The T Cell Receptor in Normal and Inflamed Human Conjunctiva

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The majority of human peripheral blood and lymphoid tissue T cells express the TCR $\alpha/\beta$ heterodimer, while the TCR $\gamma/\delta$ is expressed on only a small subset of T lymphocytes. However, the majority of murine intraepithelial lymphocytes and most Thy-1+ murine dendritic epidermal cells express the TCR $\gamma/\delta$. Selective homing of avian TCR $\gamma/\delta$ bearing lymphocytes to the intestinal epithelium also has been shown. These findings have suggested that these cells play a role against transformation and infection. More recently, a role in autoimmunity also has been proposed. We examined normal human conjunctiva and inflamed conjunctiva from patients with ocular cicatricial pemphigoid (OCP), an autoimmune disorder, and atopic keratoconjunctivitis (AKC). The majority of T cells in the epithelium and substantia propria of normal conjunctiva expressed the TCR $\alpha/\beta$. Tropism of TCR $\gamma/\delta$-expressing lymphocytes to normal human conjunctiva was not present. However, in OCP, there was a statistically significant increase in the absolute number of TCR $\gamma/\delta$ cells/mm$^2$ (epithelium, 33.9 ± 10.5 [mean ± standard error of the mean] vs. 159.9 ± 51.5, $P = < 0.0008$; substantia propria, 0.10 ± 0.05 vs. 0.33 ± 0.08, $P = < 0.03$). This was not the case for AKC. These findings suggest that TCR $\gamma/\delta$ lymphocytes play a specific but undefined role in certain conjunctival inflammatory conditions and may be important in autoimmunity. Invest Ophthalmol Vis Sci 33:453–459, 1992

T cells recognize antigen (Ag) through heterodimer receptors that are noncovalently associated with the CD3 complex. Two structurally distinct types of CD3-associated T cell receptors (TCR) have been described. The TCR $\alpha/\beta$, a 90 KDa disulfide-linked heterodimer composed of $\alpha$ and $\beta$-glycoprotein subunits, exist on the majority of peripheral blood and lymphoid tissue T cells. They recognize peptide fragments of Ag bound to products encoded by the major histocompatibility complex (MHC) and are responsible for known forms of cell-mediated immunity. The TCR $\gamma/\delta$ are expressed on a small subset of T cells in the peripheral blood and lymphoid tissue (>0.5–16%). The ligands and restriction elements recognized by this TCR are unclear. However, some specific antigens that $\gamma/\delta$ T cells can recognize have been identified. These include mycobacterial antigens (including heat shock proteins) and tetanus toxoid. The limited germline diversity also has suggested that the TCR $\gamma/\delta$ bearing lymphocytes might recognize antigen in the context of relatively nonpolymorphic antigen-presenting molecules.

The majority of murine intestinal intraepithelial lymphocytes express the TCR $\gamma/\delta$. Selective homing of avian TCR $\gamma/\delta$-expressing cells to the intestinal epithelium also has been shown. Most Thy-1+ murine dendritic epidermal cells express the TCR $\gamma/\delta$. The homing of these cells to the epithelia has implied that such TCR $\gamma/\delta$-expressing lymphocytes are involved in surveillance of epithelial cell integrity and may represent a first line of defense against infection and transformation of epithelial cells. In addition, the site-specific localization of $\gamma/\delta$ T cells bearing certain V gene pairs and the differences in diversity of the junctional regions has led to the hypothesis that each cell population may perform distinct functions related to their anatomical site. The marked tropism of the TCR $\gamma/\delta$ lymphocytes for the counterpart normal human epithelia has not been observed. However, in one study, the relatively small percentage of TCR $\gamma/\delta$ cells in the gut were noted to localize preferentially to the epithelium rather than to the lamina propria.

We have studied normal and inflamed human conjunctiva, an epithelial tissue not previously examined, to determine if tropism of TCR $\gamma/\delta$-expressing cells occurs under normal and pathologic conditions. Inflamed conjunctival tissue was obtained from patients with ocular cicatricial pemphigoid (OCP), a systemic autoimmune disorder with conjunctival cicatriz-
tion, and from patients with atopic keratoconjunctivitis (AKC), a chronic manifestation of several ocular surface disorders in the context of atopic dermatitis caused by Type I and probably Type IV hypersensitivity. The monoclonal antibodies $\beta F1$, specific for the human TCR $\alpha/\beta$-expressing lymphocytes, and TCR $\delta 1$, which binds to all T-cells bearing TCR $\gamma/\delta$, were used.

