Immunobiology

Zeitschrift für Immunitätsforschung

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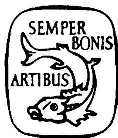

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Editorial Comment

Starting with Volume 156, 1979, the name of the «Zeitschrift für Immunitätsforschung» has been changed to

«Immunobiology»

The «Zeitschrift», founded in 1909 by Paul Ehrlich, was the first immunological journal to be published in the world. The journal has a long-lived reputation as being an important source of scientific information based on the contributions of famous immunologists. The increased use of English as the common scientific language has now prompted the Editorial Board to change the traditional German title to «**Immunobiology**». With this title change the journal emphasizes its international character as a forum for the publication of a variety of different articles in the broad field of immunology.

The Editorial Board of Immunobiology

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Generation of Effector Cells from T Cell Subsets. I. Similar Requirements for Lyt T Cell Subpopulations in the Generation of Alloreactive and H-2 Restricted Killer Cells

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Abstract

Lyt T cell subsets involved in the generation of H-2 restricted and alloreactive cytotoxic effector cells were analysed using anti Lyt antisera. Our data show that Lyt 1, 2, 3^+ T cells are required for the induction of primary and secondary H-2 restricted and TNP-specific killer cells. In contrast, primary and secondary H-2 restricted and virus-specific T effector cells were obtained from selected Lyt 2, 3^+ T cell populations and were not dependent on the presence of Lyt 1, 2, 3^+ T cells. Allogeneic responses to selected K, I, or D region differences were obtained only in the presence of Lyt 1, 2, 3^+ T cells; yet alloreactive killer cells were effectively generated from selected Lyt 2, 3^+ T cell populations deprived of Lyt 1, 2, 3^+ T cells, when responder and stimulator cells differed at either K + D, K + I, I and D regions or in the entire H-2 region.

Taken together, the results suggest that there is no qualitative difference between alloreactive and H-2 restricted cytotoxic responses in their requirements for particular Lyt T cell subsets. The findings indicate that the number of different antigenic determinants rather than their association with MHC self determinants is critical for the requirement of Lyt 1, 2, 3^+ T cells during the sensitization phase.

Introduction

It is now well established that the effector functions of thymus derived lymphocytes involved in the regulation of the immune response are mediated by T cell subpopulations. The classification of the T cell lineage into subsets was made possible by the discovery of cell surface markers.

Using the Lyt alloantigen system, described by BOYSE and co-workers (1, 2), it has been demonstrated that T lymphocyte subsets with known functional capacities also show characteristic distribution patterns of these surface structures (3, 4, 5, 6). Current information suggests that in the mouse T cells expressing the Lyt 1^+, Lyt 2, 3^- surface phenotype play an obligatory helper or accessory role in most immune responses (4, 5). In contrast, T cells which express the Lyt 1^-, Lyt 2, 3^+ phenotype develop both the capacity to suppress immune responses as well as the ability to elicit alloreactive cytotoxic activity (5, 6, 7, 8).

However, it has recently been shown by CANTOR and BOYSE that the generation of H-2 restricted cytotoxic lymphocytes specific for TNP-modified syngeneic cells requires the presence of Lyt 1, 2, 3^+ cells in the induction phase (9). The authors suggested that the Lyt 1, 2, 3^+ cells probably represent the killer cell precursor population but it is still possible that these cells represent the helper cell population involved in the generation of cytotoxic effector cells from Lyt 2, 3^+ killer cell precursors. The finding by BURAKOFF et al. (10) that the H-2 restricted and TNP-specific cytotoxic activity generated from a cell mixture containing the Lyt 2, 3^+ T cell subset from one strain and the unselected T cell population from the Lyt congenic partner was only abolished by anti-Lyt 2 antisera specific for the unselected T cell population, was interpreted in favour of Lyt 1, 2, 3 T cells consisting of H-2 restricted killer cell precursors. Similar requirements for Lyt 1, 2, 3 T cells were reported for the generation of H-2 restricted and virus specific cytotoxic lymphocytes (10), which implies that alloreactive and H-2 restricted killer cells are generated by different pathways.

The data reported in this paper show that Lyt 1, 2, 3^+ cells are required for the induction of some, but not all, H-2 restricted cytotoxic responses in vitro.

Furthermore, we demonstrate that there is also a requirement for Lyt 1, 2, 3^+ T cells in the generation of alloreactive cytotoxic activity against MHC sub regions.

Altogether, the presented data suggest that the differences seen for the induction requirements of H-2 restricted and alloreactive cytotoxic effector cells in their requirements for T cell subsets are quantitative rather than qualitative.

Materials and Methods

Mice

6 to 12 week old male or female mice were used for the experiments. All strains used were bred in our own colony: C57Bl/6, C57Bl/10, B10.D2, B10.Br, B10.A, B10.A(2R), B10.A(4R), B10.AKM, Balb/c, C.B-17, ATL, and A.AL. All mice used for the generation of anti-Lyt antisera, B6-Lyt 1.1 congenic mice (Lyt phenotype 1.1, 2.2, 3.2), B6-Lyt 2.1 congenic mice (Lyt phenotype 1.2, 2.1, 3.2), B6-Lyt 2.1, 3.1 congenic mice (Lyt phenotype 1.2, 2.1, 3.1), as well as the CE F2 Lyt 1.2 homozygous, Lyt 2.1 homozygous and Lyt 3.2 homozygous animals, originally obtained by Dr. Shen and Dr. Boyse, were also maintained in our colony.

