Title: The role of hypoxia-sensitive miRNA181a, miRNA199a, and SIRT1 in diabetes mellitus development in obstructive sleep apnea patients.

Sleep disorders are becoming an increasingly common health problem, especially in highly developed societies, including Poland. Obstructive sleep apnea (OSA) is one of the most common sleep disorders. It is estimated that it can affect even every other middle-aged man and every third middle-aged woman. It is characterized by recurrent pauses in breathing during sleep, which can result in hypoxia, arousals, and sleep fragmentation. Disturbances in the correct sleep architecture and recurrent hypoxia present in OSA patients cause not only excessive daytime sleepiness, concentration disorders, decreased work efficiency but also significantly increase the risk of car accidents. Moreover, OSA is an independent risk factor for hypertension, cardiovascular diseases, as well as disorders related to glucose metabolism. Diabetes mellitus develops in approximately 30% of OSA patients. The gold standard in OSA diagnosis is the nocturnal polysomnographic examination, during which parameters such as the electrical activity of the brain, eye movements, chest, and abdominal movements are monitored. This allows for an accurate assessment of sleep phases, arousals, and breathing disturbances. OSA is treated with a device that generates continuous positive airway pressure (CPAP), which protects the upper respiratory tract from collapsing during sleep.

This project aims to evaluate the interactions between hypoxia-sensitive molecules SIRT1 and microRNAs in order to understand their role in the development of diabetes in patients with OSA. MicroRNAs are small RNA molecules that are designed to inhibit or activate specific genes. Previous studies have shown that some microRNAs levels are changed in OSA patients. Moreover, some of them (*miRNA181a, miRNA199a*) also influence the expression of *SIRT1* which is a factor influencing insulin secretion and insulin sensitivity. Assessment of SIRT1 and microRNA expression will be performed at 4-time points: before and after the diagnostic PSG examination, after a single night treatment with the CPAP, and after a 3-month CPAP treatment. This will allow not only to assess the changes of selected factors during the day and night but also to determine the impact of one-night and long-term CPAP treatment on them. In addition, hypoxia-sensitive microRNAs have both diagnostic potential and may become a new therapeutic target that will help prevent the development of diabetes.

Due to numerous complications and many comorbidities in the course of OSA better understanding of the pathomechanisms responsible for their occurrence is very important. This research will allow further development of diagnostics and therapy of sleep disorders, thus improving the health and quality of patients' lives.