IDIOTYPE-RECOGNIZING T HELPER CELLS THAT ARE NOT IDIOTYPE SPECIFIC*

By MARY McNAMARA and HEINZ KOHLER

From the Department of Molecular Immunology, Roswell Park Memorial Institute, New York State Department of Health, Buffalo, NY 14263

The network hypothesis (1) postulates that B and T cells interact via complementary idiotypic structures (2). This assumption creates a satisfying symmetry in the immune system by which both compartments would use similar receptor structures encoded by a single pool of variable genes. Experimental support for the sharing of idiotypes between B and T cells has been substantial (3–6). Most of this evidence comes from the demonstration that an antiidiotype antibody functionally interacts with T cells or can bind to T cells or T cell factors. These findings, however, do not prove that T cell receptors or factors use the same genes as B cells. On the contrary, the recent failure to detect active gene rearrangements in specific T cell clones (7, 8) indicates that T cells use other than Ig genes (9).

One approach to studying T cell receptors is to analyze their specificity and compare it with the specificity of B cells for the same determinant. With respect to the T-B interaction in the immune network, a comparative analysis of how B and T cells recognize idiotypes would address the question of T cell receptor specificity.

In a previous study we found (10) that T helper cells which recognize idiotypes as carriers for a hapten-specific antibody response recognize the TEPC-15 (T15)[1] proteins and MOPC-167 (M167) equally well. We concluded that these T cells recognize an idiotypic determinant that is shared by T15 and M167. The recognition of a common T15-M167 idiotope is typically not observed with antiidiotypic mouse antisera that distinguish between T15 and M167 (11). A conclusion from these findings is that T cells "see" idiotype differently than B cells. This hypothesis does not exclude the possibility that two kinds of idiotype-recognizing T cells exist, one that recognizes unique idiotopes and another that recognizes common idiotopes.

More recently, we used different induction modes for idiotype-recognizing T helper cells. Consistently, we only find T helper cells that recognize T15 and M167 idiotypes. This finding of non–idiotype-specific T cells, induced by antigen, idiotype, or antiidiotope, indicates that in network regulation T cells interact

differently than B cells. This in turn supports the notion (9) that antigen and idiotype receptors on T cells are structurally and genetically different than B cell receptors and antibodies.

Materials and Methods

Mice. BALB/c mice, 6–8-wk old, were obtained from Cumberland View Farms, Clinton, MA. (CBA/N × BALB/c)F1 (NBF1) male mice were obtained from Dominion Labs, Dublin, VA. Athymic nu/nu BALB/c mice were obtained from Harlan Sprague Dawley, Inc., Madison, WI, and from National Institutes of Health, Bethesda, MD.

Myeloma and Hybridoma Proteins. The T15 and M167 plasma cell tumors were obtained from Dr. M. Potter, National Cancer Institute, Bethesda, MD, and were purified from ascitic fluid by affinity column purification (12). The hybridomas F6-3 and 4C11 were prepared in our laboratory by Dr. M. Wittner of the La Rabida-University of Chicago Institute. They are specific for determinants on the T15 molecule. 4C11 is phosphoryl-choline (PC) binding-site–specific (13). The HPC104 hybridoma protein was the kind gift of Claudia Berek, Basel Institute of Immunology, Basel, Switzerland.

Antigens. Limulus polyphemus hemocyanin (Hy) was obtained from the Millipore Corp., Bedford, MA. PC-Hy was prepared by the reduction of p-aminophenylphospho-rylcholine (Biosearch, San Rafael, CA) to diazophenylphosphorylcholine followed by reaction with Hy. The trinitrophenylated myeloma and hybridoma proteins were prepared by reacting the purified proteins, which had their PC hapten-binding sites blocked by PC-chloride (Sigma Chemical Co., St. Louis, MO), with 2,4,6-trinitrobenzene sulfonic acid (Sigma Chemical Co.). After trinitrophenylation, the hapten was removed by dialysis against 1 M borate-buffered saline (BBS).

