

# A photoablation-based Vessel-on-a-chip system to elucidate human perivascular macrophages differentiation & function

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## The Vascular Gatekeepers

Tissue-resident macrophages are a heterogeneous immune cell population with specific functions dependent on their tissue of residence and microanatomical niches. **Perivascular macrophages (PvMφ)** are a conserved LYVE1+ FOLR2+ TIMD4+ subset of interstitial macrophages residing alongside blood vessels in multiple organs [1]. PvMφ have been shown to **sample blood content** [2] and to be involved in various pathological contexts such as infection and cancer. Yet, the **environmental signals** required for the **establishment of their phenotype** and the **precise blood sampling mechanisms** remain poorly understood. To address these questions, we aim to design and modulate a Vessel-on-a-chip (VoC) *in vitro* system [3] to better understand (1) how these macrophages differentiate to acquire their specific identity and (2) explore their blood sampling function in physiological and pathological settings.

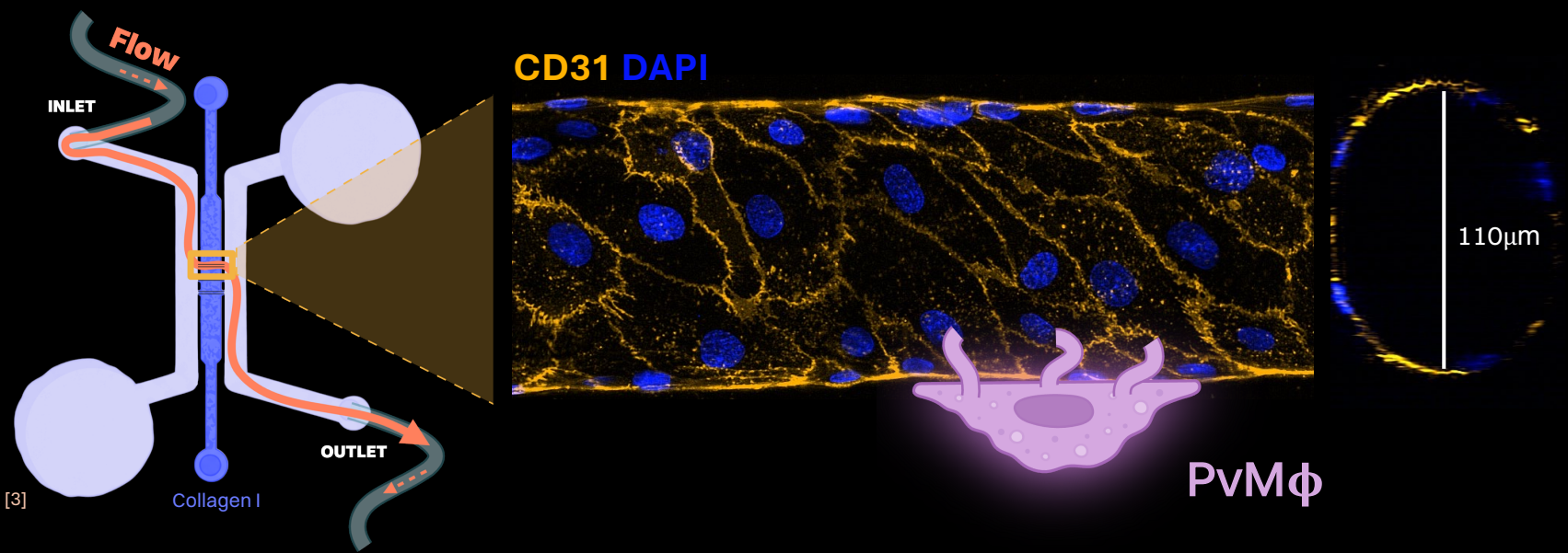
## Aims & Hypothesis

- Monocytes can extravasate from the VoC
- PvMφ identity can be acquired by circulating monocytes under particular niche signals
- PvMφ protrude through the endothelium, acting as sentinels for the bloodstream



