## Research project – objectives/hypothesis

Obesity is the one of the most important problems of XXI century. In 2014 more than 600 million subjects worldwide were classified as obese and more than 1.9 billion adults were overweight. Obesity, wherein the BMI is above 35 and is accompanied with an additional diseases is classified as morbid obesity (MO). Bariatric surgery (BS) is one of the methods of MO treatment. In contrast to diet and pharmaceutical treatment, it is characterized by high efficiency. However, BS as each therapy can have a negative consequences including: reoperation, chronic problems with the stomach and intestines, the risk of leakage of the intestinal anastomosis, or deficiencies of bioactive ingredients and micronutrients as well as essential nutrients. This procedure also causes significant changes in the composition of the gut microbiome, which may affect the composition and number of various metabolites produced by intestinal bacteria. Based on the results obtained from the previous bariatric project financial by the National Science Center: " Evaluation of effect of the Omega Loop Gastric Bypass on level of bioactive lipids in course of Morbid Obesity" I decided to continue my research by analysing the changes in fatty acids, bile acids and amino acids in stool and serum samples in the three most popular BSs performed in our research center. Each of these types of BS may have a different effect on these metabolites. We will also check whether the profile of metabolites in the stool of obese patients affects the blood metabolome, and then whether these changes have an impact on the patients' health. In contrast to few routinely analysed in clinical laboratories parameters such as serum biochemical parameters and blood morphology our research will provide the results of wide range of various plasma metabolites that may be altered in obesity and after BS, and have an impact on patients' health status. **Research** description

Three groups of patients will undergo three types of bariatric surgeries: laparoscopic sleeve gastrectomy (LSG), one anastomosis gastric by-pass (OAGB) and the Roux-Y gastrointestinal bypass (Roux -Y gastric by-pass - RYGB) and healthy non-obese people. Serum and stool samples will be collected from patients at 5 time points: 1) before starting a low-calorie diet to prepare patients for BS, 2) just before surgery, 3) 3 months after surgery, 4) 6 months after surgery, and 5) one year after surgery. At the same time points, anthropometric measurements (waist circumference, weight, height, BMI) and body composition assessment using bioelectric impedance analysis (BIA) will be performed. All patients will be examined by a team of doctors in terms of their health condition and possible co-morbidities. Standard laboratory markers will be tested on subjects by the Central Clinical Laboratory of the MUG. Metabolomics studies will include the analysis of metabolites that can be produced by the gut bacteria: short- and long-chain fatty acids, bile acids and amino acids. For this purpose, we will use the technique of gas chromatography coupled with mass spectrometry and tandem mass spectrometry coupled with liquid chromatography. Finally, the obtained results will be subjected to chemometric analysis to determine the relationship of intestinal microbiome  $\rightarrow$  metabolites of intestinal content  $\rightarrow$  serum metabolites  $\rightarrow$  patient health condition

## Significance of project

Surgical intervention in the structure of the digestive tract, especially in bariatric by-pass procedures, also causes significant changes in the composition of the microbiome, which may affect the composition and quantity of various metabolites produced by intestinal bacteria. Especially, the changes in dietary habits after BS may be important for the microbiome and metabolism of bariatric patients. Since metabolites produced by microbiome may be absorbed in the intestine of obese patients, a better understanding of the cross-talk between the host and microbiome metabolome after BS can allow the better patient selection for different procedures and may lead to the development of the next generation of weight loss therapies, as well as, metabolism improvement. The project will analyze a wide range of metabolite profiles together with clinical parameters describing the health status of patients after bariatric surgery. When we find differences in the gut metabolome, and these studies will be performed using the metagenome analysis. Our innovative approach will allow to find the relationship between intestinal microbiome, metabolome of intestinal content and serum metabolome as well as patient's health status. Furthermore, acquired knowledge may help in future to design the personalized probiotic and dietary intervention to obtain optimal effect of bariatric surgery on intestinal microbiome and patients' health.