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Development of a metastasis-on-a-chip microfluidic device to assess the metastatic abilities of cancer cells in TNBC

Flavie Woesteland¹, Aude Sivéry², Mathilde Brûlé¹, Anaïs Horochowska¹, Anthony Treizébré², Xuefen Le Bourhis¹, Chann Lagadec¹



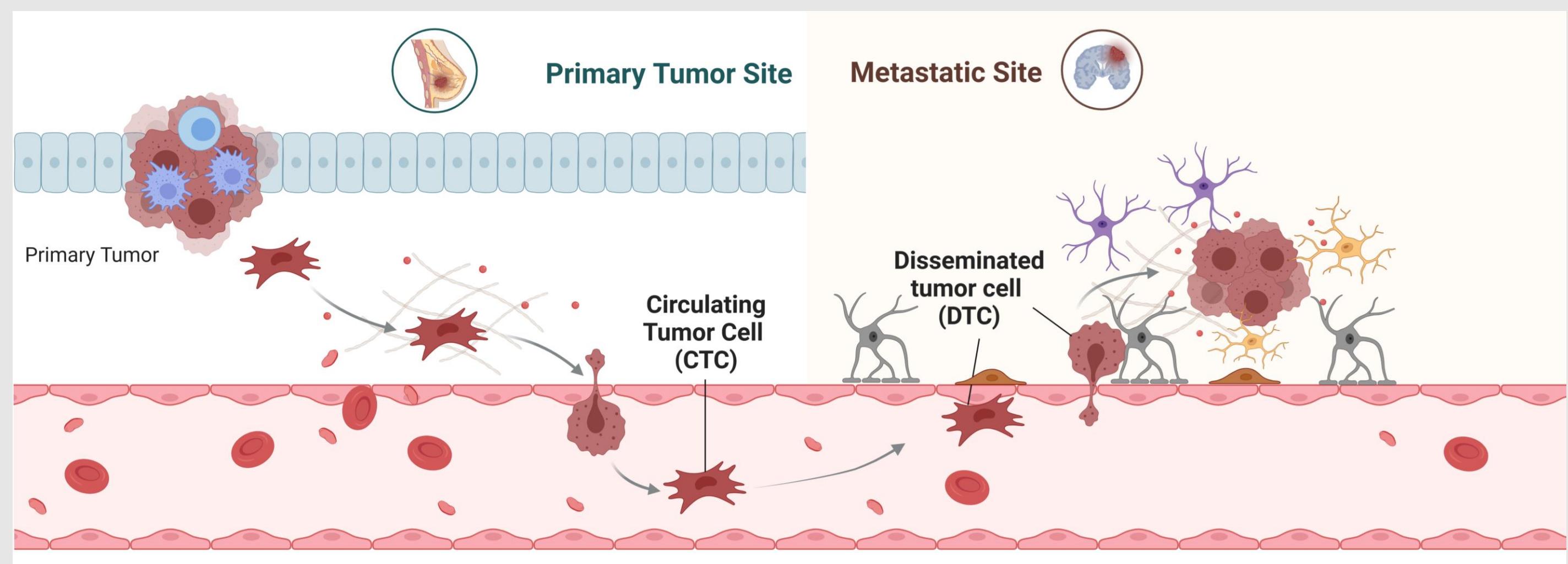
1 : Univ. Lille, CNRS, Inserm, CHU Lille, Centre Oscar Lambret, UMR9020 – UMR1277 – Canther – Cancer Heterogeneity, Plasticity and Resistance to Therapies, F-59000 Lille, France.

2 : Univ Lille, CNRS, Centrale Lille, Junia, Univ. Polytechnique Hauts-de-France, UMR 8520 - IEMN - Institut d'Electronique de Microélectronique et de Nanotechnologie, F-59000 Lille, France.

Breast cancer

- The world's most commonly diagnosed cancer
- TNBC subtype has the worst prognosis : + aggressive + metastatic
- 90% of breast cancer mortality is due to metastasis

Brain metastatic process



Which tools are available to identify key players in early metastatic brain development?