Viruses

Sendai virus (kindly provided by Dr. M.-G. Gething, ICRF, London) and influenza A virus (A/Victoria H_3N_2, kindly provided by Dr. Rott, Gießen) were grown in 10 day old embryonated chicken eggs. Harvesting and purification of virus was done as described previously (11).

Immunizations and sensitizations

Mice were injected i.p. with 100 haemagglutinating units (HAU) of infective virus. Lymphocytes from spleen and lymph nodes were removed 3–10 weeks afterwards and analyzed in

vitro. Mice were sensitized to TNP by skin painting with 30% picrylchloride in acetone and the spleen cells were removed 7 days later.

Media

MLC's were performed in RPMI 1640 supplemented with L-glutamine (2 mM final concentration), streptomycine and penicillin (50 U/ml), Hepes buffer (25 mM final concentration), 2-mercaptoethanol (2×10^{-5} M) and 10% selected fetal calf serum.

Tumor cells P-815 (H-2^d) and RBL-5 (H-2^b) tumor cells were grown in medium at a concentration of 2×10^5 cells/ml with medium change after every 48 hours.

Antisera

Anti-Thy 1.2 antiserum (AKR anti C3H) was kindly provided by Dr. B. RUBIN, Statens Seruminstitut, Copenhagen, Denmark. Anti-Lyt antisera were prepared as described by SHEN et al. (12). Briefly, anti-Lyt 1.2 antisera were prepared by injecting C3H/An mice with thymocytes from (C3H/An × CE)F2 mice homozygous for the Lyt 1.2 allele. Anti-Lyt 2.2 antisera were prepared by injecting (C3H/An × B6/Lyt 2.1, 3.2)F1 hybrids with thymocytes from C57Bl/6 mice. Anti-Lyt 3.2 antisera were prepared by injecting C58 mice with thymocytes from (C58 × CE)F2 mice homozygous for the Lyt 3.2 allele. After 1 subcutaneous injection of $50–100 \times 10^6$ donor thymocytes and three additional intraperitoneal injections of $50–100 \times 10^6$ donor thymocytes at 14 day intervals, each mouse was tested individually and those selected for further immunization were mice that produced good specific titers after removal of autoantibodies by absorption on thymocytes from the recipient strains. Selected mice were bled on days 7 and 10 after each inoculation and the sera from several bleedings were pooled and stored at −70 °C. Prior to use the Lyt antisera were absorbed once on 100×10^8 thymus and lymph node cells from the recipients and the B6 congenic strain (carrying the irrelevant Lyt allele) per ml undiluted antisera to remove autoantibodies. In a microcytotoxicity test the titer of anti-Lyt 1.2 was 1:250, the titer of anti-Lyt 2.2 was 1:250 and the titer of anti-Lyt 3.2 was 1:500 on thymocytes of strain C57Bl/6 after the removal of autoantibodies. Anti Lyt 1.2 antisera were negative on lymphocytes of B6/Lyt 1.1 congenic mice, anti-Lyt 2.2 and anti-Lyt 3.2 antisera were negative on lymphocytes of B6 Lyt 2.1, 3.1 congenic mice. The anti-Lyt 1.2 antisera as well as the anti-Lyt 2.2 antisera were used at a final dilution of 1:20. The anti-Lyt 3.2 antisera were used at a final dilution of 1:40.

For treatment of lymphocytes with antisera and complement prior to in vitro stimulation 30×10^6/ml normal lymph node or spleen cells, or nylon wool purified splenic T cells were incubated with anti-Thy 1.2 antiserum (1:20 final dilution) or the appropriate anti-Lyt antisera in RPMI 5% fetal calf serum and incubated for 30 min at room temperature. Cells were centrifuged and resuspended in freshly thawed selected rabbit serum (dilution 1:10 to 1:12) as a source of complement in 5% FCS/RPMI and incubated for an additional period of 30 min at 37 °C. The treatment of cells with anti-Lyt antisera and complement was repeated once to obtain highly purified Lyt subsets. Cytotoxic effector lymphocytes generated from lymph node or spleen cells or nylon wool purified T cells in 4–5 days MLR's were treated with Lyt antisera and complement as described above.

In vitro generation of effector cells

5×10^6 responder cells were incubated at 37 °C with 1×10^6 to 2.5×10^6 stimulator cells in 2 ml in Linbro macrotiter plates (FB 16–24 TC) and incubated for 4–6 days in humidified air plus 5% CO_2. Purified splenic T cells were obtained as described by JULIUS et al. (13). As stimulator cells, allogeneic B cells, obtained by treatment of spleen cells with anti-Thy 1.2 plus complement, TNP modified syngeneic spleen cells or syngeneic cells preincubated with viral antigens (10 µg Sendai virus, β-propiolactone inactivated/10^6 cells) for 1 hour at 37 °C were used.

