Supplementary information

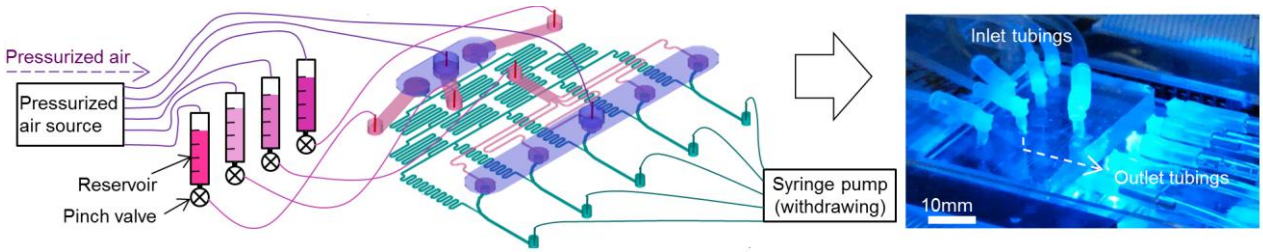
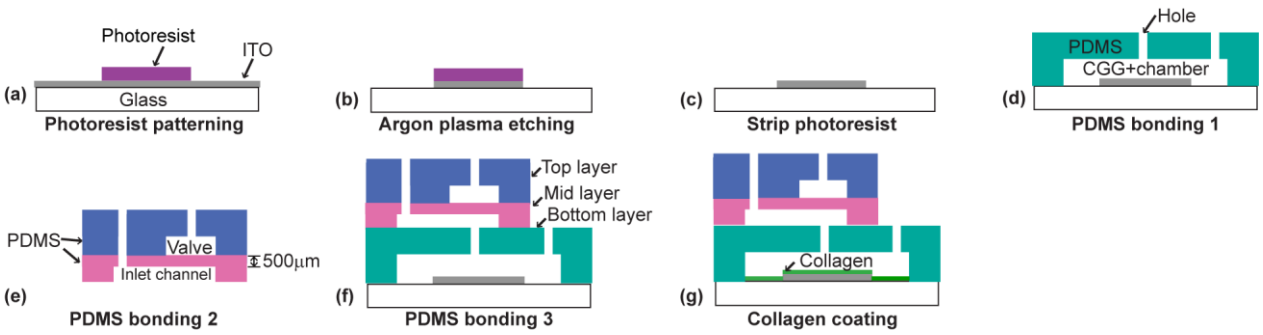


Figure S1 The perfusion system working with the cellular microarray chip for anticancer drug screening. The system included a pressurized air source, reservoirs, pinch valves, and a syringe pump. Pressurized air source was applied to keep the pressure inside the chip higher than ambient pressure (gauge pressure was 5psi) for bubble elimination[34,61,62] before cell seeding. After a bubble-free environment was confirmed, the pressurized air was released to prevent any unexpected compressive stimulus on cells.[63-65] In addition, pressurized air source was also applied to activate APV and ACV (see Fig. 1b and 4a). Moreover, pinch valves were used to regulate solution exchanges. Furthermore, the flow rate was controlled by using a syringe pump in the downstream. The right panel is the chip with tubings. A dashed arrow depicts the fluid flow path from inlets to outlets.



(h)

Part	Dimension
Membrane of APV and ACV	500 μm (thickness)
Manifold channels	200 μm (width) × 75 μm (height)
Inlet channels	1000 μm (width) × 75 μm (height)
CGG channels	200 μm (width) × 75 μm (height)
Cellular microarray chamber	1920 μm (length) × 300 μm (width) × 75 μm (height)
PIRE	640 μm (center-to-center spacing between PIREs), 185 μm (diameter of a PIRE), 20 μm (electrode width), 5 μm (inner gap), 7.5 μm (middle gap), 10 μm (outer gap)

Figure S2 Microfabrication of the cellular microarray chip. Most of the procedures (Fig. S2a to S2d) were reported in our previous work,[13] except the fabrication for the three-layer microfluidic network (Fig. S2e and S2f). (a) Photoresist was micropatterned on an ITO film. (b) The ITO film was etched using argon plasma. (c) Photoresist was then stripped off. (d) A PDMS layer was bonded to the micromachined ITO glass. (e-f) The top layer and the bottom layer of the microfluidic network were fabricated in a 10:1 (base:cross-linker agent) ratio by weight; the mid layer featured with a 500 μm-thick membrane was fabricated in a 15:1 ratio to serve as a valve. In order to ensure robust bonding between top layer and mid layer, an excess of the base was added to top layer and extra cross-linker agent was added to mid layer,[66] then the two layers defining APV and ACV were brought into conformal contact and cured by heat. ~~(f)~~ The bonding between mid layer and bottom layer was performed by oxygen plasma treatment. The chip was then plasma-sterilized[67] (50 W, 15 sccm (standard cubic centimeters per minute), 570 mTorr, 4 min.), since conventional autoclave will deteriorate the bonding strength[67] to reduce the long-term reliability of the chip. (g) The culture chambers were incubated in a collagen solution (100 μg ml^{-1}) at 37°C for 1 hour. Finally, the chip was stored at 4°C prior to use. (h) Dimensions of the cellular microarray chip.

