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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 Brulé¹, Anaïs Horochowska¹, Anthony Treizébré², Xuefen Le Bourhis¹, Chann Lagadec¹

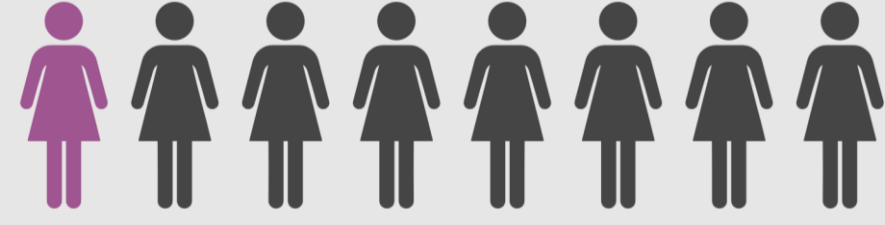


1 : Univ. Lille, CNRS, Inserm, CHU Lille, Centre Oscar Lambret, UMR9020 – UMR1277 – Canther – Cancer Heterogeneity, Plasticity and Resistance to Therapies, F-59000 Lille, France.

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.

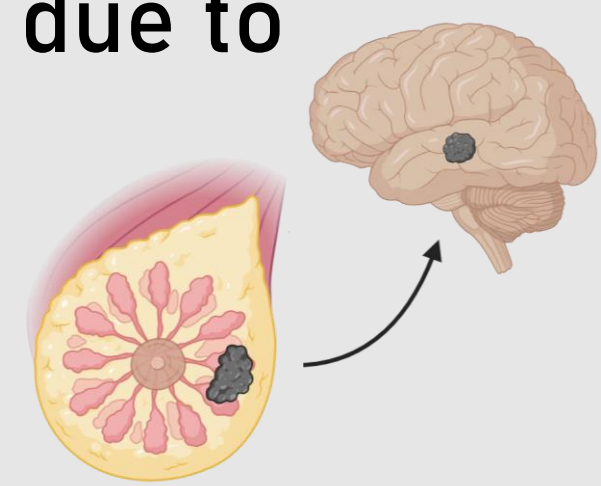
