Description for the general public

Adrenal glucocorticoid hormones play an important role in the regulation of many physiological processes such as response to stress or inhibition of immune response. They play also an important role in the regulation of metabolism, where they mainly act in antagonistic manner to insulin. Glucocorticoid concentration is precisely controlled by hypothalamic pituitary – adrenal axis, and any disturbance of this regulation leads to serious metabolic 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 glucocorticoids 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 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 urotensin II (UII).

Urotensin II is the most potent mammalian vasoconstrictor with high interspecies homology. The increased expression of this peptide and its elevated plasma levels can be found in a variety of cardiovascular diseases, such as widespread atherosclerosis. The studies have shown that UII can act as a growth factor in cancers of different origin, including the adrenal gland neoplasms. Moreover, it has been indicated that UII can affect the level of corticosterone (one of the adrenocortical hormones) in the primary culture of this gland cells. The effect of corticotropin (ACTH) and other adrenal secretagogues on UII expression and its secretion by adrenal gland cells hasn’t been identified yet.

The project will focus on determining the mechanism of corticotropin, angiotensin II and potassium ions effect on UII expression and its secretion by the adrenocortical cells. It is also planned to define intracellular mechanism of ACTH- induced UII expression. The latter goal could be achieved by means of specific pharmacological inhibitors of the signaling pathways that are important for proper adrenal function. The auto- and/or paracrine function of UII will be described using UII gene silencing and its receptor inhibition. The important part of the proposed project is to evaluate the effect of UII on the adrenocortical cells proliferation. The results obtained from this part of the study in the future may allow determining the role of UII and its receptor in the pathogenesis of the adrenal tumors.

It is planned to use a range of modern molecular biology techniques, inter alia microarray technology that 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 yet. The proposed experiments should provide information on the effect of corticotropin and other adrenal secretagogoues on UII expression and secretion, with particular emphasis on its effect on the adrenal gland cells growth and the corticosteroid biosynthesis.