Increased Frequencies of Interleukin-2– and Interferon-γ–Producing T Cells in Patients with Active Behçet’s Disease

Nakako Sugi-Ikai,1 Masatoshi Nakazawa,2 Satoshi Nakamura,1 Shigeaki Ohno,1 and Mutsuhiko Minami2

PURPOSE. To elucidate the profile of cytokine-producing T cells in patients with active or inactive Behçet’s disease (BD), the frequencies of type 1 (Interleukin-2 [IL-2], interferon-γ [IFN-γ]) and type 2 (IL-4) cytokine–producing CD4+ and CD8+ cells in peripheral blood were investigated, and the effect of immunosuppressive drugs on the profile of cytokine-producing cells was evaluated.

METHODS. Fifty-two patients with BD (32 with active and 20 with inactive BD) and 33 healthy control subjects were the subjects in this study. Patients were or were not treated with immunosuppressive drugs. Peripheral blood mononuclear cells were fixed, permeabilized, and stained for intracellular cytokines in combination with cell surface markers CD4 and CD8 for flow cytometric analysis.

RESULTS. In nontreated patients with BD, the frequencies of IL-2– and IFN-γ–producing CD4+ and CD8+ cells in active patients were significantly higher than those in inactive patients. Conversely, the frequencies of IL-4 producing CD4+ and CD8+ cells in nontreated patients with active BD were comparable with those in patients with inactive disease and in control subjects. Patients with inactive BD who were treated with immunosuppressive drugs showed significantly lower frequencies of IL-2– and IFN-γ–producing CD4+ and CD8+ cells than did treated patients with active BD.

CONCLUSIONS. The frequencies of type 1 cytokine–producing CD4+ and CD8+ cells increased in patients with active BD. Effective immunosuppressive treatments decreased the population of type 1 cytokine–producing CD4+ and CD8+ cells. These results suggest that type 1 cytokine–producing cells play an important role in the immunopathogenesis of the inflammation in BD. (Invest Ophthalmol Vis Sci. 1998;39:996–1004)

FROM THE 1Departments of Ophthalmology, and 2Immunology and Parasitology, Yokohama City University School of Medicine, Kanazawa-ku, Yokohama, Japan.

Supported by a grant from the Ministry of Education, Science, Sports and Culture of Japan and by a grant for research on Behçet’s disease from the Ministry of Health and Welfare of Japan.

Submitted for publication July 15, 1997; revised December 5, 1997; accepted January 12, 1998.

Proprietary interet category: N.

Reprint requests: Mutsuhiko Minami, Department of Immunology and Parasitology, Yokohama City University School of Medicine, 3-9 Fukaura, Kanazawa-ku, Yokohama, 236 Japan.
PATIENTS AND METHODS

Patients

Fifty-two patients with BD (35 men, 17 women) who were seen in the Uveitis Survey Clinic of the Yokohama City University Hospital, Japan, participated in the study. All had active uveitis or history of uveitis. Patients with BD did not show obvious infections when examined during the study. Average age of the patients was 36 years (range, 18–61). In 21, the complete type was diagnosed and in the remaining 31 the incomplete type was diagnosed according to the criteria of the Behçet’s Disease Research Committee in Japan.¹⁷ Patients with the complete type of BD showed all four major symptoms: oral recurrent ulcers, uveitis, genital ulcers, and skin lesions. Patients classified as having incomplete BD had three of the four major symptoms, including ocular lesions. Thirty-three age-matched, healthy adults were used as control subjects (19 men, 14 women). Average age of the healthy control subjects was 33 years (range, 25–51). All procedures adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from all patients and control subjects.

Classification of Activity

The patients were divided into two groups according to the activity of uveitis. The first group consisted of 32 active patients (16 nontreated and 16 treated with immunosuppressive drugs) who had experienced one or more attacks of uveitis monthly for the past 3 months. The second group consisted of 20 inactive patients (13 nontreated and 7 treated patients) who had experienced no attacks of uveitis for more than 6 months. Laboratory examinations on most active patients showed high levels of C-reactive protein, increased white blood cell counts, and high erythrocyte sedimentation rate. All inactive patients showed normal levels of C-reactive protein, white blood cell counts, and erythrocyte sedimentation rate and of the three major symptoms showed only oral ulcers during the study.