Cell mediated lymphocytotoxicity assay and analysis of data

Following the 5 day incubation period cytotoxic activity of effector cells was tested on either chromium labelled concanavalin A (Con A) spleen cell blasts or tumor cells. Con A blasts were

obtained by stimulating 12.5 × 10^6 spleen cells with 5 μg/ml Con A (Miles-Yeda, Ltd., Illinois 60901, Code 79-002) in 6 ml media (2, 4) and incubated for 48 hours. Con A blasts and tumor cells were labelled with ^{51}chromium. 2 × 10^4 blast cells or 1 × 10^4 tumor cells were incubated for 4 hours at 37 °C with various numbers of cytotoxic T cells in 200 μl RPMI medium (containing 10% fetal calf serum and 0.1 mM Hepes buffer, final concentration) in round bottom microtiter plates (Linbro IS-MRC-96). Afterwards, the plates were spun for 5 minutes at 1500 rpm, 100 μl of the supernatant were removed, and the isotope released from the ^{51}Cr labelled target cells was counted. An aliquot of the target cells were frozen and thawed four times so that maximum ^{51}Cr release could be determined. The percentage of ^{51}Cr release from target cells was determined using triplicate samples and calculated by the following formula:

$$\%\ \text{specific lysis} = \frac{^{51}\text{Cr release by immune cells} - {}^{51}\text{Cr release by normal cells}}{\text{max. }^{51}\text{Cr release} - {}^{51}\text{Cr release by normal cells}} \times 100$$

All measurements were performed in triplicate and the standard error of the mean was always less than 5%.

Mixed lymphocyte culture

Proliferative response of mixed lymphocyte cultures was tested by removing 100 μl from the bulk cultures and labelling with ^{3}H (thymidine) (The Radiochemical Center, Amersham Buchler, England, 2 Ci/nm) at 2 μCi/well for 12 hours. Specific incorporation was determined by substracting background responses of responder cells incubated with syngeneic irradiated cells.

Results

Generation of primary alloreactive and H-2 restricted cytotoxic lymphocytes from unselected and selected T cell populations

In order to determine the Lyt phenotype of killer cell precursors in a primary response to alloantigen or NAD (new antigenic determinants) formed by TNP or Sendai virus on syngeneic cells, lymphocytes were pretreated with either anti-Lyt 1 or anti-Lyt 2, 3 antisera and complement. Thereafter, the treated cell populations were cultured either separately or as a 1:1 mixture of the two populations selected for Lyt 1^+ or Lyt 2.3^+ T cells, respectively with the sensitizing antigen.

Figure 1 shows typical response patterns of unprimed splenic lymphocyte populations, either unselected or selected for Lyt T cell subsets and activated by allogeneic stimulators or syngeneic cells modified with TNP or Sendai virus respectively. B6 Lyt $2,3^+$ splenic T cells were able to mount a primary cytotoxic response to irradiated H-2 incompatible B10.D2 cells. The same population was unable to respond in a primary reaction to TNP haptenated syngeneic cells, even in the presence of Lyt 1^+ helper cells, which augment the cytotoxic response of Lyt $2,3^+$ T cells to the alloantigen. Balb/c Lyt $2,3^+$ T cells as well as the mixture consisting of Lyt 1^+ and Lyt $2,3^+$ T cells were very efficient in eliciting a primary cytotoxic response to virus infected stimulators. The conditions for induction of a primary antiviral cytotoxic response and the distinction from a secondary response by functional criteria have been described in a preceding paper (11). The data depicted in Figure 1 clearly demonstrate that the presence of Lyt $1.2.3^+$ cells are only required for the formation of primary H-2 restricted and TNP

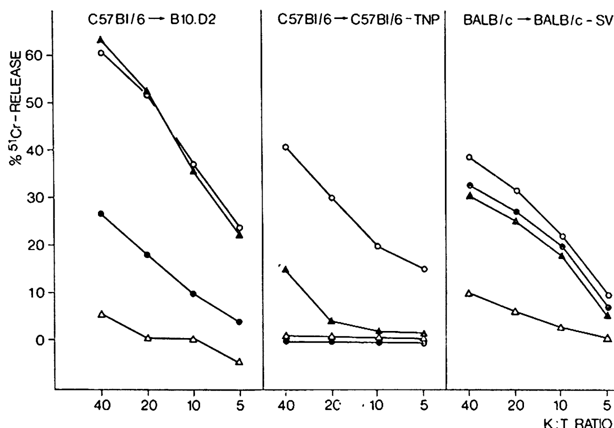

Fig. 1. Effect of pretreatment of CTL precursors specific for TNP, Sendai virus and alloantigens with anti Lyt antisera and complement prior to culture on the generation of primary cytolytic activity. 5×10^6 splenic responder cells (B6) were cultured for 5 days with 1×10^6 irradiated syngeneic TNP conjugated spleen cells or 2.5×10^6 irradiated DBA spleen cells. 5×10^6 nylon purified Balb/c T responder cells were cultivated in the presence of 1 μg inactivated Sendai virus/ml. Cultures were tested on day 5 for cytolytic activity on the relevant targets (see Materials and Methods) ○—○, unselected population; △—△, selected for Lyt 1^+ cells; ●—●, selected for Lyt $2,3^+$ cells; ▲—▲, selected for Lyt 1^+ and Lyt $2,3^+$ cells (1:1). Numbers on the abscissa indicate effector to target ratio.

specific cytotoxic lymphocytes but not for the generation of primary H-2 restricted and virus specific or alloreactive cytotoxic lymphocytes.

H-2 restricted as well as alloreactive cytotoxic effector cells generated to either TNP + self or viral + self or alloantigens respectively, were sensitive to treatment with anti-Thy 1.2 or anti-Lyt 2,3 but not to anti-Lyt 1 antisera and complement and are, therefore, Thy 1^+, Lyt 1^-, Lyt $2,3^+$ (data not shown).

