Electronic Supplementary Information (ESI) for Lab on a Chip

Electronic Supplementary Information

Controllable organization and high throughput production of recoverable 3D tumors using pneumatic microfluidics

Wenming Liu,*[a] Jian-chun Wang[ab] and Jinyi Wang*[a]

[a] *Colleges of Science and Veterinary Medicine, Northwest A&F University, Yangling, Shaanxi, 712100, China*

[b] *Energy Research Institute of Shandong Academy of Sciences, Jinan, Shandong, 250014, China.*

Abstract. This supplementary information provides all the additional information and a more detailed discussion of the current study.

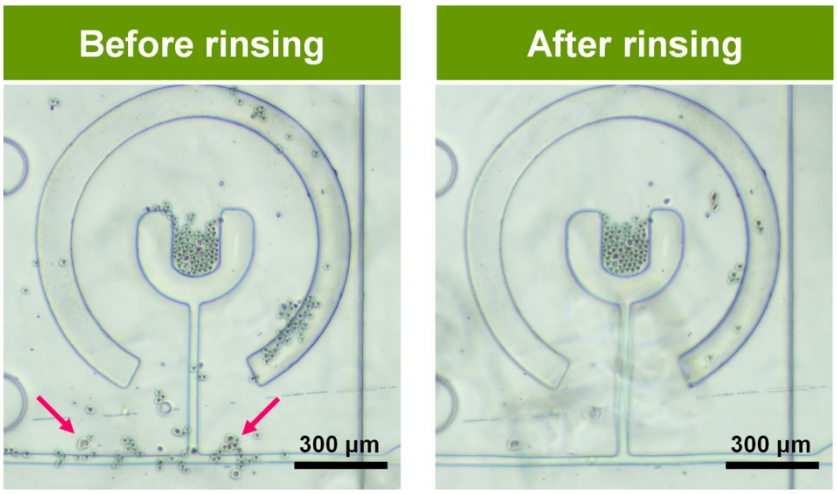

Fig. S1. Cell trapping by the micro-channel network. The channel network was originally designed for the connection between the first-generation PμSs and air inlet in the PμS layer. The height of connecting channel and PμSs were the same. The excess cells can be removed by a rinse step, however, this type of mis-trapping (red arrows) negatively impacts the specific cell localization.

