Many of these problems will also exist in fusion reactors and an obvious case to consider is what would happen if the fusion events are triggered by pulses of laser light. Laser beams deposit energy in a glass by absorption or scattering. If the pulses of light are sufficiently intense then the rate of energy deposition will cause the glass to explode[13]. For this reason one is very careful to remove strain or refractive index gradients from the glass and in normal environments the main concern is with the polish of the surface layer. Mechanical polishing leaves residual strains which may set an upper limit to the power density before fragments of material explode from the surface. Chemical or ion beam etching of this surface strain can raise the threshold level from 2 to 10 GW cm^{-2}.

In a radioactive environment fission tracks, colour centres or large scale aggregates of defects can all produce the same catastrophic events in the bulk of the specimen. Further, because the damage is unlikely to be uniform through the material there is also mechanical strain. In early fission reactors the solution was to heat the materials and anneal the damage. In later reactors this has not always been possible because of the risk of enhancing the formation of large stable defects such as voids or gas bubbles. The research on voids has also indicated that they are produced at a higher rate at high fluxes (this is the situation in a pulsed fusion system). In short, we shall need glass windows, and possibly laser materials, which are in close proximity to the fusion vessel which must not (1) distort (2) colour (3) accrete large scale defects or (4) increase the surface scatter. Problems (1), (2) and 3 are fairly intractable, (4) is certainly insoluble because sputtering of surface atoms is a consequence of radiation damage. In an insulating material the problem can be further aggravated by charge build up below the surface followed by explosions in which blocks of material are ejected. This would cause laser scatter and destruction of the glass by the subsequent laser pulses.

Clearly with a little thought we could find other potential problems. Instead, I would suggest these problems are not insurmountable. For example the oxide glasses with a large inherent vacancy concentration (for example TiO_2) are essentially self-annealing and remarkably stable to radiation damage. Similarly, if this type of material could be made of high enough electrical conductivity, yet remain transparent, then the problems of surface charge explosions might also be avoided.

1 Mees, C. E. K., and James, T. H., *The Theory of the Photographic Process* (Macmillan, London, 1966).
2 Schulman, J. H., and Compton, W. D., *Colour centres in Solids* (Pergamon, Oxford, 1963).
3 Fowler, W. B., *Physics of Colour Centres* (Academic, New York and London, 1968).
4 Greenwood, N. N., *Ionic Crystals Lattice Defects and Non Stoichiometry* (Butterworth, London, 1968).
5 Henderson, B., *Defects in Crystalline Solids* (Arnold, 1972).
6 Townsend, P. D., and Kelly, J. C., *Colour Centres and Imperfections in Insulators and Semiconductors* (Sussex University Press, Brighton, 1973).
7 Ivey, H. F., *Phys. Rev.*, **72**, 341 (1947).
8 Taylor, M. J., *Phys. Bull.*, **21**, 485 (1970).
9 Faughan, B. W., and Kiss, Z. J., *Phys. Rev. Lett.*, **21**, 1331 (1968).
10 Miller, S. E., *IEEE J. Quantum Electronics*, **8**, 199 (1972).
11 Tien, P. K., *Appl. Optics*, **10**, 2395 (1971).
12 Cheo, P. K., *Appl. Phys.* **6**, 1 (1975).
13 Teitel, R. J., *J. Nucl. Mat.*, **53**, 349 (1974).

articles

Linkage disequilibrium between *H–2* and *t* complexes in chromosome 17 of the mouse

Craig Hammerberg

Department of Human Genetics, University of Michigan Medical School, Ann Arbor, Michigan 48104

Jan Klein

Department of Microbiology, University of Texas Southwestern Medical School, Dallas, Texas 75235

Mice with t *factors belonging to the same complementation group carry similar, if not identical,* H–2 *haplotypes although these factors were derived from widely separated geographical areas. This association between* t *and* H–2 *complexes suggests more than a casual relationship between the two complexes, at least at the population level.*

CHROMOSOME 17 of the mouse carries two of the most puzzling systems in mammalian genetics, *H–2* and *t* (refs 1–3). The question whether the presence of two such highly sophisticated systems on the same chromosome is fortuitous or whether the systems could be genetically interrelated has been raised repeatedly[2–6]. In this communication we demonstrate at least one level of interrelation between *t* and *H–2* by showing the presence of a strong linkage disequilibrium in the mouse population between the two complexes.