Treatment of Patients

In the active group, 16 patients were fresh cases that had undergone no treatment (nontreated patients with active BD). The remaining 16 patients had had repeated attacks of uveitis, regardless of treatment with such immunosuppressive drugs as cyclosporin A (CyA) or FK-506. Five patients were treated with CyA and 11 patients were treated with FK-506. In the inactive group, 7 patients had been treated with CyA, and the remaining 13 patients had not been treated for at least 3 months (nontreated patients with inactive BD). Patients treated with CyA were administered doses of 2 to 5 mg/kg per day. The dosage of CyA was controlled to keep the whole-blood trough concentration at 50 to 200 mg/ml. Patients treated with FK-506 were administered doses of 0.05 to 0.15 mg/kg per day. Severely affected patients were first treated with CyA. Only when the treatment of CyA was ineffective was it replaced with FK-506.

Antibodies

Anti-human IL-2 monoclonal antibody (mAb) (mouse IgG1) and anti-human IL-4 mAb (mouse IgG1) were purchased from Genzyme (Cambridge, MA); fluorescein isothiocyanate (FITC)-conjugated goat anti-mouse IgG1 mAb from Southern Biotechnology (Birmingham, AL); phycoerythrin-conjugated anti-IFN-γ from PharMingen (San Diego, CA); and FITC- or phycoerythrin-conjugated anti-CD4 mAb, and peridinin chlorophyll-conjugated anti-CD8 mAb, and phycoerythrin-conjugated mouse IgG1 from Becton Dickinson (San Jose, CA). Anti-CD3 mAb was isolated from culture supernatant of OKT3 (ATCC, Rockville, MD) using protein G-Sepharose.

Cell Preparation and Culture

Heparinized venous blood was obtained from patients with BD and from healthy control subjects. Peripheral blood mononuclear cells (PBMCs) were isolated by ficoll-gradient centrifugation (HITOPAQ-1077, Sigma, St. Louis, MO) and washed three times with Roswell Park Memorial Institute (RPMI) 1640 (Life Technologies, Gaithersburg, MD). Peripheral blood mononuclear cells (4 × 10⁶ cells/ml) were cultured in 24-well plates (Sumitomo Bakelite, Tokyo, Japan) with RPMI 1640, supplemented with 10% fetal calf serum, 2 mM L-glutamine, 2 × 10⁻⁵ M Z-mecaptoethanol (Wako Junyaku, Osaka, Japan), 100 IU/ml penicillin, and 100 μg/ml streptomycin sulfate. These cells were cultured with immobilized anti-CD3 mAb for 0 to 48 hours at 37°C in 5% CO₂ and 85% humidified incubator. In the last 6 hours, the cells were cultured in the presence or absence of 1 μM monensin.

Immunofluorescence Staining and Flow Cytometric Analysis

For immunostaining of cytoplasmic IL-2 and IL-4, harvested cultured cells were washed twice in phosphate-buffered saline (PBS) and were fixed with 2% paraformaldehyde on ice for 15 minutes. Cells were washed twice with PBS and resuspended into 1 × 10⁶ cells in 100 μl PBS containing 0.1% saponin, 10% human type AB blood serum, and 1 μg/ml goat IgG (Chemicon, Temecula CA). After 10 minutes, the cells were incubated for 30 minutes on ice with anti–IL-2 or anti–IL-4 mAbs. Cells were washed twice in PBS containing 0.1% saponin (saponin buffer), resuspended in 100 μl saponin buffer with 1 μg/ml goat IgG, and incubated with 1.5 μg/ml FITC-conjugated goat anti-mouse IgG1 for 30 minutes at room temperature. Cells were washed twice in PBS and then resuspended in 100 μl PBS and 2 μg/ml mouse IgG (Chemicon). After 10 minutes’ incubation on ice, phycoerythrin-conjugated anti-CD4 and peridinin chlorophyll-conjugated anti-CD8 mAbs were added and incubated for 30 minutes on ice. Cells were washed twice in PBS and were resuspended in approximately 500 μl PBS. For negative controls, cells were stained with FITC-conjugated second Ab and then were stained with CD4 and CD8 antigens.

