

Neuroendocrinology is an extremely dynamically developing science and in recent years a significant progress of knowledge in this field has been observed. To a large extent, this is the result of rapid technological development generating new research opportunities. However, difficulties appearing in recent years related to both ethical issues and the increasing costs of *in vivo* animal research, and on the other hand, modern technological progress resulted in the development of completely new research methods. Studies concerning the mechanisms of neuroendocrine regulation of many processes essential for the organism functioning occurring at the hypothalamus level are particularly complicated.

A lot of attempts have been made to develop research models that could be an alternative to classical *in vivo* animal experiment in studies on the biologically active substances action at the central nervous system (CNS) level. One of the new, very promising biological research model is the dynamically developing examination technology called 'organ-on-a-chip' (OOC). OOC technology has rapidly evolved as a powerful tool for numerous applications with special reference to bioengineering, tissue engineering, molecular diagnostics and biomedical engineering research. Besides such huge multi-functional potentialities, microfluidic technology also offers the opportunity to mimic different organs to address the complexity of animal-based testing models effectively. One of the aims present project is to develop a modification of OOC system to create 'brain slides-on-a-chip' which could be an innovative technique to mimic CNS neuroendocrinal network and to some extent replicate the hypothalamic-pituitary system.

It is worth emphasizing that technological development also enables the identification and discovery of new biologically active peptides. In 2013, using a bioinformatic algorithm that utilizes information provided by the Human Genome Project a novel peptide named phoenixin (PNX) has been identified. The most important endogenous active isoforms are referred as PNX-14 and PNX-20. The amino acids sequences of this peptides have been strongly conserved during evolution and consequently have very high homology between particular vertebrate species. It is noteworthy, that this feature is characteristic for a key neuropeptide controlling vital neuroendocrine functions in vertebrates. Location of PNX in the hypothalamus nuclei indicates that it may be involved in the regulation of energy homeostasis. Moreover, PNX is characterized as a reproductive peptide which regulates GnRH expression (main hormone regulating reproductive processes), pituitary gonadotrophin secretion and is required for estrous cycle.

The studies planned in the proposed project focus on the neuromodulatory impact of PNX on the gonadotrophic axis secretory activity, which is the most important part of a complex system responsible for the control of the reproductive processes in the organism.

The unquestionable, innovative advantage of the designed project is verification of the proposed design usability - "brain slides on the chip". In both experimental systems, in 'brain slides-on-a-chip' *ex vivo* and in animal *in vivo* model the examination of changes occurring in key regulatory systems: the gonadotrophic axis, appetite control center and the GnRH pulse generator system will be monitored. Those experimental systems, difficult to perform and requiring a lot of experience, will enable to trace simultaneously the dynamics of changes in GnRH, LH and FSH gene expression, their localization and concentration in tissue. Used technique will allow to monitor changes of selected neurons, after the precise PNX administration, closely to the hypothalamus structures where the examined neuropeptide is active. Obtained results will provide also new unique data on the effects of anorexigenic/orexigenic neuropeptides on the reproduction and allow to better understand of the mechanisms underlying such disorders as anorexia, bulimia and fertility disturbances.