Immunizations. NBF1 and BALB/c mice to be used as Hy-primed donors received one intraperitoneal injection of 100 μg Hy in complete Freund's adjuvant (CFA) and were used 4 wk later. Mice to be used as PC-Hy-primed donors received an additional injection of 100 μg in incomplete Freund's adjuvant 4 wk after the initial injection and were used 4 wk later. NBF1 male mice to be used as F6-3- or 4C11-primed donors received 0.01– 15 μg of purified F6-3 or 4C11 i.v. and were used 8–10 wk later.

Anti-Thy-1.2 Treatment of Donor Spleen Cells. Glass wool-passed spleen cells were suspended in Dulbecco's modified Eagle medium (DME) (Gibco Laboratories, Grand Island, NY) with 10% agammaglobulin horse serum (AHS) (Gibco Laboratories). The cells were treated subsequently with anti-Thy-1.2 antibody from the hybridoma AT83.A.3, the kind gift of Dr. F. Fitch, University of Chicago, Chicago, IL, and low toxicity rabbit complement (Accurate Chemical and Scientific Co., Westbury, NY). The trypan blue exclusion test was used to determine viability. B cell recovery was 40%.

Donor Helper T Cell Preparation. Isolation of T cells has been described elsewhere (14). Briefly, donor spleen cells were passed over a nylon wool column. After a 1-h incubation at 37°C, T cells were eluted with 20 ml of DME with 10% AHS. Ly-2⁻ T cells were prepared by treatment of the nonadherent cells with hybridoma antibody 53-6.72 (anti-Lyt-2) (American Type Culture Collection, Rockville, MD) and low toxicity rabbit complement (Accurate Chemical and Scientific Corp.). The purity of the Ly-2⁻ population was determined by immunofluorescent staining with 53-6.72 and fluorescein-conjugated goat anti-rat immunoglobulin (Ig) (Cappel Laboratories, Cochranville, PA). 92% of the cells were Ly-2⁻.

Cell Transfers and Splenic Fragment Cultures. The splenic fragment culture system modified for the study of single T cells was used (15). Briefly, graded numbers of nylon wool–passaged, anti-Ly-2–treated cells or anti-Thy-1.2–treated cells were injected into athymic, nu/nu BALB/c mice or irradiated NBF1 recipients. 1–2 d later (in the case of the nu/nu mice) or 1–3 wk later (in the case of the NBF1 mice) the recipient spleens were removed and chopped into 1-mm cubes and the pieces were placed in individual wells of a 96-well microtiter tray (Costar, Data Packaging, Cambridge, MA) and cultured in DME with 10% AHS plus trinitrophenylated antigen at a concentration of 10^{-8} M trinitrophenyl (TNP). In vitro inhibitors, PC-chloride (Sigma Chemical Co.) and the unconjugated

myeloma proteins, T15 or M167, were added at the time of immunization. The trays were incubated at 37°C, in culture boxes that were gassed daily with a mixture of 8% CO_2 and 92% O_2. After 3 d of culturing, the antigen was removed and fresh DME containing 10% AHS was added. The cultures were continued for 12 d and the collected supernatants were assayed for anti-TNP antibody using the enzyme-linked immunosorbent assay (ELISA).

ELISA. The ELISA enzyme assay was modified (16). Briefly, 0.1 ml of the appropriate hapten-carrier protein dissolved in BBS was added to each well of a 96-well microtiter tray (Becton, Dickinson & Co., Oxnard, CA). The trays were incubated overnight at 4°C, washed with phosphate-buffered saline (PBS), and 0.2 ml of 1% bovine serum albumin (BSA) (Sigma Chemical Co.)-PBS added. After a 1-h incubation at 37°C, the trays were washed with PBS. Next, 0.025 ml of the culture supernatant fluid and 0.075 ml of 1% BSA-PBS were added to the wells (serial dilutions of affinity-purified M460 antibody were used as the standards). The trays were incubated overnight at 4°C, washed with PBS, and filled with 0.1 ml of rabbit anti-mouse Ig (Cappel Laboratories) diluted 1:1,000 in 1% BSA-PBS. After 2 h at 37°C, the trays were again washed with PBS and filled with 0.1 ml of alkaline phosphatase (Sigma Chemical Co.)-conjugated goat anti-rabbit Ig (Litton Bionetics Inc., Kensington, MD). After an overnight incubation at 4°C, the trays were washed with PBS and developed with 0.1 ml of a phosphatase substrate-diethanolamine buffer mixture (30 mg/50 ml) (Sigma Chemical Co.). The absorbance was measured on an Artek Elisa Reader at 405 nm (Artek Systems Corp., Farmingdale, NY).

