SUPPRESSION OF IgE ANTIBODY PRODUCTION IN SJL MICE

IV. Interaction of Primed and Unprimed T Cells*

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By appropriate immunization, including infestation with the nematode Nippostrongylus brasiliensis to prime T helper cells that are specific for this nematode, high and persistent IgE antibody has been preferentially obtained in many strains of mice. In the SJL strain, however, the IgE antibody response was exceptionally low and transient when compared to that obtained in other strains (1, 2).

Further studies showed that the transient IgE antibody response was inherited as a recessive trait and was not linked to the H-2 gene complex, nor to the gene governing the inheritance of the Ig-1 allotype (2, 3). High and persistent IgE antibody responses were obtained in SJL mice when they were irradiated after immunization, and this high and persistent IgE antibody response was selectively suppressed by passive transfer of syngeneic normal spleen cells or thymocytes (2, 4).

It has been shown in other systems that T-T-cell collaboration is important in suppression of antibody production (5-11). Another immunization schedule was, therefore, developed to permit investigation of the mechanism of suppression of IgE antibody in SJL mice. This schedule is based on adoptive transfer into irradiated recipients. IgE antibody-producing B cells are primed with a haptenic determinant, T helper cells with one carrier, and other T cells with the same or a different carrier. The advantages of this method of immunization are multiple: the primed cells are not irradiated, the priming of T cells can be better controlled than when infestation is used, and, finally, experimental and control mice receive cells from the same pool, therefore minimizing individual variations.

The suppression of antibody production demonstrated in the following experiments is different from any other type of suppression as it is selective for IgE and is brought about by two types of T cell, one of which might have a specificity different from that of the helper T cell.

Materials and Methods

Antigens and Parasite. Method of culture of N. brasiliensis (NB) and preparation of the worm antigen (Nh) have been described (1). Proteins and their dinitrophenylated conjugates (DNP-proteins) were the same as those previously described (1).

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Abbreviations used in this paper: C, rabbit complement; DNP, dinitrophenyl; Ea, egg albumin; HBSS, Hanks' balanced salt solution; KLH, keyhole limpet hemocyanin; NB, Nippostrongylus brasiliensis; Nh, extract of Nippostrongylus brasiliensis worms.

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Animals. The following inbred mice were obtained from The Jackson Laboratory (Bar Harbor, Maine): SJL, ASW, A/WySn, C57BL/10, C3H/He, and AKR. Congenic inbred B10.S mice were a generous gift of Dr. Phillips-Quagliata (New York University Medical Center, New York). (SJL × ASW)F1 and (SJL × B10.S)F1 hybrids were bred in our animal facilities. CFW mice were obtained from Charles River Breeding Laboratories Inc. (Wilmington, Mass.). All mice were female and 8-12 wk old at the beginning of the experiments. Sprague Dawley male rats, weighing 250-300 g, were obtained from Blue Spruce Farms Inc. (Altamont, N. Y.).

The Adoptive Transfer Method. Recipient mice were irradiated 1 d before injection of spleen cells from syngeneic donors with a dose of 600 rads. Five recipients were used per group. In preliminary experiments it was ascertained that no antibody was produced after immunization with this sublethal dose of radiation. The radiation was delivered by a Gammator M apparatus (Radiation Machinery Corp. Parsippany, N. J.) which uses cesium as its source of gamma rays. The plastic cage in which the mice were held during radiation could contain five mice.