Staining of cytoplasmic IFN-γ was performed as follows. Cultured PBMCs were washed twice and stained with FITC-conjugated anti–CD4 mAb and peridinin chlorophyll–conjugated anti–CD8 mAb for 30 minutes on ice. Cells were fixed with paraformaldehyde and permeabilized with saponin buffer. A concentration of 1 μg/ml phycoerythrin-conjugated anti–IFN-γ was added for 30 minutes on ice. For negative controls, cells were stained with phycoerythrin-conjugated mouse IgG1. To ensure specificity of the staining procedure, binding of each mAb was blocked with an excess of recombinant cytokine (IL-2, IL-4, and IFN-γ; Pharmingen, San Diego, CA).

Cells were analyzed on a flow cytometer (FACScan; Becton Dickinson) equipped with a 15-mA argon ion laser and filter settings for FITC, phycoerythrin, and peridinin chlorophyll. Ten thousand cells from each sample were computed in list mode and data were analyzed with a commercial software program (CELLQuest; Becton Dickinson). Analysis gates were set to include only single, forward scatter-positive events with appropriate negative controls.
RESULTS

Percentage of CD4+ and CD8+ Cells

The percentages of CD4+ and CD8+ cells in PBMCs were compared among patients with active BD, patients with inactive BD, and healthy control subjects. Paraformaldehyde fixation and treatment with saponin permeabilization did not affect the percentage of CD4+ and CD8+ cells (data not shown). There were no significant differences in the percentages of CD4+ cells in PBMC among patients with active BD (37.4 ± 6.5%), patients with inactive BD (36.9 ± 6.7%), and healthy control subjects (36 ± 6.8%). There were also no significant differences in the percentages of CD8+ cells among patients with active BD (26.5 ± 6.5%), patients with inactive BD (22.9 ± 5.5%), and healthy control subjects (23.1 ± 7.3%). The percentage of CD4+ and CD8+ cells did not change until after at least 24 hours’ stimulation with anti-CD3 mAb. Because white blood cell counts in peripheral blood of patients with active BD were higher than those of healthy control subjects, absolute numbers of CD4+ and CD8+ cells in peripheral blood of patients with active BD were higher than those of healthy control subjects (data not shown).

Specificity of Intracellular Cytokine Staining

Peripheral blood mononuclear cells from patients with BD and patients with atopic dermatitis were used for examination of the specificity of intracellular cytokine staining (Fig. 2). The frequency of IL-4-producing CD4+ cells was low in patients with BD and in healthy control subjects. Therefore, to examine the specificity of IL-4 staining, we used PBMCs from patients with atopic dermatitis in whom there was a high frequency of IL-4-producing cells (Fig. 2B). Peripheral blood mononuclear cells were stimulated for 6 hours with immobilized anti-CD3 mAb in the presence of monensin. These cells were stained with anti-IL-2 (Fig. 2A) or anti-IL-4 mAbs (Fig. 2B) in the presence (Fig. 2, solid line) or absence (Fig. 2, shaded) of an excess amount of the corresponding recombinant cytokine and were analyzed by flow cytometry. Anticytokine staining showed a distinct proportion of CD4+ cells expressing each cytokine. In addition, mAb binding to the cells with recombinant cytokine was completely blocked, thus demonstrating the specificity of the stain (Fig. 2, solid line). The same results were obtained in CD8+ cells.

Kinetics of Frequencies of Intracellular Cytokine Producing Cells after Stimulation with Anti-CD3 Monoclonal Antibody

We examined the kinetics of the frequencies of IL-2-, IFN-γ-, and IL-4-producing cells in patients with BD and in healthy control subjects. Peripheral blood mononuclear cells from 10 healthy control subjects were cultured with immobilized anti-CD3 mAb and were harvested at different intervals from 0 to 48 hours after onset of the stimulation. Frequencies of IL-2- and IFN-γ-producing CD4+ cells reached a peak at 6 hours’ stimulation (Figs. 3A, 3B). Similar to CD4+ cells, frequencies of IL-2- and IFN-γ-producing CD8+ cells also peaked at 6 hours of culturing (Figs. 3D, 3E). The frequency of IL-4-producing cells was low in patients with BD and in healthy control subjects, and the peak of kinetic activity could not be defined strictly. However, the frequencies of IL-4-producing cells from 0 to 10 hours of stimulation was relatively high, compared with those after 10 hours (Figs. 3C, 3F). In patients with BD, frequencies of each cytokine-producing cell showed the same kinetics as those of healthy control subjects (data not shown). Thus, we examined the frequency of cytokine-producing cells at 0 hours and 6 hours of culturing in the following experiments.
CD4⁺ cells in nontreated patients with active BD was also markedly higher than in nontreated patients with inactive BD and in healthy control subjects (Fig. 4B). Between nontreated patients with inactive BD and healthy control subjects, frequencies of IL-2- and IFN-γ-producing CD4⁺ cells were not significantly different (Figs. 4A, 4B). No difference was observed in the frequency of IL-4-producing cells among patients with active BD, patients with inactive BD, and healthy control subjects (Fig. 4C). The frequency of IL-4-producing cells was low (3%-5%) in patients with BD and in healthy control subjects. However, in our experiments, patients with atopic dermatitis showed a high frequency of IL-4 producing CD4⁺ cells, and that indicated that our assay system for detecting IL-4-producing cells was sensitive enough.

