transcriptome analysis of double-labelled transgenic tilapia expressing GFP and RFP in LH or FSH cells, respectively, we identified genes specifically enriched in each cell type. Analysis of the RNA-seq discovered 4 types of SST-Rs: sstr2, sstr3, sstr5 and sstr5x3. The specific localization of each SST-R was identified by In Situ hybridization with specific probes for each of the SST-Rs. SST-R2 and SST-R5x3 were expressed on LH and FSH cells, while SST-R5 was exclusively expressed on LH cells. Interestingly, SST-R3, which was expressed on GH secreting cells, was also expressed on both gonadotropin-secreting cells. Transactivation assays, using COS7 cell line transfected with tilapia SST-Rs together with the reporter plasmid CRE-luc, demonstrated an effect through the cAMP/PKA pathway. Signal transduction analysis demonstrated that SST agonist (Octreotide; IC50 = 0.8-60nM) decreased the cAMP/PKA pathway, while an opposite effect was found when SST antagonist (Cyclosomatostatin; EC50 = 0.1 - 188 nM) was used. To understand the physiological effects of somatostatin on gonadotropins and GH release, we examined the effect of ip injection (100 µg/kg BW) of somatostatin agonist and antagonist on plasma FSH, LH and GH levels. SST agonist decreased plasma GH and FSH levels, as fast as two hours post injection and their levels remained low until the end of the experiment. On the other hand, SST antagonist increased LH and FSH levels two hours post injection, but while FSH levels remained high during the entire experiment, LH levels went back to basal levels afterwards. Our results show - for the first time in fish - a direct effect of SST on gonadotropin release, that could serve as a bridge between the GH-axis and the GTH-axis. The research was funded by the Israel Science Foundation (ISF) no. 1540/17.

Neuroendocrinology and Pituitary
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Spatial Transcriptomics for the Analysis of Human Pituitary Development

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The pituitary develops from oral ectoderm in contact with the adjacent hypothalamus. However, the precise mechanisms underlying pituitary development in concert with plural tissues are not fully understood, especially in human. A protocol to induce pituitary cells from human induced pluripotent stem cells (hiPSCs) has been established and applied to study pituitary development and disorders. In the method, oral ectoderm and hypothalamus are induced in one organoid, which enables recapitulation of the interactions between these tissues during embryonic development. It leads to self-organization of pituitary cells. Recently, spatial transcriptome technology has been developed and is suitable for the analysis of tissue interactions. Here, we utilized spatial transcriptomics to analyze pituitary organoids, especially focusing on the mechanisms regulating pituitary progenitor cell differentiation. Spatial transcriptomics revealed that the organoids consisted of several cell populations including hypothalamus, oral ectoderm, neural retina, and cortex neuron cells. Pituitary progenitor cells, characterized by the upregulation of *LHX3*, were included as part of the oral ectoderm population. Further analysis of the population identified human pituitary progenitor-specific genes including many causal genes for congenital hypopituitarism (CPH). Finally, using spatially resolved gene expression data, we examined the hypothalamic population that was in contact with pituitary progenitor cells and identified hypothalamic factors that might regulate progenitor cell differentiation in a paracrine manner. The genes upregulated in the pituitary progenitor and neighboring hypothalamus cell populations are potential causal gene candidates for CPH. In conclusion, spatial transcriptomics provides a novel platform to analyze tissue interaction networks during human pituitary development.

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Synergistic Control of KNDy Neuronal Influence on Energy Balance by Ghrelin and Estradiol

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The gut peptide, ghrelin, mediates negative energy homeostasis and the neuroendocrine control of energy homeostasis by acting through its receptor, growth hormone secretagogue receptor (GHSR). GHSR, expressed in hypothalamic *K*isspeptin/*N*eurokinin B/*D*ynorphin (KNDy) neurons in the arcuate (ARC), is well known to regulate energy balance. We have previously shown 17-beta-estradiol (E2) robustly increases *Ghsr* expression in KNDy neurons, enhancing their sensitivity to ghrelin. We hypothesize that E2-induced increase in GHSR expression augments KNDy sensitivity in a fasting state by elevating ghrelin to reduce energy expenditure in females. We developed a *Kiss1*-specific GHSR knockout to determine the role of GHSR in ARC KNDy neurons and fed them either a low-fat diet (LFD) or a high-fat diet (HFD). Knockout (experimental) females were resistant to HFD in terms of body weight gain, adiposity, and food intake compared to HFD-fed controls. HFD-fed experimental females also exhibited slower glucose clearance compared to HFD-fed controls. Experimental females, regardless of diet, exhibited elevated fasting (5h) glucose. Metabolic rates ($V.O_2$, $V.CO_2$) and energy expenditure (heat) were not different. Respiratory Exchange Ratio (RER) was elevated in LFD-fed females, indicating the utilization of carbohydrates over fat for energy. Further meal pattern analysis revealed a reduction in meal duration in HFD-fed females, but elevated meal frequency, while HFD-fed experimental females exhibited a reduced meal size. In two separate meal pattern experiments, experimental and control females were fasted for 24h and refed or injected with ghrelin (I.P. 1mg/kg) or saline. We observed a striking delay in refeeding behavior in experimental females compared to controls during the refeeding period after fasting. After injection, control females responded to ghrelin with a rapid and sustained increase in food intake which was blunted in experimentals. Collectively, these data suggest that GHSR activation in