MUTUAL RECOGNITION OF PARENTAL AND F1 LYMPHOCYTES

Selective Abrogation of Cytotoxic Potential of F1 Lymphocytes by Parental Lymphocytes

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The injection of F1 hybrid animals with parental spleen or lymph node cells leads to the activation of specific parental lymphocytes which recognize major histocompatibility complex (MHC) -coded antigens of the other parental haplotype expressed by the F1 host (1). Such recognition can result in graft-vs.-host (GVH) reactions which are frequently associated with depressed in vivo cell-mediated immune functions, such as resistance to bacterial infection (2), skin graft rejection (2, 3), T-helper cell dysfunction (4), as well as antibody responses to thymic-dependent and -independent antigens (5-8). The depression of T-cell-mediated lympholysis (CML) responses by cells from F1 hybrid mice injected with parental lymphocytes has not been reported but could provide a useful approach for investigating T-cell receptors because self MHC-restricted as well as allogeneic CML responses can be analyzed.

This report describes an experimental system in which intravenous injection of F1 hybrid mice with parental T-splenic lymphocytes can result in the abrogation or severe depression of CML potential. This loss of CML activity did not appear to be specific for self determinants because responses to alloantigens, trinitrophenyl (TNP)-modified F1 cells (TNP-self), and TNP-modified parental cells were all affected. However, an unexpected finding was the observation that the parental-induced CML depression was dependent upon the H-2 type of the injected parental lymphocytes. Thus, the injection of H-2<sup>+</sup>, H-2<sup>A</sup>, or H-2<sup>D</sup>, but not H-2<sup>B</sup>, parental lymphocytes resulted in depressed CML potential. These findings are discussed with respect to (a) the selective resistance of F1 mice to H-2<sup>B</sup> parental lymphocytes, and (b) the possibility that F1 lymphocytes recognize idiotypic determinants specific for non-H-2<sup>B</sup> antigens on H-2<sup>B</sup> lymphocytes, but not those for H-2<sup>B</sup> antigens on non-H-2<sup>B</sup> lymphocytes.

Materials and Methods

Mice. All mice used in this study were purchased from The Jackson Laboratory, Bar Harbor, Maine, except the (C57BL/6 × DBA/2)F<sub>1</sub> (B6D2F<sub>1</sub>), which were obtained from the Animal Production Unit, National Cancer Institute. Male mice, 6-8 wk of age, were used throughout these studies, except where otherwise noted.

Injection of F1 Hybrid Mice with Parental or F1 Spleen Cells. Cell suspensions were prepared in...
Hanks' balanced salt solution (HBSS) from the spleens of parental or F1 hybrid donors by
gentle teasing with a syringe fitted with an 18-gauge needle. The cell suspensions were filtered
through sterile nylon mesh to remove debris and cell clumps and exposed to NH₄Cl lysing
buffer to remove erythrocytes. The cells were then washed, counted, and resuspended in a vol
of 0.5 or 1.0 ml in HBSS and injected intravenously via the tail vein into normal F1 hybrid
mice.

Treatment of Spleen Cells with Rabbit Anti-Mouse Brain Serum. B10.BR spleen cells were
incubated at 25°C for 30 min, with a 1:10 dilution of rabbit anti-mouse brain serum (RAMB)
(Litton Bionetics, Kensington, Md.). The cells were then washed and incubated at 37°C for 30
min, with a 1:3 dilution of guinea pig complement (Grand Island Biological Co., Grand Island,
N. Y.). The cells were washed twice and injected into (B10 × B10.BR)F1 mice. B10.BR spleen
cells were also incubated with antiserum or complement alone as controls.

The In Vitro Generation and Assay for Cell-mediated Lympholysis. The CML potential of spleen
cells from the above injected mice were tested 4-28 d later by in vitro sensitization against
TNP-self and allogeneic spleen cells, as described elsewhere (9). The responding cells were
cultured with 2,000-rad-irradiated stimulating cells for 5 or 6 d, and the effectors generated
were assayed in a 4-h ⁵¹Cr-release assay (9) on 48-h phytohemagglutinin (PHA)-stimulated
(phytohemagglutinin M, Grand Island Biological Co.) splenic blasts. The percent lysis was
calculated as previously described (9) and standard errors of the mean have been excluded
from the figures for simplicity because they were usually <5% of the means.

