Description for the general public

Psoriasis is a common, non-infectious skin disease with an unpredictable and relapsing nature. The prevalence of psoriasis is approximately 2-4% in developed countries. The first symptoms of the disease can appear at any age, but they usually occurs before the age of 30 years and affects both men and women. Typical characteristics of psoriasis are skin lesions in size from few millimeters to tens of centimeters, the usually forms dry, red patches covered with scales. The scales usually cover the elbows, knees, lower back, scalp and nails. In some cases even the entire skin surface is covered by the disease. Among the factors that contribute to the formation of psoriasis are mentioned: stress, bacterial infections, metabolic diseases, certain drugs, poor hygiene and hormonal changes. With the exception of the rare heavy forms, psoriasis does not impair the general condition of patients, but is often negatively perceived by the surroundings and the burdensome treatment reduced the quality of life of the patient.

Although the pathogenesis of psoriasis is not fully understood, there is much evidence suggesting a key role of the dysregulated immune function in the development of psoriasis, including mast cells. In the traditional meaning, mast cells are involved in defending the body against parasites, bacteria and other microbes. Their main role is to cause the local inflammation (including allergy) in response to foreign substances.

The skin is not only a protective barrier against mechanical, physical and chemical factors or microorganisms, but is also an important sensory organ. Psoriatic skin morphology analysis shows that it is rich in cutaneous innervaion and mast cells accumulate just adjacent to the nerve endings. These anatomical proximity of these both types of cells is also reflected in their interactions. Activated mast cells secrete proteases, which can modify some of the functions of neurons, eg. the production of so-called neuropeptides. These small molecules are released primarily from skin sensory endings and may activate other cells, including skin-infiltrating immune cells and other skin cells, and then influence the development of inflammation in the skin. This phenomenon, known as neurogenic inflammation may underlie many inflammatory diseases.

In the project, we propose to investigate the effect of endogenous proteins SLPI (secretory leukocyte protease inhibitor) for the development of neurogenic inflammation in the skin in a mouse model of psoriasis. Research on this issue will be pursued in stages and the scope of work will primarily involve analysis of mast cell infiltrates, distribution of subcutaneous nerves, expression of protease activated receptors type 2 (PAR2), selected neuropeptides and trophic factors in a healthy and psoriatic skin of wild type mice and mice with a genetic deficit of SLPI.

We assume that SLPI, because of its antiprotease activity, limits the development of neurogenic inflammation and determines the maintenance of optimal functioning of the immune mechanisms in the skin. The results of the proposed project will significantly increase the knowledge about the function of mast cells in psoriasis. They will also contribute to better understanding of the fundamental processes related to the role of mast cells in inflammatory diseases, which may have an important cognitive significance on a new pathogenic mechanism of inflammatory diseases and in the future will help to develop effective treatments for psoriasis and other diseases with similar etiopathogenesis.