γδ T cells of the murine vagina: T cell response in vivo in the absence of the expression of CD2 and CD28 molecules

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Abstract

While little is known about their activation requirements and function, the intraepithelial T cells of the murine vagina express TCR complexes in which the antigen recognition components and the signaling components have unusual features. These vaginal T cells express an invariant Vγ4/Vδ1 TCR and appear to be the only intraepithelial γδ T cells that exclusively use FcR γ chains in their TCR complex. To further characterize the vaginal γδ T cells we isolated them from normal mice and from mice injected systemically with an activation-inducing dose of anti-TCR mAb. The isolated γδ T cells were examined by flow cytometry for their surface expression of a panel of adhesion proteins, activation antigens and cellular interaction molecules (CD44, CD62L, CD45RB, LFA-1, CD2 and CD28). The patterns of expression observed indicate that the vaginal γδ T cells of normal mice show the phenotype of effector T cells. The adhesion/co-stimulatory molecules CD28 and CD2 were not detected on vaginal γδ T cells, an interesting finding since the absence of CD2 from other T cells has been suggested to result in anergy. However, vaginal γδ T cells are responsive to TCR-mediated signals since injection of normal mice with pan-anti-TCR antibody or stimulating anti-γδ TCR antibody resulted in an increase in cell number and increased expression of transferrin and IL-2 receptors. These results indicate that vaginal γδ T cells might utilize other co-stimulatory molecules, if any, in connection with TCR-induced activation and differentiation. While the physiological function of vaginal γδ T cells remains unknown, the expression of an invariant Vγ4/Vδ1 TCR, their exclusive use of γ chain homodimers in their TCR, and the absence of CD2 and CD28 co-stimulatory molecules are a novel combination of properties that suggests specialized functional properties. Although vaginal γδ T cells share some features in common with γδ T cells that reside in other epithelial tissues, such as skin and intestine, the present studies provide additional evidence that vaginal γδ T cells are a highly specialized and distinct T cell population.

Introduction

Immunologic protection of the host against microorganisms encountered at anatomical sites that are environmental barriers (e.g. skin, intestine) involves specialized lymphoid cell populations that can differ considerably from site to site. The regional immunology of the skin has been investigated in great detail (1,2), and much is known about the specialized immune cells and functions of the intestinal and bronchial mucosal lymphoid systems (3,4). For other environmental barrier sites, such as the vagina, the available information is more scarce and though the interest is increasing, knowledge in the field is still at an early stage of development. The existence of a well-defined model system like murine vagina is of great importance. Earlier investigations show that there is considerable change in the composition of the cell populations of hematopoietic origin in the murine vagina and cervix during the estrous cycle (5,6). It was shown that the dominant population of leukocytes in this location (~75%) is the neutrophil granulocyte (7). T cells and B cells are present in much less numbers, and the quantity of lymphocytes is dependent on the phase of the estrous cycle, being the highest at
diestrous and the lowest at estrous (6). The major antigen-presenting cells are the Langerhans cells (8,9). The macrophages and B cells represent <1%, and the ratio of NK cells is ~1% of the cells of hematopoietic origin (6,7). As was published by Nandi and Allison (10), the T cells of the murine vagina are memory T cells; of totally thymus-dependent origin, and the ratio of αβ γδ TCR expressing cells is ~1:1. In previous publications, Ibraghimov et al. showed that the CD4+/αβ TCR+ cells of normal murine vagina appear to be a phenotypically distinct T cell lineage (11,12). In the present analysis we investigated the other major subpopulation of T cells in the murine vagina, the γδ T cells which reside in the vaginal epithelium above the basement membrane (13). They comprise up to 30% of the CD3+ cells in the vagina. According to the expression of CD4, CD8, CD44, CD62L and HSA surface antigens they are double-negative T cells with a memory phenotype (10).

