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THE EXPRESSION OF SYNDECAN-1 IN PSORIATIC EPIDERMIS

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Abstract

Psoriasis is a chronic inflammatory skin disease characterized by exaggerated keratinocyte proliferation. Current opinion indicates that psoriasis is driven by T cell-mediated immune responses targeting keratinocytes. However, psoriasis cannot be explained solely on the basis of T-cell activation, and it is likely that an intrinsic alteration in epidermal keratinocytes plays a very important role in disease expression. Syndecans comprise a major family of cell surface heparan sulfate proteoglycans. Several studies indicate their role in adhesion, cell-extracellular matrix interactions, migration, keratinocyte proliferation and differentiation, inflammation, and wound healing. To determine the expression of syndecan-1 in psoriasis, skin samples from 29 patients with fully developed psoriasis and skin samples from 14 healthy volunteer persons with no personal or family history of psoriasis were immunohistochemically examined using monoclonal antibody against syndecan-1. The expression of syndecan-1 was analyzed in whole mount section of psoriatic and non-psoriatic skin biopsies under high magnification (x400). In addition, the intensity and topography of reaction in the cell, as well as localization of positive cells in the epidermis were evaluated. Strong syndecan-1 reactivity in epidermal cells in all non-psoriatic and psoriatic samples was observed. Statistical analysis showed no significant differences between two analyzed groups ($p>0.05$). In normal skin syndecan-1 was expressed in full thickness of the epidermis. The strongest reaction was observed in membranes and intercellular junctions of spinous and granular layer while basal cells showed weaker expression that was confined to cytoplasm. In psoriatic skin syndecan-1 was expressed in the membrane and intercellular junction of cells located in thickened and elongated rete ridges of the epidermis. The strongest reaction was in basal and suprabasal layers and expression diminished through spinous layer. Cells in spinous layer loose syndecan-1 expression, which is opposite pattern to normal skin. Our results

suggest that aberrant skin expression of syndecan-1 may be involved in the development of psoriasis.

Key words: Psoriasis, Immunohistochemistry, Syndecan-1

Psoriasis is a chronic inflammatory skin disease characterized by exaggerated keratinocyte proliferation. It is estimated that the prevalence of psoriasis varies from 1% to 2% and increases with age. Current opinion indicates that psoriasis is driven by T cell-mediated immune responses targeting keratinocytes. However, psoriasis cannot be explained solely on the basis of T-cell activation, and it is likely that an intrinsic alteration in epidermal keratinocytes plays a very important role in disease expression [4].

Syndecans comprise a major family of cell surface heparan sulfate proteoglycans. Syndecans at the cell surface function as coreceptors by binding to ligands and increasing ligand concentration in the pericellular vicinity of their signaling receptors. Several studies indicate their role in adhesion, cell-extracellular matrix interactions, migration, keratinocyte proliferation and differentiation, inflammation, and wound healing. In adult tissues, syndecan-1 is predominantly expressed by epithelial cells and plasma cells, and expressed to a lesser degree by other cells types (e.g. fibroblasts, endothelial cells) [1].

To determine the expression of syndecan-1 in psoriasis, skin samples from 29 patients (17 female and 12 male, average age 47.3 years) with fully developed psoriasis and skin samples from 14 healthy volunteer persons (8 female and 6 male, average age 49.8 years) with no personal or family history of psoriasis were immunohistochemically examined using monoclonal antibody against syndecan-1 (CD138, clone MI15, dilution 1:25, DAKO, Denmark). Immunohistochemical analysis was performed following microwave streptavidin immunoperoxidase (MSIP) protocol on DAKO TechMateTM Horizon automated immunostainer (DAKO). A sample of plasmacytoma that was strongly positive for syndecan-1 was used as a positive control. The diagnosis of psoriasis was histologically confirmed in all cases and each specimen was re-evaluated by three pathologists (D.T., M.V. and B.K.). None of the patients had received any topical treatment for at least one month prior the study. Skin samples of both groups measured between 0.3 and 0.8 cm (average 0.54 cm). The expression

of syndecan-1 was analyzed in whole mount section of psoriatic and non-psoriatic skin biopsies under high magnification (x400). In addition, the intensity and topography of reaction in the cell, as well as localization of positive cells in the epidermis were evaluated. Statistical analysis was performed using χ^2 test. The level of significance was set at $p < 0.05$.