Materials and Methods

Biopsy specimens were obtained—after informed consent was acquired—from the conjunctiva of 12 healthy individuals with no known ocular disease who were undergoing cataract surgery; 10 patients with immunopathologically proven active OCP at various stages of disease, with evidence of immunoreactants at the basement membrane zone; and 11 patients with atopic blepharoconjunctivitis or keratoconjunctivitis as defined by chronic conjunctivitis in the context of atopic dermatitis (with or without asthma or hay fever), with no identifiable cause of the ocular inflammation other than atopy. The patients were not age and sex matched. The biopsy specimens were obtained under identical conditions. The surgical specimens were obtained after the administration of peribulbar anesthesia. The remainder of the conjunctival specimens were obtained immediately after the subconjunctival injection of 2% lidocaine. The specimens, 4 mm $\times$ 4 mm, were harvested from superior, nasal, or temporal bulbar conjunctiva adjacent to the limbus. Each specimen was bisected for light microscopy and for immunohistochemical analysis.

Specimens for immunoglobulin staining were frozen rapidly at $-25^\circ$C and embedded in Tissue Tek OCT compound (Ames Company, Division of Miles Laboratory, Elkhart, Indiana). Four-micron sections were then cut in a cryostat, mounted on gelatin-coated slides, and stored at $-70^\circ$C. T cell subsets were characterized through a four-step immunoperoxidase method using a panel of monoclonal antibodies. In brief, the serial 4 µm cryostat sections were air dried and fixed in acetone. Sections were first incubated in normal goat serum, then incubated for 45 min with the panel of primary monoclonal antibodies. Working dilutions of primary antibodies were, if not recommended by the supplier, determined by using human lymphoid tissue obtained from patients with chronic tonsillitis. After phosphate-buffered saline (PBS) rinsing and a 30 min block for endogenous peroxidase using 0.3% H$_2$O$_2$ in PBS, all sections were incubated for 45 min with a 1:500 dilution of Biotin-SP-AffiniPure goat anti-mouse IgG (H&L) (Jackson Immunoresearch, West Grove, PA). After a final incubation with a 1:1000 dilution of peroxidase-conjugated streptavidin (Jackson Immunoresearch Laboratories), the reactions at sites of antibody binding were developed in peroxidase substrate containing 3-amino-9-ethylcarbazole and hydrogen peroxide in 0.1 M acetate buffer. The specimens were then fixed in formalin, counterstained with Gill’s No. 3 hematoxylin, and coverslipped with Vinol 205 (Air Products and Chemical, Allentown, PA).

Experimental controls were tissue sections incubated without the primary antibodies. Positive brown reaction on cell surface was counted in 5 representative high-power fields (400X) for each of the specimens with a 10 mm $\times$ 10 mm ocular grid (measuring an absolute area 0.25 mm $\times$ 0.25 mm [0.0625mm$^2$]) on a light microscope. A 2mm $\times$ 10 mm grid (measuring an absolute area 0.25mm $\times$ 0.05mm [0.0125mm$^2$]) was used for epithelial counts. Mean cell counts per high-power field were converted to counts/mm$^2$ by dividing epithelial counts by 0.0125 and subtracting propria counts by 0.0625. All counts were performed in masked fashion.

Statistical Analysis

Means and standard errors of the mean were calculated for each cell type in normal and inflamed specimens. The Mann-Whitney nonparametric test was used for statistical analysis because of the wide distribution of cellular infiltrates among some of the OCP specimens (see Results). Based on ranking, the test does not depend on a given distribution but works for a range of distributions. In addition, it is not concerned with specific parameters (such as mean in analysis of variance) but only with the distribution of variates.

Monoclonal Antibodies

The monoclonal antibody TCR $\delta 1$, specific for human TCR $\delta$-chain, was a gift from Dr. Michael Brenner (Dana Farber, Boston MA) and from T Cell Sciences (Cambridge, MA). The antibody $\beta F1$, specific for human TCR $\beta$-chains was obtained from T Cell Sciences (Cambridge, MA). The anti-Leu 4, anti-Leu 3, and anti-Leu 2a antibodies, specific for human CD3, CD4, and CD8, respectively, were obtained from Becton Dickinson (Mountain View, CA). Anti-OKT6 specific for CD1 was obtained from Ortho Pharmaceutical (Raritan, NJ).