The γδ T cells of the murine female genital tract belong to a rather unique family of T cells. Although they are of polyclonal origin (14), the TCR genes expressed by these cells are non-variant Vα/4/Vγ1 (13). A comparable situation occurs with skin γδ T cells where the homogenous TCR expressed is Vγ3/Vδ1 (15). The non-variant nature of the TCR implies that the antigen recognizing capability of these γδ T cells is very restricted (15–16). It has been suspected that similar to the skin γδ T cells, female genital tract γδ T cells also recognize stress-induced self-antigen (18). γδ T cells expressing the same TCR species also reside in the murine uterus. Their number is elevated and phenotype is activated (IL-2Rα chain+) during pregnancy, further supporting the view that their cognate antigen is of non-infectious origin (19). The second unique feature of these cells was recently reported by Park et al. (20), who presented evidence that murine vaginal γδ T cells were the only epithelial γδ T cells that exclusively use FcγR α chain homodimers instead of ζ chains in their TCR complex. This unusual combination of a unique recognition unit and a unique signaling structure raises the possibility that these γδ T cells might have unusual activation properties. To address this we investigated the surface expression of a panel of known adhesion/co-stimulatory molecules and activation markers on vaginal γδ T cells from normal mice or from mice injected systemically with an activation-inducing dose of anti-TCR mAb. We found unique phenotypic features which suggest that the determinants of γδ T cell activation in the vaginal epithelium are highly specialized.

**Methods**

**Animals**

Virgin, female BALB/c, C57Bl/6 and DBA/2 mice (8–12 weeks old) were obtained from Harlan Sprague Dawley (Indianapolis, IN) and housed in the animal facility at the University of Iowa. Three strains of mice were used to control for possible strain-specific patterns. In order to analyze the vaginal γδ T cells under stimulatory conditions each of the mice was given 25 µg of the mAb 2C11 (anti-CD3), or 25 µg UC7-13D5 (stimulatory anti-γδ TCR) or 25 µg GL3 (non-stimulatory anti-γδ TCR) antibody i.p. in PBS. Control mice received PBS only. Mice were sacrificed either 24 or 72 h after injection with antibody.

**Cell preparations**

For FACS analysis mononuclear cells from the vagina of 10 mice from each strain were prepared according to the following protocol: the vagina was dissected from the mouse, cut into 1.0 mm pieces with a single edge razor and incubated for 1 h at 37°C in HBSS containing 5% DNase I. The tissue debris was retained on a CMN-74-B nylon filter sheet (Small Parts, Miami Lakes, FL) and the cells which passed through the filter were fractionated by HBSS/40%/70% Percoll gradient centrifugation at 600 g for 15 min and collected from the 40%/70% interface. For RT-PCR the vaginal cells were isolated using the method described by Iohara et al. (13). The vaginas of four mice were cut and digested in HBSS supplemented with 0.25% trypsin/5% DNase for 1 h at 37°C. After removing the tissue pieces the digestion was stopped by transferring the cells into media containing 10% newborn bovine serum. Each vagina yielded ~10⁶ cells.

Small intestinal intraepithelial cell preparations were done as described by Lefrancois (21).

**mAb**

FITC-labeled RM2-5 (anti-CD2), FITC-labeled 7D4 (anti-CD25) and FITC-conjugated 16A (anti-CD45RB), biotin-labeled 37.51 (anti-CD28) and rat IgG2 antibody (anti-2,4,6 trinitrophenyl specific, used as isotype control), unlabeled GL-3 (non-stimulatory anti-γδ TCR), UC7-13D5 (stimulatory anti-γδ TCR), 2C11 (anti-CD3), and phycoerythrin (PE)-labeled GL-2 (anti-Vδ4) and 2.4G2 antibody (FcγR/II/III) were purchased from PharMingen (San Diego, CA). Phycoerythrin-labeled mAb Mel-14 (anti-CD62L), unlabeled IM 7.8.1 (anti-CD44) and cyantilated M17/4 (anti-LFA-1) were kindly provided by Dr Morris Dailey (University of Iowa). FITC-labeled C2 (anti-transferin receptor) was a gift from Dr J. Kemp (University of Iowa) and unlabeled UC5-10A6 (anti-Vδ2) was provided by Dr J. Bluestone (University of Chicago).

