Supplementary Information (SI) for Lab on a Chip.

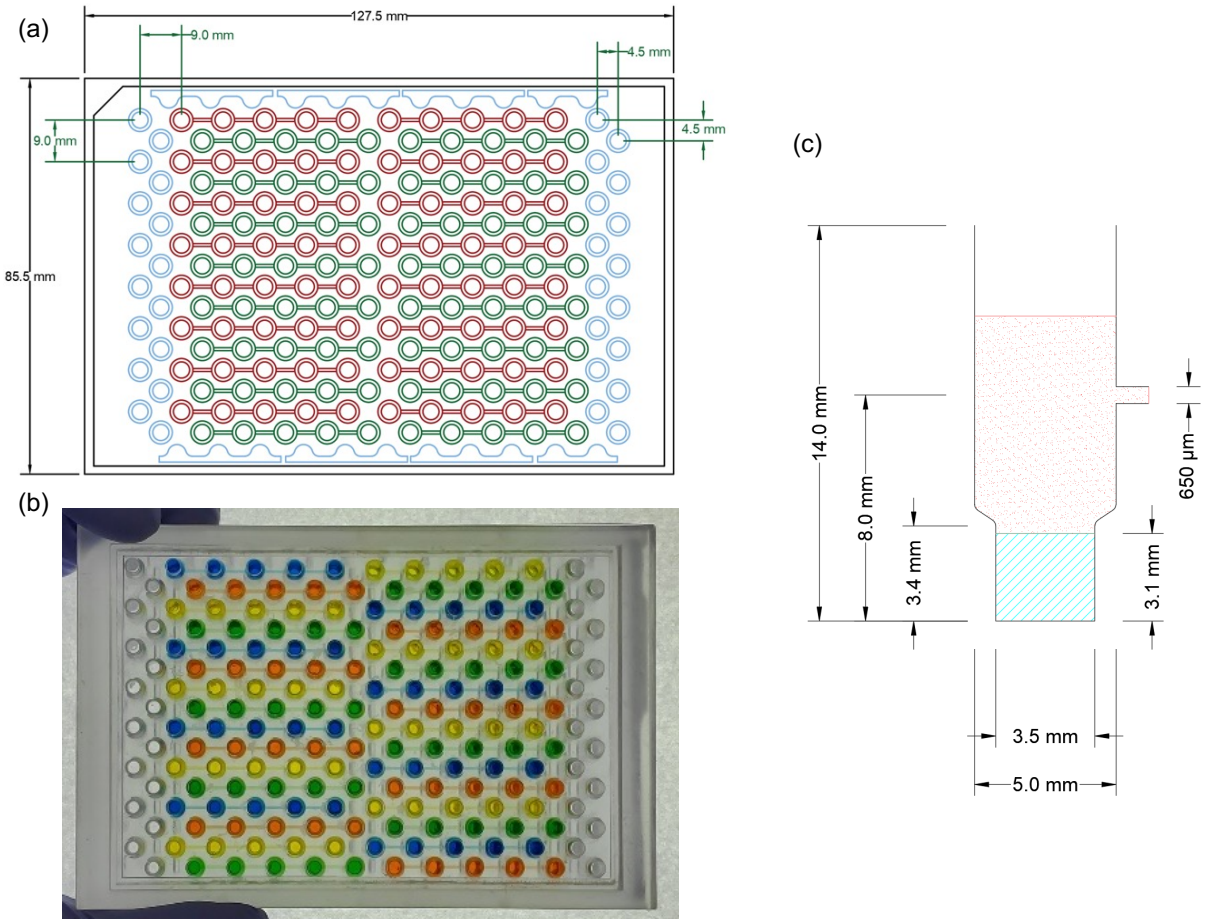

Fig S1. a) Top view of the tissue chip design with dimensions of the plate and well-well distances shown. b) Bottom view of the fabricated tissue chip containing water in the side wells and food coloring dyes in the tissue compartments. Each color represents an independent unit, and the fluid level is higher than the channels. c) Dimensions for each well and the channels. The bottom cylinder has an inner diameter of 3.5 mm, similar to wells of a 384-well plate. Filling the chamber with 30 µL collagen (shown in cyan) nearly loads the cylinder in the bottom of the compartment, which then widens at the top to increase media capacity and media-air surface area (media shown in light red).

