Supplementary Figure 1. Adaptive and innate lymphocytes in psoriasis and healthy controls. Percentage of circulating blood CD4+ T cells (CD3+CD4+) (A), CD8+ T cells (CD3+CD8+) (B), NK-like T cells (CD3+CD161+) (C) NKT cells (CD3+6B11+) (D), and NK cells (CD56brightCD3- (E) and CD56+CD16+CD3- (F)) was measured by flow cytometry, gated on CD3 (CD4, CD8, 6B11) and lymphocytes (NK cells, CD161+ T cells), respectively. Psoriasis patients and healthy controls did not show significant differences in any of the cell types analyzed. Psoriasis patients had a mean of 29 (+4.7) Vγ9Vδ2 T cells / μl peripheral blood (G).
Supplementary Figure 2

Peripheral \( \gamma \delta \) T cells do not express gut homing markers, up-regulate CLA upon exposure to IL-12 and are present in psoriatic skin. Expression of the gut homing markers CCR9 and CD103 (\( \alpha E\beta 7 \) integrin) were analyzed on peripheral T cells of 5 healthy individuals by flow cytometry. While total CD3+ T cells expressed low levels of CCR9 and CD103 (A), no circulating \( \gamma \delta \) T cells with gut homing phenotype could be detected (B). To investigate CLA regulation peripheral \( \gamma \delta \) T cell lines were either left unstimulated or stimulated with HMB-PP (1nM) or SEB (100ng/ml) for 3 days (all with and without IL-12). IL-12 induced a more than two fold up-regulation of CLA in all conditions independent of activation while activation by itself did not induce CLA (one representative experiment (n=3), done in triplicates) (C). To verify the exposure to IL-12 on CLA expression we analysed \( \gamma \delta \) T cells by flow cytometry using fresh PBMCs. Fresh PBMCs were cultured for 3 days with 10 ng/ml IL-12 or with medium alone before staining for flow cytometry. IL-12 induced a distinct up-regulation of CLA on fresh \( \gamma \delta \) T cells (one representative experiment, n=4) (D). 5 \( \mu \)m sections of frozen healthy and psoriatic lesional and non-lesional skin were stained for the \( \gamma \delta \) antigen by immunohistochemistry. The arrows indicate \( \gamma \delta \) expressing cells. \( \gamma \delta \)+ cells were present in dermis and epidermis of psoriasis skin (E). In addition they were detected in non-lesional skin of psoriasis patients (F). \( \gamma \delta \)+ cells were rarely seen in healthy skin (G).
**Supplementary Figure 3**

**A**  
Vγ9Vδ2 cells counts in psoriatic skin (A)  

![Image](367x490 to 396x547)  

37.5 Vγ9Vδ2 T cells in 1 cm skin section

![Image](307x213 to 515x280)  

2000 5 μm-thick sections correspond to 1 cm² of skin

![Image](398x293 to 427x353)  

37.5 x 2000 = 75 000 Vγ9Vδ2 T cells estimated in 1 cm² of skin

![Image](405x355 to 420x360)  

A patient with 50% of body surface area affected (= 10300 cm² of skin) has 75,000 cells/cm² skin x 10300 cm² = 7.7 X10⁸ Vγ9Vδ2 T cells in affected psoriatic skin

Vγ9Vδ2 cells counts in psoriatic blood (A)

![Image](405x362 to 420x364)  

9.8 Vγ9Vδ2 T cells in 1 μl peripheral blood

![Image](398x603 to 413x679)  

9.8 Vγ9Vδ2 T cells x 5.4 L blood = 0.53x10⁸ Vγ9Vδ2 T cells in peripheral blood

**14 times more Vγ9Vδ2 cells in psoriatic skin than in peripheral blood**

**B**

<table>
<thead>
<tr>
<th></th>
<th>psoriatic skin</th>
<th>peripheral blood</th>
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<tr>
<td></td>
<td>PASI score</td>
<td>cells/cm²</td>
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<td>Patient A</td>
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<td>7.5x10⁴</td>
</tr>
<tr>
<td>Patient B</td>
<td>24.1</td>
<td>8.8x10⁴</td>
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Supplementary Figure 3. Calculation of absolute numbers of Vγ9Vδ2 T cells in total psoriatic skin. Vγ9Vδ2 T cells in blood and psoriatic skin of one patient (Patient A) were estimated. In his lesional psoriatic skin, 6 Vδ2 expressing T cells were detected in 1.6 mm of a 5 µm section corresponding to 37.5 cells in 1 cm of 5 µm thick skin. A 1 cm² area of skin is equivalent to 2x10³ 0.5 µm-thick sections, therefore we multiplied 37.5 by 2x10³. This resulted in 7.5x10⁴ Vγ9Vδ2 T cells / 1 cm² of psoriatic skin. Clinical examination revealed that 50% of the body surface area were covered by psoriasis plaques. Patient A had – as calculated from his body size (178 cm) and weight (86 kilos) - a total body surface area of 2.06 cm², 50% of which corresponds to 10300 cm² of psoriatic skin. We calculated Vγ9Vδ2 T cell numbers in this patient’s affected skin by multiplying Vγ9Vδ2 T cell number in 1 cm² by the affected skin surface area resulting in an approximate number of 7.7x10⁸ Vγ9Vδ2 T cells (STD: +1.3*10⁸). To put this number into context we calculated the approximate number of Vγ9Vδ2 T cells in his peripheral blood. A differential blood count and flow cytometry for Vγ9Vδ2 T cells in peripheral blood taken at the same time as the biopsy was used to deduct absolute T cell numbers in peripheral blood resulting in an absolute number of 9.8 Vγ9Vδ2 T cells in 1 µl of peripheral blood. The total blood volume of this patient was calculated to be 5.44 l, resulting in an approximate total of 0.53x10⁸ Vγ9Vδ2 T cells in his circulation. Remarkably at the time of biopsy, Patient A had more than 14 times higher numbers of Vγ9Vδ2 T cells in his psoriatic skin than in his peripheral blood (A). The calculation for Patient A is summarized in (B). We could confirm these data in a further patient (Patient B) with a PASI of 24.1 with a 25 fold increase of Vγ9Vδ2 T cells in his psoriatic skin compared to peripheral blood (8.66 *10⁸ (± STD 1.5*10⁸) in skin, 3.4*10⁷ in peripheral blood) (B).
Supplementary Figure 4. The potential role of Vγ9Vδ2 T cells in skin immunology. We propose that Vγ9Vδ2 T cells are immediate response tissue surveillance cells that can have both, protective and pathogenic roles. Vγ9Vδ2 T cells are attracted to perturbed skin via CCL20 released by keratinocytes and produce growth factors such as IGF-1, FGF-2 and VEGF important for wound healing and angiogenesis. In addition Vγ9Vδ2 T cells are possibly involved in tumour immunosurveillance through their recognition of stress-upregulated self antigens such as IPP and MICA/B.

However, Vγ9Vδ2 T cells could be pathogenic in psoriasis where they might initiate and amplify the inflammatory loop by producing psoriasis-relevant cytokines (IL-17, IFN-γ and TNF-α) and chemokines (CCL3, CCL4, CCL5 and IL-8), thus attracting a plethora of immune cells to the evolving psoriatic lesions. Finally, they produce growth factors (IGF-1, FGF-2, VEGF) and antimicrobial peptides (S100A7, S100A8, β-defensin-2) also playing a role in psoriasis pathogenesis.