**Flow cytometric analysis**

For three-color analysis, cells in HBSS containing 10% BCS, 10 mM HEPES and 0.02% NaN₃ were stained with saturating specialities of labeled antibodies (2.5–5 µg/ml) on ice for 30 min in the presence of 2.4G2 antibody to inhibit FcγR-mediated binding. Following the incubation step with antibodies the cells were washed three times and incubated with PE- or Cy5-labeled avidin (PharMingen) under the same conditions. To determine the level of unspecific binding we used samples incubated with isotype control antibody or fluorochrome-conjugated avidin without incubation with the primary antibody. The excess of the dye-labeled avidin was removed by three washing steps and the samples were analyzed on a four-decade Becton Dickinson FACS 440 flow cytometer (Becton Dickinson, Mountain View, CA). The data were collected and analyzed using a VAX computer equipped with DESK software.
Vaginal γδ T cells represent a unique T cell lineage. Allison (10); Vγ4, CCA AAG AAT GTG TAG TTC; Cγ1/2, GAA TTC TAG ATG TCT GCA TCA AGC CT. The Vγ1.1 primers were constructed on the basis of published sequences of Iwamoto et al. (22): Vγ1.1, GGG GGT ACC GCA AAA AAG TTT GAG TAT CT; Jγ4, GGG AAG CTT GTC TGG GGG AAT TAC TAG GAG.

In order to get better quality pictures of the PCR product of the mRNA of the TCR, we performed a second PCR under the same conditions with an additional 10 cycles.

Results

Comparative analysis of adhesion molecules and activation markers expressed by intraepithelial γδ T cells of murine vagina and small intestine under physiological conditions

In the present studies we found that the γδ T cells in the mouse vaginal epithelium expressed the CD44 antigen at a very high level compared to their small intestinal counterparts and the CD62L expression was undetected, a finding similar to the small intestinal γδ T cells (Fig. 1B and C). We also observed that the vaginal γδ T cells were dull for the CD45RB antigen, which is in contrast with their small intestinal counterparts (Fig. 1D). In the peripheral lymphoid system αβ and γδ

Analysis of co-stimulatory molecules expressed by the intraepithelial γδ T cells of the murine vagina and small intestine under physiological conditions

We next examined the vaginal γδ T cells in parallel with the small intestinal γδ T cells for their expression of co-stimulatory molecules (Fig. 2). We detected a higher level of expression of the LFA-1 antigen on the murine vaginal γδ T cells, compared to those in the small intestine (Fig. 2A). Furthermore, like the majority of the intestinal γδ T cells, the whole population of normal murine vaginal γδ T cells was negative for the CD2 adhesion/co-stimulatory molecule. The vaginal αβ T cells, however, expressed this antigen (Fig. 2B). In addition to the lack of CD2 antigen, we detected no surface expression of the CD28 co-stimulatory molecule on the vaginal γδ T cells or on their small intestinal counterparts. On the other hand, the vaginal αβ T cells were positive for CD28 (Fig. 2C).

We observed that the vaginal γδ T cells were dull for the CD45RB antigen, which is in contrast with their small intestinal counterparts (Fig. 1D). In the peripheral lymphoid system αβ and γδ

RNA isolation and RT-PCR

Poly(A) RNA was isolated using the Micro-FastTrack Kit of Invitrogen (San Diego, CA) according to the manufacturer’s recommendations. cDNA synthesis was performed in a 40 µl volume containing 0.5 µg oligo dT/18mer, 40 units of RNasin, 400 units of M-MLV reverse transcriptase and 5 mM of each dNTP. The reaction was incubated for 2 h at 42°C, then aliquots of the mixture were directly used for PCR, which was performed on a HyBond DNA Thermal Cycler under the following conditions: 94°C for 90 s, 60°C for 90 s, 72°C for 90 s. The reactions were subjected to 35 cycles followed by an extension step at 72°C for 7 min. The reaction buffer consisted of 50 mM KCl, 20 mM Tris–HCl, pH 8.3, 100 µg/ml BSA, 10 pM of each primer, 0.2 mM of each dNTP and 1 U Taq polymerase. The concentration of MgCl2 was 1.5 mM.

The Vγ4–Cγ1/2 primers were as described by Nandi &

Table 1. Expression of adhesion/costimulatory molecules on γδ T cells of different organs of normal DBA/2 mice

