Circulating CLA+ T cells from psoriasis patients manifest a different frequency and activation state between acute and chronic stages

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Introduction

CLA^+ T cells constitute a relevant subset of circulating memory T cells in the pathological mechanisms of psoriasis (Schon *et al*, 2005; Gottlieb, 2005) and other T-cell mediated diseases (Santamaria-Babi, 2004). In uninvolved skin, distant from the plaque edge, a significant infiltration of CLA^+ T, $CD8^+$, and memory $CD45RO^+$ T cells has been shown to develop. This phenomenon seems to occur before epidermal hyperproliferation takes place (Davison et al, 2001; Vissers et al, 2004). A recent study has shown a correlation between the number of circulating CLA^+CD8^+ T cells and the severity of the disease (Sigmundsdottir et al, 2001). However, it is not known the frequency and phenotype of this circulating skin-homing population between acute and chronic state psoriasis. Therefore we were interested in determining whether there were differences in the frequency of circulating $HLA\text{-}DR^+$ T cells in either CLA^+ or CLA^- subsets in different types of psoriasis.

Material and methods

Thirty-one adult patients with psoriasis (15 acute psoriasis vulgaris and 16 chronic psoriasis) and eleven healthy subjects were studied. Patients presenting "acute lesions" including those patients who had suffered an acute relapse of psoriasis of less than six weeks duration (15 patients) included 7 guttate psoriasis and 8 plaque psoriasis patients. Patients presenting "chronic lesions" defined as chronic and stable psoriatic plaques persisting for more than six weeks (16 patients).

Results

Guttate psoriasis patients showed significantly the lowest percentage of circulating CLA^+ $CD4^+$ cells compared with acute plaque psoriasis and controls (8,8 ± 4,9 vs 16,0 ± 5,4 (p=0,009) and 16,7 ± 8,0 (p=0,03), respectively (Figure 1). Flow cytometry data from representative individuals are shown in Fig 2A and 2B.

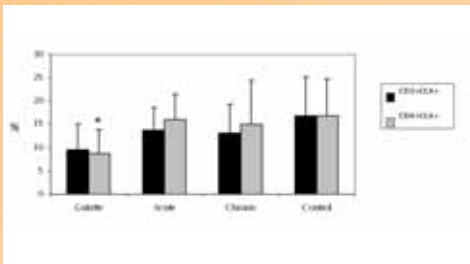

FIG 1.Percentage of circulating $CD3^+CLA^+$ and $CD4^+CLA^+$ cells in guttate psoriasis, acute plaque psoriasis, chronic psoriasis, and controls. Percentage of circulating $CD3^+CLA^+$ (black bars) or $CD4^+CLA^+$ lymphocytes (grey bars). Flow cytometric analysis were performed with PBMC from either guttate psoriasis (n=7), acute plaque psoriasis (n=8), chronic psoriasis (n=16) and healthy controls (n=11). *Values are expressed as mean ± SD, * p=0.009.*

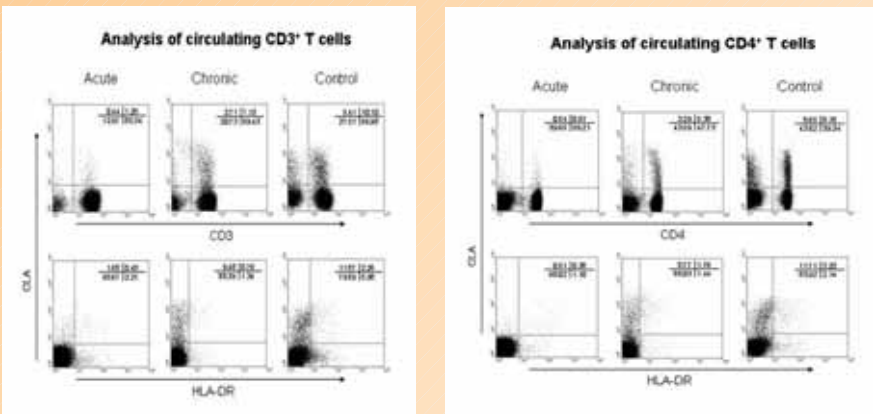

FIG 2A/2B. FACS analysis of a representative individual. Peripheral blood mononuclear cells from the study subjects were stained with HECA-452-FITC, anti-CD3-PerCP and either anti-HLA-DR both conjugated to PE. The same staining was performed with anti-CD4-PerCP antibody instead of anti-CD3-PerCP. Specific staining was determined for each marker using appropriate isotype control antibodies. Analysis was performed using a FACScalibur flow cytometer (Becton Dickinson, San Jose, CA).

