

DESCRIPTION FOR THE GENERAL PUBLIC

According to the World Health Organization (WHO), brain diseases account for almost 35% of all human diseases. The essence of protecting the brain against harmful factors and at the same time an obstacle to transport drugs is the blood-brain barrier (BBB), which defines the range of molecular exchange between the brain, blood and cerebrospinal fluid. The blood-brain barrier results from interactions of tightly packed endothelial cells lining the blood vessels of the brain with pericytes embedded in the basement membrane, and astrocytes - the major brain component. Conducting pharmacological and preclinical studies to understand the processes leading to neurodegeneration and to protect the brain against them is difficult due to the lack of appropriate animal models modeling neurological diseases in humans. At the same time two-dimensional in vitro cultures are not able to adequately recreate the complex machinery of the blood-brain barrier cellular interactions.

To meet the challenges in searching for new pharmacological strategies, scientists working on this project plan to reconstruct this complex cellular system in the form of a three-dimensional spheroid mimicking mechanisms of molecular response and signaling in the BBB. This system has been already proposed in science, but there is still the lack of reliable and efficient methods which would produce spheroids with a reproducible structure and function. An additional issue to be solved in this project is the development of a comprehensive analytical technology that will provide a set of molecular parameters determining the mechanism of interactions in the cellular aggregate and illustrating the distribution of individual cells. Currently, molecular and imaging techniques are used to determine the presence and concentration of specific proteins, the secretion of signaling mediators or gene sequences require an advanced instrumentation and a complicated, destructive sample preparation. Hence, we propose to combine the novel molecular imaging techniques based on registration of vibrational spectra with a set of markers determined by conventionally used molecular methods. It is also intended to compare function of the normal and diseased blood-brain barrier and to apply model of the novel cell-gene therapy to determine the functional range of the designed model. The gathered knowledge will allow screening potential drugs and pharmacological strategies to treat neurological diseases.