**Frequencies of Type 1 and Type 2 Cytokine-Producing CD8⁺ Cells after 6 hours' stimulation in Nontreated Patients with Active and Inactive Behçet's Disease**

We compared frequencies of IL-2-, IFN-γ-, and IL-4-producing CD8⁺ cells in nontreated patients with active and inactive BD, and healthy control subjects after 6 hours' stimulation with immobilized anti-CD3 mAb. Frequencies of IL-2- and IFN-γ-producing CD8⁺ cells in nontreated patients with active BD was markedly higher than in nontreated patients with inactive BD and in healthy control subjects (Figs. 4D, 4E). There was no significant difference in frequencies of IL-2- and IFN-γ-producing CD8⁺ cells between nontreated patients with inactive BD and healthy control subjects (Figs. 4D, 4E). The frequency of IL-4-producing cells in nontreated patients with active BD was comparable with that in patients with inactive BD and with that in healthy control subjects (Fig. 4F).

**Frequencies of Type 1 and Type 2 Cytokine-Producing CD4⁺ and CD8⁺ Cells without Stimulation in Nontreated Patients with Active or Inactive Behçet's Disease**

We compared frequencies of IL-2-, IFN-γ-, and IL-4-producing CD4⁺ and CD8⁺ cells immediately after isolation (0 hours’ stimulation) in nontreated patients with active and inactive BD and in healthy control subjects. The frequencies of IL-2-producing CD4⁺ and CD8⁺ cells in nontreated patients with active BD was higher than in nontreated patients with inactive BD and in healthy control subjects (Figs. 5A, 5D). The frequency of IFN-γ-producing CD4⁺ and CD8⁺ cells in nontreated patients with active BD was markedly higher than that in healthy control subjects (Figs. 5B, 5E). The frequencies of IL-4 producing CD4⁺ and CD8⁺ cells (0 hours’ stimulation) in nontreated patients with active BD were comparable with those in patients with inactive BD and with those in healthy control subjects (Figs. 5C, 5F).

**Effect of Treatment with Immunosuppressive Drugs on the Frequencies of Type 1 and Type 2 Cytokine-Producing Cells in Patients with Behçet's Disease**

To determine the effect of immunosuppressive drugs on the frequency of IL-2-, IFN-γ-, or IL-4-producing cells, we investigated the frequencies after 6 hours’ stimulation with immobilized anti-CD3 mAb. Sixteen patients in the active group and 7 patients in the inactive group were undergoing treatment with CyA or FK-506 when this study was performed. Peripheral blood mono-
nuclear cells from 13 treated patients with active BD and 6 treated patients with inactive BD were used for cytoplasmic IL-2 and IL-4 staining. Peripheral blood mononuclear cells from 6 treated patients with active BD and 5 treated patients with inactive BD were examined for cytoplasmic IFN-γ.

The frequency of IL-2-producing CD4+ cells in treated patients with inactive BD was significantly lower than in treated patients with active BD (Fig. 6A). Furthermore, the frequency of IL-2-producing CD4+ cells in treated patients with active BD was significantly lower than in healthy control subjects. The frequency of IFN-γ-producing CD4+ cells in treated patients with inactive BD was significantly lower than in treated patients with active BD and in healthy control subjects (Fig. 6B). Frequencies of IL-2- and IFN-γ-producing CD8+ cells in treated patients with inactive BD were significantly lower than in patients with active BD (Figs. 6D, 6E). Frequencies of IL-4-producing CD4+ and CD8+ cells in treated patients with inactive BD were comparable with those in treated patients with active BD, and with those in healthy control subjects (Figs. 6C, 6F).