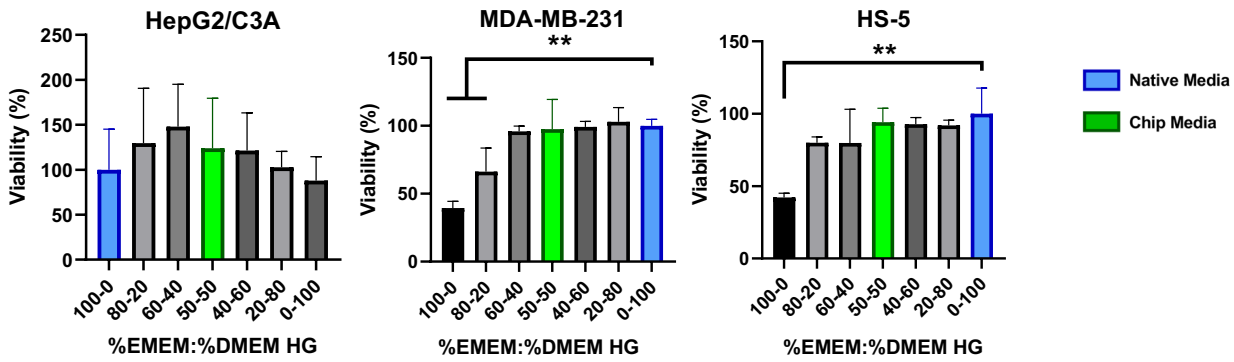

Fig S2. Effects of different ratios of EMEM:DMEM HG (high glucose) on the viability of HepG2/C3A liver cells, MDA-MB-231 breast cancer cells, and HS-5 bone marrow stromal cells. **p<0.01. Each bar shows an average of 4 replicates or more and error bars show standard errors.

