# Ph.D. projects in progress

**1.**

**Mentor:** Mária Deli, Alexandra Bocsik

**Doctoral School:** University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

**Ph.D. student:** Ilona Gróf

**Title of the research topic:** Human lab-on-a-chip models of biological barriers

**Description of the research topic:** New integrated and miniaturized model systems are increasingly used for the study of biological barriers in biomedical research and drug development. Our research group in a close cooperation within the Insitute of Biophysics of BRC has developed a a microfluidic device integrating several functions that was successfully used to the complex investigation of blood-brain, intestinal and lung barrier culture models (Walter et al., 2016). The biochip allows the co-culture of 2 or 3 cell types, the flow of culture medium, microscopy and real-time measurement of the electrical resistance of the cell layers and permeability studies. The goal of the study is to develop new human cell based co-culture models to study the respiratory and intestinal epithelium. We plan to investigate the models of nasal, lung and intestinal barriers in co-culture with endothelial cells in both physiological and pathological conditions in collaboration with groups from the Insitute of Biophysics of BRC, the University of Pécs and the University of Artois, France.

**2.**

**Mentor:** Mária Deli, Fruzsina Walter

**Doctoral School:** University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

**Ph.D. student:** Ana Raquel Santa Maria

**Title of the research topic:** In vitro models of the blood-brain barriers using an integrated microfluidic device

**Description of the research topic:** The prediction of CNS drug distribution in humans is still a challenge in drug discovery and development. Recent advencements in cell culture and microfluidic chip techniques make it possible to develop more complex models to better mimic the barriers of the CNS. The aim of the project is to establish and characterize new models of the CNS barriers using a recently developed lab-on-a-chip device in BRC HAS (Walter et al. 2016). During the project the following major tasks will be completed: (i) establishment and characterization of double and triple co-culture models (endothelial cells, pericytes, astrocytes) of the blood-brain barrier (BBB) using a custom integrated microelectronic device (BBB on a chip); (ii) studying the effect of flow on rat and human

co-culture BBB models. The project will be implemented in the frame of the Brain Barriers Training (BtRAIN) European Ph.D. Training Network (H2020-MSCA-ITN-2015 675619).

**3.**

**Mentor:** Mária Deli, András Harazin

**Doctoral School:** University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

**Ph.D. student:** Lilla Barna

**Title of the research topic:** The blood-brain barrier as a therapeutic target

**Description of the research topic:** Brain capillaries, which form the anatomical basis of the blood-brain barrier, participate in the maintenance of the homeostasis of the nervous system by their influx transporters and physical and chemical defense systems. Solute carriers and and other transporters of cerebral endothelial cells carry nutrients from the blood to the brain, while active efflux pumps block the entry of toxic molecules present in the blood. The defense systems of the blood-brain barrier are damaged in several systemic and neuronal pathologies, like acute pancreatitis, epilepsy or neurodegenerative diseases. In these pathological conditions the function of the transporter and efflux pumps is damaged andf the permeability of the blood-brain barrier is increased. The dysfunction of the blood-brain barrier contributes to further neuronal loss and the aggravation of the diseases. Recently, the blood-brain barrier was identified as as a potential new therapeutic target. In our research group the effects of pathological factors damaging the blood-brain barrier and potential protective molecules are investigated on culture models of the blood-brain barrier.

**4.**

**Mentor:** Mária Deli, Zsófia Hoyk

**Doctoral School:** University of Szeged, Doctoral School of Theoretical Medicine

**Ph.D. student:** Beáta Barabási

**Title of the research topic:** Analysis of blood-brain barrier characteristics in inflammatory conditions using animal models and endothelial cell cultures

**Description of the research topic:** The blood-brain barrier (BBB) is a dynamic interface between the circulating blood and the brain parenchyma. The BBB is formed by endothelial cells that interact with pericytes and astroglial endfeet surrounding brain capillaries. The interendothelial tight junctions of the brain capillaries restrict the penetration of hydrophilic solutes through the paracellular pathway. Consequently, brain nutrients are taken up from the blood and metabolic waste is removed from the brain by membrane transporters of endothelial cells. BBB

dysfunction is often observed in different pathological conditions, the common feature of which is inflammation. However, little is known on the link between different inflammatory factors and the cellular and molecular components of the BBB. Based on our previous results morphological characteristics of the BBB under inflammatory conditions will be analyzed in an animal model, and using an in vitro BBB model. It will be determined which cellular and molecular elements contributing to the barrier function are altered and which inflammatory factors are linked to this change. The better understanding of the interactions between the BBB and different inflammatory factors will contribute to the development of new therapeutic strategies. The project is funded by GINOP and EFOP research grants of the Biological Barriers Research Group.

**5.**

**Mentor:** Mária Deli, Szilvia Veszelka

**Doctoral School:** University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

**Ph.D. student:** Gergő Porkoláb

**Title of the research topic:** Examination of nanoparticles in cell culture models of the blood-brain barrier

**Description of the research topic:** Pharmaceutical treatment of most disorders of the central nervous system (CNS), like neurodegenerative diseases or brain tumors, is far from satisfactory due to the poor penetration of drugs to the brain. Most pharmaceutical drug candidates have a low permeability across the blood-brain barrier. Colloidal drug targeting systems, so-called nanocarriers hold the greatest promise for future clinical application. The aim of our research to design and investigate different biodegradable and biocompatible nanoparticles which can encapsulate hydrophilic or lipophilic therapeutic agents. Targeting nanoparticles with different ligands of nutrient transporters present at the blood-brain barrier can increase the efficacy of drug transport to the brain.

**6.**

**Mentor:** Mária Deli, Fruzsina Walter

**Doctoral School:** University of Szeged, Faculty of Science and Informatics, Doctoral School of Biology

**Ph.D. student:** Judit Vigh

**Title of the research topic:** Investigation of brain organoids and neurovascular cell types in novel microelectronic lab-on-a-chip devices

**Description of the research topic:** Three dimensional cell culture organoid models emerge as new tools in modern in vitro neuroscience to investigate development, pathologies and cell-cell interactions. In our cutting-edge experiments we plan to integrate brain organoids in an already tested and published lab-on-a-chip device (Walter

et al., 2016) and also in novel micro- and bio-electronic models. The goal is to study cellular interactions between the neurovascular unit and brain organoids derived from healthy and diseased tissues. The investigation will lead to the deeper understanding of the pathomechanism of neurodegenerative diseases and the development of future treatments.