Results

Response of PC-primed NBF1 Male T Helper Cells to TNP-T15 and TNP-M167. In previous studies (10, 17), we have shown that PC-Hy priming of BALB/c mice stimulates T helper cells that recognize various PC-binding idiotypes. It was postulated that the idiotype-recognizing helper T cells are stimulated via an idiotype circuit. In the present work, we investigated the cellular induction pathway of these idiotype-recognizing T helper cells and in so doing further defined their specificity. To determine if the inducing cell in the induction loop is a T cell, we used NBF1 PC-Hy-primed males as the T cell donors in the experiment. These NBF1 mice have an X-linked immune defect that renders their B cells unresponsive to PC (18); therefore the antigen priming will have no effect on the NBF1 B cells. Graded numbers of PC-Hy-primed Ly2⁻ T cells were transferred to nu/nu athymic recipients. Splenic fragment cultures were prepared and immunized with TNP-T15 or TNP-M167. Culture supernatants were assayed on days 9 and 12 for anti-TNP activity. As can be seen in Fig. 1, PC-primed NBF1 T helper cells are able to recognize both T15 and M167. Furthermore, the number of responding fragment cultures is dependent on the number of transferred T cells. Therefore, a precursor frequency for the T cell populations responding to each of the antigens can be calculated, using the previously determined (10) splenic homing efficiency of 25–30%. The frequency of T15-recognizing T helper cells is 3.5×10^{-4}; for M167-recognizing T helper cells, 8.5×10^{-4}. Statistically and within the experimental variation, these frequencies are not different.

To further substantiate the conclusion that PC-Hy priming stimulates a T cell which then induces the idiotype-recognizing T helper cell, we had to exclude the possibility of a B-T induction loop. B cells from PC-Hy-primed BALB/c were cotransferred with normal NBF1 T cells into irradiated NBF1 recipients. After 1–3 wk, splenic fragment cultures were set up and immunized with TNP-
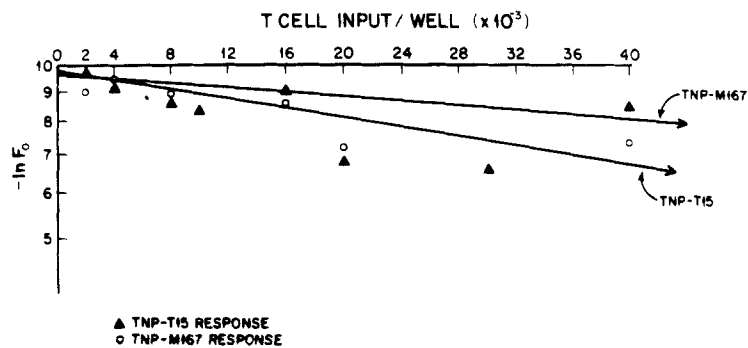
FIGURE 1.   Number of transferred T helper cells per well is plotted against the fraction of nonresponding fragment cultures ($-\ln F_0$). Splenic fragment cultures were immunized with TNP-T15 or TNP-M167 at 10^{-8} TNP.

TABLE I

B Cells from PC-Hy-primed BALB/c Mice Do Not Induce Idiotype-specific Help for TNP-T15

Cells transferred from PC-Hy-primed BALB/c*	T cells cotransferred from normal NBF1 male (× 10^6)[‡]	Anti-TNP-positive wells[§]
—	—	0 ± 0
5 × 10^6 spleen cells	—	41.7
5 × 10^6 B cells	—	0 ± 0
5 × 10^6 B cells	10^6	1 ± 0

* Mice used as PC-Hy-primed donors were primed with 100 µg in CFA 8 wk before use and 100 µg PC-Hy in IFA 4 wk before use. B cells were prepared by treating whole spleen cells with anti-Thy-1.2 and rabbit complement. Cells were injected into normal male NBF1 recipients that had been x-irradiated with 800 rad 6–8 h before cell transfer.