Results
Depressed Cytotoxic Responses in F1 Hybrid Mice Injected with Parental Spleen
Cells. (C57BL/10 × B10.A)F1 hybrid mice [(B10 × B10.A)F1] were injected intravenously with either 2 × 10⁷ B10.A or 2 × 10⁷ C57BL/10 (B10) spleen cells. The cytotoxic potential of spleens from these two groups of mice was compared with that from untreated F1 control mice 14 d later by in vitro sensitization to (a) parental spleen cells modified with trinitrobenzene sulfonate (B10.A-TNP or B10-TNP), or (b) B10.D2 allogeneic spleen cells. The results, shown in Fig. 1, indicated that the injection of B10.A spleen cells abolished the ability of the spleen cells in the F1 mice to generate CML responses to B10.A-TNP, B10-TNP, or B10.D2 stimulating cells (compare Fig. 1B, E, and H with A, D, and G). In contrast, the injection of B10 spleen cells did not result in any detectable loss of CML potential to either B10.A-
TNP or B10-TNP (compare Fig. 1C and F with A and D). Thus, the injection of
B10.A but not B10 parental spleen cells resulted in the abrogation of CML. This
abrogation appeared not to be haploype-specific at the cytotoxic effector cell level
because the B10.A spleen cells affected the CML to TNP-self through either the H-2ᵃ
or H-2ᵇ haplotype as well as to alloantigens.

Kinetics of Depressed Cytotoxic Potential and Mortality in F1 Hybrid Mice Injected with
B10.A Parental Spleen Cells. Female (B10 × B10.A)F1 mice were injected intravenously with 2 × 10⁷ syngeneic F1, B10.A, or B10 spleen cells. At 4, 7, 14, and 21 d later, the spleens of the injected F1 mice were tested for CML potential by in vitro sensitization to (B10 × B10.A)F1-TNP (TNP-self). The results are summarized in
Fig. 2. Cytotoxic potential was abolished within 4 d of injection of B10.A parental
spleen cells and remained completely depressed throughout the 3-wk period. In this
experiment, some depression of CML potential was detected on the 4th and 14th d
after injection of B10 parental spleen cells.

A number of the injected F1 mice used for CML studies in Fig. 2 were set aside and
used for survival studies. Within 10 d most of the F1 mice injected with B10.A spleen
cells exhibited signs of weight loss, hunched posture, and ruffled fur. The mice injected
## Cell-mediated cytotoxicity to TNP-self and alloantigens, using spleen cells from (B10 × B10.A)F₁ mice

**Fig. 1.** Cell-mediated cytotoxicity to TNP-self and alloantigens, using spleen cells from (B10 × B10.A)F₁ mice: A, D, and G, uninjected; B, E, and H, injected with B10.A parental spleen cells; or C and F, injected with B10 parental spleen cells. Effector cells were generated by sensitization with: A, B, and C, B10.A parental spleen cells modified with 1 mM trinitrobenzene sulfonate (TNBS) (○), or with unmodified B10.A cells (■); D, E, and F, B10 parental spleen cells modified with 10 mM TNBS (○), or with unmodified B10 cells (■); G and H, B10.D2 allogeneic spleen cells (○), or with unmodified (B10 × B10.A)F₁ syngeneic spleen cells (○). Effectors were assayed on 48-h PHA-stimulated spleen blasts from: A, B, and C, B10.A parental spleen cells modified with 10 mM TNBS; D, E, and F, B10 parental spleen cells modified with 10 mM TNBS; or G and H, unmodified B10.D2 allogeneic spleen cells.

