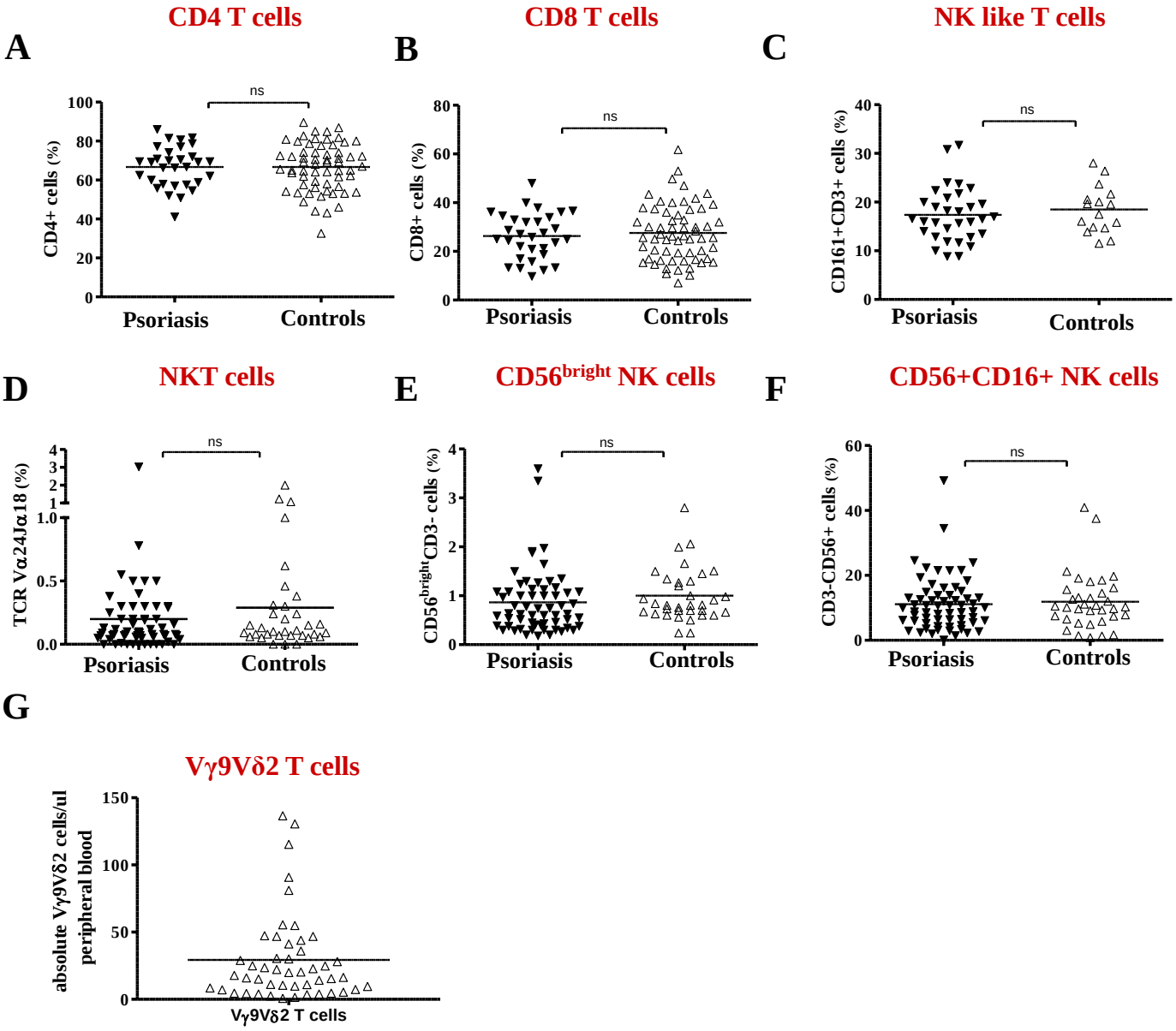
