

Metastasis on-a-chip platform to follow in real-time the extravasation process and collect extravasated cancer cells

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Aude Sivery, Flavie Woesteland, F. Soncin, Xuefen Le Bourhis, A. Treizebre, et al.. Metastasis ona-chip platform to follow in real-time the extravasation process and collect extravasated cancer cells. OncoLille Workshop, Jan 2024, Lille, France. hal-04547891

HAL Id: hal-04547891 https://hal.science/hal-04547891v1

Submitted on 16 Apr 2024 $\,$

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Metastasis on-a-chip platform to follow in real-time the extravasation process and collect extravasated cancer cells

<u>Aude SIVERY¹</u>, Flavie WOESTELAND², Fabrice SONCIN^{3,4}, Xuefen LE BOURHIS², Anthony TREIZEBRE¹, Chann LAGADEC²

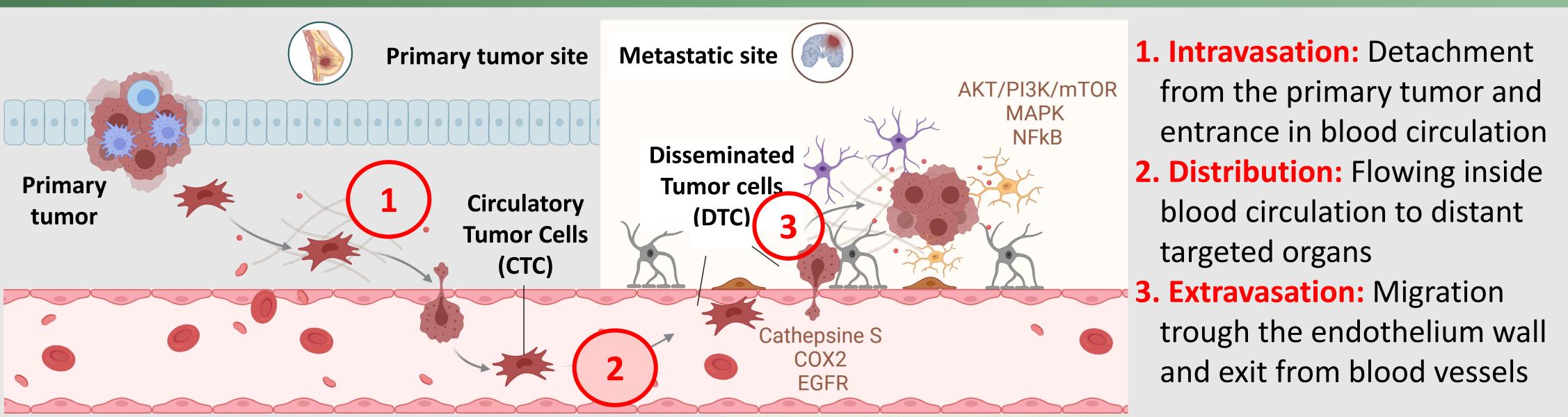


1: Univ Lille, CNRS, Centrale Lille, Junia, Univ. Polytechnique Hauts-de-France, UMR 8520 - IEMN - Institut d'Electronique de Microélectronique et de Nanotechnologie, F-59000 Lille, France. 2: Univ. Lille, CNRS, Inserm, CHU Lille, Centre Oscar Lambret, UMR9020 – UMR1277 – Canther – Cancer Heterogeneity, Plasticity and Resistance to Therapies, F-59000 Lille, France. 3 : CNRS/IIS/Centre Oscar Lambret/Lille University SMMiL-E Project, CNRS Délégation Hauts-de-France, 43 Avenue le Corbusier, 59800 Lille, France. 4: CNRS, IRL2820, Laboratory for Integrated Micro Mechatronic Systems, Institute of Industrial Science, University of Tokyo, 4-6-1 Komaba, Meguro-ku, Tokyo 153-8505, Japan