### Relative Frequency of B10.A Spleen Cells Required to Effect Depressed F₁ Hybrid Cytotoxic Response

To estimate the minimal number of injected B10.A spleen cells required to effect the depressed cytotoxic potential in the F₁ hybrid, (B10 × B10.A)F₁ mice were injected intravenously with different numbers of B10.A spleen cells ranging from 1.25 to 20 × 10⁶ per recipient. 2 wk later, spleen cells from the F₁ mice were sensitized in vitro to TNP-self and allogeneic stimulating cells. The results, summarized in Fig. 4, indicate that injection of as few as 5 × 10⁶ B10.A spleen cells results in complete abrogation of both the modified self and allogeneic CML. Both responses were severely depressed, although not totally abolished, by injection of 2.5 × 10⁶ cells. The
Cell-mediated cytotoxicity to TNP-self, with spleen cells from (B10 × B10.A)F1 mice: A, D, G, and J, injected with (B10 × B10.A)F1 syngeneic spleen cells; B, E, H, and K, injected with B10.A parental spleen cells; and C, F, I, and L, injected with B10 parental spleen cells. Effector cells to TNP-self were generated by sensitization with (B10 × B10.A)F1 syngeneic spleen cells modified with 10 mM TNBS (O) or with unmodified (B10 × B10.A)F1 syngeneic spleen cells (C) at varying times after injection: A, B, and C, 4 d; D, E, and F, 7 d; G, H, and I, 14 d; and J, K, and L, 21 d. Effectors were assayed on 48-h PHA-stimulated spleen blasts from (B10 × B10.A)F1 syngeneic spleen blasts modified with 10 mM TNBS.

Comparison of Depressed Cytotoxic Responses in Other F1 Hybrid Mouse Combinations. Because the injection of (B10 × B10.A)F1 mice (H-2b × H-2a) with B10 parental spleen cells resulted in only marginal (Fig. 2) or no (Fig. 1) depressed CML, experiments were performed with other parental and F1 combinations to determine whether depressed CML potential would be selective for one parental haplotype. (B10 × B10.BR)F1 mice (H-2b × H-2b), B6D2F1 mice (H-2b × H-2d), and (AKR × DBA/2)F1 (AKD2F1) mice (H-2k × H-2a) were injected with 2 × 10^7 spleen cells from the respective parental strains. 1–2 wk later, the cytotoxic potential of spleen cells from the injected F1 mice were compared with either un.injected F1 mice or F1 mice injected with syngeneic F1 spleen cells. The cytotoxic results for TNP-self and alloantigens (except for B6D2F1) obtained from these three strains are summarized in Figs. 5, 6, and 7. In both the (B10 × B10.BR)F1 (Fig. 5) and B6D2F1 (Fig. 6) mice, depressed

| (B10xB10 A)F1 MICE INJECTED WITH: | DAYS AFTER INJECTION: |
|-----------------------------------|----------------------|
| 2x10^7 (B10xB10 A)F1 Spleen Cells | 4 | 7 | 14 | 21 |
| 2x10^7 B10-A Spleen Cells         | A | D | G | J |
| 2x10^7 B10 Spleen Cells           | B | E | H | K |

Fig. 2. Cell-mediated cytotoxicity to TNP-self, with spleen cells from (B10 × B10.A)F1 mice: A, D, G, and J, injected with (B10 × B10.A)F1 syngeneic spleen cells; B, E, H, and K, injected with B10.A parental spleen cells; and C, F, I, and L, injected with B10 parental spleen cells. Effector cells to TNP-self were generated by sensitization with (B10 × B10.A)F1 syngeneic spleen cells modified with 10 mM TNBS (O) or with unmodified (B10 × B10.A)F1 syngeneic spleen cells (C) at varying times after injection: A, B, and C, 4 d; D, E, and F, 7 d; G, H, and I, 14 d; and J, K, and L, 21 d. Effectors were assayed on 48-h PHA-stimulated spleen blasts from (B10 × B10.A)F1 syngeneic spleen blasts modified with 10 mM TNBS.

injection of 1.25 × 10^6 spleen cells did not detectably reduce the cytotoxic potential to either TNP-self or alloantigen.
Fig. 3. Survival of (B10 × B10.A)F1 mice injected with: 2 × 10^7 (B10 × B10.A)F1 syngeneic cells (○); 2 × 10^7 B10.A parental cells (● – ●); or 2 × 10^7 with B10 parental cells (● – ○).

