Abstract

Psoriasis and atopic dermatitis (AD) are chronic inflammatory skin disorders with similar symptoms but different etiology. They manifesting in flushed skin changes due to epidermis hyperplasia and systemic inflammation with immune cells infiltration into the diseased skin regions. Psoriasis and AD are increasingly common in the developed world, but their pathophysiology is not fully understood. The knowledge of mechanisms inducing these disorders is crucial to improve the effectiveness of new therapies, which nowadays rely on alleviating the symptoms, but not eliminating the cause of the disease.

One of the known phenomenon in pathophysiology of psoriasis and AD is an increased expression of secretory leukocyte protease inhibitor (SLPI) in the skin. There is limited knowledge about the factors regulating expression and the role of this protein in skin pathophysiology. The aim of the study was to identify the cell source of SLPI protein, investigate the regulation of SLPI gene expression in the epidermis and describe the function of this protein in psoriasis and AD development. Implementation of these aims contribute to better understanding of inflammatory skin disorders pathophysiology and in a consequence developing effective therapies.

The research results described in this PhD thesis show that keratinocytes are the main cellular source of SLPI protein in skin lesions, both in psoriasis and AD. In addition immune cells infiltrating the skin are also the producers of this protein. It was demonstrated for the first time that SLPI+ eosinophiles localize in atopic lesions. Psoriatic skin is infiltrated by neutrophils differ in immunoreactivity for SLPI and neutrophil elastase. They are distributed on a different skin depth.

To determine the factors regulating SLPI gene expression in the epidermis, the model of three steps of keratinocytes differentiation was prepared. Using primary human keratinocytes obtained the cultures of undifferentiated cells, partially differentiated cell in 2D and terminally differentiated cells 3D (organotypic cultures). It was proved that differentiation process does not influence on SLPI gene expression but several factors were identified as a SLPI modulators. Double-strand, synthetic RNA and *S.aureus* infection belongs to them. Skin environment associated with chronic inflammation, typical for psoriasis and AD, influence SLPI gene expression as well.

Using mouse models of psoriasis and atopic dermatitis it was demonstrated that SLPI gene expression significantly changes during the experiments, but it does not influence the disease development. The results described in the PhD thesis are insufficient to answer the question about the function of SLPI protein in psoriasis and AD. In spite of it, published data and results of research conducted in Department of Immunology, also in a context of this PhD thesis findings suggest protective role of SLPI in pathophysiology of the diseases.