Microfluidic cancer cell invasion assay

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Abstract

Inhibiting metastasis is one of the main problems in cancer treatment. Therefore, it is of great importance to understand the underlying mechanisms on the molecular level. Here, we present a microfluidic chip which allows analyzing the morphology and speed of cancer cells during invasion in gradient of different chemical cues. The platform facilitates automated time-lapse imaging of the invasion process itself (rather than just migration) and furthermore holds significant potential for drug screening.

Metastasis occurs inside the body on long time scale. However, analyzing this process at cellular resolution *in vivo* seems difficult. Furthermore, *in vivo* models do not allow monitoring the effect of chemical gradients. To overcome these limitations, we have developed a microfluidic platform for 2D invasion assays. The microfluidic chip includes a time-stable flow-free gradient generator and a device for cell patterning on fibronectin coated glass. The chip is manufactured as two layers of PDMS using soft lithography. The alignment and bonding of the two layers is achieved by depositing a thin layer of PDMS pre-polymer on the bottom surface of the upper layer, excluding the channels, and an additional baking step. The upper PDMS layer features a channel filled with air and is designed to pneumatically control the position of a spacer located underneath, in the lower PDMS layer. This spacer allows the separation of cancer and non-cancer cell lines during their seeding in the microfluidic chip. Subsequently, the spacer is pulled up enabling the two populations to spread and invade into each other.

In a proof-of-concept experiment we have used non-small lung cell carcinoma cells H1299, tagged with mCherry (from Uri Alon library, Weizmann Institute of Science) and 3T3 fibroblasts and successfully demonstrated the feasibility of the assay. In particular, we show that human derived cancer cells can be patterned in the microfluidic chip and selectively exposed to gradients of various compositions. This approach for studying metastasis is fully compatible with automated live cell imaging and should allow drug screens, optionally including patient-derived primary cells.