Breast cancer

→ The world's most commonly diagnosed cancer

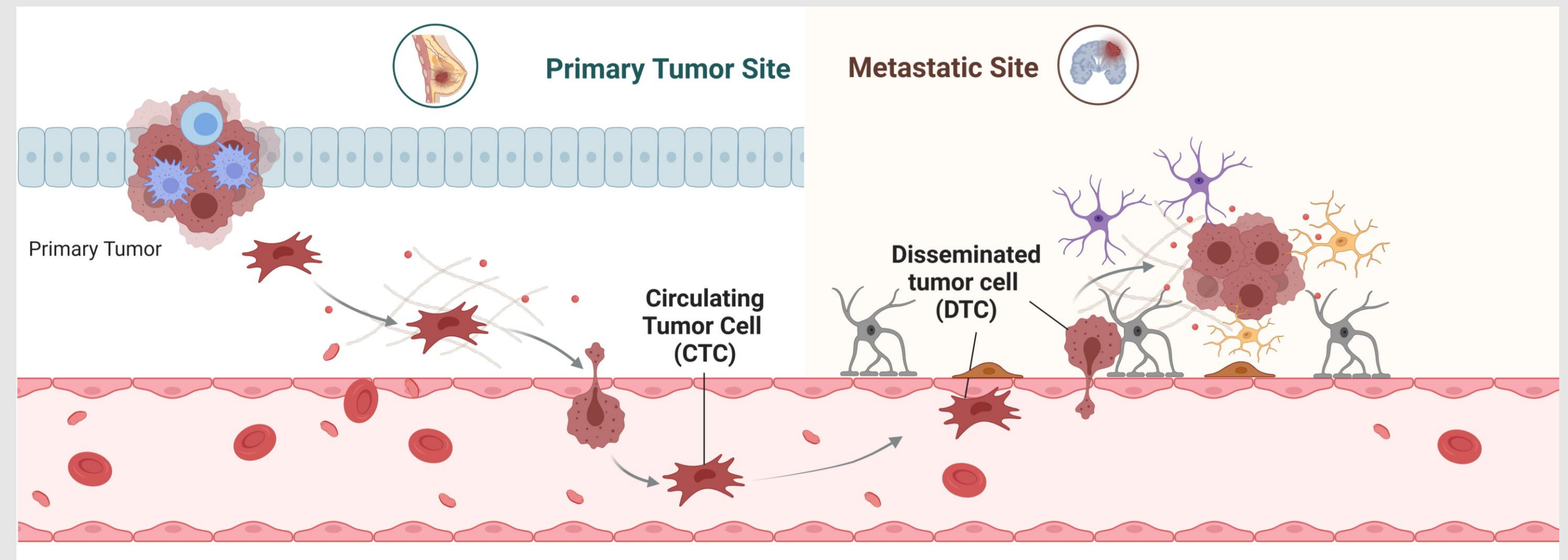


→ TNBC subtype has the worst prognosis :
+ aggressive + metastatic

→ 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

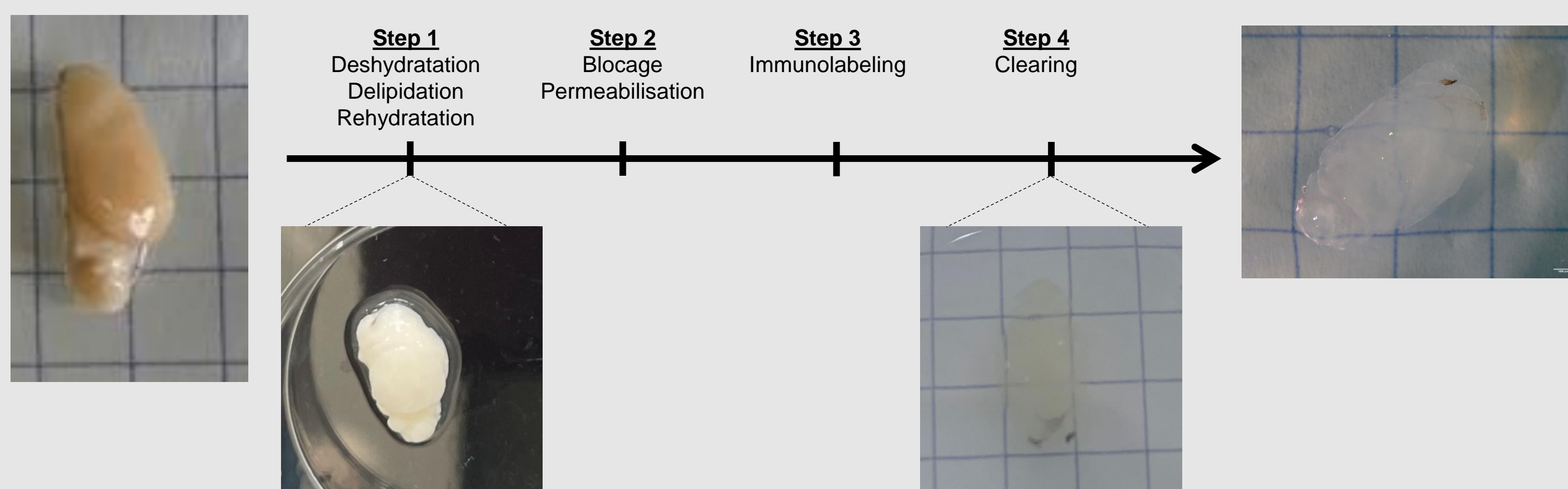


Figure 1 : Clearing by iDisco

→ LightSheet microscopy

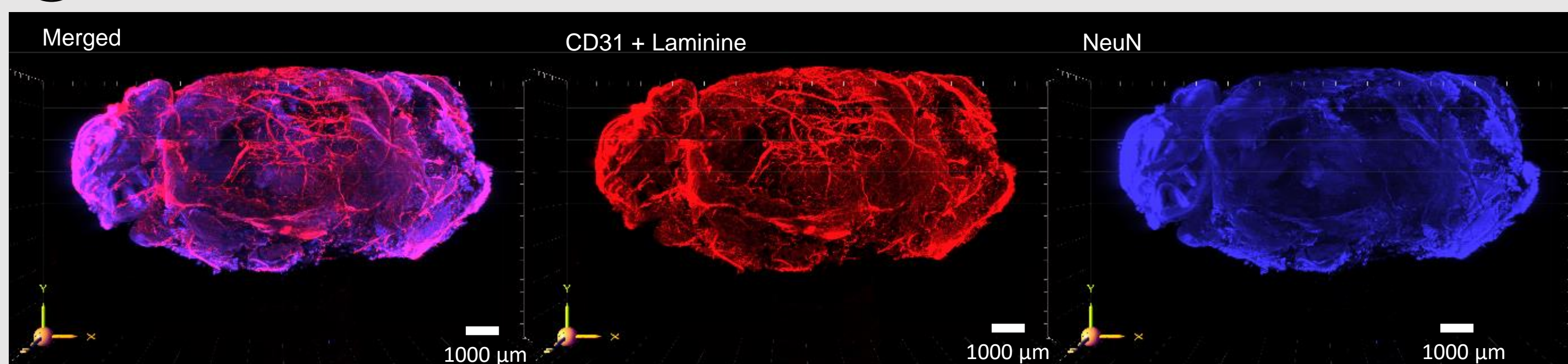


Figure 2 : Immunolabeling of blood vessels (CD31 + Laminine – red) and neurons (NeuN – blue) of half brain after iDisco.

