origin: 1. The group of the "dd" stock mice,

Table 1. Genetic Marker of Inbred Strains

Chromo. number	3	?	3	3	4	19	3	?	?	?	?	1	?	?	1	5	3
Genetic Marker	Adh-1	Adh-2	Adh-3	Adh-3t	Adh-1	Adh-2	Adh-3	Ahd-4	Ahd-5	Ahd-6	Ahr-1	Akp-1	Alr-1	Alr-2	Aox-1	Aox-2	Car-2
DD/Tbr	a	a	a	a	b	a	a	a	b	a	a	b	a	b	a	a	a
DDf	a	a	a	a	b	a	a	a	b	a	a	b	a	b	a	a	a
KF	a	a	a	b	b	a	a	a	a	a	a	b	a	b	a	a	b
DDD	a	a	b	b	b	a	b	a	a	b	b	b	a	a	a	b	b
DDO	a	a	—	—	b	a	—	—	—	—	b	—	—	—	a	a	—
ddY	a	a	a	a	b	a	—	—	—	—	b	—	—	—	a	a	—
DDN	a	a	a	b	b	a	—	a	—	a	b	a	a	—	a	a	a b
SHN	a	a	a	a	a	a	a	a	a	a	a	a	a	b	a	a	a
SLN	a	a	a	a	a	a	—	a	—	a	a	a	a	—	a	—	a
GR	a	a	a	a	b	a	—	—	—	a	a	a	—	—	a	a	a
NFS	a	—	a	a	b	a	a	a	a	a	b	a	a	a	a	a	b
BALB/c	a	a	a	a	b	a	—	a	—	—	b	a	a	—	a	a	—
C57BL	a	a	b	b	a	a	b	a	b	b	a	a	a	b	a	a	a

(Continued)

Genetic Marker of Inbred Strains

Chromo. number	?	5	4	7	8	17	2	3	3	7	2	1	6	9	9	4	1	5	2	9	9
Genetic Marker	Cbr-1	Dao-1	Gpd-1	Gpi-1	GR-1	H-2	Hao-1	Hao-1	Hao-2	Hbb	Hc	Idh-1	Ldr-1	Mod-1	Mpi-1	Mup-1	Pep-3	Pgm-1	Sdh-1	Thy-1	Trf
DD/Tbr	a	b	b	a	a	b	a	a	a	d	l	a	a	a	b	a	c	b	a	b	b
DDf	a	b	b	a	a	b	a	a	a	d	l	a	a	a	b	a	c	b	a	b	b
KF	a	a	b	a	a	b	—	a	s	o	b	a	a	b	b	a	b	a	a	b	b
DDD	b	a	b	a	a	—	c	a	s	o	b	a	a	a	b	a	b	a	a	b	b
DDO	—	—	—	—	—	b	—	—	d	o	a	a	a	a	—	a	c	a	—	b	b
ddY	—	—	b	a	—	—	a	a	s	—	a	a	a	b	—	a	b	a	—	b	—
DDN	—	—	b	a	a	b	a	a	s	l	b	a	a	b	—	a	b	a	a	b	b
SHN	a	a	a	a	a	—	a	a	d	o	b	a	a	a	b	a	b	a	a	b	b
SLN	—	—	a	b	a	—	a	a	s	o	b	a	a	a	b	a	b	a	a	b	b
GR	—	—	b	b	a	—	a	a	s	o	a	a	a	a	b	b	b	b	a	b	b
NFS	b	a	b	b	a	—	a	a	d	o	a	b	a	a	—	a	b	a	—	b	b
BALB/c	—	—	b	a	a	d	a	a	d	l	a	a	a	a	b	a	a	a	a	b	b
C57BL	a	a	a	b	—	b	a	a	s	l	a	a	a	b	—	b	a	a	a	a	b

