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Supporting Information

Statistic Single-Cell Analysis of Cell Cycle-Dependent Quantum Dot Cytotoxicity and Cellular Uptake Using Microfluidic System

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I. Single cell capture on the microfluidic device

Microwell diameter was designed to range from 25 to 40 μm to optimize the size. Cells conveniently entered into larger microwells but they also were easily to be flushed out. As a result, cell occupancy was higher than 90% at the diameter of 30 and 35 μm while it decreased to 88% at the diameter of 40 μm. The percentage of single cell reached the highest at the diameter of 25 μm (Figure S1).

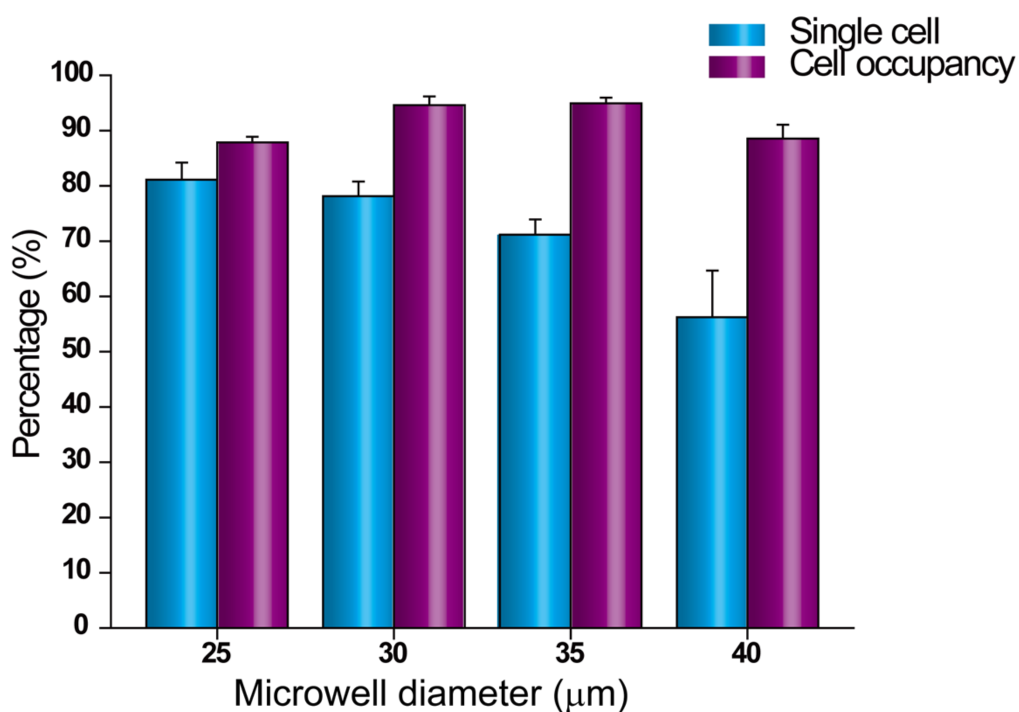

Figure S1. The percentage of single cell and cell occupancy at different diameter of microwells.

II. Concentration of QD solution simulation in the microchannels

QD and blank solution diffused from channel 1 and 3, respectively, into channel 2 from the low microchannels. At static condition, the diffusion reached balance and QD concentration become stable after a few hours. Software Comsol Multiphysics was utilized to simulate this process and data showed that the time taken to reach balance was different on the two microfluidic device (Figure 3A and S2). 5 h was cost to reach balance on the 1.5 mm-microfluidic device while it needed 10 h to become balance on the 5.0 mm-microfluidic device. QD concentration in channel 2 on the 1.5 mm-microfluidic device was higher than that on the 5.0 mm-microfluidic device all through the process.