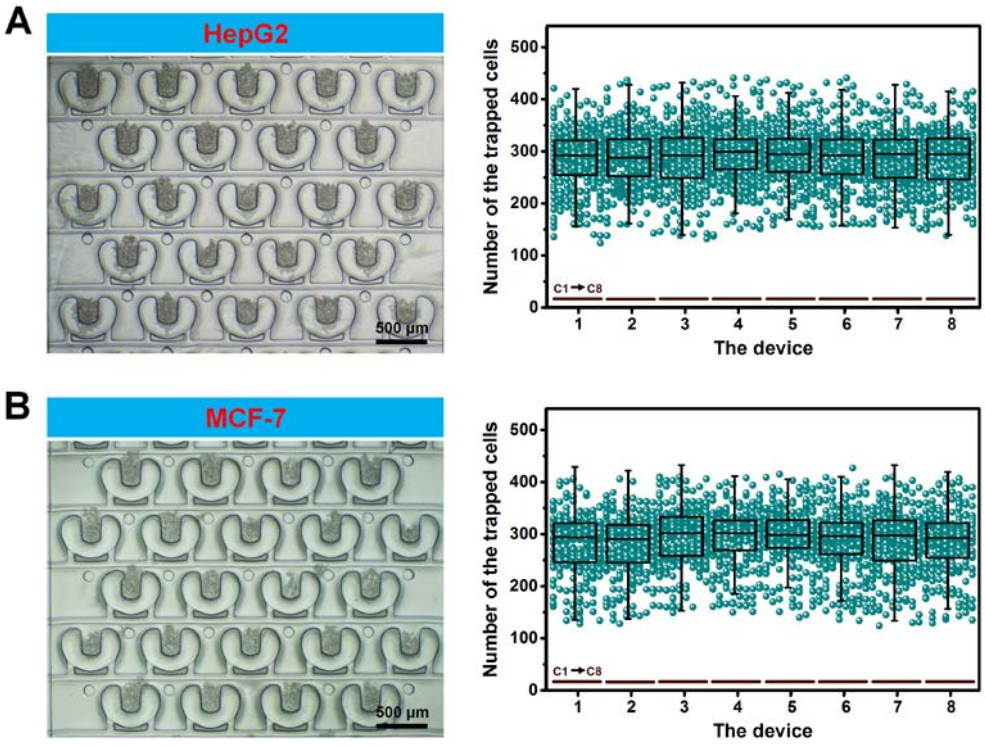

Fig. S2. Parallel positioning of tumor cells by PμS array. (A) Optical image of HepG2 cell trapping in the microchamber (left), and the quantitative analysis of HepG2 cell localization (right). (B) Optical image of MCF-7 cell trapping in the microchamber (left), and the quantitative analysis of MCF-7 cell localization (right).

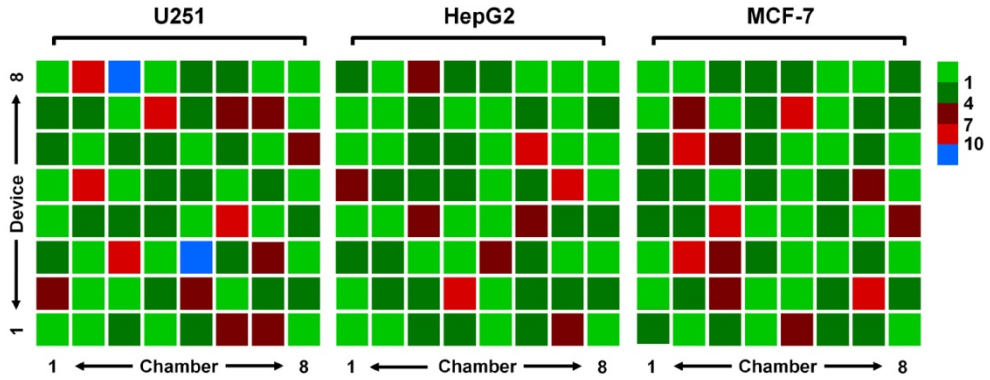

Fig. S3. Quantitative analysis of precise cell localization by PμS in the microchamber pre-modified by BSA. The data presents the number of excess cells remaining at the non-specific trapping region in the chamber.

