Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder, commonly characterized by repetitive behaviors and impaired social skills, including verbal and nonverbal communication that begins in infancy. Concerns over ASD are alarming, as many people are diagnosed yearly. Moreover, patients suffer from co-occurring conditions, including epilepsy, depression, anxiety, and gastrointestinal problems. At the same time, the increasing prevalence of overweight and obesity, described as a “global epidemic" affects both sexes of all ages. Overweight or obesity is a preexisting condition in 40% of women who become pregnant. Findings show maternal obesity and exposure to a high-fat diet (HFD) during early development are associated with an increased risk of developing mental, and behavioral disorders, neuroinflammation, and metabolism disturbances. Epidemiological studies also identify maternal obesity as a significant risk factor for neurodevelopmental disorders, including ASD. The microbiota-gut-brain axis consists of a complex network and multiple pathways that allow signals to be sent between the microbiota and the brain, demonstrating that gut microbiota can influence many neurological disorders such as ASD. Particularly, the mechanism by which gut-fetal brain interactions regulate neurodevelopmental disorders remains largely unknown.

The gut virome constitutes a major portion of the microbiome, with bacteriophages having the potential to remodel bacteriome structure and activity. Recent studies suggest that the gut virome can also impact an individual's health, similarly to the gut bacteriome. The human gut virome is greatly influenced by diet. The relationship between the virome and bacteriome in the gut and their impact on neurodevelopmental disorder is not yet fully understood. This significant gap is a major obstacle to progress in comprehending the origins of ASD and developing effective prevention or treatment strategies.

Hence, the proposed study may shed new light on the role of gut virome in ASD. Using two preclinical models of ASD-like behavior – HFD-induced maternal obesity and BTBR mice – we want to identify alterations in the virome that may correspond to manifested social and repetitive behavior disorders. We will also evaluate the impact of changes in the gut bacteriome and virome on neuroinflammatory and neurodevelopmental processes in selected brain regions important for ASD pathogenesis, but still insufficiently studied in this context (hippocampus and cerebellum). All studies will be performed on mice of both sexes to identify possible differences that may account for the higher incidence of ASD in males.

Currently, there are no effective intervention strategies for the prevention or treatment of ASD symptoms. Therefore, we will use novel fecal virome transplantation (FVT) strategy to minimize the development of ASD-like disorders. The virus-like particles (VLP) taken from feces of healthy mice will be transfer to offspring of obese mothers and BTBR mice. Then, the effectiveness of the FVT will then be evaluated in a series of behavioral tests and molecular experiments using the modern analytical and bioinformatics tools. We believe that the results of the project will become a breakthrough for understanding the role of virome in regulating the gut-brain axis in the context of social behavior disorders and such a wide prevalence of ASD in the global population.