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Staphylococcal Enterotoxin B Stimulates Expansion of Autoreactive T Cells That Induce Apoptosis in Intestinal Epithelial Cells: Regulation of Autoreactive Responses by IL-10

Komei Ito,* Hiromasa Takaishi,* Yide Jin,* Fei Song,* Tim L. Denning,** and Peter B. Ernst*‡‡

T cell responses to self Ags and normal microbial flora are carefully regulated to prevent autoreactivity. Because IL-10-deficient mice develop colitis, and this response is triggered by luminal flora, we investigated whether IL-10 regulates the ability of microbial Ags to induce autoreactive T cells that could contribute to intestinal inflammation. T cells from wild-type mice were primed with staphylococcal enterotoxin B (SEB) in vitro, which induced an autoreactive proliferative response to syngeneic feeder cells. The cells were predominately CD3+ and CD4+. T cells from IL-10-deficient mice were constitutively autoreactive, and SEB priming enhanced this further. The autoreactive, proliferative response of T cells from wild-type mice was suppressed by IL-10 in the primary or secondary culture, and this effect was inhibited by neutralizing Abs to the IL-10R. To confirm that an autoreactive repertoire was expanded after SEB priming, we used CBA/J mice (Mls-1a) in which autoreactive T cells recognizing the endogenous viral superantigen are depleted (Vβ6, 7, 8.1 TCR-bearing cells). However, SEB rescued these autoreactive T cell repertoires. Adding anti-MHC class II Ab blocked the autoreactive response. SEB-primed splenic or colonic T cells also induced apoptosis in syngeneic intestinal epithelial cells that was blocked significantly by IL-10. Thus, microbial Ags have the potential to abrogate self tolerance by stimulating autoreactive T cells that become cytolytic to target cells. IL-10 plays a protective role in maintaining self tolerance after microbial stimulation by preventing the activation of T cells that contribute to epithelial cell damage. The Journal of Immunology, 2000, 164: 2994–3001.
suggest that highly immunogenic stimuli, such as staphylococcal enterotoxin B (SEB), are capable of inducing autoreactive T cells that express a repertoire that recognizes self Ags, proliferate in response to syngeneic cells, and are capable of injuring syngeneic cells through cell-mediated immunity. In addition, these responses are regulated by IL-10. The implications for the roles of these responses in immune-mediated disease of the intestine are discussed.

Materials and Methods

Mice

IL-10−/− 129/SvEv mice (H-2b, 1-E+) were provided by DNAX Research Institute (Palo Alto, CA) and were bred in the Animal Resource Center of the University of Texas Medical Branch (Galveston, TX). Wild-type 129/ SvEv mice were purchased from Taconic Farms (Germantown, NY) and were bred under the same conditions. C57BL/10 IL-10−/− mice (H-2b, 1-E+, Mls-1a) and wild-type controls, CBA/J mice (H-2b, Mls-1a), as well as C57/HeJ mice were purchased from The Jackson Laboratory (Bar Harbor, ME). The animal research committee of the University of Texas Medical Branch approved all procedures used in these studies.

Cytokines and Abs

Recombinant murine IL-10 was provided by Schering-Plough (Kenilworth, NJ). Hybridomas producing anti-mouse CD8 (53-6.72, TIB-105) or anti-mouse I-Aβ (10.2.16, TIB-93) were purchased from American Type Culture Collection (Manassas, VA) and grown according to the instructions provided. Supernatants were used as a source of Ab. Anti-mouse I-E, I-Aβ Ab (M5/114) were produced from ascites and were concentrated using ammonium sulphate sedimentation by Dr. Victor Reyes (University of Texas Medical Branch). Anti-IL-10R Ab (1B1.2) was provided by Dr. K. W. Moore (DNAX, Palo Alto, CA). The activity of rIL-10 and the neutralizing activity of this Ab were confirmed as previously described (25) using the IL-10-dependent mouse mast cell line (MC9, American Type Culture Collection CRKL 8306), in which 0.1 μg/ml Ab inhibited the proliferation of 2 × 105 MC9 cells in the presence of 1 ng/ml mouse rIL-10 and 5 pg/ml mouse rIL-3 (data not shown). Isotype controls for mouse IgG (ChromPure Mouse IgG) and rat IgG (ChromPure Rat IgG) were purchased from Jackson ImmunoResearch Laboratories (West Grove, PA). PE- or FITC-conjugated anti-mouse CD3, CD4, or CD8 was purchased from Caltag (Burlington, CA). FITC-conjugated anti-mouse Vβ3, Vβ6, Vβ7, Vβ8.1, Vβ8.2, biotin-conjugated anti-mouse TCR-αβ, PE-conjugated anti-mouse CD8, biotinylated-human IL-10 (26), and isotype controls for the corresponding Abs were obtained from PharMingen (San Diego, CA). Streptavidin-PE was purchased from Sigma (St. Louis, MO).