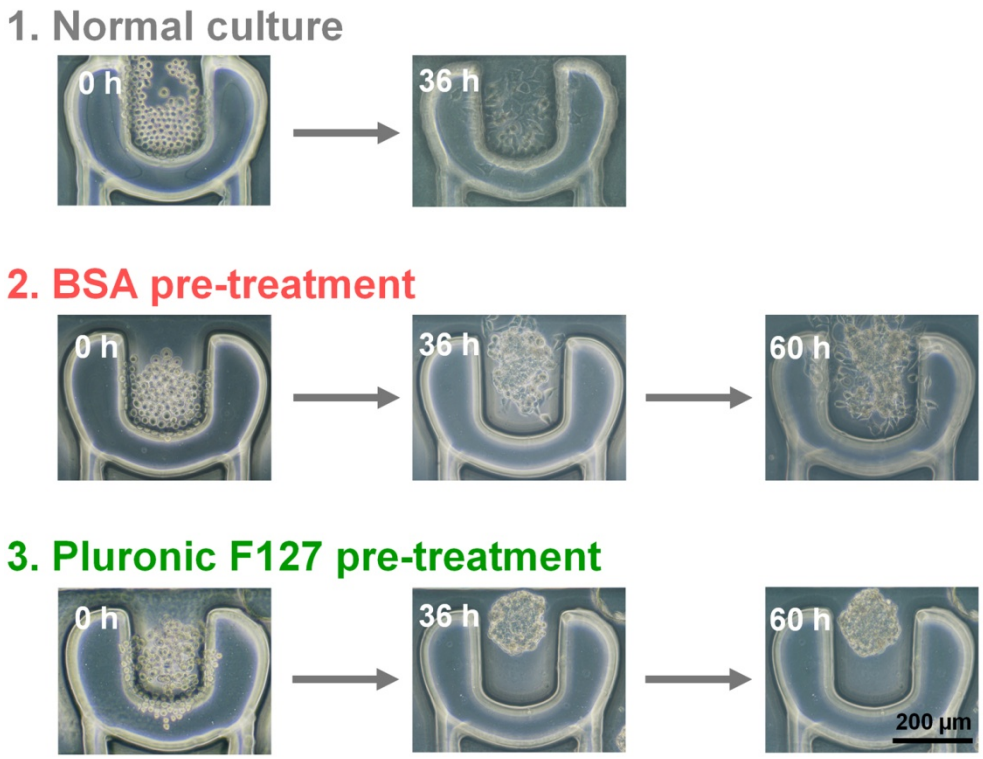

Fig. S4. Adhesion and 3D tumor formation of HepG2 cells in the PDMS chamber with different pre-modification, including treatment-free, BSA treatment and Pluronic F127 treatment. The results show that Pluronic F127 can highly prevent the HepG2 cell adhesion and promote the formation of 3D tumors, compared with BSA.