<table>
<thead>
<tr>
<th>γδ T cells</th>
<th>CD44</th>
<th>CD62L</th>
<th>CD4RB</th>
<th>LFA-1</th>
<th>CD2</th>
<th>CD28</th>
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<tr>
<td>Normal spleen</td>
<td>high and low</td>
<td>+ and −</td>
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<td>high and low</td>
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<td>Normal intestine</td>
<td>high</td>
<td>−</td>
<td>high</td>
<td>low and −</td>
<td>+ and −</td>
<td>−</td>
</tr>
<tr>
<td>Normal vagina</td>
<td>very high</td>
<td>−</td>
<td>low</td>
<td>very high</td>
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level of the CD44, CD62L, CD45RB, LFA-1, CD2 and CD28 antigens would change. In addition we analyzed the changes in the expression of activation markers including the IL-2R α chain, transferrin receptor and Thy-1. We observed no changes in the expression of the adhesion and co-stimulatory molecules (data not shown); however, we detected an increased level of the IL-2R α chain by 24 h (Fig. 3A and B). The elevated expression level of the IL-2R α chain returned to the physiological level by 48 h (data not shown). Changes in the expression of the transferrin receptor were not detected until after 72 h (Fig. 3C and D). The presence of Thy-1 antigen on vaginal γδ T cells is strain-dependent and considered to be a differentiation marker rather than an activation marker (10). In BALB/c and DBA/2 mice there are both Thy-1+ and Thy-1− γδ T cells in the vagina. Following stimulation, the proportion of Thy-1+ γδ T cells showed a remarkable elevation (Fig. 3E and F). While it is not certain that the expression of Thy-1 antigen by these cells is indicative of activation, it is clear that the increased frequency of Thy-1+ cells was a consequence of engagement of TCR by the anti-CD3 mAb. These findings establish that the CD2+ CD28− vaginal γδ T cells responded with expression of proliferation-associated markers following engagement of their TCR.

To determine whether the induced proliferation of murine vaginal γδ T cells was dependent on the simultaneous stimulation of αβ T cells, we used a stimulating antibody specific for the γδ TCR. In a parallel group of mice we used a non-stimulating antibody specific for the γδ TCR. Our data show that the murine vaginal γδ T cells proliferate equally well to anti-γδ TCR stimulation as to the anti-CD3 stimulation (Fig. 4). Since we detected an elevated level of γδ T cells in the murine vaginal samples after treatment with the stimulating γδ TCR antibody, but not after treatment with the non-stimulating anti-γδ TCR antibody, we conclude that the anti-CD3-induced proliferation of the murine vaginal γδ T cells is not due to the anti-CD3-promoted αβ T cell activation, but is a direct consequence of engagement of the TCR on the γδ cells by the stimulating mAb.

Analysis of the γδ TCR usage of murine γδ T cells after systemic stimulation to determine the source of the proliferating cells

To investigate the source of the increased numbers of vaginal γδ T cells following systemic administration of anti-TCR antibody (Fig. 5A and B) we considered two possibilities. First, it was possible that the increase was due to an influx of circulating γδ T cells. To address this possibility we examined the vaginal γδ T cells for the presence of Vγ4+ and Vγ2+ T cells, because these γδ TCR species are characteristic of the splenic/circulating pool of γδ T cells. We found by FACS analysis that the increase in vaginal γδ T cells after systemic stimulation was not due to immigration of Vγ4+ or Vγ2+ T cells (Fig. 5C and D).

Since a mAb specific for Vγ4+ is not available, we used RT-PCR to detect the Vγ4 population of γδ T cells. We examined the vaginal γδ T cells after stimulation to determine whether they still expressed the γδ TCR species observed prior to stimulation. As shown in Fig. 6, the γδ TCR species characteristic of the normal murine vagina were still present after systemic stimulation. These findings indicate that either the increase came from proliferation of cells already residing in the vagina or there was a selective recruitment of Vγ4 TCR+ cells from systemic sources.

Discussion

The murine vagina is a mucosal barrier that has some structural and immunologic features in common with the intestine. Each has an endogenous microflora, a secretory epithelial component, and is exposed to a wide assortment of potentially immunogenic materials. Since the intraepithelial lymphocyte (IEL) populations of γδ T cells at these sites might play a significant role in host defense, we were interested in comparing their characteristics. On the basis of the expression pattern of cell surface markers like CD44, CD62L and the display of cytotoxic functions, the γδ T cells of the small intestine are considered to be effector cells (21). In this report we present evidence that the γδ T cells of the murine vaginal

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**Fig. 2.** Expression of the known major co-stimulatory molecules by the αβ and γδ T cells of murine vagina, and small intestinal γδ T cells of DBA/2 mice. Expression level of (A) LFA-1, (B) CD2 and (C) CD28. The cells were gated on the basis of forward and orthogonal light scatter, selecting the lymphoid population and the expression of the αβ or γδ TCR. Dotted line, αβ T cells; thick line, γδ T cells of the murine vagina; thin line, γδ T cells of murine small intestine. Fluorescence intensity is presented on a log scale.
Vaginal γδ T cells represent a unique T cell lineage