Results

Normal Conjunctiva

Lymphocytes were identified easily in the epithelium and substantia propria in normal human conjunctival sections with mean cell counts/mm$^2$ of
189.3 ± 27.3 and 41.8 ± 7.5, respectively. CD4+ and CD8+ cells were identified with a CD4/CD8 ratio of 0.74 ± 0.07 in the epithelium and 0.75 ± 0.17 in the substantia propria. The majority of the lymphocytes expressed the TCR α/β in the epithelium and substantia propria with a TCR α/β/CD3 ratio of 0.97 ± 0.17 and 0.85 ± 0.06, respectively (Table 1). The TCR γδ-expressing cells, as a proportion of CD3+ cells (TCR γδ/CD3), represented a small fraction of the lymphocytes in the epithelium and the substantia propria (0.18 ± 0.06 and 0.10 ± 0.05, respectively) (Table 1). There were relatively more γδ T cells in the epithelium than in the substantia propria. However, this was not statistically significant (0.18 ± 0.06 vs. 0.10 ± 0.05, P = 0.54; Table 1). The CD8+ cells had a predominant basal epithelial distribution, a characteristic not seen with CD4+ cells or the TCR α/β-or γδ/ε-expressing lymphocytes. Langerhans’ cells (CD1+) were seen in the epithelium and substantia propria in approximately equal numbers (Table 1).

Conjunctiva From OCP

The conjunctiva from OCP patients showed an immunohistochemical cellular profile markedly different from that of normal conjunctiva. There was a statistically significant increase in CD3+ cells in the epithelium (189.3 ± 27.3 vs. 408.6 ± 92.6, P < 0.004) and substantia propria (48.1 ± 7.5 vs. 476.7 ± 225.2, P < 0.002). This increase was especially marked in the substantia propria (0.18 ± 0.06 vs. 0.10 ± 0.05, respectively). The CD8+ and CD3+ cells had a predominant basal epithelial distribution, contrasting sheets of cells and a rare specimen having minimal lymphocytic infiltrate (data not included).

Examination of the TCR expression from OCP conjunctiva revealed statistically significant increases in TCR α/β and TCR γδ lymphocytes in the epithelium and substantia propria as compared to normal conjunctiva (Table 1). Many of the lymphocytes expressed the TCR α/β, with a significant proportion expressing the TCR γδ (Figs. 1 and 2). An occasional specimen demonstrated dense aggregates of lymphocytes with a significant proportion of cells expressing the TCR γδ (Fig. 3). The mean cellular infiltrate of TCR γδ-expressing cells per high power field varied over a large range, with occasional specimens demonstrating sheets of cells and a rare specimen having minimal lymphocytic infiltrate (data not included).

A statistically significant increase in the TCR γδ-expressing lymphocytes, as a percentage of CD3+ cells (TCR γδ/CD3), was seen in the OCP specimens as compared to normal controls in the epithelium and the substantia propria (0.39 ± 0.07 vs 0.18 ± 0.06, P < 0.02; 0.33 ± 0.08 vs 0.10 ± 0.05, P < 0.03, respectively). This was not true for the TCR α/β-expressing lymphocytes as a percentage of CD3+ cells (TCR α/β/CD3) as compared to normal controls in the epithelium.

Table 1. Mean conjunctival mononuclear cell subpopulations identified by monoclonal antibodies*