Table 2. Esterase Isoenzyme Patterns of Inbred strains of mice of Nara

Chromo. number	8	8	11	8	8	8	8	8	8	14	8	9	9	9	14	9	3	9	?	8	8	22	8	23	8	24	?	25	3	26	3?
Genetic Marker	Es-1	2	3	5	6	7	9	8	8	10	11	13	9	9	14	9	16	17	18	?	8	22	8	23	8	24	?	25	3	26	3?
DD/Tbr	b	b	c	b	a	b	a	b	a	b	a	b	b	r	r	a	a	a	a	a	d	c	c	a	a	b	b	b	b	r	
DDf	b	b	c	b	a	b	a	b	a	b	a	b	b	r	r	a	a	a	a	a	d	c	c	a	a	b	b	b	b	—	
KF	b	b	c	b	a	b	a	b	a	b	a	a	a	r	r	a	a	a	a	a	d	c	c	f	b	b	a	a	r		
DDD	b	b	c	a	a	b	a	b	a	a	b	a	a	r	r	a	a	a	a	a	d	c	c	a	a	a	a	a	r		
DDO	—	b	c	—	a	b	a	b	a	a	a	a	a	r	r	a	a	a	a	a	d	c	c	—	b	b	b	b	—		
DDN	b	b	c	a	a	b	a	b	a	a	b	a	a	r	r	a	a	a	a	a	d	c	c	a	a	a	a	a	—		
SHN	b	b	c	b	a	b	a	b	a	a	a	b	b	r	r	a	a	a	a	a	d	c	c	a	a	b	a	a	r		
SLN	—	b	c	—	a	b	a	b	a	a	a	a	a	r	r	a	a	a	a	a	d	c	c	—	b	b	a	—			
GR	—	b	b	—	a	b	a	b	a	b	a	a	a	r	r	a	a	a	a	a	d	c	c	—	b	b	a	—			
NFS	b	b	a	b	a	b	a	b	a	a	a	b	b	r	r	a	a	a	a	a	d	c	c	f	b	b	a	a	r		
BALB/c	—	b	a	—	a	b	a	b	a	a	a	a	a	r	r	a	a	a	a	a	d	c	c	—	a	a	a	—			
C57BL	a	b	a	b	a	b	a	b	a	—	a	a	a	—	—	—	a	a	a	a	d	c	c	a	a	b	a	a	r		

Table 3. Comparison of the variable genetic markers between inbred mouse strains of Nara

Strains	No. different markers Total No. of markers	Percentage of different markers
DD/Tbr-DDD	9/26	35%
DD/Tbr-KF	7/29	24%
DD/Tbr-DDN	5/27	18%
DD/Tbr-SHN	3/31	10%
DD/Tbr-GR	6/28	21%
DD/Tbr-BALB/c	4/31	13%
DD/Tbr-C57BL	12/36	33%
KF-DDD	3/26	12%
DDO-ddY	3/16	18%
ddY-DDN	3/24	13%
DDN-KF	3/25	12%
SHN-GR	8/28	25%
SHN-SLN	2/32	0.1%
BALB/c-C57BL	12/29	41%
BALB/c-NFS	4/24	17%

including DD/Tbr, DD/Tbrf, KF, DDD, DDO, ddY and DDN. 2. The group of mice of Swiss origin, including SHN, SLN, GR and NFS. 3. One strain of American origin: BALB/c. 4. A second strain of American origin: C57BL.

Inbreeding of these mice was done mainly in Japan, except for the GR, NFS, BALB/c and C57BL strains. The genealogy of the strains inbred in Japan is given in Figs. 1, 2. The mice of the random bred "dd" stock were inbred in quite a number of different Japanese laboratories from the late 1940. The SHN and SLN strains were inbred from a random bred Swiss stock with simultaneous selection for high mammary cancer incidence.

Tables 1, 2 shows the results of a survey for genetic markers, mainly isoenzymes, in these strains. The patterns of the GR, C57BL and BALB/c strains are identical to those of these strains in the Amsterdam colony [23], National Cancer Institute [24] and the Jackson Laboratories [54]. The NFS strain is relatively unknown in this respect and shows a unique marker pattern. The SHN and SLN strains are very similar: 30/32 marker are identical (see also Table 3 for comparison of strains).

The mice of the "dd" stocks are, however, quite different from each other and one wonders whether genetic, unrelated to that of this stock, has been crossed into some of these strains. The differences ranges from 12% to 35% (between DD/Tbr and DDD). If one compares this with the 41% difference in these markers between BALB/c and C57BL, two totally unrelated strains, it is clear that the various inbred strains from the "dd" stocks are not related at all, though it appears that two strains DDD and DDN are quite identical in esterase patterns.

