

Development of new perfusion system on human *in vitro* Blood-Brain Barrier biochip for toxicity assessment

Yoann Müller¹, Casimir de Rham¹, Loris Gomez Baisac¹, Luc Stoppini^{1,2} and Adrien Roux^{1,2*}

¹ Tissue Engineering Laboratory, HEPIA/HES-SO, Geneva, Switzerland
² Swiss Centre for Applied Human Toxicology, SCAHT, Basel, Switzerland

*E-mail: adrien.roux@hesge.ch

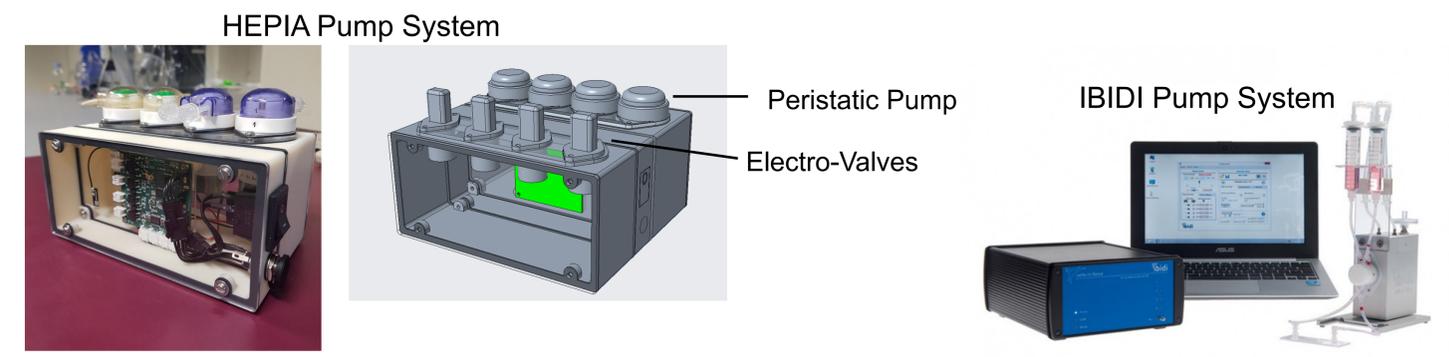


Introduction

The latest developments in *in vitro* Blood-Brain Barrier (BBB) model use the powerful of human pluripotent stem cells origin (hiPS, cord blood cells) and recent cell culture technics (3D culture and co-culture). Development of new technical tools mimic physiological conditions such as shear stress on endothelial cells or continuous renewal of medium. Specific readouts such as Trans-Endothelial Electrical Resistance (TEER), permeability coefficient (P_{app}) and immunolabelling are typical parameters to characterize the BBB. Combination of biological, technical and readouts will lead to "next generation OoC".

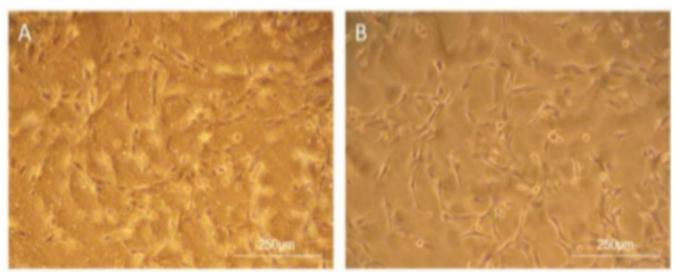
Material & Methods

Our in-house perfusion system is composed of 4 peristaltic pumps and 4 valves allowing us to perform up to 4 experiments simultaneously. This platform can be installed inside the incubator and remotely control by Bluetooth with a user-friendly graphical user interface (GUI). We used the commercial IBIDI pump system to set up and validate our in-house perfusion system. Two human BBB cells type were used for the validation; hCMEC/D3 and CD34⁺ derived cells.