While studying the polymorphism of serologically detectable H–2 antigens among wild mice[7] we H–2 typed strains carrying various *t* factors because most of these factors have been extracted from wild mouse populations, and there was a good chance that they carried the wild-derived *H–2* haplotypes. The *t* bearing strains were from our mouse colony or that of Dr Dorothea Bennett at Cornell University Medical College. The former were strains at various stages of transfer of individual *t* factors (originally obtained from the late Professor L. C. Dunn) on the inbred background of strain C57BL/10Sn (B10); the

Table 1 H-2 antigens in *t*-bearing strains of mice.

Factor	*H-2* haplotype	H-2 antigens 1	2	3	4	5	6	7	8	11	13	23	25	31	105	106	107	108	109	Ia antigens 101
t^{12}	*t12*	—	—	—	—	5	—	—	—	—	—	—	—	—	—	106	107	—	—	.
t^{w32}	*t12*	—	—	—	—	5	—	.	.	—	—	—	—	—	—	106	107	—	—	—
t^{w2}	*w5*	—	—	"3"	—	—	"6"	C	8	—	—	—	—	31	105	—	107	—	—	—
t^{w8}	*w5*	—	—	"3"	—	—	?	.	.	—	.	—	—	31	105	—	107	—	—	—
t^{0}	*w5*	—	—	"3"	—	—	?	.	.	—	.	—	—	31	105	—	107	—	—	—
t^{1}	*w5*	—	—	"3"	—	—	?	.	.	—	.	—	—	31	105	—	107	—	—	—
t^{6}	*tw1*	—	—	—	—	C	—	—	—	—	"13"	—	—	—	—	—	—	108	—	—
t^{w1}	*tw1*	—	—	—	—	C	—	—	—	—	"13"	—	—	—	—	—	—	108	—	—
t^{w71}	*tw1*	—	—	—	—	—	—	.	.	—	.	—	—	—	—	—	—	108	—	—
t^{w73}	*tw1*	—	—	—	—	?	—	.	.	?	.	—	—	—	—	—	—	108	—	—
t^{w12}	*tw1*	—	—	—	—	?	—	.	.	?	.	—	—	—	.	—	—	108	—	—
t^{w5}	*tw5*	"1"	—	—	—	5	—	—	—	11	—	C	25	—	—	—	—	—	109	101
t^{w75}	*tw5*	—	—	—	—	?	—	.	.	11	.	—	25	—	—	—	—	—	109	—

(Antigens H-2.2, 4, 9, 15, 16, 17, 18, 19, 28, 30, 32, and 33 were found to be absent in all tested t strains.)
A dot indicates not done. Quote marks indicate a similar but not identical antigen. C, cross-reacting antigen. A question mark indicates that presence or absence of an antigen is uncertain.

latter were mostly outbred animals maintained as balanced lethal lines in combination with the *brachyury* chromosome (*T/t*). The detailed results of this typing will be presented elsewhere; here we summarise the data and demonstrate a correlation between *t* complementation groups and *H-2* haplotypes.

The first step in H-2 typing was to use cells from t strains as targets for haemagglutinins and/or cytotoxins produced against known H-2 antigens. This provided limited information about the t strains, since few positive reactions were observed. Most known H-2 antigens were absent in the t strains; however, those present had a distribution more or less coinciding with the classification of *t* factors into complementation groups (antigens 1–31 in Table 1). Thus, t^{12} and t^{w32}, two members of the t^{12} group, both carry H-2.5 and t^{w5} and t^{w75}, two members of the t^{w5} group, carry antigens H-2.11 and H-2.25. In addition, t^{w1}, t^{w71} and t^{w12}, all members of the t^{w1} group and t^{w73}, which seems to define a new complementation group[13] also lack most known H-2 antigens. The two semi-lethal factors, t^{w2} and t^{w8} have a similar antigenic pattern. But the factors belonging to the t^{0}group, t^{0}, t^{1} and t^{6}, possess different antigenic patterns.