Cell isolation

Single-cell preparations were made by mincing spleen and lysing RBC in ammonium chloride (0.15 M), potassium carbonate (1 mM), and EDTA (0.1 mM) buffer (pH 7.3) lysing buffer; using standard techniques (27). Colonic mucosal T cells were isolated using a modification of a previously described procedure (28). Briefly, large intestines from five C57/HeJ mice were isolated and flushed, lymphoid nodules were removed, and tissue was opened longitudinally in HBSS (Life Technologies, Grand Island, NY). Tissue was cut into 2 to 5-mm segments and stirred at 37°C for 45 min in DMEM containing 50 U/ml of type VII collagenase (Sigma), 0.5 mg/ml of dispase grade II (Roche, Indianapolis, IN), 0.01% gentamicin (Life Technologies), and 1× PBS. After collecting the cell suspension in the supernatant, the enzymatic treatment was repeated again. Pooled supernatants were filtered through nylon wool, and enriched lymphocytes were centrifuged through a discontinuous 44/70% Percoll (Pharmacia, Alameda, CA) gradient for 18 min at 800 × g for 18 min. Cells at the interface between the 70 and 44% layers were collected and washed. Approximately 95% of the lymphocytes were viable, as measured by trypan blue exclusion.

T cell stimulation

T cells prepared from spleen or colon (2.5 × 106 cells/ml) were stimulated with 10 μg/ml SEB (Sigma) in RPMI 1640 (Life Technologies) containing 10% FCS (HyClone, Logan, UT) as a primary stimulation. After 72 h of incubation the cells were washed three times to remove the residual SEB and resuspended in 10 μg/ml SEB in RPMI 1640. After 4 days of resting, cells were washed once, and 2 × 105 viable responder cells were cultured with 2.5 × 105 syngeneic feeder cells in 96-well flat-bottom plates. Feeder cells were prepared by incubating fresh splenocytes with 100 μg/ml of mitomycin C (Sigma) at 37°C for 30 min and washing three times. In some experiments recombinant mouse IL-10 and/or anti-IL-10R Ab (1B1.2) was added in either the priming or secondary stimulation. T cells were also activated with anti-CD3 or PMA (5 ng/ml) and ionomycin (500 ng/ml; Sigma) as previously described (29) to compare their autoreactivity with that of SEB–primed cells. To detect proliferative responses, responder cells were incubated for 72 h, and [3H]thymidine incorporation was determined by liquid scintillation counting using a Liquid Scintillator (Beckman, Fullerton, CA). All experiments were performed in triplicate.

Purification of T cells

In some experiments MHC class II+ cells or CD8+ cells were depleted to obtain highly enriched CD4+ T cells (30). Spleen cells or mesenteric lymph node cells (1 × 105) were incubated in DMEM containing 10% FCS with M5/114 (anti-MHC class II) and/or 53-6.72 (anti-CD8) Abs for 30 min on ice. After being washed three times, cells were incubated at 4°C with sheep anti-rat IgG Ab-coated magnetic beads (Dynabeads M-450; Dynal, Oslo, Norway) in DMEM at one bead per cell for 20 min while rotating. Magnetic bead-binding cells were removed using a magnetic separator (PerSeptive Biosystems, Framingham, MA). Flow cytometric analysis always revealed the residual MHC class II+ or CD8+ cells to be <1%. The recovered cells were resuspended in RPMI and used for culture.

Flow cytometry of surface Ag expression

One million cells were incubated in PBS-0.1% azide containing fluorescence- or biotin-conjugated Abs on ice for 30 min. When using biotin-conjugated Abs, cells were washed once and incubated with streptavidin-PE or streptavidin-biotinylated-human IL-10 (26), and isotype controls for the corresponding Abs were obtained from PharMingen (San Diego, CA). Streptavidin-PE was purchased from Sigma (St. Louis, MO).