Fig. 4. Cell-mediated cytotoxicity to TNP-self and alloantigens, with spleen cells from (B10 × B10.A)F1 mice: A and G, un.injected; B and H, injected with 20 × 10^6 B10.A parental cells; C and I, injected with 10 × 10^6 B10.A parental cells; D and J, injected with 5 × 10^6 B10.A parental cells; E and K, injected with 2.5 × 10^6 B10.A parental cells; F and L, injected with 1.25 × 10^6 B10.A parental cells. Effector cells were generated: A-F to TNP-self by sensitization with (B10 × B10.A)F1 syngeneic cells modified with 10 nM TNBS (●) or with unmodified (B10 × B10.A)F1 syngeneic cells (○); or G-L to allogeogenic determinants by sensitization with unmodified B10.D2 allogeneic cells (○) or with unmodified (B10 × B10.A)F1 syngeneic cells (○). Effectors were assayed on 48-h PHA-stimulated spleen blasts from: A-F (B10 × B10.A)F1 syngeneic spleen cells modified with 10 mM TNBS; or G-L unmodified B10.D2 spleen cells.
CML responses were observed when B10.BR or DBA/2 parental spleen cells were injected. However, in neither of these combinations did the injection of $H-2^b$ B10 or B6 parental spleen cells result in depressed CML. These results resemble the $(B10 \times B10.A)F_1$ observations illustrated in the preceding figures in that injection of only the non-$H-2^b$ parental cells resulted in depressed CML. In contrast to these three $F_1$ combinations, AKD2F1 CML potential was depressed by injection of either AKR or DBA/2 parental spleen cells, although the reduction in responsiveness to TNP-self was not as pronounced (Fig. 7). Also, only a slight depression was detected in the allogeneic CML. These results indicate that the injection of parental spleen cells expressing the $H-2^{k,n,d}$ haplotypes results in severely depressed or abrogated CML potential, whereas the injection of $H-2^b$ parental spleen cells results in marginal or no reduction in CML activity. The data also suggest that C57BL background genes may be important because the results of AKD2F1 mice were not as clear.

Depressed $F_1$ Cytotoxic Response Depends upon a Radiosensitive, Parental $T$
Lymphocyte. Spleen cells from B10.BR mice were either unirradiated or irradiated with 500, 1,000, or 2,000 rads of α-irradiation and then injected (20 × 10^6 per recipient) into (B10 × B10.BR)F1 mice. 2 wk later, the cytotoxic potential to TNP-self and alloantigen was tested. The results (Fig. 8) indicate that the depressed F₁ response depends upon injection of a radiosensitive population of B10.BR spleen cells, because irradiation with as little as 500 rads abolished the cytotoxic depressive effect of the B10.BR cells.

Spleen cells from B10.BR mice were incubated with RAMB, complement, or RAMB plus complement before injection (20 × 10^6 per recipient) into (B10 × B10.BR)F1 mice. 2 wk later, the cytotoxic potential to TNP-self was compared in these mice with that from uninjected F₁ mice. The results are shown in Fig. 9. Injection of B10.BR spleen cells that had been incubated with RAMB with or without complement did not result in depressed CML potential. The apparent lack of a complement requirement might imply that the F₁ host provided an in vivo source of complement or that the abrogation of CML depression with RAMB was complement independent. These results are compatible with the CML depressive activity of B10.BR spleen cells being a result of a population of T-lymphocytes.
Fig. 7. Cell-mediated cytotoxicity to TNP-self and allogeneic determinants, with spleen cells from AKD2F1 mice: A and E, uninjected; B and F, injected with 2 × 10⁷ syngeneic AKD2F1 spleen cells; C and G, injected with 2 × 10⁷ AKR parental spleen cells; or D and H, injected with DBA/2 parental spleen cells. Effectors were generated: A, B, C, and D, to TNP-self by sensitization with AKD2F1 syngeneic spleen cells modified with 10 mM TNBS (○) or with unmodified AKD2F1 cells (□); or E, F, G, and H, to allogeneic determinants by sensitization with B6 allogeneic spleen cells (●) or with unmodified AKD2F1 spleen cells (□). Effectors were assayed on 48-h PHA-stimulated spleen blasts from: A-D, AKD2F1 syngeneic spleen cells modified with 10 mM TNBS; or E-H, unmodified C57BL/6 spleen cells.

