Microfluidic Device to Study Breast Cancer Cell Migration

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Primary CNF Tools Used: Objet30 Pro 3D Printer

Abstract:

Bone metastasis through the dissemination of cancer cells worsens the prognosis of patients with advanced breast cancer. Migration of breast cancer cells is a fundamental process for breast cancer metastasis and is dependent on surrounding microenvironment. Cancer cell response to chemical signals and extracellular matrix (ECM) has been studied to understand the migration of cancer cells using microfluidic devices [1-2]. How bone ECM, mainly mineralized collagen, regulates breast cancer cell migration, however, is unclear.

Here, we utilized biomimetic approach in conjunction with microfluidic device to investigate the role of bone ECM on breast cancer migration.

Summary of Research:

Three-dimensional computer-aided design (3D CAD) software (Inventor, Autodesk) was used to design a microfluidic device for studying breast cancer migration. The device is composed of central channel for bone ECM deposition and two channels for chemical gradient and breast cancer cell seeding.

To guide the cancer cell entrance into the central channel, arrays of trapezoidal posts were placed between central channel and side channels (Figure 1). CNF's 3D printer (Object30 Pro, Stratasys) was used to fabricate a mold for this microfluidic device, casted with polydimethysiloxane (PDMS, Sylgard 184, Dow Corning) (Figure 2). To verify liquid flow within microfluidic channels, first, holes for liquid flow were punched at the end of each channel. Then, the PDMS microfluidic device and glass coverslip were treated with plasma cleaner and the channels of the device were bonded, facing the surface of a plasma treated glass coverslip for binding.

Aqueous solution containing red dye was injected at the inlet of each channel and filled all microfluidic channels (Figure 3). However, post structure of the device is not enough to provide high resolution and there are striation patterns in the microfluidic channel, which will be an issue for solution leakage (Figure 4).

Conclusions and Future Steps:

The 3D printer is a tool for fast and cost-effective fabrication. However, the resolution is limited to sub-millimeter structures of microfluidic devices.

To increase the resolution of our microfluidic device, a soft photolithography technique is required. In the future, an epoxy-based negative photoresist will be coated on a silicon wafer and patterned using a photomask.

References:

[1] Lab on a Chip (2017), Vol. 17, 3851.

[2] PNAS, 2012, Vol. 109, 13515.

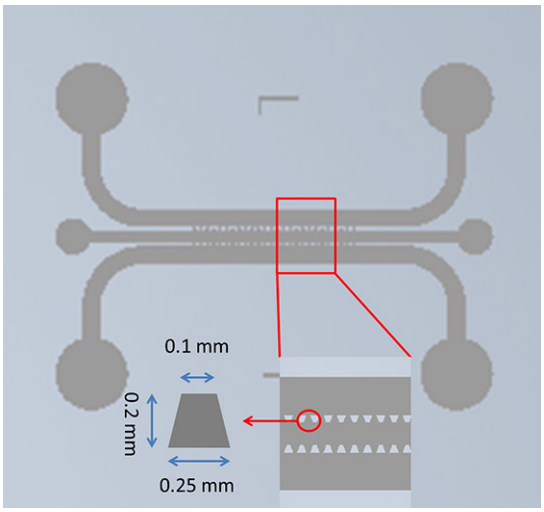

Figure 1: Design and dimension of microfluidic device. The device is composed of three channels and the array of arrays of trapezoidal posts between channels will provide the entrance of breast cancer cells into bone ECM. The smallest dimension of posts is 100 µm.

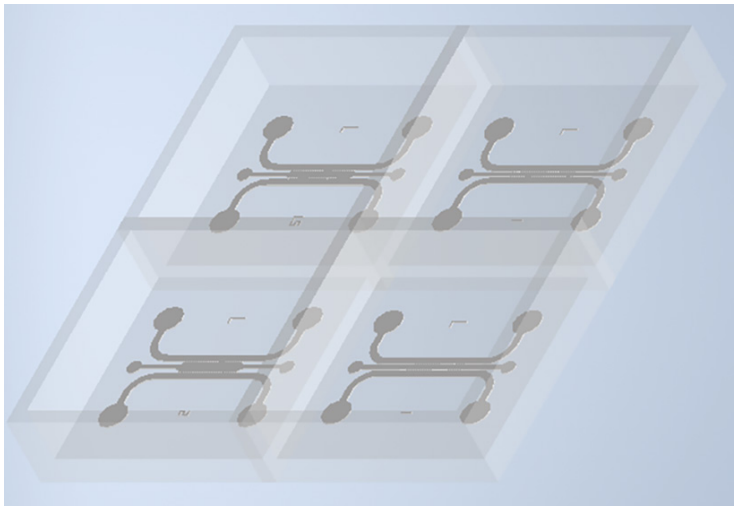

Figure 2: Mold design to cast PDMS microfluidic device. The mold has four microfluidic devices and each device has different central channel widths (1-2 mm).

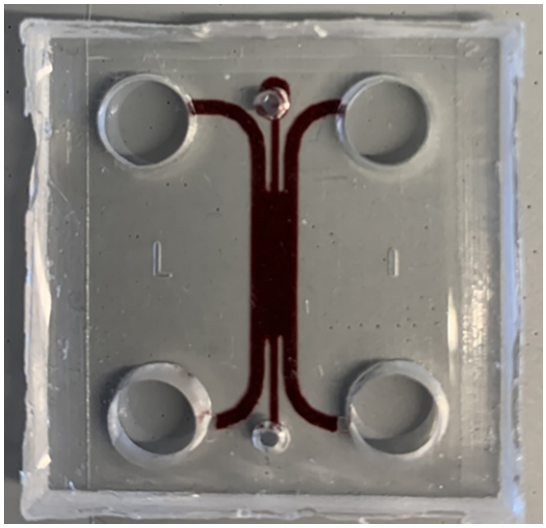

Figure 3: PDMS casted microfluidic device with fluidic channels. Plasma treated PDMS device was bound on plasma treated glass coverslip. Solution containing red dye was injected into holes of each channel.

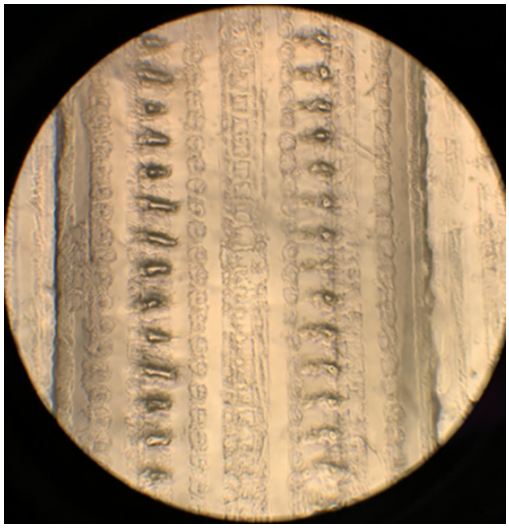

Figure 4: Low resolution of posts within central channel. Each post has different resolution and striation pattern was observed on the surface of PDMS device.