

popular abstract

The goal of the project is to estimate the role of Nampt protein in regulation of pituitary gland function. Pituitary gland combined with hypothalamus create hypothalamo-pituitary axis, which regulates the physiological function of many key organs of peripheral organs, one of which is adrenal cortex. This regulation occurs through the so called hypothalamo-pituitary-adrenal axis (HPA), which leads precise regulation of adrenal hormone secretion.

Nampt is the protein with pivotal role for the production of chemical compounds that are clue for the cellular respiration process. In last two decades Nampt is also known to be secreted as hormone to blood circulation system by adipose tissue. Secreted Nampt stimulates the function of many organs.

The research on circulating Nampt shows that Nampt is required for growth and division of cells. Because of that Nampt levels in blood serum is elevated during the growth or pregnancy. Its elevated levels are also observed in pathological processes such as tumor progression or inflammation. Due to that observations Nampt and its inhibitors (chemicals that stop its activity) are investigated as a potential new drug, that will slow down the tumor progression. Some of this inhibitors are during clinical trials.

Despite many evidences for Nampt influence on wide range of tissues, there are no data about its influence on hypothalamo-pituitary-adrenal axis physiological activity. The preliminary studies performed for that project shows that Nampt is required for correct hormone secretion by adrenal gland as well as stimulates pituitary gland for releasing adrenal stimulating hormones. The results of this studies shows that Nampt undoubtedly stimulates HPA axis through pituitary gland.

The realization of proposed project will help to described the mechanism of observed phenomena. For that purpose I would like to use commercially available pituitary cells AtT20. This cell produce corticotrophin (ACTH), which mediates the interaction between pituitary gland and adrenals. I plan to perform the experiments that will explain how Nampt influence regulation of this cells. To obtain that goal, the cells incubated in the presence of Nampt and the control cells will be analyzed for the dynamics of all gene expression by microarray method. The microarray method will help to estimate which genes are activated as a consequence of Nampt treatment. Additionally I would like to check if Nampt influence the pituitary gland in the similar way to CRH (the hormone that stimulates the pituitary gland to ACTH secretion). In the last cycle of experiments I would like to investigate the interaction between the pituitary gland and adrenal cells, within combined incubation of this two HPA components.

The results of this project will not only help to better understand the biology of hypothalamo-pituitary-adrenal axis, but also can reveal the new, previously unknown interaction between the adipose tissue and the HPA axis.