# Development of a vascularized *in vitro* model of neuroinflammatory and cancerous pathologies

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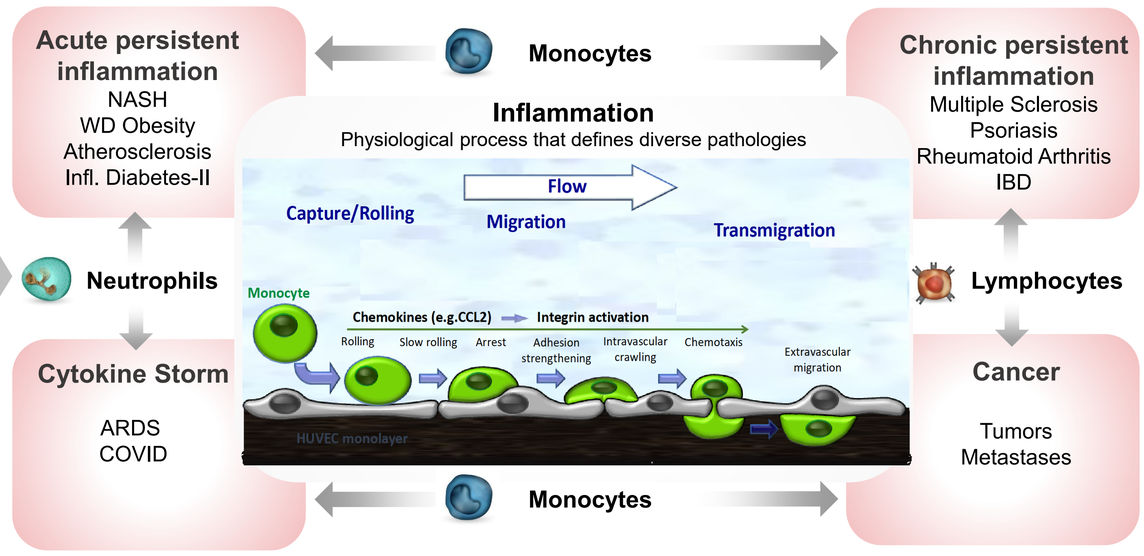
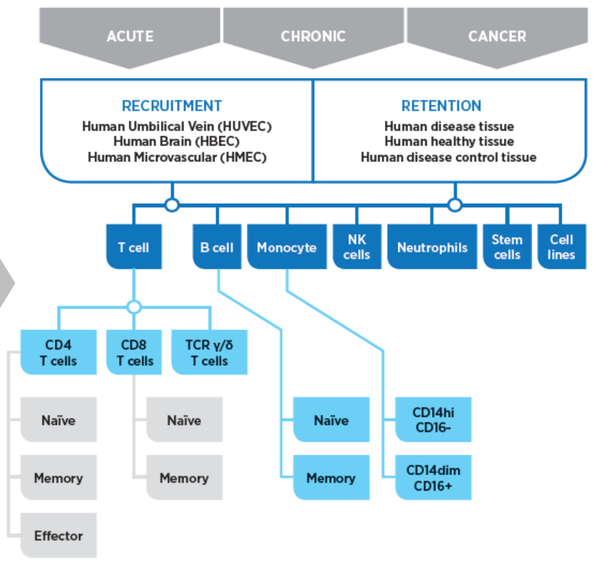
***Introduction*** *: Drug development is a complex and costly process with many hurdles. Indeed, only 5-10% of drugs that enter the preclinical development proceed to clinical trials and, of those, only 10% enter the market. These low success rates are explained by the difficulty in translating findings from animal research to clinical application, due to species differences, low relevance of animal models, complexity of human disease and ethical concerns in animal experimentation. To overcome these obstacles, we propose the development of a human-based and biologically relevant in vitro fluidic Microphysiological System (MPS) to model neuroinflammatory and cancerous pathologies, and usable for preclinical drug screening. With such platform, drug efficacy will be quantified under flow conditions with circulating human immune cells using proprietary methods established at MesenFlow.*

