Aberrant expression of bradykinin b2 receptor in the epidermis of patients with psoriasis vulgaris

Sir,

A constant serine protease activity is crucial for steady desquamation and the function of skin barrier.[1] The human tissue kallikrein gene family encodes for 15 secretory serine proteases responsible for the steady desquamation of corneocytes.[1] The psoriatic epidermis contains high levels of all kallikreins.[2] The kallikreins levels in the stratum corneum and serum of patients with psoriasis are dependent on the severity and phenotype of psoriasis.[2] Tissue kallikrein (encoded by kallikrein 1 gene) functions as a serine protease and is capable of liberating kinin peptides from kininogens by enzymatic reaction. The released kinins exhibit a wide variety of effects by activating kinin b1 and b2 receptors (b1r and b2r).[3] It is unknown whether the downstream receptors of kinin are expressed in skin lesions of psoriasis vulgaris.

Envision methods were used for immunohistochemical staining. The normal tissue and chronic plaque psoriatic lesions were stained with antibodies specific for human b1r (Biorbyt, Cambridge, UK) and human b2r (BD Biosciences, USA). B1r was expressed at a level comparable to b2r in positive controls. Normal human skin samples were obtained from six volunteers (two females and four males, 36.5 ± 10.5 years old). B1r was nearly undetected in the normal epidermis [Figure 1a] and appendages [Figure 1b-e]. In contrast, b2r was immunohistochemically detected in the stratum granulosum, stratum spinosum, and stratum basale of normal epidermis [Figure 1a]. No expression of b2r was observed in the stratum corneum [Figure 1a]. B2r showed diffuse staining and the intensity of b2r expression was much higher in the nucleus than that in the cytoplasm [Figure 1a]. The skin appendages, with the exception of intradermal sensory nerves, showe distribution of b2r, specifically [Figure 1b-e]. We obtained chronic plaque lesions of psoriasis vulgaris from six patients (three females and three males, 39.0 ± 7.3 years old), who were free of any medication. In psoriasis vulgaris, b1r was nearly undetected in the psoriatic epidermis and appendages [Figure 2a-d]. In contrast, b2r expression was intense, and it was detected in the stratum granulosum, stratum spinosum, and stratum basale [Figure 2a]. The appendages, with the exception of intradermal sensory nerves, also showed specific distribution of b2r [Figure 2b-d]. In the cells of psoriatic epidermis, b2r showed diffuse cytoplasmic staining, but it showed a granular staining in the nucleus [Figure 2a]. Moreover, the intensity of b2r expression was lower in the cells of psoriatic epidermis than that in the cells of normal epidermis, and cells in the psoriatic epidermis were frequently negative for cytoplasmic or nuclear staining [Figure 2a]. In psoriatic lesions and the adjacent skin, b1r was not detected [Figure 3a]. In contrast, b2r was detected both in psoriatic lesion and in its adjacent skin, and the number of cell layers expressing b2r was increased in psoriatic lesions compared to that in the adjacent skin [Figure 3b and c]. However, the intensity of b2r expression was lower in the psoriatic epidermis than that in its adjacent skin [Figure 3b and c]. B2r expression gradually decreased depending on the epidermal thickness [Figure 3b and c]. We scored both the staining intensity (negative = 0, weak = 1, moderate = 2, and strong = 3) and the proportion (0%–5% =0, 6%–25%

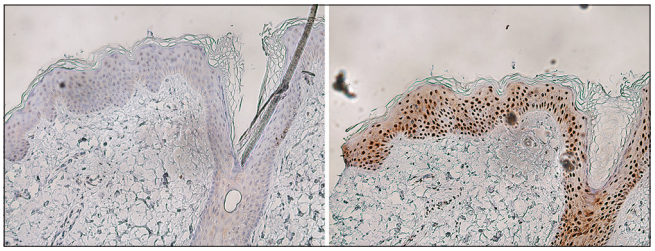

Figure 1a: Normal epidermis: immunohistochemistry of b1r and b2r in normal human skin in left panel and right panel, respectively

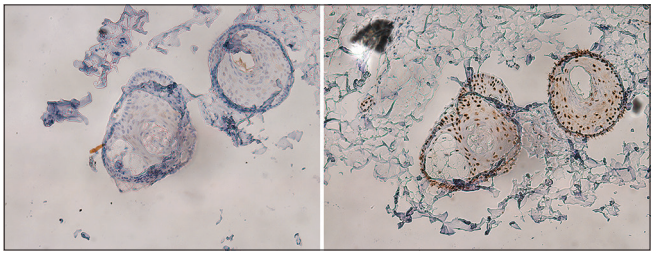

Figure 1b: Hair follicular epithelium: immunohistochemistry of b1r and b2r in normal human skin in left panel and right panel, respectively