Cytokine assay

The IL-2 concentration of culture supernatant was detected by bioassay using the CTL-2 hybridoma (27). Cells (5000/50 μl medium) were incubated with 50 μl of samples or standards (recombinant human IL-2, Genzyme, Cambridge, MA) in triplicate for 24 h. [3H]thymidine (1 μCi/well) was added during the last 8 h of incubation, and [3H]thymidine incorporation was detected as described above. Specific IL-2 activity (units per milliliter) was calculated according to the standard curve of the identical assay.

Cytotoxicity assay

The cytotoxic activity of SEB–primed effector cells (splenocytes or colonic mucosal lymphocytes) was detected by the JAM assay (31) using Mode-K cells (duodenal epithelial cell line from C57/HeJ origin (32)) as target cells. Effector cells from C57/HeJ mice were stimulated with 10 μg/ml of SEB for 18 h, washed three times, and used as effector cells. In some experiments cells were pretreated with recombinant mouse IL-10 and/or anti-IL-10R Ab (1B1.2) for 2 h before addition of SEB. Mode-K cells were labeled with 10 μCi/ml of [3H]thymidine for 4 h, washed three times, and used as target cells. Labeled Mode-K cells (1 × 105) were added to each well of a 96-well flat-bottom plate and incubated with increasing numbers of effector cells up to a 40:1 E:T cell ratio. After 24 h of culture, the amount of tritium, which was retained only in the live cells, was counted by gamma counter. Data are expressed as the percent survival and are calculated by dividing the counts per minute of samples with that of Mode-K cells only (average of 18 wells). In some experiments, supernatant from SEB–primed responder cells was checked for cytotoxicity. Culture inserts (0.4 mm pore size; Transwell, Corning Costar, Cambridge, MA) were also used between effector and target cells.

Statistical analysis

Paired Student’s t test (two tailed) was performed to compare the mean values of two corresponding datasets.

Results

Induction of autoreactive T cells by SEB

To determine whether activation of splenic T cells by a microbial Ag could induce autoreactive responses, splenocytes from IL-10 7 Abbreviations used in this paper: SEB, staphylococcal enterotoxin B; KO, knockout; IEL, intestinal intraepithelial epithelial lymphocytes; FasL, Fas ligand.

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their response to medium alone. Proliferative response to syngeneic feeders without priming compared with p
neic feeder cells. Medium-primed IL-10-deficient splenocytes also showed significant autoreactive response after secondary stimulation with syngeneic feeder cells. SEB-primed splenocytes showed active response of SEB-primed cells (Fig. 2). We also examined whether IL-10 inhibited the autoreactive proliferative responses, and IL-10-deficient cells tend to be autoreactive without priming (Fig. 1).

**IL-10 inhibits the autologous response in both induction and effector phases**

We examined the possibility that IL-10 regulates the induction of the autoreactive response by SEB in vitro. Spleen cells from C57BL/10 IL-10-deficient and wild-type mice were primed with 10 μg/ml SEB or medium for 3 days. Subsequently, primed cells were incubated with medium alone or with syngeneic feeder cells, and secondary proliferative responses were detected. SEB-primed splenocytes showed significant autoreactive response after secondary stimulation with syngeneic feeder cells. Medium-primed IL-10-deficient splenocytes also showed autoreactive responses. Data are expressed as the mean ± SEM for nine observations from three independent experiments. *, p < 0.05 for the mean proliferative response to syngeneic feeders without priming compared with their response to medium alone. **, p < 0.05 for the mean proliferative response to syngeneic feeders after priming with SEB vs medium alone.

KO (C57BL/10) or wild-type mice were primed with SEB in vitro (Fig. 1). The primary proliferative response to 10 μg/ml of SEB of splenocytes from IL-10 KO mice was comparable to that of wild-type splenocytes. SEB-primed splenocytes from C57BL/10 mice showed a significant proliferative response after secondary culture with mitomycin C-treated syngeneic feeder cells. The magnitude of the secondary response in IL-10-deficient mice of the same strain was comparable to that of wild-type mice. In contrast, medium-primed splenocytes from wild-type mice did not respond to the secondary stimulation with the syngeneic feeders, whereas those from IL-10-deficient mice underwent a significant proliferation in response to the syngeneic feeders, albeit less than that observed after priming with SEB. Interestingly, 67.6 ± 5.2 U of IL-2 were produced in the supernatant of SEB-primed splenocytes from IL-10-deficient mice, which was higher than that in wild-type (46.1 ± 3.1). Adding recombinant mouse IL-10 (10–100 ng/ml) to the culture suppressed the IL-2 production of both IL-10 KO and wild-type splenocytes, whereas the constitutive proliferative response observed in IL-10 KO mice was not affected. These data indicate that priming with SEB induced autoreactive proliferative responses, and IL-10-deficient cells tend to be autoreactive without priming (Fig. 1).

