SHARED IDIOTYPIC DETERMINANTS ON ANTIBODIES AND T-CELL-DERIVED SUPPRESSOR FACTOR SPECIFIC FOR THE RANDOM TERPOLYMER L-GLUTAMIC ACID^{60}-L-ALANINE^{30}-L-TYROSINE^{10}*

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T lymphocytes produce a wide variety of effector and regulatory substances. Among these is the suppressor factor (T_sF)[1] obtained from suppressor T cells (T_s) stimulated by the synthetic copolymer L-glutamic acid^{60}-L-alanine^{30}-L-tyrosine^{10} (GAT), in mice of Ir nonresponder haplotype (H-$2^{p,q,s}$) (1). This laboratory has studied GAT-T_sF in detail and found that it (*a*) is sensitive to pronase, (*b*) is 40,000–50,000 daltons, (*c*) bears I-region, and more specifically, I-J determinants, (*d*) has specific antigen-binding activity, (*e*) lacks conventional immunoglobulin C_H and light-chain determinants, and (*f*) acts across H-2 and Ig allotype differences, in part by inducing a second population of T_s from virgin T cells (T_{s_2}) (1–7).

The presence of an antigen-binding site on a molecule or a tightly bound molecular complex also containing determinants coded for by major histocompatibility complex (MHC) genes raises the question of the nature of this binding site. Is it a new class of highly specific combining region coded for by the MHC itself, or is it in fact an immunoglobulin V region associated in a functional way with MHC products? The recent description by Ju et al. (8, 9) of a guinea pig antiserum detecting a common idiotype (CGAT) possessed by a majority of anti-GAT antibodies in all mouse strains tested, regardless of Ig allotype or Ir gene status, provided a means to explore this issue. The CGAT idiotype is present in the serum of all mice producing anti-GAT antibodies and probably represents a germ line gene product (9). Thus, it might be predicted that if V region gene products were involved in GAT-T_sF formation, CGAT determinants would be found on GAT-T_sF molecules. The present report describes the results of studies with anti-CGAT immunoadsorbents to test for the presence of CGAT determinants on nonresponder derived GAT-T_sF. The data reveal that both DBA/1 (H-2^q, Ig-1^c) and SJL (H-2^s, Ig-1^b) GAT-T_sF can be specifically adsorbed to

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[1] *Abbreviations used in this paper:* αCGAT, anti-CGAT idiotypic antiserum; αI-J^s, anti-I-J^s alloantiserum; CGAT, cross-reactive idiotype of GAT-specific antibodies; GA, random copolymer of L-glutamic acid^{60}-L-alanine^{40}; GAT, random terpolymer of L-glutamic acid^{60}-L-alanine^{30}-L-tyrosine^{10}; GT, random copolymer of L-glutamic acid^{50}-L-tyrosine^{50}; MBSA, methylated bovine serum albumin; MHC, major histocompatibility complex; NGPS, normal guinea pig serum; PBS, phosphate-buffered saline; PFC, plaque-forming cell(s); SRBC, sheep erythrocytes; T_s, suppressor T lymphocyte; T_sF, T lymphocyte-derived suppressor factor(s); T_{s_2}, T_sF induced suppressor T cell; V region, variable region of immunoglobulin.

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and eluted from anti-CGAT-Sepharose columns, while DBA/1 T_sF specific for the related polymer L-glutamic acid^{60}-L-alanine^{40} (GA) is not bound to such anti-idiotype columns, in concordance with the absence of CGAT idiotype in anti-GA antibodies (9). Further, it is demonstrated that the active T_sF recovered from the anti-CGAT-immunoadsorbents still possesses I-J determinants. The limitations and implications of these findings are discussed with respect to the possible structure of GAT-T_sF and other antigen specific T-cell products.

Materials and Methods

Mice. SJL (H-2^s, Ig-1^b) female and DBA/1 (H-2^q, Ig-1^c) male GAT-nonresponder mice were purchased from The Jackson Laboratory, Bar Harbor, Maine. BALB/c (H-2^d, Ig-1^a) GAT-responder male or female mice were obtained from either Health Research Farms, West Seneca, N. Y., or Charles River Breeding Laboratories, Wilmington, Mass. All mice were maintained in our animal facilities on standard laboratory chow and acidified water ad lib, and used at 2–4 mo old.

