Evaluation of the brain microbiome and proteome as well as the role of fecal microbiota transplantation (FMT) in schizophrenia - studies in a methylazoxymethanol acetate (MAM-E17) rat model.

Schizophrenia is a neurodevelopmental disorder characterized by a complex clinical picture, who can be distinguished between positive symptoms (presence of psychotic symptoms), negative symptoms (lack of motivation, social withdrawal) and cognitive symptoms (impaired abstract thinking). Inflammatory factors seem to play a role in its formation, but also the gut-brain axis and factors influencing its functioning. The disease affects 0.5% to 1% of the global population regardless of nationality, ethnicity, social class or sex . It manifests between the ages of 21 - 25 years in males and 25 - 30 years in females and is persistent, lifelong, and stigmatizing for most.

A specific composition of the gut microbiome guarantees homeostasis of the human organism. Scientific evidence shows that disturbances in the composition of the microbiome, especially the large intestine, play an important role in the course of many diseases, such as inflammatory bowel disease, metabolic diseases or allergies, but they also affect the functioning of the gut-brain axis and the development of the brain. Information on the relationship between the composition of the intestinal microbiome (especially the deficiency of probiotic bacteria) and the development of inflammatory processes that influence the development of schizophrenia appears in the literature more and more often.

Taking into consideration the arguments above and the need for further research on the role of the gut microbiota in the etiopathogenesis of schizophrenia and the possible influence of fecal microbiota transplantation (FMT) on the symptoms and regression of this disease we set ourselves in our project the following objectives: a comprehensive evaluation (qualitative and quantitative, using the next-generation sequencing [NGS] method) of the composition of the microbiota of large intestine in schizophrenia rat model and control group of rats before the introduction of FMT (from control group to schizophrenia group and from schizophrenia group to control group), following FMT and additionally a comprehensive evaluation of the composition of the microbiota of blood and brain tissue when experiment will be finished. Simultaneously, an analysis of the correlation of data obtained from NGS sequencing with the results of behavioral tests and data from proteome profiling of selected regions of the brain will be carried out.

We will use schizophrenia animal model (a neurodevelopmental model of rats- Sprague-Dawley animals, obtained by administration of methylazoxymethanol (MAM) to females on day 17 of pregnancy, causing anatomical, functional and behavioral disorders in the offspring corresponding to those observed in patients with schizophrenia.

The obtained results during the implementation of this project may shed light on the causes and pathomechanism of schizophrenia. They can also contribute to the development of a new model of schizophrenia therapy, based on the modification of the gut microbiota composition with FMT, as well as the development of new drugs, individually designed for each patient and acting systemic in operation (new generation probiotics, antibiotics). It is possible that, on the basis of the data obtained in the course of this project, it will be feasible to determine the gut and blood microbiota profiles predisposing to the development of schizophrenia, or to faster remission and maintaining it longer.