Galanin as the modulator of glucocorticoid secretion and its role in Cushing Disease.

Galanin is a neuropeptide discovered over 40 year ago with unclear physiological role. Analysis of genes expression shows that galanin is produced mainly in pituitary gland, specifically by corticotroph cells – a specified subtypes of pituitary cell that secret ACTH. ACTH is the hormone responsible for the stimulation of the glucocorticoids by adrenal gland.

Pituitary corticotroph cells can undergo neoplastic transformation and form corticotroph pituitary tumors that secrete excessive amount of ACTH. It cause a set of pathogenic signs and symptoms diagnosed as Cushig's Disease (CD). These tumors that cause CD produce galanin as well. Only few previous experimental studies on the galanin role suggested that this neuropeptide have stimulatory effect on adrenal secretion. As the chemical compounds that suppress galanin effect are available the better understanding of galanin-related regulation may be used for developing a therapy approach for CD patients

Our scientific hypothesis is that galanin coregulates secretion of glucocorticoids by adrenal gland through mechanism, that remains to be determined, and that modulating its activity may be potentially utilized in CD treatment.

The planned procedures are directly aimed to:

- Evaluate the function of galanin in glucocorticoids secretion by adrenal cells in cell culture model
- Evaluate the possible auto-regulatory effect of glanian on pituitary corticotroph in cell culture model
- Investigate the physiological role of the galanin secreted by pituitary tumors in whole body context by the use of murine model.
- Determining the expression of galanin and galanin receptors in human normal anterior pituitary and corticotroph tumors to determine the role of this neuropeptide in these tumors.

Thus this project combines human tissue samples analyzes with in vitro and in vivo experiments.

To our best knowledge, relevance of galanin in adrenal regulation and pathophysiology of CD is poorly understood and targeting the galaninergic system has not previously been considered as therapeutic approach for CD. This project will provide insight in the mechanism of the regulation of HPA axis, which is a basic regulator of pituitary and adrenal secretion. The results will expand the knowledge in the field of endocrinology and possibly provide a background for further application studies on improving the pharmacological treatment of corticotroph pituitary tumors. The improvement of the treatment CD patients is still needed as the stabilization of pathological secretion of glucocorticoids in the patients is challenging and it is directly responsible for disease symptoms.