Antigens. GAT (lot 6, mol wt 32,500) was obtained from Miles Laboratories Inc., Miles Research Products, Elkhart, Ind. and GA (lot 1, mol wt 36,000) was purchased from New England Nuclear, Boston, Mass. All antigen solutions, conjugates with methylated bovine serum albumin (MBSA), GAT-sheep erythrocytes (GAT-SRBC), and Sepharose-4B immunoadsorbents were prepared as previously described (4, 10).

Preparation of Specific T_sF. Crude GAT- and GA-T_sF were prepared as extracts of pooled spleens and thymuses of either DBA/1 or SJL mice immunized i.p. 3–6 d previously with 100 μg GAT or GA in aluminum-magnesium hydroxide gel (Maalox, William H. Rorer, Inc., Ft. Washington, Pa.) (1). These crude suppressor materials were then partially purified by adsorption onto and elution from either GAT- or GA-Sepharose columns, respectively (4). This procedure has been shown to remove a serologically active fragment of GAT from the suppressor material bearing I region determinants, and was utilized to prevent possible interference by ligand (GAT) with binding of anti-CGAT antibody directed toward a combining site-associated idiotypic determinant.

Preparation and Characterization of Anti-CGAT Antiserum and Immunoadsorbents. The purification of anti-GAT antibodies and production of the anti-idiotypic antiserum have been detailed elsewhere (8). Briefly, ascites fluid containing anti-GAT antibodies from D1.LP mice was precipitated with 40% ammonium sulfate. The γ-globulin fraction was passed through a Sepharose 4B column to which an anti-H-2^b antiserum [(B10.A × A)F_1 anti-B10] was coupled and then passed over a GAT immunoadsorbent. The anti-GAT antibodies were then eluted with an acid buffer and used to immunize guinea pigs. The resulting guinea pig anti-idiotypic serum was rendered specific for anti-GAT idiotypic determinants by precipitation, then adsorption with normal mouse immunoglobulins.

The specific anti-idiotypic serum or control normal guinea serum was then coupled to CNBr-activated Sepharoe 4B (Pharmacia, Uppsala, Sweden). All immunoadsorbents contained approximately 2 mg of protein per milliliter of packed beads.

Affinity Chromatography of GAT- and GA-T_sF. All manipulations were carried out at 4°C. Small (0.3–0.5 ml) columns of either anti-CGAT-Sepharose or control normal guinea pig serum (NGPS)-Sepharose were washed extensively with phosphate-buffered saline (PBS), pH 7.2, then loaded with 1 ml purified GAT-T_sF or GA-T_sF. The T_sF was run into the gel over a 1-min period, and allowed to incubate for 60–90 min, then a 2-bed volume PBS wash collected and termed filtrate. The columns were then washed with at least 10-bed volumes of PBS and the adsorbed material eluted over a 30-s period with 2-bed volumes of pH 2.5 glycine-HCl buffer. This collected material was rapidly neutralized with 1 N NaOH and termed eluate. All filtrates and eluates were stored at −20°C in small aliquots and thawed only once, immediately before use. In one series of experiments, the eluate of an anti-CGAT immunoadsorbent loaded with SJL GAT-T_sF was passed over an anti-I-J^s [(3R × 9R)F_1 anti-B10.HTT]-Sepharose column and both the filtrate and eluate assayed for suppressive activity. All factor dilutions are calculated based on 6×10^8 cells/ml as neat T_sF, and assuming all T_sF applied to a column to be present in any given filtrate or eluate.

Assay of T_sF Activity. All assays for GAT-T_sF and GA-T_sF activity before and after immunoadsorbent passage were performed in vitro according to previously described techniques (6, 7). In certain experiments, factors and column fractions were tested directly by addition to modified Mishell-Dutton cultures of syngeneic or allogeneic nonresponder spleen cells, by using GAT-MBSA or GA-MBSA as stimulating antigens. In other experiments, factors and column fractions were added to cultures of BALB/c responder spleen cells and incubated for 2 d to permit induction of suppressor cells (T_{s_2}) (7). These precultured cells were then washed and added in graded numbers to fresh cultures of syngeneic BALB/c spleen cells with GAT as antigen. All cultures were harvested and assayed for specific IgG PFC on day 5, by using a modified Jerne plaque assay with GAT-SRBC as indicator cells. Data are expressed as either specific PFC per (7.5×10^6 cell) culture or

$$\text{as percent control response} = \frac{\text{response in presence of specific } T_sF \text{ or } T_{s_2}}{\text{response in presence of control } T_sF \text{ or cells}} \times 100\%.$$

