

Obesity and overweight - the scourge of the 21st century! The World Health Organization (WHO) reports that the problem of obesity affects 400 million and overweight over 1.6 billion adults worldwide. It is estimated that in 2030 the percentage of adults with obesity and overweight will increase to 50%. Obesity, apart from the obvious consequences, which include arterial hypertension, heart disease or cancer, also disturbs the functioning of the reproductive system, which in turn can lead to infertility. In obese women, the function of the hypothalamic-pituitary-ovary axis is dysregulated, the secretion profile of both gonadotropins and steroid hormones, and the expression of key steroidogenic enzymes change; *eg.* elevated levels of lutropin, androstenedione, estrogens and leptin are observed, and the accompanying insulin resistance and hyperinsulinemia lead to hyperandrogenism, which in turn contributes to anovulation and a decrease in endometrial sensitivity. As a consequence, the implantation of the embryo is reduced, the risk of miscarriages and complications around pregnancy is increased. In addition, there is a close relationship between obesity and reproductive pathologies, polycystic ovary syndrome (PCOS), endometriosis and ovarian cancer. The increase in the incidence of infertility and the social costs constitute the starting point for a global discussion on the search for optimal systemic solutions increasing the chances of improving the effectiveness of infertility prevention and treatment. The current research focuses on discovering new markers of female fertility and proper regulation of the reproductive function. The group of hormones that link between reproduction and the metabolic status of the body include adipokines, growth factors and neuropeptides. The aim of the project is to understand the role of novel adipokine – asprosin in the regulation of female reproduction. Asprosin is a hormone involved in the regulation of food intake, the body's energy balance, as well as sugar and lipid metabolism through binding to OLFR737 (in mouse; OL4M1 in human); little is known about its reproductive function. The research carried out in the project will include: *(i)* determination of asprosin gene and protein expression and its receptor, as well as cellular localization in hypothalamic, pituitary and ovarian cells, blood concentration depending on the stage of the oestrous cycle and metabolic status in lean and obese mice; *(ii)* the direct influence of asprosin on endocrinology function, proliferation, apoptosis and activation of protein kinases of hypothalamic, pituitary and ovarian cells; *(iii)* to study the influence of asprosin on the an *in vitro* mouse oocytes maturation, and to explain the molecular mechanisms of the observed changes; *(iv)* an *in vivo* studies involving the administration of asprosin to wild-type mice and mutants (lacking the asprosin gene) in order to determine the reproductive parameters of females: regularity of the oestrous cycle, the level of reproductive hormones and metabolic hormone in the plasma, the global transcriptome and selected proteins in the cells of the hypothalamus - pituitary - ovary axis. Importantly, to confirmed mouse model and improve my hypothesis, I will use also human granulosa cells from obese and non-obese women. The obtained results will bring a great deal of new knowledge about the regulation of the functioning of hypothalamic, pituitary and ovarian cells in different metabolic status of the organism, which will allow us to expand our knowledge of markers of reproductive function and their molecular mechanisms. My project will also bring clinical benefits, including manipulating the function of hypothalamus, pituitary and ovarian cells, improving the *in vitro* fertilization protocols, or as a new marker to increase the rate of reproductive success. The project will be implemented in international cooperation with the INRAE (*French National Research Institute for Agriculture, Food and the Environment*) in France, which will also have a positive impact on the scientific development of the team.