**Polycional stimuli induce autoreactivity**

As SEB, which stimulates about 20% of T cells, induced autoreactivity, we examined the hypothesis that polyclonal stimuli in general have a potential to induce autoreactivity. Splenocytes from CBA/J mice were primed with SEB as well as anti-CD3 or PMA plus ionomycin, and secondary responses to the feeder cells were detected. All these polyclonal stimuli induced the secondary autoreactive responses, and these responses were inhibited by IL-10 in the secondary cultures (Fig. 3). SEB expands T cell populations expressing an autoreactive repertoire in Mls-1a mice

To determine the expansion of autoreactive T cells, we employed the model involving endogenous viral superantigens in mice. Mice that have the integration of Mtv-7 genome derived from mouse mammary tumor virus are designated Mls-1a (33, 34). Mls-1a mice, such as CBA/J, have only a marginal number of T cells bearing TCR Vβ6, -7, and -8.1 chains, because these populations are depleted in the thymus due to the endogenous viral superantigen Mls-1a (33, 35). Expansion of these T cell populations directly indicates the expansion of autoreactive T cells in Mls-1a mice.

SEB-primed autoreactive T cell lines from CBA/J splenocytes were established by growing cells with feeder cells in medium containing IL-2. After several weeks of culture, TCR Vβ-chain usage was determined by flow cytometric analysis. More than 95% of the cells expressed CD4 and TCR αβ (P. Ernst et al., unpublished observations). Although freshly isolated splenocytes from CBA/J mice contain only a marginal number of Vβ7+ T cells (2% of CD3+ cells), this population increased to 12% in the T cell lines. T cells recognizing the endogenous viral superantigen and bearing the Vβ6 TCR were also expanded in the T cell lines (Fig. 4). Splenocytes from C3H/HeJ mice (Mls-1b) also had more Vβ6+ or Vβ7+ T cells after expansion in response to SEB. Vβ8.1+ T cells are depleted in Mls-1b strains; however, we detected 9% of Vβ8 cells in the freshly isolated splenocytes from both CBA/J and C3H/HeJ strains, because the Ab also recognizes Vβ8.2+ cells. Expansion of this population was also observed in the T cell lines. In other experiments anti-Mls-1a Ab (33) partially inhibited the secondary response of SEB-primed CBA/J cells, suggesting that part of the autoreactive response was directed toward the Mls-1a Ag itself (data not shown). These data provide direct evidence that priming with superantigen abrogated self tolerance and expanded autoreactive T cells in vitro.

**Autoreactive T cells responses are mediated by CD4+ T cell responses**

Because Th cells are capable of transferring disease in several models of colitis, the role of CD4+ Th cells in the secondary autoreactive response was determined. CD8-depleted cells showed

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**FIGURE 1.** SEB induces proliferative responses to self Ags. Spleen cells from C57BL/10 IL-10-deficient and wild-type mice were primed with 10 μg/ml SEB or medium for 3 days. Subsequently, primed cells were incubated with medium alone or with syngeneic feeder cells, and secondary proliferative responses were detected. SEB-primed splenocytes showed significant autoreactive response after secondary stimulation with syngeneic feeder cells. Medium-primed IL-10-deficient splenocytes also showed autoreactive responses. Data are expressed as the mean ± SEM for nine observations from three independent experiments. *, p < 0.05 for the mean proliferative response to syngeneic feeders without priming compared with their response to medium alone. **, p < 0.05 for the mean proliferative response to syngeneic feeders after priming with SEB vs medium alone.
a comparable level of secondary response as the splenocyte preparation (Fig. 5A). Moreover, addition of anti-MHC class II Ab to the secondary culture, but not an isotype control Ab, significantly blocked the autoreactive response in all three strains examined (Fig. 5B). These observations suggest that CD4+ T cells mediated the autoreactive response. Adding IL-10 in the primary or secondary culture of CD8-depleted cells suppressed the secondary response, indicating that the regulatory effect of IL-10 was independent of the presence of CD8+ T cells (Fig. 5A).