‡ Donor T helper cells were prepared by passage of spleen cells over nylon wool columns and subsequent treatment with anti-Ly-2 and rabbit complement and transferred into the x-irradiated recipients at the same time as the B cells. 1, 2, or 3 wk after cell transfer the mice were sacrificed.

§ Splenic fragment cultures were immunized in vitro with TNP$_7$-T15 at 10^{-8} M TNP. 288 cultures were assayed for anti-TNP antibody at days 6, 12, and 15 by ELISA.

T15. As seen from the results in Table I, the PC-primed B cells were not able to induce help for the T15 idiotype. As a positive control, whole spleen cells from PC-Hy primed BALB/c transferred to NBF1 recipients did function as T helpers for the TNP-T15 response. These results show that B cells from primed donors are not sufficient to induce unprimed T cells to become T15-recognizing helper cells. Collectively, the data from this and the preceding experiment indicate that PC-Hy priming involves only T cells in the induction loop for idiotype-recognizing helpers.

Double Immunization with TNP-T15 and TNP-M167.   From the calculated frequency data for T15 and M167 helper cells, the tentative conclusion can be drawn that the population of T helper cells induced by PC-Hy can recognize the T15 and M167 idiotypes equally well. To further support this assumption, we

TABLE II

Response of PC-HY-primed LY-2⁻ T Cells to TNP-T15 and TNP-M167

NBF1 male donor treatment*	No. of donor cells injected ($\times 10^6$)‡	In vitro antigen§	Anti-TNP-positive wells‖
PC-Hy	—	TNP-T15	2
	2.4		28
	—	TNP-M167	3
	2.4		33
	2.4	TNP-T15 + TNP-M167	23

* Donor mice were prepared as in Table I.
‡ Donor T cells were prepared as in Table I and transferred into nu/nu athymic BALB/c recipients.
§ Splenic fragment cultures were stimulated in vitro with TNP_7-T15 and/or TNP_{12}-M167 at 10^{-8} M TNP.
‖ 96 cultures were assayed by ELISA for anti-TNP activity on days 9 and 12.

compared the number of positive cultures obtained when the fragment cultures were immunized with one or both of the TNP idiotypes. If separate populations of T helper cells are present, each of which recognizes one idiotype, double immunization should produce an additive effect in providing help to B cells responding to TNP.

PC-primed, Ly2⁻ T cells from donor NBF1 males were transferred to nu/nu recipients and the splenic fragment cultures were immunized with TNP-T15, TNP-M167, or a combination of the two. As can be seen from the results in Table II, double immunization does not increase the number of positive anti-TNP foci; rather, the single and double immunization yield the same results within experimental variation. The failure to produce additive responses cannot be due to a limiting amount of TNP-specific B cells cells since the singly immunized cultures' response is not lower than the doubly immunized cultures'. This result indicates that PC priming induces a single population of T cells which does not distinguish between T15 and M167.

Fine Specificity of the Help for T15 and M167.   A further analysis of the T helper population that recognizes T15 and M167 was performed by inhibition experiments involving either nonconjugated idiotypes or free PC hapten as in vitro inhibitors. We first determined if a shared determinant on the two idiotypes was the target of recognition for the T cells. Fragment cultures were prepared and immunized with TNP-T15 or TNP-M167. Unconjugated T15 or M167 were added as inhibitors. If separate T helper populations for T15 and M167 exist, the antigenic stimulation of each population should only be inhibited by the stimulation idiotype. However, as is seen from Table III, either idiotype used singly blocks the majority of the response to both T15 and M167. Also, the inhibition of T cell help with T15 and M167 combined is not more efficient than the inhibition with either one. This finding was made with cultures immunized with TNP-T15 and with TNP-167 (Table III). These results support