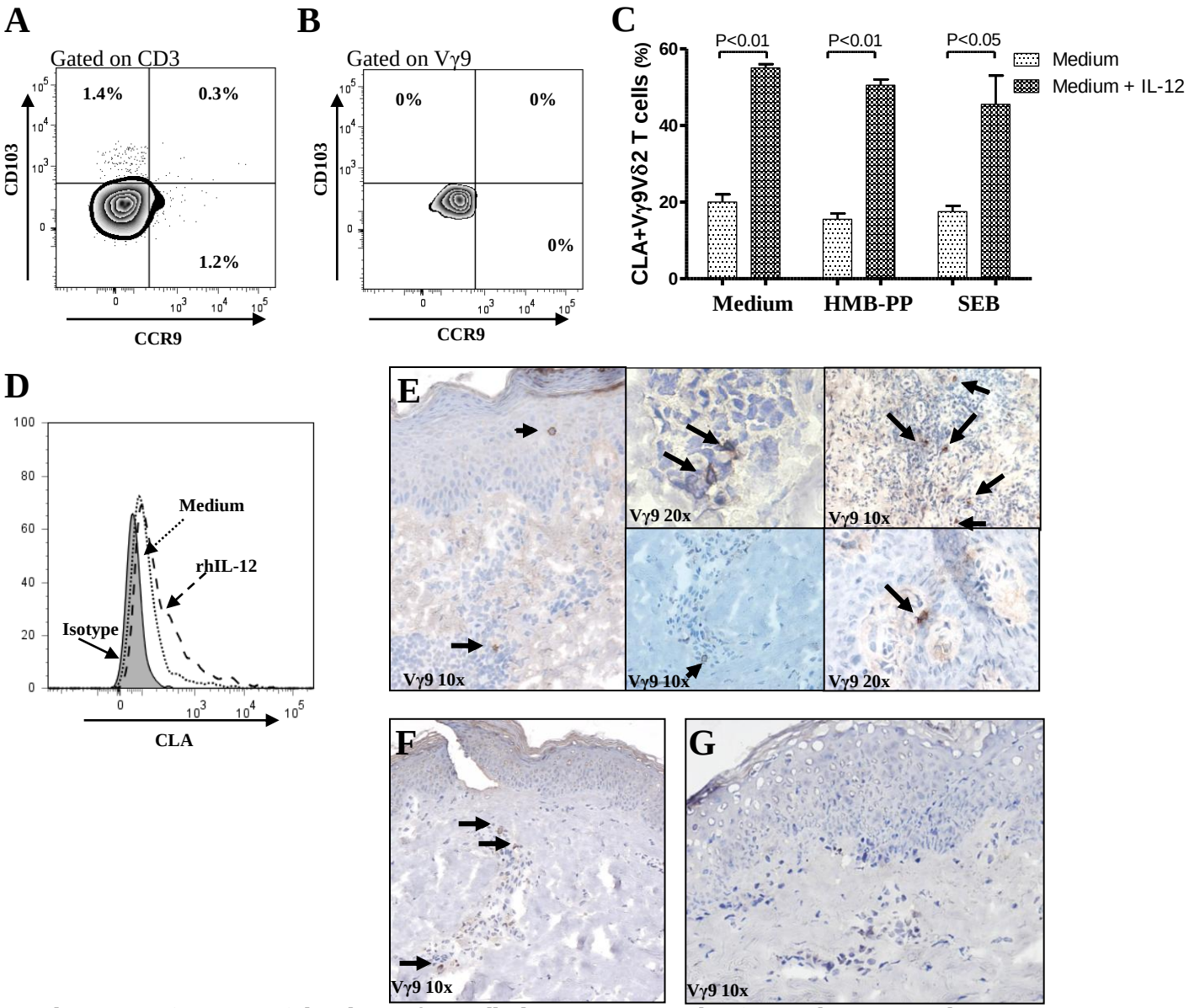
Supplementary Figure 1