Fig. 8. Cell-mediated cytotoxicity to TNP-self and alloantigens, with spleen cells from (B10 × B10.A)F1 mice: A, uninjected (●); injected with B10.A parental cells (□—□), injected with B10.A parental cells, irradiated with 500 rads (○), 1,000 rads (△), or 2,000 rads (▲). Effectors were generated: A, to TNP-self by sensitization with (B10 × B10.A)F1 syngeneic spleen cells modified with 10 mM TNBS (solid line) or with unmodified (B10 × B10.A)F1 syngeneic spleen cells (○ — ○); or B, to allogeneic determinants by sensitization with unmodified B10.D2 allogeneic spleen cells (solid line) or with unmodified (B10 × B10.A)F1 syngeneic spleen cells (○ — ○). Effectors were assayed on 48-h PHA-stimulated spleen blasts from A, (B10 × B10.A)F1 syngeneic spleen cells modified with 10 mM TNBS or B, unmodified allogeneic B10.D2 spleen cells.
Fig. 9. Cell-mediated cytotoxicity to TNP-self from (B10 × B10.BR)F1 mice: uninjected (○); injected with untreated B10.BR parental cells (▲); injected with B10.BR parental cells treated with complement (▼), with RAMB (△), or with RAMB plus complement (□—□). Effector cells to TNP-self were generated by sensitization with (B10 × B10.BR)F1 syngeneic spleen cells modified with 10 mM TNBS (solid line) or with unmodified (B10 × B10.BR)F1 syngeneic spleen cells (○—○). Effectors were assayed on 48-h PHA-stimulated spleen blasts from (B10 × B10.BR)F1 syngeneic spleen cells modified with 10 mM TNBS.

Discussion

This report has demonstrated (a) that F1 hybrid mice injected with non-H-2<sup>b</sup> parental spleen cells become incapable of generating T-cell-mediated cytotoxic responses to either TNP-self or alloantigens; (b) that the unresponsiveness is induced by a relatively low number of radiosensitive parental T lymphocytes; (c) that the unresponsive state appears early, persists for at least 3 wk, and is associated with late mortality; and (d) that such depressed F1 T-cell immune potential is not induced by injection of H-2<sup>b</sup> parental T cells. Interpretation of our findings require that we consider both the phenomenon in which injection of F1 mice with non-H-2<sup>b</sup> parental spleen cells resulted in severely impaired CML potential, and that in which F1 mice injected with H-2<sup>b</sup> parental spleen cells did not result in abrogation of cytotoxic potential.

The observation that injection of non-H-2<sup>b</sup> parental spleen cells into F1 mice resulted in depressed CML activity could be a result of some type of parental-induced immunoincompetence in the F1 hybrid or to active suppression induced by the parental lymphocytes. A future report will demonstrate that lymphocytes from F1 mice injected with parental spleen cells are capable of suppressing CML response of spleen cells from normal F1 mice (Manuscript in preparation.).

The observation that injection of parental spleen cells expressing the H-2<sup>b</sup> haplotype did not result in depressed CML activity could be accounted for by at least two mechanisms. First, the component of H-2<sup>b</sup> spleen cells responsible for depressed CML could be relatively less reactive against the alloantigens expressed on the F1 cells than that of spleen cells from H-2<sup>k,a,d</sup> mice. Second, the F1 host could be resistant (possibly immune) to the H-2<sup>b</sup>, but not to the H-2<sup>k,a,d</sup>, parental T-lymphocytes. Such resistance or immunity could be associated with recognition by F1 lymphocytes of idioptypic determinants for H-2<sup>k,a,d</sup>-coded alloantigens on H-2<sup>b</sup> parental lymphocytes (10-13). The first of the above two mechanisms could be excluded and the second mechanism would be likely if we could abolish the putative F1 resistance, thereby permitting the
$H-2^b$ T-cells to initiate the CML depression. Data to be reported later (Manuscript in preparation.) demonstrate that the spleens of 850-rads-irradiated F1 mice injected with $H-2^b$ parental spleen cells are potent suppressors of the CML response by spleen cells from normal F1 mice. Furthermore, the CML responses of F1 mice can be depressed by injection of either B10 or B10.A parental spleen cells when the inoculum is increased to 5 x 10^7 cells (Unpublished observations.). Thus, it appears that the second mechanism, i.e., that there is F1 resistance mediated by a radiosensitive population of F1 cells, is correct. These results indicated that such resistance or immune potential to parental lymphocytes (possibly expressing idiotypic determinants) is not equivalent for the two parent haplotypes in $b \times k$, $b \times a$, and $b \times d$ F1 mice, because resistance was detected only to the $H-2^b$ parent. Such differential resistance in these F1 mice raises the possibility of genetic control for recognition of the parental determinants by F1 cells.