TABLE III

Inhibition of Idiotype-specific Recognition In Vitro by Idiotypes

NBF1 T cell donor treatment*	In vitro antigen[‡]	In vitro inhibitor[§]	Anti-TNP–positive wells[‖]	Percent inhibi-tion[¶]
PC-Hy	TNP-T15	—	30	—
		T15	4	87
		M167	2	93
		T15 + M167	4	87
	TNP-M167	—	33	—
		M167	2	90
		T15	12	64
		T15 + M167	7	79

* Donor mice were primed with PC-Hy and Ly-2⁻ T cells prepared as described in Table I. 10^6 Ly-2⁻ T cells were injected into athymic, nu/nu BALB/c recipients.

[‡] The splenic fragment cultures were immunized in vitro with TNP_7-T15 at 10^{-8} M TNP or with TNP_{12}-M167 at 10^{-8} M TNP.

[§] Affinity-purified myeloma proteins T15 and M167 were used as in vitro inhibitors at 10^{-9} M protein.

[‖] 48–96 fragments were cultured and assayed for anti-TNP activity on days 9 and 12 by ELISA.

[¶] Percent inhibition was calculated by the formula: [1 − (percent positive with inhibitor/percent positive without inhibitor)] × 100.

TABLE IV

PC-Hy-primed T Cells Do Not Help the Response to TNP-104 Idiotype

NBF1 donor treatment*	In vitro Ag[‡]	Anti-TNP–positive wells[§]
PC-Hy Primed	—	2
	TNP-T15	27
	TNP-167	24
	TNP-104	6

* Donor male NBF1 mice were primed and the Ly-2⁻ T cell population prepared as in Table I. 10^6 T helper cells were injected intravenously into athymic, nu/nu BALB/c recipients.

[‡] Splenic fragment were immunized with TNP_7-T15, TNP_{12}-M167, or TNP-104 at 10^{-8} M TNP.

[§] Anti-TNP–producing fragments were assayed on days 9 and 12 by ELISA.

further the hypothesis that one population of T cells recognizes a determinant shared by the T15 and M167 idiotypes.

In an attempt to localize the shared determinant, we compared the response of cultures immunized with TNP-T15 or TNP-M167 with that of cultures immunized with TNP-104. 104 is an anti-PC hybridoma that, unlike 167, has a completely different H chain than T15 (19). The absence of help generated for 104 by PC priming indicates that the T15/M167 helper cells, while not idiotype specific, appear to be H chain idiotope-specific (Table IV).

Inhibition experiments using PC as the in vitro inhibitor were also performed. Fig. 2 shows the inhibition of the B cell response to TNP-T15 and TNP-M167 by increasing the amounts of free PC. T cell help for TNP-T15 and TNP-M167
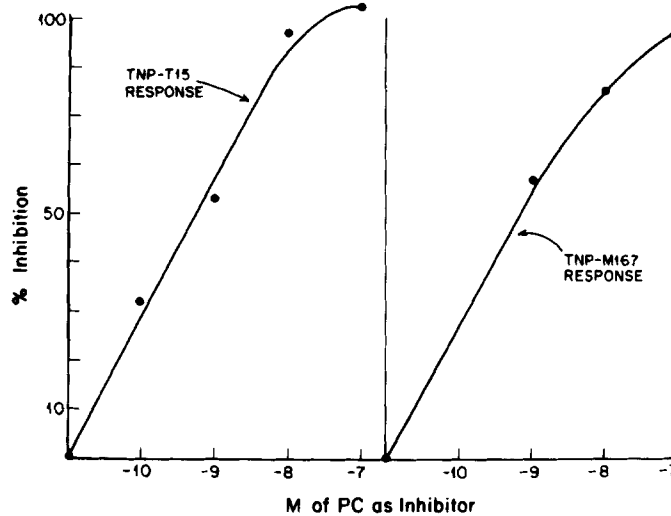
FIGURE 2. In vitro inhibition of carrier recognition by PC. The responses of splenic fragment cultures immunized with (A) TNP-T15 or (B) TNP-M167) in the presence of different amounts of PC are shown.

is inhibited equally well by the same concentrations of PC hapten. These results provide additional evidence for the existence of a single T helper population with receptors that recognize T15 and M167.