In vivo : Clearing and immunolabeling by iDisco

- Intracardiac injections of cancer cells in mice
- Development of brain metastases for 30 days
- Brain clearing by iDisco

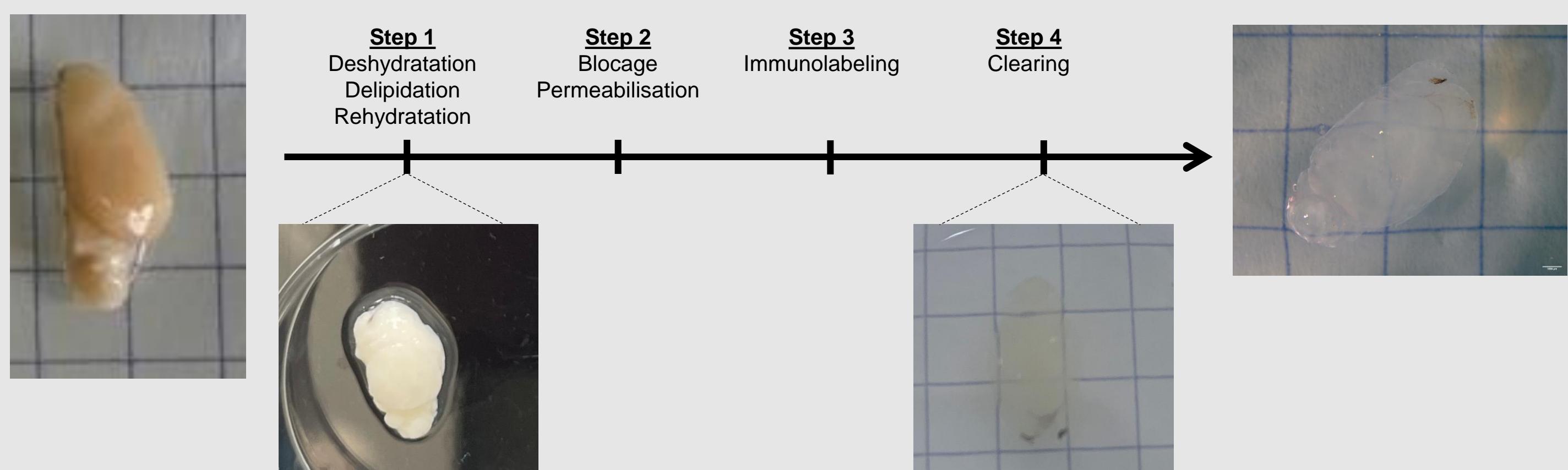


Figure 1 : Clearing by iDisco

- LightSheet microscopy

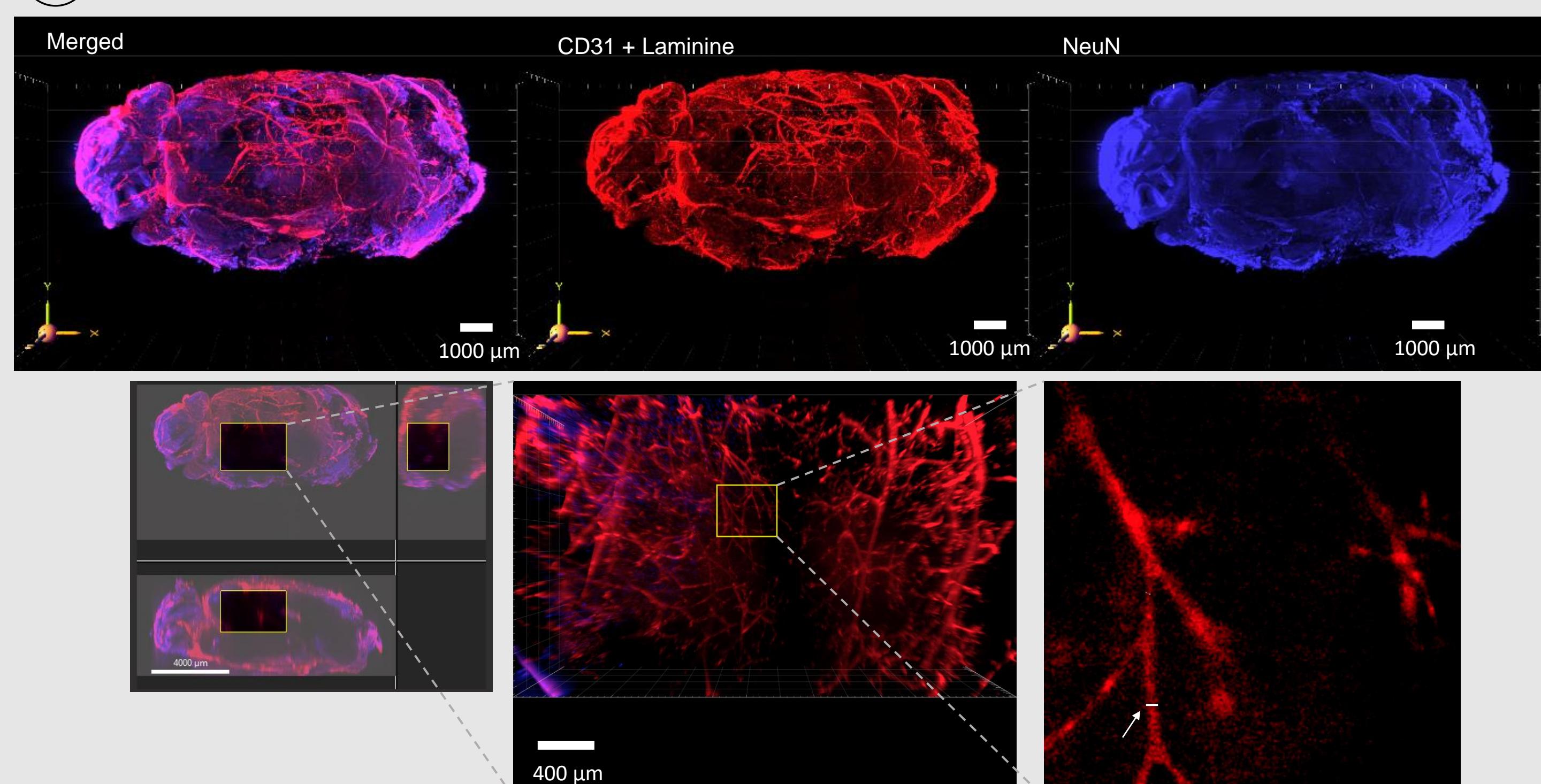


Figure 2 : Immunolabeling of blood vessels (CD31 + Laminine – red) and neurones (NeuN – blue) of half brain after iDisco.