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Normal (N = 12)</th>
<th>OCP (N = 10)</th>
<th>Pt value vs. normal</th>
<th>Atopy (N = 11)</th>
<th>Pt value vs. normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3 ep</td>
<td>189.3 ± 27.3</td>
<td>408.6 ± 92.6</td>
<td>≤0.01</td>
<td>538.4 ± 131.2</td>
<td>≤0.01</td>
</tr>
<tr>
<td>sp</td>
<td>48.1 ± 7.5</td>
<td>476.7 ± 225.2</td>
<td>≤0.002</td>
<td>669.8 ± 181</td>
<td>≤0.0006</td>
</tr>
<tr>
<td>CD4</td>
<td>185.3 ± 15.2</td>
<td>550.3 ± 139.1</td>
<td>≤0.002</td>
<td>624.8 ± 120.8</td>
<td>≤0.004</td>
</tr>
<tr>
<td>40.1 ± 3.8</td>
<td>489.5 ± 167.6</td>
<td>≤0.001</td>
<td>426.4 ± 134.4</td>
<td>≤0.002</td>
<td></td>
</tr>
<tr>
<td>CD8</td>
<td>270.0 ± 24.5</td>
<td>350.6 ± 95.1</td>
<td>NS</td>
<td>426.4 ± 70.4</td>
<td>≤0.04</td>
</tr>
<tr>
<td>53.6 ± 7.3</td>
<td>380.3 ± 162.1</td>
<td>≤0.003</td>
<td>320.5 ± 82.4</td>
<td>≤0.03</td>
<td></td>
</tr>
<tr>
<td>CD4/CD8</td>
<td>0.74 ± 0.07</td>
<td>1.66 ± 0.13</td>
<td>≤0.004</td>
<td>1.18 ± 0.16</td>
<td>NS</td>
</tr>
<tr>
<td>0.75 ± 0.17</td>
<td>1.96 ± 0.38</td>
<td>≤0.04</td>
<td>2.41 ± 0.31</td>
<td>≤0.012</td>
<td></td>
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<tr>
<td>CD1</td>
<td>84.8 ± 16.2</td>
<td>354.6 ± 60.9</td>
<td>≤0.001</td>
<td>328.8 ± 62.4</td>
<td>≤0.003</td>
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<tr>
<td>16.7 ± 3.9</td>
<td>78.0 ± 17.1</td>
<td>≤0.002</td>
<td>95.7 ± 30.7</td>
<td>≤0.06</td>
<td></td>
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<tr>
<td>TCR αβ</td>
<td>187.6 ± 30.7</td>
<td>460.7 ± 71.6</td>
<td>≤0.003</td>
<td>385.6 ± 73.6</td>
<td>NS</td>
</tr>
<tr>
<td>37.6 ± 6.8</td>
<td>437.6 ± 207.6</td>
<td>≤0.0001</td>
<td>454.4 ± 116.2</td>
<td>≤0.009</td>
<td></td>
</tr>
<tr>
<td>TCR γδ</td>
<td>33.9 ± 10.5</td>
<td>159.9 ± 51.5</td>
<td>≤0.008</td>
<td>99.2 ± 35.2</td>
<td>NS</td>
</tr>
<tr>
<td>4.1 ± 0.9</td>
<td>240.1 ± 191.3</td>
<td>≤0.002</td>
<td>90.6 ± 45.6</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>αβ/CD3</td>
<td>0.97 ± 0.17</td>
<td>1.29 ± 0.12</td>
<td>NS</td>
<td>0.86 ± 0.07</td>
<td>NS</td>
</tr>
<tr>
<td>0.85 ± 0.13</td>
<td>1.52 ± 0.48</td>
<td>NS</td>
<td>0.74 ± 0.12</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>γδ/CD3</td>
<td>0.18 ± 0.06</td>
<td>0.39 ± 0.07</td>
<td>≤0.02</td>
<td>0.14 ± 0.04</td>
<td>NS</td>
</tr>
<tr>
<td>0.10 ± 0.05</td>
<td>0.33 ± 0.08</td>
<td>≤0.03</td>
<td>0.09 ± 0.03</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

*Mononuclear cell populations expressed as cells/mm². Mean cell count of five high-power fields (×400) read with a 10 mm × 10 mm ocular grid (measuring an absolute area 0.25 mm × 0.25 mm (0.0625 mm²)) and a 2 mm × 10 mm grid (measuring an absolute area 0.25 mm × 0.05 mm (0.0125 mm²)) for the substantia propria and epithelium, respectively. Epithelial values were divided by 0.0125, and substantia propria values were divided by 0.0625 to obtain mean cell count/mm².

† Mann-Whitney nonparametric test is used for statistical analysis; P value > 0.05 considered statistically nonsignificant.
Fig. 1. OCP conjunctiva stained with monoclonal antibody βF1 specific for the TCR α/β. Note the marked cellular infiltration with TCR α/β expressing lymphocytes (X64).

