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New Phenomenon

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Dysregulated expression of inflammation-related genes in psoriatic dermis mesenchymal stem cells

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Psoriasis is a common inflammatory hyperproliferative skin disorder infiltrated predominantly by CD4-positive T-helper cells that produce pro-inflammatory cytokines such as interferon (IFN)-γ, tumor necrosis factor (TNF)-α, transforming growth factor (TGF)-β, and interleukin-17 [1,2]. In recent years, mesenchymal stem cells (MSCs) derived from patients with psoriasis have gained attention. Orciani *et al.* [3] found that the resident dermal MSCs (DMSCs) produce angiogenic and pro-inflammatory mediators, which leads to a reduction in the antioxidant capacity and contributes to the development of skin lesions in psoriasis. Recently, we have investigated the biological properties of DMSCs in psoriasis (**Supplementary Figs. S1–S3**), and these studies revealed that abnormities were already present at the level of MSCs. In prior microarray, we also identified many inflammation-related candidate targets that were significantly differently expressed in psoriasis (the data were deposited under NCBI GEO GSE42632), such as early B-cell factor-3 (*EBF3*), neural cell adhesion molecule-1 (*NCAM1*), and protein kinase C zeta (*PRKCZ*) [4].

In this study, we evaluated the mRNA and protein expression profiles of *NCAM1*, *EBF3*, and *PRKCZ* by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) and western blot assays to improve the knowledge about the role of the dysregulated inflammation-related genes in DMSCs of psoriatic patients. It was verified that the mRNA and protein expressions of *NCAM1* were significantly up-regulated (**Fig. 1A–D**). *NCAM1* has been found to be expressed on MSCs and induce TNF-α production [5,6]. However, we found that the mRNA and protein expressions of *EBF3* were markedly reduced compared with the control by qRT-PCR and western blot assays (**Fig. 1A–D**). It has been reported that methylation-associated down-regulation of *EBF3* plays an important role in a pathogenic effect of TGF-β on rheumatoid arthritis [7]. Our results showed that the expressions of *PRKCZ* mRNA and protein were also markedly reduced compared with the control (**Fig. 1A–D**). *PRKCZ* acts as a downstream molecule for TNF-α signal transduction and regulates the expression in Th1 (especially TNF-α) and Th2 cytokine production in psoriasis [8,9]. So, the down-regulated expression of *PRKCZ* may induce the reduction of TNF-α in skin lesions for immunomodulation.

Taken together, the current findings suggest that *NCAM1*, *PRKCZ*, and *EBF3* may play an important role on psoriasis at the MSC level, and for the first time to the best of our knowledge, these observations provide the evidence that human dermis MSCs may also be recruited into inflammation through cytokine-dependent mechanisms. However, the exact molecular function of *NCAM1*, *PRKCZ*, and *EBF3* in psoriasis is still unclear, and further research is required to understand how pathophysiological events in DMSCs influence psoriasis.

Supplementary Data

Supplementary data is available at *ABBS* online.