Antiidiotype Priming Induces T Help for T15 and M167.   The data described here and those reported previously (10) invoke the concept of an idiotype-nonspecific pathway of induction of T helper cells able to recognize more than one B cell idiotype. To further explore this idea, we used other priming methods that are idiotype specific to determine the fine specificity of the T inducer and T effector cells in the induction T-T cell loop.

Instead of PC-Hy we used two monoclonal anti-T15 hybridomas to prime NBF1 males. F6-3 and 4C11 are hybridoma anti-T15 antibodies previously produced in our laboratory (13). F6-3 reacts with an idiotope that is near the PC-binding site of T15; 4C11 binds to a PC-binding site idiotope since free PC inhibits the binding of 4C11 to T15. The results are shown in Table V and demonstrate that this indirect priming of T cells induces T helper cells which recognize both T15 and M167.

As seen in Table V, the dose of the priming monoclonal antiidiotypic antibody is critical. A priming dose of 10 ng of F6-3 stimulates idiotope-recognizing help, while a 10-fold higher dose suppressed the help almost completely. The situation is similar for 4C11:0.1 μg of the antibody has the optimal stimulating effect while a higher dose is not stimulatory.

Discussion

Although idiotypes on B cell receptors and antibodies are clearly defined, the expression of idiotypic specificities on T cells is controversial. The main objection to T cell Ig idiotypes arises from the failure (7, 8) to detect rearranged Ig gene segments in specific T cell lines. On the other side there is a wealth of information

NON–IDIOTYPE-SPECIFIC T CELLS

TABLE V
Low Dose Priming of Idiotype-recognizing T Help by Antiidiotypes

NBF1 T cell donor treatment[*]	Dose of priming	In vitro antigen[‡]	Anti-TNP–positive wells[§]
—	—	TNP-T15	3
—	—	TNP-M167	4
F6-3	100 ng	TNP-T15	8
	100 ng	TNP-M167	6
	10 ng	TNP-T15	42
	10 ng	TNP-M167	48
4C11	15 µg	TNP-T15	1
	15 µg	TNP-M167	1
	1 µg	TNP-T15	36
	1 µg	TNP-M167	34

[*] Donor mice received one intravenous injection of either F6-3 or 4C11 6–8 wk before use. Donor T cells were prepared as in Table 1 and 10^6 T helper cells injected into athymic, nu/nu BALB/c recipients.

[‡] Splenic fragment cultures were stimulated in vitro with either TNP_7-T15 or TNP_{12}-M167 at 10^8 TNP.

[§] 48–96 cultures were assayed for anti-TNP antibody on days 9 and 12 by ELISA.

on the serological and functional presence of T cell idiotypes of idiotypes on T cell factors (3–6, 20). One way to reconcile this dilemma is to assume that T cells produce receptors and factors that cross-react with antiidiotypic antibodies. This model allows for effective interactions between the B and T cell repertoires that are essential to achieve a controlled immune response.

In our experimental model (10, 21), we directly address the question of idiotypic receptors on T cells. We use as carrier an idiotype that is recognized by T helper cells. We can analyze this T helper cell population under limiting dilution conditions and can perform inhibition experiments in vitro during the effector phase of T helper cells. These experimental advantages permit us to precisely address the question of the size of the idiotype-specific T cell subpopulation and to investigate the nature of receptor specificity. Limiting dilution analysis and double immunization protocols indicate the presence of a single subset of T cells that can recognize two different idiotypes, i.e., T15 and M167. Inhibition data of T15 and M167 recognition support this conclusion. Furthermore, these inhibition experiments show that the heavy chains of T15 and M167, which are structurally very similar (22), are the target for idiotype-recognizing T cells. More specifically, these experiments demonstrate that T helper cells recognize a determinant on the heavy chains of T15 and M167 that is involved in the PC-binding site (10).

