Background and state of knowledge In 1997 in Geneva, the World Health Organization (WHO) declared that Obesity is a global epidemic with serious health implication (1). The number of obese is growing dramatically and it is one of the main risk factors for many of chronic diseases, including type 2 diabetes (**T2DM**). The World Health Organization data show that the number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014 (WHO website).This problem also applies to Poland where in 2014 over 62% of men and nearly 46% of women were overweight (2). Diabetes mellitus type 2, insulin resistance, cardiovascular diseases, nonalcoholic steatohepatitis, hypertension, sleep disturbances including obstructive sleep apnea are the most common complications associated with the civilization disease. The problem of etiology, clinical characteristics and potential strategies for the treatment of obesity and type 2 diabetes mellitus (T2DM) are among the most intensively studied and discussed areas in biomedical sciences. In the light of the increasing number of complications associated whit this phenomenon, understanding the homeostatic mechanisms regulating food intake, as well as body weight and peripheral tissue metabolism is a very important issue in the research of scientists from all over the world. In recent years there are more and more reports about the newly-discovered peptides, which may be involved in regulating energy homeostasis at the level of both central nervous system and many peripheral tissues. These include natural GHSR-1a agonists and antagonists. Belong to them three peptides: LEAP2 (Liver-Expressed Antimicrobial Peptide 2), ghrelin and obestatin. Modulation of GHSR-1a receptor by these peptides could be involved in the pathogenesis processes associated with obesity, insulin resistance and development of T2DM. Therefore, it seems justified to expand the knowledge about antagonists and agonists of this receptor, which in the future may translate into the definition of new therapeutic targets in T2DM and / or the development of new therapies for this disease. Due to the fact that the role of obestatin and ghrelin in pathogenesis of T2DM is relatively well known we decided to focus on role of LEAP2.

The main objective of the project is to add to the grain research the knowledge of the potential influence of GHSR-1a antagonist - LEAP2 on the regulation of carbohydrate/lipid metabolism and hormonal profile in T2DM. The project also includes in vitro studies on the effect of this peptide on the metabolism of pancreatic islets and fat cells *in vitro*.

Concept and working program Project is divided into two panels: *in vivo* and *in vitro*

In vitro* panel** will be conducted using isolated animal cells and/or cell lines involved in regulation of glucose metabolism (adipocytes and pancreatic islets). The second part of experiments (in vivo* panel**) will be conducted on murine model of type 2 diabetes. Using animal model will be investigated effect of interaction between LEAP2 and GHSR-1a receptor on metabolism and hormonal profile in T2DM.

In addition, these studies performed using both techniques: *in vitro* and *in vivo* will contribute to the development of knowledge about LEAP2 and the role of the GHSR-1a receptor in the pathogenesis of T2DM both at the molecular level (determining the intracellular transmission pathways activated by LEAP2) and peripheral.

The presentation and explanation of the effect of LEAP2 as well as interaction between GHSR-1a on metabolism in diabetes will help to clarify the thesis of the potential therapeutic use of this peptides in these pathological conditions.

1. World Health Organization (WHO) (2000) Obesity: preventing and managing the global epidemic. Report of a WHO consultation. *World Health Organ. Tech. Rep. Ser.*, **894**, i–xii, 1–253.

2. Augustynowicz, A. *et al.* (2019) Prevention of overweight and obesity undertaken by local government units in Poland. *Health Policy (New. York).*, DOI: 10.1016/j.healthpol.2019.03.006.