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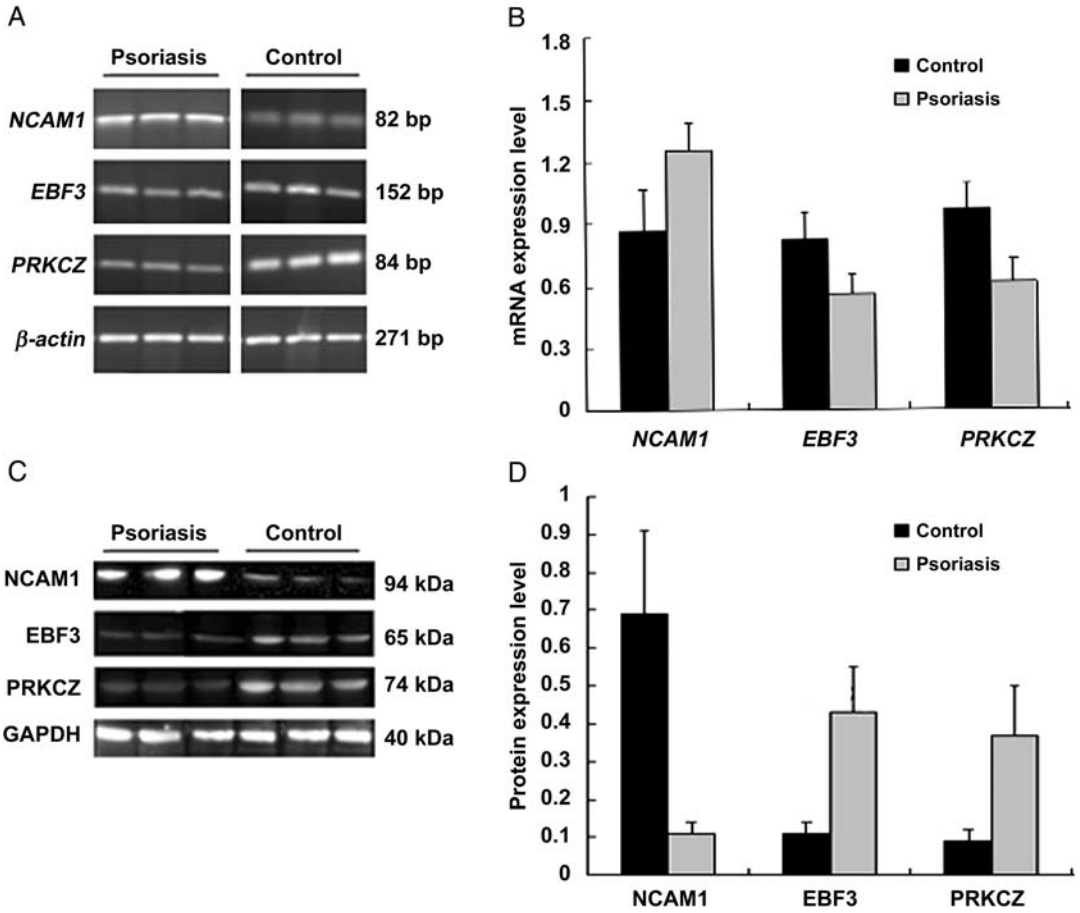

Figure 1. Analysis of mRNA and protein expression of inflammation-related genes *NCAM1, EBF3,* and *PRKCZ* in psoriatic and normal DMSCs by qRT-PCR and western blotting (A) Polymerase chain reaction products were identified using 2% agarose gel electrophoresis and photographed under UV light. (B) The relative mRNA expression levels of *NCAM1, EBF3,* and *PRKCZ*. Data were normalized to the mRNA level of *β-actin* and expressed as mean ± SD (shown in **Table 1**). (C) The protein bands of NCAM1 (94 kDa), EBF3 (65 kDa), and PRKCZ (74 kDa) is detected by western blotting. (D) Quantification of the protein levels of NCAM1, EBF3, and PRKCZ. Data were normalized to the corresponding value of the internal control GAPDH and presented as mean ± SD (shown in **Table 2**).

Table 1. Expression of *NCAM1, EBF3,* and *PRKCZ* in psoriatic and normal DMSCs determined by qRT-PCR[a]

Gene	Psoriasis ($n = 12$)	Control ($n = 14$)	P value
NCAM1	1.25 ± 0.13	0.86 ± 0.21	0.0038
EBF3	0.56 ± 0.09	0.82 ± 0.12	0.0041
PRKCZ	0.61 ± 0.11	0.96 ± 0.13	0.0109

[a]Data were normalized to that of *β-actin* and presented as mean ± SD.

Table 2. Protein levels of NCAM1, EBF3, and PRKCZ in psoriatic and normal DMSCs determined by western blot analysis[a]

Protein	Psoriasis ($n = 12$)	Control ($n = 14$)	P value
NCAM1	0.69 ± 0.22	0.11 ± 0.03	2.52648E−07
EBF3	0.11 ± 0.03	0.43 ± 0.12	1.80663E−07
PRKCZ	0.09 ± 0.03	0.37 ± 0.13	2.85533E−07

[a]Data were normalized to that of GAPDH and presented as mean ± SD.

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