Priming conditions for autoreactive T cells stimulate cell-mediated immunity to epithelial targets

To address the possibility that autoreactive T cells may be able to contribute to epithelial cell damage and inflammation in the digestive tract, Mode-K cells were used as a target for cell-mediated immunity. Splenocytes from C3H/HeJ mice (syngeneic to Mode-K) were stimulated with SEB for 18 h and checked for a cytotoxic effect by JAM assay. Fig. 6A shows that SEB-stimulated splenocytes as well as CD8-depleted cells mediated cytotoxic activity against the Mode-K target cells. Supernatant from SEB-stimulated splenocytes did not kill the target (data not shown). Furthermore, the cytotoxic effect was abolished when a culture insert was used to separate effector and target cells, indicating that this cytotoxicity was facilitated by direct contact with the target cells. Because most of the cytotoxic activity resided in the CD4+ T cells, colonic mucosal T cells, which include intestinal intraepithelial lymphocytes (IEL) and lamina propria lymphocytes (LPL) that contain increased proportions of CD4+ T cells treated with IL-10 compared with those in untreated cells. Data are expressed as the mean ± SEM for six observations from two independent experiments. C. Mononuclear cells isolated from the spleen or colon of C3H/HeJ mice were incubated in medium or primed with SEB as described in Materials and Methods. Subsequently, cells were probed for the surface expression of CD3 and IL-10 receptors. After gating on the lymphocyte population, two-color analysis was performed to detect IL-10 binding by CD3-positive T cells. This figure shows that both splenic and colonic T cells expressed IL-10R, but the level did not change after stimulation.

FIGURE 2. IL-10 inhibits autoreactive response induced by SEB. A. Splenocytes were primed with SEB in the presence or the absence of IL-10 (100 ng/ml), and secondary autoreactive responses were detected. Adding IL-10 to the primary culture suppressed the secondary autoreactive responses. Data are expressed as the stimulation index, i.e., counts per minute from culture with feeders/counts per minute from culture with medium only. The ranges of counts per minute for the different strains were: C57BL/10, 3,000–4,500; 129/SvEv, 11,000–12,000; and CBA/J, 8,000–16,000. **, p < 0.05 for inhibition by cells treated with IL-10 compared with that in untreated cells. B. SEB-primed splenocytes were given a secondary stimulation with syngeneic feeders. IL-10 (100 ng/ml), anti-mouse IL-10R Ab (1B1.2), or rat IgG (isotype control) was added as indicated. Adding IL-10 to the secondary culture suppressed the autoreactive response. The responses were restored by anti-IL-10R Ab, but not by isotype controls, in C57BL/10 and 129/SvEv strains. This Ab, however, was not effective in the CBA/J strain. **, p < 0.05 for inhibition of the responses in cells treated with IL-10 compared with those in untreated cells. Data are expressed as the mean ± SEM for six observations from two independent experiments.

FIGURE 3. Autoreactive responses occur after exposure to polyclonal stimuli. Splenocytes from CBA/J mice were primed with medium alone, SEB, plate-coated anti-CD3 Ab, or PMA plus ionomycin, and secondary responses were detected as described in Figs. 1 and 2. Data are compiled from 9 to 21 observations from 3–7 separate experiments and are expressed as the mean ± SEM. *, p < 0.05 for the autoreactive response following stimulation with a polyclonal activator vs medium. **, p < 0.05 for inhibition of the responses in cells treated with IL-10 compared with those in untreated cells.
notypes detected by FACS analysis. Depletion of CD8+ are CD4+ II Abs. These findings support the idea that the autoreactive cells

Discussion

Microbial Ags are quite capable of activating intestinal T cells in humans (9) and mice (10, 11). Recently, SEB has been shown to

cross the intestinal epithelial cell barrier (38) and stimulate T cells

(36), were stimulated with SEB and tested for cytotoxicity. Examination

of surface Ags revealed that >75% of the cells were CD3, CD4+, confirming the phenotype of colonic IEL described by others (36, 37). As shown in Fig. 6B, SEB-activated colonic mucosal

T cells kill the syngeneic epithelial cell target. Moreover, this cytoxicity was inhibited by the addition of IL-10, and the Ab recognizing the IL-10R (1B1.2) blocked the inhibition.