Visualization of blood vessels up to 10 µm of diameter

→ Stereotactic injections

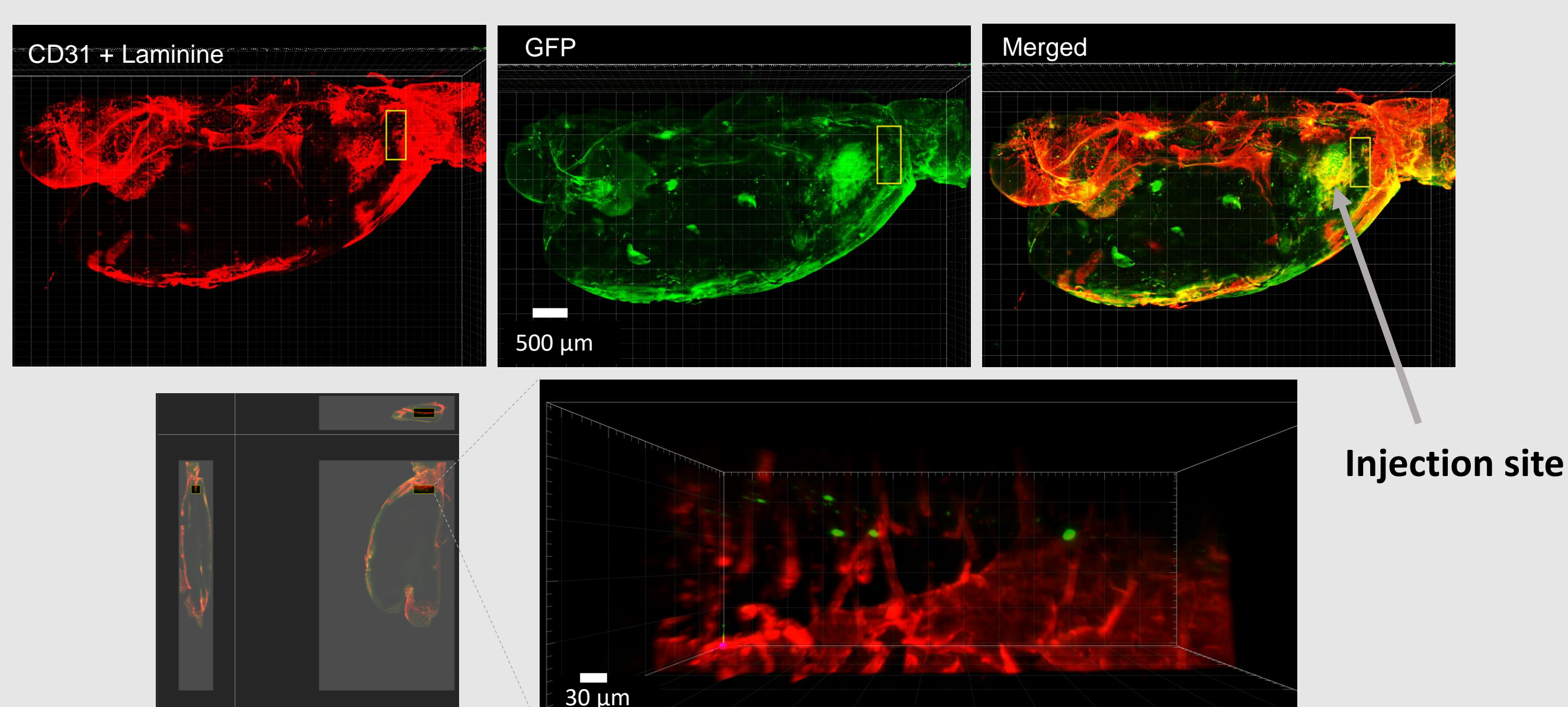


Figure 3 : Immunolabeling of blood vessels (CD31 + Laminine – red) and cancer cells (GFP – green) in half brain after iDisco

Localization of cancer cells in the brain

In vitro : Metastasis-on-a-chip

→ On-chip device to study metastasis

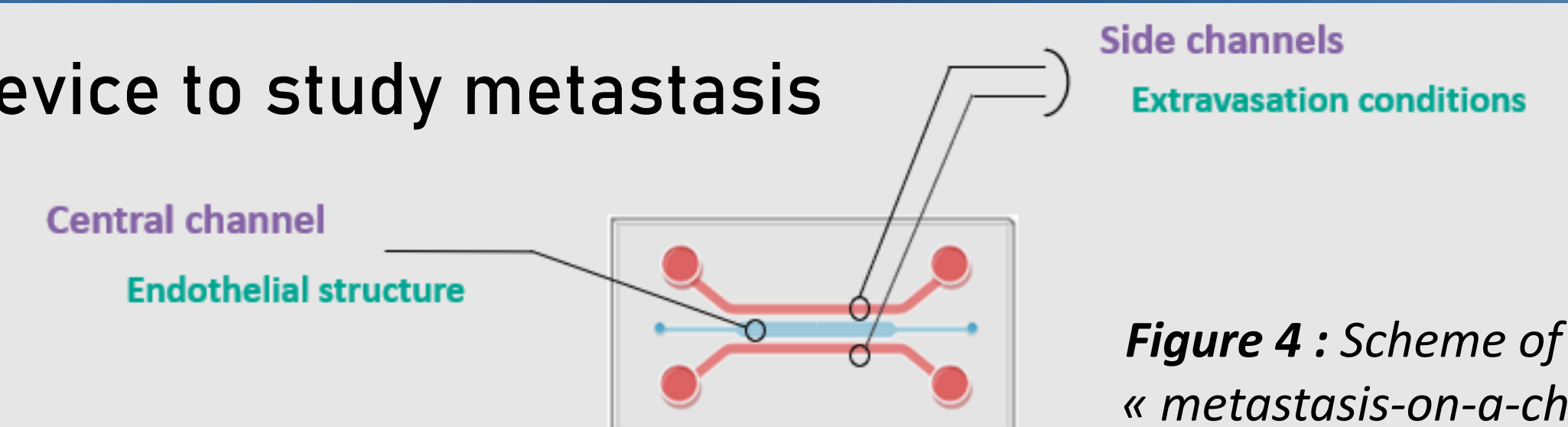


Figure 4 : Scheme of the « metastasis-on-a-chip »

