On-chip Fingerprinting Surface Enhanced Raman Scattering (SERS) Spectra Of Living Cells Via Ag@ZnO Nanocomplex Fabricated By Optothermal Effect

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Introduction: We report a microfluidic method to characterize the surface-enhanced Raman scattering (SERS) fingerprints of single living cells. The SERS substrate, a 3-demensional (3D) Ag@ZnO nanocomplex on the bottom of the microfluidic channel, is synthesized by optothermal effect catalyzed reactions. The optothermal effect catalyzed reaction can generate high-SERS-sensitive nanocomplex at any precisely controlled positions, and be incorporated into the microfluidic devices. By seamless integrating microfluidic technique with SERS spectroscopy, this hybrid device have advantages of both SERS and microfluidics: microfluidic methodology permits cells to be trapped at precisely controlled locations and reagents to be introduced into the chip to maintain cell living environments; SERS spectroscopy offers great advantages for probing the fingerprints of miscellaneous chemical and biological compounds from the cell surface in a real-time, label-free manner.

Materials and Methods: The Ag@ZnO nanocomplex clusters were formed by two sequential laser irradiation processes using the same setup: fabricating ZnO nanorods (Fig. 1a), and depositing Ag nanoparticles on the pre-formed ZnO nanorods (Fig. 1b). First, a continuous laser was focused onto a gold-coated glass slide used as the support of the microfluidic channel containing zinc nitrate and Hexamethylenetetramine solution as a precursor. The gold film absorbed the laser power and heated the surrounding precursor solutions, resulting in the formation of ZnO nanorods on the laser spot due to optothermal effect (Fig. 1a). Second, silver nitrate solution was injected into the same microfluidic device after the ZnO nanorods were prepared. The laser beam was focused onto the pre-formed ZnO nanorods, leading to the formation of Ag nanoparticles on the ZnO nanorods (Fig. 1b).

Results and Discussion: The Ag@ZnO nanocomplex was exclusively formed at the position of the laser-focusing spot (Fig. 1c). The SERS performance of the 3D Ag@ZnO nanocomplex was evaluated by detecting *4*-aminothiophenol (4-ATP) in microfluidics, where the SERS enhancement factor is estimated no ~ 2×10^6. The SERS fingerprints from the surface of single living cell was identified by integrating the 3D Ag@ZnO nanostructures in a cell-trapping microfluidic device (Fig. 1d), where a single cell were trapped on the top of each Ag@ZnO nanostructures (Fig. 1e). The SERS spectrum of the cell membrane was shown in Fig. 1f, which confirmed that cell surface is composed of proteins, carbohydrate, and lipids. Thus, the information of a living cell is visualized in a real-time, label-free manner with SERS spectrum.

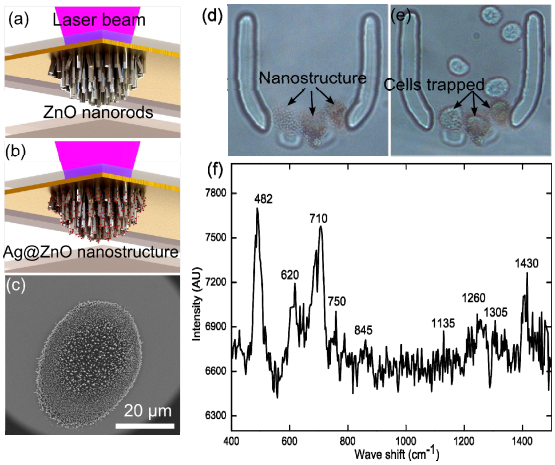

Figure 1 (a) Formation of ZnO nanorods; (b) Formation of Ag@ZnO nanocomplex as SERS substrate; (c) Scanning electron microscopy of Ag@ZnO nanocomplex; (d) Fabrication of Ag@ZnO nanocomplex in the cell trapping microfluidic channel; (e) Single cell are trapped on the SERS substrate; (f) SERS fingerprints from single, living cell surface.

Conclusions: In summary, the optothermal effect based fabrication technique allows us to fabricate SERS-sensitive substrate at prescribed location in microfluidic devices without constrains on channel design. Therefore, it is promising to combine this SERS detection scheme with microfluidic cell manipulation devices for fundamental studies in cell biology and medical diagnosis.

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References:

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