Because most known H-2 antigens were absent in t strains, we tested whether these strains carry new, so far unidentified, H-2 antigens. We immunised inbred strains and their hybrids with tissues from *t*/+ heterozygotes sharing an *H-2* haplotype (the one present in the + chromosome) with the recipient. We produced five antisera (Table 2) which were particularly useful in characterisation of t strains. Analysis of these antisera led to a definition of five new antigens, shown by linkage tests to be controlled by genes closely linked to *H-2* (data not shown). Antigens 101 and 106 to 109 were absent in all inbred strains, and H-2.106, 107 and 108 apparently occurred with a relatively low frequency among wild mice[24]. As Table 1 shows, however, the antigens are shared by some of the t strains, and this sharing, to a certain degree, parallels the classification of *t* factors into complementation groups.

One possible explanation of this peculiar antigenic similarity among members of the same complementation group is that our antisera detect not H-2 antigens, but products of the *t* loci. To test the relationship between the *t* factors and the new antigens, we first established the tissue distribution of the antigens. As Table 3 shows, the distribution of H-2.106, H-2.107 and H-2.108 is that of classical H-2 antigens since reactivity against antigens was cleared or reduced by spleen, lymph nodes, thymus, liver, kidney, heart, brain and erythrocytes. In contrast the antigen detected by the cytotoxic reactivity of H-27 is present only on spleen and lymph node cells, and the antiserum reacts only with bone-marrow-derived (B) lymphocytes and not thymus-derived (T) lymphocytes (Fig. 1). The tissue distribution of this antigen is thus indicative of an Ia antigen[8], and this antigen has been designated Ia.101. H-27 also has reactivity in the PVP-haemagglutination test in which it detects H-2.109. As this reactivity is weak, however, the assignment of H-2.109 should be considered tentative.

We also tested the molecular relationship of the new antigens to the few known H-2 antigens demonstrable in t strains. This test was based on the technique monitoring redistribution in the cell membrane of antigens combined with two layers of antibodies[9]. A typical experiment of this sort is shown in Table 4. In this experiment, pretreatment of $+H\text{-}2^{d}/t^{12}H\text{-}2t^{12}$ spleen cells with K-46 (anti-H-2.5) induced resistance to H-12 (anti-H-2.106) but not to the anti-H-2^{d} sera, K-304 (anti-H-2.4) and K-25 (anti-H-2.31) and vice versa. It thus seems that H-2.5 and H-2.106 are on the same molecule, as they are redistributed in the cell membrane together.

On the basis of these data, we conclude that antigens H-2.106 to H-2.109 are not the products of the *t* loci but typical H-2 antigens; 101 seems to be an Ia antigen. The presence of the new antigens on adult somatic tissues makes it unlikely that they are products of *t* loci, which are expressed only during embryogenesis and on spermatozoa[10].

If one accepts this conclusion, members of the same complementation group of *t* factors must have either identical or very

Table 2 Antisera detecting H-2.106, H-2.107, H-2.108, H-2.109 and Ia 101

Code No.	Recipient	Donor	*H-2* haplotype combination†	Antigens detected
H-12	(B10 × A)F_1	(B10 × T/t^{12})NT‡	(*b*/*a*)*b*/*t12*	H-2.106, H-2.107
H-25	(B10.D2 × D2.GD)F_1	t^{w2}/t^{w2}	(*d*/*g2*)*tw5*/*tw5*	H-2.107
H-11	(B10 × A)F_1	(B10 × T/t^{w1})NT	(*b*/*a*)*b*/*tw1*	H-2.108
H-26	(B10 × A)F_1	(B10 × T/t^{6})NT	(*b*/*a*)*b*/*tw1*	H-2.108
H-27	(B10 × C3H)F_1	(B10 × T/t^{w5})NT	(*b*/*k*)*b*/*tw5*	H-2.109, Ia.101

† Recipient in parentheses.
‡ Normal tail.

similar alleles at the loci coding for serologically detectable H-2 antigens. Our preliminary data on mixed lymphocyte reaction typing of t strains parallel the serological data and thus suggest that the intra-group similarity encompasses a large portion of the *H-2* complex. The significance of this finding becomes apparent when one takes into account the origin of the individual *t* factors. For example, t^{w1} was extracted before 1955, from a wild mouse captured in the New York area[11]; t^{w71} was obtained from a wild mouse trapped in 1968 in Denmark[12]; and t^{w12} was derived from a wild mouse captured in California before 1956 (ref. 13). All three factors belong to the complementation groups) and that these chromosomes have been perpetuated in mouse populations for a very long time.