Visualization of blood vessels up to 10 µm of diameter

- Stereotactic injections

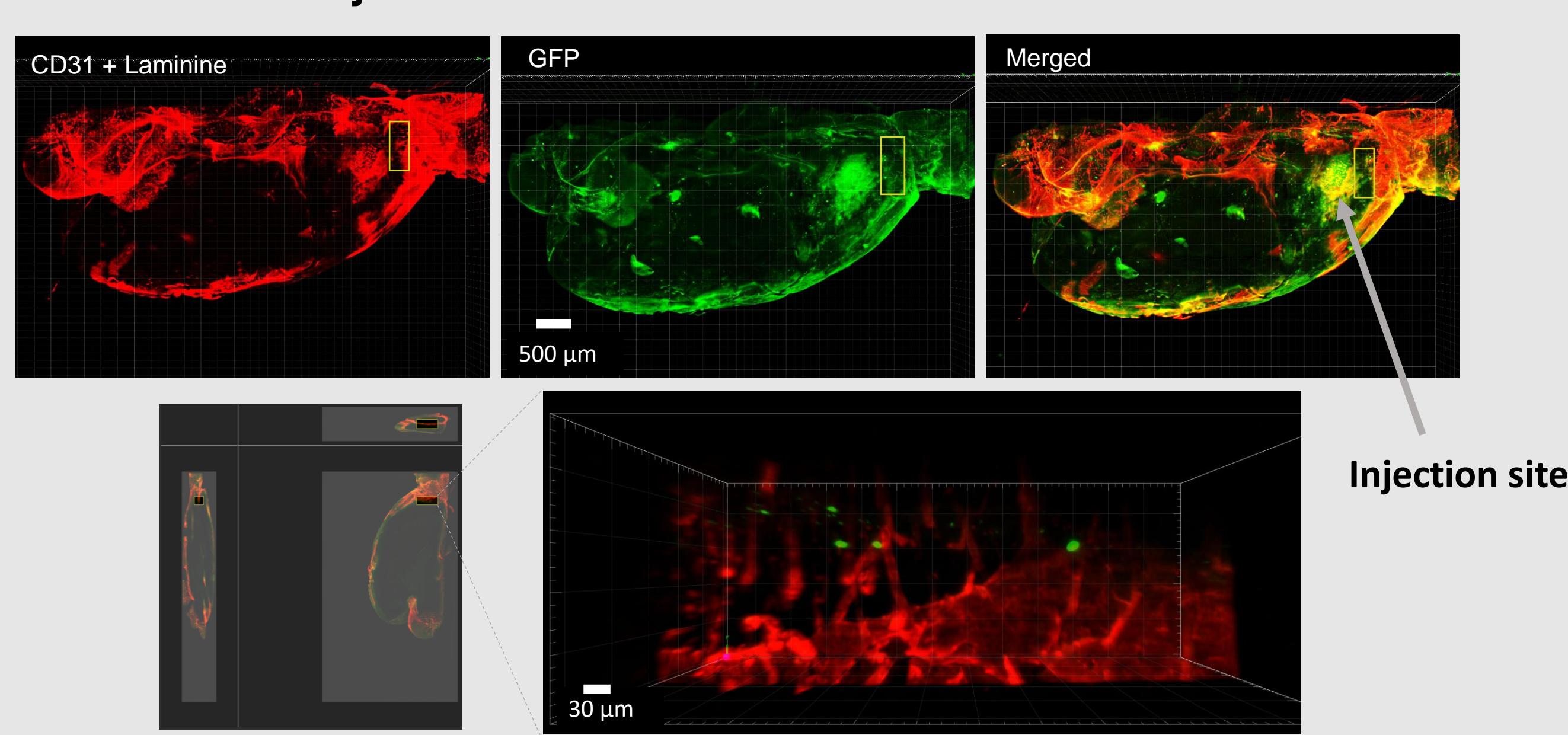
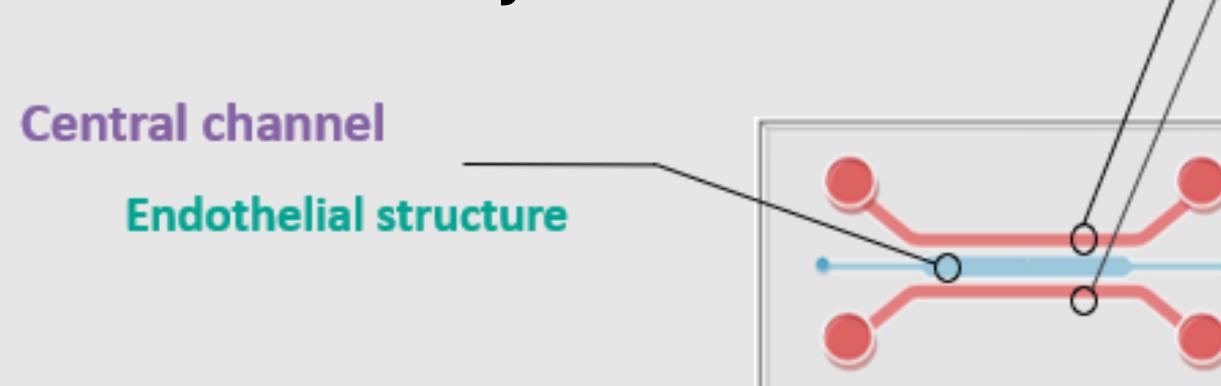


Figure 3 : Immunolabeling of blood vessels (CD31 + Laminine – red) and cancer cells (GFP – green) in half brain after iDisco

Localization of cancer cells in the brain

In vitro : Metastasis-on-a-chip

- On-chip device to study metastasis



Side channels

Extravasation conditions

Figure 4 : Scheme of the « metastasis-on-a-chip »

