

Institute : Institute of Zoology and Biomedical Research.

Topic: Expression and role of asprosin/OLFR734 in the regulation of mouse hypothalamus and pituitary cells function.

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Background information:

Obesity and overweight are increasing worldwide and have detrimental influences on several human body functions including the reproductive health. In particular, obese women undergo perturbations of the 'hypothalamic pituitary ovarian axis', and frequently suffer of menstrual dysfunction leading to anovulation and infertility. Besides the hormone disorders and subfertility that are common in the polycystic ovary syndrome (PCOS). The adipose tissue indeed, releases a number of bioactive molecules, namely adipokines, that variably interact with multiple molecular pathways of insulin resistance, inflammation, hypertension and cardiovascular risk. Obesity is conditions that alter the profiles of specific hormones such as insulin and adipokines and, thus, definitely impair the women fertility. Many reports indicate that adipokines regulate the female reproduction on hypothalamus – pituitary level. In the present project we will focus on description of adipokine – asprosin – as new regulators in female reproduction - on the hypothalamus and pituitary physiology. Asprosin is a fasting-induced glucogenic hormone, which stimulates appetitive behavior by OLFR734 receptor. It has been highlighted that elevated asprosin levels are observed in humans and mice with obesity, insulin resistance, and type 2 diabetes mellitus, however the role of asprosin in female reproduction is currently unclear.

The main question to be addressed in the project:

- mRNA and protein expression as well as immunolocalization of asprosin/OLFR737 in the mouse (obese vs control) hypothalamus and pituitary, - concentration of asprosin in plasma during estrous cycle (obese vs control), - the role of asprosin in the regulation of hypothalamus and pituitary cells (GT1-7 and LβT2, respectively) physiology: hormone secretion, proliferation, apoptosis and signalling pathways – involvement of OLFR737 in asprosin action oh hypothalamus and pituitry.

Information on the methods/description of work:

real time PCR, Western blot, ELISA, immunohistochemistry, *in vitro* culture of GT1-7 and LβT2 cell line, genes silencing, proliferation and apoptosis assays, statistical tests.

Additional information:

ability to use planned methods, using basic statistical analysis programs, knowledge of English in speech and writing, readiness to work in a team and openness to new challenges.

Place/name of potential foreign collaborator:

INRAE, Unité Physiologie de la Reproduction et des Comportements, Nouzilly, France / Professor Joëlle Dupont.

References:

Rak A, et al., Adiponectin and resistin: potential metabolic signals affecting hypothalamo-pituitary gonadal axis in females and males of different species. *Reproduction*. 2017;153(6):R215-R226.

Reverchon M, et al., Adipokines and the female reproductive tract. *Int J Endocrinol*. 2014;2014:232454.

Dupont J, et al., Involvement of adipokines, AMPK, PI3K and the PPAR signaling pathways in ovarian follicle development and cancer. *Int J Dev Biol*. 2012;56:959-67.