Generation of secondary H-2 restricted cytotoxic lymphocytes specific for TNP or viral antigen from unselected and selected T cell populations

Since different T cell populations may participate in a secondary cytotoxic response in vitro we investigated the requirements for Lyt subpopulations in the formation of a secondary H-2 restricted cytotoxic response after priming in vivo. Secondary H-2 restricted TNP specific cytotoxic lymphocytes were generated by restimulation of splenic T cells from mice previously sensitized to TNP (skin painting) with irradiated and TNP modified syngeneic cells in vitro. Primed anti-TNP specific killer cell precursors are distinguishable from virgin precursor CTL's by functional criteria. We found that only primed T cells but not unprimed T cells enriched on nylon columns were able to mount an effective TNP specific cytolytic activity in vitro (M. SIMON, unpublished observation). Secondary H-2 restricted cytotoxic lymphocytes specific for influenza A (strain A

Victoria H3N2), were obtained by restimulating nylon wool enriched splenic T cells in vitro from mice previously sensitized in vivo using virus infected cells as stimulators. Figure 2 summarizes the results of an experiment in which nylon wool purified splenic T cells either unselected or selected for Lyt subsets from C.B-17 were restimulated with TNP modified

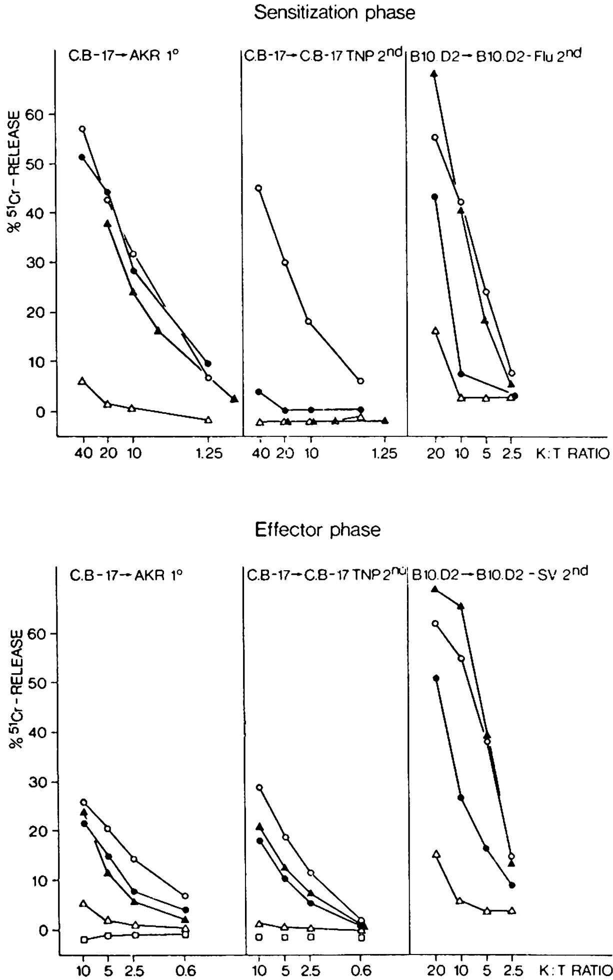

Fig. 2. Effect of pretreatment of unprimed alloreactive and primed TNP or primed influenza A virus specific lymphocytes with anti Lyt antisera and complement prior to the sensitization phase or prior to the effector phase on the generation and cytolytic activity of CTL's in vitro. 5×10^6 TNP primed C.B-17 nylon purified T cells were incubated with 1×10^6 irradiated syngeneic TNP modified stimulator cells or with 2.5×10^6 irradiated AKR spleen cells. 5×10^6 SV primed and nylon purified B10.D2 T cells were cultured in the presence of 1 µg inactivated Sendai virus/ml. Cultures were tested on day 5 in the ^{51}Cr release assay as described in Materials and Methods. ○—○ unselected populations; ▲—▲ selected for Lyt 1^+ cells; selected for Lyt $2,3^+$ cells; ●—● selected for Lyt 1^+ and Lyt $2,3^+$ cells (1:1); □—□ cells treated with āThy 1 and complement.

syngeneic cells or co-cultured with allogeneic stimulator cells from strain AKR. In addition, the secondary responses of unselected T lymphocytes as well as Lyt 1^+ and/or Lyt $2,3^+$ T cells from strain B10.D2 to influenza A modified syngeneic cells are depicted in the same Figure 2. Secondary TNP-specific killer cells were only generated from unselected populations and were not obtained from Lyt $2,3^+$ T cells alone. In most experiments the mixed population comprised of Lyt 1^+ and Lyt $2,3^+$ T cells was also ineffective in generating TNP specific cytolytic effector cells. In contrast, the mixed population was very efficient in eliciting effective responses to viral- or alloantigens. As seen before, primary alloreactivity was also obtained from Lyt $2,3^+$ T cells in the absence of Lyt 1^+ T cells. Thus, as for the primary cytotoxic response Lyt $1,2,3^+$ T cells are also involved in the generation of secondary cytotoxic lymphocytes to TNP-coupled syngeneic stimulator cells. The same population is not required during the induction of secondary responses to influenza A viral antigens (also found in secondary responses to Sendai virus; data not shown). Figure 2 also compiles data showing that alloreactive as well as secondary H-2 restricted cytotoxic effector cells specific for TNP or viral antigen are Lyt 1^- Lyt $2,3^+$.