Results

Binding of SJL and DBA/1 GAT-T_sF to Anti-CGAT-Immunoadsorbents. Partially purified GAT-T_sF from either in vivo immunized SJL or DBA/1 nonresponder mice was prepared with a GAT-immunoadsorbent. These purified suppressor factors were then applied to either anti-CGAT or control (NGPS)-immunoadsorbents, and the filtrates and eluates tested for activity directly on nonresponder spleen cells cultured with GAT-MBSA as antigen. Figs. 1 and 2 present the results of several similar experiments. Fig. 1 demonstrates that virtually all the suppressive activity of SJL and DBA/1 GAT-T_sF is removed by passage over anti-CGAT-immunoadsorbents and that the adsorbed T_sF can be fully recovered in the acid eluate of such a column. Further, these experiments reveal that both the original purified GAT-T_sF and the anti-CGAT adsorbed material can suppress not only syngeneic, but also allogeneic nonresponder spleen cells, in agreement with previous data (5). Fig. 2 summarizes a large number of similar experiments assaying immunoadsorbent treated DBA/1 GAT-T_sF preparations on SJL spleen cells in culture. These data are all in agreement with those of Fig. 1. The experiments in Figs. 1 and 2 were performed with several separately prepared batches of purified GAT-T_sF, all of which gave identical results. Taken together, these data indicate that the directly suppressive component of nonresponder GAT-T_sF is recognized and bound by immobilized antibody to CGAT determinants.

It is now appreciated that GAT-T_sF acts at least in part by inducing virgin spleen cells (T cells) to become active suppressor cells (T_{s_2}) (6, 7). This induction of T_{s_2} using nonresponder derived GAT-T_sF can occur with syngeneic and allogeneic nonresponder, as well as allogeneic responder, spleen cells. To determine if the T_sF responsible for this inducing activity was also recognized by anti-CGAT antibodies, the same filtrate and eluate materials assayed above in direct culture were used for T_{s_2} generation. BALB/c responder spleen cells were cultured for 2 d with various T_sF preparations and these cultured cells then washed and added in varying numbers to fresh BALB/c cultures stimulated by GAT. Data from one of four experiments of this type, all of which gave similar results, are presented in Fig. 3. Again, as for the direct acting material, the inducing GAT-T_sF was completely removed by the anti-CGAT-immunoadsorbent and could be recovered from the gel by acid elution. Thus, the material(s) in GAT-T_sF responsible for both direct suppression of nonresponder

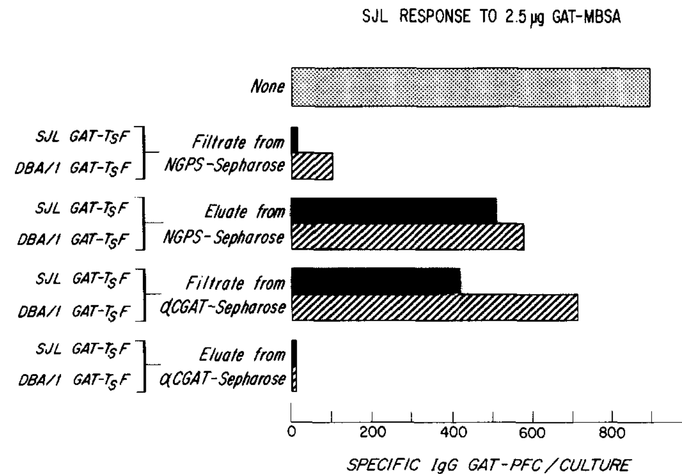

FIG. 1. Direct in vitro suppressive activity of DBA/1 and SJL GAT-T_sF before and after passage over anti-CGAT-immunoadsorbents. Purified DBA/1 or SJL GAT-T_sF was adsorbed to and eluted from either control (NGPS) columns or anti-CGAT columns, then added at a final 1/250 dilution to cultures of SJL spleen cells stimulated with 2.5 μg GAT-MBSA. Specific IgG GAT-PFC were assayed 5 d later. Data are expressed as specific PFC/culture.

lymphocytes, and induction of T_{s_2} in responder cells are adsorbed by anti-CGAT-immunoadsorbents.