This interpretation of *t* population behaviour suggests a far greater role for interdemic migration that was originally postulated. Demes have been believed to be virtually impenetrable to migrants and the migration rates were thought to be extremely low[15]. If the only source of *t* factors is, however, immigration, then the migration rates must be quite significant.

Our data also have an important implication concerning the relationship between the *t* and *H-2* systems. The data indicate that, at the population level, the two systems are interrelated in

Table 3 Tissue distribution of H-2.106, H-2.107, H-2.108, and Ia.101

	Reciprocal of titre after absorption with the following tissues*															
	Spleen		Lymph nodes		Thymus		Liver		Kidney		Heart		Brain		Erythrocytes	
Antigen	t strain†	B10	t strain	B10	t strain	B10	t strain	B10	t strain	B10	t strain	B10	t strain	B10	t strain	B10
H-2.106‡	—	128	—	128	—	128	—	128	—	128	—	128	—	128	—	128
H-2.107§	—	960	—	960	—	960	—	1,920	—	1,920	120	960	240	960	—	960
H-2.108 ¶	—	512	—	512	128	512	—	512	128	512	266	512	256	512	256	512
Ia.101‖	—	8	—	16	8	8	16	16	8	16	16	16	16	16	8	16

* Absorption was done with one part packed tissue: two parts diluted antiserum for 30 min at room temperature, then 30 min at 37 °C.

† Tissue used for absorption was from the strain against which the absorbed serum was then tested.

‡ H-12 was diluted 1: 64, absorbed, then tested against $+/t^{12}$ lymphocytes in a cytotoxic test[8] (an unpublished work with K. Artzt and D. Bennett); titre was the lowest dilution giving 50% cell lysis.

§ H-25 was absorbed first with B10.BR, then diluted 1: 10 and absorbed with the above tissues, and tested against t^{w2}/t^{w2} erythrocytes in a PVP-haemagglutination test[24]; titre was the lowest dilution giving an agglutination score of 1.

¶ H-11 was diluted 1: 64, absorbed, then tested against $+/t^{w1}$ lymphocytes in a cytotoxic test; titre was the lowest dilution giving 50% cell lysis.

‖ H-27 was diluted 1: 2, absorbed, then tested against $+/t^{w5}$ lymphocytes in a cytotoxic test; titre was the lowest dilution giving 50% cell lysis.

same complementation group and all carry *H-2* haplotypes characterised by the presence of antigen H-2.108. Thus, individual members of the same complementation group are unrelated in terms of place and time of their extraction from wild mouse population, but they have very similar *H-2* haplotypes. Similar relationships exist among members of other complementation groups. The only serious exception is the t^0 group: the t^6 factor which is classified as a member of the t^0 group, has an *H-2* haplotype which resembles that of the t^{w1} group, while t^0 and t^1 have haplotypes similar to $H\text{-}2^{w5}$. But, t^0, t^1, and t^6 are among the factors maintained for the longest time in the laboratory, and therefore they might have been modified by recombination. Supporting the contention is the fact that, for example, t^6 has a relatively low transmission ratio (0.67 C. H., unpublished). (Factors extracted from wild mice usually have transmission ratios of > 0.9; factors derived by recombination from t^{wild} factors usually have much smaller ratios.) It is possible that t^6 is a recombinational derivative of another factor (t^{w1}), while $t^0(t^1)$ or a *t* factor from which t^0 is derived may be responsible for the dispersal of the $H\text{-}2^{w5}$ haplotype among wild mice.