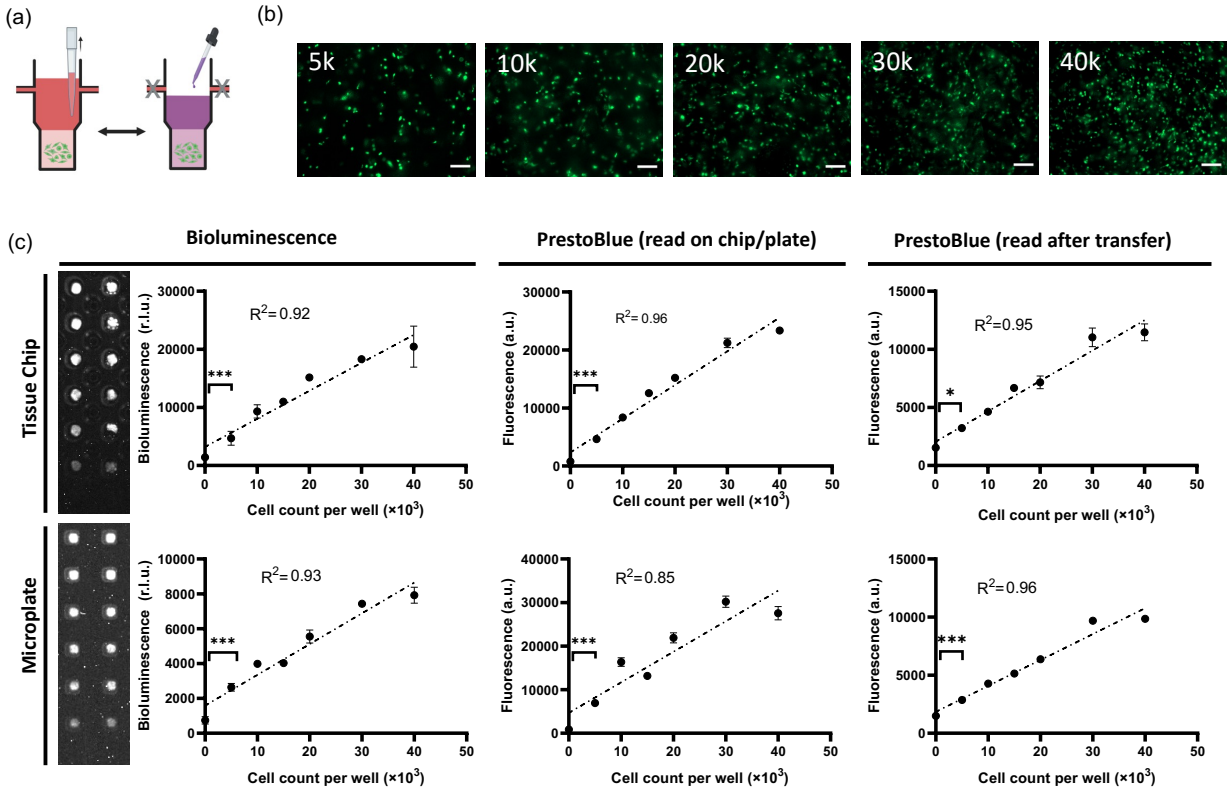

Fig S3. (a) Decreasing media volume reduces media height in the compartment to disconnect fluid flow among compartments and enables independent biochemical measurements in each tissue compartment. (b) Fluorescence images of MDA-MB-231 cells at different densities seeded in the tissue chip. Scale bar is 200 μm. (c) Bioluminescence signal intensities (left column) and fluorescence signal intensities from PrestoBlue assay (right two columns) from cells in tissue compartments (top row) and a standard 384-well plate (bottom row) for MDA-MB-231 cells at different densities. The fluorescence signal intensities were initially measured in situ in the tissue chip (middle column), followed by transferring 25 μL of the supernatant media to a standard plate to repeat the measurement and evaluate potential interference from collagen in the tissue chip (right column).

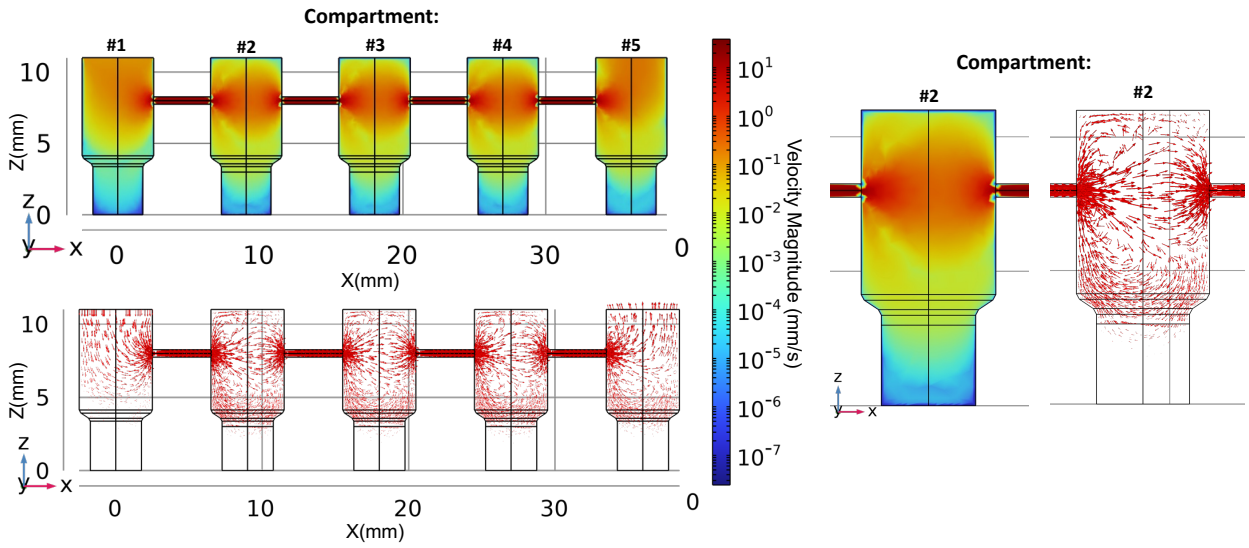

Fig S4. Heatmap and vector representations of velocity field in the tissue chip (from static mesh simulation for oxygen consumption study).