Requirements for Lyt T cell subsets in the generation of cytotoxic responses to antigens encoded by different regions within the H-2 complex

The finding that there is a different requirement for Lyt $1,2,3^+$ cells in the generation of H-2 restricted cytotoxic T cells to different modifying antigens prompted us to study the participation of Lyt T cell subsets in the induction of alloreactive T cells specific for selected MHC determinants. Lymph node cells from different mouse strains were pretreated with anti-Lyt 1 or anti-Lyt 2,3 antisera and complement. Responder populations selected for T cell subsets were co-cultured with anti-Thy 1 plus complement treated and x-irradiated spleen cells (B cells) as stimulators. The latter treatment was done to avoid a possible stimulating effect of the irradiated allogeneic T cell population (14). Responder and stimulator cells differed at either the K, I or D regions alone or were incompatible at either the K and I, K and D, I and D or the whole MHC region, respectively. The data presented in Figure 3 reveal that Lyt $1,2,3^+$ T cells are essential for the formation of cytotoxic responses to either K (ATL anti A.AL), D (B10.A anti B10.A [2R] or I (ATL anti ATH) region differences alone. This is abvious from the fact that neither the Lyt $2,3^+$ T cell subset alone nor the mixture containing Lyt 1^+ and Lyt $2,3^+$ T cells are able to mount an effective response to the appropriate antigen. In contrast, Lyt $1,2,3^+$ T cells were not required for the generation of cytotoxic activities when responder and stimulator cells differed at either the K and I (B10 anti B10.A [4R]), the K and the D (ATL anti B10.AKM), the I and D regions (B10.Br anti B10.A [4R]) or in the whole MHC complex (B10.Br anti B6), respectively. In the latter three combinations cytotoxic lymphocytes were obtained from either Lyt $2,3^+$ T cells alone or in mixed populations consisting, in addition, Lyt

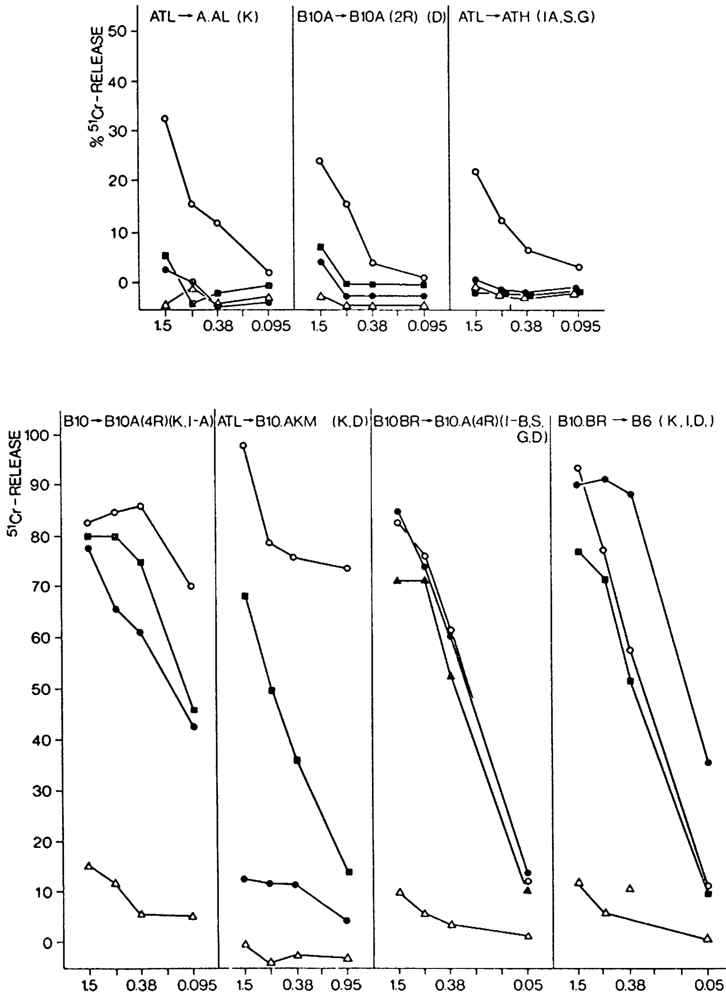

Fig. 3. Effect of pretreatment of alloreactive CTL precursors with anti Lyt antisera and complement prior to culture on the in vitro generation of cytolytic activity. 5×10^6 lymph node responder cells were cultured with 2.5×10^6 irradiated stimulator cells (B cells). Effector cells were tested on day 5 in a ^{51}Cr release assay. O—O unselected population; △—△ selected for Lyt 1^+ cells; ●—● selected for Lyt $1,2,3^+$ cells; □—□ selected for Lyt 1^+ and Lyt $2,3^+$ cells. Numbers on the abscissa indicate the number of responder cells ($\times 10^6$) cultured on day 0, the descendents of which are tested on 2×10^4 target cells.

1^+ T cells. In the experiment depicted in Figure 3, aliquots of the same ATL responder Lyt T cell subsets were used to react to either K, I or K plus D region differences. Thus, the lack of generation of cytolytic activity to K or I region differences alone from the mixed population containing Lyt 1^+ and Lyt $2,3^+$ T cells could not be due to unspecific removal of all Lyt 2,3 killer cell precursors.