The finding that *t* chromosomes within the same complementation group carry similar *H-2* haplotypes has important implications with respect to the origin of *t* factors and their role in maintaining *H-2* polymorphism. There is a wealth of experimental data indicating that wild mice live in small, relatively isolated units or demes with a social structure dominated by a single male (review in ref. 1). Because of the lethality of *t* factors, these factors can never become fixed in any particular deme and the *t* factors already present in a deme are eliminated by random genetic drift, and new factors are reintroduced into the demes[14]. The question then arises: what is the source of the reinfecting *t* factors? Do the factors represent new mutations (in the broadest sense of the word) or are the same factors reintroduced over and over by interdemic migration? Our data strongly suggest that the latter of the two explanations is correct. It seems that there is only a limited number of different *t* chromosomes among wild mice (perhaps fewer than there are that certain *t* factors are associated with specific *H-2* haplotypes. In other words, the *t* factors and *H-2* haplotypes show a strong linkage disequilibrium. What could be the significance of this disequilibrium? The simplest interpretation is that the disequilibrium is the consequence of the *de facto* close linkage of the two complexes (W. Bodmer, personal communication). As discussed by Thomson *et al*[16], linkage disequilibrium between two closely linked loci can persist over long periods if a relatively small selective effect is acting on one of these loci. For example, in a typical Northern European human population, the frequency of the *HLA1* allele is 0.16 and of the *HLA8* is 0.13. The frequency of the *HLA1*, 8 haplotype is 0.08, which corresponds to linkage disequilibrium $D = 0.06$. At the same time, the distribution of this haplotype throughout Europe suggests that it has been present at reasonable frequencies since pre-agricultural times. The association between certain *t* factors and specific *H-2* haplotypes could be an analogous example of a presistent linkage disequilibrium.

This interpretation, however, does not explain the nature of the selective effect maintaining the linkage disequilibrium. In contrast to disequilibrium in the *HLA* system, where selection acts on loci that are physically close to each other on the chromosome and where the haplotypes that are in disequilibrium show no evidence of crossing over suppression, an active suppression is a vital part of the mechanism maintaining the *t-H-2* disequilibria. Furthermore, to achieve this suppression, the mouse apparently pays a high price in the form of homozygous lethality of the embryos. One would therefore expect that there is a good reason for this costly invention. What might this reason be? We propose that the selective advantage of the linkage disequilibrium lies in the production of genetically superior sperm. It is known that the loci of the *t* complex are expressed on sperm and that they affect sperm behaviour[17]. The sperm carrying a *t* mutation has a much higher probability of fertilising an egg than the normal or the *T* sperm and the consequence of this effect is the distorted segregation observed in a $t/+ \times +/+$ mating. Circumstantial evidence indicates that a group of loci between *T* and *H-2* in chromosome 17 influences

the physiological properties of the sperm[18,19]. One can therefore envision that certain combinations of alleles at these loci result in a physiologically superior sperm, and that, for this reason, these combinations are selected for in natural populations of the mouse. When a structural aberration suppressing crossing over occurs in the chromosome carrying an advantageous combination of alleles, the alleles are permanently locked together and the chromosomal segment transmitted intact from generation to generation. Theoretically, such an advantageous combination should spread rapidly throughout the population and replace all less advantageous combinations of alleles. In reality, however, this does not happen because the chromosomal aberration also has a deleterious effect on its bearer in that it causes homozygous lethality of the embryos and the lethal effect then balances out the advantageous sperm effect. This interplay of the two opposing forces is possible because of the subdivision of wild populations into demes in which genetic drift[15] and inbreeding[20] keep the frequency of the *t* factors below deterministic expectations[21]. The result of the interplay is that the interlocked combination of alleles (a particular *t* factor) is maintained in the population in spite of the deleterious effect, but because of this effect it is prevented from completely taking over the population. Consequently, a particular *t* factor persists in the population with a stable frequency determined by the interaction between the two opposing forces, segregation distortion, and lethality. In cases where the crossing over suppression effect is strong enough to encompass the *H-2* complex, a particular *H-2* haplotype is locked together with a particular *t* factor, and a linkage disequilibrium of this combination then develops. In the history of the mouse population the locking together of the alleles occurred independently several times and involved different allelic combinations of parts of chromosome 17 and different *H-2* haplotypes.