The spleen cells of donor mice were gently teased out in sterile Hanks' balanced salt solution (HBSS) (Microbiological Associates, Walkersville, Md.) with scissors and a small forceps on melting ice. The cells were filtered through gauze and then through a small stainless sieve to remove tissue debris and clumps, and centrifuged at 170 g for 10 minutes at 4°C. The cells were washed three times with cold HBSS and finally resuspended in cold HBSS. Cell viability was estimated by the trypan blue exclusion test. Generally 80-92% of cells were viable. The appropriate number of cells were injected i.v. in 0.2-0.5 ml HBSS and immediately after the animals were injected (challenged) i.p. with the appropriate antigen in 0.5 ml sterile saline containing 1 or 2 mg Al(OH)$_3$ (See Tables). The animals were bled from the retroorbital sinus as described in (2). Briefly, 0.2 ml blood was mixed with 0.9 ml heparinized saline (10 U/ml), centrifuged, and the supernate was taken as a 1/10 dilution. Bleedings from the same groups of mice done on the same day were pooled and, if not tested immediately, stored at −20°C. The first bleeding was done 7 d after challenge and consecutively every 7 d for 4 wk. In the Tables, only the second bleeding will be presented, as the titer did not vary much in controls after the 2nd wk and, in cases when suppression occurred, the titers were the same or even lower in the third and fourth bleeding.

Donor Mice. One group of donors were healthy uninjected mice; these will be referred to as unprimed mice. The other groups were immunized as listed below. One group of mice (G1) was injected with 1 µg dinitrophenyl-keyhole limpet hemocyanin (DNP-KLH) and 3 wk later infected with 750 third-stage larvae of NB as described in (1). Spleen cells from these mice were harvested 2 wk after infestation. Two groups of mice were injected with 1 µg DNP-KLH. 3 wk later, one group (G 2) was injected with 0.2 µg egg albumin (Ea), the other group (G 3) with 10 µg Ea. The spleen cells from these mice were harvested 7 d after the injection of Ea.

One group (G 4) of mice was injected with 0.2 µg DNP-Ea and the spleen cells were harvested 4 wk later; a second (G 5) with 1 µg DNP-KLH and the spleen cells harvested 4 wk later. A third group (G 6) was injected with 10 µg Ea twice with a 2-wk interval and the spleen cells harvested 2 wk after the second Ea injection; a fourth with 10 µg KLH twice with a 2-wk interval and the spleen cells harvested 2 wk after the second KLH injection. The spleen cells from the last two groups will be referred to as hyperprimed cells. Proteins and/or protein-hapten conjugates were always injected in donor mice with 1 mg Al(OH)$_3$.

Antibody Titration. Anti-DNP antibodies were titrated as described in (2) by passive cutaneous anaphylactic reactions (PCA) in CFW mice for IgGl with a 1.5-h sensitization period (12) and rats for IgE (13) with a 2-h sensitization period (12) using as challenging antigen 0.5 mg dinitrophenyl-guinea pig serum albumin for mice and 1 mg dinitrophenyl-bovine serum albumin for rats. Doubling dilutions were used and a difference less than fourfold was not considered significant.

Depletion of T Cells from Spleen Cell Suspension. Anti-Thy-1.2 serum was a generous gift of Dr. Lloyd Old (Sloan-Kettering Institute for Cancer Research, N. Y.) and rabbit complement (C) was obtained from Accurate Chemical and Scientific Corp. (Hicksville, N. Y.). This particular batch of antiserum was used at a dilution of 1–50 and the rabbit serum as C source at a dilution of 1–15. Depletion was done as described in (2). The viability of the spleen cells was tested by the trypan blue dye exclusion test. Approximately 30% of the cells were stained.
Results

Strain Difference of Suppression of IgE Antibody Production by Injection of Unprimed Spleen Cells. Control mice were injected with $3 \times 10^7$ spleen cells which were taken from mice immunized with DNP-KLH, and infested with NB as described in materials and methods (donor mice G 1). The experimental groups were also injected with $5 \times 10^7$ spleen cells from unprimed donors. Immediately after injection of the cells, the animals were challenged with $10 \mu g$ of DNP-Nb. The antibody titers are shown in Table 1. Cotransfer of unprimed spleen cells selectively suppressed IgE antibody production in SJL, and to a lesser degree in AKR, but not in other strains of mice. It should be noted that anti-DNP IgG$_1$ antibody production was not significantly suppressed.