Table 1. MHC difference between responder and stimulator cells Δ cpm[a])

Responding cell population	K		D		I-A, S, G		K, I-A		K, D		I-B, S, G, D	
	d 3	d 4	d 3	d 4	d 3	d 4	d 3	d 4	d 3	d 4	d 3	d 4
untreated (C′)	24,686	n.d.	14,308	18,970	49,133	37,117	54,090	n.d.	49,964	43,012	n.d.	26,565
Lyt $2,3^{+}$	2,913	n.d.	5,208	4,627	14,303	9,819	8,576	20,623	6,669	38,997	n.d.	13,780
Lyt 1^{+}	1,266	n.d.	8,903	16,168	18,443	12,487	29,162	84,321	11,230	38,485	n.d.	18,288
Lyt 1^{+} + Lyt $2, 3^{+}$	4,460	n.d.	10,420	19,850	17,406	11,747	23,014	64,401	28,202	65,207	n.d.	24,120

[a]) Δ = Mean [^{3}H] thymidine uptake for allogeneic combination – mean [^{3}H] thymidine uptake for syngeneic combination.

Responder cells from the same cultures, which were tested for generation of killer cells, were also studied for their proliferative responses. The data are summarized in Table 1. As already shown by several authors (4, 5, 15) it was found that in MLC's differing at either the entire or parts of the H-2 complex pretreatment of lymph node T cells with anti-Lyt 1 antiserum plus complement removed the majority of the proliferating cells in all strain combinations tested. In the combined mixture of Lyt 1^+ and Lyt $2,3^+$ T cells the proliferative responses were restored more or less in most strain combinations. In the strain combination ATL anti A.AL, where responder and stimulator differ only in the K region, the proliferative response remained low and no cytotoxic lymphocytes were generated from the T cell population consisting of Lyt 1^+ and Lyt $2,3^+$ T cells. Similar results were obtained in studies of T cell responses to mutant H-2 K and H-2 D alloantigens in which the proliferation was shown to be dependent on Lyt $1,2^+$ cells (16). One would assume that H-2 K end antigens, when presented as the only determinants on stimulator cells, are only able to induce responses in Lyt $1,2,3^+$ but not in Lyt 1^+ or Lyt $2,3^+$ T cells. However, in two strain combinations where responder and stimulator cells differ at either only the I region or only the D region of the major histocompatibility complex Lyt 1^+ T cells could be activated. Nevertheless, there was no generation of cytotoxic lymphocytes against either I region or D region determinants from cell mixtures containing Lyt 1^+ and Lyt $2,3^+$ T cells. Since the proliferating Lyt 1^+ T cells are not able to evoke cytotoxic lymphocytes from the Lyt $2,3^+$ cell pool this finding suggests that the majority of killer cell precursors specific for I or D determinants reside in the Lyt $1,2,3^+$ T cell population.

Discussion

The aim of this study was to define the T cell subsets required for the generation of cytotoxic T effector cells specific for alloantigen or new antigenic determinants (NAD) formed by TNP or viral antigens on syngeneic cells. It is evident from the data presented that a strict distinction between alloreactive and H-2 restricted cytotoxic responses on the basis of their requirements for distinct Lyt T cell subsets during the sensitization phase is not justified. We have shown that Lyt $1,2,3^+$ T cells are necessary to generate H-2 restricted cytotoxic lymphocytes specific for TNP and for the development of alloreactive cytotoxic responses to K, I or D differences alone (i.e. when responder and stimulator cells differ at either only the K, I or D region, respectively); yet Lyt $1,2,3^+$ T cells are not required during the induction phase of H-2 restricted and virus-specific cytotoxic lymphocytes or for the generation of alloreactive killer cells when responder and stimulator cells differ at either both the K and D, K and I, I and D or the whole MHC region.

Our data on primary TNP specific cytotoxic responses are in agreement with the experiments reported by CANTOR and BOYSE (9) and BURAKOFF et al. (10). We extended these studies and found in most experiments that Lyt $1,2,3^+$ T cells are also required in a secondary response to TNP-modified target cells. Similar requirements for Lyt $1,2,3^+$ T cells in the generation of H-2 restricted CTL's have also been found in in vitro secondary responses to the male specific antigen H-Y (M. M. Simon, unpublished and [17]). This is consistent with the view that different Lyt T cell subsets discriminate between foreign non MHC antigens and alloantigens. The possibility of a separation of precursor killer cells into two subsets based on allo versus non-MHC reactivity has originally been described by CANTOR and BOYSE (9). Their assumption that killer cell precursors responsible for H-2 restricted cytotoxic responses reside within the Lyt $1,2,3^+$ cell pool while the alloreactive killer cell precursors are comprised in the Lyt $2,3^+$ T cell population was substantiated by studies of BURAKOFF et al. (10) on the generation of TNP-specific killer cells. It was found that in mixed lymphocyte populations consisting of Lyt $1,2,3^+$ and Lyt $2,3^+$ subsets derived from Lyt 2,3 congenic strains H-2 restricted effector cells expressed the Lyt 2,3 phenotype of Lyt $1,2,3^+$ cells present in the unselected T cell pool. The data were interpreted to mean that T cell clones with specificity for self plus X determinants are predominantly found in the Lyt $1,2,3^+$ but not in the Lyt $2,3^+$ subset.

We have now demonstrated that Lyt $1,2,3^+$ T cells are not required for the induction of both primary and secondary virus specific cytotoxic responses. The conditions which allow separation of primary versus secondary SV specific cytotoxic responses have been described in a preceding paper (11). BURAKOFF et al. (10) reported results suggesting that Lyt $1,2,3^+$ T cells are mainly involved in the formation of Sendai virus specific cytotoxic lymphocytes. Unfortunately, it was not indicated by the authors whether the cytotoxic activity measured was a primary or secondary antiviral response. We cannot at the moment explain the discrepancy between our and their findings, but it is unlikely that this is due to different mouse strains tested since we found similar requirements for Lyt subsets in several strains investigated.