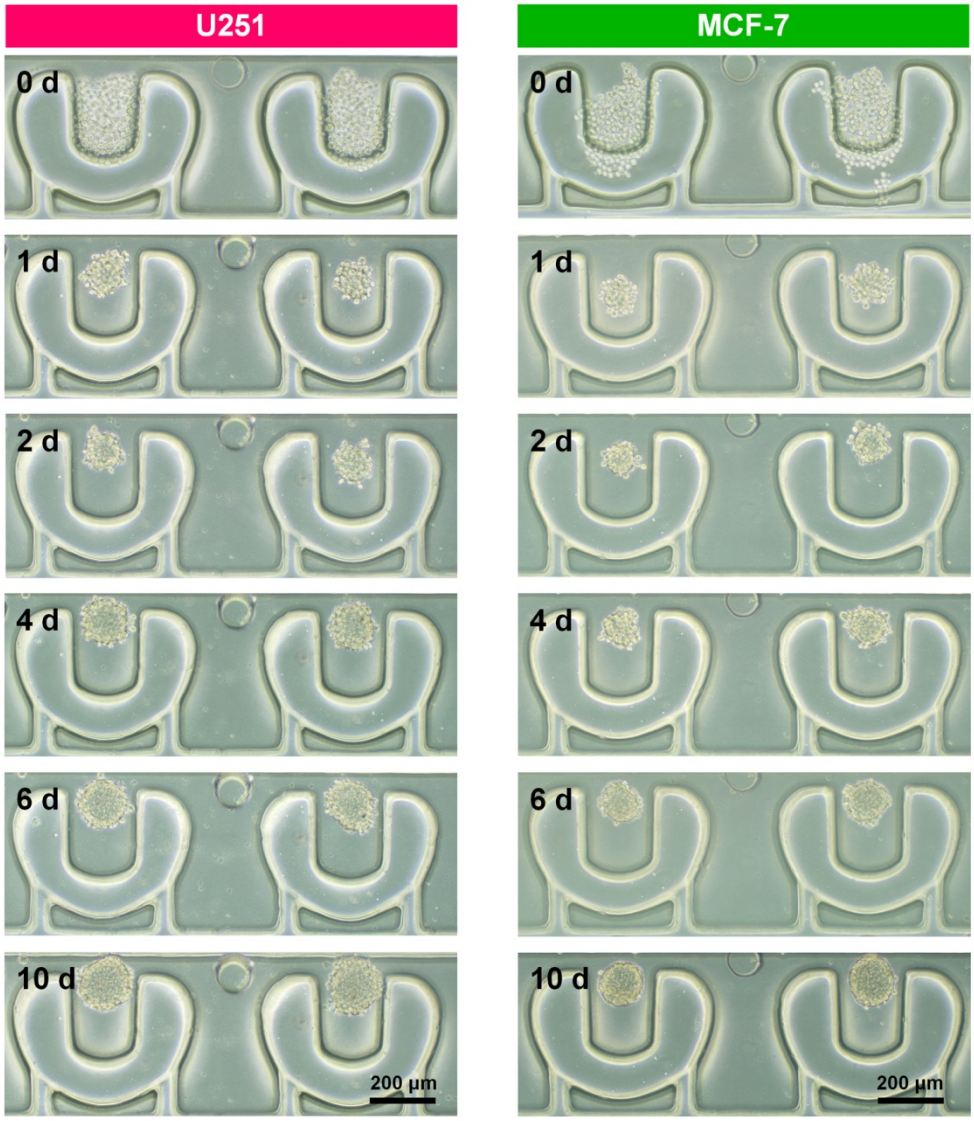

Fig. S5. Optical images of U251 and MCF-7 tumors at different time of culture in the microfluidic device.

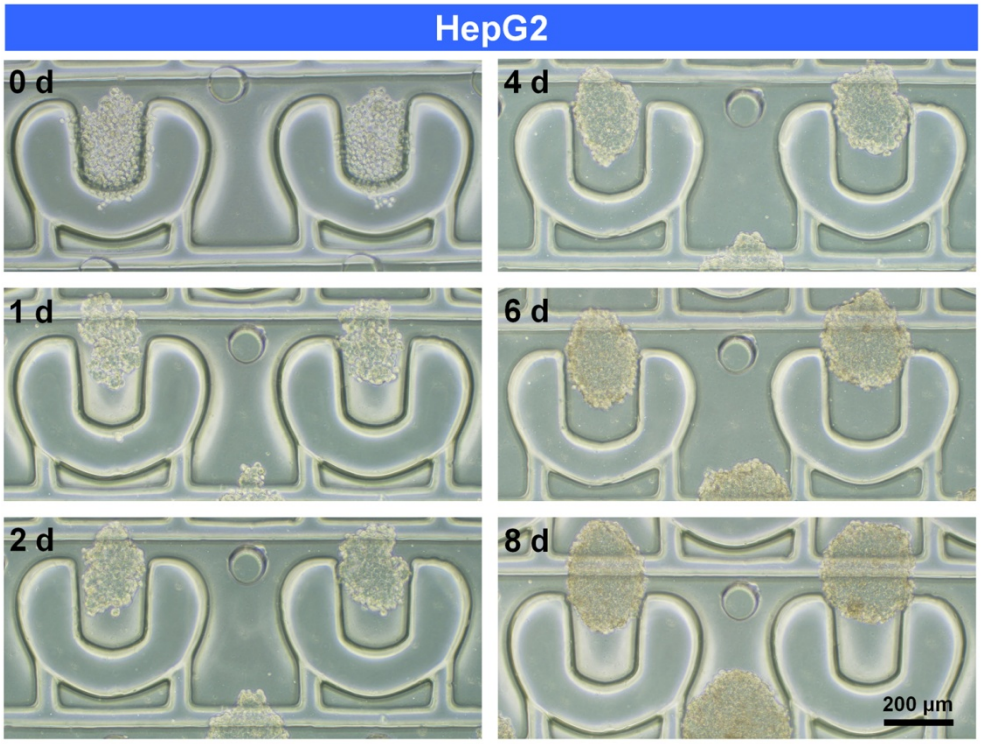

Fig. S6. Optical images of HepG2 tumors at different time of culture in the microfluidic device.

