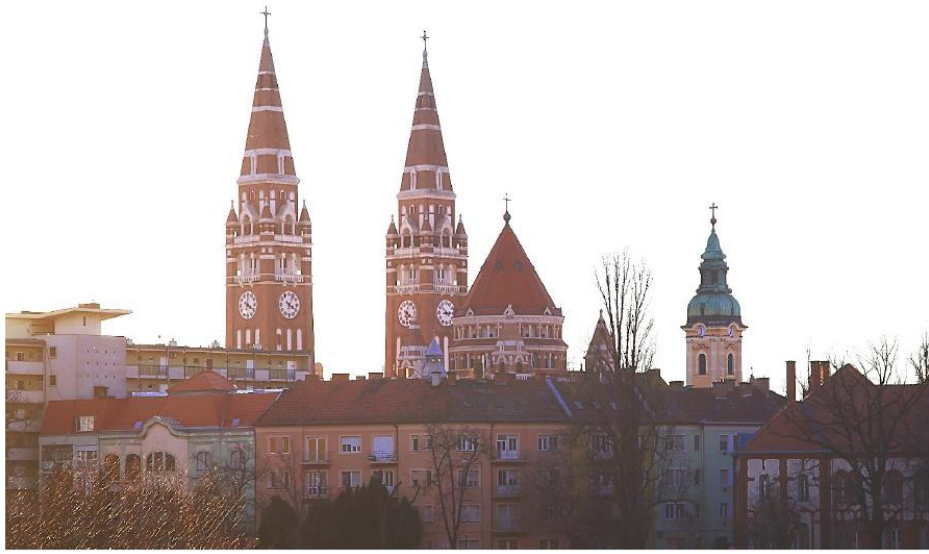




**4th Mini-Symposium on
The Blood-Brain Barrier
from Basic to Clinical Research**

24 March 2022

online meeting on [Zoom platform](#)

Organizers:

Maria A. Deli

Yoichi Morofuji

10:20 ~ 11:20 Session III - Oral presentations

Chair: Andrej Kovac

10:20 (18:20 CET, 02:20 PDT)

Fuyuko Takata (Fukuoka University, Fukuoka, Japan)

Effects of noggin treatment on fibrinogen leakage into brain through a disrupted BBB in a mouse model of traumatic brain injury

10:30 (18:30 CET, 02:30 PDT)

Yuki Matsunaga (Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan)

MAP kinase pathways in brain endothelial cells mediate contrast-induced blood–brain barrier disruption

10:40 (18:40 CET, 02:40 PDT)

Judit Vigh (Biological Research Centre, Szeged, Hungary)

Investigation of the effects of novel ecdysteroids on the blood-brain barrier

10:50 (18:50 CET, 02:50 PDT)

Ilona Gróf (Biological Research Centre, Szeged, Hungary)

Examination of the pentapeptide carrier WYKYW for large protein constructs on blood-brain and epithelial barrier models: intracellular delivery or shuttle action?

11:00 (19:00 CET, 03:00 PDT)

Lilla Barna (Biological Research Centre, Szeged, Hungary)

Investigation of untargeted and targeted magnetic nanoparticles on a human blood-brain barrier model

11:10 (19:10 CET, 03:10 PDT)

Beáta Barabási (Biological Research Centre, Szeged, Hungary)

The effects of pro-inflammatory IL-6 and anti-inflammatory IL-10 on the morphology and function of cultured brain endothelial cells from wild type and ApoB100 transgenic mice

11:20 ~ 11:30 Closing Remarks

Yoichi Morofuji

Session III-5

Investigation of untargeted and targeted magnetic nanoparticles on a human blood-brain barrier model

Lilla Barna^{1,2}, Anikó Szecskó¹, Mária Mészáros¹, Szilvia Veszélka¹, Sándor Valkai¹, András Dér¹,
Mária A. Deli¹

¹ Institute of Biophysics, Biological Research Centre, Eötvös Loránd Research Network, Szeged, Hungary; email: barna.lilla@brc.hu

² Doctoral School in Biology, University of Szeged, Szeged, Hungary

The blood-brain barrier (BBB) represents an active interface between the blood and the brain, which prevents many drugs from entering into the brain. Magnetic nanoparticles (MNPs) can be candidates to increase the brain penetration of pharmaceuticals. They can be designed with different surface coatings and targeting ligands, and delivered by magnetic force. Our aim was to investigate the ability of untargeted and targeted MNPs to cross a human blood-brain barrier culture model with the use of an external magnet.

The human BBB model was established by co-culture of human cord-blood stem cell derived vascular endothelial cells and brain pericytes. Glutathione targeting of red fluorescent starch coated MNPs was performed by biotin neutravidin binding. Cell viability was measured by impedance, MTT assay and double cell nuclei staining. Function of the barrier was tested by electrical resistance (TEER) in cultures and permeability measurements were performed for MNPs and marker molecules. Fluorescently labeled MNPs and immunostained cell junctions were visualized with confocal microscopy.

Magnetic field up to 100 mT was not toxic to endothelial cells. Untargeted or targeted MNPs did not damage endothelial cells up to 300 µg/ml concentration. Both untargeted and targeted MNPs crossed culture inserts without cells, the total amount of MNPs could be recovered from the basal compartments within 60 minutes. Contrarily, only 2% of MNPs passed through the human BBB model. The integrity of the barrier was not changed during the process. Both untargeted and targeted MNPs entered the endothelial cells, but showed different localization as visualized by confocal microscopy. Untargeted MNPs were located consistently in almost all the cells, while targeted MNPs entered only into a subpopulation of cells. The presence of magnetic field did not influence the localization of MNPs.

We demonstrated that magnetic field and MNPs did not influence the viability of endothelial cells. Untargeted and targeted MNPs crossed culture inserts, but their penetration across the human BBB model was very low. MNPs entered into endothelial cells, the localization of untargeted and glutathione-targeted MNPs showed different pattern.

Keywords: human blood-brain barrier model, magnetic nanoparticles, magnetic field

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