

According to the World Health Organization (WHO), depression is the fourth most common disease in the world and the leading cause of suicide. Experts predict that by 2030 it will be the most diagnosed disease in the world. The steadily increasing number of depressed patients, as well as the number of suicides, is an alarming factor. Nowadays, the main depression treatment options are psychotherapy combined with pharmacotherapy. Despite the available pharmacotherapy, it is a reluctant treatment option due to the many side effects and lack of knowledge of the exact mechanisms of action and long-term impact. Current efficacy studies of new drugs are mainly based on conducting experiments with animals, which pose many research barriers, *i.e.* different physiological structure or high maintenance costs. Conducting experiments on an animal's open brain is an additionally difficult process that requires specialized equipment and appropriate conditions, and raises many ethical concerns. Traditional two-dimensional (2D) cultures, on the other hand, have a simplified design, making them lack important physiopathological signals. In addition, there is a lack of clearly defined bioanalytical methods that, without the unnecessary steps of collection and preparation of *in vitro* biological samples, allowed rapid and efficient evaluation of potential antidepressants. In view of the problems described above, **the project proposes to use an Organ-on-Chip approach to develop procedures for bioanalytical evaluation of the effects of antidepressants on the neurovascular unit (NVU), considering liver metabolism.**

To achieve the goal, the project will consist of 5 tasks. Initially, the geometry of the NeuroHepaticSync microsystem will be developed to grow a model of the neurovascular unit, considering the presence of the liver model. The next stage will involve optimizing the fabrication of liver tissue and neurovascular unit models in the designed NeuroHepaticSync microsystem. In the third stage, morphological, metabolic and biochemical characterization of the obtained organ models in the NeuroHepaticSync microsystem will be carried out using standard methods. This will be followed by optimization of inflammation generation (depressed state) in the neurovascular unit model and selection of analytical methods to evaluate the resulting changes. The final stage will be to evaluate the effects of potential antidepressants on the neurovascular unit model with and without the presence of the liver tissue model using optimized analytical methods.

The proposed research topic presents an interdisciplinary approach, combining research in biotechnology, bioanalysis, innovative technologies and medical diagnostics. The proposed project will lead to a better understanding of the functioning of the neurovascular unit, as well as open new opportunities in the field of drug testing and treatment of neurological disorders. In addition, the project will create the potential for further research and development of, for example, studies of substances that increase barrier permeability or drugs for other diseases (*e.g.*, Parkinson, Alzheimer).