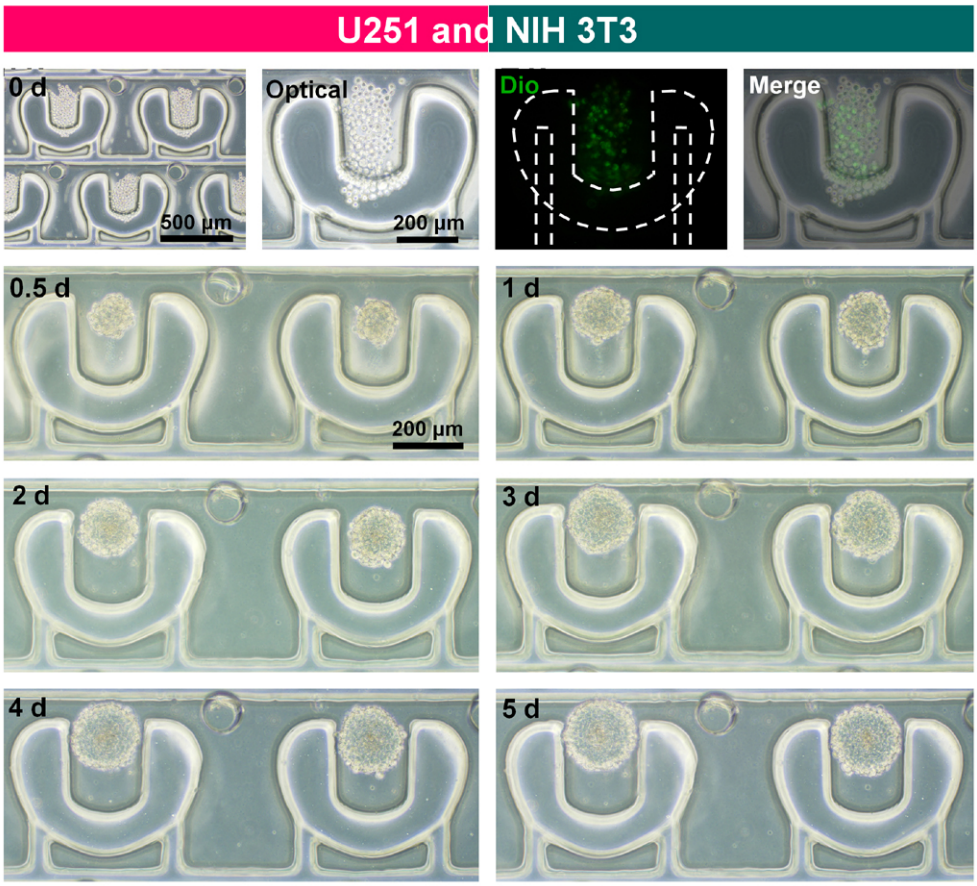

Fig. S7. Co-culture of U251 tumor cells and NIH 3T3 fibroblasts in the device. The fibroblasts were pre-stained by DiO (green) for cell tracking. The co-cultured 3D tumors presented a faster growth compared with the mono-cultured U251 tumors (Fig. S5). The cell suspension containing U251 tumor cells and NIH 3T3 fibroblasts was used in the cell loading process. The cell density for each cell type in the suspension was the same (2.5×10^6 cells/mL).

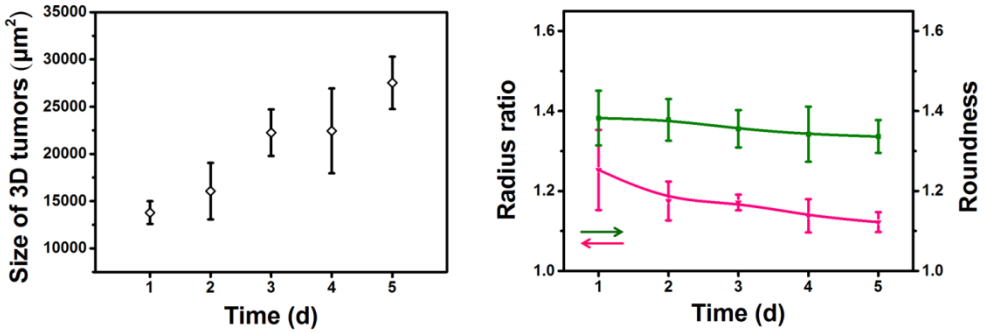

Fig. S8. Quantitative assessment of size and shape of the co-cultured tumors (U251 and NIH 3T3). Area, radius ratio and roundness of 3D tumors are used to determine the structural dynamics.

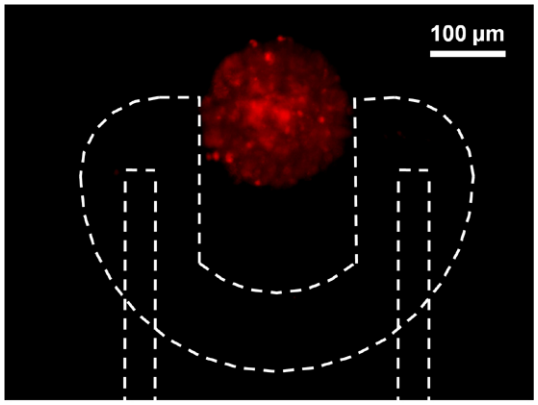

Fig. S9. Fluorescent image of 10-days cultured U251 tumor. The cells were stained by PI solution. There were several dead cells (red) accumulated in the center of 3D tumor, suggesting a start of necrotic core formation.