According to this concept most complementation groups are the result of independent occurrences of the locking together event. On the other hand, the various *t* factors of the same complementation group are all derived from the same locking together event, although they might have subsequently differentiated by mutation. Some members of a complementation group, however, might have been derived from a *t* factor of a different complementation group by a rare recombination within the *t* complex.

Whether the *H-2* complex has any evolutionary homology to the *t* complex is not known. But, the finding that antigens coded for by one of the *t* loci have a similar molecular weight as the classical H-2 antigens[22] suggests that such homology might indeed exist. In any event, it is clear that the *H-2* complex, at least at the population level, is included in the sphere of action of *t* and thus is a part of the *t* supersystem.

We thank Professor Walter Bodmer who read the draft of this manuscript and made many suggestions. We also thank Ms JoAnne Tuttle for secretarial assistance. The work was supported by grants from the National Institutes of Health.

Table 4 Susceptibility of $+H\text{-}2^d/t^{12}H\text{-}2^{t12}$ spleen cells to cytotoxic killing after anti-*H-2* and GAMIG treatment

Pretreated with*	Tested with	Dead cells at dilution of antiserum (%)		
		1:2	1:4	1:8
GAMIG (1:4)	H-12	88	85	80
H-12 + GAMIG (1:4)	H-12	25	25	25
K-46† + GAMIG (1:4)	H-12	38	30	30
K-304‡ + GAMIG (1:4)	H-12	85	82	80
K-25§ + GAMIG (1:4)	H-12	88	80	72
GAMIG (1:4)	K-46	70	60	50
H-12 + GAMIG (1:4)	K-46	30	35	35
K-46 + GAMIG (1:4)	K-46	25	25	20
K-304 + GAMIG (1:4)	K-46	70	65	60
K-25 + GAMIG (1:4)	K-46	65	60	50
GAMIG (1:4)	K-304	90	90	90
H-12 + GAMIG (1:4)	K-304	88	85	80
K-46 + GAMIG (1:4)	K-304	85	85	80
K-304 + GAMIG (1:4)	K-304	25	25	25
K-25 + GAMIG (1:4)	K-304	85	85	80
GAMIG (1:4)	K-25	85	85	80
H-12 + GAMIG (1:4)	K-25	85	80	80
K-46 + GAMIG (1:4)	K-25	85	80	80
K-304 + GAMIG (1:4)	K-25	85	85	80
K-25 + GAMIG (1:4)	K-25	25	25	20

The cytotoxicity test was performed as described by Hauptfeld *et al.* (ref.8). GAMIG, goat anti-mouse Ig (γ,κ), was produced and supplied by Dr E. S. Vitetta, University of Texas. Haplotype $H\text{-}2^d$ possesses H-2.4 and H-2.31.

* All anti-H-2 sera were used undiluted. Cells pretreated with GAMIG and tested with normal mouse serum and complement had a background of 15% cell lysis.

† K-46: (HTG × B10.D2)F_1 anti-B10; anti-H-2.5.

‡ K-304: (A.BY × B10.AKM)F_1 anti-B10.A; anti-H-2.4.

§ K-25: (A × B10.A)F_1 anti-B10.D2; anti-H-2.31.