The differences seen in the induction requirements for primary and secondary H-2 restricted TNP specific versus H-2 restricted virus specific cytotoxic responses may be explained in quantitative terms: H-2 restricted TNP-specific killer and virus-specific killer cell precursors reside in both the Lyt $1,2,3^+$ and the Lyt $2,3^+$ T cell pool but the number of virus specific cell clones is higher within the Lyt $2,3^+$ subset because of more frequent exposition of lymphocytes with possibly crossreactive viral antigens as compared to TNP determinants during ontogeny. Thus, the inability to generate primary and secondary TNP specific CTL's from the Lyt $2,3^+$ pool would be due to the small number of antigen specific clones, present in this population, which cannot be detected in the assay system. It is even

possible that similar numbers of TNP or virus specific T cell clones reside within the Lyt 2,3 cell pool yet only virus specific killer cells exceed a minimum threshold level by mitogenic activity elicited by the virus (11), which helps to expand the antigen specific T cell clones. On the other hand one could visualize a qualitative difference of the two types of antigens resulting in different pathways of activation.

Our data on the generation of cytotoxic responses to distinct alloantigens also revealed two patterns of participating Lyt subsets similar to that described for H-2 restricted responses. We found that Lyt 1,2,3 T cells are essential for the induction of alloreactive cytotoxic responses to K, I or D differences alone, thus extending results previously described by BACH and ALTER (15) for mixed lymphocyte reactions in which the responses of Lyt subsets to H-2 D alloantigens were determined. In contrast, when responder and stimulator differed in more than one region of the MHC complex, i.e. the K + I, K + D, I + D, or K, I and D regions respectively, we observed a generation of alloreactive killer cells from Lyt $2,3^+$ T cells in the absence of Lyt $1,2,3^+$ T cells.

There are several possibilities to explain the constraints for Lyt $1,2,3^+$ T cells during the induction of alloreactive responses to selected MHC region determinants:

a) From unpublished data we know that unprimed Lyt $2,3^+$ T cells contain killer cell precursors with specificities for either K or D region determinants since cytotoxic lymphocytes specific for both determinants are easily generated from the same T cell pool when responder and stimulator cells differ in more than one MHC region (M. M. Simon, unpublished). Thus, the inability of the selected Lyt $2,3^+$ T cells to respond to selected regions of the MHC cannot be due to the lack of the relevant T cell clones within this population. Therefore, other factors must control the response of Lyt $2,3^+$ T cells to selected MHC antigens.

b) Determinants encoded by only one subregion of the H-2 complex may fail, perhaps due to suppressive mechanisms to induce a cytotoxic response from the Lyt $2,3^+$ T cells which are specific for these determinants.

c) Help provided by Lyt 1^+ T cells may be not sufficient and a fraction of the Lyt 1,2,3 cell pool provide additional help.

d) Help provided by additional antigenic determinants could be operative during the generation of alloreactive killer cells from the Lyt 2,3 subset and is absent when only antigens encoded by one single MHC subregion is presented during the induction phase. This would be similar to the mechanisms described as intermolecular help by Lake and Mitchison (18, 19). They found that antigens encoded by only one MHC region are unable to initiate a humoral immune response unless additional MHC differences are present in the system.

e) Qualitative differences of the antigenic determinants may govern the requirement for Lyt $1,2,3^+$ T cells. Bach and Alter proposed that the I region is an important control element which helps to determine which

pathway of T lymphocyte differentiation will proceed in any particular situation (15). This is not easily reconciled with our data. In MLC's with responder and stimulator cells differing at the K + D, K + I or only at the I region we found no correlation between I region identity of responder and stimulator and requirement for Lyt $1,2,3^+$ T cells for killer cell induction.

f) Self restricted recognition of selected alloantigenic K, I or D products may result in the participation of Lyt $1,2,3^+$ T cells. This is not very likely since it was found by Epstein and Cohn (20), Klein et al. (21), and Billings et al. (22), that K, I, or D determinants are not recognized in a H-2 restricted manner, at least during the effector phase.

Altogether, our findings cast doubt on the simplistic model that different T cell subsets give rise to allo- or foreign non H-2 antigen specific effector cells. The data are compatible with the view that H-2 restricted as well as alloreactive precursor killer cells reside within the Lyt 1,2,3 and the Lyt 2,3 cell pool and can be generated from both T cell pools under appropriate conditions. This is also substantiated by our findings that in unselected T cell populations consisting of Lyt 1,2,3 and Lyt 2,3 lymphocytes H-2 restricted as well as alloreactive cytotoxic activity is generated from the Lyt 1,2,3 T cell pool (M. M. Simon, manuscript in preparation). This does not, however, exclude the possibility that different T cell sets within each Lyt subpopulation show preferential association with one (allo-) or the other type of antigen (X + MHC self). Since Lyt subsets do not distinguish between allo- versus foreign non MHC antigens in the generation of cytotoxic responses other factors like the number and regulatory influence of different antigenic determinants (MHC and non MHC) and/or their mitogenicity must be involved in the selection of Lyt T cell subsets required to elicit the appropriate cytolytic activity.

