

Adrenocortical hormones play an important role in regulation of many physiological processes. Among other, they are involved in response to stress, inhibition of immune response, as well as they play an important role in regulation of metabolism. Their concentration is precisely controlled and any disturbance of this regulation leads to serious health consequences. Chronic adrenal hormonal deficiency is a cause of Addison's disease, which is characterized by, inter alia, loss of appetite and reduction in body weight. On the other hand, excessive levels of adrenocortical hormones lead to the development of Cushing's syndrome, the consequences of which include development of obesity. Recent studies have shown that adrenocortical hormone levels can also be controlled by a number of bioactive peptides that may become targets for the development of new drugs or therapies associated with adrenal gland dysfunction. According to our preliminary studies, we assume that group of such peptides may include adropin.

Adropin is a newly discovered hormone peptide, characterized by extremely high interspecies homology. This peptide has a significant effect on the regulation of metabolism. It has been shown that adropin deficiency correlates with the severity of obesity and insulin resistance. On the other hand, injection of adropin to mice with induced obesity resulted in improved lipid-carbohydrate metabolism and a decreased insulin resistance. The role of adropin in the regulation of adrenocortical physiology has not been investigated. The research activities proposed in the project will focus on determining the effect of adropin on biosynthesis of rat adrenocortical steroid hormones directly, as well as indirectly, by activation of hypothalamo-pituitary-adrenal (HPA) axis. It is also planned to define the intracellular mechanism, which is activated when adropin binds to its receptor. For this purpose, a series of experiments will be carried out using specific pharmacological inhibitors of intracellular signaling pathways relevant for proper functioning of the adrenal glands. Silencing of adropin receptor expression will be used to confirm the specificity of its receptor binding. An important part of the proposed project will be to define the role of adropin in regulation of adrenocortical cell proliferation. Results obtained from this part of the study in the future may allow to determine the role of adropin and its receptor in the pathogenesis of adrenal tumors. It is planned to use a range of modern molecular biology techniques, among others microarray technology, which allows us to investigate expression of approximately 30000 genes in a single experiment.

The presented project deals with a novel issue that has not been studied by other investigators. The proposed experiments should provide information on the role of adropin in the regulation of HPA axis, with particular emphasis on its effects on the growth of adrenals and regulation of corticosteroid biosynthesis.