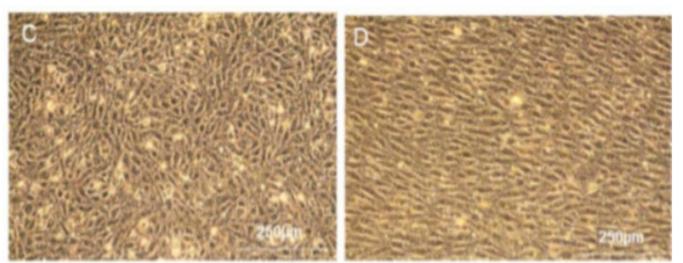


Results

Cells Visualization and Morphology

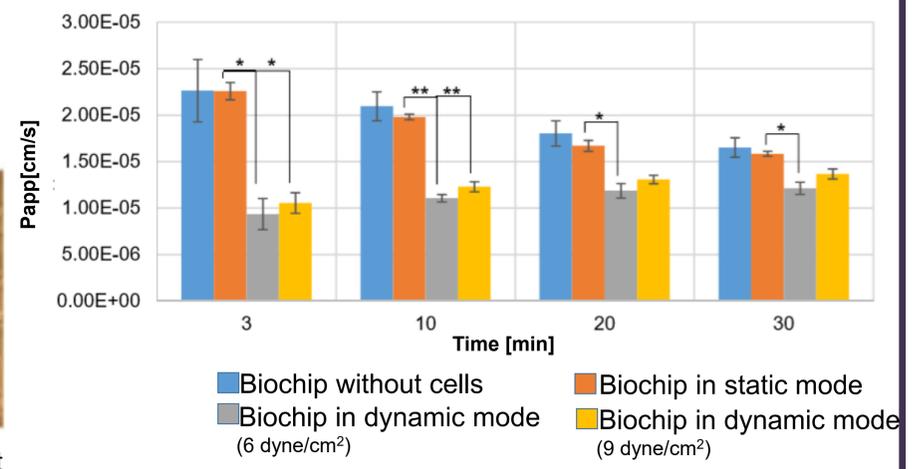


Biochip containing simultaneously confluent endothelial cells situated in the upper chamber of the biochip (A), and pericytes cells situated in the lower chamber of the biochip (B).

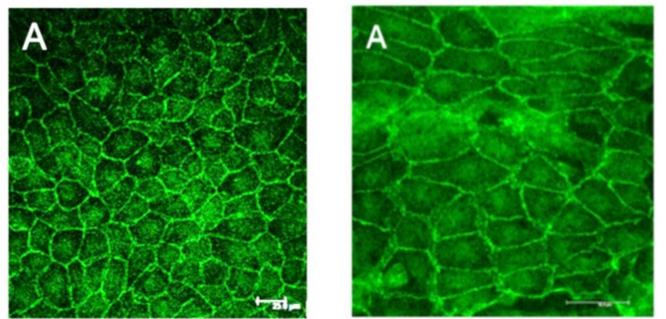


Confluent endothelial cells in a static mode (C) versus in a dynamic mode (9 dyne/cm²) (D).

Coefficient of Permeability (P_{app})

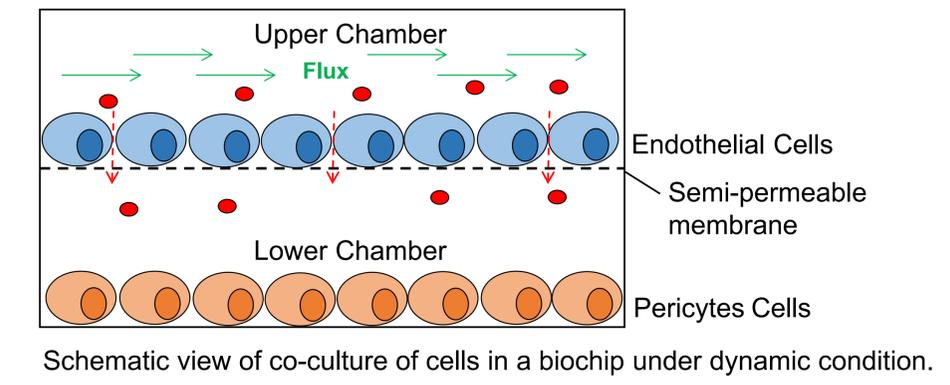
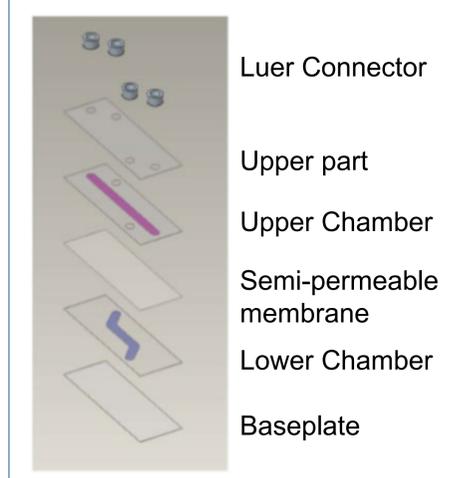


Immunofluorescence



Expression of ZO-1 by endothelial cells in a static mode (left) versus in a dynamic mode (right).

Biochip Diagram



Conclusion

We have developed biochip suitable for *in vitro* BBB model, which can be also used in any other biological cellular barrier with any perfusion system. We have shown that our peristaltic perfusion give similar results compared to the commercial IBIDI pump. With our *in vitro* platform, specific molecules or toxin can be tested and results can be observed using classical technics such as TEER, P_{app} or immunofluorescence. Implementation of the TEER in the biochip is ongoing development.