Cancer cells Extravasation: A Highly Dynamic Process Background: Metastasis

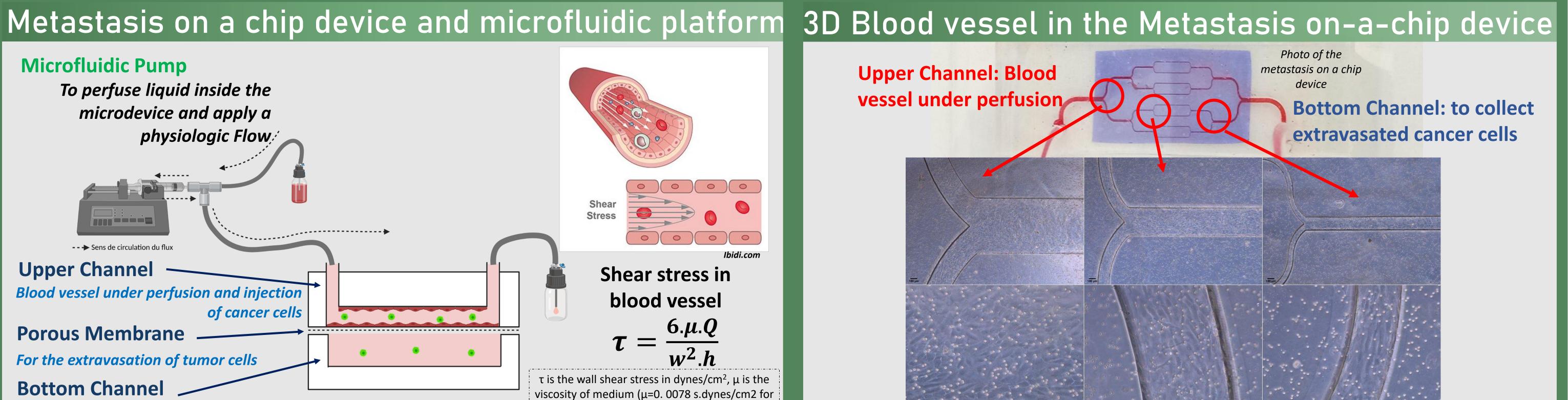
in breast cancer Most diagnosed cancer in the world





90% of mortality in breast cancer is due to the formation of metastasis

Aim of this study : Developp a metastasis on-a-chip platform to follow, collect and caracterise tumor cells that are able to extravasate



Injection of **GFP**

transfected cancer cells in

the upper channel and

following of their

migration across the

endothelium wall

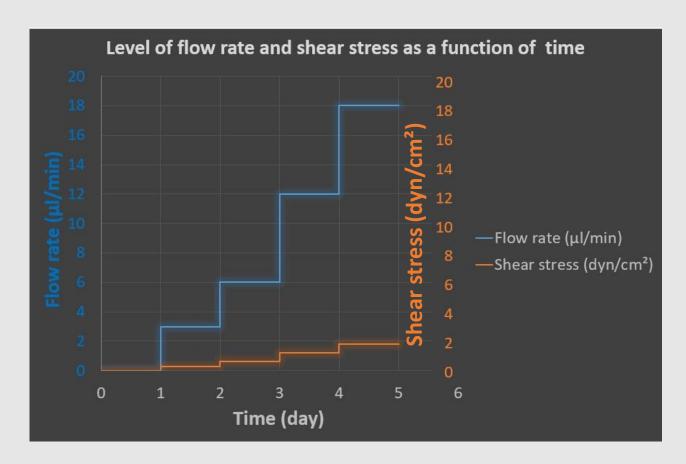
To collect extravasated cancer cells

Figure 1. Schematic Side view of the metastasis on a chip microdevice

standard culture medium), Q is the flow rate (m^3/s) , w the width (m)and h the height (m) of the channel

Figure 2. HUVEC cells inside the device after 4 days of dynamic culture conditions. From left to right inside a 800 µm, 400 µm and 200 µm channels width. All the channels have a 800 µm high. Up, 5X magnification objective. Down, 20X magnification objective, Dml1 Leica Microscope

Complete 3D endothelium



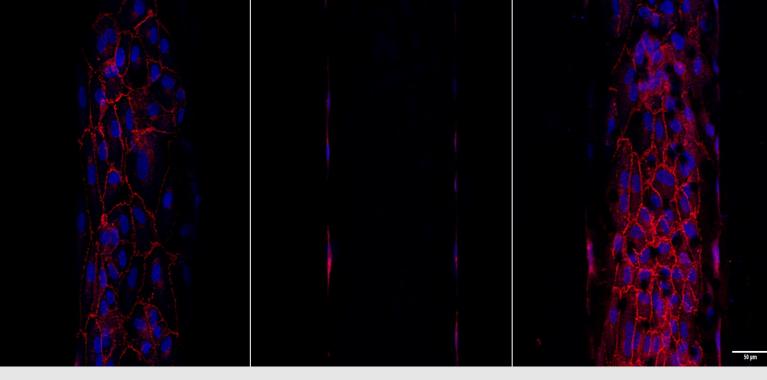
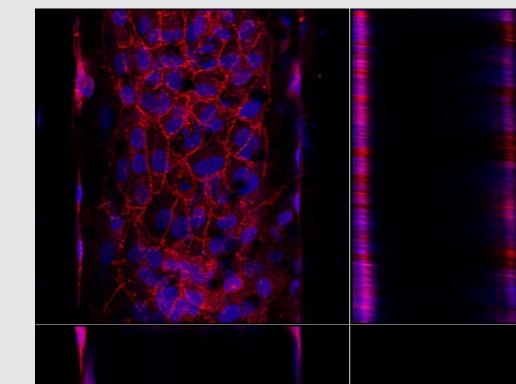


Figure 4. Confocal images inside a 200 µm channel width (Leica SP8, water immersion 25X objective). VE-cadherin (red) and Hoechst (blue) immunofluorescence staining of HUVEC inside the device at day 4 of dynamic culture condition. From left to right: Top, middle and bottom part of the channel