Figure 3 presents the frequency of circulating $CD3^+HLA\text{-}DR^+$ cells, in either CLA^+ or CLA^- subset, in the study groups. Patients with guttate or acute plaque psoriasis had the highest levels of circulating $CLA^+CD3^+HLA\text{-}DR^+$ cells (p=0.002 and p=0.0005) compared to chronic psoriasis patients and controls ,and such percentages directly correlated with PASI and BSA in acute plaque psoriasis (0.60 and 0.61, respectively). Interestingly, no significant correlation was found with PASI or BSA and the frequency of circulating CLA^-CD3^+ $HLA\text{-}DR^+$ cells in either guttate or acute plaque psoriasis patients. Conversely, in chronic psoriasis patients, both CLA^+ and CLA^- subsets of circulating $CD3^+HLA\text{-}DR^+$ cells were inversely correlated with PASI and BSA. Regarding the percentage of $CD4^+HLA\text{-}DR^+$ cells, as it is shown in Figure 4, guttate and acute plaque psoriasis patients presented significantly higher percentage of $CLA^+CD4^+HLA\text{-}DR^+$ than chronic or controls (p=0.007, p=0.0006), as in the case of $CD3^+$ cells. However, such percentages showed a lower correlation with PASI or BSA than in the case of $CLA^+CD3^+HLA\text{-}DR^+$ cells. Finally, for $CD3^+HLA\text{-}DR^+$ cells in chronic psoriasis patients, both CLA^+ and CLA^- subsets of circulating $CD4^+HLA\text{-}DR^+$ cells were inversely correlated with PASI and BSA.

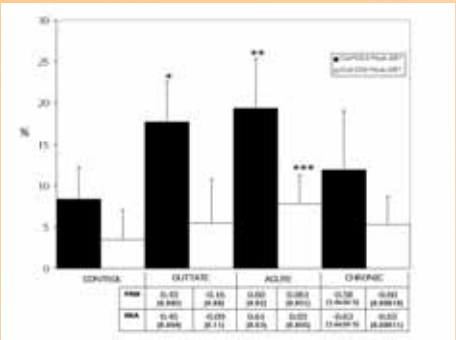

FIG 3. Frequency of circulating CLA^+ and CLA^- $CD3^+HLA\text{-}DR^+$ subsets in various psoriasis forms and correlation with PASI and BSA. *Values are expressed as mean ± SD, * p=0.002, **p=0.0005, ***p=0.0.005.*

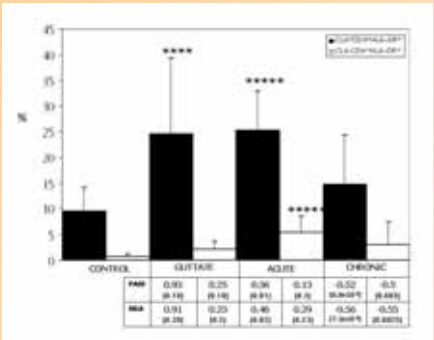

FIG 4. Frequency of circulating CLA^+ and CLA^- $CD4^+HLA\text{-}DR^+$ subsets in various psoriasis forms and correlation with PASI and BSA. *Values are expressed as mean ± SD, ****p=0.007, ***** p=0.0006, ****** p=0.0003.*

Conclusions

- In acute psoriasis, the reduced frequency of CLA^+ T cells suggests a sequestration of circulating CLA^+ T cells to skin that would support other studies showing early infiltration of CLA^+ T cells in advance of active edge of lesions.
- The increased frequency of $HLA\text{-}DR^+CLA^+$ T cells found in acute and guttate psoriasis and their direct correlation with PASI and BSA in acute psoriasis and inverse correlation with chronic psoriasis suggest that those could be memory effector T cells activated in the skin that are present in the periphery during the acute phase of psoriasis. Those results support for and early role of CLA^+ T cells in psoriasis development.
- In summary, the results obtained in this study suggest that circulating skin-seeking T cells have a probable relevance as early players in the formation of psoriasis.

Statistical analysis

Data were analyzed using the non-parametric statistic test Mann-Whitney. Correlations were calculated by the Pearson's Correlation Coefficient.

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