The autoreactive cells induced by SEB included CD4+ T cells, because most of the primed cells contained CD4+ TCRαβ+ phenotypes detected by FACS analysis. Depletion of CD8+ cells before priming did not attenuate the autoreactivity. Moreover, this autoreactivity was mediated by MHC class II molecules on the feeder cells, because this reaction was inhibited by anti-MHC class II Abs. These findings support the idea that the autoreactive cells are CD4+ T cells. As activated T cells may express only modest amounts of class II MHC, the T cells are not capable of long term expansion in the absence of feeder cells. Moreover, because SEB induces the expression of FasL on T cells, it is likely that, in time, activation will lead to a negative selection of the T cells as they die due to Fas/FasL interactions (43). The magnitude of the proliferative responses varied among strains of mice, but they were present in all strains tested. In addition, autoreactive T cells could be generated from spleen or colon, which supports our previous preliminary studies suggesting that these responses occur in gut-associated lymphoid tissue, including the mesenteric lymph nodes or intestinal Peyer’s patches (44).

CD4+ autoreactive T cells prepared from the spleens of IL-10-deficient mice displayed a level of spontaneous autoreactivity without prior priming with SEB. Despite this intrinsic autoreactivity, stimulation with SEB did not increase the response to levels greater than those observed in control mice. This somewhat unanticipated finding may reflect a ceiling for autoreactivity that is
defined by the number of autoreactive precursors and the magnitude of their expansion. It should be remembered that normally, autoreactive cells are almost nonexistent, so any increase may be quite significant. This is supported by the observation that adoptive transfer of these T cells into T cell-deficient mice can induce colitis in the recipient (24). These observations suggest that IL-10 confers a protective effect against the activation of autoreactive T cells induced by normal flora. Although there was no difference between IL-10-deficient and wild-type mice in the level of secondary autoreactive responses after priming with SEB, exogenous IL-10 suppressed the autoreactivity, including both proliferative and cytolytic effects, when delivered during the priming or secondary stimulation. IL-10R were expressed on both T cells and cells of other lineages, so the inhibitory activity of IL-10 may have been mediated at different levels.

The specificity of the effect of IL-10 was confirmed by blocking the IL-10R with anti-IL-10R Ab. This Ab was effective in the

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can be expressed on intestinal epithelial cells (51), autoreactivity of T cells recognizing this Ag must be prevented by a state of anergy. However, cytokines, such as IL-2, can abrogate anergy in autoreactive IEL (29, 52). Zinkernagel and colleagues (53) have also shown that transgenic T cells expressing a receptor recognizing a transgenic viral peptide that is expressed on pancreatic β islet cells remain anergic. However, upon stimulation with virus infection, the anergic T cells react to viral Ag and induce diabetes. Thus, presentation of a microbial Ag in an immunogenic fashion can induce autoreactivity that can contribute to disease. This may be due to antigenic mimicry between the pathogen and the host Ag or the activation of autoreactive T cells due to the burst of cytokines, such as IL-2, that are released during the infection.

Having established that autoreactive T cells can expand after exposure to SEB, we showed that these cells were capable of inducing damage to host cells. As described in Fig. 6, T cells from the spleen or colon that were activated with SEB could induce death and DNA degradation in Mode-K cells. Because SEB induces the expression of FasL on T cells (43), it is possible that apoptosis of epithelial cells was mediated by interactions between Fas and FasL. This model is supported by the results of other studies documenting the expression of Fas on epithelial cells and FasL by intestinal T cells in graft-vs-host disease (54, 55). Previous reports have suggested that changes in epithelial cell structure and function can occur after exposing tissue to SEB (41, 56). The ability of SEB to induce cytoxins (42) as well as apoptosis in epithelial cells following exposure to SEB may contribute to the T cell-mediated pathology.

As described above, colitis in many animal models is dependent on normal flora, and T cells recognizing luminal microbial Ags become activated during colitis. Moreover, adoptive transfer of T cells from colitic mice will lead to colitis in T-cell-deficient recipients. These studies suggest that microbial triggers activate a deleterious T cell response; however, a role for autoreactive T cells has not been implied previously. In this report we show that a microbial superantigen, SEB, is capable of inducing autoreactive T cells in systemic and colonic tissue and that this response is prevented by IL-10. Additional studies are required to determine the relative contribution of this process to chronic inflammatory diseases in the digestive tract.

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