DISCUSSION

Using flow cytometry, we analyzed the profile of type 1 and type 2 cytokine-producing T cells in patients with BD. We demon-
Type 1 Cytokine-Producing T Cells in Behçet's Disease

The frequency of cytokine-producing CD4+ and CD8+ cells (6 hours stimulation in vitro) from nontreated patients with Behçet's disease with immunosuppressive drugs. The frequency of each cytokine-producing cell was examined after 6 hours stimulation with immobilized anti-CD3 monoclonal antibody. Cells were stained for interleukin-2 (A, D), interferon-γ (B, E), or interleukin-4 (C, F). Frequencies of cytokine-producing cells were shown as a percentage of the CD4+ (A, B, C) or the CD8+ (D, E, F) cell population.

Figure 4. Frequency of cytokine-producing CD4+ and CD8+ cells (6 hours stimulation in vitro) from nontreated patients with Behçet's disease with immunosuppressive drugs. The frequency of each cytokine-producing cell was examined after 6 hours stimulation with immobilized anti-CD3 monoclonal antibody. Cells were stained for interleukin-2 (A, D), interferon-γ (B, E), or interleukin-4 (C, F). Frequencies of cytokine-producing cells were shown as a percentage of the CD4+ (A, B, C) or the CD8+ (D, E, F) cell population.

Increased production of Th1 cytokines such as IL-2 and IFN-γ has also been observed in patients with BD. These observations indicate that Th cells, especially Th1 cells, play an important role in immunopathology of BD. However, it is still unclear whether such increased cytokine production was caused by increased numbers of cytokine-producing T cells or enhanced ability to produce cytokines. Thus, we investigated the frequencies of cytokine-producing CD4+ or CD8+ cells at the single-cell level. In our observations, the frequency of CD4+ and CD8+ cells producing each cytokine showed a peak after 6 hours stimulation with immobilized anti-CD3 mAb (Fig. 3). The number of cytokine-producing cells after 6 hours stimulation was represented as total number of cells that produced the cytokine and the cells that were destined to produce the cytokine in our experimental system. The frequencies of
FIGURE 5. Frequency of cytokine-producing CD4<sup>+</sup> and CD8<sup>+</sup> cells (0 hours' stimulation) from patients with Behçet's disease who have not been treated with immunosuppressive drugs. The frequency of each cytokine-producing cell was examined at 0 hours (without stimulation). Cells were stained for interleukin-2 (A, D), interferon-γ (B, E), or interleukin-4 (C, F). Frequencies of cytokine-producing cells were shown as the percentage of the CD4<sup>+</sup> (A, B, C) or the CD8<sup>+</sup> (D, E, F) cell population.

IL-2- and IFN-γ-producing CD4<sup>+</sup> cells in nontreated patients with active BD were significantly higher than in patients with inactive BD and in healthy control subjects (Figs. 4A, 4B). This indicates that the patients with active BD have a greater number of Th1 cells, which contain activated and resting Th1 cells in vivo, compared with patients with inactive BD and healthy control subjects.

We also investigated frequencies of cytokine-producing cells without stimulation (0 hours). Our data showed that frequencies of IL-2-producing CD4<sup>+</sup> cells in nontreated patients with active BD was significantly higher than in patients with inactive BD and in healthy control subjects, even without stimulation in vitro (Fig. 5A). The frequency of IFN-γ-producing CD4<sup>+</sup> cells in nontreated patients with active BD was also higher than in healthy control subjects even without stimulation in vitro (Fig. 5B). Considering these findings, a high frequency of Th1 cytokine-producing cells without stimulation in patients with active BD may indicate that they have a high frequency of activated Th1 cells. Absolute numbers of activated Th1 cells were also expanded in patients with active BD (data not shown). Many investigators have reported that activated T cells were increased in patients with BD. Nakamura et al. has reported that increased number of CD45RO<sup>+</sup> CD4<sup>+</sup> and CD25<sup>+</sup> CD4<sup>+</sup> cells was observed in patients with active BD. Hamazou et al. has described that a subset of patients with
active BD had higher soluble IL-2 receptor. Yosipovitch et al. has also reported increased levels of serum soluble IL-2R and soluble IL-1β in patients with BD compared with that in healthy control subjects. Soluble IL-2R and soluble IL-1β have been shown to influence T cell activation. Thus, our data suggest that increased number of activated and resting Th1 cells in patients with active BD plays an important pathogenic role in the active phase of BD. In contrast, the frequency of Th2 cells producing IL-4 was comparable among our study groups. In this study, we used IL-4 as a marker for Th2 cells. However, Elson et al. and Seder and Prussin have reported that IL-5 is a more specific cytokine marker of Th2 cells than is IL-4. In future studies, we plan to assess Th2 cells producing IL-5.

