

Psoriasis (Ps) is one of the most common, chronic inflammatory skin disease with a complex etiology involving genetic risk factors and environmental triggers. It affects 2–3% of the European population and represents a clinically heterogeneous disorder. Although the precise etiology of psoriasis remains unclear, recent studies indicate that psoriasis is an autoimmune disease mediated by T lymphocytes, and T cells are the key in the development and occurrence of psoriatic lesions. This concept of the pathogenesis of Ps gives central role to CD4+ T lymphocytes, which have played all effector mechanisms of the immune system involved in the progress of the disease. A cornerstone of the acquired immune response is the T cell receptor (TcR)–calcium–calcineurin signaling pathway leading to T cell activation. Calcium ions (Ca²⁺) function as a universal second messenger in most of eukaryotic cells, including immune system cells and lysosomal biogenesis dependently on transcription factor EB (TFEB). As level of Ca²⁺ in serum of psoriasis patients is increased, the aim of proposed project is to thoroughly describe lysosomal compartment and metabolism and to verify whether the Ca²⁺/calmodulin/calcineurin regulation of NFAT and TFEB is common in CD4+ lymphocytes and what are effects of this mechanism. Lysosomal metabolism is a complex, multi-level process regulated by many signals and modulators. It depends on metabolic state of the cell and consists of many components, vesicles, enzymes, transcription factors and messengers. In this particular type of the cells as are lymphocytes, lysosomal metabolism is influenced also by inflammatory activation signals and takes part in cytokine production and release, what is also the point of this research. Disturbances in lysosomal metabolism in psoriasis patients CD4+ lymphocytes may result with an excessive pro-inflammatory cytokine production. On the other hand cellular stress caused by inflammatory process and dysregulation of calcium administration may result with disorganization of lysosomal compartment. Lysosomal biogenesis and metabolism is orchestrated by many specialized proteins and the aim of this project is to analyse those regulatory pathways and impact on cytokine secretion.