This conclusion appears to contradict the accepted view of idiotypes. Homologous or isologous antisera against T15 or M167 are specific for their respective idiotypes, which indicates that the B cell response to these idiotypes is idiotype specific (11, 23). It follows from these observations that B and T cells "see" idiotypes differently and that the idiotype receptors on B and T cells are different

The receptors for T15 and M167 are therefore antiidiotype-like. T cells

having these antiidiotype receptors can be stimulated with T15 and with M167 equally effectively (unpublished data). We refer to this stimulation mode as direct priming. Indirect priming of these idiotype-recognizing T helper cells has been previously demonstrated by the use of antiidiotypic antibody (21) or PC-Hy (17). In this priming mode a cellular loop is involved, since neither antiidiotype nor antigen can directly prime antiidiotypic T cells. The question arises here whether this loop is a T helper$_1$-T helper$_2$ or B-T circuit. In the present study we have obtained evidence for a T helper$_1$-T helper$_2$ loop. This evidence is the failure of B cells taken from PC-Hy-primed mice to induce T helpers from a normal donor, and the finding that these T helper cells can be induced in defective F1 mice which lack T15-producing mature B cells. The specificity of receptors on the inducing T helper$_1$ cell population would be T15-like.

If we postulate an equal tendency for T and B cells to produce variants of idiotypes, the network stability could be provided for by assuming that the number of functionally important idiotypes is limited. These determinants have been termed regulatory idiotopes (24). Other idiotopes would not be involved in interactions and clones bearing these would not participate. Functional idiotope-expression clones from the B and T cell repertoires would be selected from the changing, variant-breeding repertoires by the principle of complementarity, i.e., mutual idiotope receptor fit (25). If a variant clone arises, expressing an idiotope for which a complementary receptor does not exist, this variant clone would remain unrecognized and unstimulated, and would therefore remain small. According to this model, the idiotope repertoires of B and T cells would change steadily with time (aging), and the possibility can be envisioned that some variant clones would escape regulation by complementary T suppressor clones and could proliferate uncontrolled. In any event, a hierarchy of idiotopes may exist in which certain idiotopes are more frequent and functionally involved in T-B interactions (for recognition of help or as the target for suppression) while other idiotopes are expressed infrequently and are not recognized by complementary idiotopes.

Summary

In this study T helper cells that recognize idiotypes as carriers for a hapten-specific B cell response were analyzed under limiting dilution conditions. T helper cells, induced by phosphorylcholine-hemocyanin (PC-Hy) priming, recognize trinitrophenylated TEPC-15 and MOPC-167 (TNP-T15, TNP-167) equally well. Limiting dilution analysis indicates identical frequencies of helper cells for TNP-T15 and TNP-167. Double immunization protocols using TNP-T15 and TNP-167 fail to demonstrate additive effects. Inhibition of carrier recognition in vitro using free hapten, PC, and unconjugated T15 or M167 indicates identical specificities of helper cells for T15 and M167. Collectively, these results provide strong evidence that PC-Hy priming induces only one population of idiotype-recognizing helper cells that are unable to distinguish between the T15 and the M167 idiotopes.

The helper cell induction circuit was further analyzed. PC-Hy priming induces T15/167-specific helper T cells in X-linked immune defect-expressing F1 mice. This indicates that a B cell response to PC is not required to induce idiotype-

recognizing T cells. Adoptive cotransfer of B cells from PC-Hy-primed mice together with normal T cells fails to induce idiotype-recognizing T cells. These results indicate the existence of a T helper$_1$-T helper$_2$ induction loop. In this scheme, the T helper$_1$ cell carries T15-like receptors and the T helper$_2$ cells, anti-T15-like receptors. Monoclonal antiidiotypic antibodies specific for T15 also induce a T15/167-recognizing T helper cell population. This finding demonstrates that idiotope-specific priming induces non–idiotype-specific T cells. Evidently, the idiotypic T cell network is based on a different selection of idiotope determinants than the selection of the B cell idiotype network.

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