

Microfluidic 2D and 3D human organ-specific vasculature models to study circulating cancer cell adhesion in metastasis formation

C. Cerutti,¹ A. Luraschi,^{1,2}
L. Bettinelli,^{1,3} V. Grazioli,^{1,2}
I. Kasioulis,⁴ N. Romero,⁵ A. Granata,⁴
G. Spinetti,³ M. Rasponi,² P. Pelicci¹
¹Department of Experimental Oncology, IEO, European Institute of Oncology IRCCS, Milan, Italy; ²Department of Electronics, Information, and Bioengineering, Politecnico di Milano, Italy; ³Laboratory of Cardiovascular Research, IRCCS MultiMedica, Milan, Italy; ⁴Division of Clinical Neurosciences, Clifford Allbutt Building, Cambridge Biomedical Campus, Cambridge, United Kingdom; ⁵Department of Life, Health and Chemical Sciences, The Open University, Milton Keynes, UK

Interaction between cancer cells and Endothelial Cells (ECs), which line blood vessels, is an early and critical event in metastasis formation. Breast cancer is the most common cancer in women worldwide,

that metastasise to the brain, lung and bone, causing 90% of cancer-related death. Although animal models have contributed significantly to the understanding of cell-cell interactions and cancer research, there is a need for new alternatives to reduce the use of animal models and provide *in vivo* validation. Here, we developed human organ-specific vasculature *in vitro* models to investigate the organ tropism of breast cancer. First, we established and characterized microfluidic human vascular models of brain, lung and bone. Then, we designed, fabricated by photolithography, cultured and characterized a human microfluidic 3D Blood-Brain Barrier (BBB)-on-a-chip featuring an *in vivo*-like cylindrical geometry with brain ECs alone or in co-culture with iPSC-derived pericytes in 3D ECM matrixes. These models were characterized for the expression of endothelial and cell junction markers like PECAM1, VE-cadherin and ZO1, as well as measuring permeability. Finally, we used the microfluidic 2D and 3D models to study the interaction between human cancer cells and ECs under hemodynamic shear stress coupled to live-cell imaging. These models serve as valuable tools to uncover the molecular mechanisms underlying the interaction of cancer cells with organ-specific vasculatures, and they offer new targets for the prevention and reduction of breast cancer metastasis.

Correspondence: C. Cerutti
E-mail: camilla.cerutti@ieo.it

Conference presentation: this paper was presented at the Fourth Centro 3R Annual Meeting - The role of 3Rs in the age of One Health: where we are and where we're going - 13-15 September 2023, Università degli Studi Milano-Bicocca.

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Biomedical Science and Engineering 2023; 4:218
doi:10.4081/bse.2023.218

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