Supplementary Information

Cytotoxicity of Quantum Dots Assay on a Microfluidic 3D-culture Device Based on Modeling Diffusion Process between Blood Vessels and Tissues

Jing Wu, Qiushui Chen, Wu Liu, Yandong Zhang, and Jin-Ming Lin* Beijing Key Laboratory of Microanalytical Method and Instrumentation, Department of Chemistry, Tsinghua University, Beijing 100084, China. * To whom correspondence should be addressed: Tel/Fax: +86-10-62792343, E-mail: jmlin@mail.tsinghua.edu.cn (J.-M. Lin)

I. Characterization of cell culture chamber

The microfluidic 3D-culture device was fabricated through standard photolithography. Re-expose technology was used to manufacture different heights of main channel and cell culture chambers. As shown in Figure S1a and S1b, the height of main channel is 71 µm while the height of cell culture chambers is 38 µm. Different heights could impede mixture of cells and matrix leak into the main channel when it was infused into cell culture chambers. After condensation, almost no cell was found in the main channel (Figure S1c). Fluorescent image of calcein AM stained cells in Figure S1d also shows this phenomenon. The microfluidic device we designed satisfies research requirements in this work.



Figure S1. Different heights of main channel and cell culture chambers on the microfluidic 3D-culture device(a and b). Bright field and fluorescent images of HepG2 cells mixed with agarose and were infused into cell culture chambers (c and d).

II. Characterization of CdTe-COOH QDs

CdTe-COOH QDs were purchased from Shenzhen ZhongDS Investment Co., Ltd. (China) and some basic characterizations of them were made. Both absorption and photoluminescent spectra of CdTe-COOH QDs are shown in Figure S2a and S2b. Absorption spectra of CdTe-COOH QDs are board. Photoluminescent spectra of CdTe-COOH QDs centre at ~540 nm after being excited at 325 nm. As the concentration becomes larger the emission intensity becomes stronger. Sizes of CdTe-COOH QDs were detected by transmission electronic microscope (TEM, FEI Tecnai G² 20 S-twin). TEM image indicates the spherical shape of CdTe-COOH QDs and its radius is approximate 5 nm (Figure S2c). Bohr radius of CdTe-COOH QDs is reported to be ~ 6 nm which indicates that CdTe-COOH QDs we brought are in a confinement regime.¹ CdTe-COOH QDs were also examined by x-ray photoelectron spectra (XPS, PHI Quantera) (Figure S2d). The sample was dried in air at room temperature and the data were calibrated using the standard value for C1s at 284.8 eV. The peaks at 583 eV and 573 eV are the XPS of Te $3d_{3/2}$ and Te $3d_{5/2}$ from CdTe. Two peaks at 412 eV and 406 eV are from Cd $3d_{3/2}$ and Cd $3d_{5/2}$, respectively. All the binding energies are consistent with reports.^{2, 3}



Figure S2 (a) UV-vis absorption spectra of different concentrations of QD solutions in deionized water. (b) Photoluminescent spectra of different concentrations of QD

solutions in deionized water ($\lambda_{ex} = 325$ nm). (c) TEM images of CdTe-COOH QDs (× 790000). (d) XPS of CdTe-COOH QDs.

III. Cell culture

HepG2 cells were cultured in Dulbecco's modified Eagle's minimal essential medium (DMEM, Gibco, Grand Island, NY) containing 10% fetal bovine serum (FBS), 100 U mL⁻¹ penicillin G and 100 U mL⁻¹ streptomycin. The cells were kept in a 37 °C, 5% CO₂ humidified incubator and passaged every two or three days at a subculture ratio of 1:4 using 0.25% (w/v) trypsin solution.

IV. Intracellular ROS and GSH detection

After cells was stained by DHE and NDA, fluorescent images were taken and shown in Figure S3. Different concentrations of QD solutions cause different level of ROS generation and GSH reduction. As the concentration increases, the fluorescent intensities of ROS enhance while the ones of GSH decrease. <u>The curves calculated from these pictures are presented in Figure 5.</u>



Fig. S3 Fluorescent images of ROS and GSH varying as the concentrations of CdTe-COOH QDs changing (Scale bar: 200 µm).

References

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