As the greatest suppression was obtained in the SJL strain of mice, the following experiments were performed with this strain.

Effect of the Dose of Carrier Antigen for Priming on the Suppression of IgE Antibody Production by Unprimed Spleen Cells. To prime for IgE and IgG anti-DNP antibody-producing B cells, mice were injected with $1 \mu g$ DNP-KLH. To prime for carrier specific T cells, the mice were supplementarily immunized 3 wk later with $0.2 \mu g$ (donor mice G 2) or $10 \mu g$ (donor mice G 3) Ea. Recipients were injected with $3 \times 10^7$ cells of the above mentioned donors (donor mice G 2 or G 3), alone or in addition to the primed cells, also with $5 \times 10^7$ unprimed spleen cells. Challenge was done with $10 \mu g$ DNP-Ea. Results are presented in Table II. The production of anti-DNP IgE antibody was

![Table 1](image)

| Strain§ | Anti-DNP antibody titers* |
|---------|--------------------------|
|         | IgE | IgG$_1$ |
|         | Transferred spleen cells | Transferred spleen cells |
| SJL     | $3 \times 10^7$ primed + $5 \times 10^7$ unprimed | $3 \times 10^7$ primed + $5 \times 10^7$ unprimed |
| ASW     | 2,560 | 160 |
| B10.S   | 5,120 | 2,560 |
| A/WySn  | 2,560 | 1,280 |
| C57BL/10| 1,280 | 640 |
| C3H/He  | 1,280 | 640 |
| AKR     | 1,280 | 320 |
| (SJL × ASW)F$_1$ | 2,560 | 1,280 |
| (SJL × B10.S)F$_1$ | 5,120 | 5,120 |

* Anti-DNP antibody was titrated by PCA (see text). Titers taken 2 wk after transfer are shown.

‡ Priming of donors: $1 \mu g$ DNP-KLH + $1 \mu g$ Al(OH)$_3$ was injected i.p. 3 wk later, the mice were infested with NB. The spleen cells were harvested 2 wk later.

§ Recipient mice were challenged i.p. immediately after cell transfer with $10 \mu g$ DNP-Nb + $1 \mu g$ Al(OH)$_3$. 


selectively suppressed only in the group of mice which were injected with spleen cells from donors primed with the higher amounts of carrier protein (i.e., 10 µg) together with unprimed spleen cells. This experiment shows that the dose of carrier protein used for immunization is important to bring about an effective interaction of carrier primed T cells with unprimed spleen cells for selective suppression of anti-DNP IgE antibody production. This fact will be commented upon in the Discussion.

### Specificity of the Carrier-primed Suppressor Cells

In the experiments presented in Table II the donor mice were primed first with hapten-carrier conjugate (DNP-KLH) then with free heterologous carrier protein (Ea). To better demonstrate the specificity of the carrier-primed suppressor cells, separate donors were primed with hapten-carrier conjugate (DNP-Ea or DNP-KLH) and with free carrier proteins (Ea or KLH). Anti-DNP antibody titers, 2 wk after challenge in these experiments, are shown in Table III. One-half of the recipients were injected with 1.5 × 10^7 spleen cells from donors primed with 0.2 µg DNP-Ea and divided into six groups (See donor mice, G 4). The first group to serve as base-line control was not injected with other cells. All other groups were injected in addition with spleen cells taken from different donors as listed below: the second group with 5 × 10^7 spleen cells from unimmunized mice; the third with 1 × 10^7 spleen cells from donors hyperprimed with Ea (donor mice, G 6); the fourth with 1 × 10^7 spleen cells from donors hyperprimed with Ea and in addition with 5 × 10^7 spleen cells from unprimed donors; the fifth with 1 × 10^7 spleen cells from donors hyperprimed with KLH (donor mice, G 7); and the sixth with 1 × 10^7 spleen cells from donors hyperprimed with KLH and in addition with 5 × 10^7 spleen cells from unprimed donors. The challenging antigen was 10 µg DNP-Ea. The other one-half of recipients were used for a reverse experiment and were injected with 1.5 × 10^7 spleen cells from donors primed with 1 µg DNP-KLH (donor mice G 5). These mice were also divided into six groups and were injected exactly like the mice of the other one-half of the recipients. However, the challenging antigen in this case was 10