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 (CD56^{bright}CD3- (**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

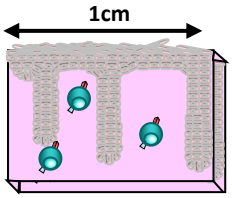


Supplementary Figure 2. Peripheral Vγ9Vδ2 T cells do not express gut homing markers, up-regulate CLA upon exposure to IL-12 and are present in psoriatic skin. Expression of the gut homing markers CCR9 and CD103 (αEβ7 integrin) were analyzed on peripheral T cells of 5 healthy individuals by flow cytometry. While total $CD3^+$ T cells expressed low levels of CCR9 and CD103 (**A**), no circulating Vγ9Vδ2 T cells with gut homing phenotype could be detected (**B**). To investigate CLA regulation peripheral Vγ9Vδ2 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 Vγ9Vδ2 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 Vγ9Vδ2 T cells (one representative experiment, n=4) (**D**). 5 µm sections of frozen healthy and psoriatic lesional and non-lesional skin were stained for the Vγ9 antigen by immunohistochemistry. The arrows indicate Vγ9 expressing cells. Vγ9+ cells were present in dermis and epidermis of psoriasis skin (**E**). In addition they were detected in non-lesional skin of psoriasis patients (**F**). Vγ9+ cells were rarely seen in healthy skin (**G**).

Supplementary Figure 3

A

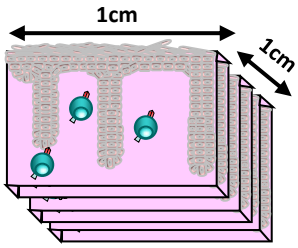
Vγ9Vδ2 cells counts in psoriatic skin (A)



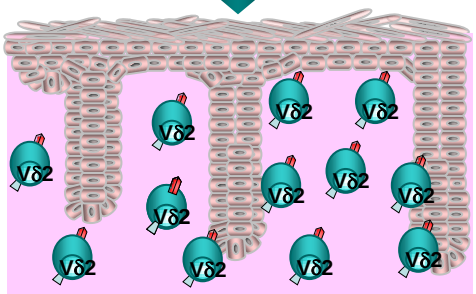
5µm thick section

37.5 Vγ9Vδ2 T cells in **1 cm** skin section

2000 5 µm-thick sections correspond to 1 cm^2 of skin

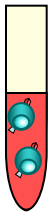


37.5 x 2000 = **75 000** Vγ9Vδ2 T cells estimated in **1** cm^2 of skin

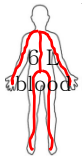


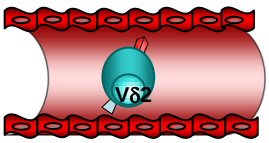
A patient with 50% of body surface area affected (= 10300 cm^2 of skin) has 75,000 cells/cm^2 skin x 10300 cm^2= **7.7 X10^8** Vγ9Vδ2 T cells in affected psoriatic skin

Vγ9Vδ2 cells counts in psoriatic blood (A)