Although the role of cytokine-producing CD8+ cells is unclear, some investigators suggest that CD8+ cells are important for induction and regulation of Th cells. We clearly showed that the frequency of IL-2- and IFN-γ-producing CD8+ cells that were stimulated with immobilized anti-CD3 mAb for 6 hours increased in patients with active BD. Frequencies of IL-2- and IFN-γ-producing CD8+ cells in patients with active BD

**FIGURE 6.** Effect of treatment with immunosuppressive drugs on frequencies of IL-2-, IFN-γ-, and IL-4-producing CD4+ and CD8+ cells. Peripheral blood mononuclear cells from treated patients with active and inactive Behçet's disease and from healthy control subjects were stimulated for 6 hours with immobilized anti-CD3 monoclonal antibody. Cells were stained for IL-2 (A, D), IFN-γ (B, E), or IL-4 (C, F). Frequencies of cytokine-producing cells were shown as the percentage of the CD4+ (A, B, C) or the CD8+ (D, E, F) cell population. Patients treated with cyclosporin A (open circles); patients treated with FK-506 (slashed circles). IFN, interferon; IL, interleukin.
was also high, even before stimulation in vitro (Figs. 5D, 5E). Salgame et al.13 have reported that CD8+ T cell clones can be divided into two subtypes according to their cytokine secretion profile. Type 1 CD8+ T cell clones are derived from healed lesions of patients with tuberculoid leprosy. They are cytotoxic and secrete IFN-γ but not IL-4. Type 2 CD8+ T cell clones derived from patients with lepromatous leprosy suppress the killing of Mycobacterium leprae by M. leprae-specific CD4+ T cell clones and secrete IL-4, IL-5, and IL-10. CD8+ T cells are thought to regulate CD4+ T cell function and development. Type 1 and type 2 CD8+ T cells exert differential effects on development of Th1 and Th2 cells.28,29 Our observations indicate that dominance of type 1 cytokine-producing CD4+ and CD8+ cells may be an important factor in the pathogenesis of BD.

Immunosuppressive drugs are important in the treatment of BD, which involves recurrent episodes of inflammation, such as repeated ocular inflammatory attacks, in many systemic or organ-specific diseases.24,25 Cyclosporin A and FK-506 inhibit the expression of genes encoding IL-2 and other cytokines.26 Our data show that successful treatment diminished the frequencies of type 1 cytokine-producing cells (in treated patients with inactive BD), whereas unsuccessful treatment did not affect the frequencies of type 1 cytokine-producing cells (in treated patients with active BD) (Figs. 6A, 6B, 6D, 6E). Furthermore, frequencies of type 1 cytokine-producing cells in treated patients with inactive BD were significantly lower (P < 0.001) than in healthy control subjects (Figs. 6A, 6B, 6D, 6E). The frequency of IL-2-producing cells in patients with BD with successful treatment dropped 1 month after immunosuppression and continued low until 6 months after the treatment. Although the frequency of IL-2-producing cells in an active patient who was unresponsive to treatment dropped 1 month after the treatment, it increased again and became higher 6 months after the treatment (data not shown). The frequency of IL-4-producing cells did not show a relative increase in patients who had benefited from immunosuppression. However, populations of CD4+ and CD8+ cells were comparable among these three groups, and the absolute number of white blood cell counts in treated patients with inactive BD was also comparable with that in healthy control subjects (data not shown). Taken together, successful CyA and FK-506 treatment may not reduce the number of type 1 T cells, but may inhibit cytokine production in type 1 T cells. Thus, the frequency of type 1 cytokine-producing cells could be one of the key markers for determining the effectiveness of treatment of patients with BD with immunosuppressive drugs. Our findings suggest that the suppression of type 1 cytokine-producing cells may be an important factor in regulating episodes of ocular inflammation. Levels of type 1 and type 2 cytokine-producing cells can be used in BD as efficient markers for assessment of disease activity and treatment.

References