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**Table II**

| Transferred spleen cells | Anti-DNP antibody‡
|-------------------------|-----------------|
| 3 × 10^7 primed with*   | 5 × 10^7 unprimed | IgE | IgG1 |
| G 1 DNP-KLH 1 µg +     | -               | 1,280 | 320 |
| + Jay 0.2 µg           |                 |       |     |
| G 2                    | +               | 1,280 | 320 |
| G 3 DNP-KLH 1 µg +     | -               | 640  | 320 |
| + Jay 10 µg            |                 |       |     |

* Priming of donors: 1 µg of DNP-KLH + 1 mg of Al(OH)3 was injected i.p. 3 wk later, 0.2 µg Ea + 1 mg Al(OH)3 or 10 µg Ea + 1 mg Al(OH)3 was also injected i.p. Spleen cells were harvested 1 wk later. The recipients were challenged immediately after cell transfer with 10 µg DNP-Ea + 1 mg Al(OH)3.

‡ For antibody titration see footnote * of Table 1.
Transferred spleen cells

|       | 1.5 × 10^7 | 1 × 10^7 | 5 × 10^7 |
|-------|-------------|-----------|-----------|
| primed with* | hyperprimed | unprimed  |           |

|       | Antigen challenge§ | Anti-DNP¶ |
|-------|-------------------|-----------|
|       |                   | IgE | IgG1 |

* Donor mice were immunized with either 0.2 μg DNP-Ea + 1 mg Al(OH)₃ or with 1 μg DNP-KLH + 1 mg Al(OH)₃ i.p. 4 wk before transfer.

§ 10 μg of DNP-Ea or DNP-KLH and 1 mg Al(OH)₃ was injected i.p. just after transfer.

¶ Antibody titer was determined 2 wk after transfer. See footnote * of Table I.

μg DNP-KLH. In both cases, selective suppression of anti-DNP IgE antibody was brought about only when the animals were injected with spleen cells from carrier hyperprimed mice and unprimed mice. Carrier hyperprimed cells alone or unprimed cells alone did not bring about a noticeable suppression of anti-DNP IgE antibody production. It must be emphasized that when unrelated carrier protein was used to hyperprime spleen cells (KLH in the first case: upper part of Table III or Ea: lower part of Table III) no suppression was observed.

Suppression of Anti-Hapten IgE Antibody Production by Injection of Free Carrier Protein. Anti-DNP antibody titers 2 wk after challenge are shown in Table IV. Recipient mice were divided into two categories. One-half of them were injected like the group of mice shown in the upper part of Table III, omitting the two groups injected with spleen cells from mice hyperprimed with the homologous carrier protein (i.e., Ea). The mice in these groups were challenged with a mixture of 10 μg DNP-Ea, 10 μg KLH, and 2 mg Al(OH)₃. The other one-half of the recipients were injected as those shown in the lower part of Table III omitting here the two groups injected with spleen cells from mice hyperprimed with the homologous carrier protein (i.e., KLH). The mice in these groups were challenged with a mixture of 10 μg of DNP-KLH, 10 μg of Ea, and 2 mg Al(OH)₃. Anti-DNP IgE antibody production was selectively suppressed only in those groups which were injected with spleen cells from carrier hyperprimed animals and unprimed spleen cells. It must be noted that the carrier used to hyperprime donors was unrelated to the carrier conjugated to DNP. The important difference between this experiment and the preceding one is that challenge was done with two substances: the carrier-hapten conjugate used to prime B cells and
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**Table IV**