## What can MesenFlow test?

The following assays and cell types have been established by MesenFlow using single chamber HUVEC flow assays



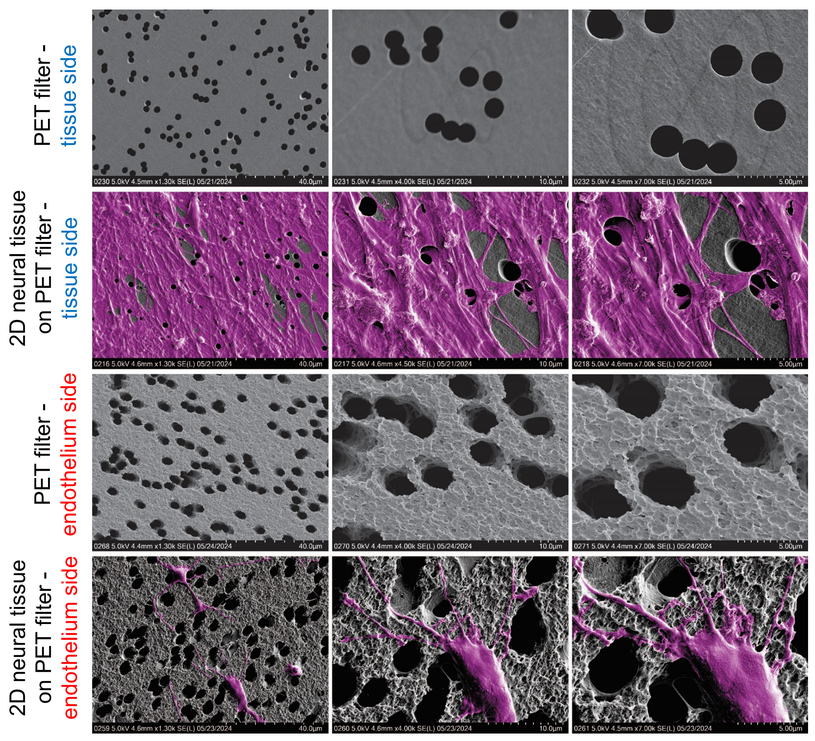

***Biology and Technology*** *: MPS developed by HEPIA for MesenFlow Technologies is composed of two fluidic chambers separated by a porous membrane, thereby allowing co-culture of human blood vessel-like endothelial cells and organoid-like neural tissue.*

Cultured neural tissue express neuronal, glial and synaptic markers. Scanning electron microscopy confirmed such tissue protrudes through the membrane, indicating physical contacts between the endothelium and neural tissue compartments.

