**Research on Cytotoxicity of Quantum Dots and Its Influential Factors Based on Microfluidic Chip**

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Quantum dots (QDs) emerging as a new kind of nanomaterial have shown outstanding fluorescent properties and the potential for replacement of organic dyes using in biological imaging. However, cytotoxicity of QDs becomes a major impediment for their universal applications. Conventional methods of QD cytotoxicity research always need professional operation, high-cost and a long period time. As a result, there is an urgent demand to develop a novel in vitro method to understand mechanism of QD cytotoxicity and give some instructions for rational utilization of nanomaterials. In this work, we analyzed QD cytotoxicity basing on microfluidic chip in order to construct a few microfluidic platforms for in vitro cytotoxic tests and reveal some in vivo factors affecting QD cytotoxicity.

A microfluidic three-dimensional cell culture device was successfully developed to imitate the diffusion process between blood vessels and tissues. The device is composed of a main channel and cell culture chambers. The cell culture chambers were designed to be different distance apart from the main channel and were divided into “close chambers” and “far chambers”. Fluorescein sodium and fluorescein isothiocyanate conjugated to bovine serum albumin (FITC-BSA) were used as model molecules to verify the diffusion process between main channel and cell culture chambers. Cell autophagy inhibitor 3-methyladenine (3-MA) was utilized to prove that cell autophagy played an important role in QD cytotoxicity.

A microfluidic cell density gradient generator was successfully developed to study the relationship between cell density and QD cytotoxicity. The microfluidic cell density gradient generator is composed of eight parallel channels which are respectively surrounded by 1-8 microwells. The sizes of microwells were optimized and the surfaces of them were modified in advance. Cells fall into microwells by gravity and the cell densities were decided by microwell number. QD cytotoxicity was observed to be obvious cell density-dependence. Comparing to cell densities infused by pipette tips, the microfluidic method exhibit higher efficiency, controllability and reproducibility.

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