



## Simulation and experimental development of blood brain barrier Organ on Chip

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### Abstract:

Nanotechnology is a cutting-edge field that extends different possibilities for the study and treatment of different diseases. In this work the most widespread neurodegenerative disease, Alzheimer disease (AD), has been studied under Blood Brain Barrier (BBB) in vitro model. An alternative animal-free in vitro model has been developed for a low cost, easy to work system that simulate the main drug access to the brain, the BBB, by means an Organ-on-a-chip devices. Two different 3D BBB-on-a-chip configurations has been studied, optimized and compared: the sandwich and the lateral platforms. The sandwich configuration was fabricated in a multilayer fashion, integrating two perpendicular channels separated by a 1  $\mu\text{m}$  pores polycarbonate membrane. Meanwhile the lateral configuration was fabricated in a horizontal design with parallel channels separated by 100  $\mu\text{m}$  distances stacks. In the second channel a 3D hydrogel is inserted as a membrane. Photolithographed electrodes were included in the design in each of the channels to measure the BBB permeability by Transepithelial/transendothelial electrical resistance (TEER). COMSOL Multiphysics was used to simulate fine elements of both configurations, considering the liquid flow, pressure and volume of liquid crossing the membrane, shear stress and the electrical field for both configuration to study, which is on theory the most efficient strategy. Lateral BBB-on-a-chip platform was tested experimentally, fabricating the chips and cell seeding it with a tri-culture of first; human astrocytes and pericytes inside the hydrogel in the second channel, to simulate the brain interstitial fluid (ISF) and then endothelial cells in the first channel to growth up the vascular barrier generated by this cells. Confocal fluorescence microscope was used in combination with immunostaining to characterize the formed cells barrier and to show the correct development of tight junctions between the adjacent brain endothelial cells.

### Biography:

Dr. Mir received the Degree in Chemistry in 1998 and in 2006 her PhD in biotechnology. She realized different predoctoral stages in Greece and UK. From 2007, she held a postdoctoral position in Max Planck Institute, Germany. Since 2008, she joins the Institute for Bioengineering of Catalonia (IBEC), as Senior CIBER researcher, combined with her teaching as



associate professor in the University of Barcelona. Along her carrier she was managing European, National and industrial research projects, supervising PhD students and collaborating in congresses as scientific committee. Her main interests are electrochemical biosensor, point-of-care technologies, implantable-sensors and organ-on-a-chip for biomedical applications.

### Recent Publications:

- L Rivas, S Dulay, S Miserere, L Pla, S Berdún-Marín, J Parra, E Eixarch, E Gratacós, M Illa, M Mir<sup>✉</sup>, J Samitier<sup>✉</sup> (Equally senior contribution) Micro-needle implantable electrochemical oxygen sensor: ex-vivo and in-vivo studies, *Biosens. & Bioel.* 2020, 153, 112028-112036
- Perez, J.; Dulay, S.; Mir, M.\*; Samitier, J. Molecular architecture for DNA wiring. *Biosensors & Bioelectronics.* 2018, 121, 54 - 61.
- Gallego, I.; Manning\*, B.; Prades, J.D.; Mir, M.; Samitier, J.; Eritja, R. DNA-Origami-Driven Lithography for Patterning on Gold Surfaces with Sub-10 nm Resolution. *Advanced Materials.* 2017, 29 (11), 1-7
- IB Tahirbegi; WA Pardo, M Alvira, M Mir, J Samitier, Amyloid A $\beta$ 42, a promoter for magnetite nanoparticles formation in Alzheimer's disease, *Nanotechnology*, 2016, 27, 465102-465109
- S Teller, IB Tahirbegi, M Mir, J Samitier, J Soriano, Magnetite-Amyloid $\beta$  deteriorates activity and functional organization in an in vitro model for Alzheimer's disease, *Scient. Rep.* 26 (5), 2015, 17261-16.

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