Fig. 2. OCP conjunctiva stained with monoclonal antibody TCR δ1 specific for the TCR γ/δ. There is significant infiltration with TCR γ/δ expressing cells (X64).

Fig. 3. OCP conjunctiva stained with monoclonal antibody TCR δ1, which is specific for the TCR γ/δ. Note the dense cellular aggregate that is located in the substantia propria with a significant proportion of cells expressing the TCR γ/δ (X40).

Fig. 4. Atopic keratoconjunctivitis conjunctiva stained with monoclonal antibody βF1. Note the significant infiltration of lymphocytes expressing the TCR α/β (X40).

Fig. 5. Atopic conjunctiva stained with monoclonal antibody TCRδ1. Only rare TCR γ/δ expressing cells are present (arrows) (X40).
The conjunctiva from AKC patients also revealed a marked lymphocytic infiltrate (CD3+ cells). Once again, the substantia propria infiltrate was much more notable. Although the CD4/CD8 ratio was altered in the epithelium and the substantia propria with an increase in the proportion of CD4+ cells, it was statistically significant only in the substantia propria (Table 1). In addition, a statistically significant increase in the Langerhans’ cell (CD1+) population was noted in the epithelium and the substantia propria.

A statistically significant increase in the TCR α/β-expressing cells was noted only in the substantia propria of the AKC specimens as compared to controls (epithelium, 385.6 ± 73.6 vs 187.6 ± 30.7; P is NS; substantia propria, 454.4 ± 116.2 vs 37.6 ± 6.8; P = <0.009) (Table 1, Fig. 4). The mean number of TCR γ/δ-expressing cells per mm² was increased in the epithelium and substantia propria of AKC conjunctiva as compared to normal controls, but it was not statistically significant (Table 1). In addition, in contrast to OCP conjunctiva, there was no increase in the proportion of TCR γ/δ-expressing cells as a percentage of CD3+ cells (TCR γ/δ/CD3) in the epithelium or substantia propria of AKC specimens as compared to controls (Fig. 5).

Discussion

With the discovery of the TCR cDNA during the search for the TCR α cDNA and the later discovery of the TCR δ genes, it became clear that vertebrates have a second TCR, the TCR γ/δ, the function of which has remained enigmatic. However, the observations that the majority of murine intestinal intraepithelial lymphocytes express the TCR γ/δ,16 that there is selective homing of avian TCR γ/δ cells to the intestinal epithelium17,18 and that most Thy-1+ murine dendritic epidermal cells express TCR γ/δ19,20 have implied that homing of these TCR γ/δ lymphocytes to the epithelia may be important in surveillance of epithelial cell integrity and may represent a first line of defense against infection and transformation of epithelial cells. However, the situation is less than clear because such localization has not been found for TCR γ/δ cells in comparable epithelial tissues in man.8

In the present study, we examined the human conjunctiva, an epithelial tissue not previously investigated but one that is an integral and very active participant in the immunologic system of the eye. The marked increase in CD3+ cells and Langerhans’ cells in OCP and AKC conjunctiva corroborates other studies on alterations in T cell sub-populations that have been previously noted.29-31 Similar to the findings of Groh,8 the TCR γ/δ-expressing cells made up a minority of the CD3+ cells in the epithelium and substantia propria (0.18 ± 0.06 and 0.10 ± 0.05, respectively). Thus, the marked tropism noted in the murine and avian epithelial tissues is not present in the human conjunctiva. There were, however, relatively more TCR γ/δ-expressing cells as a fraction of CD3+ cells (TCR γ/δ/CD3) in the conjunctival epithelium compared to the substantia propria. This difference was not statistically significant but is similar to the findings in one study in which the relatively small percentage of TCR γ/δ cells in the gut were noted to localize preferentially to the epithelium rather than the lamina propria.

Although the TCR γ/δ-expressing lymphocytes represent a small population of the CD3+ cells, they still constitute a significant population of T cells and may play a significant role in ocular mucosal immunity. The γ/δ TCR repertoire differs in various tissues in mice,16,18,26,28 and selective differences in V gene usage also has been noted in humans.32,33 This site-specific localization of γ/δ T cells that bear certain V genes has led to the hypothesis that each cell population might perform distinct functions related to their unique anatomical location. Studies are in progress to determine if such compartmentalization of α/β or γ/δ subsets occurs in human conjunctiva.