*Suppression of Anti-hapten Antibody Response by Injection of Free Carrier*

| Transferred Spleen Cells | Anti-DNP* |
|--------------------------|-----------|
| 1.5 × 10⁷ primed with*   | 1 × 10⁷ hyper-primed with‡ | 5 × 10⁷ unprimed | DNP-Ea |
|                          | +                     | -                  | +          |
| G 1 DNP-Ea               | -                     | -                  | DNP-Ea     |
| G 2 DNP-Ea               | -                     | +                  | +          |
| G 3 DNP-Ea               | -                     | -                  | KLH        |
| G 4 DNP-Ea               | -                     | +                  | KLH        |
| G 5 DNP-KLH              | -                     | -                  | DNP-KLH    |
| G 6 DNP-KLH              | +                     | -                  | KLH        |
| G 7 DNP-KLH              | -                     | +                  | +          |
| G 8 DNP-KLH              | -                     | +                  | +          |

* Priming with DNP-Ea or DNP-KLH was the same as that described in Table III, footnote*.
‡ Hyperpriming was the same as that described in Table III, footnote*.
§ 10 µg DNP-Ea, 10 µg KLH, and 2 mg Al(OH)₃ were mixed and injected together into mice of G1 to G4 just after transfer. 10 µg DNP-KLH, 10 µg Ea, and 2 mg Al(OH)₃ were mixed and injected together i.p. into mice of G5 to G8 just after transfer.

**Table V**

*Both Types of Suppressor Cells are Thy-1-Positive Cells*

| Transferred spleen cells | Anti-DNP* |
|--------------------------|-----------|
| 1.5 × 10⁷ primed with*   | 1 × 10⁷ hyper-primed with‡ or untreated | 5 × 10⁷ untreated | DNP-Ea |
|                          | treated‡ or untreated | -                  | KLH |
| G 1 DNP-KLH              | Not injected | Not injected | 1,280 |
| G 2 DNP-KLH              | Not injected | Untreated     | 1,280 |
| G 3 DNP-KLH              | Anti-Thy-1.2 and C | Untreated | 640 |
| G 4 DNP-KLH              | Normal mouse serum and C | Untreated | DNP-KLH |
| G 5 DNP-KLH              | Untreated     | Anti-Thy-1.2 and C | 320 |
| G 6 DNP-KLH              | Untreated     | Normal mouse serum and C | 80 |

* Mice were primed with 1 µg DNP-KLH and 1 mg Al(OH)₃ i.p. 4 wk before transfer.
‡ Donors were primed with 10 µg KLH and 1 mg Al(OH)₃ i.p. two times with 2-wk interval. Spleen cells were transferred 2 wk after the second injection.
§ Anti-Thy-1.2 + C or normal mouse serum + C treatment of transferred cells.
|| 10 µg DNP-KLH and 1 mg Al(OH)₃ were injected just after transfer.
† Antibody titer determined 2 wk after transfer. See also footnote* of Table I.

T helper cells and the free carrier used to immunize animals which we term here as hyperprimed (also see Discussion).

Effect of Anti-Thy and C Treatment on Carrier Hyperprimed and on Unprimed Cells. All mice were injected with 1.5 × 10⁷ cells from donors primed with DNP-KLH. All, except group I, were injected with 5 × 10⁷ unprimed spleen cells. In addition, four
groups were also injected with $1 \times 10^7$ spleen cells from donors hyperprimed with KLH. Both types of cells, unprimed and hyperprimed, were left untreated or were treated with anti-Thy-1.2 and C, as described in Materials and Methods. In controls, cells treated with normal mouse serum diluted 1–50 instead of anti-Thy-1.2 were injected. The results are presented in Table V. When either of the spleen cells were treated with anti-Thy-1.2 and C there was much less suppression of IgE antibody production than when the same cells were treated with normal mouse serum. The partial suppression observed when the unprimed cells were treated with the antisera and the hyperprimed cells were left untreated will be commented upon in the Discussion.

