CELL CULTURE AND IN VIVO STUDY OF MICROVESICLES FOR DRUG DELIVERY ACROSS BARRIERS

Szilvia Veszelka[1] – Péter Sipos[2] – Lóránd Kiss[1,2] – Alexandra Bocsik[1,2] – Petra Hülper[3] – Piroska Szabó-Révész[2] –Mária A. Deli[1]

[1] Laboratory of Molecular Neurobiology, Institute of Biophysics, Biological Research Centre, Hungarian Academy of Sciences, Temesvári krt. 62, Szeged, Hungary, e-mail: veszelka.szilvia@brc.mta.hu
[2] Department of Pharmaceutical Technology, University of Szeged, Hungary
[3] Department of Pediatrics, University of Göttingen, Germany

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Efficient drug delivery across biological barriers, like the intestinal and blood-brain barriers is a central problem in pharmaceutical treatment of disorders [1]. Most pharmaceutical drug candidates, hydrophilic molecules, biopharmaceuticals, and efflux transporter ligands have a low permeability across barriers. To solve this unmet therapeutical need colloidal drug delivery systems utilizing physiological transporters of the barriers hold a great promise. The aim of our study was to test nanosized, biocompatible and biodegradable vesicles which can encorporate both hydrophilic and hydrophobic drug cargos and present on their surfaces ligands for solute carrier (SLC) proteins. Glucose analogues and amino acids were used to achieve increased specificity and efficacy for drug delivery across barriers. Bilayered microvesicles of non-ionic surfactants, niosomes are able to encapsulate solutes and serve as potential drug carriers. Niosomes with an average hydrodynamical size of 200 nm were prepared containing different ligands and their combinbations, and Evans blue-albumin as a model molecule. Human Caco-2 intestinal epithelial and D3 brain endothelial cells, a model of the blood-brain barrier [2], were used for toxicity measurements by colorimetric methods and real-time cell microelectric sensing, permeability experiments and morphological examinations. The presence of glucose and amino acid ligands on microvesicles increased the uptake of Evans blue-albumin to the cells and its penetration across the cell layers. A kinetic in vivo study in nude mice by eXplore Optix, a near infrared fluorescence time-domain optical imaging demonstrated the elevated accumulation of Evans blue-albumin in the brain after the intravenous injection of glucose analogue and amino acid labeled niosomes. These results indicate that microvesicles labeled with SLC transporter ligands can be used for targeting hydrophilic biomolecules across barriers.

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