- Vascular-like structure in the central channel

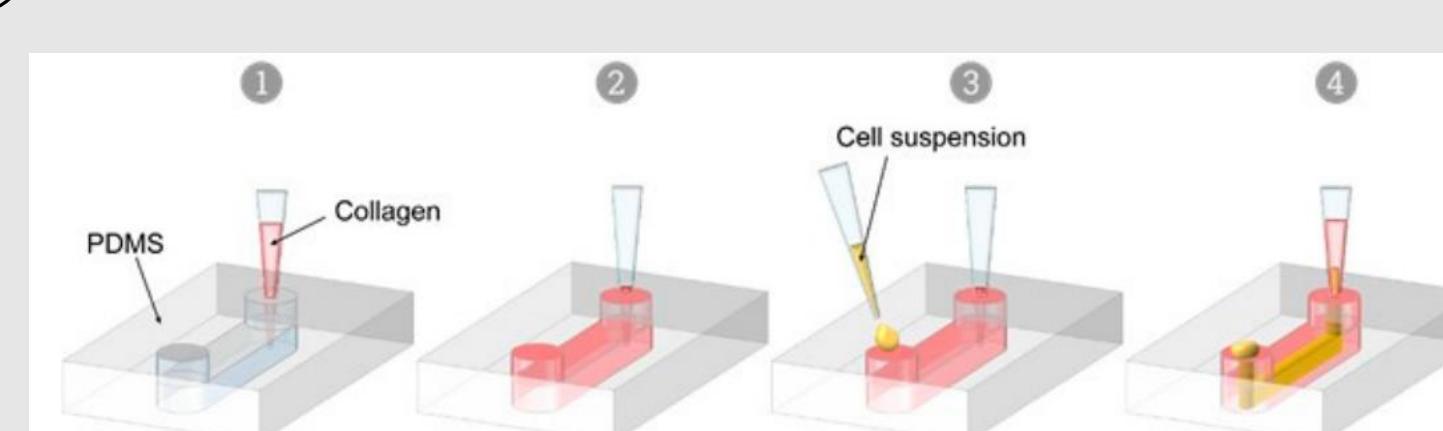


Figure 5 : Principle of viscous finger patterning to obtain an endothelial structure in the central channel
Delannoy et al, 2022.