9.8 Vγ9Vδ2 T cells in **1 µl** peripheral blood





9.8 Vγ9Vδ2 T cells x 5.4 L blood= **0.53x10^8** Vγ9Vδ2 T cells in peripheral blood

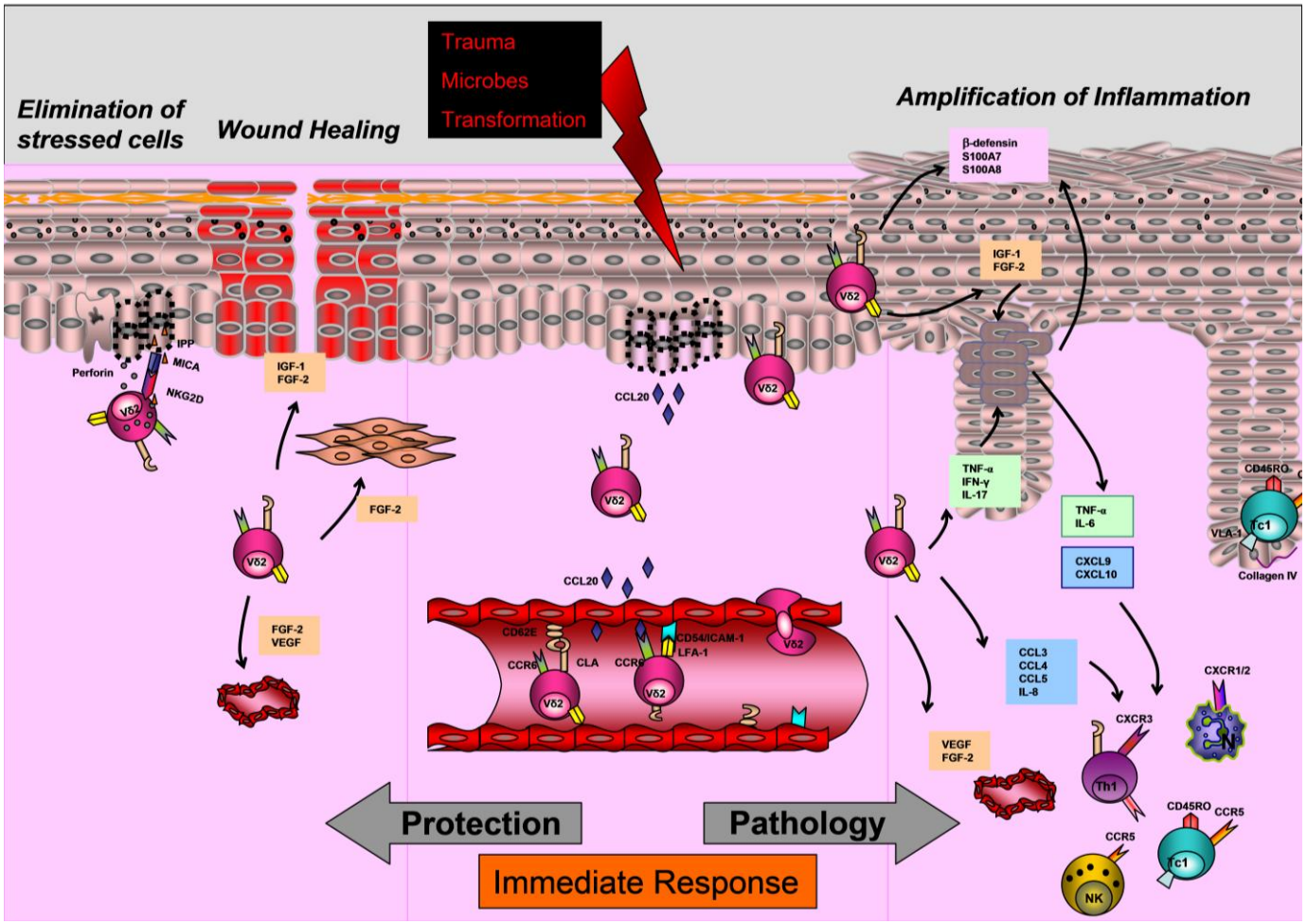
14 times more Vγ9Vδ2 cells in psoriatic skin than in peripheral blood

B

		psoriatic skin			peripheral blood		
	PASI score	cells/cm2	% affected	absolute numbers Vγ9Vδ2	% of Vγ9Vδ2	absolute number Vγ9Vδ2	Fold increase in skin
Patient A	25	$7.5x10^4$	50%	$7.73x10^8$	2.4%	$5.3x10^7$	14
Patient B	24.1	$8.8x10^4$	49%	$8.66x10^8$	1.6%	$3.4x10^7$	25

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 cm^2 area of skin is equivalent to $2x10^3$ 0.5 µm-thick sections, therefore we multiplied 37.5 by $2x10^3$. This resulted in $7.5x10^4$ Vγ9Vδ2 T cells / 1 cm^2 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 cm^2, 50% of which corresponds to 10300 cm^2 of psoriatic skin. We calculated Vγ9Vδ2 T cell numbers in this patient's affected skin by multiplying Vγ9Vδ2 T cell number in 1 cm^2 by the affected skin surface area resulting in an approximate number of $7.7x10^8$ 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 resulted 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 $0.53x10^8$ 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 an 25 fold increase of Vγ9Vδ2 T cells in his psoriatic skin compared to peripheral blood (8.66 *10^8 (± STD 1.5*108) in skin, 3.4*10^7 in peripheral blood) (**B**).

Supplementary Figure 4



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.