Fig. 4. Comparison of the relative increase of the αβ and γδ T cells of murine vagina of DBA/2 mouse strain after 72 h of i.p. administered PBS, anti-CD3 (2C11), stimulating (UC7-13D5) or non-stimulating (GL3) anti-γδ TCR antibody. Percentiles of the cells expressing αβ or γδ TCR in the lymphoid gate of the samples were calculated by Versaterm software; 30,000 events/sample were counted. The αβ and γδ T cell numbers of control mice treated with PBS only were taken as 100%. The average values ± SD of three different experiments are shown.

Fig. 3. Expression of activation markers on γδ T cells of murine vagina of the DBA/2 mouse strain before and after systemic stimulation with anti-CD3 antibody as described in the section of Methods. Panels (A) and (B) compare IL-2R α chain expression 24 h after injection of the antibody or PBS. Panels (C)–(F) show the expression of transferrin receptor or Thy-1 antigen 72 h after injection of anti-TCR antibody or PBS. The cells were stained with FITC-labeled anti-IL-2R α chain, or anti-transferrin, or anti-Thy-1.2 antibodies together with biotin-conjugated anti-γδ-TCR followed by an incubation step with avidin–Cy-5. The cells were gated on the basis of forward and orthogonal light scatter, selecting the lymphoid population; 30,000 events/sample were counted. Percentiles of the different populations within the lymphoid gate of the samples were calculated by Desk software. Fluorescence intensity is presented on a log scale.

Fig. 5. TCR analysis of γδ T cells of murine vagina of DBA/2 mice 72 h after stimulation. (A) αβ and γδ T cells of unstimulated murine vagina. (B) αβ and γδ T cells of murine vagina 72 h after stimulation. The cells were stained with PE-conjugated anti-Vγ4 TCR and Cy-5-labeled anti-Vδ2 TCR antibodies. In the case of splenic sample we used FITC-labeled anti-FcRγII/III and anti-αβ TCR antibodies for negative gating.

epithelium have the phenotype that is attributed to activated/effector T cells. This conclusion is based on the expression pattern of CD44, CD62L, CD45RB and LFA-1 antigens. Nandi and Allison described that the γδ T cells of the murine vaginal epithelium express CD44 at high levels but do not express CD62L (10). We expand that data by showing that the vaginal γδ T cells express the CD44 and LFA-1 adhesion proteins at very high levels compared to the intestinal γδ IEL, levels that are often a reflection of cellular activation. Furthermore, the expression level of these antigens on the vaginal γδ T cells
Fig. 6. Expression of V\textsubscript{166} and V\textsubscript{4} TCR mRNA in stimulated and unstimulated spleen (lanes 1 and 2) and vaginal samples (lanes 3 and 4) of DBA/2 mice 72 h after stimulation. A total of 10\textsuperscript{6} cells from mice were pooled and used as a source of mRNA. A 35 cycle RT-PCR of murine V\textsubscript{166} and V\textsubscript{4} TCR and a 30 cycle RT-PCR of murine \(\beta\)-actin was visualized on 1.5% agarose gels. The size of the PCR product was estimated by comparison to a 100 bp incremental DNA ladder. In order to get better quality pictures of the PCR product of the mRNA of the TCR, we performed a second PCR under the same conditions with an additional 10 cycles.

does not change after systemic activation. These findings differ from those reported for the intestinal \(\gamma\delta\) T cells where a qualitatively similar expression pattern of these adhesion proteins occurs, but where their level of expression increases after TCR-dependent stimulation (26). Comparison of the pre- and post-anti-TCR treatment levels of expression of this panel of adhesion molecules suggests that prior to anti-TCR treatment, the intraepithelial \(\gamma\delta\) T cells of the vagina from normal mice had already been activated. The CD8\textsuperscript{+} T cells of the small intestine, including the \(\gamma\delta\) T cells, express a high level of the CD45RB antigen (27), as do the \(\gamma\delta\) T cells of the skin (28). Our data show that the vaginal \(\gamma\delta\) T cells are dull for CD45RB. This finding further supports our conclusion that the vaginal \(\gamma\delta\) T cells from normal mice appear to be terminally differentiated effector cells.

