Fetal Alcohol Spectrum Disorders (FASD) affect individuals whose mothers consumed alcohol during pregnancy. It is the most common non-genetic cause of intellectual disability in children. Characteristic features of FASD include abnormal facial morphology, growth retardation, and impairments in learning, memory, and social behavior. Despite widespread knowledge about the harmful effects of alcohol, particularly on the fetus during pregnancy and breastfeeding, children with FASD continue to be born worldwide. Therefore, it is crucial to educate patients and seek effective treatments and support for affected individuals.

To date, no effective treatment for FASD has been found, neither pharmacological nor non-pharmacological in the form of psychotherapy. Individuals with FASD receive pharmacological assistance, which can only alleviate their symptoms but not cure them. These include medications commonly used for ADHD, depression, or sleep disorders, depending on the individual needs of the patients. Research indicates that the endogenous cannabinoid system plays an important role in learning and memory processes as well as in neuronal myelination.

In the planned study, we will use a rat model of FASD. FASD will be induced by administering alcohol to rats from postnatal days 4 to 9. This period corresponds to the third trimester of human pregnancy, during which the brain undergoes its most intense development. Subsequently, in animals with the developed FASD model, we will administer a compound (JZL-184) that enhances the action of the natural endocannabinoid system. It works by inhibiting the MAGL enzyme, responsible for breaking down one of the endogenous cannabinoids, known as 2-AG. We hypothesize that this therapy may be safer than using exogenous cannabinoids, such as cannabidiol. In the first stage of the project, we will determine the optimal dose of this compound based on behavioral studies.

Next, in the second stage of the research, we will investigate whether providing stimulating environmental conditions improves the cognitive abilities of the animals. For this purpose, we will use an enriched environment in animal studies as the equivalent of non-pharmacological therapy in humans. For children with FASD, this therapy involves providing activities that stimulate their development, such as educational games and toys, puzzles, sensory activities, or other enriching experiences.

The third part of the project will involve combining both procedures. We will evaluate the impact of the enriched environment on enhancing the efficacy of pharmacological therapy using JZL-184. We will examine whether the enriched environment amplifies the effectiveness of JZL-184 with regard to memory and learning processes.

Our research aims to determine how the proposed therapy affects memory and learning in rats and what changes occur in their brains. Analyses of myelination and the endocannabinoid system conducted after each stage will help us better understand the neurobiological mechanisms underlying these processes. The findings may contribute to the development of more effective methods for treating FASD. By combining pharmacological and environmental interventions, this study aims to explore a comprehensive approach that could not only alleviate existing deficits but also prevent the further progression of cognitive and neurological impairments associated with FASD. This project could pave the way for translational research that, in the future, could influence clinical practice and interventions for individuals affected by this disorder.