The pituitary gland is an neuroendocrine gland that produces hormones which regulate many important life functions, including growth, puberty, reproduction and fertility, pregnancy, lactation, and stress responses. It controls the work of other secretory glands and is a bridge between the brain and the rest of the body. For this reason, the pituitary is often called a master gland. The pituitary gland is physically associated with the hypothalamus, and physiologically part of the three axes: hypothalamic-pituitary-adrenal gland, hypothalamic-pituitary-gonadal and hypothalamic-pituitary-thyroid. Disorders of the former can lead to depressive states, while failure of the latter can lead to problems with ovulation, potency and fertility. Perturbations in thyroid hormone regulation are associated with wide spectrum of disorders (e.g. hypothyroidism or hyperthyroidism and their further consequences).

Completion of the Human Genome Project's sequencing gave a unique opportunity to systematically study different regions of the genome in relation to its biological activity. Perhaps one of the biggest surprises of the post-genome era is the vast amount of transcription emanating from the **non-coding regions of the genome**. It is now evident that **non-coding RNAs** (ncRNAs) being transcribed from these regions play key roles in regulatory networks determining cell fate and behavior, in a myriad of different conditions, and across all species studied so far. Among few others we can distinguish, **microRNA** (miRNA), **long non-coding RNA** (lncRNA) and **circular RNA** (circRNA). The repertoire of ncRNAs depends on cell and tissue type and the developmental stage. Many of them perform regulatory functions, e.g. a single microRNA can regulate dozens or hundreds of protein-coding genes and thus affect the metabolism and structure of the cell. Taking the pituitary gland as an example – deficiency of a single miRNA, miR-7a, in the pituitary gland of mice caused a dramatic phenotype, namely low levels of gonadotropic and sex steroid hormones, malformations in the ovaries and testes and, consequently, infertility. However, how long non-coding RNAs and circular RNAs are involved in the regulation of molecular processes in pituitary cells is very poorly understood, with a handful of exceptions.

The central hypothesis of the project: non-coding RNA, including lncRNA and circRNA may be involved in the regulation of gene expression in pituitary cells, and the modulation of the secretory functions of this gland. **The main goal of the project** is to explore and expand knowledge on circRNA and lncRNA biology, their interactions with miRNA and proteins in the pituitary. We will examine the expression patterns of circRNA /lncRNA with respect to individual secretory cells types, their location and function in pituitary cells. As a research model, we will use cell lines and pituitary tissues isolated from mice. In a special and in-depth manner, we would like to explore a regulatory RNA network made up of the circRNA Cdr1as, lncRNA Cyrano, miR-7 and miR-671, which has been characterized in the mammalian brain as being associated with the proper functioning of excitatory neurons [Piwecka et al. 2017, *Science*]. All these ncRNAs are expressed in the pituitary gland, however, intriguingly, the preliminary studies suggest that their functions may differ compared to the one observed in neurons.

To achieve these goals, we will apply cutting-edge new technologies like single-cell RNA sequencing (scRNA-seq) and RNA imaging at the single-molecule resolution. We will also implement an innovative approach for studying RNA:protein interactions that is currently developed in our laboratory in order to explore the functions of ncRNAs. The ambition of the project's investigators is to combine the efforts of molecular, cellular, and systems biology to answer the question of how non-coding RNAs affect the regulation of molecular processes in pituitary secretory cells. This innovative approach holds promise to bring a substantial and beyond state-of-the-art advance in the understanding of RNA regulatory functions in the neuroendocrine system. We anticipate that the project will generate a great resource and foundation for understanding physiological disorders of the pituitary gland in the future.