Figure 3. Flow rate and shear stress as a function of time, from day 0 to day 5 of dynamic culture conditions

Physiological shear stress between i 0,6 and 1,8 dyn/cm², applied step-by-i step during 4-5 days

The presence of adherent junctions troughout the entire microdevice reveal a complete 3D endothelium after 4 days of dynamic culture conditions



Follow in real time the extravasation events

1. Following in real-time tumor cells extravasation

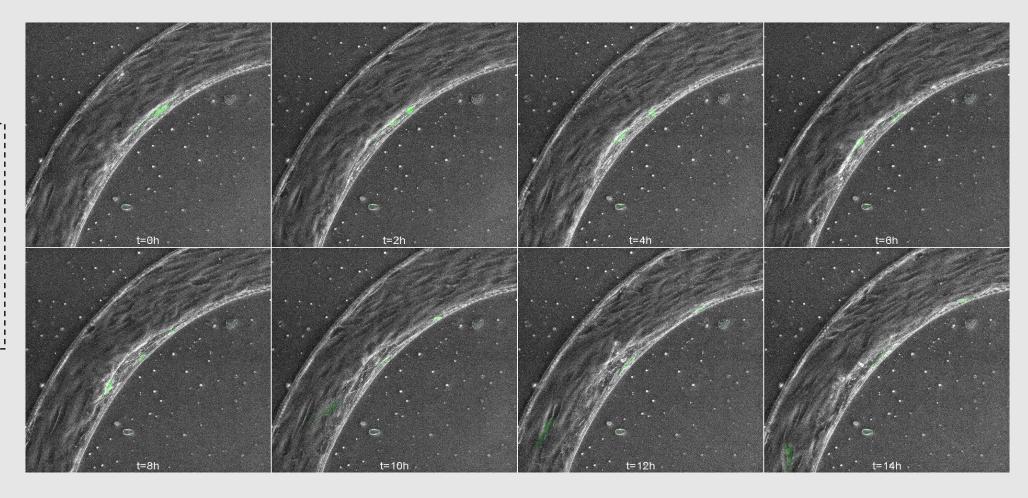
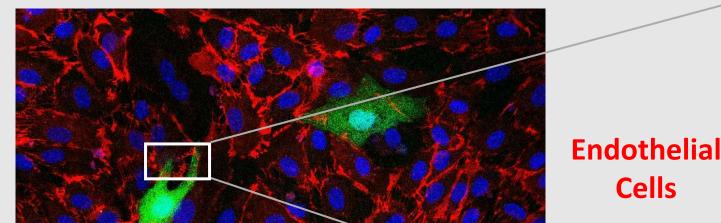


Figure 6. Timeline of interaction between MDA-MB-231-GFP cells and HUVEC endothelium during 14 h. 1h after their injection on HUVEC endothelium, the green fluorescence of GFP MDA-MB-231 cells were recorded

2. Live cells imaging to detect rare extravasation events Porous Membrane



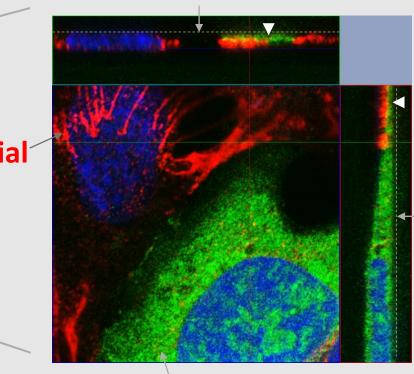


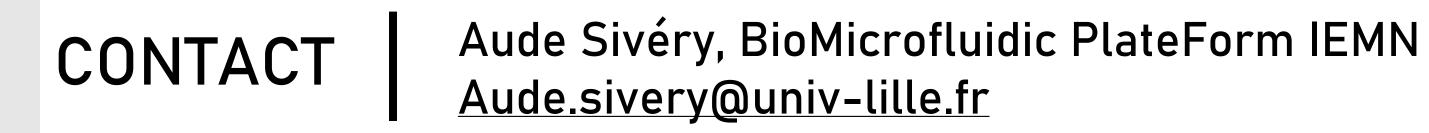


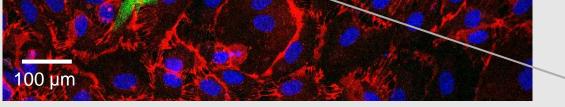
Figure 5. Orthogonal views in a 200 µm channel width obtained by confocal microscopy (Leica SP8, water immersion 25X objective). VE-cadherin (red) and Hoechst (blue) immunofluorescence staining of HUVECs inside the device at day 4 of dynamic culture conditions

Outlooks

(
ightarrow) Modify the collecting channel to a more complex microenvironment in order to mimic specific targeted organs

 \rightarrow Complete characterization of extravasated cancer cells (stemness, migration, profil...)





Cancer cells

Figure 7. Cancer cells adhesion on endothelial wall. Cancer cells (GFP, green), nucleus (Hoechst, blue), adherent junctions (VE cadherin, red)

3. Collecting extravasated cells

