Epidermis is an external barrier that limits the inward and outward passage of water and provides protection for organism against microorganisms, UV radiation, toxic agents and mechanical stimuli. It is established upon terminal differentiation process during which basal keratinocytes proliferate and move upwards forming 4 epidermal layers. These layers differ in terms of morphology and function due to differential gene expression in each layer. When disturbances in differentiation process occur, they may be caused by disorders at the genetic and/or epigenetic level. Epigenetics refers to heritable changes in gene expression that do not involve changes in the DNA sequence. Epigenetic changes occur naturally in the differentiation processes but can be also influenced by factors such as age, environment/lifestyle, and disease. From the inner perspective, epigenetic mechanisms include both chemical alternations of DNA and DNA - wrapped proteins, so-called histones. Histone modifications include acetylation, methylation, phosphorylation or ubiquitination and are introduced by appropriate enzymes. In this project we will investigate the significance of selected histone modifications for the process of epidermal differentiation in general and EDC gene expression in particular. EDC stands for “epidermal differentiation complex” which is a cluster of genes encoding proteins of high importance for epidermal formation. To this end, we will alter the expression of enzymes that introduce selected histone modifications using HaCaT cells, a model of human keratinocytes. As a silencing strategy, we decided to use the novel and effective CRISPR/Cas9 approach, which allows for a precise and selective elimination of protein expression by introducing a deletion into a gene sequence. Since the process of epidermal differentiation is jeopardized in common skin disorders, such as psoriasis and atopic dermatitis, the outcome of our studies may increase our understanding of mechanisms that orchestrate epidermal differentiation, which when imbalanced leads to a number of pathologies associated with barrier malfunctions. In a further perspective, the research may contribute to development of individualized dermatological therapies.