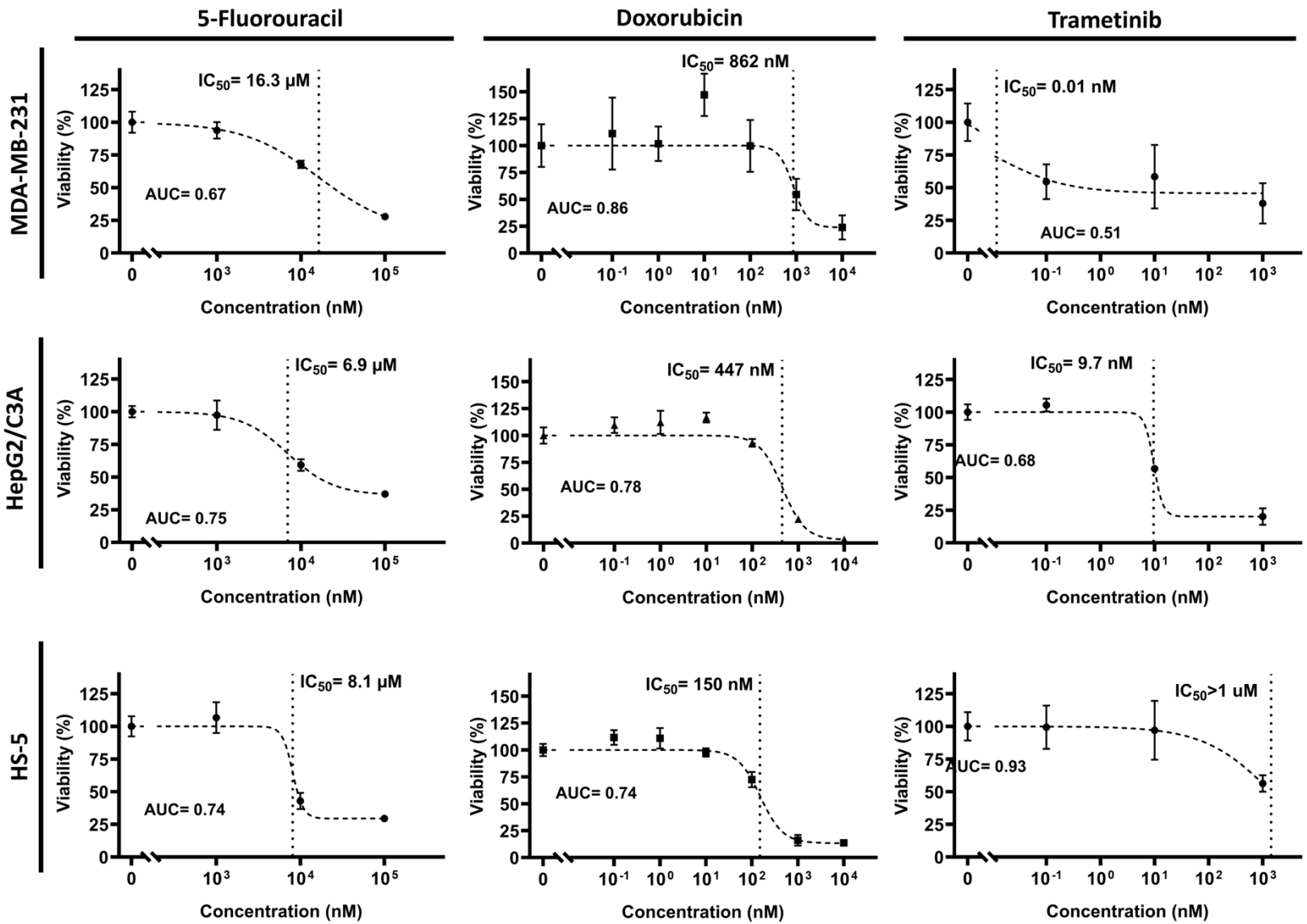

Fig S5. Dose responses of different cells in 3D cultures in a 384-well plate to three different drugs.