

Summary - general public

Food choice and eating habits have dramatically changed in Poland and other countries over the last fifty years. Nowadays our society faces not only a notorious excess of caloric intake, but also a decrease in physical activity. Consequently, the escalating global epidemic of overweight and obesity is taking over many parts of the world. Obesity leads to long-term health problems. Generally speaking, excessive accumulation of fat modifies the function of our body, promoting different diseases, such as diabetes, cardiovascular disease or cancer. Besides the impact for public health, costs for treating obesity had almost a ten-fold increase from 1998 to 2007 in Europe. Even more stunning, current research suggests that obesity leads to negative health consequences for our offspring.

The adipose tissue, or fat tissue, has been generally known as a storage of excessive fat. However, today we know that fat tissue also secretes many vital substances, like the hormone leptin, into blood stream. As a hormone, leptin, is capable of regulating other organs function, controlling from instances the appetite, as well as the ovarian function. Thus, during obesity, leptin level in the blood is unusually high, but fails to signal. As a consequence, the function of the ovaries is disrupted. When we reproduce, we pass our biological features on to our offspring through the sexual cells, also named gametes (the oocyte and the sperm). In addition to the gene code (the DNA), which contains the genetic information for all biological functions in our body, the gametes also transmit to the offspring the machinery responsible for turning genetic instructions into working proteins, as well as its programming — a phenomenon known as epigenetic. Importantly, our life experiences, environmental factors or exposition to unusually high or low levels of hormones, like leptin, can determine changes in the epigenetic regulation of the DNA of the gametes. What is more, the lipids, which are primarily known as an energy storages, may also work as signalling substances. Amongst others, these are vital for the function of the organ. Analysing the lipidome will provide a picture of total lipid components in the cell, and will help us to understand the regulation of cellular processes. Thus, in the present research proposal we will address how altered levels of leptin during obesity promotes epigenetic and lipidomic changes in the oocyte (female gamete) and cumulus cells (oocyte accompanying cells) during different periods of development and on the embryo development during pregnancy, affecting this way the next generation. As a result, we will be able to clearly understand: (i) the extent to which altered leptin level affects oocyte on different developmental stages during obesity; (ii) if putative changes established in the oocyte due to impaired leptin signals are preserved in the embryo and may affect embryo development during pregnancy. Different mouse models with high levels of leptin or deficient in leptin will be used, representative of variable levels of obesity and blood hormones, and consequences of obesity in female mice reproductive tract will be assessed and followed up in the first offspring generation.

The present proposal exploits the synergies between two institutes, the Institute of Animal Reproduction and Food Research (IARFR), Olsztyn, Poland and the Babraham Institute (BI), Cambridge, UK. With an extensive background in reproductive medicine and endocrinology, the candidate has been producing a relevant body of preliminary data on obesity and ovarian failure. The access to adequate methodology and animal models for the study of obesity is enabled at IARFR. This permits that the animal protocol will be undertaken in IARFR and further analyses will be performed at the BI, which provides the methods and state-of-the-art facilities for epigenetic analysis. Understanding how obesity impacts the oocyte and embryo epigenetic reprogramming will allow us firstly to improve fertility in obese women and secondly to assess the potential health consequences on the offspring. Undeniably, our results will shed light on the basis for establishment of obesity-related co-morbidities, such as cardiovascular-disease and cancer in offspring. Considering that nowadays the global number of clinically obese people is over 300 million, and is continuing to escalate, new insights on the impact of obesity on gametes and gestation and its epigenetic consequences for the offspring are extremely relevant for public health.