DBA/1 GA-T_sF Fails to Bind to Anti-CGAT-Immunoadsorbents. We have previously demonstrated that the CGAT idiotype is absent from mouse antibodies induced by the related copolymer GA (9). This finding suggested the possibility that GA-T_sF might lack CGAT-determinants and thus serve as an appropriate specificity control for the anti-CGAT column. Therefore, GA specific T_sF was prepared from DBA/1 mice, and purified on GA-Sepharose. This material was then passed over control or anti-CGAT-immunoadsorbent columns and tested in culture with DBA/1 spleen cells and GA-MBSA. Table I presents one such experiment. DBA/1 GAT-T_sF run in parallel with the GA-T_sF was fully adsorbed onto and recovered from the anti-GAT-immunoadsorbent, as shown repeatedly above. However, no significant binding of GA-T_sF to the anti-CGAT-immunoadsorbent occurred. These data imply that the interaction of GAT-T_sF with anti-CGAT antibodies is not due to a nonspecific affinity of this material for T_sF bearing I region determinants nor is it likely to be merely a reflection of charge effects resulting from the large glutamic acid content of GAT, because a similar effect would be expected with GA-specific T_sF as well.

Presence of Both CGAT Idiotypic Determinants and I-J^s Determinants on GAT-T_sF. GAT-T_sF has been shown to bear I region, more specifically, I-J subregion controlled determinants (2, 3). It was therefore of interest to determine if the anti-idiotype reactive suppressor material studied above also possessed such I-J determinants. To answer this question, the active eluate of an anti-CGAT column loaded with SJL (I-J^s) GAT-T_sF was passed over an anti-I-J^s Sepharose immunoadsorbent. Table II details the results obtained with the parent materials and the alloantiserum adsorbed T_sF. It is clear that the factor responsible for suppressive activity in the anti-CGAT eluate also possesses I-J^s determinants.

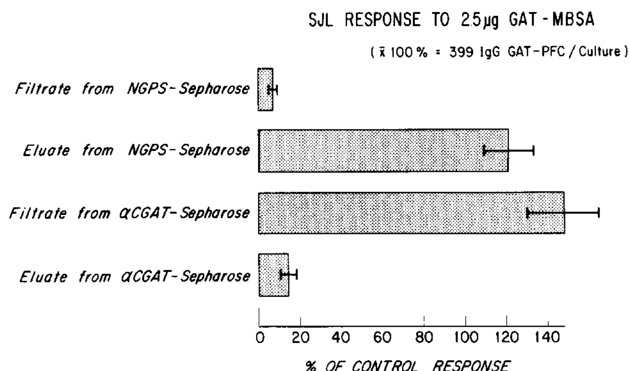

FIG. 2. Direct in vitro suppressive activity of DBA/1 GAT-T_sF before and after passage over anti-CGAT-immunoadsorbents. Purified DBA/1 GAT-T_sF was adsorbed to and eluted from either control (NGPS) columns or anti-CGAT columns, then added at a final 1/250 dilution to cultures of SJL spleen cells stimulated with 2.5 μg GAT-MBSA. Specific IgG GAT-PFC were assayed 5 d later. Data are expressed as percent control response for several combined experiments.

Discussion

The experiments presented above represent a first approach to the understanding of the nature of the antigen combining site on specific T-cell-derived suppressor factors. The results indicate that GAT-specific T_sF can be adsorbed by and eluted from immunoadsorbents prepared from a guinea pig anti-idiotype antiserum recognizing a common (cross-reactive) determinant found on most murine anti-GAT-antibodies. This adsorption appears to be related to the antigen binding specificity of the T_sF, because GAT-T_sF but not GA-T_sF, can be adsorbed by anti-CGAT-immunoadsorbents. Both direct suppressive activity on nonresponder spleen cells, and T_{s_2} inducing potential with responder spleen cells are selectively retained by anti-CGAT columns, and the active $CGAT^+$GAT-T_sF eluted from such a column still possesses I-J determinants. Further, the data indicate that the great majority of GAT-T_sF molecules bind to anti-CGAT-immunoadsorbents, based on the virtually complete removal of suppressive activity on the anti-CGAT immunoadsorbent.

