Conference abstract SL-19

Evaluation of a Blood-Brain Barrier *in vitro* Model Based on Primary Rat Cells

W. NEUHAUS [1], E. SUBILEAU [2], C. CHESNE [2], D. GRUBER [3], S. TÖGEL [4], W. KLEPAL [3], C. R. NOE [5]

[1] PharmaCon GmbH, Riglergasse 4/5, 1180, Vienna, Austria
[2] Biopredic International, 8-18 rue Jean Pecker, 35000, Rennes, France
[3] Dep. for Cell Imaging and Ultrastructure Res., University of Vienna, Althanstraße 14, 1090, Vienna, Austria
[4] Dep. of Pharm. Techn. and Biopharm., University of Vienna, Althanstraße 14, 1090, Vienna, Austria
[5] Dep. of Medicinal Chemistry, University of Vienna, Althanstraße 14, 1090, Vienna, Austria

E-mail: christian.noe@univie.ac.at (C. R. Noe)

Sci Pharm. 2009; 77: 186 doi:10.3797/scipharm.oephg.21.SL-19

The blood-brain barrier (BBB) maintains the homeostasis between the central nervous system and the blood circulation [1]. Until now, no standard *in vitro* model of the BBB is available. In this contribution a novel BBB *in vitro* model based on primary rat brain microvasculature endothelial cells (RBMEC) and primary rat glial cells (RGC) is introduced. The cells were isolated from Wistar rats and were provided by the company Biopredic Int. RBMEC were co-cultured with RGC in a 12-well Transwell system. The development of the barrier was monitored by the measurement of the transendothelial electrical resistance (TEER). The RBMEC *in vitro* model was used for several studies after app. 8-10 days in culture reaching the maximum TEER (> 100 Ohm*cm^2). Barrier integrity of two different batches was characterized by transport experiments with the paracellular marker APTS-dextran [2]. Following transport studies with several drugs (benzodiazepines, NSAIDs, …) revealed significant differences between paracellular and transcellular transport routes. Scanning as well as transmission electron microscopy confirmed the monolayer structure of RBMECs and the formation of tight junctions. Application of cytokines as TNF-α and IL-6 caused a decrease of TEER of RBMEC layers. Additionally, up – or downregulation of mRNA levels of adhesion molecules as well as of tight junctional proteins determined by RT^2-PCR proved the usability of the novel model for studies concerning inflammatory processes. In conclusion, compared to other BBB *in vitro* models, the introduced model exhibited significantly increased tightness, a greater range to distinguish between the transport of several drugs and a higher sensitivity to inflammatory stimuli.

[1] Abbott NJ, Rönnbäck L, Hansson E. Astrocyte-endothelial interactions at the blood-brain barrier. Nature Rev Neurosci. 2006; 7: 41–53. doi:10.1038/nrn1824

[2] Neuhaus W, Plattner VE, Wirth M, Germann B, Lachmann B, Gabor F, Noe CR. Validation of in vitro cell culture models of the blood-brain barrier: Tightness characterization of two promising cell lines. J Pharm Sci. 2008; 97: 5158–5175. doi:10.1002/jps.21371

Presented at the 21st Scientific Congress of the Austrian Pharmaceutical Society April 16th to April 18th 2009, Vienna, Austria.