Internship Proposal

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Proposal At: 2024-01-24

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Project Title:
Blood brain barrier (BBB) permeability and uptake studies of novel lipid nanoparticles (LNPs) under physiological and inflammatory conditions

Level:

Master Student

Project Summary:

The blood brain barrier (BBB) shields the brain against drug therapeutics via paracellular, transcellular, transporter, and extracellular matrix proteins. (1) In vitro models used to study BBB permeability and cellular uptake of drugs and nanoparticles rely on the use of plastic inserts coated with different proteins, e.g. collagen type I, Matrigel, that are absent at the BBB BM level. Our group has developed thin membranes by interfacial self-assembly between peptide amphiphiles (PAs) and hyaluronic acid (HA) resembling the nanostructure of BMs. (2,3) We use this in vitro BBB model as a screening platform to study LNPs and pharmacological drugs BBB uptake and permeability under physiological and inflammatory conditions.

We aim to investigate and quantify the uptake and permeability of novel LNPs (already characterized) on the developed BBB cellular model. Results will contribute to the optimization of LNPs formulation to enhance drug delivery into the central nervous system.

Work to be developed by the student:

Culture of human brain endothelial cells on PA/HA BMs under physiological and inflammatory induced conditions. Cell characterization (cell staining and immunofluorescent assays). Quantify LNPs uptake in the BBB model (characterization and quantification of cellular uptake by flow cytometry and confocal microscopy) both under physiological and pathological scenarios.

Live-cell imaging to access and quantify the permeability of the BBB model.

References:

1- MG Barbato, RC Pereira, H Mollica, AL Palange, M Ferrreira, P Decuzzi, A permeable on-chip microvasculature for assessing the transport of macromolecules and polymeric

nanoconstructs, J. Colloid Interface Sci, 2021

2- X Pang, W Li, L Chang, JE Gautrot, W Wang, HS Azevedo, Hyaluronan (HA) immobilized on surfaces via self-assembled monolayers of ha-binding peptide modulates endothelial cell spreading and migration through focal adhesion, ACS Applied Materials & Interfaces 13 (22), 2021

3- DS Ferreira, Y-A Lin H Cui, JA Hubbell, RL Reis, HS Azevedo, Molecularly Engineered Self-Assembling Membranes for Cell-Mediated Degradation, Adv Healthc Mater, 2015

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