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An electrochemical-TUNEL method for sensitive detection of apoptotic cells†

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An electrochemical-TUNEL method was developed for a cell sensor. A 3-D bio-interface based on CNT@PDA-FA was employed in the cytosensor, which significantly improved the cell capture. By coupling with a QD-based nanoprobe and electrochemical stripping analysis, the cytosensor exhibited attractive performance for detection of apoptotic cells.

Apoptosis or programmed cell death has been implicated in a wide variety of diseases, including cancer.^{1,2} Several standard techniques, such as electron microscopy, TUNEL assay, and flow cytometry, have been successively developed for the detection of apoptosis. Among them, the TUNEL kit has been put into commercial application by virtue of the high sensitivity and accuracy of the TUNEL assay.³ As for the traditional TUNEL method, fluorescence labelling was an essential critical step. However, nonspecific fluorescence labelling due to the long detection time or insufficient cell immobilization might lead to false positive signals. With increasing clinical demands and expectations, other techniques are gradually becoming relevant, such as micro-fluidic devices, single molecule spectroscopy, and electrochemical methods. The combination of different technologies could integrate their benefits to improve the detection sensitivity.^{4,5}

Electrochemical biosensors for cell apoptosis have attracted much attention due to their low cost, convenient operation, rapid detection, and good sensitivity.^{6–9} However, several key factors such as biocompatibility, specificity and conductivity need to be considered during the fabrication process of electrochemical biosensors. In our previous reports, several electrochemical platforms were developed for selective detection of cells with three-dimensional (3D) architectures.^{10–13} In

this research, we designed a nanocomposite with carbon nanotubes coated with polydopamine and folic acid (CNT@PDA-FA) to fix the target cell. The nanocomposite could not only retain the same advantages as normal carbon nanotubes, but also have a high affinity towards folate receptor over-expressed tumor cells. A biotin-dUTP composite was linked with 3'-OH ends generated by DNA fragments in the process of cell apoptosis under the function of the TdT enzyme. Streptavidin decorated SiO₂-QDs could connect with biotin-dUTP based on the specific recognition between biotin and streptavidin. A large number of CdTe QDs were assembled onto the silica spheres, which greatly amplified the electrochemical signals. By being coupled with the electrochemical stripping technique, an electrochemical platform was developed for the detection of apoptotic cells as shown in Fig. 1.

We have fabricated an improved interface using a dopamine (DA) modified carbon nanotube for the immobilization of FA. Fig. S1 in the ESI† shows the typical SEM images of pristine and dopamine modified carbon tubes. It can be observed that the sample displayed a similar one dimensional structure but the diameter increased a little after dopamine modification.

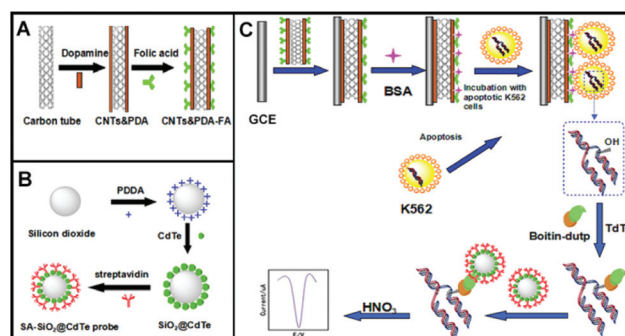


Fig. 1 The principle image of the biosensor for the detection of apoptotic cells. (A) preparation of the CNT@PDA-FA, (B) preparation of SA-SiO₂@CdTe and (C) electrochemical detection of apoptotic cells.

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