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Abstract

Psoriasis is a chronic inflammatory skin disease with unknown etiology. Infiltration of inflammatory cells as the initial event in the development of new psoriatic plaques together with the defined inflamed areas of such lesions this argues for an immunological disease with a local production of a causal antigen. Pso p27 is a protein expressed in psoriatic plaques and is shown to participate in complement activating immune complexes in the skin lesions. Recently we suggested that the Pso p27 antigen most probably is generated from SCCA-molecules by digestion with highly specific endoproteases. In this communication we substantiate this relationship and postulate an intracellular generation of Pso p27 antigen from SCCA molecules.

Introduction

Psoriasis is a chronic inflammatory skin disease which afflicts about 2 % of the general population. The association between psoriasis and selected MHC molecules and the well-defined skin lesions argues for an immunologic disease caused by a specific and locally expressed antigen [1, 2]. The psoriasis associated antigen, Pso p27, is to our knowledge the only locally expressed antigen recognized by complement activating antibodies obtained from psoriatic scale [3, 4]. Using specific antibodies against Pso p27 we have demonstrated the presence of Pso p27 antigen in mast cells in psoriatic lesions [5]. The antigen is not present in uninvolved psoriatic skin or in skin biopsies from healthy controls [5, 6]. The positive correlation between disease activity and quantity of Pso p27 antigen is significant [6, 7]. In this way Pso p27 fulfill important criteria for a localized causal antigen. Sequencing of the Pso p27 has demonstrated homologies with Squamous Cell Carcinoma Antigens (SCCAs). This includes conformities with SCCA1 as well as SCCA2 [8]. Pso p27 is a smaller protein compared to SCCA molecules, and analysis have shown that the N-terminal - and the C-terminal ends of SCCA-molecules are not present in Pso p27 [8].

Based on this knowledge we have suggested that Pso p27 is generated by a posttranslational modification of SCCA molecules [8]. In the present study we substantiate this assumption and indicate that an enzymatic digestion of SCCA-molecules takes place both in dermal mast cells and epidermal cells in the psoriatic skin lesion.

Methods

Indirect immune fluorescence of biopsies obtained from psoriatic skin lesions

Skin punch biopsies were taken from psoriatic lesions and shock frozen in liquid nitrogen. Thin sections from the biopsies were cut and stored at -80°C. Before performing indirect immunofluorescence the sections were air dried at room temperature and fixed 15 min in aceton. The sections were incubated with rabbit anti-SCCA antiserum, ab47726, (Abcam, Cambridge, UK) and biotinylated murine monoclonal anti-Pso p27 antibody (3A3D10) [6,7] diluted in phosphate buffered saline containing 0.05% Tween 20 (PBS-T). After washing with PBS-T the sections were incubated with Fluorescein Isothiocyanate conjugated swine anti-rabbit antibodies (DAKO, Glostrup, Denmark) and Molecular Probes® Streptavidin-conjugated Alexa 594 (Invitrogen Life Science, Carlsbad, CA, USA). After thorough washing with PBS the sections were mounted with Vectashield Mounting Medium H-1000 (Vector Laboratories, Burlingame, USA)

Results

Indirect immune fluorescence of psoriatic skin lesions using rabbit antiserum against the N-terminal end of SCCA molecules and a specific monoclonal antibody against Pso p27 is shown in figure 1. The presence of SCCA-molecules in the epidermis is visualized with green fluorescence (fig 1A) while the monoclonal antibody against Pso p27 is detected in epidermal cells close to surface of the skin and in the scale with red fluorescence (fig 1B). The psoriatic skin lesion presented in figure 2 demonstrates the concomitant presence of SCCA-antigens and Pso p27 antigen in dermal cells. However, a minority of dermal cells are recognized
with anti-SCCA antiserum only as indicated in fig 2A, while other cells are recognized by monoclonal antibody against Pso p27 and negative with respect to the anti-SCCA antiserum (fig 3).

Discussion

Much effort has been put forward in the search for etiological agents associated with chronic inflammatory - or autoimmune diseases. During the last decades we have focused on a protein, Pso p27, associated with psoriasis [6-8]. Pso p27 is expressed in psoriatic lesions and is not detected in uninvolved psoriatic skin or skin biopsies from healthy controls [6, 7]. Through analysis of antibodies obtained from psoriatic scale, we have demonstrated the potential role of Pso p27 as an antigen in psoriasis [3]. Based on sequence homologies between Pso p27 and SCCA molecules we have hypothesized that Pso p27 is generated by post-translational modifications of SCCA molecules [8]. In this study we used a SCCA specific antiserum and a monoclonal antibody against Pso p27 on psoriatic skin lesions in indirect immune fluorescence to describe the relationship between the molecules. The fact that some cells are positive for SCCA only and other specific for Pso p27 demonstrate the suitability of assay system.

Our observation of SCCA in epidermal cells is in accordance with earlier findings [9], and the detection of Pso p27 antigen near the surface of the skin and in the scale indicate an epidermal translational process from SCCA molecules to Pso p27. The presence of both SCCA molecules and Pso p27 in the same dermal cells points to intracellular generation of Pso p27. We have shown earlier that the Pso p27 positive dermal cells in psoriatic lesions are mast cells [5]. Together with the suggestion of mast cells as antigen presenting cells [10] and the well documented association between psoriasis and selected MHC-I molecules the observations described are particularly challenging.

The presence of Pso p27 epitopes in affected organs in other chronic inflammatory diseases [11-13] makes it reasonable to assume that these epitopes are generated through similar processes as suggested for psoriasis [8]. If so, enzymatic digestion of SCCA-molecules with highly specific endoproteases may play a key role in the pathogenesis of various chronic inflammatory diseases. Expression of retroviruses has been associated with various chronic diseases [14] including psoriasis [15, 16], but their potential role with respect to pathogenesis is not demonstrated. In view of cleavage sites recently described for the HERV-K associated endoprotease [17] compared with sequence analysis of Pso p27 [8] it is tempting to reflect on whether retrovirus associated endoproteases may have a role in the generation of Pso p27.

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References

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Illustrations

Illustration 1

Figure 1. Double labelling of a thin section of a psoriatic plaque detecting SCCA (A) and Pso p27 antigen (B).

![Illustration 1](image1)

Illustration 2

Figure 2. Double labelling of a thin section of a psoriatic plaque demonstrating concomitant presence of SCCA (A) and Pso p27 antigen (B) in dermal cells. A SCCA positive cell without detectable Pso p27 antigen is indicated by arrow (A).

![Illustration 2](image2)
Illustration 3

Figure 3. Double labelling of a thin section of a psoriatic plaque demonstrating dermal cells positive with respect to Pso p27 antigen without detectable SCCA.
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