→ Vascular-like structure in the central channel

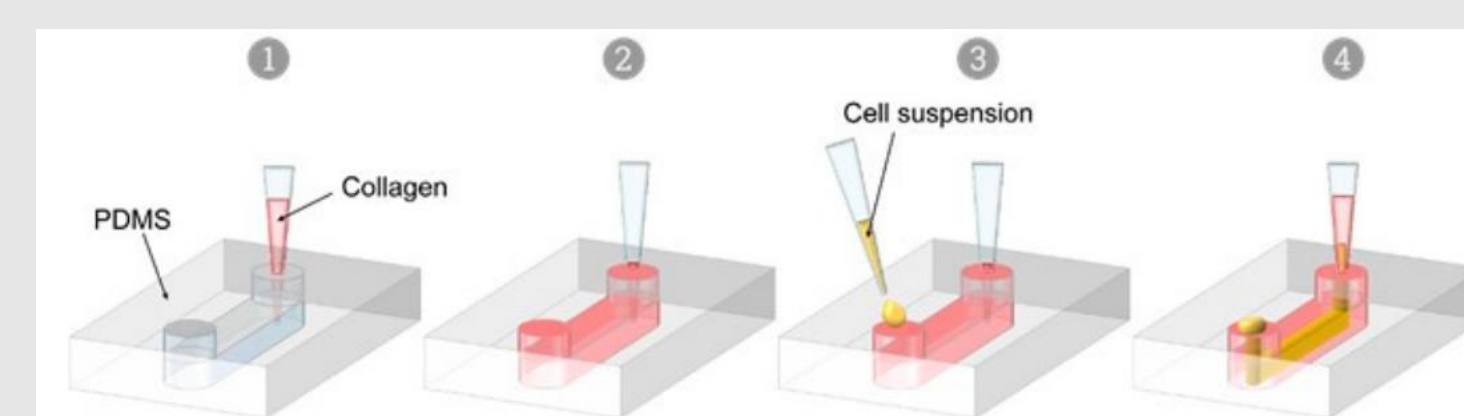


Figure 5 : Principle of viscous finger patterning to obtain an endothelial structure in the central channel
Delannoy et al., 2022.

