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Review

Enzyme-based signal amplification of surface-enhanced Raman scattering in cancer-biomarker detection

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ABSTRACT

Technologies that use surface-enhanced Raman scattering (SERS) have experienced significant growth in biomedical research during the past four years. SERS signal amplification based on enzyme action recently attracted considerable attention due to the need for ultrasensitive bioassays and the trend towards miniaturized assays. This review highlights recent developments in SERS signal-amplification techniques based on enzyme action for cancer-biomarker detection, including multiplexed detection and identification of DNA, single-nucleotide polymorphisms, small bioactive molecules, protein, and tumor cells.

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1. Introduction

Among optical detection methods, surface-enhanced Raman scattering (SERS) has become a powerful spectroscopy technique since its development in 1974 [1,2]. It has been under active investigation in biological detection because of the following advantages. In addition to high sensitivity and selectivity, the fingerprints of individual molecules permit excellent multiplexing capabilities because of the very narrow spectral width of Raman peaks (typically 10–100 times narrower than fluorescence peaks) [3,4]. It is well known that SERS has broad applications in biological detection, including small bioactive molecules [5–7], proteins [8–11], nucleic acid [12–14], and cells [15–17].

As a result, the number of research articles on SERS in biomedical applications has grown exponentially. Several reviews have covered the preparation of SERS substrates {e.g., nanofabrication techniques [18], surface functionalization [19]} and their performance in specific applications {e.g., label-free detection [20] and clinical translation [21]}. Nevertheless, there are still many challenges associated with the development of SERS technology

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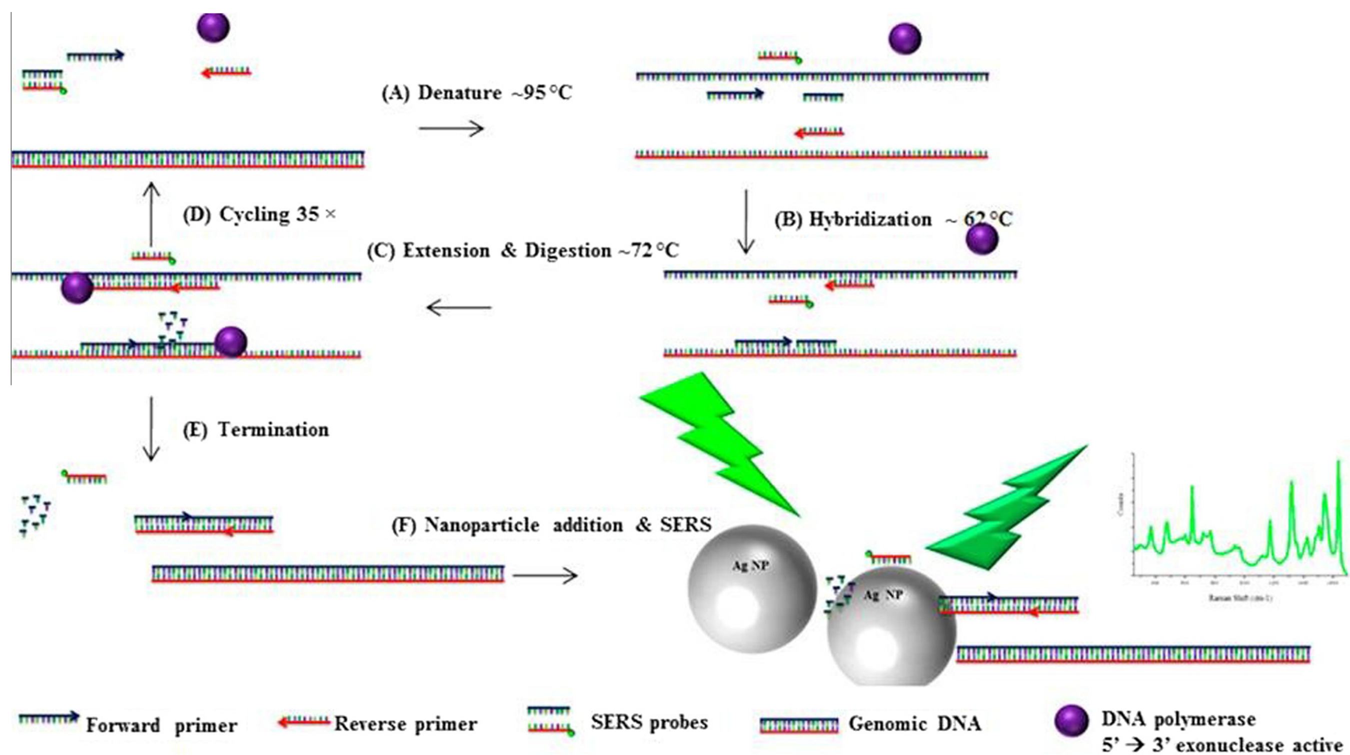