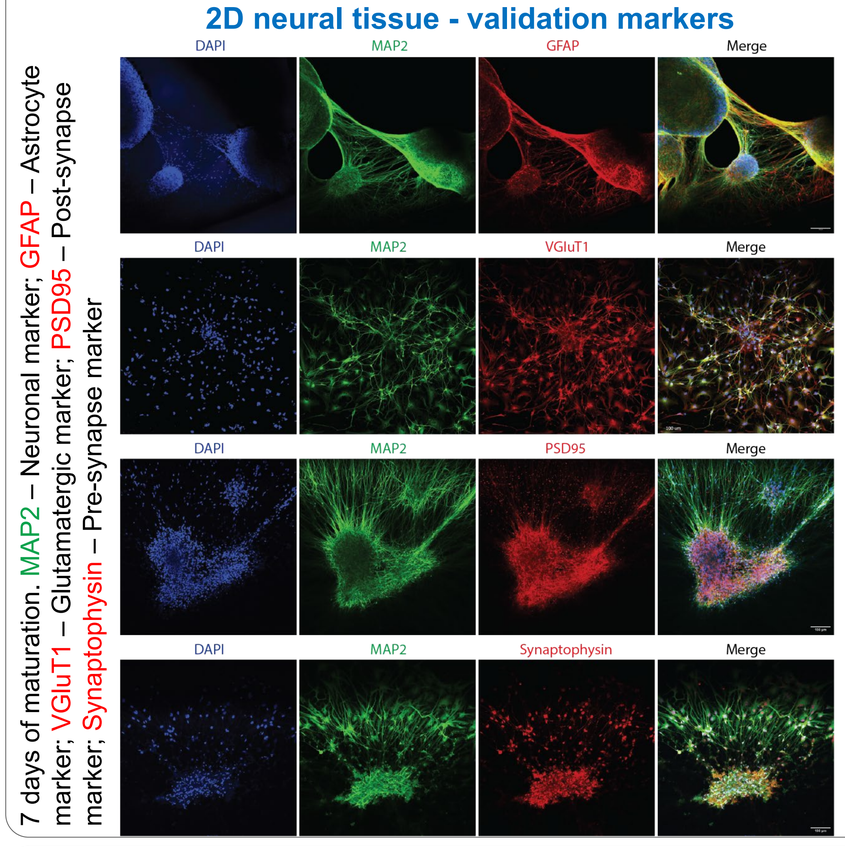
The fluidic and transparency properties of the MPS enable the assessment of human immune cell transmigration across the endothelial cell barrier, under flow conditions.

The MPS prototype has been further multiplexed to support six different co-cultures, where we will be able to establish healthy, inflammatory and/or cancerous neural pathological vascularized models within the same MPS.

### Cell-cell contact between both chambers




### 2D neural tissue - validation markers

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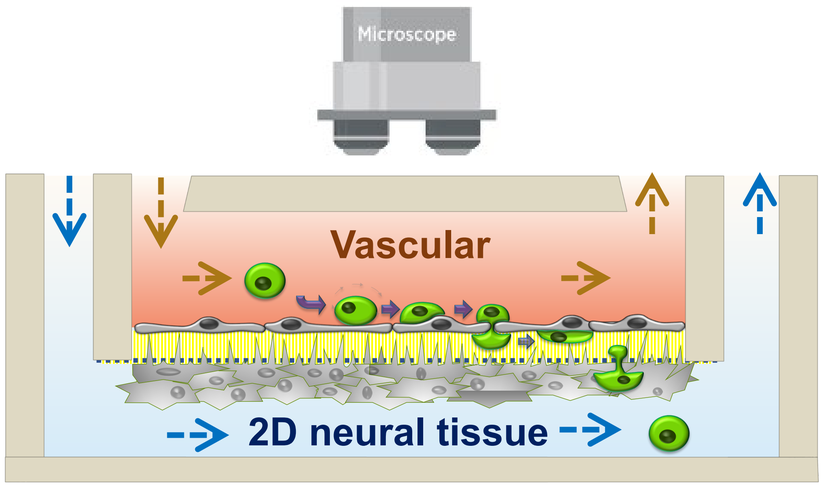
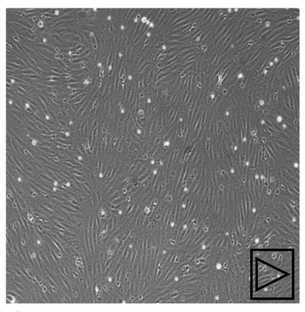