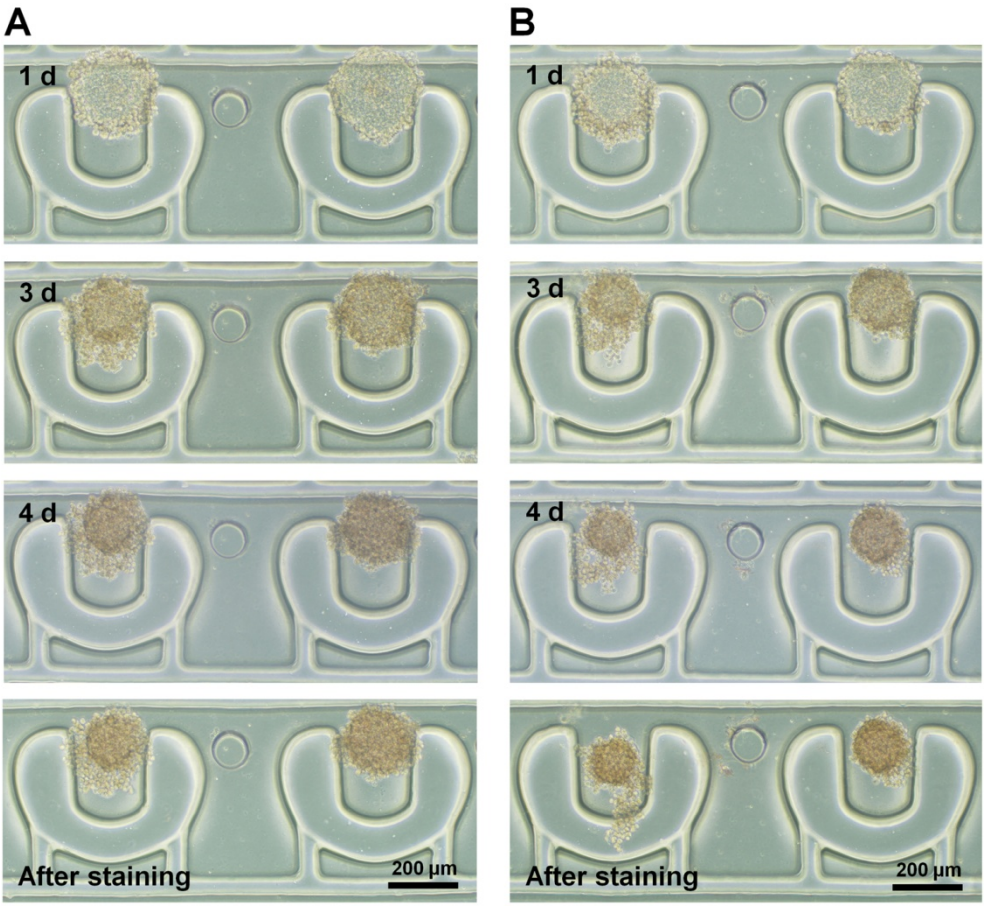

Fig. S10. Optical images of U251 tumors treated by paclitaxel-loaded 0% FD-NPs (A) and 50% FD-NPs (B) at different times. Two pictures at the last row were acquired after FDA/PI staining, corresponding to the fluorescent images of Figure 6D and E respectively.