In contrast to normal human conjunctiva, we have found that the conjunctiva from OCP patients contained a disproportionately increased number of TCR γ/δ-expressing cells, a finding not noted in the AKC patients. The significance of this finding is unclear. These two disorders have different underlying immunologic mechanisms. OCP is an autoimmune disease with a variety of systemic abnormalities, including elevated serum IgA, circulating autoantibodies directed against the conjunctival epithelial basement membrane, and HLA association.22-24 On the other hand, AKC is a chronic manifestation of several ocular surface disorders in the context of atopic dermatitis caused by Type I and probably Type IV hyper-
sensitivity. Our observation is intriguing because increased \( \gamma/\delta \) T lymphocytes have been identified in other human autoimmune disorders, such as in the synovial fluid of rheumatoid arthritis patients and in certain cases of polymyositis. Thus, there is a possible role of TCR \( \gamma/\delta \) cells in autoimmune disease.

In addition, specific antigens that \( \gamma/\delta \) T cells recognize, such as heat-shock proteins (HSP), have been identified. These are highly conserved proteins found in all organisms. Increased synthesis of these proteins occurs in response to many environmental stresses, including inflammation, fever, irradiation, viral infection, malignant transformation, exposure to oxidizing agents, heavy metal ions, ethanol, and anoxia. The 65 KDa mycobacterial heat-shock protein is highly conserved, not only among bacteria, but also in eukaryotes, so that some T cells might respond to epitopes common to both the bacterial and eukaryotic antigens. Because HSPs may be produced at sites of inflammation, T cells initially induced by bacterial antigens conceivably could mediate autoimmune disease. This notion is supported by recent in vitro data that suggest TCR \( \gamma/\delta \)-expressing lymphocytes play a role in autoimmune diseases and may recognize ligands by a mechanism similar to that of TCR \( \alpha/\beta \)-expressing lymphocytes.

The limited germline diversity of the TCR \( \gamma/\delta \)-expressing cells also suggests that they might recognize antigen in the context of relatively nonpolymorphic antigen-presenting molecules. Non-MHC-restricted \( \gamma/\delta \) T cell activity has been shown for tumor targets and recently for a human TCR \( \gamma/\delta \) clone that can recognize non-MHC-encoded CD1, a molecule that might serve as an antigen-presenting molecule for these cells. This is extremely intriguing in face of our past and present findings of significant increases in Langerhans' cells, which express CD1 and are known to be antigen-presenting cells in the epithelium and the substantia propria of OCP and AKC conjunctiva. However, the increased TCR \( \gamma/\delta \)-expressing lymphocytes in only OCP conjunctiva suggests that clonal expansion of TCR \( \gamma/\delta \) cells may be a result of specific antigens localized selectively in OCP conjunctiva in addition to CD1. Specific antigens that \( \gamma/\delta \) T cells recognize, such as mycobacterial antigens (including heat-shock proteins) and tetanus toxoid, have been identified, and we are currently examining normal and inflamed conjunctiva for HSP expression. Recent evidence suggests that extrathymic expression of \( \gamma/\delta \) cells bearing certain V gene segments may be an important feature in determining the peripheral TCR \( \gamma/\delta \) repertoire in man. Finally, immunohistopathologic studies have clearly demonstrated complement and immunoglobulin deposition in the epithelial basement membrane of OCP conjunctiva, the classic hallmark of this disease. Although the particular OCP autoantigen has not yet been identified, we can only speculate on its role in disease pathogenesis and its potential as an antigen for TCR \( \gamma/\delta \) cells.

Thus, the marked epithelial tropism of \( \gamma/\delta \) T cells noted in the murine and avian models is not present in normal human conjunctiva. However, these cells make up a significant proportion of the lymphocytes in OCP conjunctiva, a systemic autoimmune disorder. Their specific role is, however, unclear, and their role in autoimmunity is being investigated. Whether \( \gamma/\delta \) T cells are significantly increased in other conjunctival inflammatory or infectious processes will need to be studied.

Key words: atopic keratoconjunctivitis, autoimmunity, conjunctiva, ocular cicatricial pemphigoid, T cell receptor (TCR)

Acknowledgments

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References