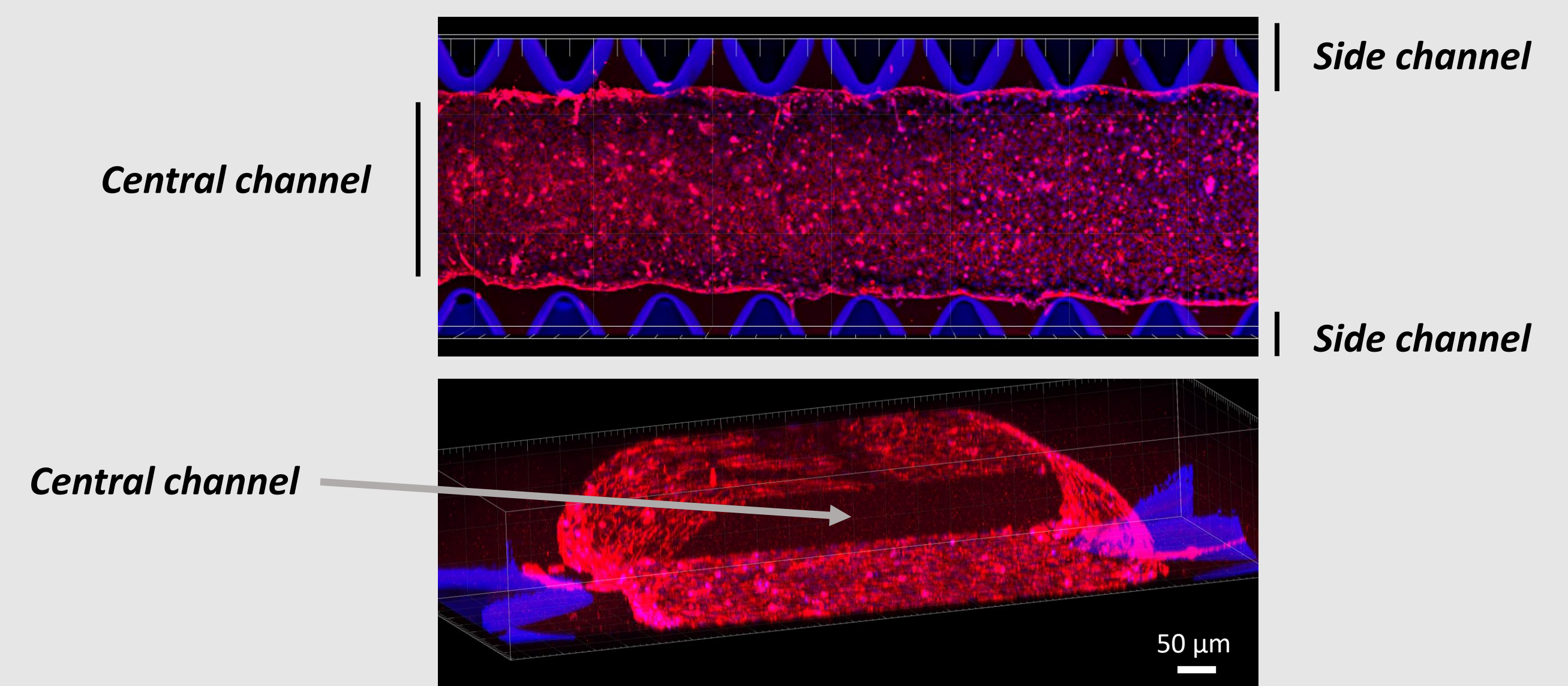


Figure 6 : Obtention of a vascular-like structure in the central channel
Adherent junctions (VE cadherin – red) & nucleus (Hoechst – blue)

→ Following of breast cancer cells under different conditions

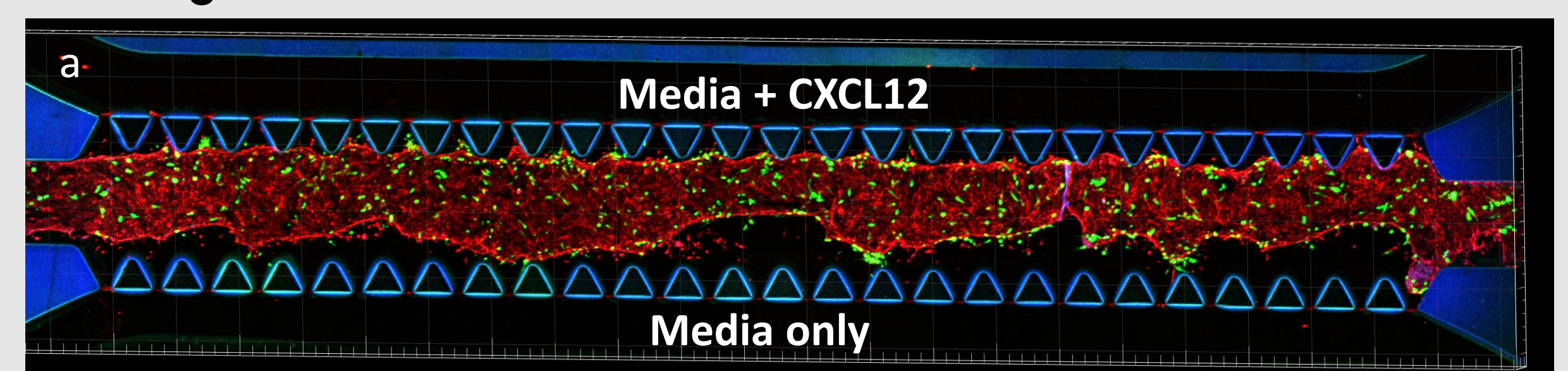