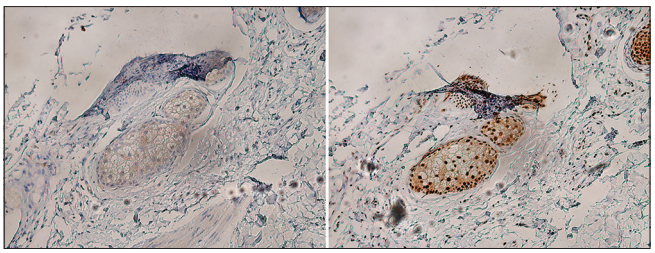

Figure 1c: Sebaceous glands: immunohistochemistry of b1r and b2r in normal human skin in left panel and right panel, respectively

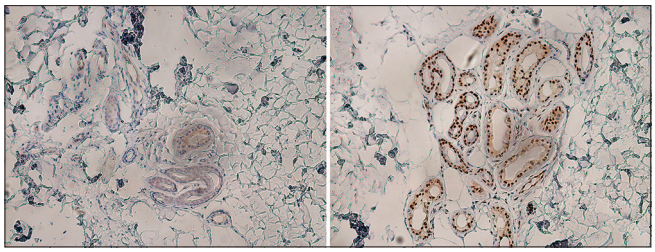

Figure 1d: Eccrine sweat glands: immunohistochemistry of b1r and b2r in normal human skin in left panel and right panel, respectively

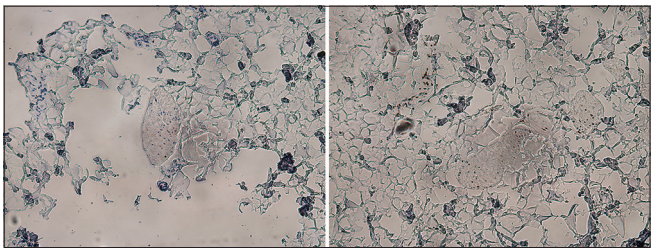

Figure 1e: Intradermal sensory nerve: immunohistochemistry of b1r and b2r in normal human skin in left panel and right panel, respectively

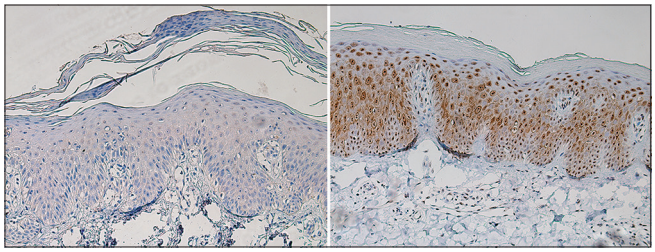

Figure 2a: Psoriatic lesions: immunohistochemistry of b1r and b2r in psoriasis vulgaris in left panel and right panel, respectively

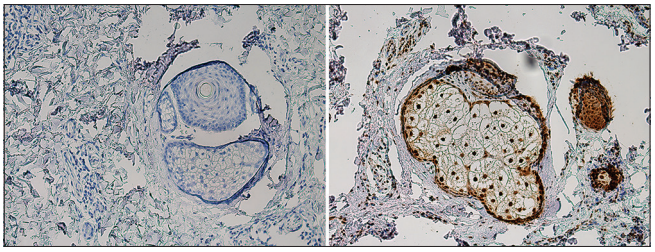

Figure 2b: Hair follicular epithelium and sebaceous glands: immunohistochemistry of b1r and b2r in psoriasis vulgaris in left panel and right panel, respectively

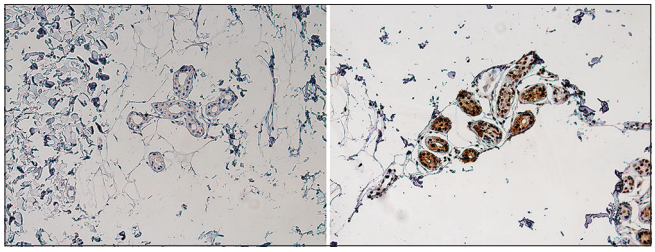

Figure 2c: Eccrine sweat glands: immunohistochemistry of b1r and b2r in psoriasis vulgaris in left panel and right panel, respectively

