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

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

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