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

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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 cancer¹. 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 capabilities². 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 gel³. 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

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