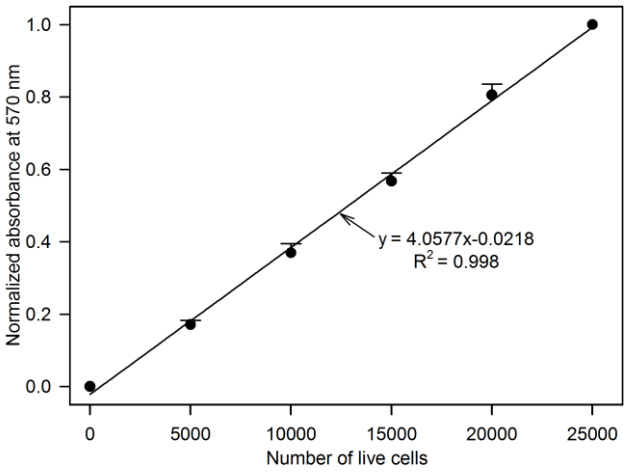


Figure S3 The correlation between number of live cells and absorbance obtained from MTT assay. The data shows an increase in absorbance as a result of number of live cells. A linear regression of the data proves the capability of MTT assay for interpreting quantities of live cells. (MCF7 cells were cultured overnight in wells of 96-well plates before performing MTT assay; data were means ± SEM, n=5)

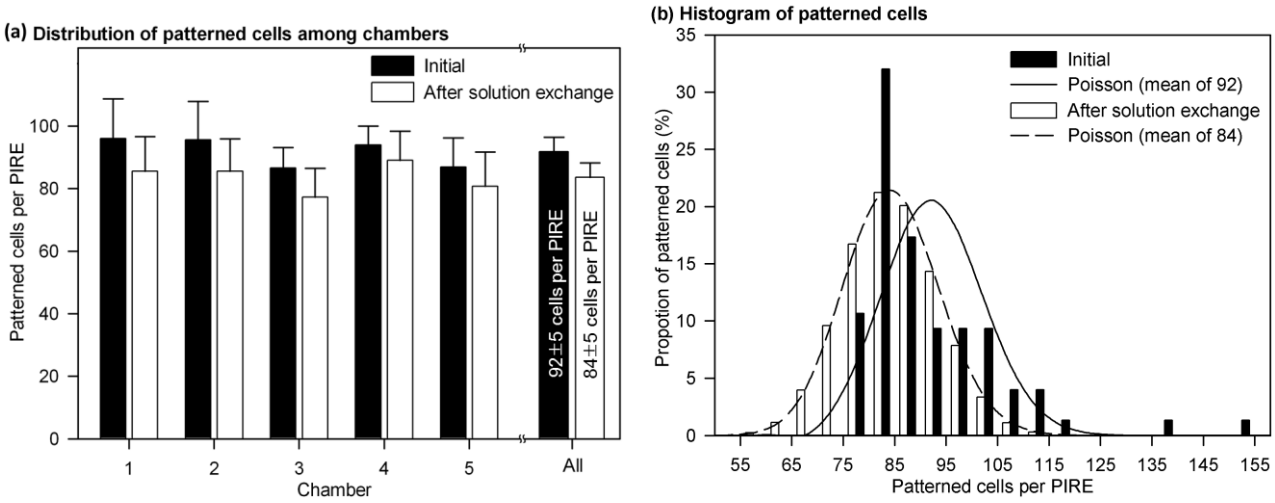


Figure S4 (a) "All" represented the mean of all chamber's distribution of pattern cells. Right after DCP, 92±5 cells were patterned on a PIRE. After solution exchange, 84±5 cells remained on a PIRE. There was no significant difference in cell amount among the chambers. (data were means ± SD, n=5; single factor ANOVA, $P < 0.05$) (b) The histogram of initially patterned cells (black bars) on a PIRE generally followed the Poisson distribution for a mean of 92 (solid line); after a solution exchange, the histogram of remained cells (white bars) turned to highly agree with the Poisson distribution for a mean of 84 (dashed line). (n=75)

Table S1 A comparison of IC_{50} values from the cellular microarray chip, 96-well plates, and literature

Drug	IC_{50} from cellular icroarray chip (μg ml^{-1})	IC_{50} from 96-well plates (μg ml^{-1})	IC_{50} from literature (μg ml^{-1})
Cisplatin	29.9	22.2	14.4 [43] 24.0 [44] >15.0 [45]
Docetaxel	12.1	12.8	14.1 [46]

Video S1: After solution exchange for culture medium, vital patterned cells attached well to the substrate, and then some cells migrated from PIREs to surrounding areas.

Video S2: At t=0 h of drug perfusion, although cells became flat and polygonal in shape, cells still retained good vitality.

Video S3: At t=24 h of perfusion (no drug), a polygonal cell morphology, good vitality and a significant cell proliferation were found.

References

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