Discussion

Cotransfer of syngeneic spleen cells from primed mice and from unprimed mice into irradiated mice may bring about a selective suppression of the hapten-specific IgE antibody production in SJL and to a lesser degree in AKR mice (Table I). These results confirmed our earlier observations (2, 4, 14). It must be noted that the recipient mice, irradiated with 600 rads, which is a sublethal dose of radiation in the SJL strain, were unable to produce antibody of any class when they were immunized in the same way as those mice which were injected with primed spleen cells, as has been observed in preliminary experiments (not shown).

Using the adoptive transfer method, we confirmed our previous results, i.e., that unprimed T cells are capable of selectively suppressing IgE anti-DNP antibody production (2, 14). One of the advantages of the adoptive transfer method is that all mice are injected with primed and unprimed cells of the same pools and for this reason the control and experimental groups can be compared with greater confidence and precision. The other advantage is that it is possible to regulate the number of primed cells which cannot be regulated by active immunization. As it is impossible to quantitate with precision the antigenic stimulus provoked by infestation with living larvae of NB, we devised a new schedule where defined hapten-protein conjugates were used for immunization. Using different amounts of hapten-carrier protein conjugates in several preliminary experiments, it became evident that the population of primed cells might contain two types of T cells: one which is a T helper cell; the other a T cell (Table V) which is necessary to bring about anti-DNP IgE suppression, and that the priming of this second type of T cell is favored by higher amounts of antigen. The experiments presented in Table II exemplify this point. In this experiment, B cells were primed with DNP-KLH, T cells with Ea. The interaction of carrier-primed (Ea) T cells and anti-hapten antibody (anti-DNP)-producing B cells requires, in most of the cases, that the hapten (DNP) should be coupled to carrier for effective challenge. This fact was demonstrated several years ago when the carrier effect was first described (15). Therefore, the challenging antigen was DNP-Ea. Anti-DNP IgE antibody was selectively suppressed only in the group which was injected concomitantly with spleen cells from donors primed with the higher amount of carrier (10 \( \mu \)g) and spleen cells from unprimed donors.

The dose of the carrier used for priming therefore has a decisive influence in selective anti-DNP IgE suppression.

Okumura and Tada (16) have shown already that repeated injections of high amounts of antigen are very effective to adequately prime suppressor cells.
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For this reason, and because of the results of the experiments presented in Table II, we hyperprimed donors with higher and repeated injections of a carrier protein and used cells from these donors to study the suppression of IgE antibody production by cells from different donors primed with low amounts of hapten-carrier conjugates. For drastic and selective suppression of IgE antibody production, the simultaneous injection of hyperprimed cells and unprimed cells was necessary. Spleen cells, taken from donors that were hyperprimed by the same carrier which was used for priming the helper T cells and for challenge, were very effective in the suppression of hapten-specific anti-IgE antibody production; spleen cells, from donors hyperprimed by an unrelated carrier, however, were without any effect if the free carrier protein was not injected with the challenging antigen (Table III). However, when the free carrier, which was used to hyperprime donors, was mixed with the challenging antigen, very effective and selective IgE suppression was obtained (Table IV). Therefore, the priming of T cells, which plays a crucial role in suppression of selective anti-hapten IgE production, is antigen specific. However, this specificity is not necessarily the same as that of the antigen which primes helper T cells. It has been shown with anti-Thy-1.2 serum and C that both interacting cells (i.e., the hyperprimed and unprimed) are T cells (Table V).

It must be emphasized that IgG1 anti-DNP antibody was not significantly different in control and experimental groups in any of the experiments, therefore, the suppression in this system is specific for the production of the IgE class of antibodies.

