Supplementary Material (ESI) for Lab on a Chip

Exploring Cancer-Associated Fibroblast-Induced Resistance to Tyrosine Kinase Inhibitors in Hepatoma Cells Using a Liver-on-a-Chip Model

Madhu Shree Poddar,^a Yu-De Chu,^b Gaurav Pendharkar,^c Cheng-Hsien Liu^{*acd} and Chau-Ting Yeh^{*bef}

^{*a.*} Institute of Nanoengineering and Microsystems, National Tsing Hua University, Hsinchu, 30044, Taiwan, R.O.C.

^{b.} Liver Research Center, Chang Gung Memorial Hospital, Taoyuan 333, Taiwan, R.O.C.

^{c.} Department of Power Mechanical Engineering, National Tsing Hua University, Hsinchu 30044, Taiwan, R.O.C.

^{d.} College of Semiconductor Research, National Tsing Hua University, Hsinchu 30044, Taiwan, R.O.C.

^{e.} Institute of Stem Cell and Translational Cancer Research, Chang Gung Memorial Hospital, Taoyuan 333, Taiwan, R.O.C.

f. Molecular Medicine Research Center, Chang Gung University, Taoyuan 333, Taiwan, R.O.C.

*E-mail: liuch@pme.nthu.edu.tw (C.-H. L) and chautingy@gmail.com (C.-T. Y)

Supplementary Figures

Figure S1



Figure S1. **Operation of the liver lobule-on-a-chip.** The sequential operation of the liver lobule-on-a-chip from Step 1 to Step 8 was illustrated.



Figure S2. Sorafenib and Lenvatinib IC₅₀ graphs.

The above graphs represent the IC₅₀ of Sorafenib (a) and Lenvatinib(b). Lenvatinib (SML3017, Sigma-Aldrich) and Sorafenib (S7397, Selleckchem, Houston, TX, USA) were evaluated at different concentrations (ranging from 100 to 0.1 μ M) to obtain their relative IC₅₀ values in order to measure drug sensitivity. In a 96-well plate, both fibroblasts and liver cancer cells were planted at a density of 5 × 10³ cells per well, along with the full growth media.



Figure S3. **Top view of the liver lobule-on-a-chip.** The illustration shows the dimension details of the liver lobule-on-a-chip to ensure reproducibility. The unit is mm.

Supplemental Videos

Video S1 captures the complete sequence of activities involved in loading cells, concreting gelma, and washing the cells within the chip. Initially, Cancer HepG2 cells are loaded, followed by the concreting of gelma through UV exposure with the aid of an exposure mask. Subsequently, excess cells are removed through a washing process, and this identical procedure is then applied to the second type of cells, Fibroblast 3T3.

Video S2 shows the demonstration of the chip's operation using dye-labeled cells.