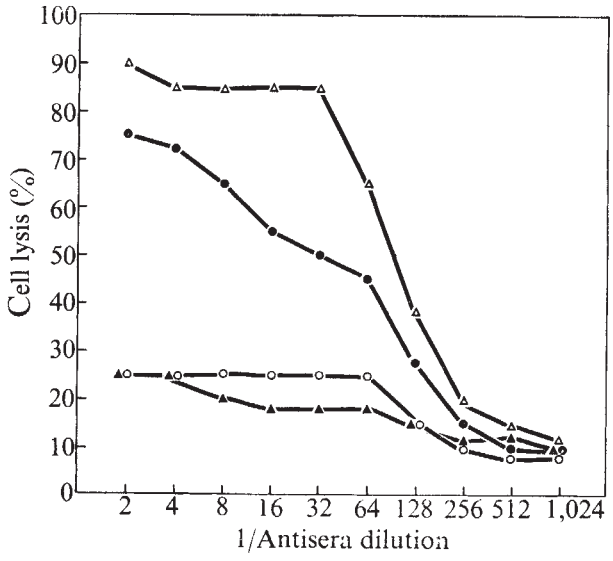

Fig. 1 Cytotoxic reactivity of anti-Ia.101 and anti-Thy-1.2 (θ-C3H) sera with thymus-derived lymphocytes (T cells) and bone-marrow-derived lymphocytes (B cells) from t^{w5} spleen. T cells were obtained by filtration of spleen cells through nylon fibre columns[23]. B cells were prepared by the method of Hauptfeld *et al.*[8]. The cytotoxicity test was performed as described by Hammerberg *et al.*[8] (unpublished). ○, anti-Thy-1.2 reactivity against B cells from t^{w5} spleen; ●, anti-Ia.101 reactivity against B cells from t^{w5} spleen; △, anti-Thy-1.2 reactivity against T cells from t^{w5} spleen; ▲, anti-Ia.101 reactivity against T cells from t^{w5} spleen.

Received August 12; accepted October 6, 1975.

1 Klein, J., *Biology of the Mouse Histocompatibility-2 Complex* (Springer, New York, 1975).
2 Gluecksohn-Waelsch, S., and Erickson, R. P., *Curr. Top. devl Biol.*, **5**, 281–316 (1970).
3 Artzt, K., and Bennett, D., *Nature*, **256**, 545–547 (1975).
4 Gorer, P. A., Lyman, S., and Snell, G. D., *Proc. R. Soc.*, **B135**, 499–505 (1948).
5 Snell, G. D., *Folia Biol., Praha*, **14**, 335–358 (1968).
6 Bodmer, W. F., in *Defence and Recognition* (edit. by Porter, R. R.), 295–328 (Butterworths, London, 1973).
7 Klein, J., *A. Rev. Genet.*, **8**, 63–77, (1974).
8 Hauptfeld, V., Hauptfeld, M., and Klein, J., *J. Immun.*, **113**, 181–188 (1974).
9 Hauptfeld, V., Hauptfeld, M., and Klein, J., *J. exp. Med.*, **141**, 1047–1056 (1975).
10 Yanagisawa, K., Pollard, D. R., Bennett, D., Dunn, L. C., and Boyse, E. A., *Immunogenetics*, **1**, 57–67 (1974).
11 Dunn, L. C., and Suckling, J. A., *Genetics*, **41**, 344–352 (1956).
12 Dunn, L. C., and Bennett, D., *Evolution*, **25**, 451–453 (1971).
13 Dunn, L. C., *Proc. natn. Acad. Sci. U.S.A.*, **43**, 158–163 (1957).
14 Lewontin, R. C., and Dunn, L. C., *Genetics*, **45**, 705–722 (1960).
15 Anderson, P. K., in *Mutation in Population* (edit. by Honcariv, R.), 17–21 (Academia, Praha, 1966).
16 Thomson, G., Bodmer, W., and Bodmer, J., in *Histocompatibility Testing* (edit. by Kissmeyer-Nielsen E.) (Munksgaard, Copenhagen, in the press).
17 Yanagisawa, K., Pollard, D. R., Bennett, D., Dunn, L. C., and Boyse, E. A., *Immunogenetics*, **1**, 91–96, (1974).
18 Dunn, L. C., and Bennett, D., *J. Reprod. Fert.*, **20**, 239–246 (1969).
19 Bennett, D., and Dunn, L. C., in *Proc. Symp. Immunogenetics of the H-2 System* (edit. by Lengerova, A., and Vojtiskova, M.) 90–103 (Karger, Basel, 1971).
20 Levin, B. R., Petras, M. L., and Rasmussen, D. I., *Am. Nat.*, **103**, 647–661 (1969).
21 Bruck, D., *Proc. natn. Acad. Sci. U.S.A.*, **43**, 152–158 (1957).
22 Vitetta, E. S., Artzt, K., Bennett, D., Boyse, E. A., and Jacob, F., *Proc. natn. Acad. Sci. U.S.A.*, **72**, 3215–3219 (1975).
23 Julius, M. H., Simpson, E., and Herzenberg, L. A., *Eur. J. Immun.*, **3**, 645–649 (1973).
24 Hammerberg, C., Klein, J., Artzt, K., and Bennett, D., *Transplantation* (in the press).