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RESEARCH AREA

Investigation of peptide carriers on culture models of biological barriers

Targeted delivery of protein drugs into cells and through biological barriers to achieve a more effective therapeutic effect is an area of intensive research. Several strategies exist already for delivery to the intracellular space, however the drugs that enter by endocytosis are unable to be effective due to entrapment in vesicles or degradation by lysosomes. We are investigating carriers that can be conjugated to a peptide or protein drug to enter cells and avoid lysosomal degradation. The aim of the research is to investigate these peptide carriers in culture models of different biological barriers for the delivery of large biomolecules. In this work, comparative study of several peptide carriers are performed on the culture model of endothelial and epithelial barriers, such as the blood-brain barrier, cornea-, lung-, and intestinal epithelium. In our experiments, we characterize the viability, integrity, and morphological changes of intercellular junctions of the cell layers. We study the intracellular localization of peptide carriers as well as their penetration through cell layers. Furthermore, passage of fluorescent proteins loaded into peptide-targeted nanoparticles through barrier models is tested. The expected results may contribute to the development of new types of carrier systems for the delivery of drugs or biopharmaceuticals across biological barriers, which may contribute to a better cure for diseases.

TECHNIQUES AVAILABLE IN THE LAB

Sterile lab work; In vitro cell culture works; isolation of primary cultures from brain and brain microvessels; double and triple co-culture models of biological barriers; experiments with brain organoids; cell culture models in microfluidic chips; electric resistance measurements of cell layers; cellular uptake and permeability assays; permeability of drugs across culture models; immunohistochemistry; phase contrast, fluorescent and confocal microscopy; spectrofluorometry; toxicity measurements (MTT/LDH tests, double cell nuclei staining, impedance based real-time cell monitoring assay).

SELECTED PUBLICATIONS

Bocsik, A., **Gróf, I.**, Kiss, L., Ötvös, F., Zsíros, O., Daruka, L., Fülöp, L., Vastag, M., Kittel, Á., Imre, N., Martinek, T.A., Pál, C., Szabó-Révész, P., Deli, M.A. (2019) Dual Action of the PN159/KLAL/MAP Peptide: Increase of Drug Penetration across Caco-2 Intestinal Barrier Model by Modulation of Tight Junctions and Plasma Membrane Permeability. **Pharmaceutics** **11**: 73.

Veszélka, S., Tóth, A., Walter, F., Tóth, A.E., **Gróf, I.**, Mészáros, M., Bocsik, A., Hellinger, É., Vastag, M., Rákhely, G., Deli, M.A. (2018) Comparison of a Rat Primary Cell-Based Blood-Brain Barrier Model With Epithelial and Brain Endothelial Cell Lines: Gene Expression and Drug Transport. **Front Mol Neurosci** **11**: 166.

Imre, N., Hetényi, A., Szabó, E., Bodnár, B., Szkalicity, A., **Gróf, I.**, Bocsik, A., Deli, M.A., Horvath, P., Czibula, Á., Monostori, É., Martinek, T.A. (2020) Routing Nanomolar Protein Cargoes to Lipid Raft-Mediated/Caveolar Endocytosis through a Ganglioside GM1-Specific Recognition Tag. **Adv Sci (Weinh)** **7**: 1902621.

Gróf, I., Bocsik, A., Harazin, A., Santa-Maria, A.R., Vizsnyiczai, G., Barna, L., Kiss, L., Fűr, G., Rakonczay, Z. Jr, Ambrus, R., Szabó-Révész, P., Gosselet, F., Jaikumpun, P., Szabó, H., Zsembery, Á., Deli, M.A. (2020) The Effect of Sodium Bicarbonate, a Beneficial Adjuvant Molecule in Cystic Fibrosis, on Bronchial Epithelial Cells Expressing a Wild-Type or Mutant CFTR Channel. **Int J Mol Sci** **21**: 4024.

Katona, G., Sipos, B., Budai-Szűcs, M., Balogh, G.T., Veszélka, S., **Gróf, I.**, Deli, M.A., Volk, B., Szabó-Révész, P., Csóka, I. (2021) Development of In Situ Gelling Meloxicam-Human Serum Albumin Nanoparticle Formulation for Nose-to-Brain Application. **Pharmaceutics** **13**: 646.