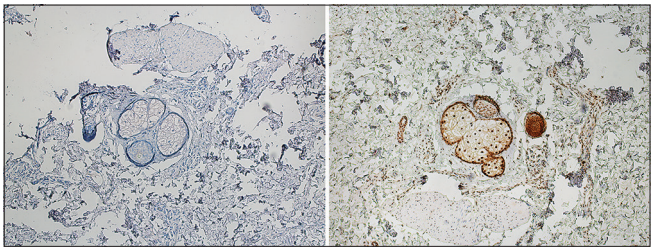

Figure 2d: Intradermal sensory nerve: immunohistochemistry of b1r and b2r in psoriasis vulgaris in left panel and right panel, respectively

=1, 26%–50% =2, 51%–75% =3, 76%–100% =4) of positive cells and then calculated the final score by multiplying the intensity and the proportion scores. Analysis of b2r scores revealed that the mean score of stratum granulosum decreased from 8.73 ± 2.15 in adjacent skin to 4.47 ± 2.26 in psoriatic skin ($P < 0.001$). Similarly, the mean score of staining in the stratum spinosum decreased from 10.6 ± 1.80 in adjacent skin to 4.93 ± 1.49 in psoriatic skin ($P < 0.001$). However, there was no significant difference in the mean score of stratum basale staining between adjacent skin (6.80 ± 1.66) and psoriatic skin (5.73 ± 1.83) ($P = 0.105$).

Although b1r may amplify and play a dominant role in chronic inflammation processes, the involvement of b1r in the pathogenesis of psoriasis seems to be excluded, due to the absence of expression of b1r in both normal skin and chronic plaque lesions of psoriasis vulgaris.[4] Results from a previous study suggest a protective role of b2r in ischemic injury.[5] Kallikrein, by acting on b2r, reduces ischemia-reperfusion-induced apoptosis of neuronal cells and inhibits inflammatory cell accumulation in the ischemic brain.[5] The decreased expression of b2r in chronic plaque lesions of psoriasis vulgaris indicates a protective role of b2r. Moreover, the intensity of b2r expression was dependent on the epidermal thickness, suggesting the implication of b2r in the pathogenesis of psoriasis. B2r may serve as candidate target for the diagnosis and treatment of psoriasis. However, further studies are needed to explore this hypothesis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patients have given their consent for their images and other clinical information to

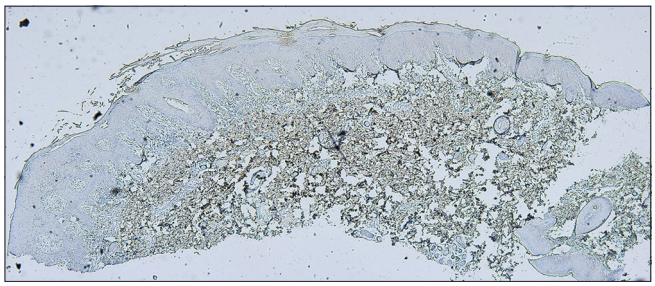

Figure 3a: Immunohistochemistry of b1r in psoriatic lesion and adjacent skin

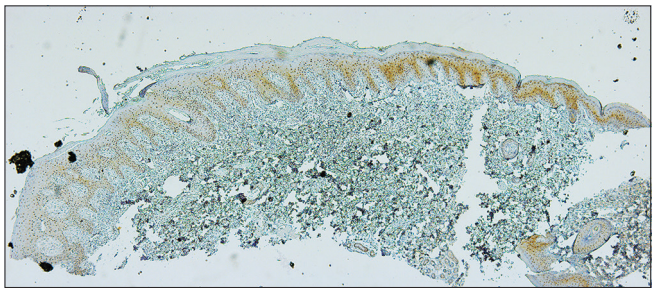

Figure 3b: Immunohistochemistry of b2r in psoriatic lesion and adjacent skin

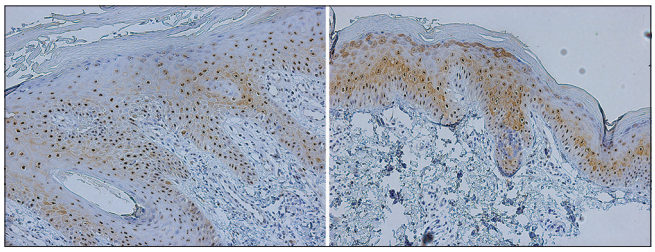

Figure 3c: Immunohistochemistry of b2r in psoriatic lesion and adjacent skin in left panel and right panel, respectively

be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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