The limited genetic studies included in this report are of additional interest, because depressed F1 CML potential was observed by injection of spleen cells from either parental strain in only one of the four combinations tested, i.e., AKD2F1 injected with AKR or DBA/2 parental spleen cells. This contrasts with the results obtained in the other three combinations, i.e., (B10 x B10.A)F1, (B10 x B10.BR)F1, and B6D2F1, in which injection of cells from the parent expressing the $H-2^a$, $H-2^k$, or $H-2^d$ haplotypes, respectively, but not the parent expressing the $H-2^b$ haplotype (common to all three of these F1 combinations, but not common to the AKD2F1), led to depressed cytotoxic potential. This genetic pattern is consistent with F1 anti-parent natural resistance to the $H-2^D-Hh-1$ (14) determinant expressed by homozygous $H-2^b$ hemopoietic cells, and demonstrated by F1 resistance to marrow grafts (14, 15) and GVH (16). Furthermore, the observation that CML depression in AKD2F1 mice injected with parental spleen cells was not as dramatic as that in the F1 strains (injected with non-$H-2^b$ parental cells) which expressed C57BL background genes, could indicate an effect of non-$H-2$ linked genetic factors in the F1 resistance patterns.

The similarities and differences between our study and that of Bellgrau and Wilson (12, 13) are worth considering. These investigators have shown that F1 hybrid rats can be specifically immunized with parental lymphocytes, and that such immunized F1 rats become resistant to lethal GVH disease after sublethal irradiation and challenge with the same parental lymphocytes (12, 13). Their results have been interpreted to mean that the F1 rats were immunized to allogeneic receptors expressed by the parental lymphocytes (12, 13). Two discrepancies appear to exist between our results and those of Bellgrau and Wilson (12, 13). First, a similar immunization protocol of F1 animals by parental lymphocytes resulted in resistance to GVH in their studies, whereas it resulted in immunosuppression in our experiments. Second, sublethal irradiation was required to induce GVH disease leading to death of the F1 rats (12), whereas we were able to induce mortality (possibly a result of GVH disease) in unirradiated F1 mice. A more careful analysis of our immune suppression and GVH disease results indicates that these phenomena were parental strain specific, because the B10.A spleen cells initiated both CML suppression and GVH disease, whereas the B10 spleen cells did not. Thus, our findings do not contradict the F1 parental rat study when we consider the F1 and B10 mouse results. Our present interpretation of the results is that the (B10 x B10.A)F1 mice possess resistance to the B10 but not to the B10.A parental lymphocytes, and that this resistance is radiosensitive. In the rat
studies, it is possible that F₁ rats possess natural immunity to both parental haplotypes, that this immunity is radiosensitive, and that it can be primed to generate a population of radioresistant immune cells which protect against GVH disease. Studies are in progress to establish whether (a) the natural resistance we detect in (H-2^b × H-2^a)F₁ mice to H-2^b parental T lymphocytes has any anti-H-2^a receptor specificity; (b) these F₁ mice are genetically deficient in their immune potential against anti-H-2^b receptors expressed on H-2^a T-lymphocytes; and (c) (H-2^b × H-2^a)F₁ mice can be selectively and specifically immunized against only the anti-H-2^a receptors on H-2^b or allogeneic lymphocytes.

Summary

Four different combinations of F₁ hybrid mice [(C57BL/10 × B10.A)F₁, (C57BL/10 × B10.BR)F₁, B6D2F₁, and AKD2F₁] were injected intravenously with spleen cells from parental strains. The T-cell-mediated cytotoxic potential of spleen cells from the injected F₁ mice was assessed from 4 to 21 d later by in vitro sensitization with trinitrophenyl-modified parental or syngeneic F₁ spleen cells (TNP-self) or with allogeneic spleen cells. The cytotoxic potential of the F₁ mice to TNP-self as well as to alloantigens was abolished or severely depressed throughout this period when the respective H-2^k'''d parental spleen cells were injected. In contrast, the cytotoxic potential was unaffected or only marginally reduced when H-2^b parental cells were injected. The induction of depressed cytotoxic activity was shown to be a result of a population of parental radiosensitive T lymphocytes. The results should be discussed with respect to (a) the genetic and mechanistic parameters associated with the differential depressive effects of parental cells expressing H-2^b vs. H-2^k'''d antigens, and (b) the use of this system for investigating allogeneic receptors on T-lymphocyte populations.

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