A MICROFLUIDIC-COMPUTATIONAL PLATFORM FOR ANALYZING VASCULAR AND EXTRAVASCULAR MASS TRANSPORT

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Considerable advances have been made in microfluidic devices and their applications since the development of soft lithographic techniques [1]. We developed a PDMS based double channel chip consisting of two microfluidic channels that mimic the vascular and extravascular compartments. The two channels are designed to be confined by sidewalls and connected by a membrane composed by arrays of pillars constituting a permeable vascular wall [2]. The inner surface of the vascular channel is uniformly coated with Human Umbilical Vein Endothelial Cells (HUVEC) resulting in well-controlled 3D model of blood vessel with endothelial barrier functions. In **Figure.1A** and **B**, the photolithographic, etching, and replica molding steps needed for realizing double-channel chips are presented together with an image (right) of the vascular channel after cell seeding and self-organization in a tubular shape. The extravascular compartment can be integrated with tumor cells of different type, potentially organized in a 3D fashion inside an extracellular matrix or with extracellular matrix components. The integration of the two compartments allow us to study the transport and permeation of therapeutic molecules, nanomedicines and cells through the endothelial barrier and the efficacy of the administered treatment. Other applications such as modeling of metastatic cell and leucocytes adhesion and migration across the endothelial barrier allow us to characterize cell extravasation from the vascular bed. The vascular transport and subsequent adhesion dynamics of nano-constructs and cells to the vascular channel are also predicted using a 3D computational framework based on coupling Lattice Boltzmann (LB) and Immersed Boundary (IB) methods. The fluid solver for the incompressible Navier-Stokes equations is based on the three dimensional D3Q19 Lattice-Boltzmann Method. The dynamics of deformable nano-constructs and cells is simulated through a neo-Hookean membrane constitutive model coupled iteratively with the fluid (**Figure.1C**). The combination of microfluidic chips and computational modeling provides a formidable tool for boosting our understanding on disease development and drug delivery.

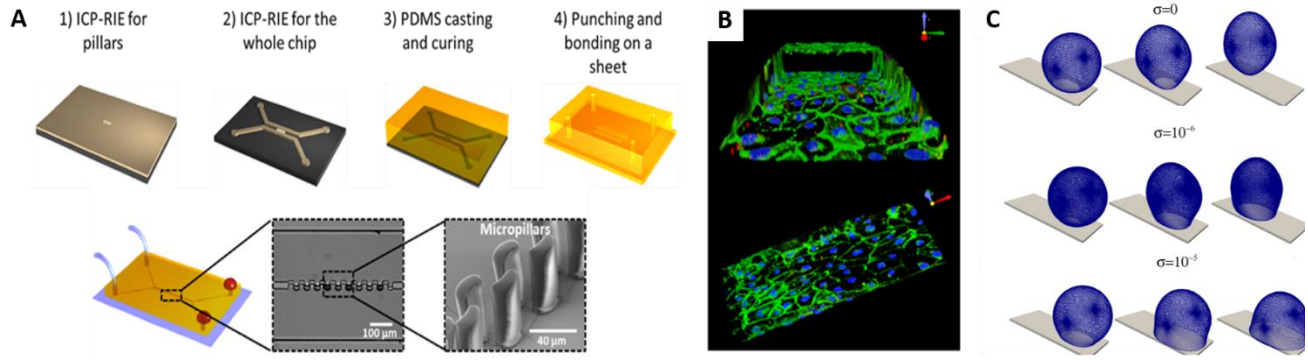

Figure 1. Double-channel microfluidic chips. A. Fabrication steps and SEM images. B. Confocal images of a confluent HUVEC monolayer cultured in the vascular compartment, where nuclei are stained in blue and VE-cadherin receptors are stained in green. C. Adhesive interactions at the wall and deformation of a circulating cell.

ESSENTIAL REFERENCES

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