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SCUOLA DI MEDICINA



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24th International Symposium
on Signal Transduction at the
Blood-Brain Barriers

PROGRAM AND
ABSTRACT BOOK

Bari (ITALY)
September, 21-23 2022

SJH

cARLA: A SMALL MOLECULAR COCKTAIL FOR ROBUST INDUCTION OF BLOOD-BRAIN BARRIER PROPERTIES

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Introduction: To bridge the translational gap between animal studies and clinical trials, human blood-brain barrier (BBB) models are needed. Current *in vitro* BBB models, however, do not recapitulate either the tightness or the endothelial identity of the human BBB.

Aims: Recently, the role of several signaling pathways were described in BBB development. We hypothesized that targeting multiple pathways simultaneously could lead to a better and more robust induction of BBB properties in cultured human brain endothelial cells.

Methods: We used a screen of small molecular compounds to identify combinations that increase the impedance of endothelial monolayers derived from human stem cells. As validation, TEER and permeability measurements were performed in vascular endothelial cells co-cultured with brain pericytes. Differences in mRNA expression were quantified by MACE-seq and visualized by confocal microscopy at the protein level. To measure the efflux pump activity and negative surface charge of endothelial cells, we performed a bidirectional transport assay of rhodamine 123 and zeta potential measurement by dynamic light scattering, respectively.

Results: We identified a combination of small molecules targeting three different cellular signaling pathways, which we termed cARLA. cARLA treatment increased the impedance and TEER of the human BBB model and decreased the permeability of fluorescein and albumin in an additive fashion. At the mRNA, protein and functional level, we found that cARLA treatment robustly induced a complex BBB phenotype by upregulating the level of tight junction proteins, efflux pump activity and glycocalyx density in endothelial cells.

Discussion: Our data suggests that cARLA treatment robustly induces complex BBB properties in human stem cell-derived endothelial cells.

- 06** 17.30 - 17.45 Blood-brain barrier organoids and brain diseases - modelling cerebral malaria and Lyme neuroborreliosis induced barrier dysfunction
Yvonne Adams, Anja R. Jensen (Denmark)
- 07** 17.45 - 18.00 cARLA: a small molecular cocktail for robust induction of blood-brain barrier properties
Gergo Porkolab (Hungary)
- 08** 18.00 - 18.15 iPSC-Derived neurovascular unit model to study neuroinvasion of parechovirus A3
Pamela E. Capendale (The Netherlands)
- 09** 18.15 - 18.30 From DNA methylation to protein function: Selection and evaluation of regulated targets in human cerebral ischemia *in vitro* models of the blood-brain barrier
Winfried Neuhaus (Austria)

18.30 - 19.30 POSTER SESSION

19.30 Welcome Aperitivo

Thursday, September 22, 2022

SESSION 3

08.30 - 10.15

The Brain Barriers in Neuroinflammatory and Neuroinfectious Diseases

Chairs: Elga de Vries (The Netherlands), Egle Solito (United Kingdom)

- 08.30 - 09.00 Plenary Lecture**
Sara Salinas (France)
Viral interactions with brain barriers: a focus on emerging neurotropic viruses
- 010** 09.00 - 09.15 B-cells and where to find them in multiple sclerosis
Carla Rodriguez-Mogeda (The Netherlands)
- 011** 09.15 - 09.30 Interaction of the hypervirulent CC17 Group B *Streptococcus* with choroid plexus cells of the blood-cerebrospinal fluid barrier
Julie Guignot (France)
- 012** 09.30 - 09.45 Rapamycin rescues loss-of-function in blood-brain barrier transmigrated regulatory T cells
Paulien Baeten (Belgium)
- 013** 09.45 - 10.00 Tick-borne encephalitis - mouse and human research model
Martin Palus (Czech Republic)
- 014** 10.00 - 10.15 The effect of astrocyte-derived fatty acid-binding protein 7 on blood-brain barrier breakdown in LPS-induced sepsis in mice
Deniz Altunsu (Turkey)
- 10.15 - 10.45 Coffee break