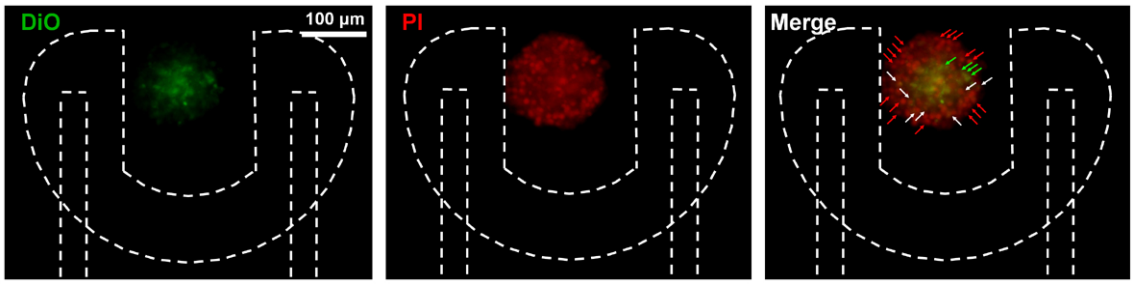

Fig. S11. Fluorescent images of cocultured U251 tumor treated by paclitaxel-loaded 50% FD-NPs for 2 days. The coculture was kept for 5 days before the drug treatment. The fibroblasts were pre-labeled by DiO (green) for cell tracking, and the dead cells were stained by PI (red). The result showed large number of dead cells in the tumor, and it seemed that more U251 tumor cells (red arrows) were killed by paclitaxel-loaded 50% FD-NPs than fibroblasts (white arrows). Meanwhile, some fibroblasts (green arrows) in the peripheral rim of 3D tumor were still live. The result suggests that folate promotes selective cytotoxicity of drug-loaded NPs against tumor cells.

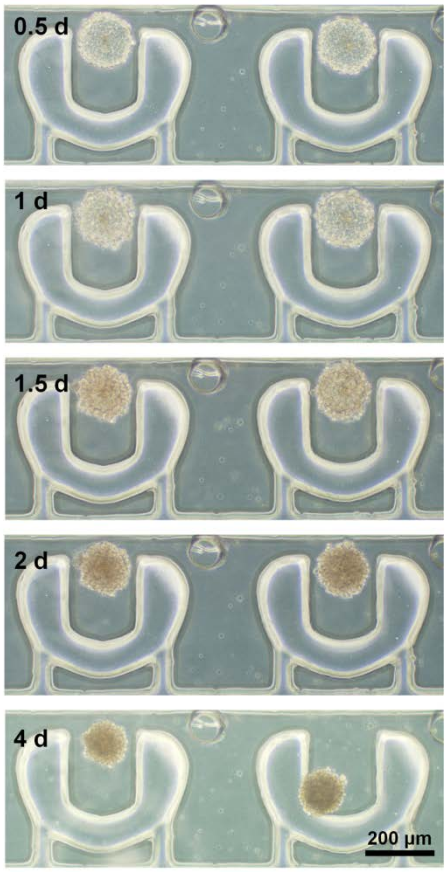

Fig. S12. Size dynamics of cocultured U251 tumors treated by paclitaxel-loaded 50% FD-NPs at different times. There were fewer cells dispersed around the cocultured 3D tumors, compared with the monocultured U251 tumors (Fig. S10).

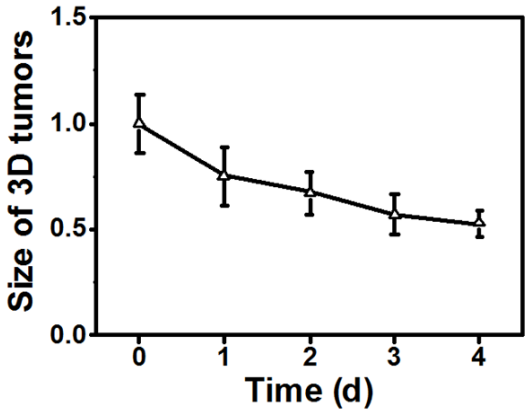

Fig. S13. Normalized size dynamics of cocultured U251 tumors along with the treatment using paclitaxel-loaded 50% FD-NPs.

ESI Movies

Movie S1. Precise localization of U251 cells in the PμSs, and the non-trapped cells can pass through the chamber and over the connecting channel.

Movie S2. Recovery of U251 tumors using a simple off-switch for the PμSs and a rinse step.

Movie S3. Recovery of HepG2 tumors from the microfluidic device.