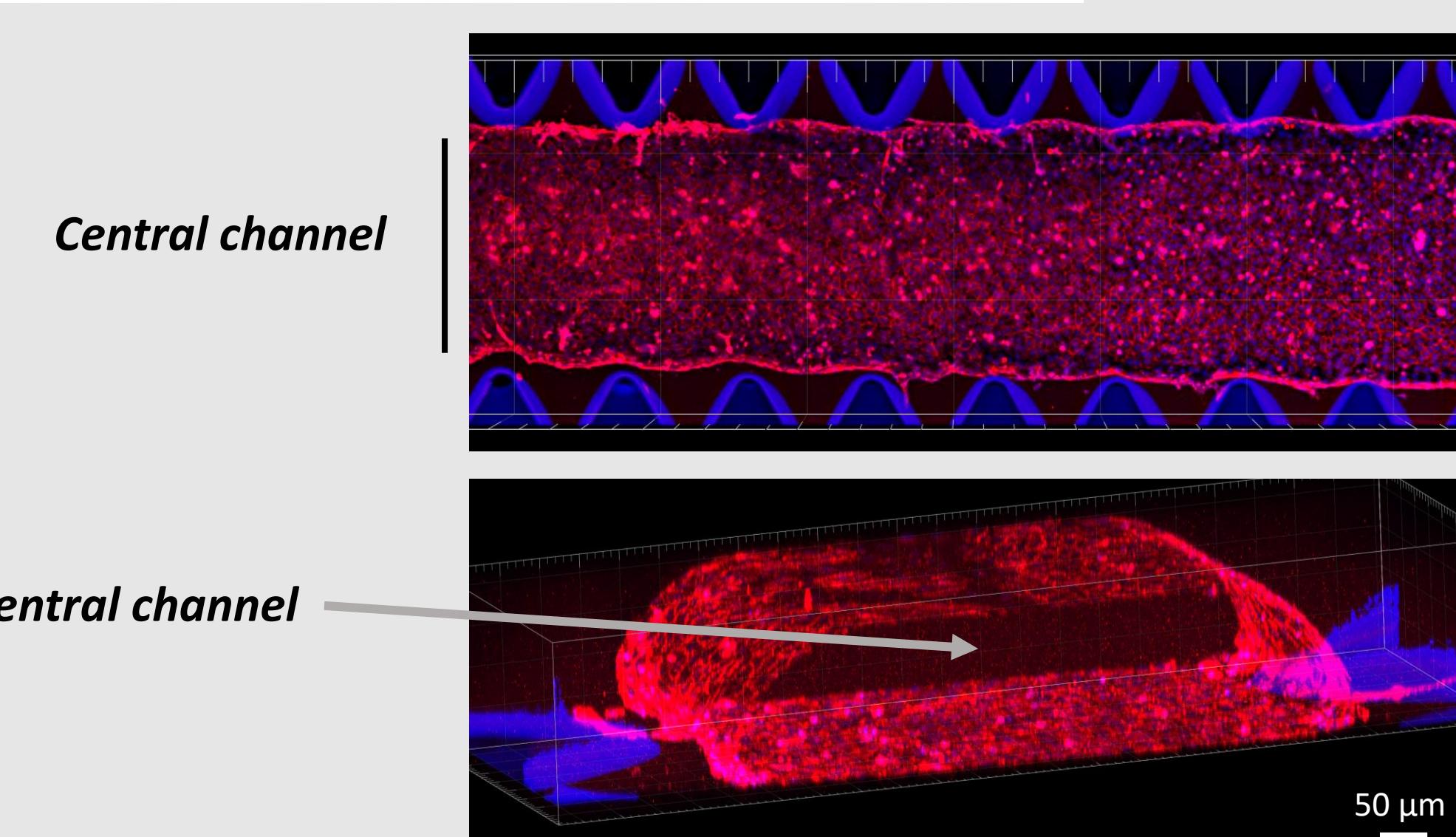


Figure 6 : Obtention of a vascular-like structure in the central channel
Adherent junctions (VE cadherin – red) & nucleus (Hoechst – blue)

- Following of breast cancer cells under different conditions

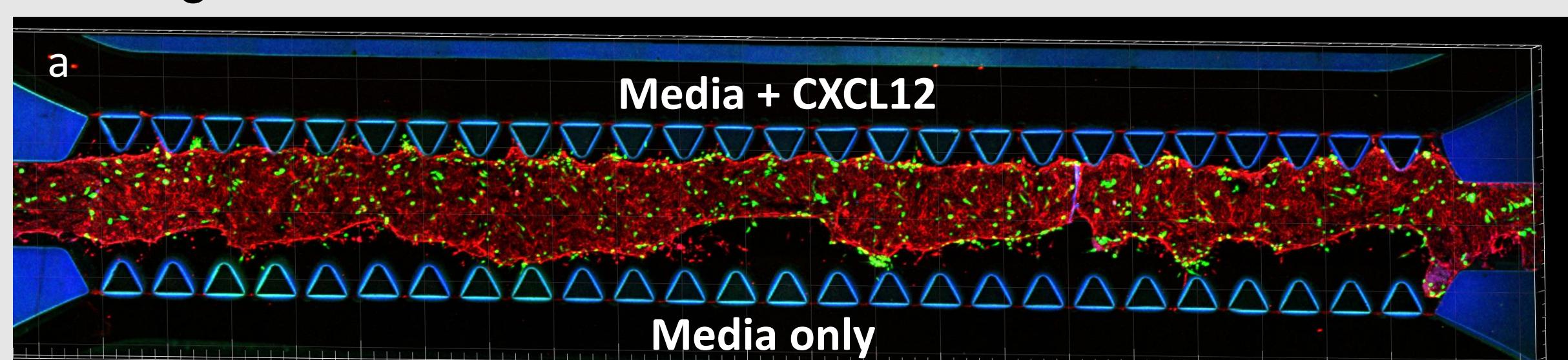
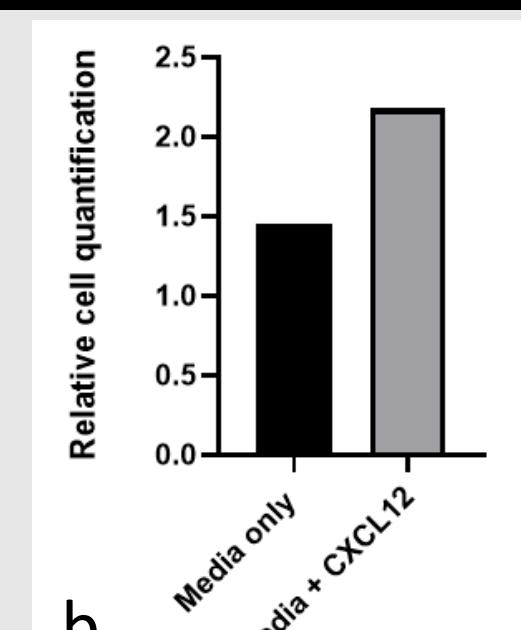


Figure 6a : Breast cancer cells in the vascular-like endothelium
Cancer cells (GFP – green); nucleus (Hoechst – blue); adherent junctions (VE cadherin – red)

Figure 6b : Relative quantification of cells attracted to CXCL12 or to media only channel



Perspectives

- Co-culture with brain cells (astrocytes, pericytes) to reach brain physiological conditions

- Apply a flow to model physiological conditions

CONTACT

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