Model of Nanoparticles Transport across the human Blood-Brain-Barrier Microvasculature

Sharon WL Lee[1,2,3], Marco Campisi[4], Tatsuya Osaki[5], Luca Possenti[6], Giulia Adriani[3], Clara Mattu[4], Roger D. Kamm[6], Valeria Chiono[4]

[1] Singapore-MIT Alliance for Research & Technology, Singapore.

[2] NUS, Yong Loo Lin School of Medicine, Singapore.

[3] Singapore Immunology Network, A*STAR, Singapore.

[4] Dept. of Mechanical & Aerospace Engineering, Politecnico di Torino, Italy

[5] Dept, of Chemistry, Materials & Chemical Engineering, Politecnico di Milano, Italy.

[6] Dept. of Mechanical Engineering, Massachusetts Institute of Technology, USA.

The blood-brain-barrier (BBB) represents a near-impenetrable hurdle against the delivery of therapeutic to the central nervous system. Since only small compounds can cross the BBB, this reduces the treatments available for neurodegenerative diseases and cancer[1]. Polymer nanoparticles (NPs) have emerged as a potential solution for delivering therapeutics across the BBB to brain targets. The development of in vitro methods for quantifying NP transport behavior represents an invaluable tool for assessing therapeutic delivery capabilities[2]. In this work, we modelled NP transport across a previously established 3D *in vitro* microfluidic model of the human BBB, where a self-assembled microvasculature from human induced-pluripotent stem cell-derived endothelial cells, brain pericytes and astrocytes are supported within an extracellular matrix and fibrin gel[3]. Differences in NP transport were observed between commercially available polystyrene and in-house produced polyurethane NPs. The platform was also capable of elucidating the effect of surface-grafted human holo-transferrin, an attractive brain-associated ligand, on NP transport across the BBB. Importantly, a pre-clinical model and protocol are presented for reliably testing the transport capabilities of nanocarriers, with the aim to optimize their design for therapeutic delivery across the human BBB.

References

1. Pardridge, W. M. *Expert Opin. Drug Deliv.* 5247, 1–13 (2016).
2. Crawford, L. *et al, J. Control. Release* 240, 251–266 (2016).
3. Campisi, M. *et al*. *Biomaterials* 180, 117–129 (2018).

Funding

Following funds are acknowledged: NRF, SMART BioSyM IRG (SWLL, RDK); BIOMODE, Compagnia San Paolo (MC, VC, RDK); A. and E. Rocca Foundation (LP); EU Horizon 2020 program MSCA, 658665 (CM); NSF, EBICS (CBET-0939511) (TO, RDK).