

A Short Note on An in vitro Model for Blood Brain Barrier Permeation

Abstract

The ability to permeate across the blood brain barrier (BBB) is essential for drugs acting on the central nervous system (CNS). Thus, systems that allow rapid and inexpensive screening of the BBB-permeability properties of novel lead compounds are of great importance for speeding up the drug discovery process in the CNS-area. We used immortalized porcine brain microvessel endothelial cells (PBMECIC1-2) to develop a model for measurement of blood-brain barrier permeation of CNS active drugs. Investigation of different cell culture conditions showed, that a system using C6 astrocyte glioma conditioned medium and addition of a cyclic AMP analog in combination with a type IV phosphodiesterase inhibitor (R020-1724) leads to cell layers with transendothelial electrical resistance values up to 300 n.cm². Permeability studies with U- [4~]sucrose gave a permeability coefficient P, of 3.24 + 0.14 x 10⁻⁴ cm/min, which is in good agreement to published values and thus indicates the formation of tight junctions in vitro.

Keywords: Blood brain barrier • in vitro model • immortalized porcine • brain • microvascular endothelial cells

Introduction

The ability to permeate across the blood brain barrier (BBB) is important for medicine performing on the central system (CNS). The transfer of compounds from the blood into the brain opening fluid is regulated by the operate of brain capillary epithelium cells. in contrast to peripheral epithelium, brain microvessel epithelium cells square measure characterised by the presence of tight living thing junctions, 320 R. B a u e r et al.: clearance curve of the PBMECIC1-2 culture was denoted postscript [1]. Whereve postscript is that the product of permeability x extent given in pl/min (or 10⁵ cm³/min). The slope of the clearance curve for the management filter was denoted terrorist organization. The postscript worth for the epithelium cell monolayer postscript, was calculated from: $IPS = IPS_f - IPS_s$. The PS, values were divided by the extent of the Falcon BIOCOATTM culture inserts (4,2 cm²) to come up with the epithelium permeableness constant letter, in centimeters per minute Influence of seeding density on the TEER worth Rubin et al. recommended a density of thirty six.000 cells/cm² for porcine brain epithelium cel1s.13 Thus, cells were plated at a seeding density of forty.000 cells/cm² and eighty.000 cells/cm² and fully grown in conditioned medium as delineate higher than. The time course of the individual TEER values were measured. As shown in Figures 1a and one b, a seeding density of eighty.000 cells/cm² results in slightly improved TEER values and remarkably higher dependableness (6 freelance experiments). Higher seeding densities (up to 250.000 cells/cm²) didn't result in an additional improvement of each TEER and dependableness. Influence of various culture conditions [2]. The positive result of things secreted by astrocytes on the barrier adjustment of brain epithelium cells is well do~urnented. '~T~h'u~s~, 's~ev eral coculture-based systems square measure rumored. To avoid the experimental issues of cocultures however still bring home the bacon the positive effects of astrocytes, astrocyte

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conditioned medium (ACM) is used as an alternate.* Figure two shows the time course of the TEER for cells fully grown exclusively in ACM obtained from rat C6-glioma cells vs. those for cells fully grown [3].

Description

The ability to permeate across the blood brain barrier (BBB) is important for medicine performing on the central system (CNS). The transfer of compounds from the blood into the brain opening fluid is regulated by the operate of brain capillary epithelium cells. in contrast to peripheral epithelium, brain microvessel epithelium cells square measure characterised by the presence of tight living thing junctions, 320 R. B a u e r et al.: clearance curve of the PBMEC1-2 culture was denoted postscript,, wherever postscript is that the product of permeability x extent given in pl/min (or lo5 cm3/min) [4]. The slope of the clearance curve for the management filter was denoted terrorist organization. The postscript worth for the epithelium cell monolayer postscript, was calculated from: $IPS = \frac{PS}{A}$, -IPSf The PS, values were divided by the extent of the Falcon BIOCOATM culture inserts (4,2 cm²) to come up with the epithelium permeableness constant letter , in centimeters per minute Influence of seeding density on the TEER worth Rubin et al. recommended a density of thirty six.000 cells/cm² for porcine brain epithelium cel1s.l3 Thus, cells were plated at a seeding density of forty.000 cells/cm² and eighty.000 cells/cm² and fully grown in conditioned medium as delineate higher than. The time course of the individual TEER values were measured. As shown in Figures la and one b, a seeding density of eighty.000 cells/cm² results in slightly improved TEER values

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Conflict of Interests

None

Acknowledgments

None

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