Dual Chamber – 3 µm pore PET filter
Optimization of co-culture on MPS ongoing

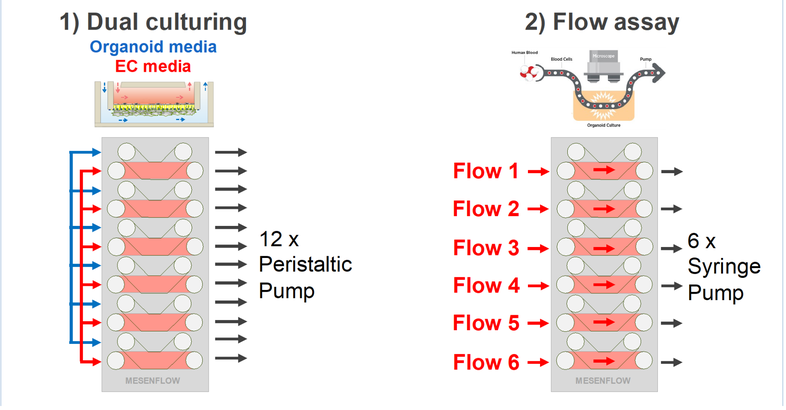
### Imaging profile for captured and migrated leukocytes in MPS validated for automated AI analysis



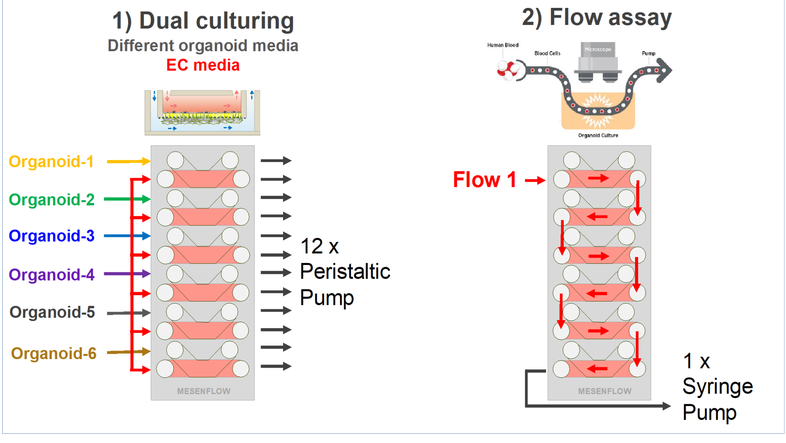
See the video sequence at poster session

Analysis
Cell Counts
FACS

### Strategy-I: Multi-throughput – Screening $IC_{50}$ values



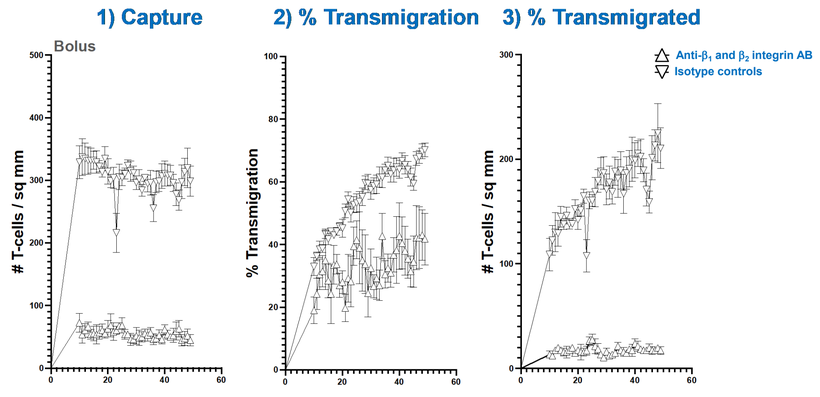

### Strategy-II
### Multi-organoid - physiological modelling
### Tissue targeting of drugs and BBB penetration




### AI counts (validation in MPS ongoing)

- HUVECs stimulated with TNF-a
- T-cell recruitment assay under flow (single chamber)


Capture & transmigration timecourse measurements made using proprietary AI platform developed by MesenFlow




***Conclusions*** *: HEPIA has built a multiplexed MPS prototype that will enable up to six different vascularized healthy, inflammatory, and/or cancerous neural pathological conditions models to run in parallel used by MesenFlow. Additionally, AI-based algorithms allow fast and accurate data acquisition and analysis. Multiplexing in this way increases the number of human leukocyte trafficking models and data acquisition throughput. We envision that the use of such a MPS for preclinical drug screening could have significant impact in reducing the costs and number of animals involved in drug development.*

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