Obesity is a major public health problem worldwide that increases the risk of hypertension, cardiovascular disease, type 2 diabetes and cancers. Moreover, it has become a common cause of death, with approximately 2.8 mln of people dying each year due to its complications. Unfortunately, for over few decades a dramatic increase in its prevalence has been observed also among children and adolescents. The abovementioned changes are reflected, e.g. in the increased rate of bariatric surgeries performed in recent years. In 2014, WHO announced that nearly 39% of the world adult population was overweight and 13% obese.

Therefore, in the light of the abovementioned, the main aim of our project is to evaluate the possibility of an inhibition of the excessive lipid accumulation in the adipose tissue of obese individuals. Detailed analyses will encompass the regulation of the intracellular pathway responsible for the translocation of fatty acid transporters and resultant influx of lipids into adipocytes. More specifically, a key factors are to assess the involvement of AS160/TBC1D4 and TBC1D1 in the fatty acid transporters trafficking in the subcutaneous and visceral adipose tissue of people with obesity. Previously published literature data clearly indicate that both homologs regulate cellular glucose uptake *via* translocation of GLUT-4 storage vesicles from intracellular compartments to the plasma membrane. Moreover, it has been suggested that the lipid accumulation commonly observed in obesity and metabolic syndrome results from an increased transmembrane transport of long chain fatty acids (LCFA) regulated mainly by fatty acid transport proteins, including: fatty acid translocase (FAT/CD36), membrane fatty acid-binding protein (FABPpm) and fatty acid transport proteins (FATP 1, 4). The before-mentioned fact is quite important given that obesity is a metabolic disease defined by excessive accumulation of fats, mainly triacylglyceroles (TAG), in amounts higher than energetic demand of human organism. The resultant positive net energy balance leads to a lipid over-accumulation mainly in the triacylglycerols (TAG), diacylglycerols (DAG) and ceramides (CER) fractions. The latter two (DAG and CER) were shown to directly interfere with the insulin signaling pathway, thus inducing insulin resistance of a given tissue. Therefore, in the proposed project we will analyzed the relationship between fatty acid transporters expression and intracellular lipid content (TAG, DAG, and CER), not only in the patients, but also in the cell cultures (primary adipocytes). Moreover, the major value of the proposed study will be to determine the involvement of AS160/TBC1D4 and TBC1D1 proteins in the regulation of total, plasma membrane and mitochondrial expression of fatty acid transporters in primary adipocytes extracted from the subcutaneous and visceral adipose tissue. The samples will be derived from severely obese patients (BMI > 35 kg/m^2) with or without metabolic syndrome and the levels of the aforementioned variables will be compared with their counterparts from the tissues of healthy individuals (BMI < 25 kg/m^2). For this reason we will conduct AS160/TBC1D4 and TBC1D1 genes silencing and determine their effect on the adipose tissue lipid metabolism.

Importantly, the proposed study is not only original but also characterized by a high potential for application. If AS160/TBC1D4 and TBC1D1 prove to be important regulators of fatty acid transporters trafficking it will open new therapeutic horizons for the regulation of intracellular lipids uptake. The latter shall allow for a reduction of their surplus influx and, therefore, reduce their adipocyte over-accumulation, which is a main cause of obesity and its associated comorbidities.