

## Description for the general public

The aim of the project is to understand the role of the mitochondrial MOTS-c peptide in the functioning of the pancreas and adipose tissue. With the current state of knowledge, its meaning and properties remain, in the context of the two above-mentioned tissues, completely unknown. This peptide was discovered three years ago, in 2015, and from the very beginning it has been shown to be important in the metabolism of carbohydrates and fats. It was also found that by peripherally acting it is able to sensitize tissues such as skeletal muscles to insulin and to prevent obesity in mice. Interestingly, it is believed that it can also play an important role in the cell cycle, contributing to longevity. In this situation, the willingness to learn more about its meaning and function in the pancreas and in adipose tissue becomes natural.

This peptide, encoded in mammalian mitochondrial DNA, thus becomes a potentially important protein in modern civilization diseases such as second type diabetes or obesity. The complicated etiology of these diseases does not give them a chance for their easy and quick treatment, and the most important role in therapy is played by prevention. This happens, among others, because these diseases have very complex causes, the mechanisms of which are still not known in many cases. The very fact of discovering more and more new peptides makes us realize how much work still needs to be done in getting to know their function in the organism before we can get therapeutic effects thanks to this knowledge. Research on the MOTS-c therefore seems to fit well into today's needs and can produce results that give hope for a more effective treatment against diabetes or obesity.

Research in the project will be carried out on two models related to the pancreas and adipose tissue. These will be alpha and beta cells of established lines grown *in vitro* from the pancreas islets producing glucagon and insulin, and adipocytes that produce hormones characteristic of adipose tissue such as leptin and adiponectin. The second model will be used pancreatic islets isolated from experimental animals and adipocytes isolated directly from adipose tissue. At this stage of the research, it is planned to obtain tissues from rats and pigs. This is related to the different anatomical structure of the pancreas and the islets themselves in these species and therefore potentially different results that can be obtained. It should be mentioned that the model of the pancreas anatomically closer to a human is represented by a pig, however a rat remains still more widespread in the literature.

The research will concern, firstly, the location of the MOTS-c peptide in the pancreas and adipose tissue, and if it is confirmed, the effect of pancreatic hormones such as insulin and glucagon and adipose tissue hormones such as leptin and adiponectin on its secretion. Second, the effect of MOTS-c peptide itself on the secretion of these hormones and the effect of MOTS-c on the survival and proliferation of endocrine cells of the pancreas and adipose tissue. At the end, it is planned to determine the basic intracellular pathways that activate MOTS-c causing its physiological effects. All these aspects are important in better understanding the mechanisms of energy homeostasis and, consequently, the origin and the course of diabetes and obesity.