Investigation of the fine antigen specificity of antibodies bearing the CGAT idiotype has revealed that antibodies elicited by GAT and L-glutamic acid^{50}-L-tyrosine^{50} (GT), but not GA, possess CGAT determinants, and that the idiotype from GAT induced antibodies preferentially bound to GT, rather than to GA.[2] These data imply that CGAT determinants are related to an antigen combining site specific for GAT or GT, but not GA, and that not all antibodies reactive with highly anionic polypeptides are bound by anti-CGAT antisera. Similar results were obtained with GAT-T_sF versus GA-T_sF in this study. The question still remains as to whether or not GT-T_sF is $CGAT^+$. The serological data might lead one to predict that GT-T_sF would be $CGAT^+$, but the lack of cross-suppression shown by GAT-T_sF and GT-T_sF in vitro (7) is difficult to reconcile with this hypothesis. Tests of GT-T_sF binding to anti-CGAT-immunoadsorbents are under way to resolve this question.

[2] Ju, S-T., M. E. Dorf, and B. Benacerraf. 1978. Idiotypic analysis of anti-GAT antibodies. III. Determinant specificity and immunoglobulin class distribution of CGAT idiotype. Manuscript submitted for publication.

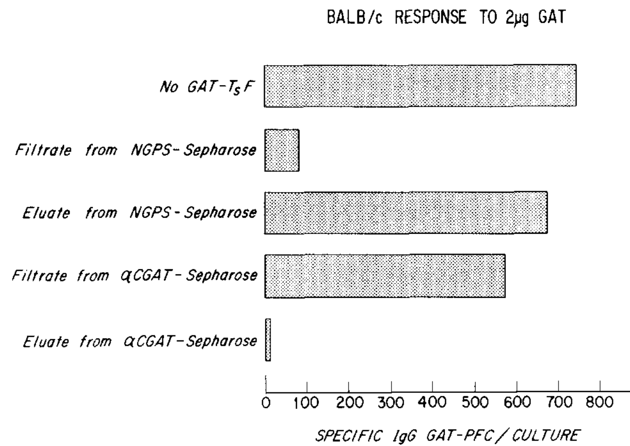

FIG. 3. Capacity of DBA/1 GAT-T_sF to induce T_{s_2} in responder BALB/c spleen cells before and after filtration over an anti-CGAT-immunoadsorbent. Purified DBA/1 GAT-T_sF was adsorbed to and eluted from NGPS- or anti-CGAT columns, then added at 1/250 final dilution together with 50 ng/ml GAT to virgin BALB/c spleen cells. After 2 d incubation, these cells were washed and 2 $\times$ 10^5 viable cells added to fresh modified Mishell-Dutton cultures of 7.5 $\times$ 10^6 BALB/c spleen cells, stimulated with 2 μg GAT. Specific GAT IgG PFC were assayed 5 d later.

Although the most likely interpretation of the data presented in this paper is that GAT-T_sF shares (a) combining site(s) with anti-GAT antibodies (i.e., possesses at least a part of an immunoglobulin V region), certain limitations of these experiments must be made clear. Although the starting immunogen consisted of $(NH_4)_2SO_4$ fractionated, GAT affinity column purified antibodies that were also passed over an anti H-2^b immunoabsorbent in an effort to remove I-region coded T-cell products, it is still theoretically possible that the anti-CGAT-serum contains antibodies made directly to GAT-specific T-cell products which copurified with the immunoglobulins and were not removed by the anti-H-2 column. Responder mice are known to be capable of producing GAT-T_sF,[3] and Kontiainen et al. have reported preparation of anti-idiotype-like antisera to antigen purified T_sF given in trace amounts according to immunization protocols similar to those used to raise anti-CGAT antisera (11). The involvement of such putative anti-T-cell factor antibodies in studies of anti-idiotypic reactivity of T-cell products is also a possibility in the earlier helper factor experiments of Mozes (12), in which no attempt was made to remove I-coded materials from the immunogen. However, if such anti-T-cell product antibodies exist in the anti-CGAT reagent, they are not directed against mouse T_sF as a class because GA-T_sF is not bound by anti-CGAT columns. Rather, they must resemble immunoglobulin specific anti-CGAT antibodies in that they detect GAT specific products obtained from strains differing at both H-2 and Ig-1 loci. To resolve this issue, we are now cloning B-cell hybridomas secreting $CGAT^+$ antibodies to provide immunoglobulin material free of potential T-cell products.[4] These pure antibodies will then be used to absorb the anti-CGAT antiserum to determine whether or not it is antibody to immunoglobulin which actually binds the T-cell-derived GAT-T_sF.