The expression pattern and level of the three known major co-stimulatory/adhesion molecules (LFA-1, CD2 and CD28) reflects both the differentiation state of the T cell and the co-stimulatory requirements of the different environments (29). The B7/CD28 counterpair of co-stimulatory molecules augments a prolonged T cell response at a very low amount of antigen (29). This pathway is used by all \(\alpha\beta\) and \(\gamma\delta\) T cells of the blood and secondary lymphoid organs, such as spleen and lymph nodes (30,31). Nandi and Allison showed that the \(\gamma\delta\) T cells of the murine vagina express no CD28 antigen (10). We point out that the expression of CD28 on vaginal \(\gamma\delta\) T cells does not change following cellular activation via their TCR.

The binding of CD2/LFA-3 molecules initiates strong antigen-independent adhesion and induction of large amounts of IFN-\(\gamma\) (29). Our findings show that the \(\gamma\delta\) T cells of the murine vagina do not express CD2. The lack of the co-stimulatory molecule CD2 results in anergy in \(\alpha\beta\) T cells, as has been well-documented in lpr and gld mutant mice, and for some of the \(\alpha\beta\) T cells of the normal murine intestinal IEL (24,32). All of the \(\gamma\delta\) T cells in the murine skin and spleen express CD2, and those in the spleen are also positive for CD28 (27,30). The intestinal \(\gamma\delta\) T cells do not express CD28 and the majority of them are CD2\textsuperscript{+} (24,25). However, as we show with the stimulation experiments, the absence of these co-stimulatory molecules on the murine vaginal \(\gamma\delta\) T cells does not seem to have any effect on their ability to be activated and proliferate. We infer from these findings that if the \(\gamma\delta\) T cells of the murine vagina use co-stimulatory pathways they differ from those used by the \(\gamma\delta\) T cells of the spleen or the skin. One of the possible candidates might be the LFA-1 molecule, because it is a potent co-stimulatory molecule on memory/effector cells, and has been shown to be involved in antigen-dependent T cell proliferation and the effector phase of cytotoxic responses (29). The very high expression of LFA-1 by both the \(\alpha\beta\) and \(\gamma\delta\) T cells of the murine vagina suggests a particular importance of the LFA-1/ICAM-1 pathway in this environment. Further, another candidate for the co-stimulatory role might be the CD69 molecule. In the presence of phorbol myristate acetate, anti-CD69 mAb have been shown to induce proliferation of human and murine T cells (33). However, other possibilities can also be envisioned. For example, the anti-mucosal addressin (\(\alpha\)M290) antibody has been shown to enhance anti-CD3-induced activation of human T cells (34). In CD28 knockout mice, CD43 has been shown to be a major co-stimulatory molecule (35). Although vaginal \(\gamma\delta\) T cells do not express the two major co-stimulatory molecules CD2 and CD28, they do express CD69, CD43 and \(\alpha\)M290 at high densities (our unpublished observations). Whether these antigens function as co-stimulatory molecules on vaginal \(\gamma\delta\) T cells, and if so what their relative importance might be, are questions that remain unanswered.

Previous data from our laboratory showed a strong in situ proliferation of CD4\textsuperscript{+} \(\alpha\beta\) T cells in the murine vagina in response to a systemically delivered TCR stimulus (12). The unusual TCR usage of murine vaginal \(\gamma\delta\) T cells provided an opportunity for easy detection of any immigrant \(\gamma\delta\) T cells following systemic stimulation. The present findings with \(\gamma\delta\) T cells parallel our earlier findings with \(\alpha\beta\) T cells and indicate that the increase of \(\gamma\delta\) T cells in response to systemic activation results from a local proliferation of resident \(\gamma\delta\) T cells, although a contribution by recruitment/retention of \(\alpha\beta\) TCR\textsuperscript{+} cells from other sites, can not yet be totally excluded.

In summary, vaginal \(\gamma\delta\) T cells are particularly interesting because (i) they combine an invariant TCR with the unusual signaling structure of FcR \(\gamma\) chain homodimers, (ii) they remain totally responsive to TCR-mediated signals in spite of the lack of the known major co-stimulatory molecules and (iii) they express some features indicative of activation in the absence of any apparent pathologic condition. These findings suggest that vaginal \(\gamma\delta\) T cells represent a distinct T cell lineage and imply that they have specialized functions.

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Abbreviations

IEL intraepithelial lymphocyte
PE phycoerythrin

References