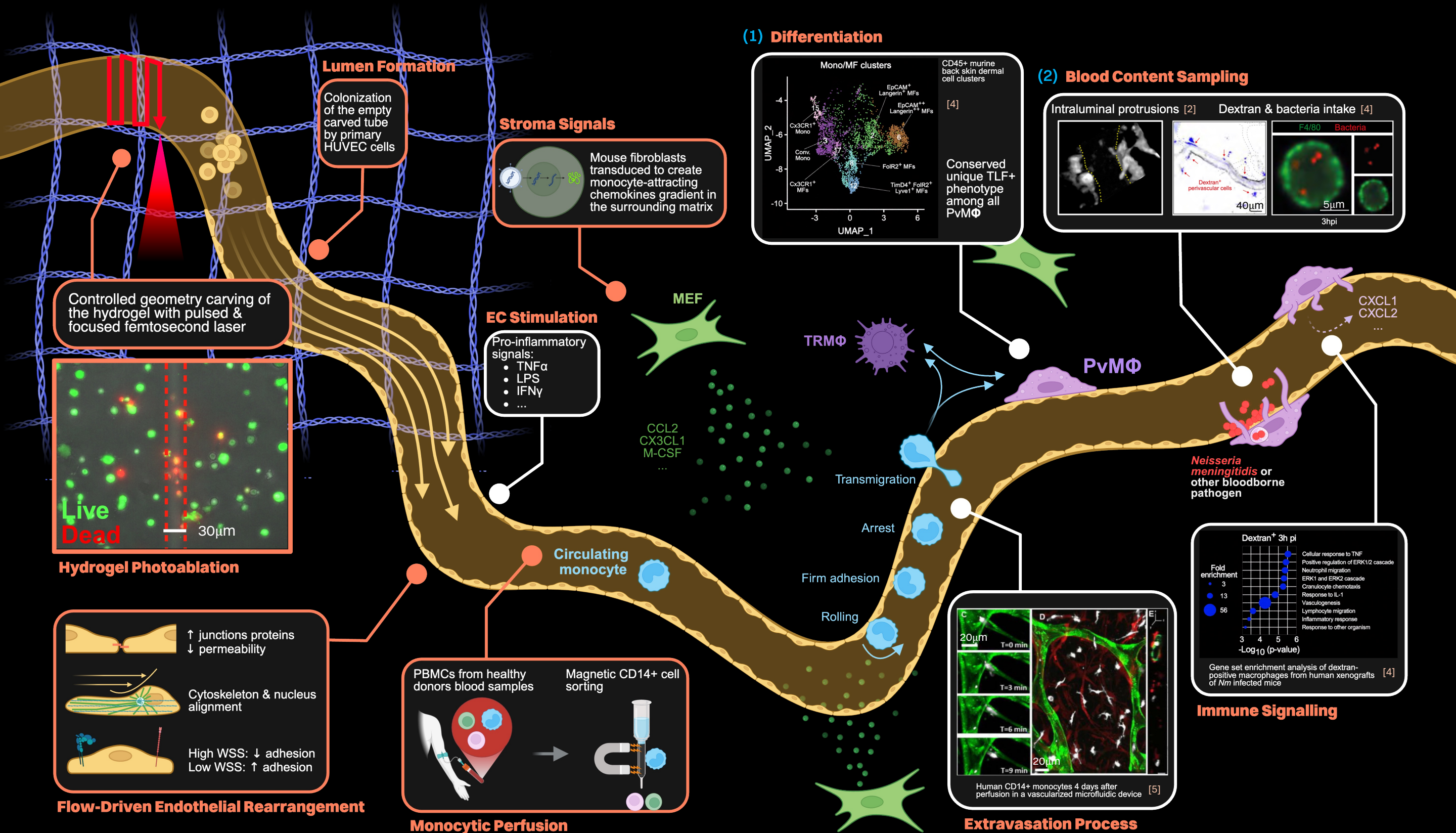
## The *in vitro* Human Venule Blueprint

Architecture of the 3D Microfluidic VoC Model



## Monocyte-derived PvMφ : towards *in vitro* Recruitment, Differentiation & Function

High-Resolution Tracking of the Monocyte-to-PvMφ Transition in a Biomimetic Niche



## Key Message

The microfluidic approach allows for control of the complex vascular niche to:

- Recapitulate an all human simplified physiological system
- Elucidate biochemical & mechanical cues of the perivascular space essential for PvMφ identity
- Bypass challenges of human xenograft & intravital murine microscopy

## Perspective

PvMφ in the VoC system becomes a relevant model for vascular infection by *Neisseria meningitidis* and its induced immunological response.

## References

- [1] Dick et al, Science 2022
  - [2] Barreiro et al, eLife 2016
  - [3] Pinon et al, eLife 2025 ☆
  - [4] Obino et al, under publication ☆
  - [5] Boussommier-Calleja et al, Biomaterials 2020
- ☆ conducted in our lab

## Thanks to

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