[3] Pierres, M., R. N. Germain, and B. Benacerraf. Manuscript in preparation.
[4] Pierres, M. Manuscript in preparation.

TABLE I
Lack of DBA/1 GA-T_sF Binding to Anti-CGAT-Sepharose Immunoadsorbent

Cultured cells*	Antigen‡	DBA/1 T_sF§		PFC/culture‖	Suppression¶
		Specificity	Treatment		
					%
DBA/1 spleen	GAT-MBSA	—	—	431	—
DBA/1 spleen	GAT-MBSA	GAT	NGPS-Sepharose filtrate	<15	100
DBA/1 spleen	GAT-MBSA	GAT	NGPS-Sepharose eluate	424	2
DBA/1 spleen	GAT-MBSA	GAT	αCGAT-Sepharose filtrate	416	3
DBA/1 spleen	GAT-MBSA	GAT	αCGAT-Sepharose eluate	<15	100
DBA/1 spleen	GA-MBSA	—	—	492	—
DBA/1 spleen	GA-MBSA	GA	NGPS-Sepharose filtrate	<15	100
DBA/1 spleen	GA-MBSA	GA	NGPS-Sepharose eluate	634	0
DBA/1 spleen	GA-MBSA	GA	αCGAT-Sepharose filtrate	86	83
DBA/1 spleen	GA-MBSA	GA	αCGAT-Sepharose eluate	686	0

* Responding spleen cells in modified Mishell-Dutton cultures.
‡ 2.5 μg per culture.
§ See Materials and Methods.
‖ Specific IgG plaque-forming cells (PFC)/(7.5×10^6 cell) culture.
¶ Comparison to no factor added group.

If, as is likely, it is antibody to idiotypic determinants on anti-GAT antibodies that bind GAT-T_sF, then several possible interpretations of the structural relationship between the binding regions of GAT-T_sF and antibody may be considered. Because of the high frequency and broad representation of CGAT determinants on anti-GAT antibodies of not only mice, but other species such as the rat (9), it is clear that there has been extensive evolutionary conservation of a major GAT binding site. Therefore, the combining region of the GAT-T_sF may have arrived at a configuration similar to immunoglobulin V regions by convergent evolution of independent genetic units, one in the MHC (for T_sF) and the other in the Ig germ line V genes. Because of the absence of $CGAT^-$ mouse strains, it is not possible to rule out this interpretation on a genetic basis. However, it is not unreasonable to assume that if both GAT-T_sF and anti-GAT immunoglobulin possess similar or identical idiotypic specificities, that they are coded for by the same genes, i.e., Ig V region genes. Such a model is consistent with the growing data on the presence of shared idiotypic specificities on B cells or Ig and T cells or T-cell products. These data include the studies of Binz and Wigzell on antibodies and T cells specific for allo-MHC determinants (13), of Black et al. and Hämmerling et al. on streptococcal A carbohydrate specific immune responses of A/J and BALB/c mice (14, 15), Krawinkel et al. on nylon fiber purified mouse B- and T-cell products (16), Cosenza et al. on phosphorylcholine specific helper T cells (17), and the recent data of Pincus et al. on (T, G)-A—L specific antibody and helper T cells (18) as well as the above mentioned work of Mozes on (T, G)-A—L helper factor (12), and the recent detailed studies of Bach et al.[5] on azobenzenearsonate specific T_sF.

If one puts aside for the moment alternative explanations for these data, what picture emerges of the relationship between T-cell antigen specific effector molecules

[5] Bach, B., A. Nisonoff, B. Benacerraf, and M. Greene. Manuscript in preparation.

