Concerns over autism spectrum disorder (ASD) are alarming, as many people are diagnosed yearly. Moreover, patients suffer from co-occurring conditions, including epilepsy, depression, anxiety, and gastrointestinal problems. Unfortunately, there is no cure for ASD, some medications can help treat only co-occurring symptoms. At the same time, the increasing prevalence of overweight and obesity, described as a “global epidemic" affects both sexes of all ages. Accordingly, the incidence of maternal obesity has also been increasing. Overweight is a preexisting condition in 40% of women who become pregnant. Maternal obesity has short- and long-term consequences, for both the mother and offspring. Literature suggests a relationship between maternal obesity and the risk for ASD – children born to these mothers have a 36% higher risk of being diagnosed. Recent findings indicate that dysbiosis of the maternal gut microbiome during pregnancy alters fetal neurodevelopment, contributing to abnormal brain structure and function underlying maladaptive, autism-like behaviors in offspring. Gut microbiome composition is driven primarily by diet; an unbalanced is associated with an increasing burden of disorders, such as ASD.

Microbiota in the gut regulates the biochemical, physiological, and neuronal functions of the host. Dysbiosis, a disruption of the gut microbiota, has been linked to diseases of the metabolic, immune, and neurological systems. There is continuous interaction between gut bacteria and the brain via the microbiota-gut-brain axis. Intriguingly, ASD and other neuropsychiatric disorders such as depression, and anxiety are influenced by gut microbiota compositions. In this project, we aim to uncover previously unknown mechanisms governing the interaction between maternal gut microbiota and fetal brain development, eventually leading to the development of ASD. Moreover, it is unclear how gut microbiota metabolites – particularly short-chain fatty acids (SCFAs) contribute to ASD pathogenesis. In light of this understanding, this project has three specific goals: 1) Assess the impact of high-fat diet (HFD)-induced maternal obesity and SCFAs interventions on fetal brain development; 2) Investigate molecular characteristics of ASD in offspring following HFD-induced maternal obesity and SCFAs interventions by determining the impact of microbiota and dietary interventions on downstream signaling molecules of the ERK1/2 pathway, microglial activity, myelination, and the structural changes in the offspring's brains underlying ASD; 3) Determine the impact of SCFA interventions on the prevention development of ASD-like behaviors in offspring from obese mothers. The research will use a mouse model of maternal diet-induced obesity. Both male and female offspring will be analyzed to identify possible molecular differences that may cause the varying incidences of ASD based on gender (ASD is more often diagnosed in boys than in girls). It is known that boys are diagnosed with ASD several times more often than girls, and this study aims to define the potential molecular reasons for this phenomenon. The project will combine *in vivo* and *in vitro* methods, behavioral, molecular, and neurochemical tools, and the latest brain imaging methods, such as magnetic resonance imaging (MRI) and electron microscopy.

Although our understanding of microbiota-host interactions has considerably increased over recent years, there is still an unmet requirement for a deeper understanding of the complex microbiota-gut-brain communication. ASD begins during prenatal life, the least researched and understood of all the developmental stages of ASD. This glaring gap is a major barrier to progress in ASD research and as well as effective treatment. The current state of the art also cannot effectively address more targeted issues, then we would like to shed new light on through the implementation of the presented project.