Fig. 1. A PCR reaction incorporating the SERS primer as an internal probe to be partly digested by the polymerase. (A) Denaturation of the DNA using heat. (B) Hybridization by cooling the sample. (C) Extension phase. (D) and (E) After the reaction, a double-stranded PCR product and short single-stranded dye-labeled sequences. (F) SERS detection (Reproduced from [38] with permission).

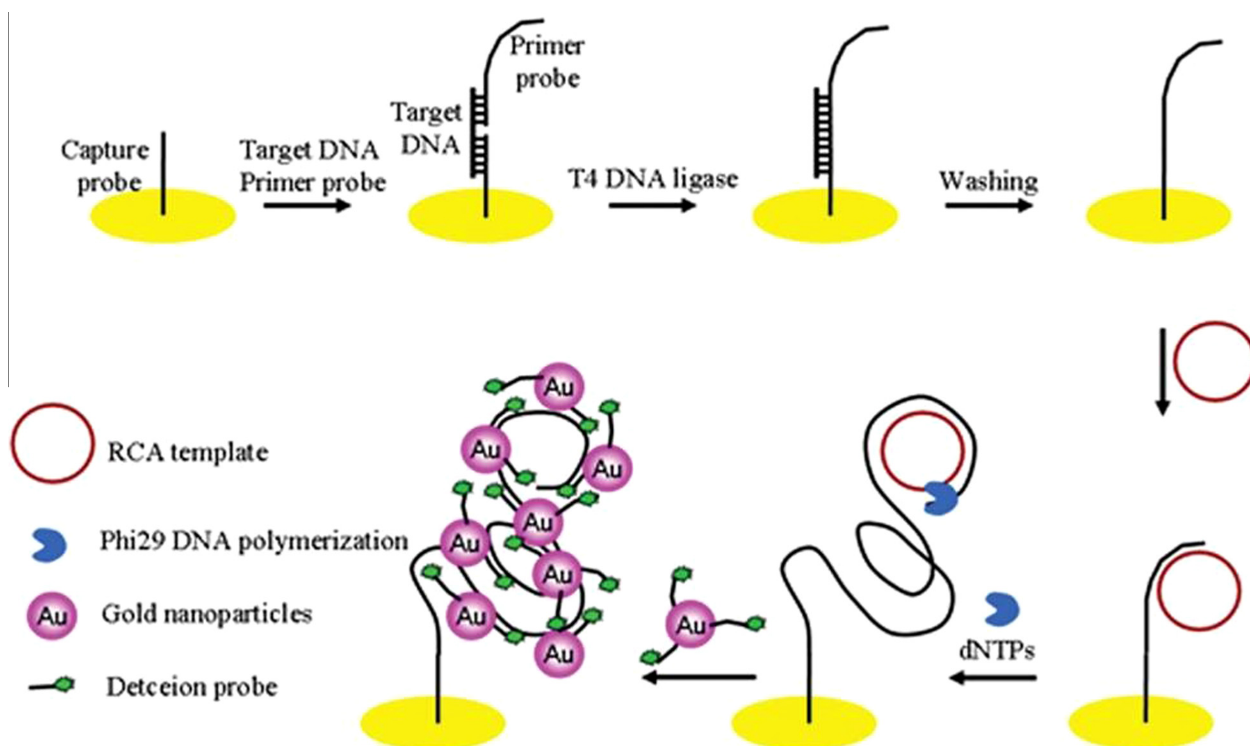

Fig. 2. The RCA-based SERS assay for DNA detection (Reproduced from [33] with permission).

(e.g., the ultrasensitive detection of biomolecules is required for first responders in order to facilitate timely and appropriate action) in the event of a biological attack.

Many efforts have therefore been devoted to realizing the ultrasensitive SERS detection by using signal-amplification methods for bioanalysis with sensitivity, selectivity, wide dynamic range, and

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