



HAL
open science

Development of a biomimetic bone on chip to study kidney cancer metastasis: ONCOTRAP

Elisa Lambert, Beatrice Cesana, Catherine Pillet, Joris Kaal, Jules Heraud,
Claude Cochet, Odile Filhol, Elisa Migliorini

► To cite this version:

Elisa Lambert, Beatrice Cesana, Catherine Pillet, Joris Kaal, Jules Heraud, et al.. Development of a biomimetic bone on chip to study kidney cancer metastasis: ONCOTRAP. EUROoCS annual meeting, Jul 2024, Milan, Italy. hal-04718061

HAL Id: hal-04718061

<https://hal.science/hal-04718061v1>

Submitted on 2 Oct 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Development of a biomimetic bone-on chip to study kidney cancer metastasis: ONCOTRAP

Elisa Lambert^{1*}, Beatrice Cesana¹, Catherine Pillet¹, Joris Kaal², Jules Heraud³, Claude Cochet¹, Odile Filhol-Cochet¹, Elisa Migliorini¹

¹ Université Grenoble Alpes, CEA, INSERM U1292 Biosanté, CNRS EMR 5000 BRM, 38000 Grenoble, France.

² CEA LETI DTBS, 38000 Grenoble, France

³ SIS2M-LIONS CEA CNRS, UMR 3299, CEA Saclay, 91191 Gif-sur-Yvette, France

*elisa.lambert@cea.fr

The majority of the solid tumors generate metastasis in different organs like the bone. This late tumor stage is considered as a lethal disease as the patient prognosis is very poor and treatments are partially efficient. In the case of kidney cancer, 30% of patients are metastatic at diagnosis, despite improvements in medical imaging and target therapies. Predicting the evolution of cancer would be helpful for biologists to choose the best therapeutic strategy. Due to unethical issues of animal models and its lack of representation of human tissue behavior, alternatives such as organ-on-chip appear with the potential to study the aggressiveness of metastatic cells and to test anti-metastatic drugs. Unfortunately few bone-on-chip devices have been so far developed [1]. We have designed a metastasis-on-chip to study patient kidney cancer cells invasion towards bone niche. Herein, to recreate a bone niche, we aim to use human Periosteum Derived Stem Cells (hPDSC) that differentiate into osteoblasts in the presence of Bone Morphogenetic Protein 2 (BMP2). BMP2 delivery is usually regulated by extracellular matrix components such as the glycosaminoglycan heparan sulfate (HS). A biomaterial already developed by our team promotes osteogenic differentiation through the interaction HS/BMP2 [2].

The microfluidic chip is made of two main chambers (Figure 1): in chamber1 (Ch1), renal tumoroids are inserted in a collagen 3D matrix [3], in Ch2 hPDSC are differentiated into bone on the biomaterial. A channel with pillars connects the two chambers. Thanks to numerical simulation, we predicted and validated the flow direction of both inlets and found optimized flow rates for cell culture and functionalization of the Ch2 with the biomaterial. We use a counter pressure effect to reduce the risk of molecules diffusion in Ch1. We set up a microfluidic bench based on pressure flow controllers to control precisely in space the functionalization of the biomimetic platform. We have successfully built up, step by step, the biomaterial in only the bone chamber. hPDSCs differentiation to bone is validated with osteogenic differentiation markers such as Osterix and Alkaline Phosphatase. In the next future we will insert the renal tumoroid in the Ch1 to study the cancer invasion.

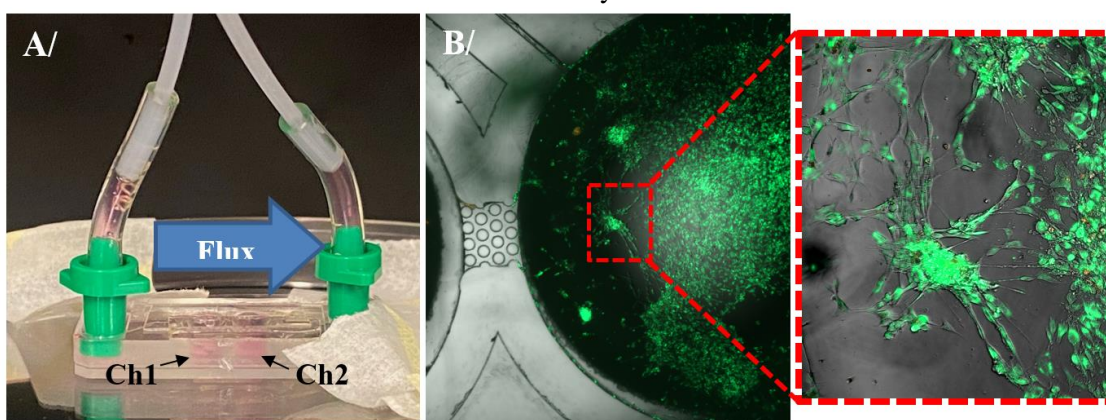


Figure 1 Culture of undifferentiated hPDSC cells under flux at a flow rate of 5 μ L/min during 3 days. (a) Picture of the microfluidic chip with the two chambers. (b) hPDSC cells are in Ch2 and were labeled with PKH67 to distinguish them from the kidney cancer cells.

Acknowledgments

The MetasTRAP project has been funded by the interdisciplinary program Focus Organoïde-sur-Puce of CEA lead by the pilot committee: Carole Bresson, Anselme Perrier and Fabrice Navarro. This project is in collaboration with IMAC (Invasion Mechanisms in Angiogenesis and Cancer) and BRM (Biomimetism and Regenerative Medicine) teams of CEA-IRIG-Biosanté lab (UMR_1292).

References

- [1] Hao S, Ha L, Cheng G, Wan Y, Xia Y, Sosnoski D M, Mastro A M and Zheng S-Y 2018 A Spontaneous 3D Bone-On-a-Chip for Bone Metastasis Study of Breast Cancer Cells *Small* **14** 1702787
- [2] Sefkow-Werner J, Machillot P, Sales A, Castro-Ramirez E, Degardin M, Boturny D, Cavalcanti-Adam E A, Albiges-Rizo C, Picart C and Migliorini E 2020 Heparan sulfate co-immobilized with cRGD ligands and BMP2 on biomimetic platforms promotes BMP2-mediated osteogenic differentiation *Acta Biomater.* **114** 90–103
- [3] Séraudie I, Pillet C, Cesana B, Bazelle P, Jeanneret F, Evrard B, Chalmel F, Bouzit A, Battail C, Long J-A, Descotes J L, Cochet C and Filhol O 2023 A new scaffold-free tumoroid model provides a robust preclinical tool to investigate invasion and drug response in Renal Cell Carcinoma *Cell Death Dis.* **14** 622