The moderate suppression, when only cells from hyperprimed donors were injected without unprimed spleen cells, can be explained by the probable presence of some unprimed T cells in the population of spleen cells from hyperprimed donors (experiments in Tables II–V).

Our previous results on IgE suppression were confirmed in other laboratories (17).Suppressor cells and suppressor factors for IgE production were also shown by others (18–22). However, cellular interactions were not investigated by these authors.

Tada (5) showed that an Lyt-2,3 suppressor cell produces a suppressor factor which then reacts with an Lyt-1,2,3 cell which accepts this suppressor factor and an amplification loop is interposed before the actual suppressor cells act on the target cell. Eardley et al. (7), Cantor et al. (8), and McDougal et al. (9), studying IgM plaque-forming cells in vitro, showed in their system that Lyt-1 cells may act as helper cells for amplifying suppression and called this feedback suppression. However, we cannot infer from these in vitro results what could happen in vivo in regard to IgE anti-hapten antibody production.

It is possible that the carrier injected into the recipients may induce T cells from the unprimed population for suppressor activity or for amplifying activity. These T cells induced from the unprimed cells could then interact with the carrier specific hyperprimed cells. Another possibility is that the carrier antigen, after interacting with the carrier-specific hyperprimed T cell, induces suppressor cells from the unprimed T-cell population in a way similar to that shown by Tada (5) (see above).

Still another possibility is that the free carrier is acting only on the carrier hyperprimed cell and the unprimed T cell is in someway necessary to bring about suppression. The suppressor cell might act either on the T helper cell or directly on the IgE-producing B cell. A particular aspect of the antibody suppression obtained in the SJL strain of mice is the selectivity for the IgE class of antibody. Selective
suppression of IgE class was also demonstrated by Kishimoto et al. (19, 20). These authors showed that if before immunization with DNP-ovalbumin mice are preimmunized with DNP-coupled mycobacteria, IgE, but not IgG1 anti-DNP and even IgE anti-ovalbumin antibodies, are suppressed. This suppression was caused by DNP-specific suppressor T cells. We found in our experiments that suppression of anti-hapten IgE antibody production could be induced by carrier-specific T cells, but only when the challenging antigen contained the same carrier, albeit unconjugated to the challenging hapten-carrier conjugate. In addition, an interaction between these hyperprimed T cells and unprimed T cells was necessary.

The type of suppression described in this work is quite different from types previously described for the following reasons: it is class specific (only IgE antibody is suppressed); it results from the interaction of two sets of T cells, one hyperprimed and the other unprimed; and finally, the specificity of the hyperprimed T cells can be unrelated to the specificity of the helper T cells.

Summary

The mechanism of selective anti-hapten IgE antibody production was studied in SJL mice. Using an adoptive transfer method of spleen cells into syngeneic recipients irradiated with a sublethal dose of 600 rads, it was demonstrated that for the suppression of anti-dinitrophenyl (DNP) IgE antibody production the interaction of two subsets of T cells is necessary. DNP-primed B cells and carrier-primed T helper cells are taken from donors primed with small amounts of DNP-carrier conjugates. Without injection of other cells, high titer and persistent anti-DNP antibodies are produced in the recipients. The two subsets of T cells that are active in suppression of IgE are taken from two types of donors: one donor is immunized (hyperprimed) with larger amounts of carrier protein twice, the other is an unprimed donor. The carrier for hyperpriming the first type of donor may be unrelated to the carrier used for priming the helper T cells. To bring about anti-DNP IgE suppression it is necessary that the animals should be challenged with the same DNP-carrier conjugate used for priming the B and T helper cells. If the hyperprimed donors were immunized with a heterologous, unrelated carrier, then this heterologous unconjugated carrier must also be injected together with the homologous DNP-carrier conjugate. In these conditions, anti-DNP IgE antibody production is suppressed, but the production of anti-DNP IgG1 antibody is not diminished.

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