DESCRIPTION FOR THE GENERAL PUBLIC

Skin provides a physical, immunological and biochemical barrier between the host and the external environment. The epidermis of the skin is primarily composed of keratinocytes, which undergo multiple stages of differentiation and proliferate from the basal layer to the stratum corneum. Keratinocytes are specialized cells responsible for barrier functions, cohesion and mediating immunological responses via the release of cytokines. The cytokine secretion profiles vary in response to various external stimuli, which may lead to the acute or chronic inflammation, posing significant problems in dermatology. In human, the most common skin diseases are psoriasis and skin cancer.

Psoriasis is a chronic, recurring skin condition affecting 1 to 3% of human population. The etiology of this disease, involving both genetic and immunological factors, for instance enriched proliferation of keratinocytes upon stimulation via activated lymphocytes T or the action of pro-inflammatory cytokines (IL-1, IL-6, IL-8 or TNF- α), is still not fully understood. Skin cancer is one of the most frequent cancers among human. The two most common types of cancer are basal and squamous cell carcinoma. Several risk factors including prolonged exposure to solar UV radiation, immunosuppression or genetic factors may contribute to the development of skin cancer and epidermal dysplasia.

There are a number of modulators that control inflammation and play important role in maintaining skin homeostasis. *Zc3h12a* family encodes 4 proteins, of which MCPIP1 negatively regulates inflammation. It possesses RNAse activity and can degrade transcripts of pro-inflammatory cytokines such as IL-1β or IL-6. *In vivo* and *in vitro* studies revealed that MCPIP1 is also a negative regulator of NF- κB and AP1 transcription factors, which control a number of cellular processes such as proliferation, differentiation or apoptosis. Recent studies indicated a potential role of MCPIP1 in psoriasis suggesting that *Zc3h12a* gene may be essential to distinguish between normal and psoriasis affected skin. However, a direct role of MCPIP1 in the regulation of skin physiology as well as in various skin disorders has never been shown. **Therefore, the main aim of our research will be to investigate the role of MCPIP1 protein in the physiology and pathology of epidermis with the use of a unique mouse model in which the *Zc3h12a* gene is conditionally deleted in epidermis.**

To accomplish the research goal, our studies will be divided into several steps. At first, we plan to use basic techniques for functional analysis of epidermis to characterize potential changes in the morphology and function of mouse epidermis lacking MCPIP1 protein. Additionally, we will perform some global transcriptome analysis of cKO mouse epidermis. Next, we will develop a mouse model of psoriasis and with the use of histological techniques, mass spectrometry and next generation sequencing will investigate whether and how MCPIP1 may be involved in the pathology of psoriasis. Finally, we want to use the mouse model of skin cancer to study whether MCPIP1 is involved in cancer progression or metastasis.

We believe that our research will reveal how MCPIP1 protein regulates physiological processes in epidermis. Additionally, studies on the role of MCPIP1 in the pathogenesis of psoriasis or skin cancer should lead to a much better understanding of the molecular basis of those diseases and as a result may contribute to the discovery of new medical therapies.