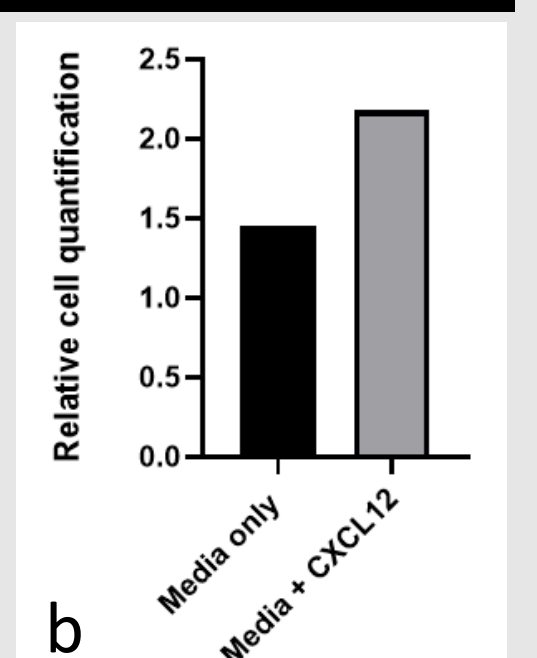


Figure 6a : Breast cancer cells in the vascular-like endothelium
Cancer cells (GFP – green) ; nucleus (Hoechst – blue) ; adherent junctions (VE cadherin – red)

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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