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References

1. BOYSE, E. A., T. MIYAZAWA, T. AOKI, and L. J. OLD. 1968. Ly-A and Ly-B: Two systems of lymphocyte isoantigens in the mouse. Proc. Roy. Soc. Lond. B. Biol. Sci. **170:** 175.
2. BOYSE, E. A., K. ITAKURA, E. STOCKERT, A. IRATANI, and M. MIURA. 1971. Ly-C: a third locus specifying alloantigens expressed only on thymocytes and lymphocytes. Transplantation (Baltimore) **11:** 351.
3. KISIELOW, P., J. HIRST, H. SHIKU, P. C. L. BEVERLEY, M. K. HOFFMAN, E. A. BOYSE, and H. F. OETTGEN. 1975. Ly antigens: markers for functionally distinct subsets of thymus-derived lymphocytes of the mouse. Nature (Lond.) **253:** 219.
4. SHIKU, H., P. KISIELOW, M. A. BEAN, T. TAKAHASHI, E. A. BOYSE, H. F. OETTGEN, and L. J. OLD. 1975. Expression of T cell differentiation antigens on effector cells in cell-mediated cytotoxicity in vitro: evidence for functional heterogeneity related to surface phenotype of T cells. J. Exp. Med. **141:** 227.

5. CANTOR, H., and E. A. BOYSE. 1975. Functional subclasses of T lymphocytes bearing different Ly antigens. I. The generation of functionally distinct T cell subclasses is a differentiation process independent of antigen. J. Exp. Med. **141**: 1376.
6. CANTOR, H., and E. A. BOYSE. 1975. Functional subclasses of T lymphocytes bearing different Ly antigens. II. Cooperation between subclasses of Ly^+ cells in the generation of killer activity. J. Exp. Med. **141**: 1390.
7. JANDINSKI, J., H. CANTOR, T. TADAKUMA, D. L. PEAVY, and C. W. PIERCE. 1976. Separation of helper T cells from suppressor T cells expressing different Ly components. I. Polyclonal activation: suppressor and helper activities are inherent properties of distinct T cell subclasses. J. Exp. Med. **143**: 1382.
8. FELDMAN, M., P. C. L. BEVERLEY, M. DUNKLEY, and S. KONTAINEN, S. 1975. Different Ly antigen phenotypes of in vitro induced helper and suppressor cells. Nature (Lond.) **258**: 614.
9. CANTOR, H., and E. A. BOYSE. 1976. Regulation of cellular and humoral responses by T cell subclasses. Cold Spring Harb. Symp. Quant. Biol. **XLI**: 23.
10. BURAKOFF, S. J., R. FINBERG, L. GLIMCHER, F. LEMONNIER, B. BENACERRAF, and H. CANTOR. 1978. The biological significance of alloreactivity. The ontogeny of T cell sets specific for alloantigens or modified self antigens. J. Exp. Med. **148**: 1414.
11. KOSZINOWSKI, U., and M. M. SIMON. 1979. Generation of virusspecific cytotoxic T cells in vitro. I. Induction conditions of primary and secondary Sendai virus specific cytotoxic T cells. Eur. J. Immunol., in press.
12. SHEN, F.-W., E. A. BOYSE, and H. CANTOR. 1976. Preparation and use of Ly antisera. Immunogenetics **2**: 591.
13. JULIUS, M. H., E. SIMPSON, and L. A. HERZENBERG. 1973. A rapid method for the isolation of functional thymus derived murine lymphocytes. Eur. J. Immunol. **3**: 645.
14. VON BOEHMER, H. 1974. Separation of T and B lymphocytes and their role in the mixed lymphocyte reaction. J. Immunol. **112**: 70.
15. BACH, F. H., and B. J. ALTER. 1978. Alternative pathways of T lymphocyte activation. J. Exp. Med. **148**: 829.
16. WETTSTEIN, P. J., D. W. BAILEY, L. E. MOBRAATEN, J. KLEIN, and J. FRELINGER. 1978. T lymphocyte response to H-2 mutants. I. Proliferation is dependent on Ly 1^+2^+ cells. J. Exp. Med. **147**: 1395.
17. SIMPSON, E., and P. C. L. BEVERLEY. 1977. T cell subpopulations. (Mandel, T. E., Cheers, C., Hosking, C. S., McKenzie, I. F. C., Nossal, G. J. V.) Eds.) Progress in Immunology III, North Holland, Amsterdam-New York. p. 206.
18. LAKE, P., and N. A. MITCHISON. 1976. Regulatory mechanisms in the immune response to cell-surface antigens. Cold Spring Harbor Symp. Quant. Biol. **XLI**: 589.
19. MITCHISON, N. A., and P. LAKE. 1977. Associative control of the immune response to cell surface antigens. Immunol. Commun. **5**: 795.
20. EPSTEIN, R., and M. COHN. 1978. T cell inhibition of humoral responsiveness. I. Experimental evidence for restriction by the K- and/or D-end of the H-2 gene complex. Cell. Immunol. **39**: 110.
21. KLEIN, J., C. L. CHIANG, and V. HAUPTFIELD. 1977. Histocompatibility antigens controlled by the I region of the murine H-2 complex. II. K/D region compatibility is not required for I-region cell-mediated lymphocytotoxicity. J. Exp. Med. **145**: 450.
22. BILLINGS, P., S. BURAKOFF, M. E. DORF, and B. BENACERRAF. 1977. Cytotoxic T lymphocytes specific for I region determinants do not require interactions with H-2K or D gene products. J. Exp. Med. **145**: 1387.

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