TABLE II

Presence of I-J^s Determinants on SJL GAT-T_sF Eluted from Anti-CGAT-Sepharose Immunoadsorbent

Cultured cells*	Antigen	GAT-T_sF‡	PFC/culture§	Suppression‖
				%
SJL spleen	2.5 μg GAT-MBSA	—	500	—
SJL spleen	2.5 μg GAT-MBSA	Filtrate from NGPS-Sepharose	<20	100
SJL spleen	2.5 μg GAT-MBSA	Eluate from NGPS-Sepharose	520	0
SJL spleen	2.5 μg GAT-MBSA	Filtrate from αCGAT-Sepharose	800	0
SJL spleen	2.5 μg GAT-MBSA	Eluate from αCGAT-Sepharose	<20	100
SJL spleen	2.5 μg GAT-MBSA	Filtrate from αI-J^s Sepharose loaded with eluate of αCGAT-Sepharose	400	20
SJL spleen	2.5 μg GAT-MBSA	Eluate from αI-J^s Sepharose loaded with eluate of αCGAT-Sepharose	<20	100

* Responding spleen cells in modified Mishell-Dutton cultures.
‡ See Materials and Methods.
§ Specific IgG PFC/(7.5 × 10^6 cell) culture.
‖ Comparison to group receiving no T_sF.

and immunoglobulin? Rat T-cell products specific for alloantigens, as studied by Binz and Wigzell, possess idiotypes in common with antibodies of the same specificity (13), but both genetic and serologic studies found no evidence of MHC association with these T-cell materials (19). On the other hand, Krammer and Eichmann found the idiotypic pattern of alloreceptors on mouse T lymphocytes can be influenced genetically by both Ig allotype and MHC linked loci, though the presence of either type of gene product in the actual receptor was not demonstrated (20). The present study clearly suggests a physiochemical association of both MHC (I–J) coded products and V region determinants in the GAT-T_sF. A minimal model incorporating the bulk of these and other related data would postulate that T cells produce materials with shared Ig V region determinants, presumably reflecting the presence of true Ig V region gene products. These V region products are either (*a*) part of a single chain also including I region coded material in which the V region portion provides antigen binding specificity and the I region portion provides biologic effector function (e.g., help, suppression, H-2 restricted cell-cell communication) in a manner similar to Ig Fc regions or (*b*) joined by disulfide or noncovalent bonds to a second chain containing the I region material, forming a tightly bound molecular complex with a similar distribution of functions. This model would provide a single explanation for certain Ir gene effects in terms of both cell interaction and factor activity in that lack of formation or functional expression of the proper I region-V region complex would preclude T-cell activity for the given antigen specificity of the V region and the particular I region effector function involved. Further, this model can accommodate either an altered self concept of T-cell antigen recognition, based on appropriate V region selection and/or mutation, or a dual receptor model involving recognition of a physically linked nominal antigen and H-2 interaction site. Current advances in biochemical analysis of T-cell idiotype positive material will provide evidence for or against this model in the near future. Towards this end, the development of T hybridomas producing large quantities of active specific suppressor factor will provide an important tool, and efforts are underway to derive such hybridomas producing $CGAT^+$ GAT-T_sF to be studied in parallel with the monoclonal $CGAT^+$ anti-GAT antibodies now being isolated.

Summary

T-cell derived suppressor factors (T_sF) specific for the random copolymers L-glutamic acid^{60}-L-alanine^{30}-L-tyrosine^{10} and L-glutamic acid^{60}-L-alanine^{40}, referred to as GAT and GA, respectively, were prepared and partially purified on the appropriate antigen immunoadsorbents. GAT-T_sF obtained from nonresponder DBA/1 (H-2^q) and SJL (H-2^s) mice were passed over immunoadsorbents prepared from normal guinea pig serum (NGPS) or guinea pig anti-idiotype antiserum (anti-CGAT) specific for a common cross-reactive idiotype found on most anti-GAT antibodies in all mouse strains tested. Both the directly suppressive activity of the GAT-T_sF and the ability of GAT-T_sF to induce new suppressor T cells (T_{s_2}) in vitro were adsorbed to and fully recoverable from the guinea pig anti-CGAT-Sepharose immunoadsorbent, while the T_sF passed through the control NGPS-Sepharose without appreciable binding. The SJL GAT-T_sF specifically eluted from anti-CGAT-immunoadsorbents was shown to still possess I-J determinants. These data provide evidence suggesting a sharing of V region structures between B-cell antibody and T-cell suppressor factor specific for an antigen (GAT) under Ir gene control, in agreement with earlier studies on T and B-cell alloreceptors, T-cell helper factors, and T and B-cell receptors for conventional antigens.

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