Strong syndecan-1 reactivity in epidermal cells in all non-psoriatic and psoriatic samples was observed (Table 1). Statistical analysis showed no significant differences between two analyzed groups ($p > 0.05$). In addition, dermal appendages and some endothelial and inflammatory cells were also positive. In normal skin syndecan-1 was expressed in full thickness of the epidermis. The strongest reaction was observed in membranes and intercellular junctions of spinous and granular layer while basal cells showed weaker expression that was confined to cytoplasm (Fig. 1A). In psoriatic skin syndecan-1 was expressed in the membrane and intercellular junction of cells located in thickened and elongated rete ridges of the epidermis (Fig. 1B). The strongest reaction was in basal and suprabasal layers and expression diminished through spinous layer (Fig. 1C). Cells in most upper part of spinous layer showed no expression of syndecan-1 (Fig. 1D).

In our study, syndecan-1 was expressed in all samples of normal skin. The strongest reaction was in suprabasal, differentiating epidermal cells which are consistent with previous investigations [2,6,8]. To our knowledge there are no reports about expression of syndecan-1 in psoriasis. We observed strong syndecan-1 expression in all 29 psoriatic samples but pattern of expression was different compared to normal skin. The strongest expression was in proliferating basal and suprabasal layers and expression diminished with cell differentiation. Cells in spinous layer loose syndecan-1 expression, which is opposite pattern to normal skin.

A role of syndecan-1 in wound healing, epidermal cell proliferation and migration is under extensive research [3,5,7,9]. Stepp and al. [9] recently reported that syndecan-1 knockout mice display impaired proliferation and migration of corneal keratinocytes in eye

abrasion wound healing. The wounded syndecan-negative corneas failed to initiate proliferative burst 24 hours after wounding. In addition, the migration of corneal cells was hampered by the absence of syndecan-1 [9]. Elenius et al. [5] studied wound healing in mice that overexpress syndecan-1 in several tissues, including skin and blood. The elevated levels of shed syndecan-1 ectodomain in these animals inhibit both re-epithelization and remodeling of the newly laid matrix in dermis [5]. Ojeh et al. [7] in our investigation showed role of syndecan-1 in regulation of keratinocytes proliferation during skin development and wound healing. They generated transgenic mice that overexpress syndecan-1 in the basal layer of the epidermis that harbors epidermal stem cells and transit amplifying cells. Transgenic mice exhibited hyperproliferative skin lesions that were characterized by normal cornified layer, occasional parakeratosis in the granular layer, and increased number of spinous cell layers. The number of suprabasal cell layers was increased and flattening and anucleation of the cells were delayed but terminal differentiation was preserved. The extent of the hyperproliferations varied between different skin locations and between individual mice. Some lesions also contained localized areas of remarkably thickened epidermis that involved some downgrowth into the dermis [7]. Similarities of lesion that exhibited transgenic mice with psoriatic lesion are remarkable. Increased number of suprabasal and spinous cell layers, delayed flattening and anucleation, parakeratosis, remarkably thickened epidermis with downgrowth into the dermis are all histological characteristic of psoriatic skin. In addition, in our investigation similar expression of syndecan-1 in psoriatic skin and transgenic mice was also observed. The strongest expression of syndecan-1 in psoriasis was in proliferative basal cell layer like in transgenic mice and expression diminished through spinous to cornified layer of the epidermis [7].

Our results suggest that aberrant skin expression of syndecan-1 may be involved in the development of psoriasis. Further studies on larger patient series and in various stages of psoriatic lesions are welcome.

