ABSTRACT
We present high throughput micro assembly of cell containing microgels using railed microfluidics. Heterogenous micropatterning of cell matrix has been achieved using rail-based fluidic self assembly, enabling low cost fabrication of cell matrix array by eliminating need for sequential lithography or manual assembly.

KEYWORDS: Railed microfluidics, Hydrogel, Self-assembly.

INTRODUCTION
Micro patterning of hydrogel to encapsulate multiple cell types in 3D matrix has been extensively studied due to its application in tissue engineering and cell based microarray[1]. In these applications, it is important to locate different cells in desired locations on a chip in order to study cell-cell interaction or form heterogeneous tissue culture. Patterning of multiple cell types involves in sequential repetition of multiple photolithographic steps or time-consuming pick-and-place assembly of microgels. Of the interest is to minimize the time and cost required for the cell patterning. Recently, we have demonstrated ‘railed microfluidics,’ a fully deterministic way of guiding and assembling microstructures inside a fluidic channel by fabricating grooves (“rails”) on the channels and polymeric microstructures with ‘fin’ that fit with the grooves (figure 1 inset)[2]. In this paper, we demonstrate the application of the rail-based assembly to cell and tissue engineering. Based on the accurate guiding and assembly using rails, heterogeneous cell matrix array is simply fabricated without sequential photolithographic steps.

EXPERIMENTAL

Figure 1 A schematic diagram of the experiment for the assembly of cell microgel in a microfluidic channel. (a) Fabricating microgels encapsulating cell in a railed microfluidic channel. (b) Pipetting microgels in microgel suspension. (c) An assembling microgels using pipetting and pushing them into rail-patterned channel.
Unique aspect of our approach is to separately fabricate microgels with multiple cell types in a channel for microgel production and assemble them at once in a channel for cell matrix assembly (Fig. 1). First, a cell suspension dispersed in a hydrogel (PEG-DA) was introduced into a microgel producing channel with multiple grooves (rails). Then microgels were in-situ polymerized on a rail using patterned UV light through mask (Fig. 1a).

RESULTS AND DISCUSSION

The fin structure on the cell-containing microgel fits with ‘rail’ so that the microgel can travel along the rail (Fig. 2). The finned microgels were then pipetted out of the channel for microgel production after washing with PBS (phosphate buffered saline) (Fig. 1b). Second, we introduced the cell-containing microgels to an assembly channel in order to fluidically self-assemble them into a cell matrix (Fig. 1c).

Figure 2 Prefabricated Microgel encapsulating HeLa cells stained with PI (propidium iodide). (Scale bar: 100μm) (a) A coded microgel fabricated on the rail (b) fluorescence microscope image of the microgel.

The finned microgels were guided along the rails in the assembly channel to the desired location due to the shape matching of the fin and the rail (Fig. 3).

Figure 3 Sequential images that microgel is introduced into the microchannel with guidance of rail after pipetting them into microfluidic channel.

Figure 4 (a) The array of microgel assembled and aligned by the rail. Fluorescence microscope image (Right ) (b) The assembly of heterogeneous microgels in a cross-shaped microchannel. Microgel of HeLa cell stained with PI and Microgel of HeLa cell tranjected with GFP was introduced and assembled on the microfluidic channel. (Left) (Scale bar: 100μm)
We demonstrated the assembly of prefabricated microgel in a groove-patterned microfluidic channel. The microgels were stopped at the end of the rail and assembled to form an ordered cell matrix shown in Fig. 4(a). By flexibly designing the assembly channel, heterogeneous patterning of different microgel can be done with one assembly step. For example, different microgels prefabricated in the microgel producing channels are assembled by designing multiple inlets and rails (Fig. 4b). Microgel formation and assembly can be done in the same microfluidic channel for more complicated assembly.

![Figure 5](a) Three vertical channels for cell suspension, a horizontal channel for the assembly of heterogeneous microgel using rail-type groove. (b),(c) 3x3 checkerboard composed of heterogeneous cell microgel. (Scale bar: 100μm)

Microgel formation and assembly can be done for more complicated assembly. 2D heterogeneous checker board pattern made of 293 and HeLa cell was fabricated in a channel. Three vertical channels were intersected with a horizontal channel with multiple assembly rails in the center (Fig.5a). After microgels were in-situ polymerized at the assembly rail from the cell containing hydrogel flown vertically over the multiple horizontal assembly rails, PBS from horizontal channel pushes the microgels horizontally along the rail to form the checkerboard pattern.

**CONCLUSIONS**

We have used railed microfluidics as a method for guiding and assembling microstructures inside a microfluidic channel. The controllability of rail based assembly would be applicable to wide range of application in cell chips and tissue engineering.

**ACKNOWLEDGEMENTS**

This work was supported by the Korea Science and Engineering Foundation(KOSEF) grant funded by the Korea government(MOST) (2007-04049)

**REFERENCES**
