DESCRIPTION FOR THE GENERAL PUBLIC

Psoriasis is one of the most common, chronic, non-infectious skin diseases affecting app. 3% of population, which means that more than 125 million people are suffering for it now. It can occur in any age, although it is most common in people between 15 and 35 years of life. Currently, it is impossible to cure psoriasis. Patients use lifelong symptomatic treatments. Due to the different course of disease in individual persons, and the number of available pharmaceuticals and methods of treatment, the correct choice of curative agents, or their combination is a long process, often not bringing the expected results.

The main problem is multifactorial nature of the disease, which means that the exposure, and the severity are dependent both on a genetic predisposition, disturbances of the immune system, but also on environmental impact. As a result of long-term overproduction of proinflammatory cytokines and the influx of T-cells into the skin, there is excessive activation and overgrowth of skin cells - keratinocytes, resulting in the formation of psoriasis plaques, painful, and reddened changes. Such complicated process of pathogenesis is still subject requiring the extension of current knowledge, mainly towards identifying potential causes.

Despite the constantly updated knowledge about both induction and the development of psoriasis, the factors that may be the cause of the disease are still sought. The current theories indicates, that psoriatic keratinocytes are characterized by lack of differentiation (a process that is driven i.a. by lysosomes) compared to normal cells and, that they are able to express MHC class II molecules on the cell surface under the strong influence of interferon gamma (IFN-γ) secreted by Th lymphocytes. However, there are no literature data linking the two above phenomena, which may connect endosomal-lysosomal system perturbation in the presentation of antigens with MHC II molecules on the surface of keratinocytes with an abnormal enzymatic processing of antigenic proteins, which is the starting point for the research proposed in this project. The first step of this project will be determination of localization and quantitative and qualitative changes of the endosomal-lysosomal system organelles and next correlating the obtained data with the results of subsequent studies, i.e. monitoring of intracellular antigen processing and determination of activity of endosomes and lysosomes producing ligands for the MHC class II molecules on an *in vitro* model, i.e. a commercial culture of primary human keratinocytes cell line (cytokine mix-stimulated cell line model of psoriatic inflammation and a control model) and on *in vivo* material i.e. skin biopsies and blood of psoriatic patients and healthy individuals as a control.

The obtained results may be important for the development of knowledge about the causes of immune disturbances in psoriasis, including antigen processing pathway in keratinocytes, and also for further investigations of diseases, not only dermatological, but also autoimmunological ones. Analysis of phenomena at immunological and molecular level are necessary to provide new information that will help to improve diagnosis of the disease and, consequently, to the development of targeted, personalized therapy for psoriasis patients.