REFERENCES

1. Bartlett AH, Hayashida K, Park PW (2007) Molecular and cellular mechanisms of syndecans in tissue injury and inflammation. *Mol Cells* 24: 153-166, DOI not available
2. Bayer-Garner IB, Smoller BR (2001) The expression of syndecan-1 is preferentially reduced compared with that of E-cadherin in acantholytic squamous cell carcinoma. *J Cutan Pathol* 28: 83-89, DOI 10.1034/j.1600-0560.2001.280204.
3. Bayer-Garner IB, Sanderson RD, Smoller BR (2002) Syndecan-1 is strongly expressed in the anagen hair follicle outer root sheath and in the dermal papilla but expression diminishes with involution of the hair follicle. *Am J Dermatopathol* 24: 484-489, DOI not available
4. de Rie MA, Goedkoop AY, Bos JD (2004) Overview of psoriasis. *Dermatol Ther* 17: 341-349, DOI 10.1111/j.1396-0296.2004.04037.
5. Elenius V, Gotte M, Reizes O, Elenius K, Bernfield M (2004) Inhibition by the soluble syndecan-1 ectodomains delays wound repair in mice overexpressing syndecan-1. *J Biol Chem* 279: 41928-41935, DOI doi:10.1074/jbc.M404506200.
6. Inki P, Larjava H, Haapasalmi K, Miettinen HM, Grenman R, Jalkanen M (1994) Expression of syndecan-1 is induced by differentiation and suppressed by malignant transformation of human keratinocytes. *Eur J Cell Biol* 63: 43-51, DOI not available
7. Ojeh N, Hiilesvuo K, Warri A, Salmivirta M, Henttinen T, Maatta A (2008) Ectopic expression of syndecan-1 in basal epidermis affects keratinocyte proliferation and wound re-epithelialization. *J Invest Dermatol* 128: 26-32, DOI 10.1038/sj.jid.5700967.
8. Sanderson RD, Hinkes MT, Bernfield M (1992) Syndecan-1, a cell-surface proteoglycan, changes in size and abundance when keratinocytes stratify. *J Invest Dermatol* 99: 390-396, DOI not available

9. Stepp MA, Gibson HE, Gala PH, Iglesia DD, Pajooohesh-Ganji A, Pal-Ghosh S, Brown M, Aquino C, Schwartz AM, Goldberger O, Hinkes MT, Bernfield M (2002) Defects in keratinocyte activation during wound healing in the syndecan-1-deficient mouse. *J Cell Sci* 115: 4517-4531, DOI 10.1242/10.1242/jcs.00128.

Table 1. The intensity of syndecan-1 expression in psoriatic and non-psoriatic skin

	Psoriatic skin	Non-psoriatic skin
ISI 0*	0 (0%)	0 (0%)
ISI 1*	0 (0%)	0 (0%)
ISI 2*	0 (0%)	0 (0%)
ISI 3*	29 (100%)	14 (100%)
Total	29 (100%)	14 (100%)

*To evaluate the level of syndecan-1 expression, the percentage of positive cells and the staining intensity were graded on a scale of 0 – 3. Staining percentage was labeled as: 0 = 0% cells; 1 = 1- 33% positive cells; 2 = 34 – 66% positive cells; and 3 = more than 66% positive cells. Staining intensity was denoted as: 0 = no staining; 1 = weak staining; 2 = moderate staining; 3 = strong staining. For each sample, the staining percentage and staining intensity scores were multiplied to give staining index. Immunohistochemical staining index (ISI) was labeled as: 0 = zero; 1 – 3 = low; 4 – 6 = moderate; and 9 = high.

Figure 1. (A) In non-psoriatic skin syndecan-1 was expressed in full thickness of the epidermis. The strongest reaction was observed in membranes and intercellular junctions of spinous and granular layer. The basal cells in non-psoriatic skin showed weaker expression of syndecan-1 that was confined to cytoplasm. (B) In psoriatic skin syndecan-1 was expressed in the membrane and intercellular junction of cells located in thickened and elongated rete ridges of the epidermis. (C) The strongest reaction was in basal and suprabasal layers and expression diminished through spinous layer. (D) Cells in most upper part of spinous layer in psoriatic skin showed no expression of syndecan-1. (The bar in B indicates 200 μm . A, C and D are of the same magnification, and bars indicate 50 μm .)





