ISTITUTO ITALIANO
DI TECNOLOGIA

PHD Neurosciences, curriculum “Neurosciences and Neurotechnologies, XXXVII cycle
Project title:

Engineering the blood-brain barrier: regulation of the crossing of molecules and nanomaterials through the transcellular and paracellular pathways

Tutors: Valentina Castagnola and Fabio Benfenati

The project involves the development of blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier (BCSFB) models with increasing complexity, from brain endothelial monolayer to co-cultures, 3D organoids, and microfluidic systems. These models will be employed to study different complementary aspects of the barriers’ functionality and integrity, such as the expression of thigh-junction proteins that are known to seal the paracellular spaces.
The interactions of BBB and BCSFB with carbon-based nanomaterials will be evaluated in terms of toxicology and nanomaterials capability for barrier crossing through transcellular pathways. In parallel, it will be investigated the possibility to selectively and reversibly modulate the opening of tight paracellular spaces for therapeutic purposes. In a second phase, the project aims to develop efficient molecular tools to increase glucose transport across the BBB in Glut1-deficiency (GLUT1DS). Glucose transporter type 1 (Glut1) is a critical protein allowing glucose efflux to the brain through the BBB. Monoallelic or bi-allelic mutations in the Glut1 encoding gene - SLC2A1 - result in a clinical spectrum of neurological disorders, including very rare and highly severe autosomal recessive De Vivo Syndrome and relatively common autosomal dominant conditions, typically featuring intractable seizures, intellectual disability, ataxia, and dystonia, starting from infancy. Even modest increases in glucose transport through the BBB are expected to be clinically beneficial in this context. Transient permeabilization of the BBB will be explored using inhibitory peptides for a key tight-junctions component, Claudin-5. To model GLUT1 deficiency, human brain endothelial cell line (hBMEC/D3) will be genetically modified, or brain endothelial cells derived from patients’ induced pluripotent stem cells (iPSCs) will be used. The efficacy of the treatment will be assessed using biophysical readouts such as the measurement of transendothelial electrical resistance or apparent permeability of fluorescent probes.
The successful and ideal candidate is a highly motivated scientist with a strong teamwork attitude and interest in smart material interfaces with cells and tissues. She/he should have a master degree in Life Sciences and/or Tissue Engineering (Medicine, Bioengineering, Biology, Pharmacy, Biotechnologies, or similar) and a good background in cell-material interfaces.
For further information, please contact dr. Fabio Benfenati (fabio.benfenati@iit.it) and dr. Valentina Castagnola (valentina.castagnola@iit.it).