This view is substantiated by the patterns of endogenous mammary tumor virus genes as shown in Figure 3. Within the "dd" group, the patterns of the DDD, DDN and DDO resemble each other very much, but this pattern is very different from that of the KF strain and also of the DD/Tbr and DD/Tbrf strains. The latter strain has very few endogenous MTV genes (not more than two), even fewer than the BALB/c strain. The

other dd stock mice may have 4-6 endogenous viral genes, because EcoRI cuts the MTV genome in 2 fragments.

The patterns of the SHN strains are very similar, with one or two more bands in the SLN. Both strains have a high and early mammary tumor incidence. In case of the SHN strain this is due to the Mtv-4 locus [37].

The NFS pattern of viral genes looks like that of the GR, though the tumor incidence is very low.

Discussion

The results presented here clearly show that the various inbred strains derived from the wellknown "dd" stock are occasionally as much different from each other as totally unrelated strains of American and European origin. If one considers endogenous MTV gene patterns as a good parameter for relatedness, one could classify the strains of Nara into three categories: 1. Group 1: DDD, DDN, DDO (and perhaps ddY), 2. Group 2: KF, 3. Group 3: DD/Tbr strain and its fosternursed substrain DD/Tbrf.

However, this distinction is less clear if one considers the isoenzyme patterns, because few of these markers are characteristic for one of the three groups. One could say that the Pgm-1^b marker is typical for the DD/Tbr strains as opposed to the other strains in group 1 and 2, but one cannot find markers indicative of the other groups only.

If the two genes of endogenous MTV of the DD/Tbr stock represent the common ancestor genes of this virus in the "dd" stock mice, it follows that the additional genes of the other strains, notably of group 1, are recent reintegrations which occurred in the past 30 years. However, the endogenous genes of the dd stock are known not to get expressed at all [36] and it is therefore hard to speculate that they are the genes which would be amplified in the other stocks. Since it is hardly conceivable that the DD/Tbr stock lost endogenous MTV genes as compared to the strains of group 1, it follows that some of these endogenous viral genes were introduced

by other genetic material, e. g. from mice of Swiss stock origin or other unknown origin. This speculation is not wholly unwarranted because of the similarities in several endogenous viral gene sizes of the Swiss stock and dd stock strains.

This could also be deduced from some of the marker patterns. The rare Hbb^s gene, e. g. is present in Nagasawa's SLN stocks is also observed in some dd stock mice. Recently Yonekawa et al. also [65] showed that a closed colony ddY has a mixture of *domesticus* and *molossinus* mitochondrial DNAs suggesting that the original dd stock was contaminated with another mice of different origin. It should be emphasized, however, that more extensive studies on genetic marker patterns of Japanese inbred strains are necessary to understand the genetic relationships between these strains as they occur now. For the mice kept at Nara such studies are being planned and executed.

This work was supported in part by Grants-in-Aid for Cancer Research 4010410 and 4010411 from the Ministry of Education, Science and Culture, Japan.

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我国で系統維持されている近交系マウスにおける 遺伝子マーカーと内因性乳癌ウイルスについて

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主として奈良医大で維持されている dd 系マウスをはじめ、近交系マウスの遺伝的背景を明確にするために、遺伝子マーカーおよび内因性乳癌ウイルス (MTV) の動態について調べた。アイソザイムを中心に他の遺伝子マーカーとの組み合わせの結果、共通の祖先を有する dd マウス群においても、それぞれのマウスにより遺伝的に異なる点が明らかになった。またその幅は、dd 系とはまったく異なった由来のマウス系より大きい。内因性 MTV の DNA への組み込みの分布でみると、dd

系は次の群に分けられる。すなわち、1) DDD, DDN, DDO 2) KF, 3) DD/Tbr である。特に DD/Tbr 系とその外因性 MTV を除去した DD/Tbrf 系の MTV のゲノムは他の系統と比較して最も少ない。一方、スイス由来の SHN 系および SLN 系では互によく似たゲノムの分布を示すが、NFS 系、GR 系のスイス由来を含め他のすべての系とは、まったく異なった分布を示した。