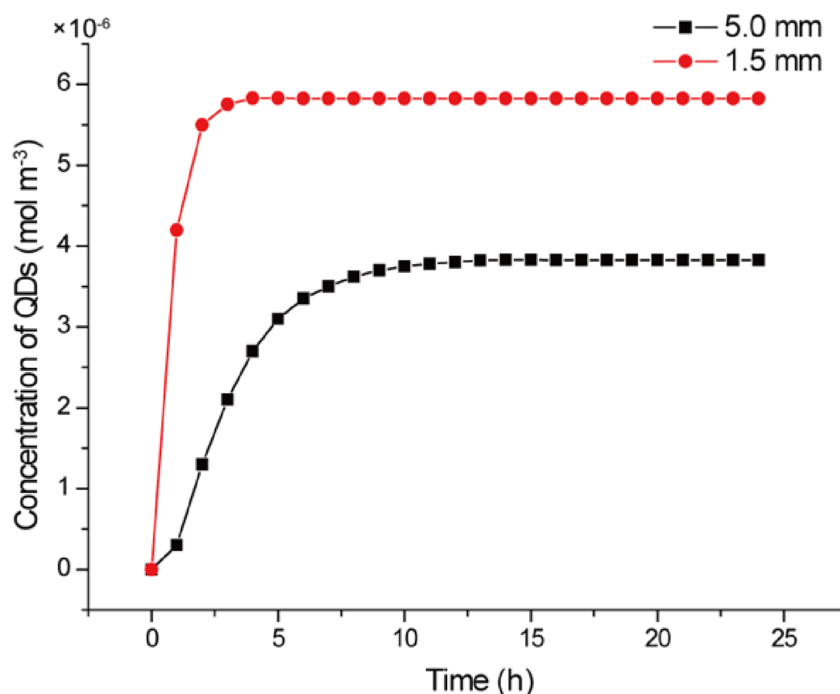

Figure S2. Curves of QDs concentration simulation in the channel 2 on the two kinds of microfluidic chips with different lengths (1.5 mm and 5.0 mm) of microchannels under static condition.

III. QD cytotoxicity detection by CCK-8 assay kit

Stocking solution of QDs (5 mg mL^{-1}) was serially diluted by cell culture medium into the desired concentrations (0, 1, 3, 5, 10, 20, 30 μg mL^{-1}) and treated on the HepG2 cells for 24 h and 48 h, respectively. Cell viability was detected by CCK-8 assay kit and the absorbance of controlled group was designated to be 100%. QD cytotoxicity shows obvious concentration-dependence that cell viability decreases as the concentration of QDs increasing. The IC_{50} value is 25 μg mL^{-1} for the 24 h treatment. It is clear that QDs almost bring no adverse impact on the cells at the concentration of 5 μg mL^{-1} both under 24 h and 48 h treatment. As a result, the concentration of 5 μg mL^{-1} was chosen in this work to ensure that the QD treatment has no influence on the cell cycle.

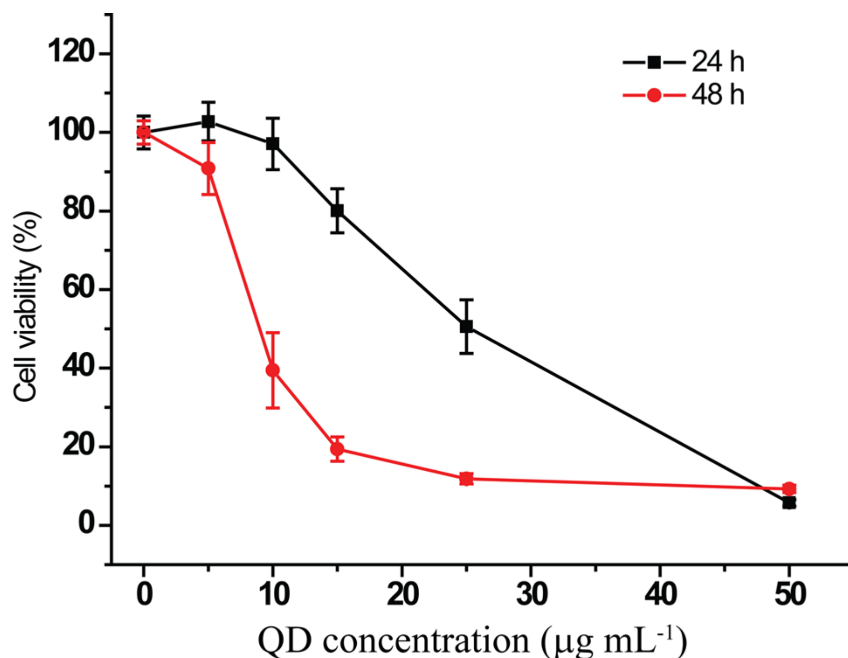

Figure S3. Cell viability of HepG2 cells was detected by CCK-8 assay kit under QD treatment with different concentrations.